POSTER ABSTRACTS

135. Fosfomycin Susceptibilities Among Uropathogenic Extended Spectrum Beta-Lactamase-producing *Enterobacteriacea*

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Background. Antimicrobial resistance among uropathogens is a global problem with limited therapeutic alternatives. The Urinary Tract Infection Drug Resistance Index (UTI-DRI) in the South-Atlantic Region of the United States has steadily increased in the last decade by 60% (baseline 16.9 in 1999 to 27.1 in 2010). Fosfomycin is a broad-spectrum antimicrobial that has attracted interest for the treatment of lower UTIs caused by Gram-negative uropathogens resistant to commonly used antimicrobials. Data regarding antimicrobial susceptibilities for *Enterobacteriaceae*in the United States are extremely scarce.

Methods. Retrospective review of urines cultures performed at Integrated Regional Laboratories (IRL) serving 14 acute care (ACF) and 5 long-term care facilities (LTCF) in South Florida between January 2013 and December 2013. Urine cultures were from hospitalized patients, emergency departments and residents in LTCF. Only *Enterobacteriaceae* isolates that tested non-susceptible to extended spectrum beta-lactam agents were included in the analysis. Isolates were considered to be ESBL-producing if they were intermediate (I), susceptible dose-dependent (SDD), or resistant (R) to any 3rd or 4th generation cephalosporin per the 2013 Clinical Laboratory Standards Institute (CLSI) breakpoints. Fosfomycin Kirby-Bauer disk diffusion susceptibilities were determined with a 200 ug disk using 2014 CLSI breakpoints: >16 S, 13-15 I, <12 R.

Results. ESBL-producing *Enterobacteriaciae* from 290 ACF and 87 LTCF urine cultures were analyzed. The number of *E. coli* isolates ranged from 3-35 in ACF and 2-40 in LTCF. 93% of isolates in ACF and 97% in LTCF were susceptible (Table). *Klebsiell*a and *Proteus* strains were less susceptible than *E. coli*strains.

Table: Number and percent of urinary isolates susceptible to fosfomycin

Species	ACF	LTCF
E. coli	202/209 (97%)	75/76 (99%)
K. pneumoniae	60/70 (86%)	9/10 (90%)
K. oxytoca	4/4 (100%)	No data
P. mirabilis	5/7 (71%)	0/1 (0%)
All	271/290 (93%)	84/87 (97%)

Conclusion. Fosfomycin has excellent in vitro activity against urinary ESBL-producing *Enterobacteriacea* strains, especially *E. coli*, in South Florida acute and long-term care facilities.

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136. Management of positive urine cultures in hospitalized adults without symptoms of urinary tract infection

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Background. The Infectious Disease Society of America (IDSA) Guidelines for the Diagnosis and Treatment of Asymptomatic Bacteriuria (ABU) state that treatment of a positive urine culture without symptoms is not indicated except in pregnant women and patients undergoing surgical urologic procedures. Despite this, literature demonstrates a lack of understanding of the appropriate management of ABU. Previous studies have not addressed which factors influence antibiotic prescribing in ABU.

Methods. This is a retrospective descriptive cohort study to evaluate the current practice for the management of ABU in hospitalized adults at Baystate Medical Center from July 1, 2012 to June 30, 2013. ABU was defined as a positive urine culture (> 10,000 CFU of a single organism) without signs or symptoms of a urinary tract infection (UTI). Exclusion criteria were pregnancy, surgery during admission, history of renal transplant, other acute infectious diagnosis, symptoms of UTI, Alzheimer's disease, and dementia. Patients were randomized and reviewed for inclusion and exclusion criteria until the target number of 100 ABU cases was reached. Data were analyzed using descriptive statistics with 95% confidence intervals.

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Results. Antibiotics were prescribed in 57% of ABU cases (95% CI 46.9 to 66.4). Greater extent of pyuria (95% CI -73.7 to -15.8), urine CFU count >100,000 (95% CI 18.3 to 66.3), and gram negative isolate (95% CI 6.3 to 49.7) are associated with antibiotic prescribing. Hospitalists and residents cared for 48% and 37% of all patients respectively, and prescribed 42% and 38% of antibiotics. One case of *Clostridium difficile* infection was observed in the non-antibiotic group and 2 in the antibiotic group (95% CI -5.4 to 7.7).

Conclusion. ABU is frequently treated with antibiotics despite published guidelines. Misinterpretation of urinalysis, specifically extent of pyuria, may be influencing providers to prescribe antibiotics for ABU. Urine culture results may also be influencing antibiotic prescribing, specifically high CFU counts and gram negative isolates. This information can be used to create an educational intervention targeted towards hospitalists and residents to decrease the prescribing of antibiotics in ABU.

Disclosures. **All authors:** No reported disclosures.

137. Developing an Approach to Evaluating the Quality of Antibiotic Prescribing in Hospitalized Patients with Community-Acquired Pneumonia (CAP) and Non-catheter Associated Urinary Tract Infection (UTI)

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Background. Although CDC recommends that hospitals implement antibiotic stewardship programs, standard methods to evaluate antibiotic prescribing (AP) are not well established. The Emerging Infections Program (EIP) field tested an approach for evaluating inpatient AP quality for CAP and UTI.

Methods. A convenience sample of adult patients on antibiotics for clinician-documented CAP or UTI during a 2011 10-state antimicrobial use prevalence survey were selected for chart abstraction. Diagnostic tests, antibiotics, and infection signs/symptoms were collected from medical records. We calculated the proportions of: 1) CAP patients with recommended antibiotics and cultures according to the 2007 IDSA and American Thoracic Society guideline; 2) UTI patients with compatible signs/symptoms and urine cultures; 3) patients with final culture results before discharge.

Results. Records were reviewed for 41 CAP and 132 UTI patients in 36 hospitals among 8 EIP sites. Of 19 CAP patients for whom guidelines recommend blood and respiratory cultures, 7 (37%) did not have a blood culture and 14 (74%) did not have a respiratory culture. Among 31 CAP patients who had either culture (whether recommended or not), 3 (10%) had a positive culture and 1 (3%) had a final result prior to discharge. Of 33 CAP patients not needing intensive care, 4 (12%) did not receive a guideline-recommended inpatient antibiotic regimen. Of 132 UTI patients, 51 (39%) lacked a documented sign/symptom and 22 (17%) did not have a urine culture collected before antibiotic start. Of 54 (41%) UTI patients with signs/symptoms and a positive culture, culture results were not final prior to discharge for 8 (15%).

Conclusion. Cultures to inform evaluation of CAP and UTI inpatient AP quality were often not collected or results were unavailable. CAP patients frequently did not have documentation of culture collection in accord with recommendations. UTI patients frequently did not have documentation of key elements of UTI diagnosis, and results to inform AP were not available during the hospitalization in some patients with signs/symptoms and a culture. More work is needed to define objective measures of AP quality and understand barriers to timely availability of microbiology data to inform inpatient AP.

Disclosures. **All authors:** No reported disclosures.

138. Do Criteria-Based Urine Cultures Contribute to Unnecessary Antibiotic Use at a Community Teaching Hospital?

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Background. Asymptomatic (Asx) bacteriuria is commonly treated with antibiotics despite evidence demonstrating no benefit. Reliance on urinalysis (UA) or urine culture (UCx) without consideration of patient (pt) symptoms may contribute to overtreatment. A criteria-based urine culture (CB-UC) process relies on UA triggers to determine need for UCx. The purpose of this study was to assess the impact of CB-UC on

inpatient antibiotic prescribing and development of antimicrobial resistance at a community teaching hospital.

Methods. A retrospective cohort study was conducted of adults admitted between January 1 and September 30, 2013 who had a UA performed meeting criteria for UCx. Pts were excluded if discharged before results of UCx were available, neutropenic, or history of renal transplant within a year. UCx was prompted by ≥ 1+ bacteria, yeast, ≥ 3 white blood cells (WBC) per high power field (hpf) for men or ≥ 10 WBC/hpf for women. Data collected included pt characteristics, UA and microbiologic data, antibiotic regimens, and clinical outcomes. Pts were compared based on presence of urinary tract infection (UTI) symptoms and further stratified based on receipt of UTI treatment (tx).

Results. 300 pts were included, 241 in the Asx group and 59 in the symptomatic group. Demographics were similar between groups. Approximately 58% of UCx were negative. *E.coli*was the most frequently isolated organism (43%). The most common empiric treatments were fluoroquinolones (48%) and cephalosporins (44%). In the symptomatic group 80% of pts received tx, while 20% of Asx pts received tx. No statistical difference in new antimicrobial resistance at 6 months was found between groups. A subgroup analysis of Asx pts found that those who received tx had more new antimicrobial resistance (11.3% vs 4.4% p = 0.044). Risk factors associated with tx in Asx pts included UA with bacteria present (OR 9.6, 5.0 – 143), ≥10 WBC (OR 2.5, 2.0 – 3.4), or a positive UCx (OR 2.6, 2.0 – 3.5).

Conclusion. Over half of CB-UCs were negative and approximately 20% of Asx pts received UTI tx; this was significantly associated with development of antimicrobial resistance. These results support the need for revision of the CB-UC process and antimicrobial stewardship interventions to reduce tx of Asx bacteriuria.

Disclosures. **All authors:** No reported disclosures.

139. Descriptive study of patterns of urine testing and antibiotic use in an inpatient physical medicine and rehabilitation population

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Background. Asymptomatic bacteriuria (ASB) is common in patients admitted to inpatient rehabilitation (IPR) units. Current guidelines recommend against routine urine testing in asymptomatic patients, including patients with spinal cord injuries (SCI). Screening for urinary tract infections (UTI) is prompted by subjective observations that may not relate to infection; however, a positive urine screen frequently prompts antimicrobial prescribing even in the absence of symptoms.

Methods. A retrospective case control study was conducted at a university-affiliated academic medical center with a 76-bed IPR unit. 181 IPR patients hospitalized between August 2013 and October 2013 were randomly selected. The documented reasons for urine testing and results, antibiotic use, demographic information, comorbidities, and urinary catheter data were collected. SAS V9.3 was used to analyze the data. The primary objective was to determine patient factors that prompted screening and treatment and to document specific UTI symptoms. A secondary objective was to describe appropriateness of antimicrobial use.

Results. 104 patients had orders for urinalysis and/or culture. Only 17 patients (16.3%) who were screened had specific UTI symptoms as defined by the National Health Safety Network (NHSN). Among the 61 patients who were ordered antibiotics, 38 patients had ASB (62.3%). Neurogenic bladder in SCI patients is a known risk factor for UTI. Of those screened in our study, 36 patients (35%) had documented neurogenic bladder, while 10 (13%) patients without screening had neurogenic bladder (OR = 3.4, 95% CI = 1.6-7.4, p = 0.002). Results from a multivariate analysis determined the following factors associated with urine screening.

Variable		OR	95% CI	p-value
Actual LOS	Per week (7 days)	2.1	(1.4, 3.2)	0.0006
WBC Count	≥11,000	4.6	(1.4, 15.8)	0.014
Symptoms		153.4*	(32.5, ∞)	<.0001
IPR Unit	General	Baseline		0.018
	Stroke	4.2	(1.3, 13.9)	
	SCI	1.8	(0.6, 5.6)	
	Traumatic Brain Injury	0.14	(0.01, 2.4)	

Conclusion. The primary use of antimicrobial agents on the IPR units at our institution is for the treatment of ASB. The practice of routine urine screening for asymptomatic patients should be revisited. This project identifies an opportunity for targeted antimicrobial stewardship efforts.

Disclosures. **All authors:** No reported disclosures.

140. Improved Practice and Decreased Antibiotic Utilization for Urinary Indications in Long Term Care Facilities After an Educational Intervention

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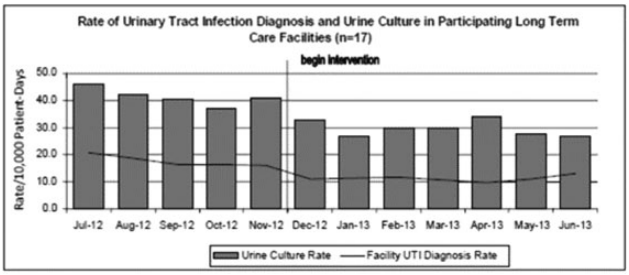
Background. Antibiotics are among the most commonly prescribed medications in long-term care facilities. Reports show that 25-75% of systemic antimicrobials are prescribed inappropriately, often for asymptomatic bacteriuria.

Methods. We developed a collaborative program to improve the management of suspected urinary tract infection in the elderly. The program provided useful tools for promoting a careful approach to indications for urine testing (including the appropriate evaluation of mental status changes) and the interpretation of urine test results. The curriculum reviewed appropriate culture and treatment indications during 2 full day workshops, webinars, four conference calls and one-to-one coaching sessions. To analyze the effectiveness of the program we measured urine culture rates, facility rates of diagnosis of urinary tract infection, and *C. difficile* infection rates before and after the program.

Results. Seventeen long term care facilities throughout Massachusetts participated and submitted monthly data. Urinary tract infections decreased by one-third after the intervention (IRR = 0.67, CI = 0.59, 0.76) and urine cultures decreased by one quarter (IRR = 0.73, CI = 0.66, 0.79). Incidence of *C. difficile* decreased by nearly one-half after the initiation of the collaborative (IRR = 0.55, CI = 0.39, 0.78).



Conclusion. Following a collaborative program to improve practice in testing and diagnosis of bacteriuria, there was a decrease in infection diagnoses and urine cultures rates reflective of an improved understanding of when to culture and an improvement in appropriate diagnosis. During this time period, there was a marked decrease in *C. difficile* infection rate which may have been due in part to decreased antibiotic usage, although this was not measured. These data support a reasonable model for other health care systems to utilize to improve care of long-term care facility residents who are at risk for unnecessary antibiotic treatment for asymptomatic bacteriuria.

Disclosures. **All authors:** No reported disclosures.

141. Urine Culture Optimization: A Powerful Antimicrobial Stewardship Strategy

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Background. Inappropriate collection of urine cultures (UC) has the potential to increase the likelihood of antimicrobial prescription for asymptomatic bacteriuria. Antimicrobial overuse can lead to increased cost, mortality and morbidity related to antimicrobial resistance and *Clostridium difficile*. We postulated that a quality improvement strategy to optimize collection of UCs would effectively reduce the unnecessary use of antibiotics.

Methods. The Antimicrobial Stewardship (ASP) team at our hospital initiated interventions aimed at optimizing UC collection in our Emergency Department (ED). Our interventions consisted of a creation of a Working Group involving the ED staff and an Infection Preventionist (IP) trained in Frontline Ownership (FLO) techniques. Thinking sessions involving staff were facilitated by the same IP utilizing FLO principles; the sessions reviewed process, policy and encouraged UC utilization dialogue. Session summaries and UC volume run charts were shared biweekly serving as continuous feedback to the ED. Antimicrobial use was determined through financial charge data and standardized as defined daily doses/1,000 patient days.

Results. Pre-intervention UC rate was (0.09 per ED patient visit) compared to after intervention (0.06 per ED patient visit), representing a 24% reduction (p < 0.002) (Figure 1). Use of ciprofloxacillin in the ED from 9.8 to 8.0 (DDD/1,000 ED Visits) an 18 %(p = 0.02) reduction (Figure 2).

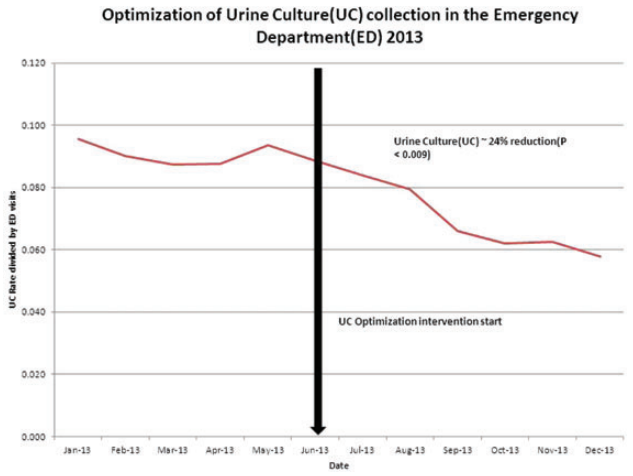

Figure 1. Urine Culture (UC) testing reduction in the Emergency Department (ED) 2013 from pre-intervention UC rate was (0.09 per ED patient visit) compared to after intervention (0.06 per ED patient visit) a 24% reduction (p<0.002).

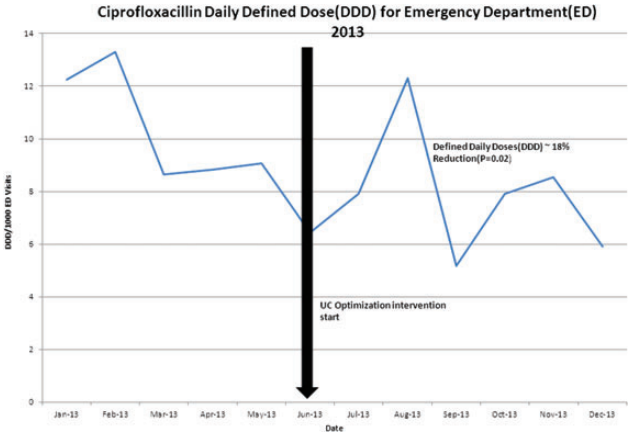

Figure 2. A reduction of Ciprofloxacillin's Daily Defined Dose (DDD) for the Emergency Department in 2013 from pre-intervention mean 9.8 (DDD/1,000 ED Visits) to post intervention mean of 8.0(DDD/1,000 ED Visits) an 18 %(p=0.02) reduction

Conclusion. Our intervention in the ED using FLO methodology, effectively reduced UC testing and in turn reduced the ciprofloxacin. Our novel intervention represents an upstream approach to ASP, capitalizing on frontline staff engagement in stewardship interventions. Optimizing microbiologic evaluation is an important stewardship tool to prevent inappropriate use of antimicrobial agents.

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142. Retrospective, multicenter, point prevalence study of urinary tract infection (UTI) data for a city-wide antimicrobial stewardship initiative

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Background. Antimicrobial stewardship optimizes patient care via promoting appropriate antimicrobial use. Institutional data demonstrates UTI as the most common indication for antimicrobial initiation, but diagnosis remains challenging and treatment of asymptomatic bacteriuria is common. The purpose of this study was to evaluate antimicrobial prescribing practices for UTIs in the acute care setting using a standardized chart audit tool as part of an antimicrobial stewardship initiative.

Methods. Four hospitals participated in this retrospective, multicenter, point prevalence survey using a standardized CDC-endorsed chart audit tool. Data were captured on a single day at each hospital in January or February 2014. Patients were included if they were receiving antimicrobial(s) for an indication of UTI per order indication or if not available, through positive urine culture (1 hospital). Data collected included demographics, presenting symptoms, urinalysis and urine culture, empiric and pathogen-guided treatment and total inpatient duration of therapy.

Results. Of 91 patients included, 59 (65%) were female. Hospital medicine service was the primary team for 61 (67%). Eighteen (20%) patients were asymptomatic and 29 (32%) presented with only one UTI related symptom. Commonly reported signs and symptoms included leukocytosis (27%), fever or rigors (23%) and new onset delirium (19%). Urine culture was obtained in 83 patients; Gram negative organisms (64%) were the most common pathogens. After applying McGeer Criteria to 66 patients without an indwelling urinary catheter, only 7 (11%) met both symptomatic and microbiological criteria for UTI. Ceftriaxone, ciprofloxacin and sulfamethoxazole-trimethoprim were the most commonly used antimicrobials for monotherapy. The median duration of therapy for those patients meeting McGeer Criteria was five days.

Conclusion. These results demonstrate an over-use of antimicrobials for UTI in the absence of diagnostic criteria. Using a standardized, CDC-endorsed chart audit tool facilitated rapid project implementation and led to timely identification of a stewardship intervention targeting appropriate diagnostics that could be implemented across a multi-institution collaborative.

Disclosures. **All authors:** No reported disclosures.

143. The Frequency of Antibiotic Treatment of Positive Urine Cultures in Hospitalized Patients that are not UTIs: A Three Hospital Survey

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Background. Antibiotic overuse is a problem among hospitalized patients that increases costs and fuels the emergence of antimicrobial resistance. Although many assert that treatment of positive urine cultures that are not urinary tract infections (UTIs), such as asymptomatic bacteriuria and contaminated cultures, are a driving force behind inappropriate antibiotic use, there are few data assessing the validity of this claim.

Methods. We reviewed 299 urine cultures from unique individuals at 3 medical centers in Los Angeles (a community hospital, a county hospital, and a private tertiary care medical center) using a standardized chart abstraction form. For each positive culture, we assessed for symptomatic urinary tract infections (SUTI) using both IDSA and NHSN criteria, and evaluated antibiotic treatment and indications.

Results. Of the 299 positive cultures, criteria for SUTI was met infrequently: 29% using IDSA criteria, and 29% using NHSN surveillance criteria. Concordance between IDSA and NHSN criteria was only 66%. Among the 163 patients not using antibiotics for another reason whose urine culture did not meet clinical SUTI IDSA criteria, 38% (n = 62) received antibiotics directed at urine studies within 1 day after urine culture collection. Among 171 patients not meeting SUTI criteria by NHSN criteria and not receiving antibiotics for other reasons, 42% (n = 71) received antibiotics directed at urine studies. On day 4 after culture, 50% (59/119) of non-SUTI by IDSA criteria and 43% (53/122) by NHSN criteria were receiving antibiotic treatment. Factors associated with antibiotic receipt for a non-SUTI by IDSA criteria 1 day and 4 days after culture were the same: hospital identity, presence of leukocyte esterase, positive nitrite, and urine leukocyte count.

Conclusion. In our 3 center survey, antibiotic treatment of positive urine cultures that were not SUTI was prevalent both empirically and after culture results were finalized, especially among patients with leukocytes in the urine. Our data suggest that inappropriate antibiotic treatment of positive urine cultures that do not represent UTIs is highly prevalent and a potential target for antimicrobial stewardship programs aiming to reduce inappropriate inpatient antibiotic use.

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144. Unexpected Intramuscular Ceftriaxone Prescribing Patterns in a Multi-campus Ambulatory Care Health System

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Background. Intravenous ceftriaxone (CTX) is commonly used due to its broad spectrum activity and convenient dosing. Intramuscular (IM) CTX has a more limited role and is primarily used to treat sexually transmitted infections (STI). We noted an unexpectedly high number of IM CTX prescriptions in our ambulatory care system and initiated a quality improvement project to investigate its use.

Methods. In July 2013, retrospective chart reviews were conducted for IM CTX prescriptions issued between June 2012 and June 2013. 556 prescriptions were identified and 20% of charts from each campus were reviewed to identify indications for therapy. Based on the results, in August 2013 an intervention that included clinic

stock adjustment and staff education was completed. A post-intervention review was conducted for IM CTX prescriptions issued between October 2013 and March 2014 to evaluate the impact of the intervention.

Results. IM CTX prescriptions decreased by 63.9% in the 6 months following the intervention (227 vs 82). Many patients received a one-time CTX dose in clinic and were also prescribed an oral antibiotic to complete the treatment course. The most common indications in the pre-intervention period were skin and soft tissue infections (SSTI) (34.2%), lower respiratory tract infections (20%) and STI (18.3%) compared with STI (44.4%) and SSTI (38.9%) in the post-intervention period. Pre-intervention, one campus was identified as an outlier with over 3-fold the number of prescriptions of any of the other campuses. Although that campus remained the highest user, total IM CTX prescriptions decreased 76.7% post-intervention, with one provider accounting for 28.6% of prescriptions.

Conclusion. Even with very familiar and frequently prescribed agents such as ceftriaxone, opportunity exists for improved antibiotic utilization. As IM CTX requires administration, most often by nurses, improved prescribing practices may also reduce unnecessary utilization of nursing resources. Prescriber and pharmacist education and adjustment of CTX clinic stock can be successful antimicrobial stewardship strategies to decrease inappropriate antimicrobial utilization in the outpatient setting.

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145. Differences in Antimicrobial Use and Susceptibilities for Gram Negative Organisms between Intensive Care Units and the Emergency Department: Implications for Antimicrobial Stewardship

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Background. Antimicrobial use and susceptibility patterns of common Gram negative (GN) organisms differ within hospital units. Antimicrobial stewardship strategies emphasize that empiric antimicrobial therapy should be patient specific, guided by local data and the presumptive site of infection.

Methods. Retrospective review of the microbiology surveillance system (VigilanzÒ) comparing antimicrobial susceptibilities patterns of bacterial isolates between hospital adult intensive care units (ICUs) and the emergency department (ED), at Jackson Memorial Hospital (1550 beds, Miami, FL) from June 2012 to June 2013. Only the first positive isolate per patient was included. Antibiograms were categorized by patient location in Surgical ICU (SICU), Medical ICU (MICU), and ED. Antimicrobial use was measured in days of therapy (DOT)/1,000 patient days. Proportions of bacteria susceptibilities to specific antibiotics were compared between patient locations using chi-square test of Fisher's exact test where appropriate. Any post-hoc testings were performed using Bonferroni's adjustment for family-wise error rate.

Results. 4,980 bacterial isolates were analyzed. 1289 (26%) ED, 536(11%) MICU, 349(7%) TICU, 318 (6%) SICU, 302(6%) NSICU. *Pseudomonas aeruginosa* susceptibilities to cefepime differed between ED 89%, MICU 75%, SICU 66% ($p = <0.0001$), ED vs SICU ($p = 0.0164$) was significant. *P. aeruginosa* isolates were more susceptible to meropenem in the ED than MICU and SICU (93% vs 72% $p = 0.0078$ and 93% vs 53% $p < 0.0001$ respectively). *Klebsiella pneumoniae* susceptibilities to cefepime differed between ED 91%, MICU 75% and SICU 85% ($p = 0.0197$), ED vs MICU ($p = 0.0174$) was significant. Antimicrobial use in DOTs differed between units: vancomycin was the most used antibiotic in all units. Meropenem used differed between units, ED used less 16.53gr/1,000 patient days. MICU used more cefepime than other units.

Conclusion. There are differences in antimicrobial susceptibilities between units. GN organisms were more susceptible to cefepime and meropenem in the ED than in specific unit (MICU, SICU). We also observed that cefepime was used more in the MICU. Further analysis are needed to determine if antimicrobial use correlates with trends in antimicrobial resistance for each unit.

Disclosures. **All authors:** No reported disclosures.

146. Review of Empiric Echinocandin Therapy for Candidemia

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Background. Candidemia represents up to 9% of all blood cultures, of which the majority are due to azole-sensitive species. The 2009 IDSA guidelines recommend empirically starting fluconazole ($7/day at 2013 GW hospital pharmacy pricing) for candidemia until species identification. The exceptions are for patients with moderately severe to severe illness, patients who are neutropenic, or patients with recent azole exposure. In clinical practice however, echinocandins ($117/day) are started empirically in the majority of patients with candidemia without clear benefit, but at significantly increased financial burden.

Methods. We reviewed the hospital records of any patient at the George Washington University Hospital with candidemia over a 6-year period from January 1, 2008 through December 31, 2013, and evaluated the empiric antifungal therapy used in relation to the *Candida* species and patient clinical status. Fluconazole sensitivity was routinely tested for all *Candida* species after January 1, 2011.

Results. 163 patients (97 men, 66 women) with a mean age of 58 years old had 411 positive blood cultures for *Candida*, of which 74.8% were hospital-acquired. 51.5% of patients were in the ICU and 83.4% had a central venous catheter at the time of their candidemia. Infectious Diseases consultation was requested in 70.2% of cases and the 30-day mortality was 39.3%. C. *albicans* accounted for the majority of episodes (34.7%), followed by *C. parapsilosis* (30%), *C.glabrata* (19.5%), and *C. krusei* (3%). 46.8% of the *C. glabrata* isolates after January 1, 2011 were azole-resistant, but accounted for only 10.4% of all candidemias over this time period. An echinocandin was started empirically in 70.9% of cases, but was switched over to fluconazole in 51.9% of these cases. No ID consult was obtained in 56 episodes of candidemia and in 19 (33.9%), of these an echinocandin was the sole therapy used for azole-sensitive *Candida* species. This occurred only in 15.9% of cases when an ID consult was requested, which was statistically significant.

Conclusion. Echinocandins are used as empiric therapy for candidemia in the majority of patients despite a low prevalence of azole-resistant *Candida* species resulting in significantly increased cost despite no definitive mortality benefit.

Disclosures. **All authors:** No reported disclosures.

147. An antibiotic stewardship program in the emergency department decreased piperacillin-tazobactam use and increased guideline-concordant antibiotic prescribing for uncomplicated cystitis

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Background. Antimicrobial stewardship programs aim to optimize antibiotic use to improve patient outcomes. Data regarding the impact of stewardship efforts in the Emergency Department (ED) are limited. We extended our inpatient antimicrobial stewardship program to our ED and report on antibiotic use before and after this initiative.

Methods. We developed a quarterly report of antibiotics administered standardized by 1,000 patient encounters (PE) to monitor use over time. Initial interventions were focused in two areas: 1) Prospective audit and feedback to decrease unnecessary use of piperacillin-tazobactam (pip-tazo) was initiated in October 2012. Cefepime was the recommended anti-pseudomonal agent, where appropriate. 2) Increasing adherence to treatment guidelines for uncomplicated cystitis, beginning in January 2013. Nitrofurantoin was the recommended first-line agent. To measure the impact of these interventions on antibiotic utilization, we performed a retrospective pre/post-intervention evaluation of adults >18 years who received at least one dose of an antibiotic in the ED. Days of antibiotic therapy (DOT)/1,000 PE were compared between time periods using interrupted time-series analysis to detect changes in level and trend before and after the intervention.

Results. Pip-tazo use was significantly decreased by -3.2 DOT/1,000 PE (95% CI -5.8 to -0.7) immediately after the intervention ($p = 0.02$). Cefepime use increased by 1.9 DOT/1,000 PE (95% CI -0.8 to +4.7) immediately after the intervention ($p = 0.05$). Among cases identified with uncomplicated cystitis, nitrofurantoin use significantly increased by 8.3 DOT/100 cases (95% CI 0.9-15.8) immediately after the intervention ($p = 0.03$). Cephalexin use decreased by -15.8 DOT/1,000 cases (95% CI -32.5 to +0.8) immediately after the intervention, ($p = 0.05$).

Conclusion. Antibiotic stewardship initiatives can result in rapid practice change in the ED which can be monitored through use of longitudinal antibiotic utilization data. Future interventions should aim to expand the focus of antibiotic stewardship initiatives in the ED.

Disclosures. **All authors:** No reported disclosures.

148. Use of a Skin and Soft Tissue Protocol to Reduce Emergency Department use of Ertapenem in a 325 Bed Community Hospital

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Background. Skin and soft tissue infections (SSTI) are a common presentation in the emergency department. The most common pathogens that cause SSTI are *Staphylococcus aureus* and *Streptococcus pyogenes.*

The IDSA guidelines for SSTI recommend that the empiric treatment for simple SSTI be treated with anti-staphylococcal penicillins or a first or second generation cephalosporin. Ertapenem may appear to be a good choice to treat SSTI due to its broad spectrum of activity against both gram positive and gram negative bacteria. However, the guidelines state that ertapenem should be saved for complicated infections or for infections caused by bacteria resistant to our first line options.

In 2011 a protocol for the treatment of SSTI in the emergency department was implemented at McKay- Dee Hospital in hopes of standardizing the approach to treating SSTI in the emergency department.

The primary outcome was to determine the effect the protocol has had on the use of ertapenem to treat SSTI in the emergency department. A relative decrease of 25% would show efficacy of the implemented protocol.

Methods. Using ICD9 codes, patients treated for SSTI in the emergency department immediately prior to and after the protocol was implemented were identified. The electronic medical record was then reviewed to determine what medication the patient received. The overall percentage use of ertapenem was determined for each group and evaluated using the chi squared test. In the 2007-2008 group 1298 patients were evaluated, 281 were excluded, 996 met the inclusion criteria. In the 2011-2012 group 1158 patients were evaluated, 163 were excluded, 995 met the inclusion criteria.

Results. In the 2007-2008 group 322 (32%) patients received ertapenem. In the 2011-2012 group 140 (14%) patients received ertapenem. The difference in ertapenem usage was found to be statistically significant (P <0.0001).

Conclusion. To maintain the effectiveness of ertapenem its use should be reserved for complicated SSTI or SSTI caused by bacteria resistant to first line options as recommended by the IDSA guidelines. Based on the data collected it appears that the protocol helped to decrease the use of ertapenem to treat SSTI in our emergency department.

Disclosures. **All authors:** No reported disclosures.

149. Impact of a Clinical Decision Support Tool in the Emergency Department on Antimicrobial Prescribing Patterns for the Treatment of Pneumonia

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Background. The National Hospital Inpatient Quality Measures identifies community-acquired pneumonia (CAP) as a core measure. The Joint Commission and Centers for Medicare and Medicaid Services assess rates of compliance with the standards established for core measures. The primary objective of this project was to evaluate the impact of a clinical decision support (CDS) tool in our Emergency Department (ED) on the rate of guideline concordant empiric antibiotic selection for the treatment of CAP.

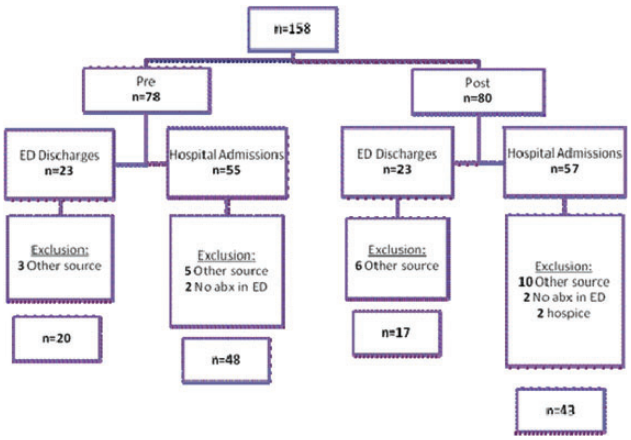
Methods. To improve risk factor identification and appropriate antibiotic selection for CAP at Penn Presbyterian Medical Center, the pharmacy and ED collaborated with infectious diseases and informatics representatives in the development and implementation of an electronic antibiotic CDS tool. This CDS tool was created within the ED's electronic medical record and computerized physician order entry system to guide empiric antibiotic selection for patients presenting with CAP.

To assess impact the pharmacy department conducted a pre-implementation and post-implementation, retrospective evaluation of patients that presented to the (ED) with a primary or secondary ICD-9-code indicative of pneumonia between February 1, 2012-April 30, 2012 (pre-implementation control group) and February 1, 2013-April 30, 2013 (post-implementation of the CDS tool).

Results. Sixty-eight patients were included in the pre-implementation arm and 60 included in the post-implementation arm.

In order to further validate the impact of clinicial decision support tools on patient outcomes, future studies with a larger patient population should be developed.

	Pre	Post	p-value
Appropriate empiric antibiotic selection			
Total	36/68 (52.9%)	44/60 (73.3%)	<0.001
ED discharge only	18/20 (90.0%)	16/17 (94.1%)	0.647
Hospital admission	18/48 (37.5%)	28/43 (65.1%)	< 0.001
Excess antibiotic days (median)	0.5	0	



Conclusion. Results demonstrate that the implementation of a CDS tool to guide antibiotic selection in the Emergency Department significantly improved adherence to national guidelines and decreased days of excess antibiotics. This represents a low-maintenance and sustainable intervention.

Disclosures. **All authors:** No reported disclosures.

150. Changes in Nursing home Reimbursement Associated with Improvement of Antibiogram Data in an Urban Community Hospital

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Background. Multidrug resistant organism infections (MDROI) remain a threat in hospitals and Nursing Homes . East Orange General Hospital (EOGH) has had vigorous infection control practices and an antibiotic stewardship program in place for 5 years. It was noted that the EOGH Antibiogram showed gains against MDROI.

The Federal Government changed NH reimbursement in 2011 leading Nursing Homes to transfer fewer patients .We hypothesize that this would lead to decreased admissions to hospitals and a decrease in MDROI. We report on our experience from 2011-13

Methods. The study comprised of inpatients at EOGH. Admissions were 8023, 7515, 6928 for 2011, 2012 and 2013 respectively, of these, Nursing Home patients were 1624, 1338 and 1051 in years 2011, 2012 and 2013 respectively. Antibiotic utilization statistics were gathered for antibiotics used to treat MDROI: tigecycline(TG), carbapenems(CP) and colistin(CL). The data was converted to defined daily doses (DDD). Sensitivity data was collated

Results. Nursing Home admissions declined over the study period the following percentage, 20%, 17% and 15% for 2011, 2012 and 2013 respectively.

The data for CL/ DDD adjusted for patient days decreased by 27 %, CP/DDD by 25% and TG/DDD by 10% from 2011-13.

Antibiogram sensitivities improved over the study period. *E coli* sensitivities improved for: ceftriaxone(CT) (79%-85%), levofloxacin(LV) (51%-57%), *Klebsiella pneumoniae* sensitivities improved for: gentamicin (71%-76%), imipenem(IP) (59%-64%), LV (50%-60%),CT (45%-54%). *Pseudamonas aeruginosa*sensitivities were mixed with sensitivities improving for LV (50%-62%), and decreasing for IP (70%-67%) and cefepime (80%-75%)

Conclusion. Changes in federal reimbursement affecting nursing home admissions to hospitals may have kept patients with MDROI out of the hospital, leading to the improvement of the Antibiogram.

Disclosures. **All authors:** No reported disclosures.

151. Is Nursing Home Specific Antibiogram Necessary for All Nursing Homes?

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Background. Smaller sample size in nursing homes can be one of the limitations in developing useful facility specific antibiogram. Studies looking into variability of antibiotic susceptibilities for closely located nursing homes are lacking. We examined the differences in the susceptibility results of the commonly prescribed antibiotics for the most common organism identified on urine cultures in 4 different nursing homes located within 5 miles of each other.

Methods. Using a retrospective study design, we conducted chart reviews on all patients who were managed for SAB at Vidant Medical Center and affiliated community hospitals during a one-year period (November 2012 to November 2013). Subjects were divided into two groups: those who received ID consultations and those who did not. Information on demographics, quality-of-care indicators, and clinical outcomes were obtained. Fisher's exact test and chi square analysis were used to assess differences in the two groups with $p < 0.05$ denoting statistically significance.

Results. *Escherichia coli* was the most common microorganism from urine cultures with 99 total isolates (21, 23, 19 and 36 from nursing homes A, B, C and D, respectively). When comparing sensitivities of *Escherichia coli* in nursing homes A, B, C and D, 86%, 78%, 63% and 81% of the isolates were sensitive to trimethoprim-sulfamethoxazole, respectively ($p = 0.35$); 76%, 78%, 58% and 61% to ciprofloxacin ($p = 0.33$), 90%, 87%, 89% and 81% to cefazolin ($p = 0.69$); 95%, 96%, 95% and 100% to nitrofurantoin ($p = 0.68$). The only significant difference was in the sensitivity of ampicillin (62%, 39%, 11% and 44%, p = 0.01). Other common organisms included *Klebsiella pneumoniae* (n = 38), *Enterococcus species* (n = 36), *Proteus mirabilis* (n= 34), and *Pseudomonas aeruginosa* (n = 22). The number of organisms was too small for statistical analysis for all of these isolates.

Conclusion. We have demonstrated that antimicrobial susceptibilities were similar for most antibiotics in closely located nursing homes. Antimicrobial stewardship

programs can consider developing regional nursing home antibiograms if multiple nursing homes are located in close proximity. This practice can be particularly helpful when developing antibiograms for smaller size nursing homes.

Disclosures. **P. Cook**, Gilead (investigator), Pfizer (investigator), Merck (investigator and speakers' bureau), Forest (speakers' bureau).

152. One year impact of clindamycin and ciprofloxacin administration on the human normal microflora

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Background. The purpose of this study is to assess the effect of clindamycin (150 mg qid for 10 days) and ciprofloxacin (500 mg bd for 10 days) on the skin, nasal, saliva and intestinal microflora of healthy humans for a period of one year In addition, the consequences of the emergence and persistence of clindamycin and ciprofloxacin resistant bacteria in the normal microflora were studied.

Methods. Thirty healthy subjects (15 males and 15 females) were randomly assigned in 3 groups and clindamycin, ciprofloxacin and placebo were given for 10 days period. Skin, nasal, saliva, faeces samples were collected at day -1, day 11, 1 month, 2 months, 4 months and 12 months. Agar plates were incubated in anaerobic and aerobic condition. Clindamycin and ciprofloxacin plates were also used. Bio assay was used to detect antibiotic concentration. MIC was done by the agar dilution method against 5 antibiotics.

Results. In the clindamycin group, minor effects on Coagulase-negative staphylococci (CoNS) observed on the skin microflora and normalized after 2-4 months. Nasal microflora normalized after 4-12 months. Saliva microflora normalized after 1 to 4 months. There were minor effects on the Enterococci, Bifidobacteria, Lactobacilli and Bacteroides that normalized after 2-12 months. Clindamycin was detected in faeces on day 11.

In the ciprofloxacin group, minor effect on CoNS observed and normalized after 4 months. Nasal microflora there were minor effects on CoNS and P. acnes that normalized after 2 months. In the saliva microflora there were minor effects on alpha-hemolytic Streptococci, Fusobacteria that normalized after 4 to 12 months. Initially there was no effect on the Enterococci but after 4 months there was an increase that normalized after 1 year. There were major effects on *E. coli*and on Bifidobacteria that normalized after 2 months. There were minor effects on Lactobacilli and Bacteroides. Ciprofloxacin was detected in faeces on day 11.

Conclusion. The interval of the normal microflora to be normalized after clindamycin or ciprofloxacin treatment is different for different bacterial species at different body sites. It takes 1-12 months to normalize the human microflora after treatment. No *Clostridium difficile* was detected in any of the samples.

Disclosures. **M. U. Rashid**, European Union: received funding **A. Weintraub**, European Union: received funding **C. E. Nord**, European Union: received funding.

153. Implementation of a Provider-Based Antimicrobial Stewardship Strategy at a Long Term Acute Care Hospital (LTACH) and Inpatient Physical Medicine and Rehabilitation (PMR) Facility

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Background. Antimicrobials are often overutilized in long term care facilities, particularly for urinary tract infections (UTI) and asymptomatic bacteriuria (ASB). However, limited data exists to guide antimicrobial stewardship in these settings. This study sought to determine if implementation of empiric UTI evaluation and treatment guidelines, along with education and targeted prescriber feedback would reduce the number of urine cultures ordered, prevent inappropriate treatment of ASB, and improve appropriate antimicrobial selection.

Methods. We conducted a single-center prospective cohort study with historic controls at a 96-bed LTACH and PMR facility in Philadelphia from September 2013–April 2014. Treatment guidelines were developed using unit-specific antibiograms. Guidelines were then implemented through educational sessions and distributed as pocket cards on January 15, 2014. Clinical characteristics (LTACH and PMR) and antimicrobial regimens (PMR) for UTI were compared for a 4-month pre- (PRE) and 3-month post-intervention (POST) group. All patients who had a urine culture ordered and received empiric UTI antimicrobials were included.

Results. Patients were similar in the two groups except for a higher frequency of LTACH patients with indwelling urinary catheters in the POST group (38.9% vs 15.3%; $p = 0.004$). Fewer urine cultures were ordered in POST compared to PRE group (mean cultures per month: 62 vs 92; $p = 0.037$). For the PMR unit, a total of 32 antimicrobial regimens (20 UTI, 12 ASB) were evaluated in the PRE group and 21 regimens (15 UTI, 6 ASB) in the POST group. Inappropriate treatment of ASB did not differ significantly between POST and PRE groups (6/21 [28.6%] vs 12/32 [37.5%]; $p = 0.56$). The intervention improved both empiric antimicrobial choice for UTI episodes (POST vs PRE: 13/15 [86.7%] vs 1/20 [5.0%]; $p < 0.001$) as well as appropriate dose/frequency (POST vs PRE: 15/15 [100%] vs 7/20 [35%]; $p < 0.001$).

Conclusion. A bundled stewardship intervention was effective at reducing the number of urine cultures and improving appropriate drug selection for UTI at an LTACH and PMR facility. The intervention was well received and easy to implement using limited resources, demonstrating that stewardship strategies can be successfully incorporated into long term care and other post-acute care settings.

Disclosures. **All authors:** No reported disclosures.

154. Gap Analysis of infection control practices in low and middle income countries (LMIC): Role of antimicrobial stewardship

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Background. Health-care associated infections (HAI) rates are higher in LMIC (6-18%) resulting in increased patient mortality, disability, and healthcare costs. We explored opportunity for improvement using a standardized tool - Infection Control Assessment Tool (ICAT). Prevention of Surgical site infections is a priority globally. In order to address this global health problem, we set out to further investigate specific areas where infection control practices could be improved in LMIC.

Methods. SHEA's international ambassadors were trained in specific modules by webinar using ICAT developed as a collaborative by USAID. Five out of the ten international sites completed the surgical modules-(1) Surgical antibiotics use and surgical equipment procedures, (2) Surgical practice area, (3) Sterilization and disinfection-equipment and IV fluids. Modules were scored and rated per guidelines: rating of (1) 75% -A: recommended practices are followed consistently, (2) 50-75% B-recommended practices usually followed and (3) <50%-C: training and follow-up needed on recommended practices. Data from the five sites were combined and analyzed based on World Bank country economy classification.

Results. Of the five sites, one was classified as a high income economy, three were upper-middle income economies, and one was a low-middle income economy. Scores (%) for the two surgical modules are presented in the table, categorized by income economy classification. Sterilization and disinfection scores were also low at 50% -C grade. Overall hand hygiene (HH) rates were low, an average of 33%.

Table 1

Module Section	High Income (N=1)	Upper-Middle Income (N=3)	Low-Middle Income (N=1)
Peri-Operative Antimicrobial Prophylaxis	15.8%	70.2%	47.4%
Surgical Drains	50.0%	100.0%	100.0%
Preprocessing of Surgical Instruments	25.0%	81.6%	66.6%
Preoperative Preparation of the Patient	35.7%	61.9%	50.0%
Preoperative Scrub by Surgical Personnel	50.0%	66.6%	72.2%
Barrier Precautions Used by Surgical Personnel	72.7%	81.8%	100.0%
Cleaning of Surgical Area	16.7%	82.2%	16.7%
Surgical Area Ventilation	33.3%	72.2%	33.3%
Surgical Area Traffic	50.0%	66.7%	25.0%
Surgical Area Attire	25.0%	69.4%	75.0%
Weighted Average	37.0%	72.0%	58.1%

Conclusion. Our results indicate that adherence to recommended infection control practices are suboptimal. Opportunities for improvement of infection control practices in several areas exist. Major areas of focus for improvement should be antimicrobial prophylaxis and preoperative preparation of the patient. Basic IC practices like HH, sterilization and disinfection should be addressed. Surgical site infections were not routinely monitored in these hospitals and SSI surveillance is not being consistently performed at the all the participating sites. International collaborative efforts should be established to improve IC practices.

Disclosures. **All authors:** No reported disclosures.

155. Implementation of a national surveillance program for antimicrobial use, Colombia 2012-2013

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Background. Bacterial resistance is considered a major public health problem, with greater impact on developing countries. However, in our country, few institutions of antimicrobial management programs. The objectives were to establish a national

surveillance of antimicrobial use for prescription habits and so it appropriate institutional policies set

Methods. 1. Through Management Colombian Association of infectious diseases public and private institutions in the country were invited to voluntarily form a surveillance network for rational use ofantimicrobials. 2. Antibiotic consumption was standardized using DDD x 100 day beds for consolidating information in each institution, according to the guidelines of the World Health Organization. 3. a website accessible to all institutions was developed, in order to educate, collect usage information on a monthly basis for antimicrobial, This tool allows real-time calculation of consumption rates and make institutional compared to national averages.

Results. Data from 30 institutions that make up the network of surveillance of antimicrobial use for 24 months follow-up were included. Describes the DDD per 100 beds/day of major groups of antimicrobials in Figure 1 and 2. It also was possible to establish trends in prescription of each molecule or group of intra-and inter-institutionally AB monthly in the period.

Conclusion. The creation of a network of antimicrobials was successful and from this information considered the baseline and in conjunction with the analysis of resistance profiles, it is possible to make recommendations to improve or establish antimicrobial management programs.

Disclosures. **All authors:** No reported disclosures.

156. Cost Analysis of Ertapenem Therapy for Urinary Tract Infections and Assesment of Its Suitability for Outpatient Paranteral Antibiotic Therapy in Turkey

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Background. In recent years, urinary tract infections (UTIs) due to extended-spectrum β-lactamase (ESBL)-producing gram- negative bacilli show an increased incidence both among out-patients and hospitalized group of patients in our country as well as around the world. Because of the ESBL-producing bacterial infections, patients' hospitalization, morbidity and mortality rates increase and this condition causes an increasing cost of treatment and socio-economic losses. The primary outcome of this study was to evaluate the cost of treatment with ertapenem for the treatment of UTIs due to ESBL-producing gram-negative bacilli in hospitalized patients and to calculate the estimated difference regarding costs between outpatients and hospitalized patients. Use of ertapenem in an OPAT programme is not available in our country. The secondary outcome was to assess whether ertapenem was suitable for outpatient paranteral antibiotic therapy (OPAT) programme in Turkey in future.

Methods. A total of 53 patients hospitalized between 2008 and 2010 with the diagnosis of UTI caused by ESBL-producing gram-negative bacilli and treated with ertapenem were retrospectively evaluated. The cost of ertapenem treatment as inpatient antibiotic therapy (IPAT) was calculated regarding hospital records. The estimated cost of the same antibiotic for the same patients as an OPAT programme was then calculated and the costs were compared.

Results. Ertapenem therapy was found to be safe and effective and its implementation as an OPAT programme would provide an estimated 20% reduction in projected costs. Consequently, the estimated patient bed days gained was calculated as 583 days, which constitutes about 5% of the total number of hospitalization days.

Conclusion. In our country, applying ertapenem therapy for UTIs due to ESBL-producing gram-negative bacilli, where the incidence is increasing each year, through OPAT programme will decrease the financial burden of health expenses. Also, this programme will reduce the number of inpatient bed days required for successful treatment and increase patient satisfaction.

Disclosures. **All authors:** No reported disclosures.

157. Effect of Antimicrobial Stewardship Program (ASP) on Perioperative Antibiotic Use in Cardiovascular Surgery in Japanese Tertiary Hospital

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Background. Antibiotics are needed for perioperative intensive care after cardiovascular surgery, but use is sometimes excessive, requiring intervention.

Methods. We analyzed antibiotic use and patient characteristics after scheduled cardiovascular operations (including 76 coronary artery bypass grafting and 96 valve/arch replacements) in our hospital (726 beds and 8 intensive care unit [ICU] beds), excluding cases of infective vascular disorders (i.e., infectious endocarditis and mycotic aneurysm) and emergency operations. Observation periods were 8 months in 2013 (intervention period; IP) and the same period in 2012 (pre-IP). For the intervention, an infectious disease [ID] fellow rounded on the ICU every day, and three times a week our ASP team (ID physician, clinical ID pharmacist, nurse, and microbiologist) discussed carbapenem and anti-methicillin-resistant *Staphylococcus aureus* [MRSA] drug administration for ward patients. Routine perioperative cefazolin was not included in the analysis.

Results. We analyzed 86 cases (540 patient-days [PDs] in the ICU and 3576 inpatient PDs) in the IP and 98 cases (619 ICU PDs and 4012 inpatient PDs) in the pre-IP. There were no statistically significant differences between the IP and pre-IP for male sex, age, BMI, operative bleeding, days hospitalized, ICU stay, and survival rate. MRSA and extended spectrum β-lactamase infections [ESBL] producing bacteria infections occurred in 9.3% vs 8.2% and 1.7% vs 3.1% of cases in the IP and pre-IP, respectively. Maximum sequential organ failure assessment [SOFA] scores during the ICU stay were higher in the IP (8.8 vs 7.6, $P = 0.03$, Mann-Whitney's test). Antibiotic use in the ICU did not differ significantly between periods (183.4 and 222.9 DOT/1,000 PDs), but was lower for the total hospital stay in IP vs pre-IP (142.9 vs 420.2 DOT/1,000 PDs, $P < 0.001$, chi-square test), especially for anti-MRSA drugs (17.7 vs 56.3 DOT/1,000 PDs, $P < 0.001$). The intervention shortened mean duration of anti-MRSA drug use to 5.2 from 9.8 days in the ICU and to 3.0 from 11.6 days in the ward. Total antibiotic expenditures in 8 months were 1.76 and 3.93 million JPY (IP and pre-IP, respectively).

Conclusion. The ASP team intervention decreased antibiotic use, optimizing anti-MRSA drug use, after cardiovascular surgeries without worsening patient prognosis in critical and ward care.

Disclosures. **All authors:** No reported disclosures.

158. Trends of Antibiotic Consumption in Korea according to Nation-wide Reimbursement Data (2008-2012): A Population-Based Epidemiologic Study

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Background. National data on antibiotic consumption are needed in order to develop effective strategies to foster appropriate antibiotic consumption. The objective of this study was to evaluate the quantity and the patterns of total antibiotic prescription based on reimbursement data in the Republic of Korea.

Methods. This population-based descriptive study was conducted using data from nationwide health insurance claims between 2008 and 2012. Data of systemic antibiotics for ambulatory and hospital care were collected using measurement units of the Defined Daily Dose (DDD)/1,000 populations per day according to the Anatomical Therapeutic Chemical classification. All of the analyses were performed with SAS 9.2.

Results. During study period, total consumption of systemic antibiotics showed stable trend as follows: 21.68 in 2008, 22.46 in 2009, 22.99 in 2010, 22.60 in 2011, and 23.12 in 2012. Of the total antibiotics, 83.65 % are used in the outpatients. During recent five years, penicillins were the most commonly used antibiotics, followed by second generation cephalosporins, macrolides, and fluoroquinolones. In time series analysis with an ARIMA model, total antibiotic consumption demonstrated the significant seasonality ($P < 0.001$). Total antibiotic consumption was more frequently prescribed in the influenza season than in the non-influenza season (AUD, 1.98 ± 0.16 vs 1.81 ± 0.18, $P < 0.001$). In a regression model with autoregressive errors, aminoglycosides consumption has been continuously decreased during recent five years ($P < 0.001$). Meanwhile, main antibiotic classes for infections caused by multi-drug-resistant microorganisms and metronidazole showed the upward trend ($P < 0.001$). Differences by age groups and types of healthcare institution were observed among antibiotic classes. Antibiotics used most frequently in surgical subjects to an evaluation of antibiotic prescription relevance have decreased from 2008 to 2012, in contrast with those to a non-evaluation ($P < 0.001$).

Conclusion. In conclusion, this study suggested that consumption of the broader spectrum antibiotics has been increased recently and showed the effect of appropriate public health policy associated with perioperative antibiotic prescription.

Disclosures. **All authors:** No reported disclosures.

159. Clinical pharmacists enhance an antimicrobial stewardship program in Thailand

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Background. Clinical Pharmacist (CP) is an emerging career in Thailand. We evaluated the efficacy of antimicrobial stewardship programs (ASP) featuring CP with or without infectious diseases consultation (IDC) in Thailand.

Methods. From January 1, 2012-September 30, 2012, all patients with infections admitted to 4 medicine units were prospectively followed until hospital discharge for the impact of ASP with or without IDC for outcomes: inappropriate antibiotic use, antibiotic de-escalation, duration of antibiotic use, hospital length of stay (LOS), and mortality. Patients were retrospectively categorized as patients who had CP input without IDC (Group 1), CP input and IDC (Group 2), and no CP input or IDC (Group 3). All groups received basic ASP supervised by hospital pharmacy during the study period. CP was responsible for making daily rounds, alert treating physicians on antibiotic use, and reminders on antibiotic de-escalation. Appropriate antibiotic use was retrospectively evaluated for *prehoc* prescribing criteria.

Results. The cohort was comprised of 574 patients (G1 = 104; G2 = 320; G3 = 150), with no difference in demographics in G1 and G2. Compared to G3, G1 and G2 patients were more likely to have comorbidities and advanced age. Most antibiotic prescriptions were for empirical therapy (373/574; 65%) while antibiotic prescriptions were most often prescribed for respiratory tract infection (287/574; 50%). By multivariate analysis, G1 was associated with <7days duration of antibiotic use (adjusted Odds Ratio 19.6; $P < 0.001$), while G2 was associated with less inappropriate antibiotic use (aOR = 0.03; $P < 0.001$), antibiotic de-escalation (aOR = 3.7; $P < 0.001$), and <7 days duration of antibiotic use (aOR = 6.81; $P < 0.001$). Compared to G3 (as reference), G1 and G2 were less likely to be prescribed inappropriate antibiotic use ($P < 0.001$), have de-escalation of antibiotics ($P < 0.001$), receive antibiotics <7 days ($P < 0.001$) and have subjects with shorter hospital LOS ($P < 0.001$). There were no group differences in mortality.

Conclusion. This study suggests the feasibility and efficacy of ASP featuring CP, with or without IDC, among hospitalized patients in Thailand. Appropriate antibiotic use, antibiotic de-escalation, <7 day antibiotic regimens, and shorter hospital LOS was associated with CP participation on medical teams.

Disclosures. **All authors:** No reported disclosures.

160. A Simulation Study to Assess Indicators of Antimicrobial Use as Predictors of Resistance

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Background. Indicators of antimicrobial (AM) use have been described previously, but the optimal indicator for predicting AM resistance in hospital settings, especially when including pediatric populations, is unknown. This simulation study aimed to assess if a significant difference could be found between these indicators' accuracy as predictors of AM resistance, even with entire networks of intensive care units (ICUs).

Methods. Ten different resistance / AM use combinations (combinations) were studied. Simulations were run to find out if Québec's network of ICUs or the National Healthcare Safety Network (NHSN) ICUs could have allowed the detection of predetermined differences between the most accurate and 1) the second most accurate indicator, and 2) the least accurate indicator, in more than 80% of simulations. For each indicator, simulated absolute errors were generated, for each ICU and each 4-week period, over 4 years of surveillance (absolute error = |observed prevalence or incidence – predicted prevalence or incidence|. Absolute errors in prediction were generated following a binomial distribution, using mean absolute errors (MAEs) observed in data from 9 ICUs as the average proportion; simulated MAEs were then compared using t-tests. This was repeated 1,000 times for each scenario.

Results. Main results are presented in the table.

Number of resistance / AM use combinations for which a power of 80% was reached, for different scenarios.

Measure of resistance predicted	Most accurate indicator of AM use was compared to	Number of combinations for which a significant difference was observed in >80% of simulations (N=10)	
		Québec network	NHSN
Prevalence	2nd most accurate indicator	0	2
	Least accurate indicator	5	10
Incidence	2nd most accurate indicator	1	5
	Least accurate indicator	7	10

Conclusion. The two most accurate indicators of AM use would often offer similar predictions of resistance, even in large networks. The least accurate indicators could frequently be distinguished, but not always, especially in the Québec network, which is smaller.

Disclosures. **All authors:** No reported disclosures.

161. Do Positive Anaerobic Culture Results Affect Physicians' Clinical Management Decisions?

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Background. Often routine aerobic and anaerobic cultures from body fluids, abscesses and wounds are ordered. We seek to determine whether results of anaerobic tissue and fluid cultures, with the exception of blood, affect physicians' treatment approaches.

Methods. Retrospective chart review of all adult inpatients (age ≥ 18 years) with positive anaerobic body tissue/fluid cultures between January 1, 2012 and December 31, 2012.

Data collected included subjects' ages, co-morbidities, hospital service, initial antibiotic regimen, acknowledgement in the chart of positive anaerobic culture results, and whether or not ID consultation was obtained. Culture data included specimen source, organism identification, and time to growth of anaerobic culture.

Results. 205 of 3,234 (6.34%) anaerobic body fluid/tissue cultures, from 180 patient visits, were positive. Of these 180 visits, 26 were excluded based on exclusion criteria, therefore 154 charts were reviewed.

The majority of cases with positive anaerobic cultures were surgical specimens. Only 20% (n = 31) of patient charts with positive cultures had documented physician acknowledgement, 90.3% by ID physicians. Only 8% (n = 15) had antibiotic regimens changed based on results (Figure 1). In about 25% of cases, results were reported after the patient was discharged, so no assessment of response was possible.

Nearly 70% of all patients were on appropriate initial empiric antibiotic coverage (Figure 2). Of the remaining 30% (inappropriate, unknown, or no empiric coverage), 1 regimen change was documented after culture results were known. There were no changes in cases without physician result acknowledgment.

Limitations:

1. Use of progress notes as evidence of physician acknowledgement of culture results likely misses many cases in which results were reviewed and considered in physician assessments.

2. Since only patients with positive culture results were reviewed, we cannot assess the impact of a negative result on decisions regarding need for continued antimicrobial therapy.

Figure 1. Characterization of Physician Acknowledgements and Antibiotic Changes Due to Positive Anaerobic Cultures

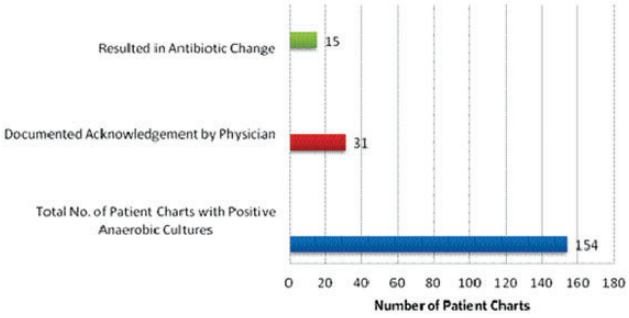
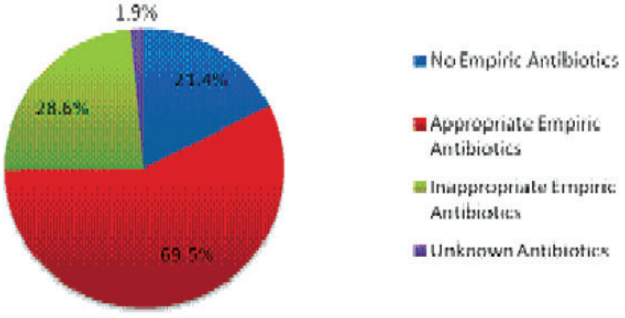
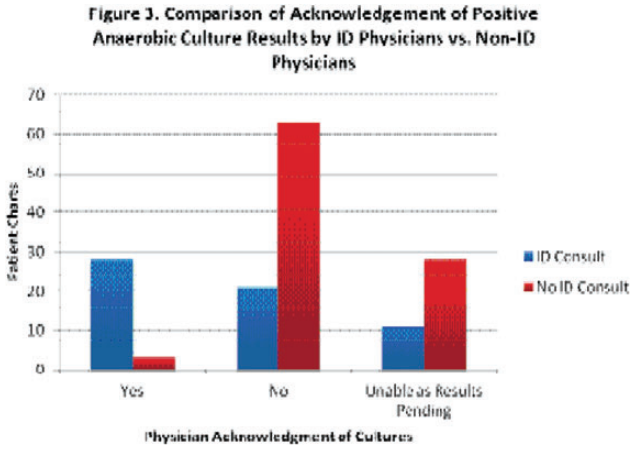


Figure 2. Empiric Antibiotic Choice for Patients with Positive Anaerobic Cultures





Conclusion. Our study suggests that positive anaerobic body fluid culture results infrequently affect physicians' treatment decisions. There may be significant opportunities for cost saving if anaerobic cultures are not routinely processed.

Disclosures. **All authors:** No reported disclosures.

162. Antimicrobial Stewardship in the Micro Lab: Selective Susceptibility Reporting and Impact on Ciprofloxacin Utilization in a Hospital Setting

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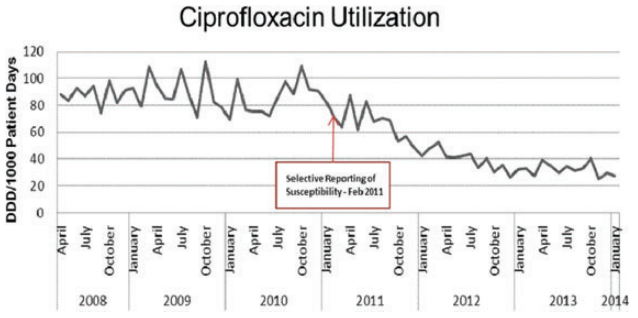
Background. Resistance to ciprofloxacin has increased markedly over the past several years in response to increased prescribing. The objective of this study was to determine the impact of selective reporting of ciprofloxacin susceptibility on ciprofloxacin utilization as part of an antimicrobial stewardship program in a hospital setting.

Methods. Our institution is a 375-bed community teaching hospital. Historically, the microbiology laboratory practice was to report ciprofloxacin susceptibility for all Enterobacteriaceae regardless of susceptibility to other agents. A selective reporting policy was created and implemented by the antimicrobial stewardship program in collaboration with the microbiology laboratory in February 2011. The policy involved the suppression (i.e., non-reporting) of ciprofloxacin susceptibility to Enterobacteriaceae when there was lack of resistance to the antibiotics on the gram negative panel. Ciprofloxacin utilization (measured by Defined Daily Doses (DDD)/1,000 patient days) 34 months before and 38 months after the intervention (policy implementation) was collected. An interrupted time series analysis was performed.

Results. Pre-intervention (April 2008-Janurary 2011), ciprofloxacin utilization was 87.9 DDD/1,000 patient days. Following the intervention (February 2011 to January 2014), ciprofloxacin utilization decreased to 45.2 DDD/1,000 patient days. This represents an approximate 50% decrease ($p < 0.0001$) in ciprofloxacin utilization after selective ciprofloxacin susceptibility reporting.



Conclusion. Selective reporting of ciprofloxacin antimicrobial sensitivity may result in a decrease of ciprofloxacin prescribing in a hospital setting when combined with a comprehensive antimicrobial stewardship program.

Disclosures. **All authors:** No reported disclosures.

163. What's Going Around? A prospective cluster randomized trial to evaluate a novel, real-time, syndromic surveillance tool's effect on clinical decision making amongst primary care providers

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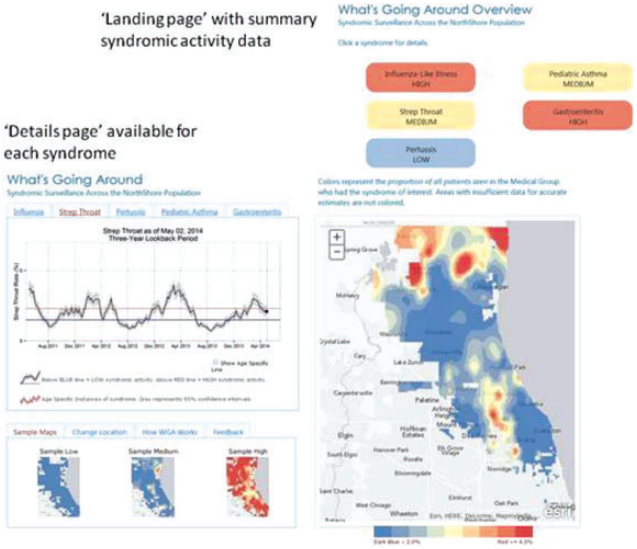
Background. A patient's epidemiological context can aid clinical decision making. NorthShore University HealthSystem is evaluating a novel, real-time, local, syndromic surveillance tool.

Methods. The What's Going Around (WGA) tool collects data daily from electronic health records (EHR), processes the data through algorithms and generates a syndromic heatmap for Influenza-like-illness (ILI), Pertussis, Group A Strep (GAS) and pediatric asthma. WGA provides these maps to clinicians inside their EHR (figure). A prospective cluster randomized trial is underway to evaluate this tool. 54 primary care practices were randomized to the WGA tool or control arms. A five month (November 1, 2013-April 1, 2014) interim analysis is being evaluated. The primary outcome is percentage of ILI visits with an antibiotic prescription. T tests and difference-in-differences (DID) calculations with a 2 year look back period were performed.

Results. The intervention arm did not prescribe fewer antibiotics for ILI visits than the control arm overall (41.1% vs 41.3%; $p = 0.90$). However, during periods of high and medium ILI activity, the intervention group experienced an absolute 2.0% and 5.1%* reduction in antibiotic prescription for ILI visits, (baseline 39.4% and 46.8%, respectively) and a 1.6% increase and 0.33%* decrease in antiviral prescription (9.7% and 2.4% baseline). For all clinic visits during periods of high and medium ILI activity there was an absolute 1.0%* and 1.7%* reduction in antibiotic prescription (baseline 21.1% and 19.1%). During periods of high, medium and low pertussis, the intervention group had an absolute 2.2%* increase, a 1.4%* reduction and a 1.4%* reduction in pertussis PCR orders (baseline 8.6%, 7.8% and 6.3%, respectively). For high, medium and low GAS, the intervention group had an absolute 3.3%* increase, 8.4%* decrease and a 6.7%* decrease in GAS specific antibiotic prescriptions (baseline 46.3%, 46.2% and 40.9%, respectively). * Results significant at $p < 0.05$ value.



Conclusion. This interim analysis suggests that an EHR-based decision support tool providing clinicians with local epidemiological information aids their decision making.

Disclosures. **All authors:** No reported disclosures.

164. Lessons Learned from Early Implementation of Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-ToF MS) with Antimicrobial Stewardship, A Pilot Study

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Background. Our goal was to describe early implementation of Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI) identification coupled with antimicrobial stewardship program (ASP) on timing, process and outcome in bacteremic patients.

Methods. MALDI at Montefiore received NYS Department of Health lab approval January 2014. A pilot for MALDI identification (IDENT) of blood cultures coupled with ASP notification (MALDI-IDENT+ ASP) was compared to a matched month of conventional IDENT (CON-IDENT) (March 2014 vs 2013) to assess feasibility and resources needed. MALDI lists were e-faxed 2-3 times/day to ASP staff who reviewed medical records for demographics, antibiotic prescribing, and timing parameters. Data collection is ongoing for statistical and program evaluation (i.e., outcomes, severity adjustment) and for pediatrics.

Results. Blood cultures from 115 patients are summarized in the table. In March 2014 >90% blood isolates were IDENT by MALDI, the majority from plates (68%) vs bottles (32%). The median time in hours to IDENT was sooner with MALDI. A trend towards earlier targeted antibiotics was also seen with MALDI-IDENT, especially for gram-negative rods (55.9 vs 85.0) and isolates identified directly from bottles (64.9 vs 77.6). These interventions required 6-10 hours daily from lab and ASP.

	MALDI-IDENT + ASP March.'14 (n=62)	CON-IDENT Mar.'13 (n=53)	p-value
Patient Demographics			
Age (mean years, range)	62 (25-94)	68 (24-93)	
Gender (% female)	40	57	
Clinical source (Top 3)	Urine (13), Abdominal (10), Bone/Joint/SSTI (9)	Urine (13), Pneumonia (10), Bone/Joint/SSTI (8)	
Sepsis (Sp) + Severe Sp/shock (%)	40	39	
Pathogen distribution			
Gram negative (n=total)	28	34	
Gram positive (n=total, *S. aureus*, other)	47, 17, 30	32, 8, 24	
Timing parameters (median hours, range)			
[A]Time to **IDENT**	31.4 (17.1-218.2)	52.2 (26.5-254.3)	<0.001
[B]Time to Antibiotic Regimen	67.5 (19.4-185.8)	79.2 (33.5-241.6)	0.07

A= Microbiological identification–time collected; B= Preferred narrowest antibiotics–time collected

Conclusion. Our preliminary results suggest shortened time to identification and tailored antibiotics. However additional data is needed for formal evaluation. Our pilot supports that MALDI can feasibly be adapted to a large urban academic center, with proper resources and close coordination between lab and ASP staff.

Disclosures. **All authors:** No reported disclosures.

165. Integrating a Rapid Diagnostic Test and Antimicrobial Stewardship: Optimizing Discharge Antibiotics in Skin and Soft Tissue Infections (SSTI)

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Background. *S. aureus* (SA) is the leading cause of SSTI. Empiric antibiotics for SSTI should have activity against methicillin-resistant SA (MRSA) and methicillin-susceptible SA (MSSA). Clindamycin is highly utilized for SSTI; however, clindamycin-resistance rates in MSSA are nearly 20% at our institution. Differentiation between MRSA and MSSA using a rapid antigen test that detects penicillin-binding protein (PBP2a) for methicillin-resistance prior to final susceptibility could allow early targeted antimicrobial therapy. This quality-improvement project aims to optimize antibiotic usage in SA SSTIs through utilization of the PBP2a rapid diagnostic test.

Methods. Baseline antimicrobial use for inpatient SA SSTIs was collected for 1 year prior to implementation. Live education regarding interpretation of the PBP2a test was provided to hospitalists and housestaff. The test was implemented for SA SSTI in January 2014. Test results were faxed to the Antimicrobial Stewardship Program (ASP) and reviewed; recommendations were made if necessary. Data was collected to assess impact of PBP2a results on antimicrobial prescribing. Targeted therapy for MSSA was defined as effective beta-lactam therapy.

Results. 163 patients were evaluated prior to PBP2a implementation. 44/163 (27%) were discharged prior to final susceptibility. Of those, 24 (55%) patients were infected with MSSA and 20 (83%) were prescribed clindamycin; 4 (17%) patients had clindamycin-resistant MSSA. In the post-PBP2a implementation interim analysis, 36 patients were reviewed; 14 (39%) patients were discharged prior to final susceptibility. Of those, 8 (57%) patients had MSSA and 2 (25%) of those were discharged with clindamycin. Among all patients, ASP intervened in 7 cases (19%); no intervention was made if therapy was appropriate (n = 13), if the team changed to an appropriate therapy (n = 9), if Infectious Diseases service was involved (n = 5), or if patient was already discharged (n = 2).

Conclusion. In this interim analysis, targeted MSSA therapy increased from 17% to 75% in patients discharged prior to final susceptibility. It appears that rapid diagnostics in combination with education likely improves targeted antibiotic therapy for SA SSTI. Further audit and feedback by ASP may improve antibiotic mismatch rates.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient **R. Selvarangan**, Alere: Investigator, Research grant **J. Goldman**, Pfizer: Grant Investigator, Research grant

166. Rapid MRSA PCR on Respiratory Specimens from Ventilated Patients with Suspected Pneumonia: A Potential Tool for Antimicrobial Stewardship

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is an important cause of ventilator-associated pneumonia. As a result, empiric therapy often includes anti-staphylococcal agents. Our objective was to evaluate the GeneXpert MRSA/SA SSTI Assay (Cepheid, Sunnyvale, CA) for use in lower respiratory tract (LRT) specimens for rapid MRSA detection as a tool in antimicrobial stewardship efforts.

Methods. For the validation of the assay, we included laboratory-derived ("spiked") bronchoalveolar lavage (BAL) specimens with known quantities of MRSA (SCC*mec* II and IV; 10^2 - 10^5 CFU/mL) and 30 banked LRT samples. For the clinical phase, we determined if LRT samples submitted to the microbiology lab met criteria for suspected pneumonia and were collected from ventilated patients. Comparator standard-of care culture results and antibiotic utilization information were collected. Antibiotic days for vancomycin and linezolid were calculated.

Results. The limit of detection for MRSA in the spiked BAL samples was 10^3 CFU/ml. The assay correctly detected MRSA in 9/9 frozen samples and excluded MRSA in 21/21 samples with other organisms (sensitivity 100%, specificity 100%). We screened 310 LRT specimens; 100 met study criteria. Ten samples tested positive for MRSA with rapid PCR, while 6 were positive in routine cultures. Rapid PCR correctly detected 5/6 positive and 89/94 negative MRSA specimens for a sensitivity of 83.3% (95% CI: 36.1-97.2%) and specificity of 94.7% (95% CI: 88-98.2%) with a negative predictive value of 98.9% (95% CI: 93.9-99.8%). A total of 748 vancomycin and 305 linezolid antibiotic days were associated with the enrolled specimens. Vancomycin and linezolid utilization would decrease by 68.4% and 83%, respectively, if they were discontinued 1 day after negative rapid PCR results.

Conclusion. A rapid MRSA PCR test performed well against the gold standard in respiratory samples from ventilated patients with suspected pneumonia. Its implementation has the potential of reducing empiric vancomycin and linezolid utilization.

Disclosures. **C. A. D. Burnham**, Cepheid: Investigator, Research support

167. Reduction in Contaminated Blood Culture Rates and Associated Costs as an Antimicrobial Stewardship Program Activity

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Background. Contamination of blood cultures (CBCx) is a common, costly, and preventable problem which can cause confusion for clinicians and leads to unnecessary hospitalization, additional testing and consultation, and unnecessary antibiotic treatment. The maximum acceptable percent of CBCx is 3% (Clinical and Laboratory Standards, College of American Pathologist). Published studies indicate the average inpatient with a CBCx accumulated $4385 - $7502 in excess hospital costs and stayed 4.5 – 5.4 additional hospital days.

Methods. We reviewed the CBCx occurrence from 2008-2012 and found our hospital CBCx rate exceeded the 3% rate over 32% of the time during this period.

Results. The most common CBCx organisms were aerobic Gram-positive cocci, with the most common organism identified being *S. epidermidis*. Identified issues resulting in CBCx included improper skin preparation and accessing a peripheral venous catheter for blood cultures. For the years 2010-2012, the Emergency Department (ED) was responsible for 33-61%, 29-74%, and 31-76% of the monthly total CBCx, respectively. The time of day CBCx were drawn during 2010-2012 were evaluated, and CBCx occurrence rose beginning at 08:00, peaked at 14:00, and declined significantly 22:00 during these three years, nearing the staff shift change. Hospital and ED costs

associated with CBCx were estimated, as well as costs incurred by the microbiology lab and pharmacy. Overall hospital cost of CBCx for the three years averaged $1,893,830, with the ED accounting for $929,500 (49%). The most commonly used antibiotic to treat CBCx was vancomycin, with an annual average hospital cost of $6,887 for the last three years evaluated. Projected hospital savings by reducing the occurrence of CBCx from the ED during these three years by 20% and 30% were $185,166 and $278,670 respectively.

Conclusion. Reducing the occurrence of CBCx may result in significant hospital savings from inappropriate hospital admissions, additional laboratory costs, and overuse of antibiotics.

Disclosures. **All authors:** No reported disclosures.

168. The Positive Blood Culture as a Stewardship Opportunity: Time to Appropriate and "Best Therapy" is a Useful Quality Gauge Across an Acute Care Hospital

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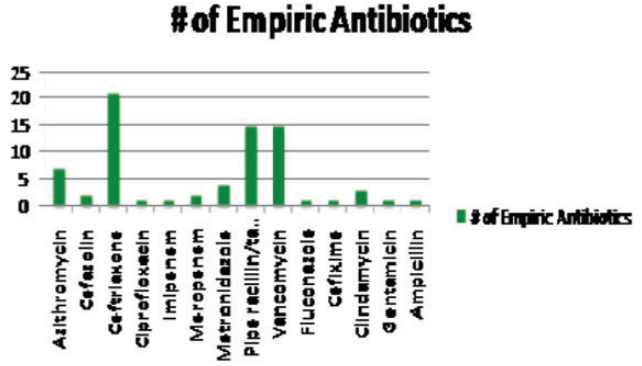
Background. To assess the appropriateness of antimicrobial therapy of patients with positive blood cultures in a tertiary care setting, the timeliness of antibiotic administration, and streamlining of therapy in response to microbiologic data generated using MALDI-tof

Methods. Over a 4-week period, all inpatients (University of Alberta Hospital) with new positive blood cultures were enrolled prospectively. Data collected included Microbiology, patient demographics, comorbidities and antimicrobial therapy. The final antimicrobial regimen was categorized as the "Best Therapy" or not, based on susceptibility testing, clinical factors including coinfections, allergies and cost. The timeliness of antibiotic therapy and streamlining was assessed based on the time of the positive culture call, the times antibiotics were ordered and administered, and the time culture, and updated susceptibility reports became available.

Results. 48 positive blood cultures were included (19%- *E. coli*, 12%- *Staph. aureus*, 10% - *Enterococcus* and 15.5% -*Streptococcus).* The most commonly suspected sources were urosepsis (24%) and pneumonia (12%). Over 80% of empiric antimicrobial orders were concordant with Microbiologists recommendations. Ceftriaxone, piperacilin-tazobactam, vancomycin and azithromycin were the most common empiric antibiotics (36.2%, 25.9%, 25.9% and 12.1% respectively). Based on final culture and sensitivities, 34.5% of empiric therapy was inadequate; however, 89.7% of all positive blood cultures patients received eventual "Best Therapy". It took a median of 2.78 hours and 6.7 hours for antibiotic initiation and change after the call from microbiology and after susceptibilities were posted respectively, significant variability in the timing of antibiotic changes (0-46 hrs) and administration (0-19.75 hrs) was noted



Conclusion. Microbiologists recommendations and initial empiric therapy are >80% concordant. The majority of patients were eventually treated with best therapy; however, there are opportunities to streamline therapy earlier in the clinical course. Finally, the time to initiate and change antibiotics varies substantially, and more data involving the processes on each unit is required in order to make improvements.

Disclosures. **All authors:** No reported disclosures.

169. Rapid Testing using Verigene® Microarray in Combination with Antimicrobial Stewardship Intervention in Gram-negative Bacteremia

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Background. Rapid identification of organism and resistance is paramount for targeted treatment in serious blood stream-infections (BSI). Verigene® Gram-Negative Blood Culture Test (BC-GN) is a multiplex, automated nucleic acid test for the identification of a broad panel of Gram-negative (GN) organisms and resistance markers from blood culture bottle positivity with a turnaround time of approximately 2 hours. We evaluated the Verigene® BC-GN assay in combination with theoretical antimicrobial stewardship team (AST) intervention in GN BSIs.

Methods. Clinical isolates from adult patients at the University Maryland Medical Center with GN bacteremia from January 2012 to June 2012 were included. Blood culture bottles were spiked with clinical isolates and processed by Verigene® BC-GN. AST reviewed charts along with Verigene® result and recommended antibiotics using derived algorithms. The time interval included in analysis was time of Gram stain report until 48 hours after susceptibility results. The intervention group's (Verigene® with AST) antibiotic recommendation was theoretically implemented at 3 hours from actual Gram stain report, and compared with the control group's actual antibiotic administration times obtained from the chart, using Student's t-test.

Results. A total of 117 isolates were tested, demonstrating 97.6% sensitivity, 99.6% specificity and overall concordance rate of 95.7% (112/117) for organism identification. Half of the *Enterobacteriaceae* isolates resistant or intermediate to ceftriaxone were detected as CTX-M (5/10) and all of the MDR *A. baumannii* were detected as OXA (7/7). The intervention group had a significantly shorter mean duration to both effective (1.4 vs 6.6 hours, $P < 0.01$) and optimal (6.7 vs 47.7 hours, $P < 0.01$) antibiotic therapy. Using proportional hazards regression, we found that the intervention group was significantly more likely to receive timely optimal antibiotic therapy compared to controls (hazard ratio 1.5, $P = 0.01$).

Conclusion. Our study demonstrated a potential decreased time to both effective and optimal antibiotic therapy in GN BSI using combined intervention of rapid testing and AST recommendation. Prospective studies are needed to further validate this strategy.

Disclosures. **J. K. Johnson**, Nanosphere: Investigator, Research support; Bio-Fire: Investigator, Research support; OpGen: Investigator, Research support

170. Outcomes of Rapid Identification for Gram Positive Bacteremia in Combination with Antibiotic Stewardship at a Community Based Hospital System

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Background. Rapid identification of Gram positive (GP) bacteria from blood cultures can help narrow antimicrobial therapy toward the offending pathogen or discontinue unnecessary antibiotics for contaminants. The Verigene® GP blood culture assay is a nucleic acid test that identifies 10 organisms and select resistance genes in 2.5 hours from positive blood cultures. This study evaluates the use of the Verigene® assay, or optimized standard identification of blood GP isolates, in combination with real-time support from the Antibiotic Stewardship Team (AST) in a community hospital system.

Methods. This multi-center, pre-post quasi-experimental study was conducted at the five hospitals that compose Scripps Healthcare. Rapid diagnostic testing was performed at a central laboratory from 7am-7pm. If cultures became positive overnight, routine identification was done first thing in the morning. Pharmacists notified physicians of results and assisted with antibiotic modifications. The primary outcomes were average time to optimal antibiotic therapy and difference in antibiotic duration for contaminants. Secondary endpoints included hospital length of stay, mortality, pharmacy and overall hospitalization costs. Adult patients with a GP bacteremia admitted in 2011 (pre-rapid testing) were compared to those admitted in 2014 (post-rapid testing).

Results. There were 110 patients in the preintervention group and 65 patients in the intervention group. The optimized GP identification process, combined with AST intervention improved time to optimal antibiotic therapy (60.6 vs 35.3 hours, $p < 0.0001$). Duration of antibiotic therapy for blood cultures considered to be a contaminant decreased in the intervention group (44.2 vs 24.5 hours, $p = 0.0171$). Length of stay (14.1 vs 9.0 days, $p = 0.0162$), pharmacy costs ($1,957 vs $1,115, $p = 0.16$), and overall hospitalization costs ($27,245 vs $16,698, $p = 0.02$) were lower in the intervention group. Mortality was similar between groups (9.1% vs 9.2%, $p = 0.55$).

Conclusion. Rapid identification of GP blood cultures with AST intervention decreased time to optimal antibiotic therapy, length of unnecessary antibiotic therapy for blood culture contaminants, length of stay, and overall hospital and pharmacy costs.

Disclosures. **All authors:** No reported disclosures.

171. Impact of Rapid Bloodstream Pathogen Identification in Hospitalized Patients

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Background. Rapid identification of blood stream infection (BSI) pathogens by polymerase chain reaction (PCR) may reduce time to effective and optimal antibiotic use and improve patient outcomes. We sought to evaluate the impact of a novel PCR system, the FilmArray Blood Culture ID (BCID) Panel (BioFire, Salt Lake City, UT). The BCID is performed directly on a positive blood culture, has 27 PCR targets (20 pathogen specific, 4 genus level, and 3 resistance genes), and takes < 2 hours.

Methods. A case-control study included hospitalized patients with clinically significant BSI identified by traditional cultures with BCID (BG, cases, November 2013-April 2014) or without BCID (TG, controls, January 2013-September 2013). Prior to BCID introduction stewardship-driven guidelines for interpretation were widely distributed, but antibiotic management was dictated by primary teams. Time from blood culture draw to effective (antimicrobial active against the pathogen) and optimal (most narrow spectrum effective therapy) therapy were the primary outcomes.

Results. Fifty five subjects each in the BG and TG groups were similar in age, comorbidity, Charleson and Pitt bacteremia scores, critical care support needs, infectious disease involvement, and immunosuppressed status. Common infection sources were central venous catheters (37.6%), genitourinary (16.5%), intra-abdominal (13.8%), and skin/bone (13.8%). Frequent BSI pathogens were *E. coli* (19.7%), *S. aureus* (16.4%), and *Klebsiella* species (9.8%) with 10.9% polymicrobial. Nosocomial infections were more common in the BG (41.8% vs 24.1%, $P = .02$) and healthcare-associated infections in TG (57.4% vs 30.9%, $P = .02$).

Outcome (*=mean)	BG (Std Dev) N=55	TG (Std Dev) N=55	*P*
Time to Effective Therapy, h*	14.9 (26.0)	14.3 (22.9)	.91
Time to Optimal Therapy, h*	47.4 (36.0)	58.6 (37.7)	.10
30-day Mortality, %	10.9	18.2	.42
Clinical Resolution, %	80	74.6	.65
Readmission, %	25.5	23.6	1.00
Days of Therapy*	26.2 (25.4)	26.2 (41.8)	.10
Length of Stay*	16.2 (12.4)	15.2 (24.1)	.03

Conclusion. Numerical improvements in time to optimal therapy, 30-day mortality, and clinical resolution were noted but not significant. The analysis was underpowered, but it is likely that clinicians are not changing antibiotic prescribing in response to BCID data. The BCID results should be paired with an antimicrobial stewardship intervention to improve its impact.

Disclosures. **M. E. Rupp**, 3M: Consultant and Grant Investigator, Consulting fee and Research grant

172. Can Procalcitonin (PCT) Be Used as an Early Marker of Sepsis in Patients with Intracranial Hemorrhage (ICH)?

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Background. To assess whether PCT can be used as a reliable early marker of sepsis in patients with ICH.

Methods. In this prospective observational study we enrolled 73 patients with ICH (defined as subarachnoid hemorrhage, subdural hematoma, epidural hematoma, intraventricular hemorrhage, intraparenchymal hemorrhage) who were febrile above 38.3 C at anytime during hospitalization. Serum PCT was measured on day one (PCT 1) and 48-72 h later (PCT2. Patients were determined to have an infection (pneumonia (PNA), urinary tract infection (UTI) or blood stream infection) based on cultures, imaging and clinical impression of the treating team and were assigned a score of 1 based on the presence of an infection that was microbiologically proven. The clinical impression regarding the cause of the fever was also noted (infection vs central fever).

Results. There was no statistically significant difference between the mean PCT1 of patients with no infection (M = 0.22 ng/ml, SD = .40) as compared to those with microbiologically proven infection (M = .45, SD = .55), p = .063. There was no statistically significant difference between the mean PCT2 among those with no infection (M = 0.21, SD = .37) as compared to those with microbiologically proven infection (M = .56, SD = .73), p = .084. However, at PCT1, those with infection based on clinical impression (M = 0.18, SD = .17) had significantly lower PCT scores as compared to those with central fever(M = 0.44, SD = .69), F(1, 72) = 6.33, p = .014. This difference did not remain significant at PCT2 (M = .22, SD = .41; M = .41, SD = .61, p = .302).

PCT1 levels were not significantly different in patients with PNA (M = 0.22, SD = .39) vs central fever (M = 0.50, SD = .67), p = .06. Similarly, PCT2 levels were not significantly different in patients with PNA (M = 0.21, SD = .38) vs central fever (M = 0.56, SD = .73), p = .09. PCT1 levels were also not different in patients with a UTI diagnosis (M = .27, SD = .46) vs central fever (M = .31, SD = .38), p = .85. There was only 1 patient with a central fever at PCT2, so we could not examine that association.

Conclusion. The results of our study indicate that serum PCT is not a reliable marker in differentiating between early sepsis and central fever in patients with ICH.

Disclosures. **All authors:** No reported disclosures.

173. Introduction of Procalcitonin Testing Did Not Reduce Antibiotic Utilization for Acute Exacerbations of Chronic Obstructive Pulmonary Disease

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Background. Acute exacerbations of chronic obstructive pulmonary disease (AECOPDs) are a frequent cause of inpatient admission and antibiotics are often used for treatment, even without a clear indication. Procalcitonin (PCT), a biomarker for bacterial infections, has been used to safely discontinue antibiotic therapy in AECOPDs. We sought to characterize the impact of PCT's introduction to our medical center on the management of AECOPDs.

Methods. Patients admitted from October 1, 2013 (the date PCT became available) to March 31, 2014 were included in the study if an AECOPD was present on admission and they were not transferred from another facility. Data were extracted through structured query and chart review. The primary outcome was antibiotic days on therapy (DOT) and secondary outcomes included 30-day readmission and mortality. Linear and logistic regression were used to model the outcomes.

Results. A total of 238 patients met inclusion criteria. Mean age was 66.7, standard deviation ±12.3, 124 (52%) patients were female, and systemic inflammatory response syndrome (SIRS) was present in 115 (48%). PCT was measured on 73 patients. Presence of SIRS and length of stay (LOS) associated with PCT measurement, while age and gender did not. Overall, PCT measurement associated with more antibiotic DOT (+56%, standard error [SE] ±9%, $P < .001$) compared to patients on whom no PCT was measured, even when adjusted for SIRS and LOS. Among those on whom PCT was measured, low PCT levels (<0.25 ng/mL) associated with fewer DOT for intravenous (IV) antibiotics (-108%, SE ±22%, $P < .001$). When adjusted for LOS, PCT measurement was not associated with readmission or mortality.

Conclusion. Measurement of PCT during episodes of AECOPD did not reduce overall antibiotic utilization, though lower levels associated with fewer days on IV therapy. The impact of PCT on antibiotic utilization demonstrated in controlled studies may not be immediately realized in local clinical practice. Whether increased provider familiarity with PCT over time and/or targeted educational efforts can affect these findings deserves further study.

Disclosures. **All authors:** No reported disclosures.

174. Usefulness of Procalcitonin in Detection and Monitoring Treatment of Bacterial Infections

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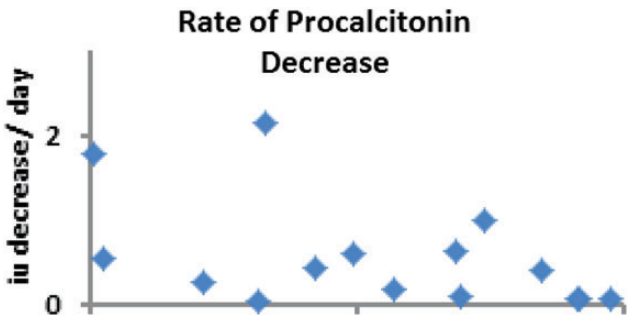
Background. The usefulness of procalcitonin (PCT) in identifying bacterial sepsis has been generally accepted based on a large body of evidence. The utility of PCT in identifying less serious bacterial infections and in monitoring the progress of treatment of bacterial infections is still controversial. At the VA New Jersey Healthcare System, our laboratory has offered PCT test since November 2013. We now have the opportunity to retrospectively review our PCT data and microbiology data along with the clinical assessment of patients to try to determine if PCT is useful in these two areas (detection and treatment monitoring).

Methods. In our Process Improvement Project, we obtained PCT and culture results from the laboratory data archive. Cases were identified and reviewed. Bacterial infection is defined as when the event was identified as such in the patient discharge summary.

Results. A total of 203 procalcitonin assays were done up to April 15, 2014, involving 130 patients and 144 positive cultures. The significance of each PCT result was manually reviewed for utility as a predictor for bacterial infection and for monitoring effectiveness of therapy. We had 54 assays in which there was presence of a positive bacterial culture done between -3 and +7 days of the assay. 32 of 54 (60%) had PCT levels of 0.1 or higher; 22 (40%) has levels <0.1. In those with levels <0.1, there was only one positive blood cultures of Staphylococcus coagulase-negative (contaminant). Most of these were UTIs and soft tissue mild infections. The positive culture group had an average value of 11.7, median of 0.16. There were 149 PCT assays with no associated cultures done and we could not analyze those with any confidence. We have 24 patients with serial values done during treatment. The rates of decreases during treatment depended on the type of infection. Decreases of >2 iu /day were seen in patients (5) with resolving sepsis.



Conclusion. 1) procalcitonin levels were increased during serious bacterial infection. Some urine and soft tissue infections do not have elevated values. 2) If initial levels are high, successful treatment will result in incremental decreases in these values. Proper application of procalcitonin should assist in the guidance of antibiotic use and determining durations of treatment of bacterial.

Disclosures. **All authors:** No reported disclosures.

175. Cost-effectiveness of a Procalcitonin-Guided Treatment Algorithm in Sepsis

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Background. Procalcitonin has emerged as a promising biomarker of bacterial infection. Published literature demonstrates that use of procalcitonin testing and an associated treatment pathway reduces duration of antibiotic therapy without impacting mortality. Procalcitonin testing, however, is an additional expenditure which may or may not be offset by treatment-related financial gains. The cost-effectiveness of procalcitonin use has not been established in patients with sepsis. The objective of this study was to determine the cost-effectiveness of utilizing a procalcitonin algorithm to guide patient care compared with standard care in patients with sepsis.

Methods. A decision analytic model was developed from a hospital perspective. Published clinical and economic data populated a cost-minimization and a cost-utility analysis across 10,000 hypothetical patient scenarios. Univariate and probabilistic sensitivity analyses assessed the robustness of our model across all likely scenarios.

Results. Our model predicted that the use of a procalcitonin algorithm dominated standard care (i.e., increased effectiveness with decreased costs). The incremental cost of procalcitonin use vs standard care saved $168 per septic episode while increasing a patients' quality of life. Secondary analyses found variables which had the potential to alter results included: compliance with algorithm adherence (<25.2%), days of antibiotic reduction (<0.28), the probability of antimicrobial-induced nephrotoxicity (<11%), or decreased nephrotoxicity through antimicrobial reduction (<0.9%). Under these circumstances, our model predicted a higher incremental cost of procalcitonin use; however, procalcitonin use remained cost-effective at our predetermined willingness-to-pay threshold.

Conclusion. Our model predicts that use of a procalcitonin-guided treatment algorithm in sepsis patients may be cost-effective. Implementing a procalcitonin-guided treatment algorithm in septic patients could improve the quality of care and decrease costs in patients with sepsis.

Disclosures. **All authors:** No reported disclosures.

176. Antibiotic Prescribing Adherence to Procalcitonin (PCT)-Generated Recommendations in Two Academic Medical Intensive Care Units (MICUs)

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Background. Using serum PCT levels to help guide antibiotic duration in adult intensive care units reduced antibiotic use without adversely affecting survival or other outcomes in randomized controlled trials. We assessed the clinical utility of real-world PCT testing in two Chicago teaching hospital MICUs.

Methods. Concurrent PCT testing and teaching/guideline interventions deployed in reverse sequence in the two MICUs were approved as quality improvement projects by both hospital IRBs, with waiver of patient consent. Recipients of systemic antibacterials were targeted for daily PCT testing only while in the MICU; results appeared in patients' electronic records; MICU physicians (MDs) used published interpretive criteria to integrate PCT results with clinical data in making antibiotic prescribing decisions. We assessed MD prescribing decision/PCT level adherence over all PCT levels and for the last PCT measurement for each episode of care.

Results. PCT was measured 1240 times in 630 care episodes (median 2 tests/episode) for 540 patients over 10 months in MICU A. Over 5 months of ongoing testing in MICU B, PCT was measured 531 times during 131 episodes of care (median 3 tests/episode) for 121 patients. PCT results and patient-level trends generally mirrored infection severity and response to therapy. At hospital A, of 173 initially low PCT values, MDs stopped antibiotics 49 (28%) times; at hospital B, initial PCT values were not responded to. Adherence to PCT-generated recommendations for all PCT levels and for the last PCT levels is displayed in Figure 1 and Figure 2.

Figure 1: All PCT Levels, Hospital A & B

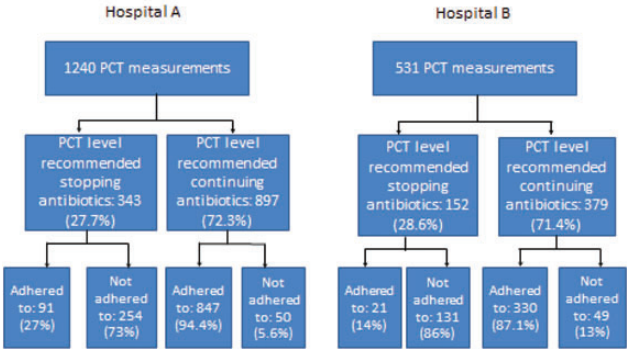
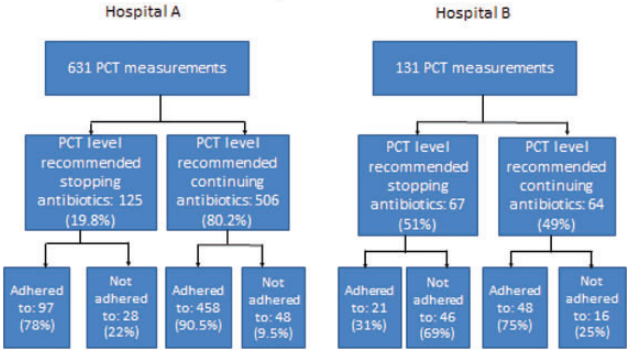


Figure 2: Final PCT Levels, Hospital A & B



Conclusion. The distribution of PCT values above and below the threshold for recommending antibiotic stopping was similar at our two academic MICUs, but MD adherence to these recommendations differed markedly, suggesting variable test acceptance. Only 20% of patients in the MICU with higher rates of adherence had PCT levels below the threshold to recommend stopping antibiotics. PCT testing after ICU discharge and improved MD education may be needed to take full advantage of PCT testing in this population.

Disclosures. **K. Singh**, Quidel: Scientific Advisor, Consulting fee **R. Balk**, Biomerieux: Research and Speaker's Bureau, Research support and Speaker honorarium

177. Management of Complicated Para-pneumonic Effusion and Pleural Empyema with Initial Parenteral Antibiotics and Early Switch to Oral Equivalent

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Background. Intravenous (IV) antibiotics had been the mainstay of therapy for children with complicated para-pneumonic effusion (PPE) and pleural empyema (PE). Whereas oral antibiotics have been used to complete a prescribed course of therapy, when to switch and how long to treat are more a matter of style than a matter of evidence or official guidelines. There is also controversy regarding the use of video-

assisted thoracoscopic surgery (VATS) vs chest tube insertion with fibrinolysis when drainage is indicated. Substantial practice variation exists.

Methods. Retrospective chart review and descriptive analysis of children managed by the pediatric infectious diseases service at Kosair Children Hospital between 2008 and 2012.

Results. A total of 59 children met inclusion criteria. All patients received IV antibiotics at admission. Sixty-seven percent of children had a surgical procedure on the day of admission or the following day; all of these were VATS, except for 2 children who had a chest tube placed and later underwent VATS. The mean time to VATS was 1.4 days [95% CI 1.08, 1.80]. In 70% of the cases that underwent drainage, no organism was identified by culture of the pleural fluid. All patients received IV antibiotics at admission and all were discharged on oral antibiotics; the mean time to switch was 7.9 days [95% CI 6.76, 9.12] and the mean duration of oral antibiotic therapy was 16.98 days [15.3, 18.64]. There were no deaths; 6 patients required repeat surgical intervention, but this was not related to use of oral antibiotic therapy.

Conclusion. Children with complicated PPE and PE can be managed effectively with early VATS and early switch from IV to oral antibiotic therapy.

Disclosures. **All authors:** No reported disclosures.

178. Impact of Delaying methicillin-resistant *Staphylococcus aureus* (MRSA) Pneumonia Treatment Until Microbiologic Documentation

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Background. Well-designed clinical studies have shown the importance of accurate empiric antibiotic coverage for critically ill patients suffering from an infection. However, these studies may lack external validity regarding the importance of early methicillin-resistant *Staphylococcus aureus* (MRSA) pneumonia due to the underrepresentation of this population. Two major clinical trials documenting the mortality benefit of early and accurate empiric antibiotics only reported 3.1% of patients having an MRSA infection and 15.6% of patients with documented *Staphylococcus aureus* infection.

Methods: This is a retrospective, descriptive, single center study to evaluate the impact on patient outcomes of delaying coverage for the treatment of MRSA pneumonia in intensive care unit (ICU) patients. The primary endpoint was to evaluate the in-hospital mortality of ICU patients with positive MRSA cultures from a respiratory source empirically treated with an anti-MRSA antibiotic compared to those not treated empirically. Secondary endpoints were to evaluate the hospital and ICU length of stay among surviving patients that received empiric or delayed therapy.

Results. From January 2010 to September 2013 total of 68 patients with similar baseline characteristics were included in the study analysis, 45 in the empiric and 23 in the delayed group. There was 24.4% mortality in the empiric treatment group compared to 26.1% in the delayed treatment group with an absolute risk increase of 1.7% (95%CI -20.3-23.5). Among 51 surviving patients the mean hospital length of stay was 20.7 days in the empiric and 21.5 in the delayed group. The mean ICU length of stay was 7.8 days in the empiric compared to 10.5 days in the delayed group, a 2.7 day absolute increase in the delayed group.

Conclusion. There does not appear to be a difference in hospital length of stay. However, the data implies a clinically meaningful increased ICU length of stay when delaying MRSA pneumonia therapy. Future study with an appropriately powered sample still necessary for more precise estimates and evaluation of adjusted results.

Disclosures. **All authors:** No reported disclosures.

180. Effect of Antimicrobial Treatment Duration on recovery of Bacteria in Sterile Specimens Submitted for Culture

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Background. Early initiation of antibiotics results in cultures that are unrevealing, resulting in potentail over use of broad-spectrum antibiotics. We performed a prospective study of PCR and electrospray ionization mass spectrometry (PCR/ESI-MS) assay in development for detection of bacteria directly from sterile surgical specimens obtained after antibiotic treatment had been initiated.

Methods. We prospectively identified 111 cases of suspected bacterial infection in which sterile specimens were submitted for culture after the initiation of antibiotics. Patients were stratified based on days of antibiotic treatment (DOT). Conventional aerobic and anaerobic culture results were compared to PCR/ESI-MS. Agreement was assessed by Kappa score.

PCR&ESI-MS vs Culture results Stratified by DOT (N=111)

	N	PCR&ESIMS-/ Culture-	PCR&ESIMS-/ Culture+	PCR&ESIMS+/ Culture+	PCR&ESIMS+/ Culture-	Kappa (95% CI)
DOT < 2	45	16	1	23	5	0.73 (0.53–0.93)
DOT 3 - 7	37	8	0	7	22	0.12 (0.01–0.23)
DOT > 8	29	7	0	5	17	0.12 (-0.005–0.25)

Results. PCR/ESI-MS detected pathogens more often than conventional culture: 71% (79/111) vs 32% (36/111). The overall Kappa score was 0.294, consistent with poor agreement. Culture and PCR/ESI-MS had strong agreeement (Kappa = 0.73) for patients with < 2 days of antibiotic treatment (table). For patients in the two longer treatment groups, PCR/ESI-MS was more likely to detect bacterial pathogens, and the discordance between culture and PCR/ESI-MS results as measured by Kappa was more than would be expected by chance.

Conclusion. In patients treated with > 2 days of antimicrobial treatment prior to collection of samples, PCR-ESI/MS was significantly more likely than conventional culture to detect pathogic bacteria directly from sterile surgical specimens. PCR/ESI-MS results were not significantly different from conventional culture for specimens collected within 48 hours of initiation of antibiotics. The advantage with antibiotic treatment durations > 2 days does not appear to demonstrate a dose response relationship. PCR/ESI-MS may provide future opportunities to target antimicrobial therapy and salvage both individual treatment regimens and institutional antimicrobial stewardship efforts when patients have received more than 2 days of antimicrobial treatment prior to diagnostic testing.

Disclosures. **R. Sampath**, Ibis BioSciences, an Abbott Company: Employee, Salary **R. Bonomo**, AstraZeneca: Grant Investigator, Grant recipient; Merck: Grant Investigator, Grant recipient; Rib-X: Grant Investigator, Grant recipient; Steris: Grant Investigator, Grant recipient; TetraPhase: Scientific Advisor; NIH: Grant Investigator, Grant recipient; VA Merit Review: Grant Investigator, Grant recipient

181. Empiric Coverage of ICU Patients for Infections Due to Beta-lactam Resistant *Pseudomonas aeruginosa* with Combination Therapy: A Needs Assessment

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Background. Empiric antimicrobials for critically-ill patients routinely include combination therapy for patients at risk for infection from *P. aeruginosa*. In 2013, in vitro susceptibility to anti-pseudomonal beta-lactams, ciprofloxacin and tobramycin among ICU isolates at of *P. aeruginosa* was < 85%, 70% and >90%, respectively. This prompted the question of whether an aminoglycoside should routinely be administered with an anti-pseudomonal beta-lactam antibiotic as empiric therapy in ICU patients.

Methods. The study aimed to describe the epidemiology and patient outcomes of infection due to *P. aeruginosa* with in vitro resistance to at least one anti-pseudomonal beta-lactam agent. A retrospective study of patients admitted to an ICU between January 1 and December 31, 2013 with at least 1 isolate of *P. aeruginosa* with in vitro resistance to at least one of the anti-pseudomonal beta-lactam agents was completed.

Results. Overall, 61 ICU patients out of 15, 311 ICU admissions (0.4%) had 100 isolates with resistance to at least one anti-pseudomonal beta-lactam agent. Nineteen (31.2%) had >1 isolate recovered during the calendar year and 38 (62.3%) had structural respiratory tract changes and/or depressed CNS function that likely predisposed to *P. aeruginosa* colonization or infection. Sepsis was listed as a diagnosis in 10 patients.

Based on empiric choices of therapy, 21 patients had a "mismatch" in therapy, based on drug administration and in vitro susceptibility results.

Twenty-one (34.4%) of 61 patients died during the hospitalization or shortly thereafter. Of these, 8 (38.1%) had received mismatched therapy. In only one case, death was possibly related to mismatched therapy.

Conclusion. The results of this study suggest that despite the concerning decrease in susceptibility of both beta-lactams and quinolones to *P. aeruginosa,* the recovery of beta-lactam resistant *P. aeruginosa* in our ICU cohort was uncommon and did not result in a significant worsening of patient outcomes. Therefore, even with decrease in susceptibilities**,** routine use of empiric combination therapy that includes an aminoglycoside does not seem warranted at this time.

Disclosures. **All authors:** No reported disclosures.

182. Correlation between Antibiotic Use and *E.coli* Resistances in a Swiss Tertiary Care Hospital

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Background. Monitoring antimicrobial use and local antimicrobial susceptibility in hospitals are important tools of antimicrobial stewardship programs. In our institution 2144, *E.coli* from clinical samples were isolated in 2011. We aimed to correlate resistance of these samples with antibiotic use.

Methods. The hospital pharmacy calculated the antibiotic use in grams for each department of the hospital for the years 2008-2011. We converted the use into defined daily doses (DDD) and expressed it as DDD/100 bed days, using the ATC/DDD system promoted by the WHO.

Antimicrobial susceptibility tests (ASTs) were routinely assessed using the disk diffusion method and results interpreted according to CLSI criteria. Resistance rates of *E. coli* represent the number of resistant isolates divided by the total number of clinical isolates for which AST was performed. All hospital departments with a total of >20 *E. coli* isolates in urine, blood or other clinical material in the year 2011 were included in the analyses. Per patient only the first isolated *E.coli* was included. The correlation

between antibiotic use from 2008-2011 and *E.coli* resistance rate in the year 2011 was determined with linear regression analyses.

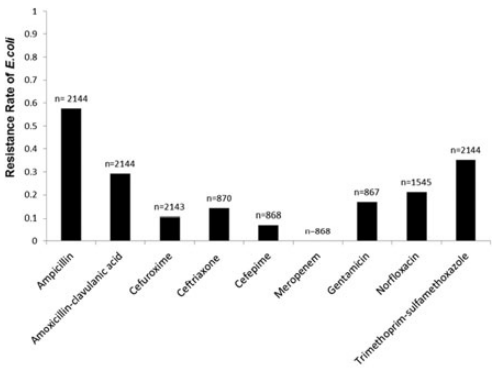

Figure 1: Hospital-wide resistance rate of *E.coli* for the analyzed antibiotics. N indicates the number of performed antimicrobial susceptibility tests for the respective substance.

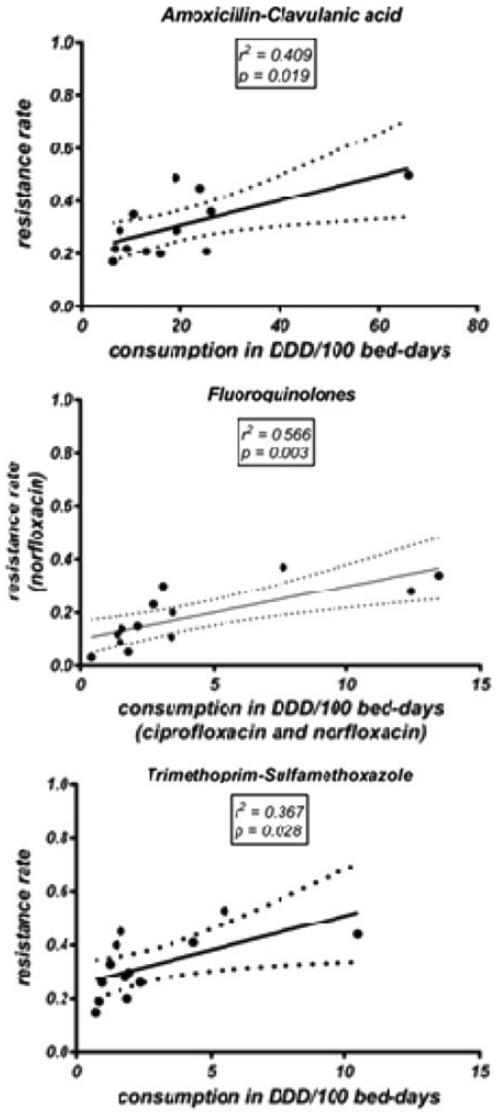

Figure 2: Linear regression analyses for use and resistance rates of *E.coli* for amoxicillin clavulanic acid, fluoroquinolones and trimethoprim-sulfamethoxazole. Each dot represe individual clinical department in our hospital.

Results. The total antibiotic consumption for the hospital was 64 DDD/100 hospital days with high variability between the different departments. The hospital-wide resistance rates of *E.coli* are summarized in Figure 1. Antibiotic use correlated with *E. coli* resistance for amoxicillin-clavulanic acid [coefficient of determination (r^2) 0.409 (p-value: 0.019)], trimethoprim-sulfamethoxazole [r^2 0.367 (p-value: 0.028)] and for fluoroquinolones (ciprofloxacin and norfloxacin), [r^2 0.566 (p-value: 0.003)]. (Figure 2) There was no correlation between use and resistance for amoxicillin, cefuroxime, ceftriaxone, cefepime, meropenem and gentamicin.

Conclusion. A correlation between inhospital antibiotic use and *E.coli* resistances was documented exclusively for antibiotics with a high consumption rate which are both available in oral and parenteral form. Two of the antibiotics in question are often prescribed for treatment of urinary tract infections. Our data could serve as basis for antibiotic-specific stewardship interventions.

Disclosures. **All authors:** No reported disclosures.

183. Evaluating Multidrug Resistance Prevalence and Antimicrobial Stewardship Preparedness in the Largest Not-For-Profit Healthcare System in the United States: Taking the First Step to Optimize Antimicrobial Use

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Background. Antimicrobial stewardship plays the most critical role to control the development of multidrug resistant organisms (MDROs). We assessed the current antimicrobial stewardship practices (ASP) in a large multi-hospital health system as the initial step for future system-wide ASP implementation.

Methods. A survey from 85 hospitals of a single healthcare system evaluated the prevalence of MDROs, and the presence of antimicrobial stewardship programs (ASPs). Questions addressed the prevalence of MDROs and local measures to optimize antimicrobial use. We compared the results based on hospital bed size (small ≤200, medium 201-500, large >500 beds).

Results. Larger hospitals had the highest reported rates of *Klebsiella pneumoniae* carbapenem resistant organisms (2.2% vs 0.7% for medium and 0.3% for small; p = 0.001). Medium size hospitals reported higher rates of carbapenem resistant to *Escherichia coli* (0.091% vs 0.018% for large and 0.015% for small; p = 0.09). There were no significant differences for extended spectrum beta lactamase producing *E. coli* (large 4.6%; medium 4.9%; small 7.9%; p = 0.51). The vast majority of hospitals (n = 81, 95.3%) produced an antibiogram, with 77 (90.6%) at least annually. ASPs were more established in large (100%) and medium (81.5%) compared to small (23.1%) hospitals (p < 0.001). Large hospitals more often restricted broad-spectrum antimicrobials (83.3% vs 63% for medium and 23% for small; p < 0.001). Prospective evaluation by pharmacists was 100% in large hospitals (44.4% for medium and 25% for small; p = 0.001). Mandatory Infectious Diseases consultation for specific broad-spectrum agents was more common in large (100%) compared to medium (40.7%) and small (9.6%; p = <0.001). Clinical pathways for specific infections were more common among large hospitals (66.7% vs 40.7% for medium and 21.2% for small; p = 0.001). Infectious Diseases pharmacist approval was rarely used.

Conclusion. The prevalence of MDROs and the presence of ASPs vary based on hospital size. Smaller hospitals may be less prepared than larger ones to address antimicrobial stewardship. Our findings contribute to a better understanding of the varied needs of our hospitals to develop future processes and optimize patient care outcome.

Disclosures. **All authors:** No reported disclosures.

184. Prevalence and Molecular Epidemiology of ESBL producing *E.coli* and *K.pneumoniae* in Lebanese Medical Centers; Strong Correlation between Antibiotic Consumption and Resistance to Cephalosporins and Ciprofloxacin

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Background. ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae* have rapidly spread worldwide creating a severe threat. The development of resistance in these bacteria is multi-factorial; antibiotic consumption is a major factor. In view of both significant increase in ESBL production and lack of efficient control of antibiotic use in Lebanon (Middle East), we conducted a study to determine the epidemiology of ESBL-related genes in *E.coli* and *K.pneumoniae,* and analyzed the correlation of antibiotic use with bacterial resistance in 3 major medical centers.

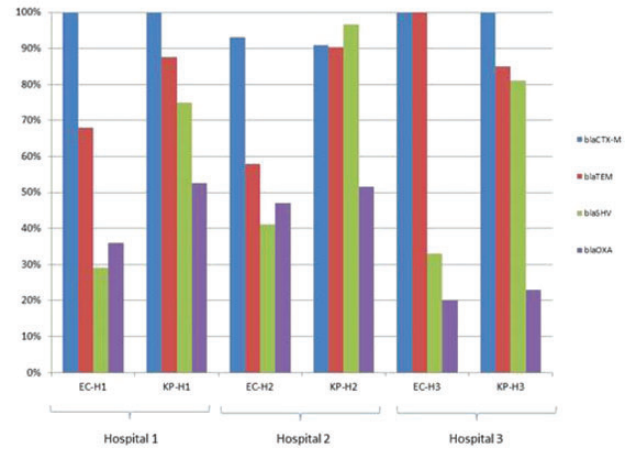
Methods. Three medical centers located in the north, south, and capital (Beirut) of Lebanon were chosen for this study. All ESBL producing *E.coli* and *K.pneumoniae* from inpatients were collected between January 2, 2012 and January 2, 2013. Only the first isolate per patient was included. Antibiotic consumption was expressed in DDD/100 bed days and Kirby-Bauer technique was used for antibiotic resistance

testing. For the phenotypic detection of ESBL, double disk synergy test and E-test were performed. PCR and multiplex PCR were used for the detection of the genes bla_{TEM}, bla_{SHV}, $bla_{CTX\text{-}M,\ and}$ bla_{OXA}. The identification of $bla_{CTX\text{-}M15}$ was done by sequencing of the gene. The association between consumption and resistance was analyzed using Spearman correlation coefficient. Pulsed Field Gel Electrophoresis (PFGE) was used to determine the clonality of the different isolates.

Results. A total of 1002 *E.coli* and 233 *K.pneumoniae* isolates were analyzed. 29.9% of *E.coli* strains and 31.1% of *K.penumoniae* were ESBL producers. Use of 3rd and/or 4th generation cephalosporins and resistance to these antibiotics were strongly correlated. In addition, the correlation factor of cephalosporin consumption vs susceptibility to ciprofloxacin in *E.coli* (Hospital 1) was as low as -0.899 and -0.886 in *K. pneumoniae* (Hospital 3). $bla_{CTX\text{-}M}$ was produced by 97% of *E.coli* and 96.7% of *K.pneumoniae*. Specifically, $bla_{CTX\text{-}M15}$ was commonly found. 22.3% of *E.coli* and 37.4% of *K.pneumoniae* co-produced the 4 studied beta-lactamases.

PFGE analysis demonstrated that there was no major clonal relationship among these ESBL producers.

Occurrence of different ESBL genes in *E.coli* and *K.pneumoniae*



Conclusion. Our data show the urgent need for antimicrobial stewardship programs in the country to control the use of antibiotic and the spread of bacterial resistance.

Disclosures. **Z. Daoud**, Merck: Grant Investigator, Research grant **S. Doron**, Merck: Grant Investigator and Speaker's Bureau, Research grant and Speaker honorarium.

185. Predicting Antimicrobial Resistance Prevalence and Incidence from Indicators of Antimicrobial Use

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Background. Indicators of antimicrobial (AM) use have been described, but the optimal indicator for predicting AM resistance in hospital settings, especially when including pediatric populations, is unknown. This study compared the accuracy of 15 different AM use indicators in the prediction of resistance, in 9 intensive care units (ICUs).

Methods. All patients admitted to participating ICUs (3 neonatal, 2 pediatric, 4 adult) between 2006 and 2010 were studied retrospectively. Prevalence and incidence of resistance in endotracheal cultures were both estimated per 4-week period. AM use was measured, per 4-week period, using 15 different indicators. Resistance / AM use combinations studied were resistance to:

- methicillin in *Staphylococcus aureus* / penicillin + 3rd generation cephalosporins + quinolones use
- aminoglycosides in coliforms / aminoglycoside use
- piperacillin-tazobactam in coliforms / piperacillin-tazobactam use
- quinolones in coliforms / quinolones use
- carbapenems in *E. coli*, *Klebsiella* sp. or *Proteus* sp. / penicillin + carbapenem + quinolone use
- carbapenems in *Pseudomonas* sp. / carbapenem use
- piperacillin-tazobactam in *Pseudomonas* sp. / piperacillin-tazobactam use
- quinolones in *Pseudomonas* sp. / quinolone use

For each combination, indicators of AM use were successively tested in regression models after adjustment for ICU type. Binomial regression was used to model prevalence and Poisson regression, to model incidence. Multiplicative and additive models were tested, as well as no time lag and a 1 period time lag. For each model, the mean absolute error (MAE) was computed. MAEs were then compared using t-tests.

Results. A statistical difference between MAEs could only be detected when using carbapenem use for predicting prevalence of resistance to carbapanems in *Pseudomonas*sp. For this combination, the most accurate indicator (courses/100 patient-days, additive model, no time lag; MAE = 0.31 cases/100 admissions) was better ($p = 0.0006$) than the least accurate indicator (recommended daily doses/100 admissions, multiplicative model, 1-period time lag; MAE = 0.43 cases/100 admissions, thus 38% bigger).

Conclusion. In our ICUs, indicators of AM use predicted resistance with similar accuracy, except for one combination.

Disclosures. **All authors:** No reported disclosures.

186. Incidence of acute kidney injury in patients receiving vancomycin and pipercillin-tazobactam compared to other antibiotic combinations

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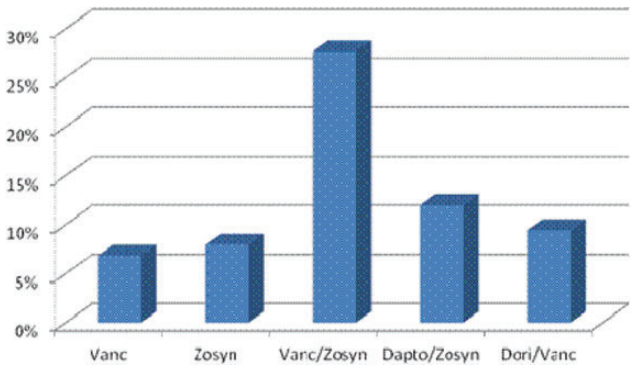
Background. Vancomycin and piperacillin-tazobactam are two of the most commonly used empiric antibiotics in hospitalized patients. Recent reports indicate a higher incidence of acute kidney injury (AKI) with this combination of antimicrobial compared with vancomycin alone

Methods. Retrospective chart review of patients admitted to tertiary medical center receiving at least 48 hours of vancomycin (V), piperacillin-tazobactam (Z), vancomycin and piperacillin-tazobactam (VZ), vancomycin and doripenem (VD) and piperacillin-tazobactam and daptomycin (ZD) for rates of AKI.AKI was defined as an increase in creatinine by 50% from baseline or ≥ 0.5 mg/dL. Other data collected included vancomycin level, vasopressor use, diabetes mellitus (DM) history, nephrotoxic agents and concurrent contrast.

Results. Data of 392 patients over a period of 2 years were analyzed. Average age in each group was: V (66), Z (67), VZ (63), ZD (58) and VD (61). Average initial creatinine in all groups was 1.1 mg/dL. AKI developed in 28% (26/94) of patients in the VZ group, 7% (3/44) of vancomycin alone, 8% (8/101) of pipercillin-tazobactam alone, 12% (12/100) of patients receiving VD and 9% (5/53) of those on ZD . Within the VZ and ZD group, those who develop AKI, was more likely be on diuretics and or ACE inhibitors. Concurrent contrast did not seem to correlate with AKI in any of the groups except for vancomycin alone group. Vancomycin trough level was higher in those with AKI in the VZ group and vancomycin alone group. Vasopressors were more likely used in the AKI group with all the combinations. DM reported more in Z, VZ, VD groups in those who developed AKI. The average patient age was higher in the AKI subset in all groups except for VZ and VD group. In VZ group, the average time to onset of AKI was 7.6 days.



Conclusion. Higher Rates of acute kidney injury seen in patients with combination of pipercillian-tazobactam and vancomycin. In addition, any two antibiotics combination had higher incidence of AKI in compare when vancomycin or pipercillin-tazobactam used alone. The risk of AKI may be higher in patients on concurrent diuretics, ACE inhibitors and those with diabetes mellitus. Further studies needed to confirm these results and to evaluate mechanism of nephrotoxicity.

Disclosures. **All authors:** No reported disclosures.

187. Colistin and its Effect on Renal Function: A Retrospective Review at an Urban Hospital

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Background. The emergence of multi-drug resistant gram negative organisms has led to the frequent use of colistin, an antibiotic first available for clinical use in 1959 but unpopular due to concerns of renal failure. Recent literature suggests colistin

nephrotoxicity may be overestimated. Aggressive, weight based dosing with an initial loading dose is recommended for colistin therapy in our institution. We completed a retrospective analysis to assess the utilization of a colistin dosing protocol and its effect on renal injury in an urban academic hospital.

Methods. All patients admitted to University Hospital who received colistin between 2010 and 2013 were reviewed retrospectively. 144 patients were identified and data abstracted included patient demographics, colistin doses, serum creatinine, use of renal replacement therapy and hospital disposition. Dosages given were compared to hospital guidelines and renal clearance (based on Cr clearance) was utilized as a measure of renal failure. Acute kidney injury (AKI) was defined as a change in creatinine greater than 0.5 mg/dL from baseline.

Results. On many occasions, colistin was not appropriately dosed. The loading dose of colistin was given correctly to 70 patients (48.61%) whereas it was not given in 70 patients and overdosed in 4 patients (2.78%). There were 1170 maintenance doses given in total: 610 correct doses (52.14%), 158 overdoses (13.50%) and 402 underdoses (34.36%). Renal function was monitored throughout hospitalization. There were only 34 patients (23.61%) who met criteria for AKI prior to start of colistin, whereas 76 patients (52.77%) met criteria for AKI after starting colistin. Additionally, there was a greater rise in creatinine with more adherence to the colistin dosage protocol. On average, there was a change in Cr of 1.72 mg/dL when colistin was dosed correctly 75-100% of the time as opposed to a change in Cr of 0.73 mg/dL when dosed correctly only 0-25% of the time.

Conclusion. Colistin is being inappropriately under-dosed as per hospital protocol approximately 50%of the time in regards to loading doses and maintenance doses. However, we still see considerable acute kidney injury, especially when adhering to hospital protocol, which contrasts with the latest literature that claims the nephrotoxic effects of colistin to be overestimated.

Disclosures. **All authors:** No reported disclosures.

188. Evaluation of Baseline QTc Interval and Azithromycin Prescribing in an Academic Medical Center

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Background. The use of azithromycin for its anti-inflammatory effect in chronic obstructive pulmonary disease, cystic fibrosis, and lung transplant recipients has increased significantly. Recently published data cited a rise in cardiovascular death in patients with azithromycin compared to other antibacterial agents. In response, the FDA released warnings regarding prescribing azithromycin in certain patient populations. Our main objective aimed to assess inpatient prescribing patterns for azithromycin and determine the potential risk for adverse cardiovascular events.

Methods. From October 1, 2012 through April 30, 2013, 1610 encounters were identified for inpatients ≥19 years of age prescribed azithromycin. One hundred patient encounters were randomly selected for evaluation. Information collected for each patient and included length of stay, reason for use, dose, duration of therapy, concomitant medications associated with QTc prolongation, culture data, telemetry charges, and baseline ECG. Patients were divided into three risk categories based on number of QTc prolonging medications ordered (Low = 1, Medium = 2-3, High ≥4) and were subsequently compared.

Results. In the study, 79% of azithromycin use was empiric for the treatment of suspected infections, 20% as an anti-inflammatory agent, and 1% as culture directed therapy. Sixty-five percent of patients received a baseline ECG prior to prescribing azithromycin and 39 of 65 (60%) had borderline or abnormal QTc prolongation. Twenty patients were concurrently prescribed medications identified as having a major drug-drug interaction with azithromycin, with an average overlap of 4.5 days. Seventy-six patients were prescribed 2 or more QTc prolonging medications, and only 32 (42%) were monitored with telemetry.

Conclusion. In a randomly selected cohort of patients receiving azithromycin therapy, a majority of patients (76%) were prescribed 2 or more QTc prolonging agents, with telemetry ordered less than half of the time. Additional studies are necessary to determine the risk of such drug combinations. Given recent warnings issued by the FDA, enhanced education is necessary for providers regarding the potential for adverse cardiac events with prescribing azithromycin.

Disclosures. **All authors:** No reported disclosures.

189. Hospital onset *Clostridium difficile* infection not a predictor of increased antibiotic use in small hospitals: an evaluation of 54 hospitals

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Background. *Clostridium difficile* infection (CDI) is one of the leading healthcare-associated infections in the United States. Antimicrobial pressure has been linked to increased incidence, severity and recurrences of CDI. As the initial step for development of a system-wide antimicrobial stewardship program for a large health system, we evaluated the relationship between antimicrobial use and hospital onset (HO) CDI standard infection ratio (SIR).

Methods. CDI SIRs were compared to the use of specific classes of penicillin, cephalosporin, carbapenem, quinolone, clindamycin, tigecycline, and total antimicrobials (defined daily dose/1,000 patient days) among 54 hospitals in one health system for the year 2013. Antimicrobial use and HO CDI SIR were compared factoring yearly patient days (≤25,000; 25,001-50,000; 50,001-75,000; >75,001) categories.

Results. The highest antimicrobial use per 1,000 patient-days was in groups with <25,000 patient days per year, (1177/1,000 patient-days). In addition, these hospitals represented the highest use of 3rd generation cephalosporins, extended spectrum penicillins, and quinolones (Table). However, HO CDI SIR did not correlate with increased antimicrobial use, and was associated with hospitals with patient-days >50,000 per year.

Antibiotic Defined Daily Doses per 1,000 patient-days in the 54 hospitals grouped by patient-days in 2013

	≤25,000 patient-days (n=18)	25,001-50,000 patient-days (n=9)	50,001-75,000 patient-days (n=9)	>75,000 patient-days (n=18)	Total mean	P-value
All antimicrobials	1177±389	716±211	782±225	695±256	874±363	<0.001
3rd generation cephalosporins	150±122	65±22	84±40	62±31	95±83	0.005
Carbapenems	26±16	37±41	33±27	28±16	29±23	0.66
Extended spectrum penicillins	196±117	141±68	39±13	42±10	146±102	0.007
Quinolones	249±145	148±71	168±77	192±155	200±133	0.23
Hospital onset CDI Standardized infection ratio	0.57±0.37	0.68±0.38	0.97±0.48	0.85±0.26	0.75±0.38	0.036

Conclusion. Hospitals with lower patient days had the highest use of antimicrobial agents, and represent an important opportunity to target the antimicrobial stewardship efforts. On the other hand, CDI SIR may not be a good surrogate to evaluate their antimicrobial stewardship outcomes.

Disclosures. **All authors:** No reported disclosures.

190. Adequacy of Prior Antibiotic Use in Patients with Clostridium difficile Infection: A Resptrospective Analysis

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Background. Clostridium difficile infections (CDI) are the main cause of healthcare associated diarrhea. Inappropriate use of antibiotics (AB) is a significant risk factor for CDI. The aim of this study is to determine the proportion of CDI patients who received inappropriate AB prior to developing CDI.

Methods. This is a retrospective cohort study to assess the proportion of newly diagnosed CDI patients whose AB regimen could have been optimized prior to CDI episode at a tertiary medical center. The study population, identified through a Microbiology lab database, included patients with a first episode of CDI between February and May 2013. Each patient's AB regimen, indications and culture results were reviewed using a standardized form. AB therapy was defined as inappropriate when ≥1 of the following were met: (1) absence of a clear and valid indication to initiate therapy; (2) deviation of initial empiric therapy from local recommendations; (3) inappropriate de-escalation or duration of therapy. Inappropriateness of AB was determined by a panel of experts in CDI and antibiotic stewardship. Ethics approval was obtained before starting the chart review.

Results. 50 patients with CDI were identified (52% male, mean age, 76yrs). 47% had received AB in the previous 5 weeks and 53% received therapy on the day of CDI diagnosis. ABs prescribed were 54% penicillin, 44% quinolones, 20% cephaloporines and 18% carbapenems for the following conditions: penumonia 24%, urinary tract infection 11%, skin and soft tissue infection 12%, 32% for other indications. 10% received antibiotics for prophylaxis.

49% (n = 24) of patients with CDI had received an inappropriate AB in the previous 5 weeks. The main sources of inappropriate use were: failure to de-escalate (n = 9; 38%); inappropriate duration (n = 13; 54%); absence of clear diagnosis on day 3 of therapy (n = 4; 20%); and failure to switch to a narrower spectrum AB despite diagnostic test results and clinical improvement (n = 9; 38%).

Conclusion. A significant proportion of CDI cases received an inappropriate course of AB in the previous 5 weeks illustrating the need to improve AB use in our hospital. Antimicrobial stewardship has been initiated and a prospective audit is being planned to investigate its effect on CDI rates.

Disclosures. **All authors:** No reported disclosures.

191. Evaluation of Oxacillin Consumption Following Implementation of a Usage Restriction Protocol: A Drug Use Evaluation and Cost Savings Analysis

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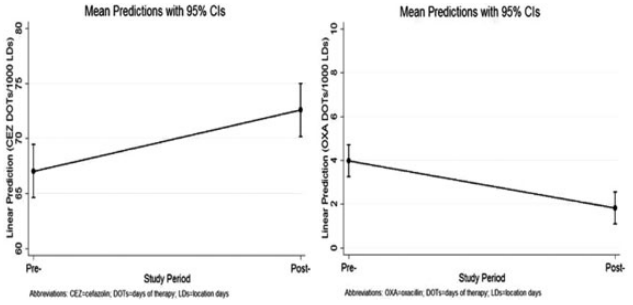
Background. Anti-staphylococcal β-lactams, such as oxacillin (OXA), are considered the drugs of choice for the treatment of methicillin-sensitive *Staphylococcus aureus* (MSSA) infections. Cefazolin (CEZ) has been shown to be equally efficacious to OXA for many MSSA infection types and is less costly than OXA. Our Antimicrobial Stewardship Program (ASP) implemented a use restriction protocol in July 2013 to limit OXA usage to patients with a central nervous system infection or with Infectious Diseases physician approval.

Methods. The Centers for Disease Control and Prevention Antimicrobial Use and Resistance Module was utilized to quantify OXA and CEZ consumption institution-wide in two time periods: August 2012 to April 2013 (pre-restriction) and August 2013 to April 2014 (post-restriction). Days of therapy (DOTs) were normalized using 1,000 patient location days (LDs) as a denominator. Calendar months were compared directly pre- and post-restriction to minimize temporal differences in antimicrobial usage. OXA and CEZ total DOTs drug costs from each study period were tabulated using purchase data and then compared. Patients receiving OXA were assessed retrospectively for adherence to the restriction protocol criteria.

Results. Mean OXA usage has decreased significantly following implementation of the restriction protocol (1.82 vs 3.91 DOTs/1,000 LDs; P = 0.0013). The by month comparison showed a trend toward decreased OXA DOTs/1,000 LDs across all months except one after implementation. 42 of 50 patients (84%) receiving OXA in the post-restriction study period met criteria for use. CEZ usage increased significantly post-implementation (72.6 vs 67.0 DOTs/1,000 LDs; P = 0.006). Reduction in OXA usage was associated with an overall cost savings of $52,309 during the study period. Projected annualized cost savings after OXA restriction are approximately $70,000.



Conclusion. Implementation of an OXA restriction by our ASP has been successful at our institution. Usage of OXA has decreased from the previous calendar year and this program resulted in notable drug cost savings. Similar restrictions may offer an opportunity for substantial cost savings among other antimicrobial stewardship programs.

Disclosures. **All authors:** No reported disclosures.

192. Vancomycin Dosing in Obese and Morbidly Obese Patients with Methicillin-Resistant *Staphylococcus aureus* (MRSA) Pneumonia

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Background. Despite the increasing burden of obesity, the optimal dose of vancomycin in obese and morbidly obsese (MO) patients with MRSA pneumonia is largely unknown.

Methods. This national retrospective cohort study included obese patients (pts; BMI ≥ 30) admitted to VA hospitals with MRSA-positive cultures from respiratory sites between 2002 - 2012. Pts initiating vancomycin (VAN) in the hospital were selected for inclusion. Exclusion criteria included death or discharge within 2 days of treatment initiation and exposure > 2 consecutive days of MRSA antibiotic therapy in the 3 days prior to treatment initiation or during treatment with VAN. Pts were included if they had appropriately collected VAN troughs and no evidence of acute kidney injury prior to VAN initiation per VAN guidelines. Logistic regression models were used to measure the effect of various VAN dosing regimens on trough levels in obese and MO (BMI ≥ 40) pts.

Results. We identified 263 obese and 73 MO pts treated with VAN with appropriately collected VAN trough levels. Total body weight ranged from 69 to 244 kg. The mean total daily dose of VAN was lower in obese vs MO pts (2005 ± 736 vs 2298 ± 923 mg, p <0.05) however the mean mg/kg/day dose was higher in obese vs MO pts (20 ± 7 vs 17 ± 7 mg/kg/day, p < 0.05). About 20% of pts in each group had a vancomycin trough level of >15-20 mg/L. The mean mg/kg/day VAN dose was also higher in obese vs MO pts with a trough of >15-20 mg/L (20 ± 7 vs 15 ± 7 mg/kg/day, p < 0.05). In obese pts, the standard dose of ~30mg/kg/day was appropriate for reaching a VAN trough of >15-20 mg/L (odds ratio [OR] 3.348, 95% confidence interval [CI] 1.2 - 9.2). In MO pts, as the mg/kg/day VAN dose increased, the odds of achieving a VAN trough of 15-20 mg/L decreased (OR 0.870, 95% CI 0.78 - 0.98).

Conclusion. We offer additional consideration on the dosing of VAN in obese and MO pts. MO patients may require a lower mg/kg/day VAN dose than obese patients to reach a trough of >15-20 mg/L. However, further research is warranted to determine which VAN trough levels are associated with the best outcomes in obese and MO patients.

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193. Impact of Weight Based Dosing Guidelines on Vancomycin Dosing and Trough Levels Including in Obese Patients

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Background. In 2009, the American Society of Health System Pharmacists, Infectious Diseases Society of America, Society of the Infectious Diseases Pharmacists released guidelines on vancomycin. Applying guidelines to a local population, particularly obese patients, has not been well-studied.

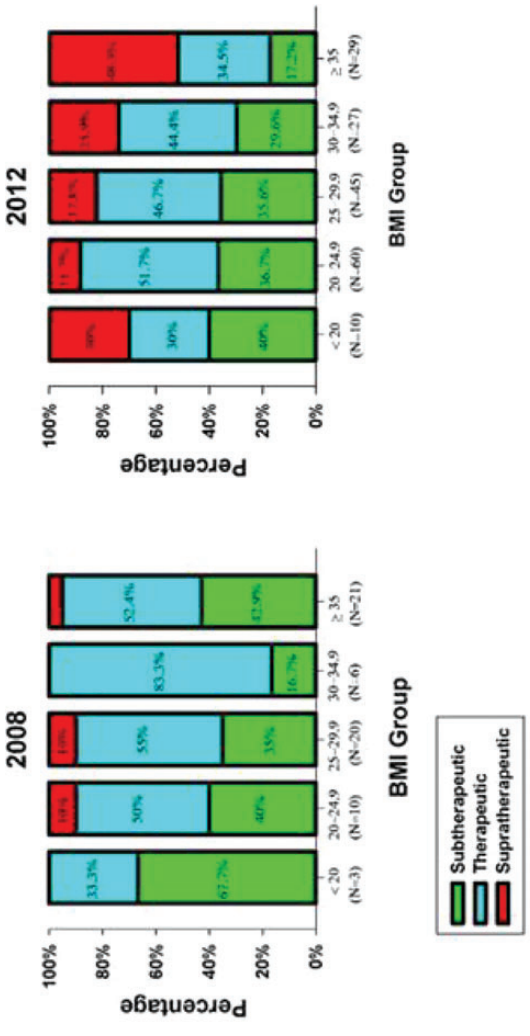

Figure 1 Percentage of Sub-therapeutic, Therapeutic and Supra-therapeutic Trough Levels by BMI comparing 2008 Conventional Dosing and 2012 Actual Body Weight Dosing, p=0.0109

Methods. A retrospective review was done on patients at an acute care, university-affiliated, community hospital who received intravenous vancomycin for suspected/documented infections before and after implementing the 2009 guidelines. Before 2009, patient received vancomycin, 1 gm every 12 hrs. After the guidelines, patients were dosed on actual body weight (ABW), 15-20mg/kg, or 25-30mg/kg in seriously ill patients, every 8-12 hrs. We compared the frequency of therapeutic troughs, nephrotoxicity and trough group levels stratified by Body Mass Index (BMI).

Results. There were no significant differences in therapeutic troughs and nephrotoxicity. Adjusted for BMI, there was a significant difference in trough levels between the two groups, p = 0.0109. However, a large number of patients in the conventionally-dosed group were excluded due to inconsistent doses. In the ABW-dosed group, there was a high number of high trough levels in 48% of patients with BMIs >35, p = 0.005

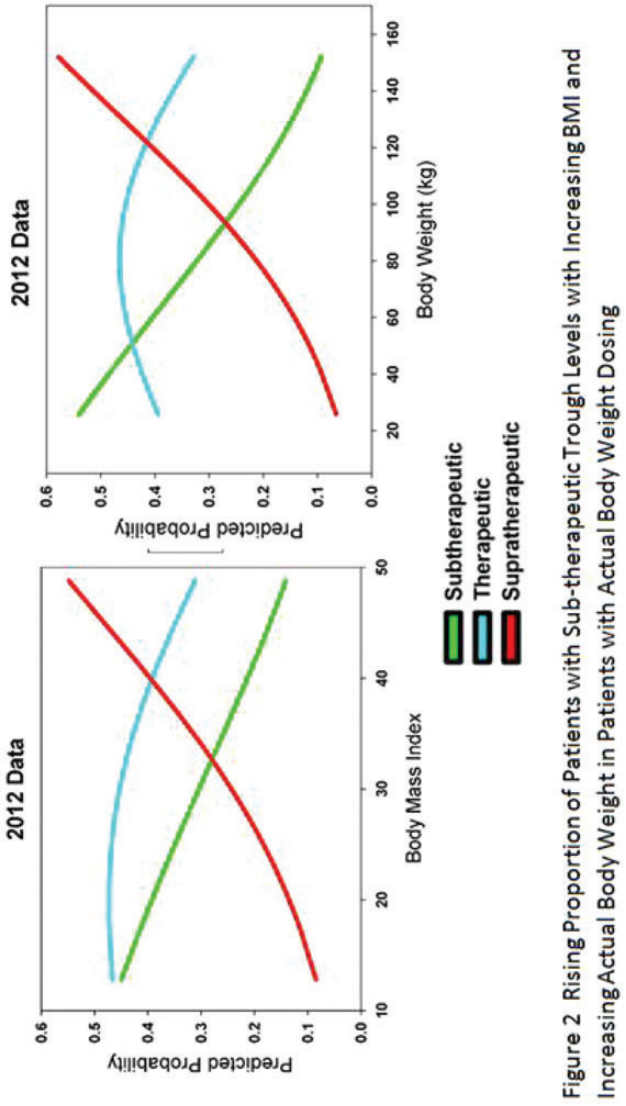

Figure 2 Rising Proportion of Patients with Sub-therapeutic Trough Levels with Increasing BMI and Increasing Actual Body Weight in Patients with Actual Body Weight Dosing

Conclusion. Obese patients may require an alternate dosing strategy as the ABW-dosing based on the 2009 national guidelines resulted in supra-therapeutic levels in patients with high BMIs. Implementing guidelines-based monitoring resulted in more consistent and appropriately drawn trough levels.

Disclosures. **All authors:** No reported disclosures.

194. Antimicrobial Stewardship Evaluation of Meropenem Use at a Large Academic Medical Center

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Background. Judicious carbapenem use in hospitalized patients is an important goal of antimicrobial stewardship program (ASP). Use of meropenem (M), the formulary carbapenem at our University hospital, is restricted to the ASP, infectious diseases (ID), and critical care. We report an ASP initiative to assess M utilization and prescribing patterns after change of ASP ordering process due to implementation of new computerized order entry system (CPOE).

Methods. M utilization was measured in days of therapy (DOT)/1,000 patient (pt) days. Microbiological data, clinical and treatment characteristics were evaluated retrospectively for all patients who received ≥1 dose of M during 2nd quarter (Q2) of 2013. A GN isolate was considered an MDRO if non-susceptible to ≥1 agent in ≥3 antimicrobial classes.

Results. In the Q2 of 2013 M use increased by mean of 62 DOT/1,000 pt-days at intensive care units [ICU], p = 0.18 and by 12 DOT/1,000 pt-days in non-ICU units, p = 0.31. Among 145 patients who received M during Q2 of 2013, 43 were in ICU at M start. Most common approval source was from ID attending (43%) followed by an approval from critical care (24%) and ASP team (21%). Positive cultures with GN organisms were present in 53% of patients, and 44% of these were MDRO. The most common site of positive culture was urine, followed by lungs and blood. Median duration of M was 7 (range 1-37) days. In ICU, twice as many patients received >14 days of therapy vs nonICU (15.9% vs 8.5%, p = 0.27). M was used as escalation of therapy in 76% of patients (only 3/59 were due to discordant initial therapy). Escalation of therapy within ≤24h was twice as frequent in ICU vs nonICU (35% vs 19%, p = 0.1). M was deescalated in 18% of patients. An additional 22% of patients could have been deescalated based on susceptibility results. In logistic regression, prior MDRO infection or colonization (within 90 days) was identified as a predictor of current MDRO infection (OR 4.12, 95% CI 1.13-15.05, p = 0.032) after adjusting for age >65 years, presence of comorbidities, need for ICU admission, and vasoactive agents at M start.

Conclusion. ASP recommendations based on our findings include: implementation of CPOE flag for patients with prior MDRO; report M monthly utilization trends to ICU and medicine teams; and collaborate on practice agreement for initiation of restricted antibiotics by ASP team.

Disclosures. **All authors:** No reported disclosures.

195. Rapid Intravenous Antibiotic Desensitization: Clinical Experience at a Single Center

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Background. Allergies to penicillin and other classes of antibiotics are common. Withholding appropriate therapy due to reported antibiotic allergy is associated with increased morbidity, mortality, and economic costs. Additionally, antibiotic choices are becoming further limited due to increasing prevalence of multi-drug resistant organisms. Rapid intravenous antibiotic desensitization (RIAD) is not a common practice but may be a useful modality to overcome problematic antibiotic allergies. Our objective was to analyze the safety and efficacy of RIAD, in both non-cystic fibrosis (CF) and CF populations, at our institution.

Methods. A retrospective review of 20 patients who underwent RIAD at a single tertiary medical center from October 2009 through March 2014.

Results. A total of 23 RIAD courses were performed on 20 patients. There were 12 females and 8 males, with an average age of 43 years (range, 21 to 81 years). There were 15 (65%) non-CF RIADs and 8 (35%) CF RIADs. Ten different antibiotics were used in 23 RIADs: one metronidazole, two cephalosporins (cefazolin, cefoxitin), three carbapenems (two meropenem, one doripenem), and 17 pencillin agents. Of 23 RIAD courses, 17 (74%) were successful. The success rate was 80% in non-CF patients and 62.5% in CF patients. Except for one patient, all completed the initial desensitization process successfully. Of the other five failures, four occurred within 24 hours of desensitization and one at 21 days into therapy. Only 1 of 23 courses resulted in increased morbidity and prolonged length of stay. The mean duration of successful antibiotic administration was 56 days. Failure of prior desensitization did not predict repeat failure.

Conclusion. RIAD is an efficacious and safe modality to overcome problematic antibiotic allergies. Our study provides encouraging results supporting the application of RIAD, especially in non-CF patients. Our study also includes the first report of successful metronidazole desensitization.

Disclosures. **All authors:** No reported disclosures.

196. Alarming AAA in Infectious Disease: Aztreonam Use, Allergy History and Antimicrobial Stewardship Collide

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Background. Background: Penicillin allergy (PA) is reported by 10 % of patients. Fewer than 10% of these have a positive skin test, allergy details are often sparse.

Increasing gram negative resistance makes empiric therapy difficult if beta lactam antimicrobials cannot be utilized. Use of alternate agents is associated with higher costs, increased length of stay and other adverse outcomes. Vancomycin is often used with aztreonam (AZ) to provide gram positive coverage, exposing patients to risk of nephrotoxicity. Stewardship team (ST) interventions can mitigate these patient outcome and cost issues.

Methods. Methods: Several stepped interventions were instituted. At our institution, AZ was frequently administered when PA was noted. Annual cost for AZ acquisition reached $360,000 annually. Requiring infectious disease (ID) approval for AZ, we decreased our use by 2/3; subsequently requiring approval directly from the ST with an investigation of allergy and antibiotic use history decreased AZ use a further 2/3 from prior year; then instituting a carbapenem graded challenge for severe or unknown PA decreased use of AZ by 50% again

Results. Results: We evaluated 212 patients between July 1, 2010 and April 22, 2014 who received at least one dose of Aztreonam. The single most frequent reason for AZ request was PA in the form of rash. In 50% of patients a history of safe beta lactam administration could be documented after review of medical records and beta lactams were utilized. Quinolones were substituted less than 10% of the time. 19 patients underwent a carbapenem graded challenge. No adverse reaction to carbapenem graded challenge was observed even in history of anaphylaxis to penicillin. 12% of AZ requests were appropriate and approved

Conclusion. These interventions have led to a marked decrease in the use of aztreonam in favor of cephalosporin and carbapenem antimicrobials, allowing for annual cost savings of $343,000 and the ability to choose from a wider selection of antibiotic agents. Clarifying PA details and administering monitored carbapenem graded challenges for severe or unknown PA can improve patient care while decreasing costs.

Disclosures. **All authors:** No reported disclosures.

197. Beta-Lactam Allergy: Documentation Matters

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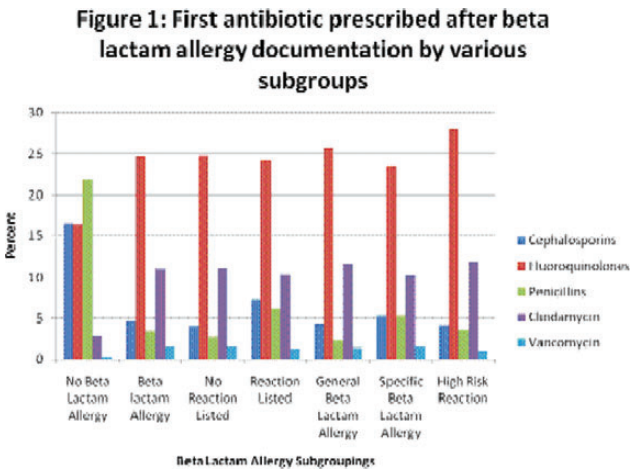
Background. Beta-lactam allergy documentation is frequently incomplete and lacks instructive value in guiding beta-lactam antibiotic rechallenge. How clinical decision-making and antibiotic choice is affected by allergy documentation is not well described.

Methods. We performed a retrospective, descriptive study of all patients seen by a NorthShore University HealthSystem primary care provider between 2008 and 2013. Beta-lactam allergy information, first antibiotic prescribed after allergy entry and subgrouping of allergy description was performed with an Enterprise Data Warehouse.



Results. The study included 234,233 total patients seen by NorthShore primary care providers of which 15.2% had a reported beta-lactam allergy. There were 21,196 unique patients with a beta-lactam allergy who received antibiotics. 79.2% had no details of the reaction documented, 58.0% did not have a specific beta-lactam identified, and 3.1% had a high risk reaction (IgE mediated or severe reaction). Patients with beta-lactam allergy were less likely than those without to receive subsequent penicillins and cephalosporins, and more likely to be treated with fluoroquinolones, clindamycin and macrolides (Figure 1). Patients with details of the reaction documented as compared to those without such documentation were more likely to receive a subsequent penicillin (6.1% vs 2.8%; $p < 0.001$) or cephalosporin (7.3% vs 4.0%; $p < 0.001$). Similarly, patients who had a specific beta-lactam identified were more likely to receive a subsequent penicillin (5.3% vs 2.2%; $p < 0.001$) or cephalosporin (5.3% vs 4.3%; $p = 0.01$). Patients with no details of the reaction documented had the same likelihood of beta-lactam rechallenge as those with a high-risk reaction: penicillin (2.8% vs 3.6%; $p = 0.22$); cephalosporin (4.0% vs 4.2%; $p = 0.84$).

Conclusion. The more complete the penicillin allergy documentation the more likely a patient was to receive a beta-lactam antibiotic and less likely to receive macrolides, fluoroquinolones or clindamycin. Providers may be assuming the highest risk reaction for those patients without an allergy description. Completing allergy documentation should be a high priority to improve quality of care and reduce costs.

Disclosures. **All authors:** No reported disclosures.

198. Evaluation of Antibiotic Use in the Neonatal Intensive Care Unit (NICU): from an Antimicrobial Stewardship (AMS) perspective

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Background. Neonatal infections result in significant morbidity, mortality and increased health care costs. Antibiotics are commonly prescribed to infants hospitalized in the Neonatal Intensive Care Unit (NICU). Broad spectrum antibiotic exposure has been associated with emergence of resistant organisms and disruption in the development of normal flora. There is paucity of data evaluating the appropriateness of antibiotic use in the NICU, based on Centers for Disease Control and Prevention (CDC) 12-Step Guidelines to Prevent Antimicrobial Resistance.

Methods. A retrospective audit of antibiotic use at a tertiary perinatal centre covering four million population was conducted during July 2010 – June 2013. Our objective was to assess the practice of antibiotic therapy for compliance to the recommendations of the CDC 12-step campaign.

Results. We audited vancomycin, meropenem and linezolid use in the NICU. Empirical use >3-day without appropriate specimens collected, or utilization despite narrower spectrum antibiotic available, were considered inappropriate use.

Agent	CDC 12-step violation	Inappropriate use examples
Meropenem	4	Continued use despite organism is sensitive to 3rd generation cephalosporins
	9	Prolonged empirical use without collecting appropriate specimens / redundant coverage with metronidazole
Vancomycin	4	Treatment for ampicillin-sensitive (amp-S) Enterococcus or methicillin-sensitive Staphylococcus aureus (MSSA)
	9	Prolonged empirical use without collecting appropriate specimens
Linezolid	4	Treatment for (amp-S) Enterococcus or MSSA or Enterobacteriaceae

Agent	Antibiotic Courses	Duration (Median days, IQR)	Antibiotic Days	Proportion of Inappropriate Prescription
Meropenem	57	3 [7, 14]	525	10/57 (17.5%)
Vancomycin	133	7 [5, 11]	1204	48/133 (36.0%)
Linezolid	35	7 [3,9]	233	6/35 (17.1%)

Conclusion. The CDC 12-Step Campaign is feasible in the NICU setting. Inappropriate antibiotic prescriptions are not uncommon in relation to the use of meropenem, vancomycin and linezolid. Attention should be focused on timely streamlining of these antimicrobials and collection of appropriate microbiologic specimens.

Disclosures. **All authors:** No reported disclosures.

199. Mandatory Antimicrobial Stewardship Program Review of Pediatric OPAT: Program Implementation and Results of Pilot Phase

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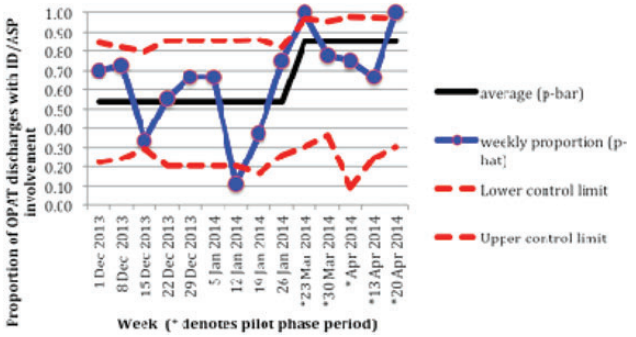
Background. Mandatory infectious disease (ID) consultation or review by an ASP is required at many adult hospitals for patients receiving outpatient parenteral antimicrobial therapy (OPAT), thus reducing OPAT overuse, lowering costs and optimizing therapy. Similar initiatives have not been reported in pediatrics. A retrospective review of OPAT at our children's hospital showed substantial opportunities to improve OPAT use. As a result, our hospital initiated mandatory ASP review prior to hospital

discharge for OPAT. We present an overview of the program implementation and pilot phase results.

Methods. Our hospital executive board selected OPAT as a priority area for quality improvement and formed a multidisciplinary implementation team. We analyzed the care process for patients receiving OPAT to identify critical time points and opportunities to notify the ASP about potential OPAT discharges. We modified several care processes to enhance detection of potential discharges. Before hospital-wide implementation, we performed a pilot intervention in two high-volume services: hospital medicine and oncology/ICS.

Results. We implemented 5 distinct care process interventions to enhance detection and recognition of plans for OPAT. These included (1) education of providers; (2) daily prospective ASP review of patients receiving IV antimicrobials via central catheter; (3) modification of the PICC order set to include notification to ASP or ID for PICCs placed for OPAT; (4) verification that OPAT was reviewed by case managers; (5) reminder system to physicians in electronic discharge software. Before program implementation, baseline ID/ASP involvement in OPAT discharges was approximately 50%. During the pilot phase, we successfully identified and reviewed 85% of OPAT cases before discharge (Figure 1). The intervention was implemented hospital-wide on May 1, 2014.

Figure 1: P chart of pre-implementation and pilot phase (*) period



Conclusion. A thorough understanding of care processes associated with OPAT is necessary to identify candidates for ASP review. The pilot phase showed marked improvement but continuous process improvement is needed to identify missed opportunities. Expanding ASP efforts to include mandatory review of OPAT can improve the appropriateness and safety of antimicrobial use in children.

Disclosures. **All authors:** No reported disclosures.

200. What Triggers an Antimicrobial Stewardship Program (ASP) Intervention in Pediatrics?

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Background. ASPs are growing in pediatrics. Many programs function by reviewing a large number of antimicrobial prescriptions on a daily basis to identify opportunities to improve or modify prescribing, thus leading to an intervention or recommendation. Little is known about the frequency with which reviewed prescriptions lead to an intervention and the patient and clinical factors most strongly associated with an intervention. A better understanding of these factors could lead to more targeted ASP reviews and more efficient use of resources. The objective was to identify the antibiotics and clinical diagnoses most strongly associated with a pediatric ASP.

Methods. We reviewed the frequency and types of interventions made by a pediatric ASP across 5 years, from March 2008–March 2013. Our program uses a prospective audit and feedback structure where prescriptions for any of 18 selected antibiotics are reviewed daily for potential interventions. Interventions were grouped into four categories: stop therapy, modify therapy (i.e., change antibiotic), optimize therapy (i.e., alter dosing or route of administration) and consult infectious diseases. We used a multinomial distribution model to determine the probability of each ASP intervention group, based on the specific antimicrobial agent or disease category.

Results. A total of 14,407 ASP reviews were included in our analysis. Among these, a total of 2,318 (16%) prompted an ASP intervention. The most common types of ASP recommendations were stop or modify therapy. The clinical diagnoses with the highest predicted probability of an intervention were community acquired pneumonia (CAP, 0.26), ear/nose/throat (ENT, 0.25), genitourinary (0.23), and respiratory infections (0.21) (Figure 1). The antibiotics with the highest predictive probability of an intervention were ceftriaxone (0.20), clindamycin (0.20), and gentamicin (0.19) (Figure 2).

Figure 1. Predicted Probability of ASP Intervention, by Diagnosis

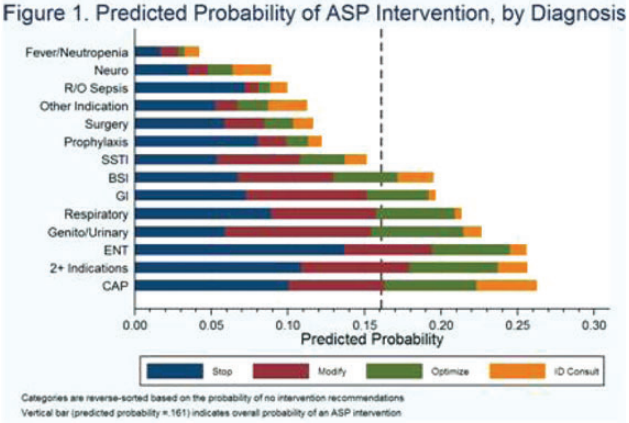
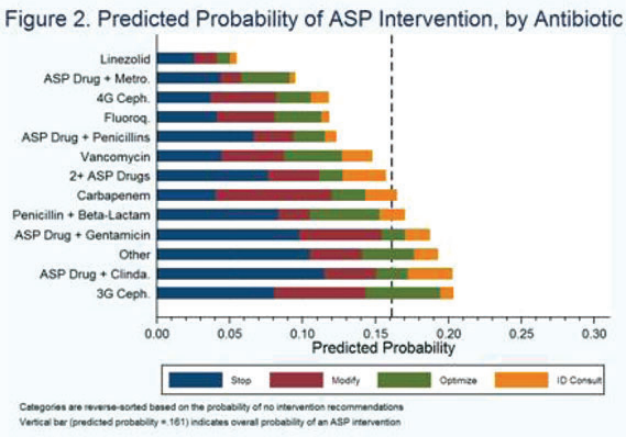


Figure 2. Predicted Probability of ASP Intervention, by Antibiotic



Conclusion. We identified several clinical diagnoses and antimicrobials that are associated with higher than average likelihood of triggering an ASP intervention. This analysis will assist in enhancing our ASP to focus not only on specific antibiotics but to also target specific conditions for review and development of clinical practice guidelines.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

201. Evaluation of Antimicrobial Stewardship Computer-Assisted Guidance for the Optimal Use of Amphotericin B

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Background. The clinical utility of amphotericin B (AmB) is limited by toxicities, particularly infusion reactions and nephrotoxicity. Practice standards support the use of pre-medications, including acetaminophen, diphenhydramine, meperidine, and normal saline fluid boluses (AmB bundle) to prevent adverse reactions, as well as close monitoring of renal function and electrolytes. To improve compliance to practice standards, VUMC initiated a computer-assisted decision support guidance for the optimal use of AmB.

Methods. This retrospective, pre-post implementation study compared compliance to AmB standard practices before and after implementation of computer-assisted decision support in November 2012. Eligible patients were defined as all adult inpatients who received at least one dose of AmB (standard or lipid formulation). All patients who received AmB from both the pre-implementation period (November 2011-October 2012) and post-implementation period (December 2012-June 2013) were eligible. The primary outcome was ordering compliance based on appropriate AmB dose and adherence to the standard practice bundle. This bundle included acetaminophen, diphenhydramine, and meperidine pre-infusion, and normal saline boluses both pre- and post-AmB administration. Secondary outcomes included incidence of nephrotoxicity and frequency of infusion-related reactions.

Results. Seventy-nine patients were included (50 pre-implementation, 29 post-implementation). Baseline demographics and renal function were similar in both groups.

Overall compliance in ordering the AmB bundle significantly increased post-implementation (12% to 48% with all components ordered correctly, $p < 0.001$). There was no significant difference in the incidence of AKI in patients pre- and post-implementation. Additionally, there was no difference in infusion-related reactions, based on patient-specific factors during the AmB infusion.

Conclusion. In conclusion, a significant increase in ordering compliance was seen after the implementation of the AmB ordering page, allowing increased compliance to standards of practice.

Disclosures. **All authors:** No reported disclosures.

202. Antifungal Stewardship: The Clinician's Perspective on Barriers to Implementation

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Background. The presence of invasive fungal infections (IFIs) significantly increases morbidity and mortality for patients with immune suppression. Incorporating antifungal stewardship (AFS) principles into clinical practice through a multidisciplinary approach can maximize the efficient use of antifungals and maximize improved patient outcomes by directing appropriate patients to receive timely antifungal therapy. Additionally, stewardship interventions and guidance can favorably impact hospital and pharmacy costs associated with antifungal overuse. A survey was designed to identify barriers influencing implementation and utilization of AFS strategies.

Methods. A survey of 267 pharmacists and physicians was conducted to characterize perspectives on the value, approach and robustness of AFS strategies and programs in their hospitals. Additionally, they were asked to specify barriers to implementing an AFS program at their institution.

Results. Only 35% of respondents strongly agreed (a rating of 6 or 7 on a 7-point scale) that their institution valued the benefits of AFS. Less than one quarter of respondents (23%) strongly agreed that their institution had a robust AFS program in place. Additionally, only 32% strongly agreed that their institution took a multidisciplinary approach to AFS. The top 3 barriers to successful implementation of AFS were identified as: 1) lack of awareness of need and/or benefit of AFS (37%); 2) limited time/compensation for AFS efforts (31%); and 3) lack of physician participation (27%).

Conclusion. The survey results demonstrate the existing system-level limitations for successful implementation of AFS. Multilevel education regarding potential benefits of a robust AFS program and its impact on patient outcomes may favorably influence these limitations.

Disclosures. **A. Safdar**, Astellas: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium; Cubist: Speaker's Bureau, Speaker honorarium **D. Goff**, Astellas: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; Cubist: Research Contractor, Research support **J. Gallagher**, Cubist: Consultant, Consulting fee; Optimer: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium; Astellas: Speaker's Bureau, Speaker honorarium; Forest: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium; Pfizer: Scientific Advisor, Consulting fee **D. Hsu**, Cubist: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium; Astellas: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Research support and Speaker honorarium **E. Eiland**, Astellas: Speaker's Bureau, Speaker honorarium; Cubist: Speaker's Bureau, Speaker honorarium **P. Smith**, Health and Wellness Partners: Employee, Salary **N. Azie**, Astellas: Employee, Salary

203. Optimization of Posaconazole (PCZ) Dosing with Multi-disciplinary Therapeutic Monitoring (TDM) Protocol

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Background. PCZ is a broad spectrum azole antifungal used for prophylaxis in high risk patients and treatment of invasive fungal infections, with activity against *Candida spp.*, *Aspergillus spp.,* and other invasive molds. TDM of PCZ is recommended to ensure efficacy with a goal therapeutic serum concentration (TC) of >700 ng/ml, some studies support a goal of >500 ng/ml for prophylaxis. Two oral formulations of PCZ are available; unlike the suspension the absorption of the tablet does not depend on an acidic environment or high fat meals. Therefore, the preference is to use the tablets although some patients may still require the suspension if unable to receive solid oral dosage forms. With an increase in utilization of PCZ at our institution we implemented a TDM protocol that recommended dietary consults for all patients receiving PCZs in which a registered dietician advises changes in fat intake or nutritional supplements and provides education to patients regarding dietary strategies to optimize absorption. We evaluated the effect of this TDM protocol on initial steady state PCZs levels.

Methods. All adult patients receiving PCZs at treatment or prophylactic doses following implementation of the TDM protocol between December 1, 2012-January 10, 2014 with a PCZ random concentration obtained were included.

Results. 68 patients received PCZs, 76.2% of those receiving PCZs for prophylaxis (32/42) and 77% of those receiving PCZs for treatment (20/26) had TCs, respectively. Median time to serum concentration was 7 days and 88% of patients had a dietician note in their chart indicating provision of patient education. Three patients (7%) receiving PCZs for prophylaxis were changed to alternative therapeutic antifungal therapy following a subtherapeutic level, while 5 patients (11.9%) receiving PCZs for prophylaxis with a subtherapeutic level were changed to alternative antifungal prophylaxis.

Conclusion. For patients requiring PCZs, strategies to improve absorption such as ensuring that doses are taken with a high fat meal are pertinent in achieving TCs. Incorporating dietary consultation in a PCZ TDM protocol resulted in a large of proportion of patients receiving the PCZ suspension achieving adequate levels for both prophylaxis and treatment.

Disclosures. **J. Pisano**, Pfizer: Grant Investigator, Research grant

204. Voriconazole Restriction in Addition to Therapeutic Drug Monitoring (TDM) Protocol Results in Optimized Dosing

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Background. Voriconazole (VRC) is a broad spectrum antifungal with activity against several medically important pathogens including *Candida spp.* and *Aspergillus spp*., often utilized as a prophylactic agent in high risk patient populations and in the management of invasive fungal infections. VRC TDM is recommended by national guidelines to ensure safety and efficacy, with a recommended therapeutic trough range of 2-5.5 mcg/dL. We previously found, prior to the implementation of a TDM protocol in addition to antimicrobial stewardship (ASP) restriction and post-prescriptive review for all patients receiving therapeutic VRC, only 44% of patients achieved adequate troughs. We sought to evaluate our success rate with achieving therapeutic trough concentrations (TTC) following the implementation of a TDM protocol in addition to targeted ASP restriction and monitoring efforts.

Methods. All adult inpatients receiving therapeutic voriconazole for either presumed or documented invasive fungal infections, with a serum trough concentration obtained between October 20, 2012-July 23, 2013 were included in this analysis. Patients that received voriconazole for prophylaxis were excluded.

Results. Twenty-five adult inpatients receiving therapeutic VRC had a serum trough concentration obtained. 80% of patients were found to have a TTC with a median trough of 4.3 mcg/dL. Among patients that received a loading dose (N = 19), 89.4% of patients achieved a TTC. Of those that did not receive a loading dose (N = 6), only 50% achieved a TTC. Trough concentrations were obtained on day 5 of therapy (median).

Conclusion. Following the implementation of a VRC TDM protocol in addition to concerted efforts by ASP in ensuring safe and appropriate utilization, rate of success in achieving TTC increased by 36-45.4%. Patients receiving a loading dose were more likely to achieve TTC on day 5 of therapy.

Disclosures. **J. Pisano**, Pfizer: Grant Investigator, Research grant

205. Antimicrobial Stewardship Knowledge, Attitudes and Practices among Healthcare Professionals in Utah

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Background. National societies and accrediting bodies advocate for Antimicrobial Stewardship (AS) Programs (ASPs) in all hospitals. Most ASP surveys have been conducted in large academic medical centers, even though most U.S. hospitals are <200 beds (72%). Very little is known about AS knowledge, attitudes and practices (KAP) among healthcare professionals in small, community hospitals (SCHs).

Methods. An anonymous 48-item AS KAP survey was administered to providers, pharmacists and administrators at 15 SCH (<200 beds) and 3 large (>200 beds) community hospitals (LCHs) within an integrated healthcare network.

Results. In total, 33 SCH and 105 LCH pharmacists completed the survey (response rates 60% and 63% respectively). Only 2 SCHs (13%) had active ASPs while

all LCHs had ASPs. Most pharmacists graduated after 1999 (54% SCH and 73% LCH). In SCH, 67% of pharmacists covered all clinical service lines, compared to 25% in LCHs. Both SCH and LCH pharmacists were familiar with the term AS (98%) and agreed AS is necessary in their hospitals (99%). Respondents strongly agreed they would like more antimicrobial education (70% SCH and 73% LCH). SCH and LCH pharmacists agreed antimicrobials were overused nationally (94% and 96%, respectively) but only 67% and 72%, respectively, felt they were overused at their hospital. Similarly, respondents agreed antimicrobial resistance is a significant national problem (88% SCH and 96% LCH) but only 45% and 54% of respondents felt it was a problem in their facilities. SCH pharmacists were less likely to call an Infectious Diseases provider for information about the treatment of infections compared to their LCH counterparts (60% SCH vs 82% LCH).

Conclusion. SCH and LCH pharmacists in Utah are aware of antimicrobial resistance and overuse, and agree ASPs are necessary; however, SCHs are less likely to have formal ASPs. SCH pharmacists are also less likely to contact Infectious Diseases for information compared to LCH pharmacists. These results will be used to support the development of ASPs at SCHs, while recognizing SCHs unique knowledge, attitudes, practices and resources.

Disclosures. **All authors:** No reported disclosures.

206. Implementing an Antimicrobial Stewardship Program

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Background. The antimicrobial stewardship program (ASP) at Providence Saint John's Health Center was implemented in June 2013. The program was developed in three phases. Each phase was three months duration.

Methods. The ASP tracked the following interventions in each phase: IV to PO, dose change, redundancy, de-escalation (of Daptomycin, Ertapenem, and Teflaro), inappropriate antibiotic combination, drug/bug mismatch, positive culture with no coverage, and duration.

Results. In phase 1 (July-September 2013), 275 interventions were made in 1109 eligible patients and 232 (84%) interventions were accepted in dose change, IV to PO, and positive culture with no coverage. Of the 16% of interventions which were not accepted, the major categories were: redundancy and restricted antibiotics. In phase 2 (October-December 2013), 215 interventions were made in 1032 eligible patients and 194 (90%) interventions were accepted in dose change, IV to PO, and positive culture with no coverage. Of the 10% of interventions that were not accepted, the major categories were: redundancy and restricted antibiotics. The most frequently made interventions in phases 1 and 2 were redundancy and de-escalation. In phase 3 (Jan-March 2014), 216 interventions were made in 1248 eligible patients and 197 (91%) interventions were accepted in dose change, IV to PO, de-escalation, restricted antibiotics and drug/bug mismatch. Of the 9% of interventions that were not accepted, the major categories were: redundancy, de-escalation and duration.

Conclusion. Overall, physicians were receptive to the ASP program and intervention acceptance increased with each phase of implementation. During phases 1 and 2, the most frequently made interventions were redundancy and de-escalation. During phase 3 the interventions changed to de-escalation, IV-PO, duration and dose change. More interventions were accepted in phase 3 than in the two previous phases. Future program intervention goals are defined duration of antibiotics by post-op category, automatic downgrade substitutions where applicable for certain antibiotics, and development of guidelines based on specific hospital needs and inappropriate antimicrobial usage. A protocol that allows the ASP program to initiate changes is a long term goal.

Disclosures. **E. Goldstein**, Merck: Investigator, Research grant

207. Metrics for Analyzing an Antimicrobial Stewardship Program's Impact on Antimicrobial Use and Cost over Time

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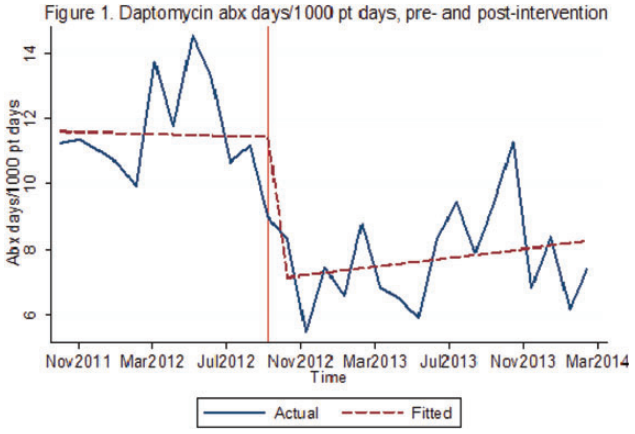
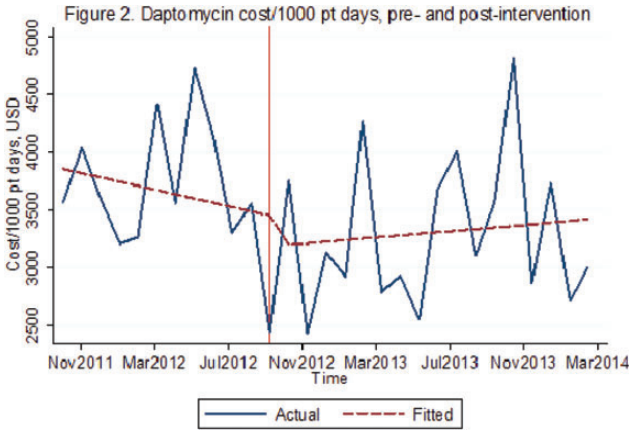
Background. Antimicrobial Stewardship Programs (ASP) are charged with ensuring responsible use of antibiotics while decreasing cost. Metrics used to assess ASP impact vary based on institution-specific goals and available resources. We present an antibiotic-specific example of utilizing multiple metrics to determine ASP impact over time at Ohio State University Wexner Medical Center (OSUWMC).

Methods. The metrics assessed by OSUWMC's ASP are antibiotic (abx) days/1,000 patient (pt) days, dispensing cost/1,000 pt days, count of unique pts administered an abx, and amount of abx dispensed (e.g., mg) per month. Abx days are defined as a count of pts administered at least one dose of an abx on a calendar day. Pt days are defined as a count of all pts admitted to OSUWMC at midnight. We analyzed data from November 2011 thru March 2014 via segmented regression analysis to explore changes in the metrics over time for daptomycin. Daptomycin use was restricted to Infectious Diseases or ASP approval and doses were rounded to the nearest 250mg upon dispense beginning January 23, 2013. Education and awareness of the intervention began November 2012. Costs were adjusted to 2014 dollars by the consumer price index. P-values $\leq$0.05 were considered statistically significant.

Results. Results of the regression analysis are shown in the table. There was a significant decrease in all metrics at the time of intervention except dispensing cost/1,000 pt days (p = 0.59). All four metrics show no change in slope pre- or post-intervention. Select metrics are shown in Figures 1 and 2.

Metric	y-intercept	Slope pre-intervention	Point change at intervention	Slope post-intervention
Abx days/1,000 pt days	11.6	-0.01 (p=0.91)	-4.38 (p=0.001)	0.08 (p=0.59)
Dispensing cost/ 1,000 pt days, $	3,893.83	-36.80 (p=0.51)	-262.68 (p=0.59)	50.43 (p=0.44)
Unique pts	71.7	0.51 (p=0.47)	-26.36 (p<0.001)	-0.56 (p=0.50)
mg dispensed	244,238.40	31.80 (p=0.99)	-77,453.45 (p=0.02)	573.80 (p=0.89)





Conclusion. Single metrics alone do not present a complete picture of the impact of ASP as changes in use and cost do not always follow the same trends. We show an antibiotic-specific example of the need to concurrently analyze multiple metrics in order to realize the full impact of ASP interventions.

Disclosures. **K. A. Bauer**, Cubist: Investigator, Research grant

208. Integrating Retrospective Antimicrobial (AM) Use Audit with Physician (MD) Education and Prospective Post-Prescriptive Review with MD Feedback: Proof of Concept with Focus on Diabetic Foot Infections (DFIs)

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Background. How best to combine MD education with more active hospital AM stewardship (AS) interventions is unclear.

Methods. We retrospectively reviewed the records of consecutive AM recipients admitted to a single inpatient teaching service (TS). We then presented pertinent findings to the TS in conference format where we also surveyed TS MDs' knowledge of the causes of common infections and antimicrobial spectra of commonly used drugs, and we began prospective post-prescriptive review and MD feedback for TS AM recipients. Because this TS is assigned most DFI admissions, we emphasized institutional DFI and other skin/soft tissue infection (SSTI) guideline (GL) treatment recommendations. We also assessed results of post-prescriptive reviews of DFI and SSTI patients admitted concurrently to TSs not exposed to this teaching intervention as a concurrent control group.

Results. Retrospective audit ("Pre"), post-prescriptive review of the targeted TS ("post") and post-prescriptive review of other TSs ("Control") results are presented in the table.

AM recommendations by treatment indication for pre intervention, post intervention group and control groups

Recommendation	N (%) Pre	N (%) Post	N (%) Control
DFI	**11**	**29**	**8**
Any AM recommendation	8 (73)	15 (52)	7 (88)
Empiric AM appropriate	3 (27)	22 (76)	3 (38)
Empiric AM too broad	7 (64)	6 (21)	3 (38)
Empiric AM too narrow	1 (9)	1 (3)	2 (25)
De-escalate AM	0	8 (28)	2 (25)
Recommendation accepted	NA	15 (100)	6 (86)
ID consult recommended	1	11 (38)	5 (63)
SSTI	**9**	**5**	**3**
Any recommendation	6 (67)	4 (80)	3(100)
Empiric AM appropriate	2 (22)	2 (40)	0
Empiric AM too broad	4 (44)	2 (40)	1(33)
Empiric AM too narrow	2 (22)	1 (20)	2(67)
Recommendation accepted	NA	4 (100)	2(67)
Total Cases	**20**	**34**	**11**

Conclusion. Integrating retrospective AM use audit results with institutional GL recommendations followed by prospective post-prescriptive review and provider feedback may enhance MD uptake and retention of educational antimicrobial stewardship interventions. DFI may be especially apt for teaching AS principles given the frequently prolonged hospital stays and positive tissue culture results of DFI patients.

Disclosures. **All authors:** No reported disclosures.

209. Results of an Antimicrobial Stewardship Intervention Involving Surgical Subspecialty Patients

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Background. Antimicrobial stewardship can improve antimicrobial use and clinical outcomes in hospitalized patients. A core antimicrobial stewardship strategy is prospective case review with real-time recommendations to prescribers; however, the impact of this intervention has not been described for surgical patients. With multi-disciplinary involvement, the antimicrobial stewardship team developed a prospective review and feedback intervention for surgical subspecialty patients.

Methods. Beginning in November 2013, an Infectious Diseases Clinical Pharmacist performed three-times-weekly prospective case review for all inpatients receiving antibiotics, other than peri-operative prophylaxis, on the following surgical services: Neurosurgery, Maxillofacial Surgery, Plastic Surgery, Otolaryngology, and Urology. When appropriate, recommendations regarding antibiotic utilization were communicated to the surgical teams. A summary of the interventions and acceptance rate over the initial 5-month period is summarized.

Results. A total of 65 patients were reviewed during the study period on the surgical services: Neurosurgery (n = 29, 45%), Maxillofacial Surgery (n = 10, 15%), Plastic Surgery (n = 8, 12%), Otolaryngology (n = 1, 1.5%), and Urology (n = 17, 26%). A total of 29 prescribing recommendations were made in those 65 patients (44% of cases reviewed). Recommendations made per surgical service include Neurosurgery (n = 15, 52%), Maxillofacial Surgery (n = 1, 3%), Plastic Surgery (n = 4, 14%), Otolaryngology (n = 1, 3%), and Urology (n = 8, 28%). The most common recommendations made were de-escalation of therapy (n = 10, 15%), antibiotic discontinuation (n = 6, 9%), and duration of therapy (n = 4, 6%). Of the recommendations made, 23 were accepted by the surgical services (79% acceptance rate).

Conclusion. A multi-disciplinary antimicrobial stewardship collaboration performing prospective case review in a surgical subspecialty population led to opportunities to improve antibiotic use in nearly half of cases with high rates of recommendation acceptance. Further evaluations should incorporate evaluating the impact of overall antimicrobial use and clinical outcomes.

Disclosures. **All authors:** No reported disclosures.

210. Audit of Prescribing Patterns for Restricted Antibiotics in an Inpatient Setting (APPRAIS): Appraisal Reveals Hospital Overuse and Underdosing of Carbapenems

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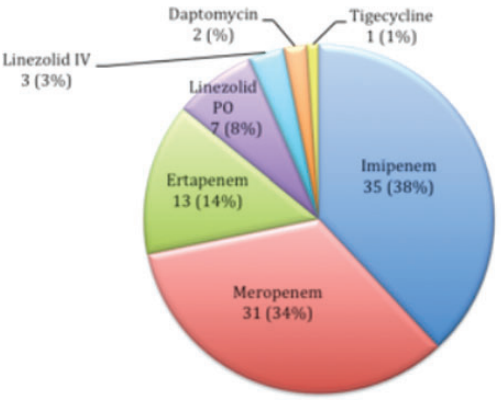
Background. This project evaluated the guideline concordance of inpatient use of restricted antimicrobials (daptomycin, imipenem, meropenem, ertapenem, linezolid and tigecycline) at the University of Alberta Hospital (UAH), examined the usability of the current formulary guidelines, and identified areas where action could be taken using stewardship to promote patient safety and appropriate antimicrobial use.

Methods. All inpatients at the UAH started on a restricted antibiotic from January 9 - February 6, 2014 were prospectively enrolled and followed. Exclusion criteria included patients under the age of 18, and any patient treated with restricted antimicrobials as outpatients in the emergency department or medical outpatient unit. Patient charts and electronic health records were reviewed to collect relevant patient, microbiological and clinical data. Indication for use and guideline concordance was determined by the researcher, Drug Stewardship Pharmacist and Physician. Data was de-identified, entered into a secure database, and analyzed using Excel pivot tables and descriptive statistics.

Results. Eighty-five patients were prescribed a total of 92 restricted antibiotics during the study period. The attending service ordered 77% of the restricted antibiotics; only 23% (n = 21/92) of orders came from the Transplant Infectious Disease or Infectious Disease service. Orders were classified as "use outside of guidelines" 28% of the time (n = 26/92). Twenty of these "use outside of guidelines" orders had appropriate non-restricted formulary options, which would have been considered equally safe and effective in the clinical situation. Fourteen percent (n = 13/92) of the restricted antibiotics were incorrectly dosed by the attending services and 9 of the 13 incorrect orders (69%) under-dosed the patient.

Figure 1. Breakdown of restricted antibiotic orders during study period



Conclusion. This study demonstrated carbapenem overuse, a concern in the current era of evolving antimicrobial resistance, and a surprisingly high dosing error rate, which is a safety concern. An educational intervention has already been implemented to address the identified dosing issue. Going forward we hope to gain institutional support for an active, ongoing stewardship program, which is a current need in this facility.

Disclosures. **All authors:** No reported disclosures.

211. Impact of Focused Medication Cost Reduction Efforts on Antimicrobial Spend

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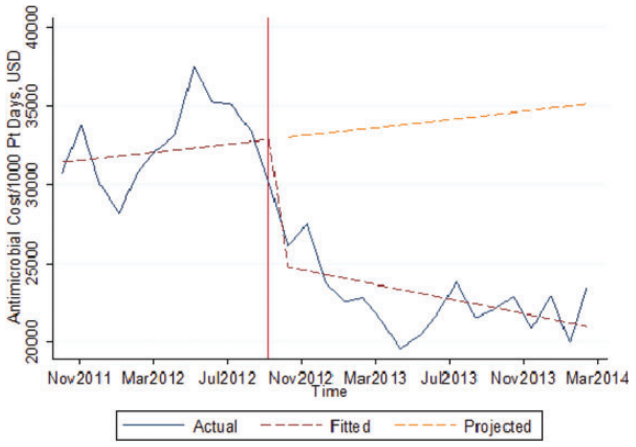
Background. The healthcare landscape is rapidly evolving and reimbursement is diminishing making efforts to decrease cost while maintaining quality of care imperative. Antimicrobials (abx) comprise a significant portion of inpatient pharmacy budgets and should be used in a clinically responsible and cost-conscious manner.

Methods. An institution-wide efficiency and effectiveness improvement (EEI) effort began in October 2012 wherein the pharmacy was charged with reducing medication expenditures by $8 million over 18 months. Areas evaluated for medication cost reduction (MCR) included inventory/formulary management, purchasing/contracting, waste reduction, and medication utilization. The institution's top 15 highest spend non-chemotherapeutic medications were initially targeted and included four abx: daptomycin, linezolid, piperacillin/tazobactam (P/T) and ertapenem. Changes in overall abx cost were evaluated using an interrupted time series analysis over two time periods [pre-EEI (November 2011-October 2012) and post-EEI (November 2012–March 2014)]. Our metric was abx cost/1,000 patient (pt) days before and after adjustment for case mix index (CMI). All costs were based on doses dispensed and were adjusted to 2014 dollars using the consumer price index. Student's t-test or Wilcoxon ranksum test was used to evaluate changes in average monthly abx cost per 1,000 pt days for each of the four target abx. P-values ≤ 0.05 were considered significant.

Results. Average monthly abx cost/1,000 pt days post-EEI was reduced compared to pre-EEI for all four target abx [daptomycin $3,605 vs $3,303 ($p = 0.22$), linezolid $4,134 vs $3,130 ($p < 0.001$), P/T $3,495 vs $2,063 ($p < 0.001$), and ertapenem $1,644 vs $1,195 ($p < 0.001$)]. Pre-EEI, mean cost/1,000 pt days was $32,543/month and there was no significant change in the monthly trend in cost/1,000 pt days ($p = 0.59$). Following EEI, abx cost/1,000 pt days dropped by $7,864 (24%) ($p = 0.001$) and the monthly decrease in abx cost/1,000 pt days was $367 ($p = 0.23$) (Figure). In Mar 2014, cost/1,000 pt days was 33% lower than the projected cost. Adjusting for CMI had no impact on the directionality or statistical significance of the results.



Conclusion. Focused abx cost reduction efforts had a significant impact on abx spend at our institution.

Disclosures. **All authors:** No reported disclosures.

212. Skills Learned during Critical Care Prospective Audit and Feedback are Utilized outside of the Stewardship Environment

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Background. Antimicrobial stewardship programs (ASP) are crucial to optimize antimicrobial utilization in critical care. Prospective audit and feedback is the major intervention used by stewardship programs, yet the impact on clinicians' antimicrobial prescribing behaviours outside of the stewardship environment is unknown. We sought to understand if skills learned during prospective audit and feedback are translated to other areas of clinicians' practice.

Methods. Antimicrobial stewardship, through biweekly prospective audit and feedback, was initiated in a 14 bed closed medical-surgical ICU at a single site of a multi-site, community hospital. ICU physicians working in the stewardship ICU also worked in another site ICU at the same community hospital where stewardship had not been formally introduced. We compared antimicrobial utilization between the stewardship and non-stewardship ICUs before and after antimicrobial stewardship implementation using time series analysis.

Results. Broad-spectrum antimicrobial use and anti-pseudomonal antimicrobial use decreased post ASP implementation in the stewardship ICU as well as the non-stewardship ICU. In the stewardship ICU broad-spectrum antibiotic use and anti-pseudomonal antibiotic use was decreased by 21.2% ($p = 0.023$) and 20.6% ($p = 0.017$) respectively compared to 29.8% ($p = 0.071$) and 38.1% ($p = 0.025$) in the non-stewardship ICU.

Conclusion. Prospective audit and feedback has the potential to change antimicrobial prescribing behaviours among ICU clinicians. Skills learned during prospective audit and feedback are translated to practice settings outside of the stewardship environment.

Disclosures. **All authors:** No reported disclosures.

213. Impact of Antimicrobial Stewardship Strategies on Antimicrobial Use: A Systematic Review

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Background. The increasing emergence of multi-drug resistant bacteria coupled with dwindling antibiotic development pipeline is a major health problem globally. As resistance is largely attributed to inappropriate antimicrobial use, antimicrobial stewardship has been implemented worldwide with varying outcomes. We performed a systematic review on the various strategies of antimicrobial stewardship.

Methods. PubMed, Cochrane Library and Embase databases from January 2000 to February 2014 and bibliographies of retrieved articles were searched. The following search terms were used: (Antibiotic OR Antimicrobial) AND (Stewardship OR Management OR Policy Or Implementation OR Restriction).The inclusion criteria were interventional studies employing audit-feedback, formulary restriction or Computerized Decision Support System (CDSS), which were carried out as Randomized Controlled Trials (RCT), Controlled Before-After (CBA) and Interrupted Time Series (ITS) studies on adult inpatients. Articles that were not written in English were excluded.

Results. Thirty-two studies were identified (21 ITS, 8 RCT and 3 CBA). Audit-feedback (15 studies) was the most common strategy, followed by formulary restriction (7 studies) and CDSS (4 studies). 10 studies were multifaceted.

A meta-analysis of 4 studies demonstrated significant improvement in appropriateness of antimicrobial use with interventions (random-effect model, OR 2.28, 95% CI: 1.03 to 5.04, $p < 0.05$). Three studies also showed significant reduction in the duration of target antimicrobial use (random-effect model, OR -1.63, 95% CI: -2.24 to -1.02, $p < 0.01$). Overall, a reduction of 18% to 70% in target antimicrobial consumption was observed (18 studies) and 9 studies showed 9% to 23% decrease in costs due to this. Antimicrobial stewardship also significantly reduced *Clostridium difficile* infection (3 studies) and incidence of resistant isolates (9 studies). No statistical difference in mortality (12 studies), length of hospitalisation (11 studies) and 30-day readmission (3 studies) was demonstrated.

Conclusion. Antimicrobial stewardship strategies are effective in improving appropriate antimicrobial use, reducing antimicrobial use, expenditures and resistance, without compromising patient safety.

Disclosures. **All authors:** No reported disclosures.

214. Social Media as a Tool for Antimicrobial Stewardship

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Background. Antimicrobial stewardship optimizes antimicrobial use in the treatment and prevention of infection. Providing prescribers with the education and tools (i.e., pathways and order sets) to guide clinical decisions surrounding antimicrobial use is central to stewardship practices. To increase the visibility and reach of our Antimicrobial Stewardship Program (ASP), we used social media platforms, Facebook and Twitter, to disseminate educational material to Internal Medicine Residents (IMRs) with the aim to increase antibiotic (Abx) knowledge and the use of our clinical pathways (CP).

Methods. IMRs consented to a pre/post intervention knowledge-based survey and agreed to follow our ASP on social media. Along with 20 basic Abx/infectious diseases (ID) questions, this survey assessed IMRs awareness of our ASP initiatives and social media usage. Over 6 months, IMRs received daily posts/tweets of basic Abx and ID trivia while promoting use of educational tools and CP on our ASP website. Engagement was encouraged with daily/monthly incentives (gift cards) given to IMRs who answered trivia questions. Categorical and continuous variables were analyzed using the chi2 and t-test to compare pre/post intervention survey responses.

Results. In total, 55 IMRs participated in the intervention, 31/55 (56%) have completed both pre/post surveys thus far. 90% and 34% of our IMRs use Facebook and Twitter respectively. 41% (n = 23) of IMRs had >1 interaction with our ASP via

social media and 18% (n = 10) had >5 interactions. Mean scores for Abx knowledge increased significantly from 11.5/20 (58%) vs 14.4/20 (72%), p = 0.01 when pre and post intervention scores were compared. No difference in post-intervention scores was seen when IMRs with and without interactions with our ASP on social media were compared (p = 0.2). The percentage of IMRs knowing how to access the ASP's internal website increased from 67% to 74%, p = 0.6. IMRs indicating they used ASP-sponsored CP as a part of clinical care increased significantly (33% vs 62%, p = 0.01).

Conclusion. Social media is a valuable tool for education and outreach to IMRs to reinforce ASP initiatives while encouraging the use of CP and educational tools to promote antimicrobial mindfulness and improve patient care.

Disclosures. **All authors:** No reported disclosures.

215. Impact of Multidisciplinary Antimicrobial Stewardship Rounds on Prospective Audit with Intervention and Feedback Recommendations

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Background. Many stewardship programs that perform prospective audit with intervention and feedback (PAIF) utilize phone calls or electronic messaging to deliver prescriber feedback. Antimicrobial stewardship ward rounds may be a more effective method to change prescriber behavior. The aim of this study was to evaluate the impact of Antibiotic Stewardship Program (ASP) rounds on the types of interventions made.

Methods. We conducted a retrospective, chart review of patients at the Hospital of the University of Pennsylvania who were evaluated by the ASP team between December 9, 2009-December 15, 2013. From December 9, 2009-November 30, 2011 (period 1), ASP Infectious Disease (ID) pharmacists called providers with antimicrobial recommendations. From December 1, 2011-December 15, 2013 (period 2), ID pharmacists also rounded with an ID physician twice weekly on patients that were identified by surveillance of antibiotic prescriptions. We characterized and compared the frequency distributions of the following successful ASP interventions during the two periods: narrowed antimicrobials, broadened antimicrobials, discontinued antimicrobials, intravenous therapy (IV) changed to oral, and recommended duration of therapy. To assess for differences in the study population over time, we randomly selected 50 patients from each period and compared demographics, microbiologic data, and antibiotic consumption.

Results. During the study period the ASP team made successful interventions on a total of 812 patients, including 365 patients during period 1 and 447 patients during period 2. Patient demographic and clinical characteristics were similar during the two periods. The number of successful interventions in the following categories increased significantly from period 1 to period 2: narrowed current antimicrobials (3.3 vs 6.0 interventions per month, p-value 0.001), IV therapy changed to oral (1.0 vs 2.0 interventions per month, p-value 0.03), and discontinuation of antibiotics (2.4 vs 4.0 interventions per month, p-value 0.05)

Conclusion. PAIF has been shown to reduce the inappropriate use of antimicrobials. In our study, the addition of ASP rounds to an established stewardship program resulted in a greater proportion of patients having antimicrobial therapy narrowed, discontinued, or converted from IV to oral.

Disclosures. **All authors:** No reported disclosures.

216. Statistical Characterization of Antimicrobial Activity: Do Common Descriptions Hold Up To Unsupervised Data Analytics?

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Background. Antibiotic spectrum is commonly described as it relates to structure or activity against resistant pathogens. Data analytics is a method of verifying these descriptors and potentially describe new patterns. Principal components analysis (PCA) is a data analytic technique that produces new uncorrelated variables in order of decreasing variability. This project examines principal components (PC) of antimicrobials as they relate to spectrum of activity.

Methods. Previously published data were utilized to determine antimicrobial activity of 70 antibiotics against 55 bacterial pathogens. Antibiotics were considered active, partially active or inactive against bacteria. Dimensionality was reduced via principal components analysis. PC1 and PC2 were correlated with clinically relevant groups of bacteria.

Results. Doripenem, imipenem, and ticarcillin-clavulanic acid had the largest PC1 scores (2.65, 2.62, and 2.53, respectively), while, daptomycin, teicoplanin, and telavancin had the smallest PC1 scores (-2.48, -2.40, -2.38, respectively). Tigecycline, chloramphenicol, and ampicillin-sulbactam had the highest PC2 scores (1.84, 1.74, and 1.50, respectively). While, tobramycin, amikacin and gentamicin had the lowest PC2 scores (-1.99, -1.99, and -1.97). PC1 score correlated to number of Gram-negative bacteria ($R^2 = 0.942$, $p < 0.001$, Figure 1). PC2 score correlated to number of non-Gram-negative bacteria ($R^2 = 0.858$, $P < 0.001$, Figure 2).

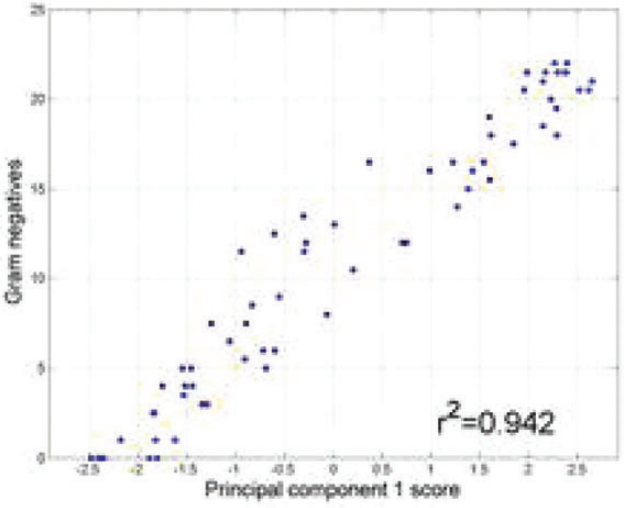

Figure 1. Principal Component 1 Score vs Gram-Negative Activity

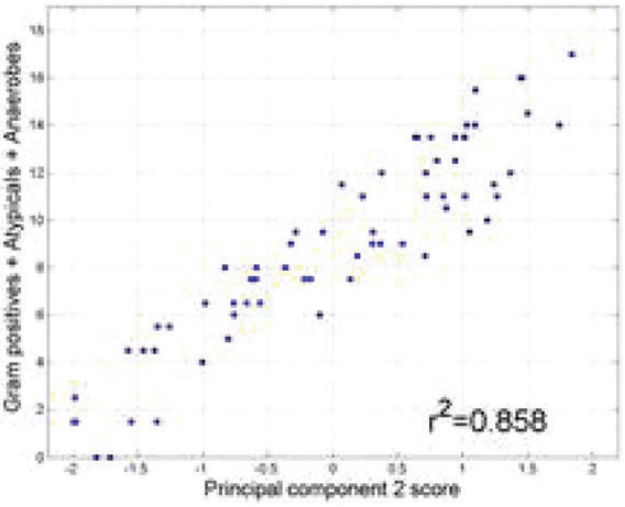

Figure 2. Principal Component 2 Score vs Non-Gram-Negative Activity

Conclusion. PCA suggested Gram-negative coverage was the major source of antimicrobial variability. PC2 described a rich interplay of Gram-positive, anaerobic and atypical activity. PCA is a valuable tool for comparing spectrum of activity between antibiotics. PC scores may also be useful in future studies on antimicrobial de-escalation.

Disclosures. **All authors:** No reported disclosures.

217. The Oregon Antimicrobial Stewardship Collaborative (OASIS). Statewide Effectiveness on Re-Survey

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Background. In 2012, the Oregon Public Health Division and Patient Safety Commission surveyed inpatient facilities to assess needs for establishing Antimicrobial Stewardship Programs (ASPs). During 2013, an ASP collaborative was conducted at 12 hospitals and all Oregon hospitals (62) were provided access to ASP resources including, webinars, learning sessions, and online materials. We re-surveyed all hospitals to assess changes following ASP collaborative and educational outreach efforts.

Methods. We re-surveyed pharmacists, physicians, infection preventionists, and laboratory personnel in 62 acute-care hospitals in Oregon via an on-line survey monkey®, using the same questionnaire from 2012. We compared ASP resources, trends, and barriers observed among these hospitals using 2012-2013 surveys.

Results. In 2013, 58 out of 62 facilities responded. The tables assess important factors affecting ASPs compared to 2012.

We saw increases in ASP formation in all hospital sizes, including non-collaborative hospitals. They were able to increase streamlining, dose optimization, and IV to PO strategies. However, despite these gains, most ASPs identified the lack of funding, staffing, and corporate suite support as limitations.

	Small: ≤ 50 beds		Medium: 50-199		Large: >200 beds	
	2013	% change	2013	% change	2013	% change
Hospitals with ASP	17(71%) n=24	+32%	14(78%) n=18	+15%	12(92%) n=13	+25%
Strong, well established ASP	2(13%) n=15	+13%	2(13%) n=15	-1%	5(42%) n=12	-8%
Funding	9(23%) n=40	+5%	6(23%) n=26	+6%	6(20%) n=30	-3%
Staffing	13(33%) n=40	+2%	11(42%) n=26	+3%	12(40%) n=30	+19%
Buy in from corporate suite	0(0%)	-3%	1(4%) n=26	0%	4(13%) n=30	+5%
Formulary Restriction	7(12%) n=59	-2%	11(20%) n=55	+8%	10(15%) n=66	+2%
Streamline De-escalation	6(10%) n=59	+4%	7(13%) n=55	+1%	7(11%) n=66	-2%
Dose Optimization/ Adjustment	9(15%) n=59	-2%	9(16%) n=55	+3%	10(15%) n=66	+3%
IV to PO	10(10%) n=98	+2%	12(16%) n=77	+3%	9(11%) n=82	+1%

Conclusion. The 2013 re-survey showed an increase of ASP establishment and activities. Although many hospitals still do not have an ASP. However, most hospitals did identify staffing, funding, and administrative barriers which will likely affect the future maintenance of these programs.

Disclosures. **All authors:** No reported disclosures.

218. Changes in Antimicrobial Prescribing Patterns Following Implementation of The Oregon Antimicrobial Stewardship Collaborative (OASC)

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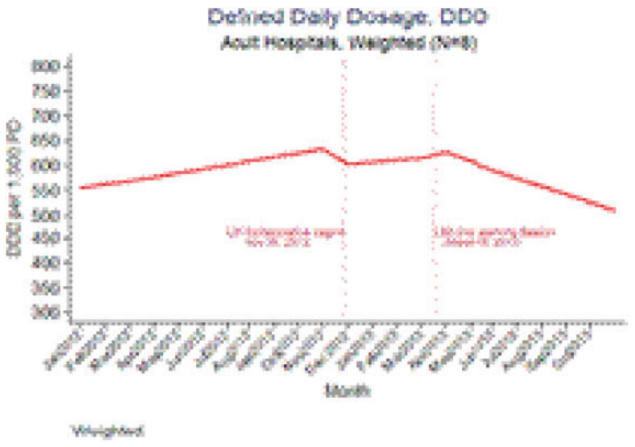
Background. We implemented OASC as a statewide model to develop and support antimicrobial stewardship programs (ASP) for hospitals.



Methods. Thirteen hospitals committed to participate in OASC, receiving educational and program support for ASP creation or expansion. The participating hospitals agreed to provide both baseline and prospective antimicrobial utilization data, in DDD (defined daily dose) and DOT (days of therapy) format. We computed DDD/DOT using General Estimating Equations (GEE) modeled with a log-linear Poisson distribution.

Results. Data for analysis was available for 8 adult hospitals: 2 small hospitals (< 50 beds), 4 medium hospitals (50-199 beds), and 2 large hospitals (≥ 200 beds). Data were divided into the following periods for analysis: baseline (January 2012 – October 2012), preparatory (November 2012 – March 2013), and post-intervention (April 2013 – November 2013).

Prior to the start of the observation period, the collaborative hospitals were prescribing on average 547.3 DDD/1,000 patient days and 572.5 DOT/1,000 patient days. The post-intervention DDD trend decreased by 4.3% compared to the baseline trend ($p = 0.001$), and 3.7% compared to the preparatory phase; during the post intervention period, DDD continued to decrease by 3.0% per month (Figure 1.). The DOT trend decreased non-significantly compared to the baseline trend.

Conclusion. In the context of a statewide ASP collaborative, we saw decreasing trends in antimicrobial prescribing when comparing post-intervention DDD trends to baseline and preparatory trends. Further, the DDD continued to decrease in the post-intervention period, suggesting a sustained impact following implementation of the collaborative.

Disclosures. **All authors:** No reported disclosures.

219. Characteristics of Antimicrobial Stewardship (AS) Activities in Community Hospitals Upon Enrollment in the Duke Antimicrobial Stewardship Outreach Network (DASON)

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Background. Community hospitals that wish to improve antimicrobial stewardship (AS) activities face barriers such as lack of dedicated personnel, resources, and/or administrative support.

Methods. We conducted an in-depth needs assessment at 10 community hospitals during months 1-2 of enrollment in the Duke Antimicrobial Stewardship Outreach Network (DASON). The DASON liaison pharmacist conducted in-person standardized interviews at each member facility to characterize AS activities and infrastructure at baseline. Results were compiled using descriptive statistics.

Results. The 10 participating hospitals had a median [IQR] bed size of 280 [220-310] and 9,849 [7,567-14,424] admissions per year. Infectious diseases (ID) physicians and ID-trained pharmacists were available in 8 (80%) and 5 (50%) facilities, respectively. Three hospitals (30%) provided dedicated PharmD funding for AS; none provided dedicated ID physician funding. Two (20%) facilities had a preexisting formal AS program. Committees with antimicrobial use oversight existed in 6 (60%) facilities, but AS subcommittees (20%) and formalized policies (30%) were uncommon. Ongoing AS activities most commonly included pharmacy-driven dose optimization (100%); empiric antibiotic selection guidelines (90%); auto-stop policies (90%); and IV-PO conversion (70%). Four (40%) hospitals performed post-prescription review; two (20%) used formulary restriction and preauthorization. Three (30%) hospitals conducted regular antimicrobial use evaluations, while 5 (50%) conducted formulary reviews annually. Few hospitals measured or reported outcomes to assess the utility of AS activities. Survey respondents cited multiple barriers to implementation: higher priority IT and clinical initiatives, personnel and staffing constraints, lack of education regarding AS, and opposition from prescribers.

Conclusion. Formalized programs and dedicated resources for AS were uncommon in community hospitals, despite ongoing AS activities and the presence of ID experts. Outcome measurements and data-driven assessments of the utility of AS activities were lacking. Efforts to support, formalize, measure, and optimize AS programs in community hospitals are greatly needed.

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220. Ongoing Impact of an Antimicrobial Stewardship Program at A Large Academic Medical Center, 7 years of experience

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Background. The University of Minnesota Medical Center (UMMC), Fairview is a 300 bed tertiary care facility. UMMC has had a long-standing, comprehensive antimicrobial stewardship program (ASP).

Methods. The stewardship team is comprised of a full-time PharmD and ID staff members who rotate through the service. The team allows providers to order restricted

antimicrobials, per hospital guidelines and policies, without upfront approval, followed by a chart review. Recommendations are placed in the electronic medical record as a progress note. Verbal recommendations may also be made. The number of patient on restricted antimicrobial, total number of interventions and acceptance rates, antimicrobial cost per patient day (pt day), antimicrobial utilization, and patient outcomes are evaluated annually.

Results. The team made 15,940 recommendation from 2007-2013; 9,569 (60%) accepted, 3071 (19.3%) agree with management, 3300 (20.7%) declined.

There was a downward trend in Hospital Acquired (HA) C. difficile diarrhea from January 2007–December 2013 from 1.2 to 0.5/1,000 pt day. From 2009-2013 a decrease was seen in HA VRE infections from 0.53 to 0.22/1,000 pt days and in HA MRSA infections from 0.2 to 0.09/1,000 pt days. Newly acquired HA ESBL infections increased from 2009-2013 at 0.09 to 0.21/1,000 pt days.

Cost savings, after adjusting for inflation, continued from year to year. The greatest cost savings was from 2006-08 in which antimicrobial doses/pt day declined by 7%, antibiotics costs declined by $7.40/pt day. In 2012, we observed our lowest antibiotic cost/pt day at $36.36 which is a difference of $19.03 before implementation of the program. We observed an increase in antibiotic cost/pt day in 2013 to $42.17 which is the same as 2011. The reasons for the increase are currently under investigation.

Conclusion. The ASP has continued to cost justify the program by reducing antibiotic use and antibiotic costs per patient day. Quality of care was not adversely affected. We began to observe a decrease in HA VRE and C. difficile infections after 3 years of operation, and MRSA after 5 years. The effects of the program and the Infection Prevention Department appear to be synergistic. Future areas for focus include rising ESBL HAIs and increased antimicrobial costs in 2013.

Disclosures. **All authors:** No reported disclosures.

221. Antimicrobial Use in Nine Intensive Care Units, Using Ten Different Indicators

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Background. Surveillance and control of hospital antimicrobial (AM) are intended to limit AM resistance. Using 10 different indicators for AM monitoring, we aimed to measure AM use in nine intensive care units in Montréal.

Methods. AM prescriptions for all patients admitted to participating ICUs (3 neonatal, 2 pediatric, 4 adult) between April 2006 and March 2010 were measured retrospectively using 10 different indicators of AM use. These indicators were obtained by combining 5 numerators [defined daily doses (DDDs), recommended daily doses (RDDs), agent-days, exposed or not, and number of courses] with 2 denominators (patient-days and admissions). Indicators were computed for by class of AM, in accordance with the Anatomical Therapeutic Chemical Classification System, and were stratified per year and ICU type. Poisson regression was used to estimate time trends and differences in AM use by type of ICU.

Results. Overall, ranking of AM use by class was similar, regardless of the indicator used. When RDDs, exposed and courses were used, the most frequently used AM classes were cephalosporins, followed by penicillins and aminoglycosides. Using agent-days, penicillins came first, followed by aminoglycosides and penicillins and B-lactams inhibitors. With DDDs, more variations were observed. From 2006 to 2010, use decreased significantly for all AM classes except 1) carbapenems use, which remained stable, and 2) trimethoprim and sulfamides use, for which results varied with the indicator used. Compared to adult ICUs: 1) aminoglycosides and penicillins use was higher in both neonatal and pediatric ICUs; 2) carbapenems, glycopeptides and quinolones use was lower; 3) for cephalosporins, clindamycin, macrolides, penicillins and B-lactams inhibitors and trimethoprim and sulfamides, use was lower in neonatal ICUs and higher in pediatric ICUs.

Conclusion. Frequency of AM prescribing varied across ICU types, but generally decreased in participating ICUs. A standard set of indicators would facilitate surveillance of AM use in a population.

Disclosures. **All authors:** No reported disclosures.

222. Impact of a City-Wide Collaborative Antimicrobial Management Program Involving All Acute Care Hospitals in Savannah, Georgia

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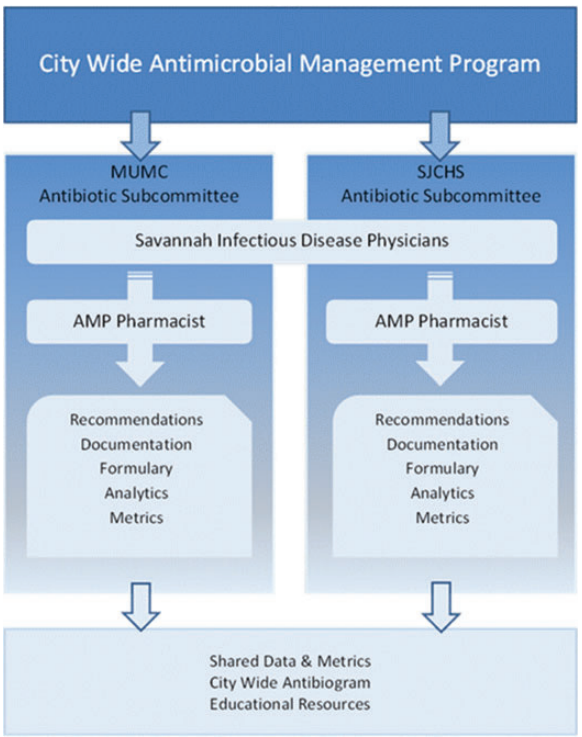
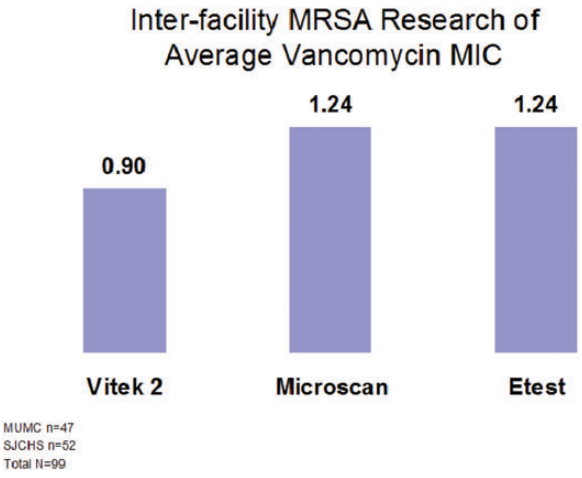
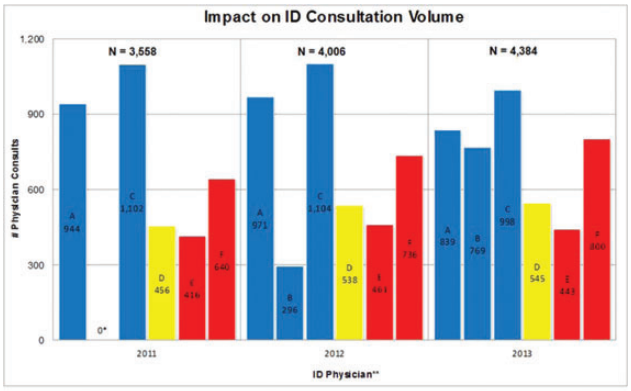
Background. In January 2012, the major health care facilities in Savannah, Georgia collaborated to create a unique city-wide Antimicrobial Management Program (AMP). Memorial University Medical Center and St. Joseph's/Candler Health System were later joined by Select Specialty Hospital (long term acute care).

Methods. Savannah's six adult infectious disease (ID) physicians see patients at each of the facilities, which share patient populations, and participate in the AMP by rotating on a weekly basis. The program achieved early success reviewing patients on carbapenems and daptomycin and rapidly incorporated patients receiving one of sixteen targeted anti-infectives medications, those on ≥4 anti-infectives, or with bug-drug mismatches. After comprehensive review by a clinical pharmacist and an ID physician, recommendations are communicated to the responsible prescriber, including other ID physicians.

Results. The integration of competing health systems, all ID physicians, and peer review bolstered the program's credibility and allowed for effective collegial interaction. The growth and influence of the AMP led to shared initiatives across facilities (Figure 1) inter-facility research, including comparisons of lab susceptibility systems (Figure 2); development of city-wide metrics; grant awards; and education, including travel to national meetings for microbiologists to evaluate new technologies and address deficiencies. All activities occurred without a negative impact on consultation volume for the ID physicians (Figure 3).







Conclusion. A city-wide antimicrobial management program is able to optimize anti-infective usage to improve patient care, generate regional metrics, expand and improve microbiology procedures, promote research, and provide educational opportunities, without negatively impacting local infectious disease practices.

Disclosures. **All authors:** No reported disclosures.

223. Teaching Antimicrobial Stewardship Globally with A Massive Online Open Course (MOOC)

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Background. Increasing recognition of the importance of effective antimicrobial stewardship (AS) demands a comprehensive freely available educational program for physicians and allied health professionals (AHPs).

Methods. We developed a MOOC entitled "Antimicrobial Stewardship: Optimization of Antibiotic Practices" and made it available at the online learning platform, Coursera (https://www.coursera.org). Full course access is free of charge and 6 continuing medical education (CME) credits are available from Stanford University's Office of CME for a nominal fee ($20).

The course consists of 26 modules ranging in length form 6-25 minutes. The content is divided into 2 parts: the first deals with the clinical science of antimicrobial use and the second with practical aspects, including stewardship program management. In addition to Stanford faculty, we recruited targeted guest lectures from leading authorities in several content areas, such as the making the business case for AS, measurements and metrics, pediatrics and the role of AS in infection prevention, long-term care and palliative medicine. Data on course use, user demographics and test results were collected.

Results. The cost of producing the course was about $6,000, ($5,000 CME accreditation fee, $1,000 copyright fees), exclusive of faculty and technical labor costs. The course debuted on 22 November 2013 and, over 5 months, amassed 23,950 registered users from 126 countries and including 124 new registrants and 825 active users the week of April 15-22, 2014. Usage data showed 73,320 total streaming views and 77,731 total video downloads, as well as 1171 examination submissions. Of 107 CME candidates (66 MDs/41 AHPs) only 95 (62 MD/33 AHP) successfully passed the CME course post-test. The difference in pass rate between these groups was not statistically significant.

Conclusion. A comprehensive antimicrobial stewardship course was developed for minimal cost and has attracted a large number of users. The MOOC format may offer a way to rapidly disseminate education to a variety of healthcare providers over a vast geographic area. Further investigation is needed into how users best engage with the material and whether this format is effective at addressing knowledge gaps in antimicrobial use best practices.

Disclosures. **All authors:** No reported disclosures.

224. Impact of an Antimicrobial Stewardship Program (ASP) on antimicrobial use and clinical outcomes at a Veterans Affairs (VA) Teaching Hospital

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Background. Antimicrobial stewardship programs (ASPs) are used as key strategies to limit the spread of antimicrobial resistance through appropriate antimicrobial utilization practices.

Methods. In September 2012, a formal ASP was implemented at a VA teaching hospital licensed for 118 beds. The ASP team of attending and fellow ID physicians, a clinical ID pharmacist and fellow, and pharmacy residents and students prospectively audited all inpatient antimicrobial use (IV and PO) daily (Monday-Friday). Antimicrobial use and clinical outcomes were compared between inpatients on antimicrobials in a 1 year period before (pre-ASP; October 2010-September 2011) and after (post-ASP; September 2012-August 2013) ASP implementation. Poisson regression models were used to calculate adjusted relative risk (RR) and 95% confidence intervals (CI) to assess ASP impact on inpatient mortality, 30-day readmission, and 14 day length of stay.

Results. Post-ASP implementation, 522 interventions were made with an acceptance rate of 77%. A total of 2659 pts (49% pre-ASP; 51% post-ASP) were included for evaluation. IV antimicrobial use in pre- and post- ASP pts decreased from 293 to 288 days of therapy (DOT)/1,000 patient days (PD) and PO antimicrobial use increased from 186 to 209 DOT/1,000 PD. The DOT/1,000 PD of several broad spectrum antimicrobial agents decreased from pre- to post- ASP periods, including piperacillin-tazobactam (-6%), 3rd/4th generation cephalosporins (-13%), fluoroquinolones (-20%), and carbapenems (-35%). IV vancomycin DOT/1,000 PD increased 6% from the pre- to post-ASP periods. Post-ASP implementation, inpatient mortality decreased significantly (adjusted relative risk [RR] 0.59, 95% CI 0.35 - 0.99), 14 day length of stay decreased non-significantly (RR 0.78, 95% CI 0.61 - 1.01) and 30-day readmission increased non-significantly (RR 1.05, 95% CI 0.91 - 1.21).

Conclusion. Our ASP was associated with improvements in use of several broad spectrum antimicrobials and clinical outcomes, including inpatient mortality and length of stay. However, further ASP efforts are needed to improve vancomycin use and 30-day readmission rates.

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225. Development of Institutional Guidelines for Management of Gram-Negative Bloodstream Infections: Incorporating Local Evidence

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Background. Appropriate empirical antimicrobial therapy is associated with improved survival in patients with bloodstream infections (BSI). Antimicrobial stewardship programs can develop evidence-based institutional guidelines for empirical antimicrobial therapy of gram-negative BSI based on local data.

Methods. Hospitalized adults with gram-negative BSI from 2011-2012 at Palmetto Health Richland and Baptist Hospitals in Columbia, SC were evaluated. Multivariable logistic regression was used to identify patients with risk factors for BSI due to gram-negative bacilli that harbor antimicrobial resistance genes (*Pseudomonas aeruginosa, Enterobacter, Citrobacter* and *Serratia* species). Antimicrobial susceptibility rates of bloodstream isolates to non-restricted antibiotics were stratified by risk of antimicrobial resistance and acute severity of illness. Retained antibiotics had predefined susceptibility rates ≥90% for non-critically ill (Pitt bacteremia score <4) and ≥95% for critically ill patients (Pitt score ≥4).

Percentage of susceptible bloodstream isolates to antibiotics by site of acquisition and Pitt score

	CA		HCA and HA	
Antibiotic	Pitt < 4 (N=128)	Pitt ≥ 4 (N=33)	Pitt < 4 (N=152)	Pitt ≥ 4 (N=77)
Ampicillin-sulbactam	71	66	60	71
Ceftriaxone	95	91	85	90
Cefepime	96	100	95	96
Piperacillin-tazobactam	98	100	95	97
Ciprofloxacin	84	82	84	75
Gentamicin	91	97	94	91

Results. Among 390 patients with gram-negative BSI, healthcare-associated (HCA) [odds ratio (OR) 3.01, 95% confidence intervals (CI) 1.52-6.32] and

hospital-acquired (HA) sites of acquisition [OR 3.68, 95% CI 1.64-8.44] were identified as risk factors for BSI due to *P. aeruginosa* or Amp-C-producing *Enterobacteriaceae* as compared to community-acquired (CA) BSI (referent). Based on stratified bloodstream antibiogram (Table), ceftriaxone was recommended for empirical therapy of CA BSI in non-critically ill patients; and cefepime or piperacillin-tazobactam for HCA, HA and critically ill patients with BSI.

Conclusion. Incorporation of risk factors for antimicrobial resistance, local antimicrobial susceptibility rates and acute severity of illness into institutional management guidelines provides an objective evidence-based approach for optimizing empirical antimicrobial therapy for gram-negative BSI.

Disclosures. **J. A. Justo**, Cubist Pharmaceuticals: Grant Investigator, Research grant **P. B. Bookstaver**, Durata Therapeutics: Scientific Advisor, Salary; Cubist Pharmaceuticals: Grant Investigator, Research grant

226. Impact of Physician Assistant Directed Antimicrobial Stewardship Consultation Service

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Background. Expansion of antimicrobial stewardship (AMS) will require innovative use of interprofessional models. The Henry Ford Hospital AMS Program expanded in 2012 utilizing a Physician Assistant (PA) supervised by an ID staff physician. This study describes the impact of a PA directed antimicrobial stewardship (PA-AMS) consult service.

Methods. IRB approved retrospective cohort of all consecutive patients evaluated by the PA-AMS from November 2012–December 2013. First consultation only included. Hospice patients excluded. Clinical success was defined as resolution or improvement of signs and symptoms of infection at last encounter, discharged alive, no antimicrobial adverse effects, no escalation of antibiotic coverage due to clinical worsening, and no 30 day readmission due to the index infection. Measures of central tendency and proportion were used to describe patient population, interventions, and outcomes.

Results. 335 patients met inclusion criteria: median age 67 years, 52% male. Comorbidies: 42% diabetes, 26% COPD, 25% CHF, 23% malignancy, 13% BPH, 5% dialysis. Reason for consult: 186 (56%) request PICC for home infusion; 44% request antibiotic management. PA-AMS diagnosis: 28% lower respiratory tract, 22% urinary tract infection, 15% skin infection, 15% bloodstream, 5% osteomyelitis; 24% no infection, 16% asymptomatic bacteriuria. Interventions: Change in diagnosis for 109 (33%). Most common diagnosis changes were for UTI (49/109, 45%), lower respiratory tract (36/109, 33%). 71/186 (38%) PICC avoided, 128/335 (38%) IV to PO switch, 28% discontinue, 16% additional diagnostics suggested, 13% de-escalate, 13% extend duration, 10% simplify, 5% broaden spectrum. Clinical success was observed in 95% of patients. 20% of patients were readmitted within 30 days, 2% readmission for index infection, 1.5% new onset C. difficile infection. 15% had outpatient clinic follow-up scheduled with PA. 36/50 (72%) attended the clinic visit.

Conclusion. PA-AMS effectively managed AMS consults and reduced unnecessary PICC placement and antimicrobial use. Patient outcomes were favorable. An interprofessional model for AMS with a PA is a reasonable approach to expanding AMS programs.

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227. Evaluation of Antimicrobial Stewardship in an Academic Medical Center Emergency Department (ED)

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Background. Current available literature supports the importance of timely follow-up and appropriate antimicrobial selection for discharged patients from the ED. We sought to evaluate the impact of implementing a pharmacist-managed antimicrobial stewardship program (ASP) in our hospital's ED by assessing measurable outcomes related to patient follow-up.

Methods. This quality assurance project included all patients with positive culture results after being discharged home from the ED. The culture review process included screening the daily laboratory patient report for positive results, collecting pertinent data, and determining if empiric therapy at discharge from ED was appropriate based on current evidence-based practice guidelines. If lab result was positive for a sexually transmitted disease (STD) or empiric therapy inappropriate, an attempt was made to contact the patient and/or PCP by phone. If available, notified of test result(s) and called in new prescription when indicated. If unavailable, letter was sent to the patient's stated home address. The control group (6 weeks) assessed the current practice of ED Physician Assistant (PA) culture follow-up and the intervention group (15 weeks) assessed the transition to ASP-pharmacist management. Data was collected retrospectively for the control phase and prospectively during the intervention period. This project was IRB approved and data was analyzed using SPSS-PC (ver. 21).

Results. During the intervention phase, attempted patient and/or PCP follow-up occurred in 72/73 (98.7%) cases vs 10/22 (45.5%) in the control group ($p < 0.001$). No differences in percentage of inappropriate empiric prescribing were seen (44.9% vs 41.2%, $p > 0.05$). Comparing control vs intervention group, STD and urinary tract infection (UTI) accounted for the majority of mistreated infections. Of the reasons for inappropriate empiric therapy, no treatment prescribed and drug-bug mismatch were the most common. In addition, a sub group analysis of STD treatment in ED patients revealed deficiencies in provider prescribing practices and as a result education was provided.

Conclusion. Implementation of an ASP in the ED can improve timeliness of culture review and provide more consistent patient follow-up while reducing the non-clinical workload of ED providers.

Disclosures. **All authors:** No reported disclosures.

228. Building Bridges: Improving Antibiotic Prescribing in the Emergency Department

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Background. Emergency room utilization in the US has increased over the last decade. Little is known about antibiotic utilization and its appropriateness in the Emergency Department (ED). Published data indicate that over 50% of patients presenting with viral upper respiratory tract infections receive inappropriate antibiotics during an ED visit. Thus, opportunities exist to improve prescribing.

Methods. We implemented an antibiotic stewardship (ASP) and infectious diseases (ID) management pilot program, designed in collaboration with the ED at the Einstein Campus of Montefiore Medical Center (a 424 bed non-profit teaching facility with over 72,000 ED visits a year and 16,000 admissions), the University Hospital of Albert Einstein College of Medicine in Bronx, NY. For 17 consecutive weeks an ID physician was notified about patients presenting with infectious conditions by ED providers or ASP staff (during antibiotic auditing and approval calls). An ID physician formally evaluated the patient and offered recommendations for antibiotic selection, dosing, duration, additional testing, and when appropriate, outpatient management. Patients who were hospitalized were offered follow up with an ID specialist.

Results. During the intervention period, 230 patients were evaluated. Of those patients, 138 (60%) were initially prescribed 'inappropriate' antimicrobial regimens. Outpatient management with discharge from the ED was recommended in 28 (12%) patients, and 28 (12%) were recommended to stop antimicrobial therapy completely. Acceptability of ASP/ID consultation was high, with 92% of ED physicians prescribing the recommended antibiotic regimen.

	N (%)	Prescribing details
Number of Consults	230	
Antibiotics prescribing inappropriate	138 (60)	Reasons, N (%): No antibiotics needed: 28 (12) Coverage too broad: 37 (16) Coverage too narrow: 27 (12) Able to switch to oral: 17 (7) Other (e.g., incorrect drug due to allergy or prior cultures, incorrect dosing) 29 (13)

Conclusion. Our pilot data suggests that a collaborative approach with early ASP and ID consultation in the ED is a feasible and acceptable model that can improve initial antibiotic prescribing, reduce unnecessary antibiotic use, improve patient safety, avert unnecessary hospital admissions and build relationships with ED staff.

Disclosures. **All authors:** No reported disclosures.

229. A Pre-clinical Interprofessional Curriculum in Antimicrobial Stewardship Improves Knowledge and Attitudes Toward Interprofessional Healthcare in Two Professional Schools

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Background. Antibiotic misuse can have serious effects on patient safety and is addressed in the health care setting by physician and pharmacist run teams. However, this is not comprehensively taught in the medical or pharmacy school curricula. Addressing this deficiency can teach an important concept as well as model interprofessional health care.

Methods. We created an online learning module, as well as branched logic interactive clinical cases for a subsequent small group session that combined pre-clinical medicine and pharmacy learners, with faculty from both schools. We used validated questions to assess knowledge and attitudes regarding antimicrobial stewardship and interprofessionalism. We used paired t-test and chi-squared tests to assess differences before and after the small group session.

Results. 280 second-year medical and third-year pharmacy students enrolled, 91% participated in the study. 90% and 93% agreed or strongly agreed that the online and small group activities were a valuable learning experience. Compared to pre-module knowledge and attitudes, there was no change ($P > 0.20$) in whether students believed that antibiotic resistance is a major public health problem (99% vs 100%), or whether only the needs of the individual patient should be considered when prescribing antibiotics (27% vs 29%). There was a higher proportion of students who were able to describe the role of each profession in appropriate antibiotic use (36% vs 81%, $P < 0.001$), communicate in a manner that engages the interprofessional team (77% vs 96%, $P < 0.001$), and describe collaborative approaches to appropriate antibiotic use (47% vs 89%, $P < 0.001$).

Conclusion. An interprofessional health education (IPE) curriculum that models an authentic work experience can be successfully developed and implemented in pre-clinical curriculum. Students have a good knowledge base of antimicrobial stewardship concepts even before completing the module. However, combining two professional schools for a coordinated IPE curriculum substantially improves knowledge and attitudes in interprofessional domains. Future studies that link IPE attitudes to patient safety outcomes are needed to continue to inform IPE curricular interventions in pre-clinical education.

Disclosures. **All authors:** No reported disclosures.

230. Antimicrobial Stewardship Strategy to Decrease Respiratory Fluoroquinolone Utilization in a Large, Urban, Healthcare System

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Background. To compare moxifloxacin use within a healthcare system after implementation of criteria for utilization and a required beta-lactam allergy assessment.

Methods. In 2009, the Seton Healthcare Family (central Texas) implemented antimicrobial stewardship with a primary target of reducing utilization of fluoroquinolones. This resulted in a dramatic decrease in utilization and cost (control group), as well as a decrease in *C.difficile* infection rates. Beginning July 2013, the infectious diseases pharmacists led physician education regarding the healthcare system's community acquired pneumonia treatment guideline (post-education group). Criteria for moxifloxacin use were implemented in December 2013 (post-restriction group). Pharmacists reviewed all moxifloxacin orders for approved criteria for use and performed beta-lactam allergy assessment on patients with reported allergies. To assess the effectiveness and fiscal impact of this program, descriptive statistics and a Mann-Whitney U test were used to compare moxifloxacin use and cost between the control group and the post-education and post-restriction groups.

Results. Hospital sites experienced an initial reduction in median days of therapy per 1,000 patient days after education [35 (IQR 16-58) vs 11 (IQR 10-25); $p = 0.076$], correlating with a 23 to 63% reduction amongst individual sites. A greater reduction was experienced after implementation of criteria for use [35 (IQR16-58) vs 6 (IQR 5-6); $p = 0.02$], correlating with an additional reduction of 40-75% following education amongst individual sites. As compared to education alone, the median monthly cost for moxifloxacin was further reduced following adoption of restriction criteria [$8016.14 (IQR $7518.42-$12198.01) vs $1217.04 (IQR $0-$2900.35); $p = 0.01$]. The annual moxifloxacin acquisition cost is expected to decrease 87% following the current restriction criteria (control $116,504.60 vs estimated post-restriction $14,604.48; p = n/a).

Conclusion. Education provided an initial reduction in moxifloxacin utilization; however, implementation of criteria for use and a required beta-lactam allergy assessment led to a more rapid and greater reduction in utilization and expenditure.

Disclosures. **All authors:** No reported disclosures.

231. Using an Algorithm to Decrease Fluoroquinolone Use and Effects on *Escherichia coli* Resistance

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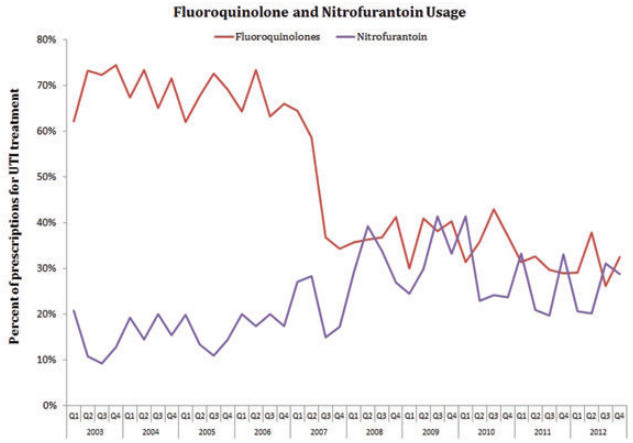
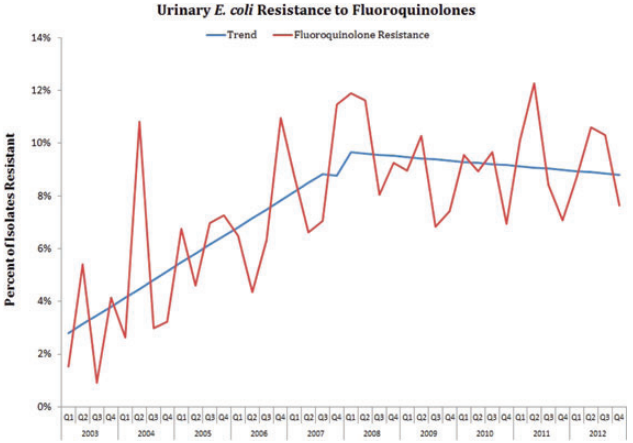
Background. Between 1999 and 2005, fluoroquinolone resistance among urinary *Escherichia coli (E. coli)* isolates increased markedly at our institution following implementation of an algorithm recommending fluoroquinolones as first line therapy for uncomplicated cystitis (UTI). In 2007, the algorithm was revised to direct providers to use nitrofurantoin as first line therapy. The objectives of this study were to evaluate changes in fluoroquinolone and nitrofurantoin prescriptions following this intervention and assess the impact on fluoroquinolone resistance in *E. coli*.

Methods. This single center, retrospective study included non-pregnant, adult outpatients diagnosed with acute cystitis and prescribed an antibiotic from the emergency department, adult urgent care clinic, or primary care clinic between 2003 and 2012. Changes in antibiotics prescribed for the treatment of UTIs before and after implementation of the algorithm in 2007 and changes in outpatient fluoroquinolone-resistant *E. coli* isolated from urine were evaluated over time.

Results. 5717 patients and 11,416 *E. coli* isolates were included. Fluoroquinolones decreased from 65% of prescriptions to 35% while nitrofurantoin use increased from 17% to 29% *($P < 0.001$)*, with the greatest impact immediately following the intervention. There was no further reduction in fluoroquinolone use in the remaining post-intervention period while nitrofurantoin use had a slight but significant downward trend. *(Figure 1)* Over the course of the study period *E. coli* resistance rates to fluoroquinolones increased from 1.5% to 7.6%, however, following the decrease in fluoroquinolone use resistance rates stabilized and decreased slightly each quarter in the post-intervention period. *(-0.3%/quarter, $P = 0.02$) (Figure 2)* There was no change in nitrofurantoin resistance, despite increased use.





Conclusion. The halt and decline of a growing population of fluoroquinolone-resistant *E. coli* found in the community followed a marked reduction in

fluoroquinolone use for UTI management. Despite increased nitrofurantoin use, there was no increase in nitrofurantoin-resistant *E. coli.* These findings suggest that antimicrobial stewardship interventions can impact the emergence of antimicrobial resistance.

Disclosures. **All authors:** No reported disclosures.

232. Assessment of Year-to-Year Variation in Combination Antibiograms for *Pseudomonas aeruginosa* (PA) after Ciprofloxacin (CIP) Restriction

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Background. Combination therapy is often employed for serious PA infections. Due to declining activity of CIP against PA at our institution, empiric use of the drug was restricted and prescribers were encouraged to add alternative agents to one of our commonly used antipseudomonal beta-lactams (BLs), piperacillin/tazobactam (P/T), cefepime (CEF), and meropenem (MER) as addition of CIP provided gain in combined activity based on a combination antibiogram. We have determined both the effects of the CIP restriction as well as general year to year variation in our combination antibiograms.

Methods. Combination antibiograms for the years 2009-12 were prepared. The relative activity for ourmost commonly used/tested agents was assessed for isolates that were resistant to one or more of our primary, BL antipseudomonal antibiotics. The basis for the analysis was the determination of percent of isolates resistant to a primary antibiotic susceptible to a secondary antibiotic. The secondary antibiotics assessed were the other primary antibiotics plus amikacin (AMK), gentamicin (GEN), tobramycin (TOB), ciprofloxacin (CIP), and aztreonam (AZM). Changes from 2009 to 2012 were assessed with Chi square analysis.

Results. The number of PA isolates tested/assessed each year ranged from 245 to 400 (duplicates excluded). Changes from 2009 to 2012 were largely non-significant although the activity of CIP against isolates resistant to P/T or MER did increase significantly subsequent to its restriction ($p < 0.04$). Regardless of primary antibiotic considered, the secondary agent most likely to be active against resistant strains was an aminoglycoside (either AMK or TOB). The second most active secondary antibiotic was also an aminoglycoside, with only one exception. These findings varied somewhat from year-to-year. The agents least likely to be active against resistant strains were AZM, CEF, and P/T.

Conclusion. The best secondary antibiotic to use in combination at our institution for known or suspected PA infections is an aminoglycoside and this information has been used to inform prescribers and clinical guidelines. While restriction of CIP did result in return of activity against some resistant strains, removal of restriction may cause re-emergence of resistance.

Disclosures. **All authors:** No reported disclosures.

233. Antibiotic Prescribing at the Time of Hospital Discharge: a Target for Antibiotic Stewardship

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Background. For common infections requiring hospitalization, the majority of antibiotic treatment occurs after hospital discharge; however, prescribing practices at the transition to outpatient care have not been well described. The objectives of this study were to describe antibiotic use and evaluate appropriateness of oral antibiotics prescribed at the time of hospital discharge.

Methods. We identified a retrospective cohort of adult inpatients who were prescribed an oral antibiotic at the time of discharge between July 1, 2012 and June 30, 2013 at an academic medical center. Two Infectious Diseases specialists independently assessed the appropriateness of antibiotic(s) prescribed from a random sample of cases. We performed a multivariate logistic regression to identify factors associated with inappropriate prescriptions.

Results. In total, 1825 unique patients were prescribed antibiotics; of these, 376 cases were randomly selected for manual review to reach 300 included cases. Antibiotics were most commonly prescribed for urinary tract infections (UTI) (n = 72, 24%), community acquired pneumonia (CAP) (n = 52, 17%), cellulitis and/or cutaneous abscess (n = 48, 16%), and chronic obstructive pulmonary disease (COPD) exacerbations (n = 23, 8%). The most commonly prescribed antibiotics were levofloxacin (n = 115, 38%), azithromycin (n = 37, 12%), and amoxicillin/clavulanate (n = 37, 12%). Median total treatment duration was 10 days (interquartile range [IQR] 7-13) with a median duration after discharge of 6 days (IQR 4-10). Of the 150 cases randomly selected for appropriateness review, the discharge prescriptions in 115 cases (77%) were independently agreed upon as being appropriate (n = 51, 44%) or inappropriate (n = 64, 56%). The most common types of inappropriate use were excessive treatment duration (n = 37, 58%) and antibiotic selection (n = 20, 31%). Multivariate logistic regression analysis did not reveal any significant factors associated with inappropriate prescribing.

Conclusion. UTI, CAP, skin and soft tissue infections, and COPD exacerbations accounted for nearly two-thirds of conditions for which antibiotics were prescribed at hospital discharge. Discharge prescriptions were inappropriate in approximately half of cases suggesting a key target for antimicrobial stewardship.

Disclosures. **All authors:** No reported disclosures.

234. Characterization of Inappropriate Antimicrobial Therapy Following Changes in Antimicrobial Stewardship Strategies

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Background. The traditional antimicrobial stewardship approach at the University of California Davis Medical Center (UCDMC) emphasized prior authorization. In 2013, UCDMC transitioned to a prospective audit with intervention and feedback model and de-restricted several antimicrobials, including cefepime, ceftazidime, piperacillin/tazobactam (PTZ), micafungin, and fluconazole. Our aim was to determine if prescription rates increased for the de-restricted antimicrobials following the stewardship strategy change.

Methods. We identified inpatient orders for the de-restricted antimicrobials using a retrospective cohort design. The pre- and post- periods examined were October 1, 2012-December 31, 2012 and October 1, 2013-December 31, 2013, respectively. Inclusion criteria were age $\geq$ 18 years, hospital admission, and receipt of >1 dose of the select agent following patient admission. Patients were excluded if the agents were recommended by the Infectious Diseases service or initiated by an outside facility. Appropriate use was assessed based on antimicrobial spectrum of activity and conformity with national or institutional guidelines.

Results. Subsequent to antimicrobial de-restriction, prescription rates per 1,000 patient-days increased by 106% for PTZ and 64% for micafungin, but decreased by 7% for cefepime and 36% for fluconazole. A trend toward increased inappropriate PTZ (n = 168) prescribing was observed for several physician services, including medical intensivists (8% vs 30%; p = 0.127), hospitalists (0% vs 25%; p = 0.147), gastrointestinal surgery (0% vs 40%; p = 0.444), cardiothoracic surgery (13% vs 60%; p = 0.217), vascular surgery (22% vs 50%; p = 0.491), and orthopedic surgery (20% vs 33%; p = 0.604). Increased inappropriate PTZ prescribing was observed for pulmonary (10% vs 43%; p = 0.033), abdominal (10% vs 36%; p = 0.515), and pelvic (0% vs 25%; p = 0.515) infections. Rates of inappropriate micafungin (n = 16) prescribing did not change.

Conclusion. Our comparison of prescribing practices identified several services and infection types that may merit intervention on PTZ selection. Continual characterization of prescribing practices following changes in stewardship strategies can identify targets for enhanced stewardship efforts.

Disclosures. **All authors:** No reported disclosures.

235. Use of electronic de-escalation alerts to facilitate prospective audit and feedback for antimicrobial stewardship

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Background. Prospective audit with intervention and feedback (PAIF) to prescribers can decrease inappropriate antimicrobial use. At our institution, PAIF previously had been performed by manual chart review limited to only several broad-spectrum antimicrobials on select inpatient units. To improve efficiency of PAIF, we developed an electronic alert to identify opportunities for de-escalation. Our aims were to determine performance characteristics of the alert and to compare the number of successful de-escalation events before and after the alert was implemented.

Methods. We used a prospective cohort study to evaluate performance characteristics of the electronic alert at the Hospital of the University of Pennsylvania, a 772-bed tertiary-care hospital from July 1, 2013 through October 31, 2013. All adult inpatients receiving a broad-spectrum antimicrobial were eligible. Using Theradoc® (Hospira, Salt Lake City, UT), an electronic alert was created and was used to notify antimicrobial stewardship pharmacists (ASP) in real-time of opportunities for de-escalation. The alert was introduced July 1, 2013, at the same time inpatient ASP resources decreased from 3.0 full-time equivalents (FTE) to 2.0 FTE. A random sample of 200 broad-spectrum antimicrobial prescriptions over the study period was reviewed by two physicians, blinded to whether an alert fired, and was used to determine performance characteristics. PPV was also determined by ASPs reviewing alerts in real-time. Successful de-escalation interventions were compared during and 1 year before the study period.

Results. The alert had a sensitivity of 77.5% (95% CI 61.1-88.6), specificity of 84.3% (95% CI 77.4-89.5), positive predictive value (PPV) of 56.4% (95% CI 42.4-69.4), and negative predictive value (NPV) of 93.5% (95% CI 87.6-96.8). The

prospectively determined PPV was 19.4% (95% CI 12.7-28.4%). The successful de-escalation interventions per month increased from 2.8 to 5.3 after introduction of the alert (p = 0.01).

Conclusion. Compared to the prior method of PAIF at our institution, electronic alerts were associated with favorable performance characteristics. The implementation of the alert was associated with an increase in successful de-escalation interventions at a time when inpatient ASP resources decreased. Electronic alerts may facilitate more efficient PAIF.

Disclosures. **All authors:** No reported disclosures.

236. Taking an Antibiotic Timeout: Utilizing an Antibiotic Renewal Template for Automatic Approval of Vancomycin and Piperacillin-tazobactam

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Background. CDC recommends an antibiotic time out after culture results become available. We devised a self-directed time out program to guide providers to (re)consider the continuation of antibiotics past day 3.

Methods. We implemented the time out program at a teaching hospital where continuation of vancomycin (VAN) and piperacillin-tazobactam (P-T) past day 3 previously required Infectious Diseases approval. We created an electronic antibiotic renewal template that included a structured review of antibiotic indications with links to local guidelines that provided automatic approval upon completion. Providers were notified of time out on day 4 via an electronic dashboard that summarized the patient's microbiological and clinical status. We assessed template utilization in the first 6 months of implementation (April to October 2013) among providers who received time out notification and determined via expert chart review whether self-continuation of VAN or P-T through day 5 was discordant with local guidelines as compared to a six-month period 1 year prior (April to October 2012).

Results. Of 145 VAN time outs, templates were completed in 55 (38%); of these, VAN was continued through day 5 in 39. VAN was allowed to expire without template completion in 77 (53%). VAN was active through day 5 despite no template in 13 (9%). 7 continuations of VAN via template (5% of timeouts) were guideline-discordant, as compared to 0/199 1y prior (p = 0.002). Overall, VAN discontinuation was higher with the time out program as compared to 1y prior: 93/145 (64%) vs 96/199 (48%), p = 0.004.

Of 105 P-T time outs, templates were completed in 52 (49.5%); of these, P-T was continued through day 5 in 33. P-T was allowed to expire without template completion in 51 (48.5%). P-T was active through day 5 despite no template in 2 (2%). 9 continuations of P-T (9% of time outs) via template were guideline-discordant, as compared to 2/93 (2%) 1y prior (p = 0.063). Overall, P-T discontinuation was similar with the time out program as compared to 1 year prior: 70/105 (67%) vs 58/93 (62%), p = 0.55.

Conclusion. The self-directed time out resulted in few guideline-discordant continuations and a higher overall rate of VAN discontinuation, suggesting that the time out prompted providers to discontinue VAN in cases where they previously might have sought Infectious Diseases approval for continuation.

Disclosures. **All authors:** No reported disclosures.

237. Evaluation of the Impact of a Clinical Decision Support Tool and Pharmacist Telephone Consultation Within 48 hours of Discharge on Unscheduled Emergency Department Encounters for Skin and Soft Tissue Infections

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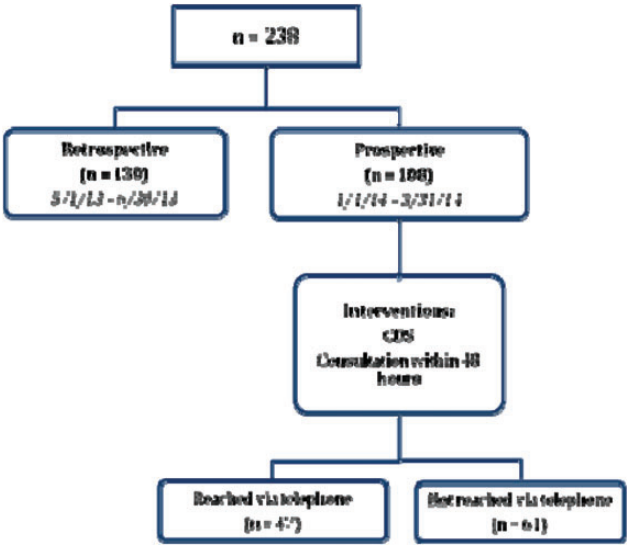
Background. The National Transitions of Care Coalition (NTOCC) describes medication-related problems as a major source of concern for emergency departments (ED), especially during the discharge process. The primary objective of this project was to evaluate the impact of a clinical decision support (CDS) tool for skin and soft tissue infections (SSTI) and pharmacist telephone consultation within 48 hours of discharge on the proportion of patients that have an unscheduled ED encounter for SSTI within 7 days of discharge.

Methods. To enhance antibiotic prescription adherence to health-system guidelines, a CDS tool was implemented into the ED electronic medical charting system. A series of pre-created SSTI discharge prescriptions for oral antibiotics were implemented to guide appropriate dosing based on patient-specific clinical data. Patients were contacted for pharmacist consultation within 48 hours of ED discharge.

To assess the impact of the interventions, the pharmacy department conducted a retrospective and concurrent evaluation of patients presenting to the ED with an ICD-9 diagnosis code of SSTI between May 1, 2013-June 30, 2013 (retrospective) and January 1, 2014-March 31, 2014 (concurrent following implementation of CDS and phone consultation).

Results. A total of 130 patients were included in the retrospective arm and 108 included in the prospective arm.

	Retrospective	Prospective (Not Reached)	Prospective (Reached)	p-value
ED re-encounters at 7 days	11.5 % (15/130)	15.8% (9/61)	4.3% (2/47)	
Hospital admissions at 7 days	1.5% (2/130)	1.6% (1/61)	0% (0/47)	
Prescription adherence to health-system antimicrobial guidelines	26.2% (34/130)	55.7% (68/122)		p<0.0001



Conclusion. Results for the primary outcome suggest that a pharmacist telephone consultation within 48 hours of ED discharge may result in a decrease in re-encounters at 7 days. Results further demonstrate that implementation of the CDS tool to guide antibiotc selection in the ED significantly improved adherence to health-system antimicrobial guidelines.

Further investigation is required to determine the impact of a CDS on ED re-encounters, hospital admissions, and patient outcomes.

Disclosures. **All authors:** No reported disclosures.

238. Changing the Culture: Spreading the Stewardship Message to a New Campus

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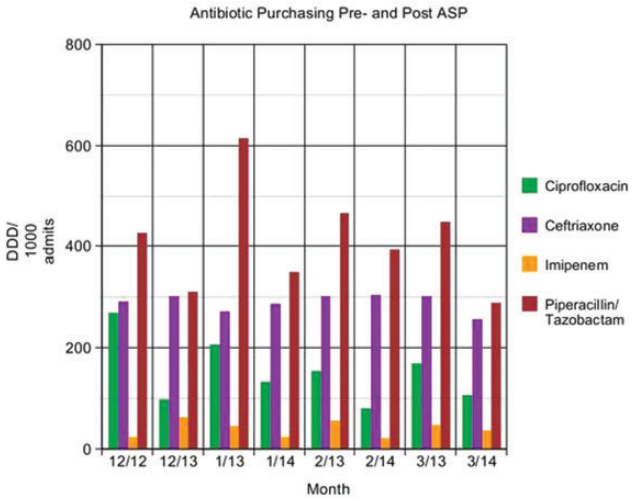
Background. As of 2014, the CDC recommends that all acute care hospitals implement Antimicrobial Stewardship Programs (ASP). Montefiore is an academic medical center with 1490 beds and ASP since 2008. Recently, Montefiore acquired a new

campus, a 369-bed acute care facility in the community with no formal ASP. A review of prescribing from 2010-2013 showed a disproportionally large consumption of IV antimicrobials, particularly quinolones. In 2013 an ID physician and ID pharmacist were hired to extend Montefiore ASP to the new campus.

Methods. ASP launched in December 2013 adapted from existing policies at Montefiore but tailored to our patients, prescribers, and pathogens. Target activities include 1) prior authorization, 2) audit and feedback at 72-hours, 3) formal ID consult for drugs of "last resort," 4) IV to PO switch, and 5) education. Prior authorization occurred on weekdays from 8am to 5pm. During off hours, pharmacy authorized antibiotic doses until the next business day with ASP follow up. Initial activities and process measures from December 2013-March 2014 are described, including purchasing data (defined daily doses [DDD] per 1,000 admissions).

Results. 224 pager requests and >500 audit interactions were reviewed from January 2014-March 2014. Overall approval rate was 75%, however only 15% were approved as requested, and adjustments were made to the remaining 85% (i.e., dose, route, duration, suggestion of alternate regimen or work-up). Approval-rate varied by drug. 77% of new requests for IV ciprofloxacin resulted in an alternative regimen due to high rates of gram-negative resistance in New York City. IV to PO switch was successful in 41% of azithromycin and 50% of levofloxacin requests. ID consults were recommended in 75 of 224 interactions (33%), and 69% of these occurred within 3 days. Formal educational outreach was provided to diverse services of >100 prescribers. Monthly DDD/1,000 admissions for 4 high volume antibiotics pre- and post ASP onset (December 2012-March 2013 vs December 2013-March 2014) is shown in the graph.



Conclusion. Our early data suggests an impact on antibiotic volume and selection by outreach to large groups of prescribers. Adaptation of the traditional academic ASP model appears successful when applied to a community hospital.

Disclosures. **All authors:** No reported disclosures.

239. A Cluster-Randomized Controlled Trial of Trained Pharmacists and Infectious Disease Clinical Fellows for Approval of Restricted Antibiotics in Hospitalized Medical Patients at Siriraj Hospital

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Background. Siriraj Hospital has implemented post-authorization of target antibiotics (piperacillin/tazobactam, meropenem, imipenem/cilastatin and doripenem) for nearly 10 years. Currently, antibiotic approval is implemented by ID clinical fellows.

Methods. During February – September 2013, we conducted a cluster randomized controlled trial in 6 general medical wards at Siriraj hospital to compare the impact of antibiotics approval by ID clinical fellows vs trained general pharmacists in terms of clinical outcomes, microbiological outcomes and antibiotic consumption and expenditure. Three wards were randomly assigned to the intervention group (the pharmacist group) while the other three wards were assigned to the control group (the fellow group). The target antibiotics can be prescribed by responsible physicians during the first 72 hr, after that an approval from the fellows or the pharmacists is required.

Results. There were 806 enrolled patients. The preliminary analysis included 161 patients with 178 prescriptions in the pharmacist group and 168 patients with 181 prescriptions in the fellow group. Baseline characteristics of both groups were comparable. The equivalence can only be proved in the superimposed infection outcome (Δ = -0.44% [-4.83 to 5.71]) but the non-inferiority of the pharmacist group could be assumed in the ID death (Δ = -3.68% [-10.65 to 3.3]), favorable clinical outcome (Δ = 3.53% [-6.75 to 13.82]) and favorable microbiological outcome (Δ = 7.67% [-1.34 to 16.67]). The defined daily dose (DDD) of target antibiotics per prescription was significantly higher in the pharmacist group (11.76 ± 11.96 vs 10.16 ± 9.50; P = 0.02). However, there was no difference in the DDD of all antibiotics per prescription (32.52 ± 38.27 vs 30.09 ± 39.62; P = 0.36) and cost of target antibiotics or all antibiotics per prescription.

Conclusion. Although the patients who received antibiotic approval by the pharmacists had significantly higher consumption of target antibiotics, there was no significant difference in antibiotic expenditure and important treatment outcomes. Therefore, the trained pharmacists could be an alternative to ID specialists for antibiotic approval in the resource limited setting. (ClinicalTrials.gov number, NCT 01797133)

Disclosures. **All authors:** No reported disclosures.

240. Effectiveness of a Pharmacist Driven Antibiotic Stewardship Program at Two Critical Access Hospitals Using a Remote Infectious Diseases Pharmacist

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Background. Guidelines recommend an infectious diseases (ID) physician and ID trained pharmacist as core members of an antibiotic stewardship program (ASP); however, many hospitals struggle to obtain these resources. The purpose of this study was to evaluate the effectiveness of a pharmacist-driven ASP in two critical access hospitals (CAHs) using a remote ID pharmacist and ID pharmacy resident within the same healthcare system as the ID specialist overseeing the ASP.

Methods. The ID specialist remotely reviewed patients receiving antibiotics at each CAH daily. The ID specialist provided recommendations to the CAH pharmacist, who then made the recommendations to the provider. For the first CAH, recommendation type and outcome were documented by the CAH pharmacists. For the second CAH, the ID specialist documented number of patients reviewed, number of recommendations made to the CAH pharmacist, number of recommendations communicated to the provider, and recommendation type and outcome.

Results. During the first year at hospital one, the ASP made 247 recommendations with an acceptance rate of 88%. Total antibiotic use decreased 4.3% and cost decreased 3.4%. During the first 6 months at hospital two, 424 patient reviews were completed by the ID specialist resulting in 85 recommendations to the CAH pharmacist. Of those recommendations communicated to the provider (N = 75, 88%), there was an 87% acceptance rate. During the first 5 months, antibiotic use decreased 12.2% and cost increased 6.2%.

Conclusion. The ASPs at these two CAHs are unique in that they are pharmacist-driven and utilize an ID pharmacist and ID pharmacy resident as the ID specialist. This study demonstrates that using a remote ID pharmacist and ID pharmacy resident is a potential model for healthcare systems to provide ASP services to multiple institutions that would otherwise not have the resources to implement an ASP individually.

Disclosures. **All authors:** No reported disclosures.

241. Effectiveness of a Stewardship Program in Reducing Antimicrobial Use in a Tertiary Care Hospital ICU in Southern Ontario

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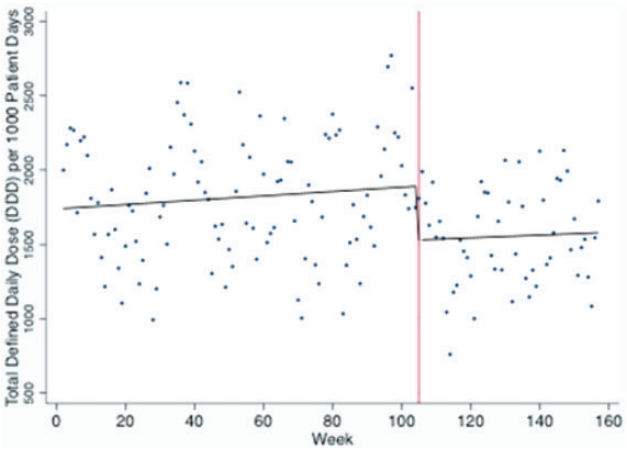
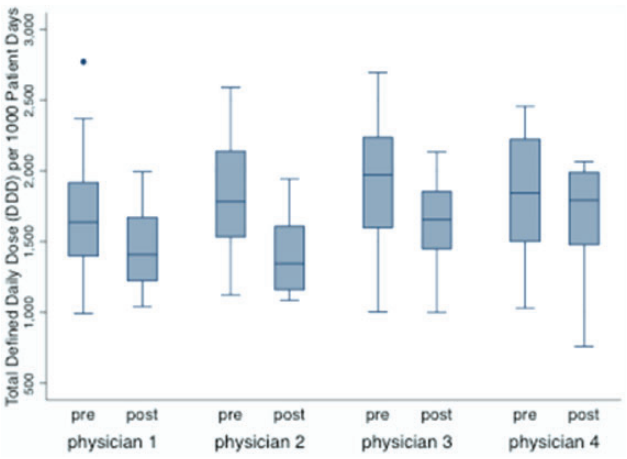
Background. While the benefits of antimicrobial stewardship programs (ASP) in reducing antimicrobial use in the intensive care unit (ICU) setting are suggested in the literature, few data exist regarding its effectiveness at the individual intensivist level. This study sought to assess the impact of an ASP in an ICU at a large tertiary care hospital on the ICU- as well as the individual intensivist level.

Methods. This study used a quasi-experimental design to compare antimicrobial utilization at the unit as well as at the individual intensivist level. Antimicrobial utilization in defined daily doses (DDD) per 1,000 patient days was collected for each of the four intensivists (1-week rotations) in a single 19-bed ICU in a tertiary care hospital in Ontario, Canada. From weeks 0-105, weekly ICU stewardship rounds were held (pre phase). From week 106 on, rounds took place twice weekly, were more formalized, and supported by teaching sessions (post phase). Average DDD were compared using segmented regression/time series analysis. ANOVA was used to compare average DDDs by phase (pre/post) and by intensivist including an interaction term.

Results. There was a 20% reduction in average DDD/1,000 patients days of antimicrobials post intervention (segmented regression, p = 0.006) (Figure 1a), mostly driven by antibiotics, and specifically piperacillin/tazobactam. Also, there was less weekly variation as demonstrated by an 18% reduction in the standard deviation in the post phase. There was a reduction in the average antimicrobial utilization in DDD/1,000 patients days for all intensivists (Figure 1b). Despite a range in this reduction from 180 to 487 in individual intensivists, the effect did not differ significantly between intensivists (ANOVA p = 0.07).





Conclusion. An ASP was effective in reducing the total weekly DDDs and the variability in utilization of antimicrobials in the ICU. The program seemed to have a similar effect on all participating intensivists.

Disclosures. **All authors:** No reported disclosures.

242. Stewardship in Community Hospitals – Optimizing Outcomes and Resources (SCORE): A Baseline Analysis of Antimicrobial Use Utilizing CDC NHSN AU Data

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Background. The SCORE study is a cluster randomized trial of antimicrobial stewardship interventions at 15 small community hospitals (SCHs, bed range: 8 – 126). Antimicrobial use in SCHs is poorly described. As a pre-intervention baseline analysis we analyzed variability in antimicrobial use in SCHs and sought to identify candidate variables to facilitate case-mix adjustment for interhospital comparison using NHSN data .

Methods. Intermountain Healthcare includes 15 SCHs that report to the NHSN Antimicrobial Use option, a validated approach for antimicrobial use measurement. Use was reported in days of antibiotic therapy (DOT)/1,000 pt days (PD) monthly from 2011-13. Floors were categorized as: 1) ICU, 2) medical/surgical, 3) pediatrics, and 4) other (e.g., labor/delivery). An average 3 year rate of antimicrobial use was calculated for floor type and facility. 95% CI were calculated assuming a Poisson distribution. A mixed effect Poisson regression model with a random hospital effect was fitted to characterize variation in antimicrobial use among facilities and floor types.

Results. Total antimicrobial utilization varied widely across the 15 SCHs (range: 134- 671 DOT/1,000 PD, coefficient of variation [CV] = 36%), Figure 1. Examination of antimicrobial use within floor types revealed significant differences in antimicrobial use (Table 1). ICUs had the highest use of antimicrobials with a mean of 893 DOT/1,000PD (range: 782 – 1158) but the lowest CV (16%) in mixed effects analysis. "Other" floors had lowest use with a mean of 74 DOT/1,000PD (range: 13 – 167) but the largest CV = 72%. Mean use in medical/surgical floors was 627 DOT/1,000 PD (range: 147 – 790, CV = 43%). Mean use in pediatric floors was 503 DOT/1,000PD (range 401 – 586, CV = 19%).

Figure 1. Total antimicrobial usage rates of 15 SCHs in Utah

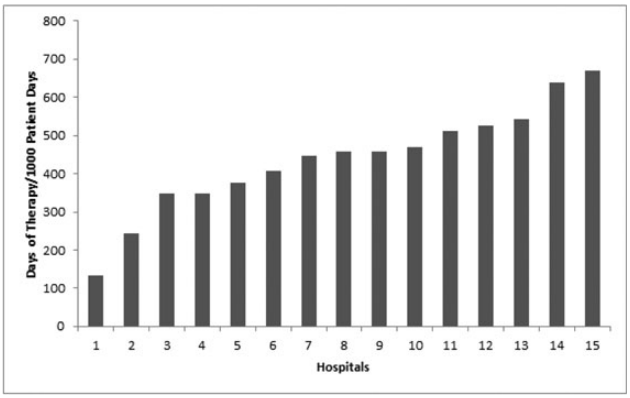

Table 1. Relative risk of antimicrobial use per floor type

Floor type	RR (95% CI)	P value
Other	reference	
Pediatrics	6.7 (6.5, 6.8)	<0.001
Med/Surg	8.8 (8.7, 9.0)	<0.001
ICU	11.1 (10.9, 11.4)	<0.001

Conclusion. There is substantial variation total antimicrobial use across SCHs. Total use is dependent, in part, on the case-mix of patients served in each facility and floor type is a promising variable for adjustment to be used for interhospital benchmarking. Nonetheless, variability in use remains substantial within floor types and is a potential target for stewardship opportunities.

Disclosures. **All authors:** No reported disclosures.

243. Role of a Dedicated Full-time Infectious Diseases Pharmacist in Antimicrobial Stewardship: a Tale of Two Veterans Affairs Medical Centers

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Background. Antimicrobial stewardship can minimize adverse events from antibiotics, development of resistance, and costs. Two potential stewardship targets are in initiation and streamlining of therapy.

Methods. We examined indicators of quality in initiating and streamlining antibiotic therapy between two Veterans Affairs (VA) hospitals with different stewardship programs: VA Greater Los Angeles (GLA), which has a dedicated full-time infectious diseases (ID) pharmacist who reviews all broad-spectrum parenteral antibiotic usage, and the Denver VA (DEN), which has a more decentralized model where individual ward pharmacists are responsible for stewardship. We reviewed a sample of 300 cases of inpatient parenteral antibiotic use (200 at GLA from October 2011-October 2012 and 100 at DEN from July 2010-June 2011).

Results. For antibiotic indication, GLA cases were more likely to have an indication for antibiotic therapy documented [199/200 (99%) vs 95/100 (95%), p = 0.017] and appropriate empirical therapy prescribed [194/200 (97%) vs 87/100 (87%), p = 0.002] but were less likely to have appropriate cultures collected [121/186 (65%) vs 82/100 (82%), p = 0.002]. For antibiotic streamlining, GLA cases were more likely to have therapy modified within 24 hours of lab data being available [133/152 (87%) vs 37/51 (73%), p = 0.016], to be converted to oral medication appropriately [100/123 (81%) vs 41/67 (61%), p = 0.003], and to have antibiotics discontinued when bacterial

infection was determined to not be present [39/50 (78%) vs 11/33 (33%), p < 0.0001]. The presence of any streamlining activity was higher at GLA regardless of whether ID consultation was obtained [174/191 (91%) vs 47/95 (49%) overall and 128/143 (90%) vs 36/70 (51%) without ID consult, p < 0.0001 for both].

Conclusion. Our findings strongly support the presence of a full-time ID pharmacist in antimicrobial stewardship, particularly in influencing streamlining of therapy, but opportunities for improvement in both initiation of and streamlining of therapy still exist even when a full-time ID pharmacist is present.

Disclosures. **All authors:** No reported disclosures.

244. Organizational Factors Associated with Antibacterial Use Among Academic Medical Centers

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Background. Interhospital comparisons of antibacterial use can inform hospitals of targets for antimicrobial stewardship strategies. Variability in patient mix and organizational features may impact on drug use. Thus, we aimed to identify organizational factors among academic medical centers that impact on the amounts of antibacterials prescribed.

Methods. Data concerning antibacterials were obtained from administrative data from 89 University HealthSystem Consortium hospitals for adult patients (age ≥ 18) for 2011. Antibacterials were measured in Days of Therapy per 100 admissions. The following data were also obtained: case mix index (CMI); bedsize (expressed as < or > the median); the % of intensive care unit days; average length of stay (LOS); a marker for market competition, the Herfindahl Index (HHI); region [Northeast (NE), South, Midwest, West]. The number of admissions per 35 UHC Clinical Service Lines (CSLs) was collapsed into 4: Surgery; Medicine; Transplant; Other [expressed as < or > the median]. Three forward stepwise regression models were conducted to identify factors associated with total antibacterial, total antipseudomonal [antipseudomonal fluoroquinolones, cephalosporins, β-lactam/β-lactamase inhibitors, and carbapenems], and anti-methicillin resistant S. aureus (MRSA) [vancomycin + linezolid + daptomycin + tigecycline + ceftaroline + quinupristin/dalfopristin] drug use.

Results. For all models, the following variables were statistically significant (p < 0.05) and positively associated with antibacterial use: LOS; region South as compared to NE; while HHI and Other CSL were significant and negatively associated with antibacterial use. In addition, Surgery and Transplant CSLs were significant and positively associated with antipseudomonals [p = 0.03 and 0.01, respectively] and the region West as compared to NE was significant and positively associated with anti-MRSA agents [p = 0.04].

Conclusion. Several factors were associated with total antibacterial, antipseudomonal, and anti-MRSA drug use, including HHI, LOS, region, and CSL type. Incorporation of these factors into interhospital analyses can aid in more meaningful antibacterial comparisons.

Disclosures. **All authors:** No reported disclosures.

245. Ceftolozane/Tazobactam Activity Tested against Aerobic Gram-negative Organisms Isolated from Intra-abdominal Infections in United States Hospitals (2013)

David J. Farrell, PhD; Helio S. Sader, MD, PhD; Robert K. Flamm, PhD; Ronald N. Jones, MD; JMI Laboratories, North Liberty, IA

Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. Timely and appropriate antimicrobial therapy is important for the management of intra-abdominal infection (IAI). Ceftolozane/tazobactam (TOL/TAZ) is a novel antibacterial with activity against *P. aeruginosa*, including drug-resistant strains, and Enterobacteriaceae, including many ESBL-producing and MDR strains. TOL/TAZ is currently under clinical development for treatment of complicated IAI.

Methods. 425 isolates (1 per patient) were collected in 27 hospitals in the USA from patients with IAI by the Program to Assess TOL/TAZ Susceptibility (PACTS) in 2013. Susceptibility (S) testing was performed by CLSI broth microdilution methods.

Results. TOL/TAZ was potent ($MIC_{50/90}$, 0.25/1 μg/mL) against 364 Enterobacteriaceae inhibiting 95.6% of isolates at ≤8 μg/mL. *E. coli* was the most common organism (43.5% of total) and had overall ESBL-/MDR-phenotype rates of 12.4/4.9%. All *E. coli* strains were S to meropenem (MEM) and 98.9% were inhibited at TOL/TAZ of ≤8 μg/mL ($MIC_{50/90}$, 0.25/0.5 μg/mL). *E. coli* S rates for gentamicin (GEN) and levofloxacin (LVX) were 85.9 and 72.3%, respectively. Among *Klebsiella* spp. (KSP; 2nd most common pathogen, 20.7%), ESBL/MDR rates were 18.2/13.6%. TOL/TAZ was active ($MIC_{50/90}$, 0.25/32 μg/mL; inhibited 89.8% at ≤8 μg/mL) against most KSP, but was less active against ESBL and MDR strains inhibiting only 43.8 and 25.0% at ≤8 μg/mL, respectively, TOL/TAZ was more active against MEM-S-ESBL phenotype KSP (Figure). S rates to GEN and LVX were 92.0 and 88.6%, respectively. TOL/TAZ ($MIC_{50/90}$, 0.5/2 μg/ml) showed greater activity than CAZ ($MIC_{50/90}$, 2/32 μg/ml) and piperacillin/TAZ (PIP/TAZ; $MIC_{50/90}$, 4/ > 64 μg/ml) against *Enterobacter* spp. *P. aeruginosa* (PSA) was the 3rd most common pathogen (13.6%); TOL/TAZ ($MIC_{50/90}$, 0.5/2 μg/mL) and amikacin ($MIC_{50/90}$, 2/8 μg/mL; 100.0% S) were the most active compounds tested. TOL/TAZ was 4- to 16-fold more active than ceftazidime (CAZ; $MIC_{50/90}$, 2/32 μg/mL) when tested against PSA.

Conclusion. TOL/TAZ was very active against aerobic Gram-negative organisms isolated from IAIs in USA hospitals in 2013. TOL/TAZ coverage against Enterobacteriaceae was comparable to MEM and greater than PIP/TAZ and CAZ. TOL/TAZ activity against PSA was greater than MEM, PIP/TAZ and CAZ.

	% Susceptible (CLSI criteria)			
Organism (no. tested)	TOL/TAZ[a]	PIP/TAZ	CAZ	MEM
All Enterobacteriaceae (364)	(95.6)[a]	89.0	87.9	97.5
E. coli (185)	(98.9)[a]	94.1	91.9	100.0
ESBL-phenotype (23)	(91.3)[a]	78.3	34.8	100.0
MDR (9)	(77.8)[a]	44.4	11.1	100.0
Klebsiella spp. (88)	(89.8)[a]	83.0	86.4	89.8
ESBL-phenotype (16)	(43.8)[a]	6.3	25.0	43.8
MEM-S-ESBL phenotype (7)	(71.4)	14.3	57.1	100.0
MDR (12)	(25.0)[a]	0.0	8.3	25.0
Enterobacter spp. (41)	(95.1)[a]	75.0	73.2	100.0
P. aeruginosa (58)	(98.3)[a]	82.8	87.9	73.7
MDR (9)	(88.9)[a]	22.2	55.5	0.0

a. Inhibited at ≤8 μg/mL.

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246. Frequency of Occurrence and Antimicrobial Susceptibility of Gram-negative Organisms Isolated from Health Care–Associated (HCA) Urinary Tract Infections (UTI) in the United States: Results from the Program to Assess Ceftolozane/Tazobactam Susceptibility (PACTS)

David J. Farrell, PhD; Helio S. Sader, MD, PhD; Robert K. Flamm, PhD; Ronald N. Jones, MD; JMI Laboratories, North Liberty, IA

Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. HCA-UTI is the most frequent HCA infection and responsible for significant patient morbidity and mortality. Ceftolozane/tazobactam (TOL/TAZ; formerly CXA-201) is currently under clinical development for the treatment of nosocomial pneumonia, complicated intra-abdominal infections and complicated UTIs. We evaluated the activity of TOL/TAZ and comparators tested against Gram-negative organisms causing HCA-UTI in United States (USA) hospitals.

Methods. In 2013, a total of 1451 unique patient organisms were consecutively collected from USA medical centers from patients with HCA-UTI. Susceptibility (S) testing was performed for TOL/TAZ (TAZ at fixed 4 μg/mL) and many comparators by reference CLSI broth microdilution methods.

Results. The most frequently isolated pathogens were *E. coli* (EC; 52.2%), *Klebsiella* spp. (KSP; 14.1%), indole-positive *Proteus* spp. (IPP; 7.2%), *Enterobacter* spp. (ESP; 6.6%) and *P. aeruginosa* (PSA; 6.2%). EC and KSP ESBL-phenotype rates were 12.1% and 17.6%, respectively. TOL/TAZ inhibited 97.4% of 1,355 Enterobacteriaceae ($MIC_{50/90}$, 0.25/1 μg/mL) and 72.9% of 107 (7.9%) multidrug-resistant (MDR) strains, 99.9% of all EC and 99.6% of ESBL-phenotype EC, and 90.2% of all KSP and 44.4% of ESBL-phenotype KSP at ≤8 μg/mL. Susceptibility (S) rates for levofloxacin (LEV) and gentamicin (GEN) were 73.4 and 89.6% for EC, 86.2 and 87.7% for KSP, 75.0 and 85.6% for IPP, and 92.7 and 94.8% for ESP, respectively. TOL/TAZ ($MIC_{50/90}$, 0.5/8 μg/mL; 92.7% at ≤8 μg/mL) demonstrated greater activity than CAZ ($MIC_{50/90}$, 0.5/ > 32 μg/mL; 76.0% S) and P/T ($MIC_{50/90}$, 4/ > 64 μg/mL; 78.9% S) when tested against ESP. TOL/TAZ ($MIC_{50/90}$, 0.25/1 μg/mL; 99.0% at ≤8 μg/mL) demonstrated greater potency than CAZ ($MIC_{50/90}$, 0.12/8 μg/mL; 88.3% S) and P/T ($MIC_{50/90}$, 4/ > 64 μg/mL; 99.0% S) when tested against IPP. TOL/TAZ inhibited 98.9% of PSA ($MIC_{50/90}$, 0.5/1 μg/mL) and 10/11 (90.9%) of MDR strains at ≤8 μg/mL. PSA had S rates to meropenem (83.0%), CAZ (90.0%), P/T (83.3%), LEV (75.6%) and GEN (90.0%).

Conclusion. TOL/TAZ demonstrated potent activity against contemporary (2013) Gram-negative bacilli, including many ESBL-phenotype and MDR strains, and may represent a valuable treatment option for HCA-UTI in the USA.

Organism (no. tested)	No. of isolates (cumulative %) inhibited at MIC (µg/mL): ≤0.25	0.5	1	2	4	8	16	≥32
Enterobacteriaceae (1355)	962 (71.0)	248 (89.3)	63 (94.0)	16 (95.1)	17 (96.4)	14 (97.4)	10 (98.2)	25 (100.0)
MDR (107)	12 (11.2)	31 (40.2)	16 (55.1)	6 (60.8)	6 (66.4)	7 (72.9)	7 (79.4)	22 (100.0)
E. coli (758)	642 (84.7)	82 (95.5)	23 (98.6)	4 (99.1)	3 (99.5)	1 (99.6)	1 (99.7)	2 (100.0)
ESBL-phenotype (92)	25 (27.2)	37 (67.4)	20 (89.1)	3 (92.4)	3 (95.7)	1 (96.7)	1 (97.8)	2 (100.0)
Klebsiella spp. (204)	135 (66.2)	36 (83.8)	8 (87.8)	2 (88.7)	1 (89.2)	2 (90.2)	3 (91.7)	17 (100.0)
ESBL-phenotype (36)	4 (11.1)	5 (25.0)	2 (30.6)	2 (36.1)	1 (38.9)	2 (44.4)	3 (52.8)	17 (100.0)
MEM-S-ESBL (20)	4 (20.0)	5 (45.0)	2 (55.0)	2 (65.0)	1 (70.0)	1 (75.0)	2 (85.0)	2 (100.0)
Indole (+) proteus spp. (104)	57 (54.8)	33 (86.5)	7 (93.3)	4 (97.1)	1 (98.1)	1 (99.0)	0 (99.0)	1 (100.0)
Enterobacter spp. (96)	44 (45.8)	20 (66.7)	8 (75.0)	2 (77.1)	8 (85.4)	7 (92.7)	3 (95.8)	4 (100.0)
P. aeruginosa (90)	6 (6.7)	52 (64.4)	23 (90.0)	6 (96.7)	2 (98.9)	0 (98.9)	0 (98.9)	1 (100.0)
MDR (11)	0 (0.0)	1 (9.1)	5 (54.6)	2 (72.7)	2 (90.9)	0 (90.9)	0 (90.9)	1 (100.0)

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247. Antimicrobial Activity of Ceftolozane/Tazobactam Tested against Gram-negative Bacterial Isolates from Hospitalized Patients with Pneumonia in United States Hospitals (2013)

David J. Farrell, PhD; Helio S. Sader, MD, PhD; Robert K. Flamm, PhD; Ronald N. Jones, MD; JMI Laboratories, North Liberty, IA

Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. Ceftolozane/tazobactam (TOL/TAZ) is a novel antibacterial with activity against *P. aeruginosa* (PSA) and other common Gram-negative pathogens (GN). TOL/TAZ is currently under clinical development for the treatment of nosocomial pneumonia, complicated intra-abdominal infections and complicated UTIs. The in vitro activity of TOL/TAZ was tested against GN in patients hospitalized with pneumonia in USA hospitals.

Methods. 1458 isolates were consecutively collected in 29 USA hospitals from patients with pneumonia in 2013. Susceptibility (S) testing was performed by CLSI broth microdilution methods (TOL/TAZ at a fixed 4 µg/mL of TAZ).

Results. PSA was the most common pathogen (39.8%) and TOL/TAZ was the most active β-lactam tested against PSA (97.6% inhibited at ≤8 µg/mL). PSA exhibited moderate S to meropenem (MEM, 78.1%), ceftazidime (CAZ; 83.0%), cefepime (FEP, 81.2%), piperacillin/TAZ (PIP/TAZ; 75.7%), levofloxacin (LVX; 72.6%), and gentamicin (GEN; 86.0%). TOL/TAZ exhibited activity against CAZ-non-S, MER-non-S PSA, and MDR PSA isolates (Figure). TOL/TAZ was active against *K. pneumoniae* (KPN; $MIC_{50/90}$, 0.5/ > 32 µg/mL) but activity was lower ($MIC_{50/90}$, 32/ > 32 µg/mL) against ESBL-phenotype KPN (31.2%); similar to all β-lactams [including MER (32.2% S)] and LEV (18.6% S) and GEN (57.6% S). TOL/TAZ inhibited 84.2% of MEM-S-ESBL-KPN at ≤8 µg/mL. TOL/TAZ was active against *E. coli* (MIC_{90}, 0.5 µg/mL), including ESBL-phenotype isolates (MIC_{90}, 1 µg/mL). TOL/TAZ inhibited 93.4 and 96.2% *Enterobacter* spp. (ESP) and *Serratia* spp., respectively, at ≤8 µg/mL, and demonstrated activity against CAZ-non-S ESP (70.3% inhibited at ≤8 µg/mL). TOL/TAZ was active against *P. mirabilis* (MIC_{90}, 0.5 µg/mL), *Citrobacter* spp. (MIC_{90}, 4 µg/mL) and indole (+) *Proteae* (MIC_{90}, 1 µg/mL). All β-lactams had limited activity against *Acinetobacter* spp.

Conclusion. In GN isolates from hospitalized patients with pneumoniae in USA hospitals, TOL/TAZ demonstrated greater in vitro activity than currently available cephalosporins, carbapenems, and P/T when tested against PSA, including MDR strains. Additionally, TOL/TAZ demonstrated greater activity than currently available cephalosporins and PIP/TAZ against Enterobacteriaceae from pneumonia specimens.

Disclosures. **D. J. Farrell**, Cubist Pharmaceuticals: Grant Investigator, Research grant **H. S. Sader**, Cubist Pharmaceuticals: Grant Investigator, Research grant **R. K. Flamm**, Cubist Pharmaceuticals: Grant Investigator, Research grant **R. N. Jones**, Cubist Pharmaceuticals: Grant Investigator, Research grant

248. S-649266, a Novel Siderophore Cephalosporin: Efficacy against *Klebsiella pneumoniae* producing NDM-1 or KPC in rat lung infection model with recreated humanized exposure profile of 2 gram dose with 1 hour and 3 hours infusion

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Background. S-649266 ('266), which was discovered by Shionogi and Co., Ltd. is a novel catechol-substituted siderophore cephalosporin with potent activity against Gram-negative pathogens including multi-drug resistant (MDR) isolates. In this study, *in vivo* therapeutic efficacy of '266 was evaluated in rat lung infection models.

Methods. Exposure profile of free concentrations of '266 in human plasma was recreated in cannulated rats derived from the PK profile with 2 g dose by 1 hour infusion in healthy volunteers (phase 1). The 2 gram human PK profiles were modeled for both 1 and 3 hour infusion. With the recreated human PK profiles, the efficacy of '266 was evaluated against 2 strains of NDM-1 producing *K. pneumoniae* and 3 strains of KPC producing *K. pneumoniae* in rat lung infection model. MIC of '266 was determined by using both CAMHB supplemented with apotransferrin (apo-T) and chelex treated Iso-Sensitest Broth(CT-ISB), and $T_{>MIC}$ was evaluated. MICs (CAMHB with apo-T/CT-ISB) were as follows: *K. pneumoniae* VA-391 (KPC producer); MIC = 0.125/8 µg/mL, *K. pneumoniae* VA-384 (KPC producer); MIC = 0.5/16 µg/mL, *K. pneumoniae* VA-361 (KPC producer); MIC = 0.125/16 µg/mL, *K. pneumoniae* Kl2 (NDM-1 producer); MIC = 1/8 µg/mL, *K. pneumoniae* NCTC13443 (NDM-1 producer); MIC = 4/16 µg/mL.

Results. The treatment with 1 hour infusion of '266 showed little or no efficacy against all the strains, but the treatment with 3 hours infusion of '266 decreased viable cells to below the limit of detection. $T_{>MIC}$required for bactericidal activity was approximately ≥80%. Viable cell numbers in lung are as follows.

Organism (no. tested)	No. of isolates (cumulative %) inhibited at TOL/TAZ MIC (μg/mL) of:								MIC_{alone}
	≤0.5	1	2	4	8	16	32	>32	
P. aeruginosa (581)	300 (51.6)	170 (80.9)	56 (90.5)	26 (95.0)	15 (97.6)	5 (98.5)	1 (98.6)	8 (100.0)	0.5/2
CAZ-non-S (99)	4 (4.0)	12 (16.2)	34 (50.5)	21 (71.7)	14 (85.9)	5 (90.9)	1 (91.9)	8 (100.0)	2/16
MEM-non-S (170)	50 (29.4)	60 (64.7)	23 (78.2)	17 (88.2)	8 (92.9)	4 (95.3)	1 (95.9)	7 (100.0)	1/8
MDR (94)	8 (8.5)	23 (33.0)	26 (60.6)	16 (77.7)	8 (86.2)	4 (90.4)	1 (91.5)	8 (100.0)	2/16
K. pneumoniae (189)	128 (67.7)	13 (74.6)	4 (76.7)	1 (77.3)	2 (78.3)	7 (82.0)	11 (87.8)	23 (100.0)	0.5/>32
ESBL-phenotype (59)	8 (13.6)	4 (20.3)	3 (25.4)	1 (27.1)	2 (30.5)	7 (42.4)	11 (61.0)	23 (100.0)	32/>32
MEM-S-ESBL (19)	8 (42.1)	4 (63.2)	2 (73.7)	1 (79.0)	1 (84.2)	1 (89.5)	0 (89.5)	2 (100.0)	1/>32
Enterobacter spp. (167)	124 (74.3)	6 (77.8)	12 (85.0)	8 (89.8)	6 (93.4)	5 (96.4)	3 (98.2)	3 (100.0)	0.25/8
Serratia spp. (156)	98 (62.8)	37 (86.5)	9 (92.3)	5 (95.5)	1 (96.2)	0 (96.2)	1 (96.8)	5 (100.0)	0.5/2
E. coli (134)	129 (96.3)	3 (98.5)	1 (99.3)	0 (99.3)	1 (100.0)	-	-	-	0.25/0.5
ESBL-phenotype (20)	17 (85.0)	1 (90.0)	1 (95.0)	0 (95.0)	1 (100.0)	-	-	-	0.25/1

Conclusion. The human PK profile of S-649266 was successfully recreated in rat. The 2g TID 3 hours infusion of '266 showed potent efficacy against *K. pneumoniae* producing NDM-1 or KPC causing pneumonia.

Human exposure profile recreated in rat	Viable cell number in lung (log CFU/lung, average±SD)				
	K. pneumoniae VA-391 (KPC)	K. pneumoniae VA-384 (KPC)	K. pneumoniae VA-361(KPC)	K. pneumoniae KI2(NDM-1)	K. pneumoniae NCTC13443 (NDM-1)
S-649266_2g TID_1hr infusion	3.7±2.3	6.4±1.1	4.3±1.9	≤1.2	4.6±2.1
S-649266_2g TID_3hr infusion	≤ 1.2	≤ 1.2	1.6±0.8	1.9±1.3	1.4±0.3
1 hr baseline controls	5.6±0.7	5.5±0.4	5.9±0.7	4.9±0.6	5.7±0.6
96 hr saline-treated controls	5.9±0.8	6.2±1.0	7.2±0.8	7.8±0.9	7.1±0.7

Disclosures. **M. Tsuji**, Shionogi and Co., Ltd.: Employee, Salary **C. Singley**, Glaxo SmithKline: Employee, Salary **T. Horiyama**, Shionogi and Co., Ltd.: Employee, Salary **R. Nakamura**, Shionogi and Co., Ltd.: Employee, Salary **R. Echols**, Shionogi and Co., Ltd.: Consultant and Employee, Salary **S. Rittenhouse**, GlaxoSmithKline: Employee, Salary **Y. Yamano**, Shionogi and Co., Ltd.: Employee, Salary **J. Shimada**, Shionogi and Co., Ltd.: Consultant and Employee, Salary

249. Activity of Plazomicin Against Contemporary Isolates of Enterobacteriaceae from New York City

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Background. Plazomicin is a next generation aminoglycoside that is not affected by most commonly-encountered aminoglycoside modifying enzymes and is currently being studied in a global Phase 3 trial enrolling patients with bloodstream infections or nosocomial pneumonia due to carbapenem-resistant Enterobacteriaceae. The activity of this novel agent was tested against a contemporary collection of Enterobacteriaceae from New York City.

Methods. Unique patient isolates of *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter* spp. were gathered from 11 hospital microbiology laboratories from November 2013 through January 2014. Isolates underwent susceptibility testing by the agar dilution method according to CLSI guidelines. Cephalosporin-resistant isolates were screened for the presence of bla_{KPC}.

Results. A total of 2866 isolates of *E. coli* (two with bla_{KPC}), 944 isolates of *K. pneumoniae* (125 with bla_{KPC}), and 216 isolates of *Enterobacter* spp. (7 with bla_{KPC}) were collected. Susceptibility results for gentamicin, amikacin, and plazomicin are shown in the table.

Among the 125 isolates of *K. pneumoniae* with bla_{KPC}, the MIC_{50} and MIC_{90} values for plazomicin were 0.5 and 1 μg/ml, respectively.

	MIC_{50}	MIC_{90} μg/ml	Range	Percent susceptible
E. coli (n=2866)				
Gentamicin	1	>8	≤0.25 - >8	85%
Amikacin	2	4	≤0.5 - >64	99.5%
Plazomicin	1	1	0.12 - 4	
K. pneumoniae (n=944)				
Gentamicin	0.5	>8	≤0.25 - >8	78%
Amikacin	2	32	≤0.5 - >64	88%
Plazomicin	0.5	0.5	0.12 - 32	
Enterobacter spp. (n=216)				
Gentamicin	0.5	2	≤0.25 - >8	92%
Amikacin	2	4	≤0.5 - 64	97%
Plazomicin	0.5	1	0.25 - 4	

Conclusion. Plazomicin is an investigational aminoglycoside with broad-spectrum activity against common Enterobacteriaceae, including multidrug-resistant strains of K. pneumoniae. Further studies with this agent are warranted.

Disclosures. **C. Urban**, Pfizer: Speaker's Bureau, Speaker honorarium; Cubist: Speaker's Bureau, Speaker honorarium **D. Landman**, Tetraphase: Research Contractor, Research grant; Achaogen: Research Contractor, Research grant **J. Quale**, Tetraphase: Research Contractor, Research grant; Achaogen: Research Contractor, Research grant.

250. Ceftazidime-avibactam Activity Tested Against a Large Collection of Enterobacteriaceae Isolates Collected in United States (USA) Hospitals in the 2011-2013 Period, Including Organisms Producing KPC- and CTX-M-variants

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Background. Increasing rates of multidrug-resistant (MDR) Enterobacteriaceae (ENT) challenges infection control and antimicrobial stewardship practices. We evaluated the activity of ceftazidime-avibactam (CAZ-AVI), a cephalosporin combined with a serine-β-lactamase (BL) inhibitor displaying activity against ENT, including those producing contemporary BLs.

Methods. 20,709 ENT isolates collected from 2011 to 2013 in 79 hospitals located in all nine USA Census regions were susceptibility (S) tested by CLSI broth microdilution against CAZ-AVI and comparators. CTX-M- and KPC-encoding genes were identified by a microarray based assay and/or reference PCR/sequencing.

Results. Overall CAZ-AVI inhibited 99.9% of isolates at ≤4 μg/mL (CLSI CAZ-S breakpoint) and was only less potent than meropenem (MIC_{90}, 0.25 and ≤0.06 μg/mL, respectively). Among 25 isolates displaying CAZ-AVI MICs at >4 μg/mL, 15 were indole-positive Proteae with MICs of 8-16 μg/mL and 3 *K. pneumoniae* (KPN) producing metallo-BLs (CAZ-AVI MIC, >32 μg/mL). Against the most prevalent bacterial species, CAZ-AVI inhibited all *E. coli* isolates, 99.9% of KPN and >99.9% of *E. cloacae* (ECL) at ≤4 μg/mL. CAZ-AVI $MIC_{50/90}$ for these species were 0.06/0.12, 0.12/0.25, 0.12/0.5 μg/mL, respectively (Table) whereas CAZ MIC_{90} values were 2, 32 and >32 μg/mL, respectively. All but one *P. mirabilis* were inhibited by CAZ-AVI at ≤0.5 μg/mL. 214 KPC-producers, 497 CTX-M-15-like and 102 CTX-M-14-like strains were identified and CAZ-AVI $MIC_{50/90}$ values for these strains were 0.5/2, 0.12/0.5 and 0.12/0.25 μg/mL, respectively. KPC-producers were very resistant to all comparators with CAZ-AVI, tigecycline ($MIC_{50/90}$, 0.5/1 μg/mL) and colistin ($MIC_{50/90}$, 0.5/2 μg/mL) being the only agents with acceptable coverage.

Organisms/Group (no. tested)	CAZ-AVI MIC (μg/mL): 50%	90%
All (20,709)	0.12	0.25
E. coli (6,486)	0.06	0.12
K. pneumoniae (4,421)	0.12	0.25
E. cloacae (2,261)	0.12	0.5
P. mirabilis (1,626)	≤0.03	0.06
KPC-producers (214)	0.5	2
CTX-M-15-like-producers (497)	0.12	0.5
CTX-M-14-like-producers (102)	0.12	0.25

Conclusion. CAZ-AVI displayed high activity against contemporary ENT isolates, including those producing prevalent CTX-M-variants in the USA, and KPC-producers that are often MDR.

Disclosures. **M. Castanheira**, Forest: Grant Investigator, Research grant **R. N. Jones**, Forest: Grant Investigator, Research grant **H. S. Sader**, Forest: Grant Investigator, Research grant

251. Characteristics and Outcomes of Complicated Intra-abdominal Infections Involving *Pseudomonas aeruginosa* from a Phase 3 Ceftolozane/Tazobactam Study

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Background. Ceftolozane/tazobactam (C/T) is a novel antimicrobial with activity against pathogens causing complicated intra-abdominal infections (cIAIs), including extended-spectrum β-lactamase (ESBL)–producing Enterobacteriaceae and drug-resistant *P. aeruginosa*. The efficacy and safety of C/T + metronidazole (MTZ) compared with meropenem (MEM) were evaluated in a randomized, double-blind phase 3 trial in hospitalized patients with cIAI. This analysis provides information on cIAI involving *P. aeruginosa*, a pathogen poorly described in cIAI.

Methods. Hospitalized patients with cIAI were randomized to 4-14 days of intravenous (IV) C/T (1.5 g) + MTZ (500 mg) every 8 hours or IV MEM (1 g every 8 hours). Baseline intra-abdominal cultures were obtained. The primary efficacy endpoint was the clinical response at the test-of-cure (TOC) visit 26-30 days after the start of study therapy.

Results. In the microbiological intent-to-treat (MITT) population (N = 806), *P. aeruginosa* was isolated in 72 (8.9%) patients (38 C/T + MTZ, 34 MEM); the incidence of *P. aeruginosa* in North America was 18%. *P. aeruginosa* was more frequently associated with polymicrobial infection (94% vs 65%). The highest incidence of *P. aeruginosa* occurred in patients with infections arising from the colon (14%) or appendix (11%). *P. aeruginosa* infections were less likely to be hospital-acquired (2.8% vs 7.1%) but occurred more commonly in those receiving prior antibiotic therapy (65% vs 57%). C/T and MEM were highly active *in vitro* against *P. aeruginosa*, with a minimum inhibitory concentration against 90% of pathogens (MIC_{90}) of 2 μg/mL and 4 μg/mL, respectively. Clinical cure rates in the microbiologically evaluable patients with *P. aeruginosa* were 100% (25/25) and 96% (27/28) for C/T + MTZ and MEM, respectively.

Conclusion. In this phase 3 study in hospitalized patients with cIAI, *P. aeruginosa* was isolated in 8.9% of MITT patients. Interestingly, *P. aeruginosa* was most commonly isolated in community-acquired infections of the colon and appendix. Prior use of MTZ and 3rd generation cephalosporins may have predisposed patients to infection with *P. aeruginosa*. Overall, patients with *P. aeruginosa* responded well to therapies in this study, as demonstrated by the high clinical cure rates.

Disclosures. **B. Miller**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **M. Wooley**, Cubist Pharmaceuticals: Employee, Salary **E. Hershberger**, Cubist Pharmaceuticals: Employee, Salary **J. Steenbergen**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **B. Busa**, Cubist Pharmaceuticals: Employee, Salary **G. Yuan**, Cubist Pharmaceuticals: Employee, Salary **R. Mensah**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **I. Friedland**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **J. Alverdy**, Cubist Pharmaceuticals: Consultant, Consulting fee

252. S-649266, a Novel Siderophore Cephalosporin: *In vitro* activity against Gram-negative bacteria

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Background. S-649266 ('266) is a novel catechol-substituted siderophore cephalosporin for injection discovered by Shionogi and Co., Ltd. In this study, *in vitro* antibacterial activity of '266 is evaluated against the clinical isolates of Gram-negative bacteria.

Methods. MIC was measured by broth microdilution method according to Clinical and Laboratory Standard Institute except that CAMHB supplemented with 20 μM of apo-transferrin (apo-T) was used for evaluation of the activity of '266. In the case of *Acinetobacter baumannii*, Iso-Sensitest Broth (ISB) supplemented with 20 μM of apo-T was used to suppress the trailing effect. Tested isolates were collected from multi-sites in North America, Europe and other regions from 2009 to 2011. Approximately 34% and 23% of tested isolates were resistant to ceftazidime and meropenem respectively.

Results. '266 showed potent *in vitro* activity against a broad spectrum of Gram-negative bacteria. MIC_{90} of '266 against 1086 strains of Gram-negative bacteria was 2 μg/mL. MIC_{90} against *Pseudomonas aeruginosa, Stenotrophomonas maltophilia* and most of Enterobacteriaceae were 1 μg/mL or less, and MIC_{90} against *A. baumannii* was 2 μg/mL. These results demonstrated the potent antimicrobial activity of '266 against a variety of Gram-negative bacteria including strains non-susceptible to ceftazidime, meropenem, levofloxacin or ciprofloxacin.

Species	N	MIC_{90} (μg/mL) S-649266	Ceftazidime	Meropenem	Levofloxacin	Cefepime
Total isolates	1086	2	>32	>16	>8	>32
Pseudomonas aeruginosa	104	1	>32	>16	>8	32
Klebsiella pneumoniae	105	0.12	>32	0.12	>8	>32
Escherichia coli	106	1	2	≤0.06	>8	8
Stenotrophomonas maltophilia	108	0.5	>32	>16	8	>32
Serratia marcescens	103	≤0.06	1	2	2	1
Enterobacter aerogenes	100	0.5	>32	≤0.06	0.5	4
Enterobacter cloacae	103	1	>32	0.12	4	8
Citrobacter freundii	100	0.12	>32	≤0.06	8	8
Acinetobacter baumannii	103	2	>32	>16	>8	>32

Conclusion. S-649266 has potent antimicrobial activity against a variety of Gram-negative bacteria under iron-deficient conditions, suggesting the potential use of '266 for the treatment of resistant strains.

Disclosures. **M. Tsuji**, Shionogi and Co., Ltd.: Employee, Salary **A. Ito**, Shionogi and Co., Ltd.: Employee, Salary **R. Nakamura**, Shionogi and Co., Ltd.: Employee, Salary **Y. Yamano**, Shionogi and Co., Ltd.: Employee, Salary **J. Shimada**, Shionogi and Co., Ltd.: Consultant and Employee, Salary

253. Activity of Eravacycline Against Enterobacteriaceae and *Acinetobacter baumannii* from New York City

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Background. Multidrug-resistant Gram-negative bacteria have become established in hospitals in New York City. Novel antibiotics are sorely needed to treat infections due to multidrug-resistant strains. Eravacycline is a novel fluorocycline, and is

not affected by common mechanisms leading to tetracycline resistance. In this study we examine the activity of eravacycline against Gram-negative pathogens from New York City, a region plagued by MDR strains.

Methods. From November 2013 through January 2014, single patient bacterial isolates were gathered from 11 hospitals in Brooklyn and Queens, NY. Isolates underwent susceptibility testing by dilution techniques according to CLSI methodology. Cephalosporin-resistant isolates were also screened by PCR for the presence of bla_{KPC}.

Results. Among 2866 isolates of *E. coli*, 87% were susceptible to cephalosporins and 99.8% to carbapenems; two possessed bla_{KPC}. For 944 *Klebsiella pneumoniae*, 67% were susceptible to cephalosporins and 86% to carbapenems; 13% possessed bla_{KPC}. For 216 *Enterobacter* spp., 75% were susceptible to cephalosporins and 95% to carbapenems; 3% possessed bla_{KPC}. For 158 *Acinetobacter baumannii*, 34% were susceptible to cephalosporins and 31% to carbapenems. The susceptibility results for tetracycline and eravacycline are listed in the table.

Among 125 isolates of *K. pneumoniae* with bla_{KPC}, the MIC_{50} and MIC_{90} values for eravacycline were 0.5 and 1.0 μg/ml, respectively. For 96 isolates of *A. baumannii* resistant to carbapenems, the MIC_{50} and MIC_{90}values were 0.5 and 2 μg/ml, respectively.

	MIC_{50}	MIC_{90} μg/ml	Range	Percent susceptible
E. coli (n=2866)				
Tetracycline	4	>16	≤0.25 - >16	59%
Eravacycline	0.12	0.5	≤0.015 - 4	
K. pneumoniae (n=944)				
Tetracycline	4	>16	1 - >16	68%
Eravacycline	0.25	1	≤0.06 - 8	
Enterobacter spp. (n=216)				
Tetracycline	2	16	≤0.25 - >16	78%
Eravacycline	0.5	1	≤0.12 - 2	
A. baumannii (n=158)				
Tetracycline	>16	>16	2 - >16%	10%
Tigecycline	2	>2	≤0.06 ->2	66%
Eravacycline	0.5	1	≤0.015 - 4	

Conclusion. Eravacycline is a novel antibacterial agent with excellent in vitro activity against *E. coli*, *K. pneumoniae*, *Enterobacter* spp. and *A. baumannii*, including multidrug-resistant isolates.

Disclosures. **C. Urban**, Pfizer: Speaker's Bureau, Speaker honorarium; Cubist: Speaker's Bureau, Speaker honorarium **D. Landman**, Tetraphase: Research Contractor, Research grant; Achaogen: Research Contractor, Research grant **J. Quale**, Tetraphase: Research Contractor, Research grant; Achaogen: Research Contractor, Research grant

254. In Vitro Activity of Ceftazidime in Combination with Avibactam vs 1825 *Pseudomonas aeruginosa* Clinical Isolates Obtained from across Canada as Part of the CANWARD Study, 2009-2013

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Background. Avibactam is a non-beta lactam beta-lactamase inhibitor, with activity against molecular class A, class C, and some class D beta-lactamase enzymes. The purpose of this study was to evaluate the in vitro activity of ceftazidime in combination with avibactam against a large collection of *Pseudomonas aeruginosa* clinical isolates obtained as part of the CANWARD study (2009-2013).

Methods. From January 2009 to December 2013, inclusive, 12 to 15 sentinel hospitals across Canada submitted clinical isolates from patients attending ERs, medical and surgical wards, hospital clinics, and ICUs (CANWARD). Each center was asked to submit clinical isolates (consecutive, one per patient/infection site) from blood (100 to 165), respiratory (100), urine (25 to 50), and wound (25 to 50) infections. Susceptibility testing was performed using broth microdilution as described by CLSI. Doubling concentrations of ceftazidime were evaluated in combination with a fixed concentration of avibactam (4 μg/mL).

Results. 1825 *P. aeruginosa* clinical isolates were obtained as a part of CANWARD. The antimicrobial susceptibility profile of these isolates is presented in the table.

Two-hundred and fifty-seven isolates (14% of the total) were multidrug-resistant (non-susceptible to at least one antimicrobial from 3 or more classes). Ceftazidime-avibactam demonstrated an MIC of ≤8 μg/mL (ceftazidime susceptibility breakpoint) vs 70.4% of MDR isolates. Further, 67.4% of ceftazidime non-susceptible isolates and 79.9% of meropenem non-susceptible isolates had an MIC of ≤8 μg/mL for ceftazidime-avibactam.

Antimicrobial	MIC_{50} (μg/mL)	MIC_{90} (μg/mL)	Susceptibility Breakpoint (μg/mL)	% Susceptible
Amikacin	4	16	≤16	93.0
Ceftazidime	4	32	≤8	82.7
Ceftazidime-Avibactam	2	8	Not defined	No data
Ciprofloxacin	0.25	4	≤1	76.7
Colistin	1	2	≤2	94.6
Gentamicin	2	16	≤4	83.0
Meropenem	0.5	8	≤2	82.0
Piperacillin-Tazobactam	4	64	≤16/4	84.7

Conclusion. The combination of ceftazidime-avibactam demonstrated improved in vitro activity over ceftazidime alone vs *P. aeruginosa* clinical isolates obtained from patients across Canada (4-fold reduction in MIC_{90}). Over two-thirds of MDR isolates evaluated were inhibited by ≤8 μg/mL of ceftazidime-avibactam.

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255. Optimization of a non-canonical anti-infective: interrogation of the target binding pocket for a small molecule inhibitor of *E. coli* polysaccharide capsule expression

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Background. The polysaccharide capsule in *E. coli* is a major pathogenic factor. Loss of encapsulation results in complete attenuation in an otherwise lethal systemic murine infection model. We have previously identified a small molecule inhibitor of capsule biogenesis (designated DU011) and identified its target as MprA, a transcriptional repressor of multi-drug efflux pumps. Unlike other proposed MprA ligands such as salicylate and 2,4-dinitrophenol (DNP), DU011 does not alter *E. coli* antibiotic resistance and has significantly enhanced inhibition of capsule expression. We hypothesized that DU011 interacts uniquely in the MprA binding pocket relative to other ligands to produce a different phenotype and sought to define critical residues in the binding pocket to optimize inhibitor design.

Methods. To identify mutations within MprA that confer resistance to DU011, a plasmid carrying *mprA* was randomly mutated in DNA repair deficient XL-Red cells. In a non-mutator strain of *E.coli*, plasmids were screened for DU011 and DNP resistance by using a capsule dependent phage assay. Individual clones were selected and the plasmids sequenced.

Results. Mutant MprA clones were identified that conferred shared and specific resistance to DU011 and DNP. Mutations mapped to the predicted binding pocket as modeled *in* silico. Biophysical studies demonstrated altered and abrogated binding of DU011 and DNP in purified mutant MprA proteins.

Conclusion. DNP and DU011 use different residues for binding to MprA, which may explain their differential effects on multi-drug efflux pump and capsule regulation. Molecules that target the amino acid residues that are part of the DU011 binding pocket would be good candidates as therapeutics that would inhibit a major pathogenic factor in *E .coli* while maintaining the repression of multi-drug efflux pumps and thereby eliminating a major mechanism of resistance to such molecules.

Disclosures. **All authors:** No reported disclosures.

256. S-649266, a Novel Siderophore Cephalosporin: Mechanisms of enhanced activity and beta-lactamase stability

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Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. Although spread of multi-drug-resistant Gram-negative pathogens causes serious problems, there are limited therapeutic options because of the lack of new promising antibacterial agents. S-649266 ('266) is a novel catechol-substituted siderophore cephalosporin antibiotic with potent antibacterial activity against Gram-negative bacteria including drug-resistant pathogens. This study investigated the mechanisms of enhanced activity and β-lactamase stability of '266.

Methods. MIC was determined by brothmicrodilution methods by using apo-transferrin (apo-T) into the medium and treatment of the medium by Chelex resin. Chelating activity of '266 and iron was evaluated by Chromeazrol B and uptake of '266 was measured by using calcein fluorescence. The kinetic parameters of '266 against carbapenemases were determined to evaluate the stability.

Results. The i*n vitro* activity of '266 increased under free iron deficient conditions such as apo-T supplemented medium. These culture conditions mimic the condition in human infection. The evaluation with Chromeazrol B showed the strong chelating activity of '266 with ferric iron. The rate of iron uptake by *P. aeruginosa* cells were enhanced by addition of '266, suggesting that '266 had siderophore activity with iron transported efficiently into *P. aeruginosa*. The catalytic efficiency (*kcat*/*Km*) of '266 against IMP-1, VIM-2, L1 were 5×10^3, 5×10^3, 2×10^4 M^{-1} s^{-1}, respectively. These values were approximately 10 to 1,000 fold lower than those of meropenem, ceftazidime, and cefepime. The relative hydrolysis velocity of '266 against NDM-1 was lower than that of meropenem. No or only a slight hydrolysis of '266 was observed against KPC-3, P99 and OXA-23, indicating the high stability of '266 to these β-lactamases.

Conclusion. The in vitro activity of S-649266 was enhanced under free iron deficient conditions which mimic the condition in human infection. S-649266, acting through siderophore receptors was transported into *P.aeruginosa*. S-649266 was more stable against carbapenemase than other cephalosporins and carbapenems. These results showed that '266 is a promising siderophore cephalosporin to treat multi-drug resistant Gram-negative pathogens.

Disclosures. **M. Tsuji**, Shionogi and Co., Ltd.: Employee, Salary **A. Ito**, Shionogi and Co., Ltd.: Employee, Salary **T. Horiyama**, Shionogi and Co., Ltd.: Employee, Salary **N. Fukuhara**, Shionogi and Co., Ltd.: Employee, Salary **R. Nakamura**, Shionogi and Co., Ltd.: Employee, Salary **Y. Yamano**, Shionogi and Co., Ltd.: Employee, Salary **J. Shimada**, Shionogi and Co., Ltd.: Consultant and Employee, Salary **Y. Ishii**, Toho Univesity Shool of Medicine: Employee, Salary **K. Tateda**, Toho Uneiversity School of Medicine: Employee, Salary

257. In Vitro Activity of Meropenem/RPX7009, a Carbapenem/β-lactamase Inhibitor Combination Tested Against Contemporary Populations of Enterobacteriaceae and KPC-producing Strains

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Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. We evaluated the activity of meropenem (MER) ± RPX7009 (RPX), a serine-β-lactamase inhibitor (BLI) tested against contemporary isolates of Enterobacteriaceae (ENT), including KPC-producing isolates.

Methods. 100 ENT clinical isolates collected during 2012-2013 were tested against MER ± RPX at fixed 4 and 8 μg/mL using CLSI reference broth microdilution methods. Additionally, 100 KPC-producing ENT were tested.

Results. Against all 200 ENT, MER/RPX displayed $MIC_{50/90}$ of ≤0.25/1 and ≤0.25/0.5 μg/mL at fixed 4 and 8 μg/mL, respectively when compared to $MIC_{50/90}$ ≤0.25/ > 8 μg/ml for MER alone (Table). Overall, 91.5/95.5% and 96.0/99.0% of ENT were inhibited at ≤1/ ≤ 4 μg/mL of MER in the presence of 4 or 8 μg/ml of RPX, respectively. MER/RPX at fixed 4 and 8 μg/mL, inhibited 80.3 and 90.8%, respectively of the *K. pneumoniae* (n = 76) isolates at ≤1 μg/mL (MER CLSI susceptible breakpoint), whereas MER inhibited only 21.1% at the same MIC. Only 32.0% of *E. cloacae* isolates (n = 25) were inhibited at 1 μg/mL of MER, but 96.0% of these isolates were inhibited by MER/RPX (at the same MIC Value) for 4 and 8 μg/mL. All *E. coli* (n = 38), *Serratia* spp. (n = 12) and indole-positive Proteae (n = 11) isolates were inhibited by ≤0.25 μg/mL of MER/RPX at fixed 4 or 8 μg/mL. MER/RPX inhibited 83.0 and 91.0% and 92 and 98 % of the KPC-producers at ≤1 and ≤4 μg/mL of MER for both BLI concentrations, compared to only 3.0% or 24.0% for MER alone, respectively.

Conclusion. These results demonstrate that MER/RPX is a good candidate for further development that could increase the treatment options against serious infections, including those caused by KPC-producers that are often resistant to most antimicrobial agents.

Organism (no. tested)	Antimicrobial agent[a]	Cumulative % inhibited at MIC (μg/mL)[b]: ≤0.25	0.5	1	2	4	8
ENT (200)	MER	50.0	50.5	51.5	54.5	62.0	71.0
	MER/RPX 4	87.0	89.0	**91.5**	94.0	96.0	98.0
	MER/RPX 8	89.5	**92.5**	95.5	98.5	99.0	99.0
K. pneumoniae (76)	MER	19.7	21.1	21.1	22.4	25.0	36.8
	MER/RPX 4	69.7	72.4	73.7	75.0	77.6	85.5
	MER/RPX 8	72.4	75.0	80.3	85.5	89.5	**94.7**
KPC-producers (100)	MER	0.0	1.0	3.0	9.0	24.0	42.0
	MER/RPX 4	74.0	78.0	83.0	88.0	**92.0**	96.0
	MER/RPX 8	79.0	85.0	**91.0**	97.0	98.0	98.0

a. MER/RPX=meropenem/RPX7009; 4=at fixed 4 μg/mL; 8=at fixed 4 μg/mL
b. MIC_{90} are bolded

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258. S-649266 Modeling and Simulation for Prediction of Efficacy and Dose Optimization

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Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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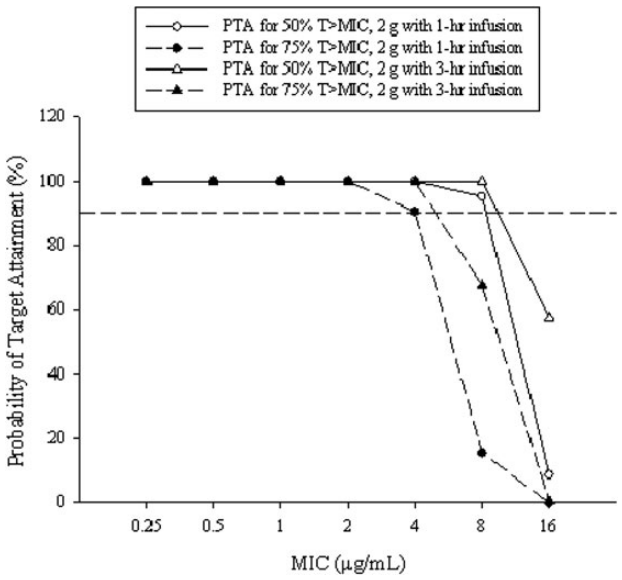
Background. S-649266 is a novel parenteral siderophore cephalosporin discovered by Shionogi and Co., Ltd. which exhibits potent efficacy against various gram negative bacteria including carbapenem resistant strains. The aim of this study is to develop a pharmacokinetic model which describes time courses of S-649266 concentrations in plasma and urine and to predict efficacy for optimizing dosage regimens.

Methods. Plasma and urine concentration data of S-649266 following single (100 to 2,000 mg) or multiple (1,000 and 2,000 mg, q8h dosing) intravenous infusions from a phase 1 study in Japan [54 healthy volunteers (49 Japanese and 5 Caucasian subjects), 1348 points in plasma, 276 points in urine] were used. The plasma and urine data were simultaneously fitted to 3-compartment disposition model by non-linear mixed effect model approach. Probability that time which free drug concentration in plasma exceeds MIC over dosing interval ($fT_{>MIC}$) attains 50% (a static effect in animal models) or 75% (1-log_{10} reduction in animal models) was calculated by Monte Carlo simulation using the developed model at certain doses with 1-hr or 3-hr infusion against MIC of 0.25 to 16 μg/mL. Time courses of urine concentrations were also simulated.



Probability of Target Attainment for 50% or 75% of $fT_{>MIC}$ at 2 g q8h

Results. The developed model well described plasma and urine concentration data. The probability of target attainment (PTA) with 2 g q8h with 1-hr or 3-hr infusion is shown in Figure 1. For 2 g q8h with either infusion time, the PTA was > 90% at 8 and 4 μg/mL of MIC for 50% and 75% of $fT_{>MIC}$, respectively. The PTA for either $fT_{>MIC}$ targets at 2 g q8h with 3-

hr infusion was higher than that with 1-hr infusion. The predicted 5th percentiles of urine concentrations over 8 hours were > 100 μg/mL at 2 g with 1-hr infusion.

Conclusion. The simulations for the subjects with normal renal function (conservative condition for S-649266 efficacy) suggested: S-649266 at 2 g q8h would exhibit efficacy for the target pathogens (i.e., carbapenem resistant *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*; MIC_{90}: 0.5, 2, 2 and 8 μg/mL, respectively). A 3-hr infusion would provide higher PTA than that for a 1-hr infusion. 2 g q8h would maintain urine concentrations at the high level.

Disclosures. **T. Katsube**, Shionogi and Co., Ltd.: Employee, Salary **T. Ishibashi**, Shionogi and Co., Ltd.: Employee, Salary **D. Tenero**, Glaxo SmithKline: Employee, Salary **T. Wajima**, Shionogi and Co., Ltd.: Employee, Salary

259. IgG mAbs against *Klebsiella pneumoniae* K1-CPS as a possible new therapeutic approach

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Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. *Klebsiella pneumoniae* (*Kp*) infections with hypervirulent (hvKp) serotypes are common in Asia and emerging in the US. Although these strains are usually sensitive to antibiotics they are highly invasive and can cause life-threatening infections including liver abscesses, pneumonia, meningitis and endophtalmitis in otherwise healthy patients. Also of concern is that ESBL and carbapenem resistance has already been noted in these strains in Asia. Most of these hvKp strains produce a hyperviscous capsular polysaccharide (CPS), which type as a K1 (50-80%) or K2 (20%) serotype. The goal was to generate monoclonal antibodies (mAb) against the K1 CPS that can be used as adjunctive therapy.

Methods. BALB/c mice were immunized with K1 CPS-conjugate to Protective Antigen of *Bacillus anthracis*. Spleen cells of mice with high IgG titers were fused to myeloma cells and hybridomes were isolated. Growth, agglutination, human serum resistance and mouse macrophage and human neutrophils phagocytosis assays were carried out with mAbs. Animal experiments were performed after intraperitoneal (i.p.) and intratracheal infections.

Results. CPS-PA conjugate successfully increased the IgG response in immunized BALB/c mice. Six distinct K1 specific IgG mAbs were isolated. Among them 4C5 (IgG1) and 19A10 (IgG3) were selected for further studies. Both mAbs were able to bind and agglutinate different clinical K1 strains. Both mAbs reduced *Kp* viability after 2h of co-incubation with the bacteria. Mabs significantly reduced the K1-*Kp* resistance to human serum. Both mAbs where opsonophagocytic 4C5 increased 100-fold phagocytosis of *Kp* by J744-macrophage cell line and also significantly increased phagocytosis of *Kp* by human neutrophils. 4C5 enhanced survival of mice injected with K1-*Kp* strains i.p. and i.t. and also decreased the bacterial cfu in liver, spleen and lung, respectively.

Conclusion. K1-CPS conjugation to PA was successfully employed to generate IgG response in mice. Both mAbs showed opsono-phagocytic characteristics and 4C5 also protected mice from 2 types of K1 infections. These results encourage efforts to develop these mAbs further for therapeutic use in humans, where they could be of great use especially if drug resistance continues to emerge in these hypervirulent K1 strains.

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260. Ceftolozane/Tazobactam for the Treatment of cUTI and cIAI Caused by ESBL-producing Enterobacteriaceae

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Session: 40. Antimicrobial Resistance: Novel Agents and Approaches to Gram Negative Infections
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Background. In the USA, extended-spectrum β-lactamases (ESBLs) are implicated in an estimated 26,000 infections resulting in 1700 deaths annually. Ceftolozane/tazobactam (C/T) is a novel antibacterial active against most ESBL-producing Enterobacteriaceae and drug-resistant *Pseudomonas aeruginosa.* C/T was studied in Phase 3 trials in patients with complicated intra-abdominal infection (cIAI) and complicated urinary tract infection (cUTI). Data from these studies were evaluated to describe the characteristics and outcomes of patients infected with ESBL- producing Enterobacteriaceae.

Methods. All trials were randomized and double-blind. In cUTI, treatment consisted of 7 days of intravenous C/T or levofloxacin, and in cIAI, 4-14 days of C/T plus metronidazole or meropenem. A baseline culture was obtained in both indications. Enterobacteriaceae were selected for ESBL characterization based on predefined criteria. Clinical and microbiological outcomes were determined 7 days post-treatment and 26-30 days after initiation of treatment in the cUTI and cIAI studies, respectively.

Results. A total of 150 patients (11%) had an ESBL-producing Enterobacteriaceae (genotypically verified) in the microbiologically evaluable population. Although most baseline characteristics were similar to the overall population, a greater proportion of patients with ESBLs were ≥65 years of age (31% vs 21%) or renally impaired (40% vs 31%) as compared with the overall population. Clinical cure rates for patients with ESBLs were 97% and 85% for the C/T arm and combined comparators, respectively. Microbiological eradication was achieved in 81% and 61% of patients in the C/T and comparator arms, respectively. At a breakpoint of 8 mg/L, 90% of ESBL-producing Enterobacteriaceae were susceptible to C/T; in the cUTI trials approximately 20% were susceptible to levofloxacin, and in the cIAI trials meropenem resistance was low (<5%).

Conclusion. Ceftolozane/tazobactam achieved high clinical and microbiological cure rates in cUTI and cIAI patients with ESBL infections. This was particularly notable, as patients with ESBLs were more likely to be elderly and/or renally impaired. C/T provides an empiric treatment option for infections caused by ESBL-producing pathogens.

Disclosures. **M. Wooley**, Cubist Pharmaceuticals: Employee, Salary **D. Cloutier**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **J. Huntington**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **J. Steenbergen**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **E. Hershberger**, Cubist Pharmaceuticals: Employee, Salary **O. Umeh**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **B. Miller**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **K. Kaye**, Cubist Pharmaceuticals: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Grant recipient and Speaker honorarium

261. Comparative *in vitro* Activity of Sitafloxacin and Other Antibiotics Against Clinical Isolates of Carbapenem-Resistant *Acinetobacter baumannii* and Carbapenem-Resistant *Pseudomonas aeruginosa* by Disk Diffusion Method

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Background. *Acinetobacter baumannii* (*AB*) and *Pseudomonas aeruginosa* (*PA*) are among the most important causes of nosocomial infections. The emergence of carbapenem-resistant (CRAB and CRPA) strains has posed a major global threat as there are few remaining treatment options. Sitafloxacin (DU-6859a) is a broad-spectrum fluoroquinolone that has been shown to exhibit activity against multidrug-resistant Gram-negative bacilli.

Methods. During January 2014 – April 2014, 216 clinical isolates of *AB* and *PA* obtained from various sites were tested for the susceptibility to various antibiotics, including, the carbapenems, sitafloxacin (SITA), ciprofloxacin (CIPRO), piperacillin/tazobactam (PIP/TAZ), cefoperazone/sulbactam (CEF/SUL), colistin, (COL) and tigecycline (TIG, tested only for *AB* isolates). The susceptibility test was performed by disk diffusion method. The zone diameter interpretive criteria as recommended in M100-S24 were applied. For agents that had no interpretive criteria by the Clinical and Laboratory Standards Institute, such as SITA, we had referred to some published studies for appropriate breakpoints criteria.

Results. A total of 123 clinical isolates of *AB* were obtained from 96 patients. Of these, 111 (90.2%) from 86 patients were carbapenem-resistant (CRAB). The susceptibility rates of CRAB isolates to SITA, CIPRO, PIP/TAZ, CEF/SUL, COL, and TIG were 58.6%, 0%, 0%, 2.7%, 100%, and 100%, respectively. SITA was significantly more effective than CEF/SUL ($P < 0.001$) but significantly less active than COL and TIG ($P < 0.001$) against CRAB. For clinical isolates of *PA*, a total of 93 were obtained from 81 patients. Of these, 41 (44.1%) from 32 patients were carbapenem-resistant (CRPA). The susceptibility rates of CRPA isolates to SITA, CIPRO, PIP/TAZ, CEF/SUL, and COL were 17.1%, 12.2%, 12.2%, 9.8%, and 100%, respectively. SITA was significantly less active than COL against CRPA ($P < 0.001$). SITA was not statistically more active than CIPRO, PIP/TAZ, and CEF/SUL against CRPA ($P = 0.53$, $P = 0.53$, and $P = 0.33$, respectively). Lastly, the susceptibility rate to SITA was significantly higher among CRAB than CRPA isolates (58.6% vs 17.1%, $P < 0.001$).

Conclusion. SITA may be considered as an alternative empirical treatment for infections caused by CRAB when COL and TIG are not tolerated. However, SITA may be less reliable for the empirical treatment of CRPA.

Disclosures. **All authors:** No reported disclosures.

262. Effect of NSAID/Corticosteroid Use on the Efficacy of Tedizolid in Acute Bacterial Skin and Skin Structure Infections: Pooled Data From the Phase 3 ESTABLISH-1 and ESTABLISH-2 Studies

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Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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Background. Tedizolid (TZD) is a novel oxazolidinone with potent activity against a wide range of Gram-positive pathogens, including MRSA, and with a favorable safety profile. In two Phase 3 trials, ESTABLISH-1 and ESTABLISH-2, TZD (200 mg once daily for 6 days) demonstrated noninferiority to linezolid (LZD) (600 mg twice daily for 10 days) in patients with acute bacterial skin and skin structure infections (ABSSSI). Use of non-steroidal anti-inflammatory drugs (NSAID) and/or corticosteroids (CS) is common in patients with ABSSSI. Due to their anti-inflammatory properties, it is possible that concomitant use of these agents may reduce lesion size and confound the primary outcome of ≥20% reduction in lesion size at the 48–72 hour visit. This subgroup analysis of pooled data from ESTABLISH-1 and -2 examined the effect of concomitant NSAID/CS use on early clinical response in patients with ABSSSI receiving TZD or LZD.

Methods. Patients with ABSSSI (lesion surface area ≥75 cm^2 and ≥1 regional or systemic sign of infection) received TZD 200 mg qd for 6 days or LZD 600 mg bid for 10 days. The use of NSAIDS/CS was documented for each patient and the primary outcome for both therapies at the 48-72 h visit was measured with/without NSAID/CS use.

Results. A total of 1333 patients were randomly assigned to TZD or LZD. Patients were mostly male (63.1%); average age of 44 years. The most common ABSSSI was cellulitis (45.3% and 45.9% in TZD and LZD treatment groups, respectively), followed by major cutaneous abscess (25.3% and 24.8%), and wound infections (29.4% and 29.3%). Overall, 44 of 664 patients (6.6%) in the TZD treatment group and 63 of 669 patients (9.4%) in the LZD group received NSAID or oral CS during the first 72 hours of treatment. Among patients receiving NSAID/CS, early clinical response rates at the 48-72 h visit were similar between TZD and LZD groups (70.5% vs 69.8%), but lower overall than compared with patients not receiving NSAID/CS (82.4% with TZD vs 80.4% with LZD).

Conclusion. Early clinical response rates were similar in patients treated with either TZD or LZD for ABSSSI in the ESTABLISH-1 and -2 trials, regardless of NSAID/CS use. This finding suggests there is an absence of bias with anti-inflammatory use in assessing early clinical response rates in ABSSSI clinical trials.

Disclosures. **T. Sandison**, Cubist: Employee, Salary **C. De Anda**, Cubist: Employee and Shareholder, Salary **A. Das**, Cubist: Consultant, Consulting fee; Cempra: Consultant, Consulting fee; Cerexa: Consultant, Consulting fee; Nabriva: Consultant, Consulting fee; Paratek: Consultant, Consulting fee; Trius: Consultant, Consulting fee; Achaogen: Consultant, Consulting fee; Durata: Consultant, Consulting fee **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

263. Gastrointestinal Safety Profile of Tedizolid: Pooled Results from Two Phase 3 Trials in Acute Bacterial Skin and Skin Structure Infections

Edward Fang; Carisa De Anda; Sonia Minassian; Shawn Flanagan; Philippe Prokocimer; Cubist San Diego, CA

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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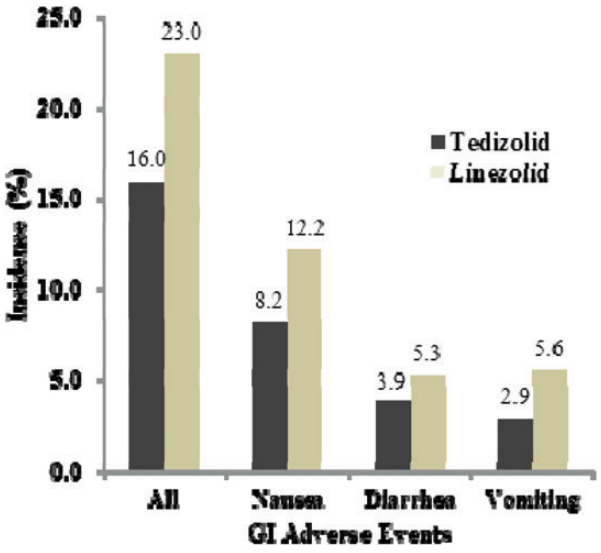
Background. Tedizolid (TZD) is a novel oxazolidinone antibacterial with potent activity against a wide range of Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), and it has a favorable safety profile. Two Phase 3 clinical trials demonstrated the noninferiority of 6 days of TZD 200 mg once daily compared with 10 days of linezolid (LZD) 600 mg twice daily for treatment of acute bacterial skin and skin structure infections.

Methods. Pooled data from 1324 patients (TZD, N = 662; LZD, N = 662) were used to compare the gastrointestinal (GI) adverse event (AE) profiles of TZD and LZD.

Results. GI disorders were the most common AEs and were reported less frequently in the TZD (16.0%) than the LZD group (23.0%); the most common AEs within this system organ class were nausea, diarrhea, and vomiting (Figure 1). The first episodes of these GI AEs occurred primarily within the first 6 days of treatment. The lower incidence of GI AEs in the TZD group was noted during this early period, when both groups were receiving active drug (Table 1). Discontinuation of study drug due to GI AEs was reported for 3 patients receiving TZD (abdominal discomfort, diarrhea, and vomiting, in 1 patient each) and for 6 receiving LZD (vomiting and nausea in 3 patients each).



Incidence of gastrointestinal adverse events

Onset of First Episode of Gastrointestinal Adverse Events

AE	Time of Onset	TZD 200 mg once daily for 6 days (N=662) n (%)	LZD 600 mg twice daily for 10 days (N=662) n (%)
GI disorders overall	0-6 days	86 (13.0)	125 (18.9)
	7-10 days	10 (1.5)	19 (2.9)
	>10 days	10 (1.5)	8 (1.2)
Diarrhea	0-6 days	19 (2.9)	27 (4.1)
	7-10 days	5 (0.8)	7 (1.1)
	>10 days	2 (0.3)	1 (0.2)
Nausea	0-6 days	47 (7.1)	70 (10.6)
	7-10 days	3 (0.5)	8 (1.2)
	>10 days	4 (0.6)	3 (0.5)
Vomiting	0-6 days	13 (2.0)	31 (4.7)
	7-10 days	3 (0.5)	2 (0.3)
	>10 days	3 (0.5)	4 (0.6)

Conclusion. Treatment with TZD 200 mg once daily for 6 days was associated with an improved GI AE profile compared with LZD 600 mg twice daily for 10 days. Most of the GI AEs occurred during the first 6 days of the study period while patients in both treatment arms were exposed to active study drug, suggesting that the difference in GI AEs may reflect a pharmacologic difference between TZD and LZD rather than a difference in duration of exposure.

Disclosures. **E. Fang**, Trius/Cubist: Employee, Salary **C. De Anda**, Cubist: Employee and Shareholder, Salary **S. Minassian**, Cubist: Consultant, Consulting fee **S. Flanagan**, Cubist: Employee and Shareholder, Salary **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

264. Results of the Surveillance of Tedizolid Activity and Resistance (STAR) Program: In Vitro Susceptibility of Gram-Positive Clinical Isolates Collected in 2013 From the United States

Paul Bien; Philippe Prokocimer; Cubist, San Diego, CA

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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Background. Tedizolid is a novel oxazolidinone antibacterial with potent activity against a wide range of Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), a key pathogen associated with acute bacterial skin and skin structure infections (ABSSSI). As part of the **S**urveillance of **T**edizolid **A**ctivity and **R**esistance (STAR) Program, the in vitro activity of tedizolid was analyzed against a variety of clinically relevant Gram-positive pathogens isolated from clinical sources in 2013.

Methods. Nonduplicate, nonconsecutive, single-patient clinical isolates of key Gram-positive pathogens (N = 1473) were collected from 36 clinical centers in the United States in 2013. Isolates underwent susceptibility testing against tedizolid in accordance with CLSI M7 and M100 guidelines at a central laboratory (Eurofins, Chantilly, VA).

Results. Tedizolid MIC values were determined for *S. aureus* (n = 1088), CoNS (n = 110), and enterococci (n = 275) from various infection/lesion sites. Tedizolid was active against all of these pathogen groups, with MIC_{90} values of 0.5 μg/mL for MRSA and MSSA; 0.25 μg/mL for CoNS; and 0.5 μg/mL for enterococci.

Pathogen	Isolates (n)	Tedizolid MIC (μg/mL)			
		Range	Mode	MIC_{50}	MIC_{90}
All *S. aureus*	1088	≤0.03-1.0	0.25	0.25	0.5
MRSA	499	≤0.03-1.0	0.25	0.25	0.5
MSSA	589	≤0.03-1.0	0.25	0.25	0.5
CoNS	110	≤0.03-0.5	0.12	0.12	0.25
Enterococcus spp	275	0.06-2.0	0.25	0.25	0.5

MIC_{50} = 50% minimum inhibitory concentration; MIC_{90} = 90% minimum inhibitory concentration

Conclusion. Based on MIC_{90} values, tedizolid retains potent activity against Gram-positive pathogens implicated in ABSSSI, including MRSA. The results obtained in this analysis are consistent with the findings obtained in tedizolid surveillance studies conducted in prior years. The serious public health problem of antibacterial resistance warrants continued surveillance of tedizolid activity.

Disclosures. **P. Bien**, Cubist: Employee, Salary **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

265. Hepatic Safety in Acute Bacterial Skin and Skin Structure Infection (ABSSSI) Patients Receiving Tedizolid (TZD) vs Linezolid (LZD)

Catherine Hardalo; Edward Fang; Carisa De Anda; Sonia Minassian; Philippe Prokocimer; Cubist, San Diego, CA

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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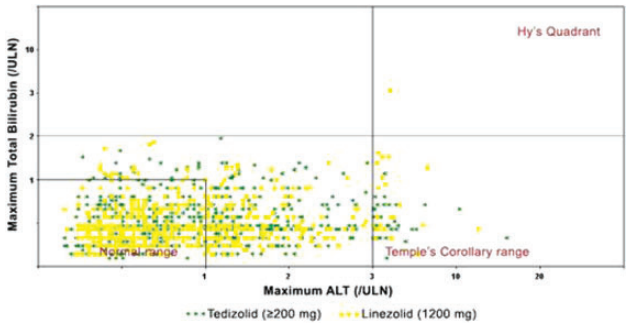
Background. TZD is a novel oxazolidinone with potent antibacterial activity against a wide range of Gram-positive pathogens. In two randomized, double-blind, Phase (Ph) 3 noninferiority trials, ESTABLISH-1 and -2, TZD 200 mg qd for 6 days was noninferior to LZD 600 mg bid in treating ABSSSI. This analysis was conducted to identify any evidence of Drug-Induced Serious Hepatotoxicity (DISH) in a large TZD clinical trial database (Ph 2 and 3) and to assess the effect of TZD in Ph 3 ABSSSI patients (pts) with normal hepatic function, hepatic impairment (HI), or hepatic disease (HD), as measured by incidence of TEAE, TEAE leading to drug discontinuation (D/C), and SAE.

Methods. Hy's Law (HL) defines DISH as unexplained serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3x upper limit of normal (ULN) + total bilirubin (TBL) >2x ULN without alkaline phosphatase elevation; Temple's corollary (TC) defines it as ALT elevation >3x ULN without TBL elevation. Pts from Ph 2 and 3 trials who received ≥1 TZD or LZD dose with ≥1 on-treatment ALT/TBL value were included. A scatterplot of maximum ALT/AST divided by ULN (/ULN) vs max TBL/ULN was generated on a $\log_{10}$ scale (figure). Safety assessments were performed as described above.

Results. The DISH population comprised 1024 TZD- and 621 LZD-treated pts who had ALT and TBL values. No TZD pts but 1 LZD patient met HL criteria after the first dose. Thirty-six TZD (3.5%) and 26 LZD (4.1%) pts met TC criteria. TZD pts had no evidence of DISH following medical review. The incidence of TEAE, TEAE leading to D/C, and SAE were similar in both arms in Ph 3 trials (Table).



Drug-Induced Serious Hepatotoxicity

Incidence of TEAE, TEAE leading to drug discontinuation (D/C), and serious AE (SAE)

	TZD (N = 662)		LZD (N = 662)	
Pts	n	%	n	%
Normal	n = 474		N = 443	
≥1 TEAE	202	42.6	183	41.3
TEAE → D/C	1	0.2	3	0.7
≥1 SAE	9	1.9	7	1.6
HI	n = 14		n = 12	
≥1 TEAE	3	21.4	5	41.7
TEAE → D/C	0	0	0	0
≥1 SAE	1	7.1	2	16.7
HD	n = 175		n = 209	
≥1 TEAE	78	44.6	98	46.9
TEAE → D/C	2	1.1	3	1.4
≥1 SAE	2	1.1	4	1.9

HI: Child-Pugh score ≥7; HD: Baseline ALT/AST >2× ULN or hepatitis C seropositivity.

Conclusion. There was no DISH signal in a safety database from Ph 2 and Ph 3 clinical trials in ABSSSI. TEAE profiles were similar for Ph 3 TZD- and LZD-treated patients with HI/HD, and those with normal hepatic function, suggesting no worsening of hepatic function.

Disclosures. **C. Hardalo**, Cubist: Consultant, Consulting fee **E. Fang**, Trius/Cubist: Employee, Salary **C. De Anda**, Cubist: Employee and Shareholder, Salary **S. Minassian**, Cubist: Consultant, Consulting fee **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

266. Dalbavancin vs Vancomycin for the treatment of acute bacterial skin and skin structure infections (ABSSSI): a subanalysis from the DISCOVER studies

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Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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Background. To compare efficacy and safety outcomes for patients enrolled in 2 prospective phase 3 ABSSSI clinical trials of dalbavancin (DAL) who received study drug only IV, with no switch to oral therapy, for a total duration of 10-14 days.

Methods. Both trials were double-blind, double dummy, randomized trials in which patients with ABSSSI were randomized to receive DAL 1g IV on Day 1 and 500 mg IV on Day 8 or Vancomycin (VAN) 1g (or 15mg/kg) IV every 12 hours (q12h) for at least 3 days with an option to switch to oral linezolid (L) 600 mg q12h to complete 10-14 days of therapy. In a pooled analysis, we identified patients who received ≥10 days of IV VAN/placebo study drug without being switched to oral therapy (oral placebo for patients in the DAL group and oral L in the VAN/L group). Efficacy and safety outcomes for this subset of patients were evaluated.

Results. 61/652 (9.4%) patients randomized to DAL completed ≥10 days of IV placebo compared to 54/651 (8.3%) of patients randomized to VAN/L who received ≥10 days of IV VAN.

Table 1: Clinical Success at EOT in patients who did not switch to oral therapy

Clinical Success at EOT	DAL n/N (%)	VAN n/N (%)
CE Population	39/56 (69.6)	34/49 (69.4)
ITT Population	42/61 (68.9)	36/54 (66.7)

Table 2: Summary of total adverse events

Number of Patients Who Experienced at Least One of	DAL N=61 n (%)	VAN N= 54 n (%)
Treatment-Emergent adverse event (TEAE)	18 (29.5)	25 (46.3)
Drug-Related TEAE	3 (4.9)	3 (5.6)
TE-Serious AE (TE-SAE)	1 (1.6)	7 (13.0)
Drug-Related TE-SAE	0	0
TE-SAE Leading to Death	0	1 (1.9)
TEAE Leading to Premature Discontinuation of Study Drug	1 (1.6)	0
TE-SAE Leading to Premature Study Drug Discontinuation	0	0

Table 3: Nephrotoxicity* on therapy

	DAL n/N(%)	VAN n/N(%)	P-Value
ITT Population	21 / 637 (3.3)	31 / 638 (4.9)	0.16
DAL vs IV VAN only	21/637 (3.3)	5/54 (9.3)	0.06
Patients who received IV treatment (DAL + IV placebo or VAN) only	1 / 58 (1.7)	5 / 54 (9.3)	0.21

*nephrotoxicity defined as a 50% increase from baseline serum creatinine or an absolute increase in serum creatinine of 0.5 mg/dL

Conclusion. Patients with ABSSSI treated with DAL had similar clinical success rates at EOT compared to those treated with IV VAN alone. Compared to patients receiving DAL, patients who received IV VAN for ≥10 days had a tendency towards more TEAEs and more nephrotoxicity.

Disclosures. **S. Puttagunta**, Durata Therapeutics: Employee and Shareholder, Salary **G. Talbot**, Durata Therapeutics: Consultant, Scientific Advisor and Shareholder, Consulting fee **M. Wilcox**, Durata Therapeutics: Scientific Advisor, Consulting fee **M. Dunne**, Durata Therapeutics: Employee and Shareholder, Salary

267. Dalbavancin for the treatment of Streptococcal Skin Infections

Sailaja Puttagunta, MD; Michael Dunne, MD; Durata Therapeutics, Branford, CT

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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Background. Streptococci are a known cause of complicated skin and soft tissue infections (cSSTI). Dalbavancin, a lipoglycopeptide antibiotic has been studied in 3 global phase 3 randomized, double-blind, controlled trials for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and cSSTI. The objective of this analysis is to evaluate outcomes for patients with streptococcal skin infections enrolled in the 3 global trials.

Methods. Patients enrolled in the 3 phase 3 ABSSSI/cSSTI trials with baseline cultures positive for streptococcal species were identified. In these trials, dalbavancin, 1 g IV on day 1 followed by 500mg IV on day 8 was compared to either IV vancomycin or IV linezolid with an option to switch to oral linezolid. The MIC distribution of streptococcal isolates and clinical outcomes for patients with streptococcal skin infections were determined.

Results. The *in vitro* MIC_{90} to dalbavancin for each strain of streptococci was ≤0.06 mcg/mL.

Table 1: Distribution of streptococci in 3 phase 3 ABSSSI/cSSTI trials

	DUR001-301/302 + VER001-9			
	Dalbavancin		Comparators	
	n	%	n	%
Baseline Isolates	N=695		N=521	
S. pyogenes	50	7.2	46	8.8
S. agalactiae	24	3.5	22	4.2
Streptococcus viridans group	17	2.4	10	1.9
S. dysgalactiae	8	1.2	2	0.4
Streptococcus Group C	5	0.7	5	1.0
Streptococcus Group G	10	1.4	7	1.3
Streptococcus anginosus Group	22	3.2	25	4.8
S. anginosus	6	0.9	4	0.8
S. constellatus	15	2.2	16	3.1
S. intermedius	6	0.9	7	1.3
Streptococcus pneumoniae	1	0.1	0	0.0
Other streptococci*	2	0.3	5	1.0

*includes S. bovis, S. gordonii, S. mitis, S. mutans, S. salivarius and other streptococcal species

Table 2: Clinical Success* at EOT by Key Target Pathogen

Baseline Pathogen	Dalbavancin n/N (%)	Comparator n/N (%)
S. pyogenes	43/45 (95.6)	37/39 (94.9)
S. agalactiae	19/21 (90.5)	12/14 (85.7)
S. dysgalactiae	8/8 (100)	2/2 (100)
S. anginosus	6/6 (100)	3/3 (100)
S. constellatus	11/11 (100)	14/14 (100)
S. intermedius	4/4 (100)	5/5 (100)

*assessed by investigators; EOT = end of treatment

Conclusion. Data from the clinical trial program confirm the *in vitro* activity of dalbavancin against strains of streptococci. Patients with streptococcal skin infections treated with dalbavancin had similar clinical success rates at EOT as those treated with the comparator regimens.

Disclosures. **S. Puttagunta**, Durata Therapeutics: Employee and Shareholder, Salary **M. Dunne**, Durata Therapeutics: Employee and Shareholder, Salary

268. Clinical Response of Tedizolid vs Linezolid in Acute Bacterial Skin and Skin Structure Infections by Severity Measure: Pooled Analysis of 2 Phase 3 Double-Blind Trials

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Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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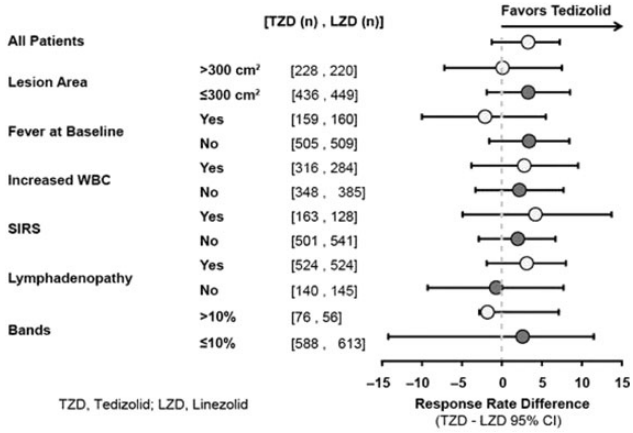
Background. There is no consensus on defining disease severity in acute bacterial skin and skin structure infections (ABSSSI) trials. In two ABSSSI, noninferiority Phase 3 trials (ESTABLISH-1 and ESTABLISH-2), 6 days of tedizolid, a novel oxazolidinone antibacterial, demonstrated noninferior efficacy to 10 days of linezolid. In this prespecified subgroup analysis, the effect of different measures of disease severity at baseline (lesion size, fever, increased white blood cell count, System Inflammatory Response Syndrome [SIRS], lymphadenopathy, and presence of immature neutrophils [bands]) on clinical response was investigated.

Methods. Eligible patients were randomized 1:1 to receive 200 mg tedizolid once daily for 6 days or 600 mg linezolid twice daily for 10 days. ESTABLISH-1 patients received oral therapy, while ESTABLISH-2 patients received IV therapy with an optional switch to oral. The primary endpoint was early clinical response (≥20% reduction in lesion area compared to baseline at 48-72 h after start of study drug). Investigator-assessed clinical response at the posttherapy evaluation (PTE; 7-14 days posttherapy) was a key secondary endpoint. Response rates to therapy were compared between tedizolid and linezolid with and without the presence of specified measures of disease severity at screening.

Results. Among the 1333 patients in the pooled intent-to-treat population, there was no difference in the specified measures of disease severity between patients randomized to tedizolid (n = 664) and linezolid (n = 669). Early clinical response rates were similar between the tedizolid and linezolid treatment groups across all evaluated severity subgroups (Figure 1). Similar response rates between the two antibacterials were also maintained for investigator-assessed clinical response at PTE across all evaluated measures of severity.



Early Clinical Response by Severity Measures

Conclusion. In the pooled data for these two phase 3 trials for ABSSSI, 6 days of TZD was consistently non-inferior to 10 days of LZD, regardless of the measure of disease severity used.

Disclosures. **T. Sandison**, Cubist: Employee, Salary **C. De Anda**, Cubist: Employee and Shareholder, Salary **E. Fang**, Trius/Cubist: Employee, Salary **A. Das**, Cubist: Consultant, Consulting fee; Cempra: Consultant, Consulting fee; Cerexa: Consultant, Consulting fee; Nabriva: Consultant, Consulting fee; Paratek: Consultant, Consulting fee; Trius: Consultant, Consulting fee; Achaogen: Consultant, Consulting fee; Durata: Consultant, Consulting fee **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

269. Comparison of the Hematologic Safety of Tedizolid and Linezolid: Pooled Results from Two Phase 3 Trials in Acute Bacterial Skin and Skin Structure Infections

Edward Fang; Carisa De Anda; Sonia Minassian; Shawn Flanagan; Philippe Prokocimer; Cubist, San Diego, CA

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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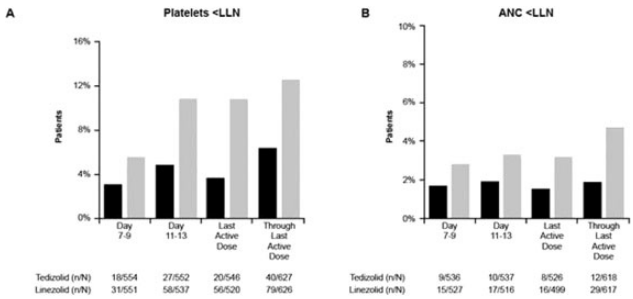
Background. Tedizolid (TZD) is a novel oxazolidinone antibacterial with a favorable tolerability profile and potent activity against a wide range of Gram-positive pathogens, including resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci. In two randomized, double-blind, Phase 3 trials in patients with acute bacterial skin and skin structure infections (ABSSSI), 6 days of TZD 200 mg once daily was noninferior to 10 days of linezolid (LZD) 600 mg twice daily. Oxazolidinones are known to inhibit mitochondrial protein synthesis, which may have an effect on hematologic parameters. Differences in pharmacokinetics and dosing characteristics between LZD and TZD may lead to a reduced potential for mitochondrial toxicity with TZD.

Methods. We compared the hematologic profiles of TZD and LZD using pooled data from the 2 trials (safety population, N = 1324). The incidence of abnormal values (<lower limit of normal [LLN]) and substantially abnormal (SA) values (for absolute neutrophil count [ANC]: <50% LLN if normal value at baseline or <50% of LLN and <50% of baseline if abnormal value at baseline; for platelets and hemoglobin: <75% LLN if normal value at baseline or <50% of LLN and <75% of baseline if abnormal value at baseline) were determined on study days 7-9, 11-13, on day of last active dose, and for the entire treatment period.



Incidence of platelet counts (A) and ANC (B) less than the lower limit of normal with TZD or LZD in two Phase 3 studies in ABSSSI

Results. At all time points, the incidence of platelet counts <LLN was lower in the TZD group (3%-6%) than in the linezolid group (6%-11%), and over the entire treatment period was 6% vs 13% (Figure 1). SA platelet counts ranged from 0.8% to 1.2% with TZD

and from 0.8% to 1.9% with LZD. Incidence of ANC <LLN was lower with TZD (<2%) than with LZD (<4%) at each time point, with rates of 1.9% and 4.7%, respectively, over the entire treatment period. SA ANC were reported in <1% in both groups at all time points. Hemoglobin changes were similar in the TZD and LZD groups.

Conclusion. Although the clinical relevance is not known, this pooled data analysis suggests that TZD 200 mg daily for 6 days may have a lower potential for adverse hematologic outcomes vs LZD 600 mg twice daily for 10 days when treating patients with ABSSSI.

Disclosures. **E. Fang**, Trius/Cubist: Employee, Salary **C. De Anda**, Cubist: Employee and Shareholder, Salary **S. Minassian**, Cubist: Consultant, Consulting fee **S. Flanagan**, Cubist: Employee and Shareholder, Salary **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

270. SYN-004, a Class A Beta-Lactamase Therapy for the Prevention of Antibiotic-Induced Disruption of Intestinal Microflora

Michael Kaleko, MD, PhD; Andrew Bristol, PhD; Sheila Connelly, PhD; Pertti Koski, PhD; Synthetic Biologics, Inc., Rockville, MD

Session: 41. Antimicrobial Resistance: Novel Agents and Approaches to Gram-Positive Infections
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Background. ß-lactam antibiotics that are excreted into the intestine can damage the microflora, which can lead to serious infections such as *Clostridium difficile (C. diff)*. SYN-004 is a potent ß-lactamase formulated for oral use with intravenous (IV) antibiotics to degrade antibiotics in the intestine.

Methods. SYN-004, formerly called P3A, was developed and evaluated by Ipsat Therapies, Helsinki, Finland. SYN-004 was engineered from the *Bacillus licheniformis* PenP enzyme to expand the hydrolysis of ß-lactams to cephalosporins, including ceftriaxone (cfx), while maintaining its anti-penicillin activity. The use of cfx is a major risk factor for the development of *C. diff*. Antibiotic hydrolysis was assessed *in vitro*. *In vivo,* SYN-004 activity was evaluated in the intestinal tract of jejunal-fistulated dogs (n = 6) following administration of oral SYN-004 (0.44 mg/kg) and IV cfx (30 mg/kg).

Results. *In vitro* antibiotic hydrolysis assays demonstrated that, compared to PenP, SYN-004 displayed improved degradation of cephalosporins: cfx, cefotaxime, cefazolin, cefoperazone, and cefuroxime. Activities against ampicillin and piperacillin were unchanged. Dog studies revealed that cfx was excreted at high levels into the intestine following IV delivery (mean $C_{max}$of 1500 µg/g of jejunal chyme), and a second cfx peak (mean 167 µg/g) was observed six hours later, after an additional feeding. Following delivery of SYN-004 ten minutes prior to IV cfx, the cfx concentration stayed low (<5 µg/g chyme) for five hours in 4/6 dogs. The other two dogs did not eat prior to dosing and showed higher cfx concentrations at the early timepoints, presumably due to delayed gastric emptying. The second peak in cfx levels was not detected in any SYN-004-treated animal demonstrating that SYN-004 was present, remained functional, and hydrolyzed the cfx in the intestines of all treated dogs.

Conclusion. SYN-004 is a potent ß-lactamase specifically engineered to hydrolyze an expanded range of antibiotics including the cephalosporins. Oral delivery of SYN-004 resulted in efficient degradation of intestinal ceftriaxone in dogs. Therefore, SYN-004 is a promising candidate to protect the intestinal microflora to prevent antibiotic-associated adventitious infections such as *C. diff*.

Disclosures. **M. Kaleko**, Synthetic Biologics, Inc.: Employee, Salary and Stock options **A. Bristol**, Synthetic Biologics: Employee and Shareholder, Salary **S. Connelly**, Synthetic Biologics: Employee, Salary **P. Koski**, Synthetic Biologics, Inc.: Consultant, Consulting fee

271. Detection, evolution and outcome of the first case of Vancomycin Resistant *Staphylococcus aureus* (VRSA) infection in Europe

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Session: 42. MRSA and VRE
Thursday, October 9, 2014: 12:30 PM

Background. In Portugal, in May 2013 a VRSA strain (MRSA with vancomycin MIC = 1024 mg/l) was isolated from pus of a toe amputation wound of a 74 year-old female patient with chronic renal failure requiring haemodialysis, diabetes mellitus and peripheral vascular disease. The patient was under treatment with vancomycin for a methicillin-resistant *Staphylococcus aureus* (MRSA) local infection. Vancomycin-resistant *Enterococcus faecalis* (VRE) and *Pseudomonas aeruginosa* were also isolated from the wound.

Methods. Antibiotic therapy with daptomycin, rifampicin and amikacin was administered for 6 weeks. Control precautions were reinforced. The strain was characterized and an epidemiological survey to monitor its possible dissemination was carried out. All isolates were characterized by multilocus sequence typing (MLST), *spa* typing, and pulsed-field gel electrophoresis (PFGE) profiling, and the structure of the *SCCmec* element of all MRSA isolates was determined.

Results. The VRSA strain was no longer found in the wound after 3 weeks, and the VRE strain after 5 weeks. Nasal swabs from 53 close contacts (2 household members (HHM), 47 healthcare workers (HCW), 4 patients) did not reveal VRSA. Methicillin susceptible *Staphylococcus aureus* (MSSA) were recovered from 14 HCW, and 5 MRSA isolates were recovered from 3 HCW, 1 HHM and 1 patient. *S. aureus* isolates presented high genetic diversity, most of them belonging to clones previously identified in Portugal.

In countries with increase in CC5-associated clones and high prevalence of MRSA and VRE, such as Portugal, VRSA may arise more frequently in the near future.

Conclusion. The VRSA strain harboured *vanA*, was ST105-II and belonged to CC5, as in 12 of the 13 cases detected in the USA. *vanA*-positive VRE may have been the donor of the *vanA* into a MRSA during co-infection and therapy with vancomycin. Transmission of the strain to contacts was not detected.

Disclosures. **J. Melo-Cristino**, Pfizer: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Gilead: Speaker's Bureau, Speaker honorarium **M. Ramirez**, Pfizer: Speaker's Bureau, Speaker honorarium; GlaxoSmithKline: Consultant, Consulting fee

272. Characteristics of USA500/Iberian Methicillin-Resistant *Staphylococcus aureus* (MRSA) Invasive Disease

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Session: 42. MRSA and VRE
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Background. Describe the clinical and epidemiologic characteristics of invasive USA500/Iberian MRSA infections and compare to USA300 and USA100 invasive disease.

Methods. Population-based surveillance for invasive MRSA disease was conducted in the 8-county metropolitan Atlanta area from 1-1-2005 to 12-31-2011 through the Active Bacterial Core surveillance program of the Georgia Emerging Infections Program. Isolates were typed by pulse-field gel electrophoresis (PFGE) and/or screened for SCC*mec* (SM) types II and IV and categorized as non-USA300 with SM IV, USA300, USA100 or other. SM IV isolates were subtyped and *spa* typed; clonal complex (CC) was inferred by *spa* type. CC8, non-USA300 that were SM IV but not IVa, were classified as USA500/Iberian. Medical records were reviewed.

Results. Among a total of 2,006 invasive MRSA infections, 36% were due to USA300, 31% USA 100, 27% (540/2,006) USA500/Iberian, and 7% other. Most invasive USA500/Iberian cases (99%) were bacteremias. Clinical syndromes included: bacteremia without focus (38%), central line-associated bloodstream infection (24%), pneumonia/empyema (12%), skin and soft tissue (9%), urinary tract (9%), bone or joint infections (7%), and endocarditis (3%). Most were healthcare-associated community-onset (72%), in men (63%) of black race (73%); 24% were in persons with HIV/AIDS. Trimethoprim-sulfamethoxazole resistance was high (97%). In-hospital mortality was 21% (110/532) for USA500/Iberian, compared to 21% (126/608) for USA100 and 14% (98/712) for USA300. On multivariable analysis, invasive USA500/Iberian infections had similar risk of in-hospital mortality as USA300 (aOR 1.34; 95% CI 0.96 – 1.87) and USA100 (aOR 0.97; 95% CI 0.70 – 1.35).

Conclusion. USA500/Iberian MRSA was a common cause of invasive disease in Atlanta. The association with healthcare exposure, HIV/AIDS and trimethoprim-sulfamethoxazole resistance was strong. In-hospital mortality for invasive USA500/Iberian MRSA infections was similar to USA100 and USA300 after adjusting for confounders.

Disclosures. **All authors:** No reported disclosures.

273. Genomic Epidemiology of Methicillin-resistant *Staphylococcus aureus* in a Neonatal Intensive Care Unit

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Session: 42. MRSA and VRE
Thursday, October 9, 2014: 12:30 PM

Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a leading cause of healthcare-associated infections (HAI). The prevalence of community-associated (CA) MRSA strains has increased in hospitals. We previously demonstrated that *spa*-type t008 CA-MRSA strains have been replacing *spa*-type t002 and t045 healthcare-associated (HA) MRSA strains among colonized infants in our Neonatal Intensive Care Unit (NICU). However, *spa*-typing lacks the discriminatory resolution to determine the cause of this epidemiological shift. Whole genome sequencing (WGS) and phylogenetic analysis may better characterize MRSA transmission in the NICU.

Methods. Since 2004, we have performed admission and weekly MRSA screening of all infants admitted to the level III NICU in Jacksonville, FL (AJIC 2011;39:35-41). Isolates from infants (n = 411) were *spa*-typed to characterize prevalent strains within the NICU. Strains identified as *spa*-type t008 (n = 55), representing the prevalent CA-MRSA lineage, and *spa*-type t045 (n = 41), representing the prevalent HA-MRSA lineage, underwent WGS and phylogenetic analysis to understand the putative replacement of HA- strains and to assess the endemnicity of CA strains within the unit. Infant demographic and clinical data were extracted electronically.

Results. A total of 5,212 infants were admitted to the NICU during the study period (2004-2011) representing 128,422 patient days (pd). The colonization prevalence among infants was 3.62 per 1,000 pd. Preliminary epidemiological and phylogenetic analysis of *spa*-type t008 and t045 strains demonstrated a complex dynamic marked by both multiple introductions of t008 strains and putative nosocomial transmission as suggested by different individuals having nearly identical MRSA WGS.

Conclusion. Our findings show evidence of multiple introductions of MRSA into the NICU, possibly due to increasing community-wide prevalence resulting in greater colonization pressure from patients, staff, and visitors. Given that *spa*-typing alone cannot distinguish introductions from the community vs nosocomial transmission (i.e., sporadic vs epidemic cases), WGS should be used as the gold standard to investigate the emergence and transmission of MRSA and to inform evidence-based, targeted control measures.

Disclosures. **All authors:** No reported disclosures.

274. Evolving Epidemiology of *Staphylococcus aureus* Bacteremia

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Background. National estimates suggest that the epidemiology of invasive methicillin-resistant *S. aureus* (MRSA) infections is changing. USA300—the most common community-associated MRSA strain in the US by pulsed-field gel electrophoresis (PFGE)—has led to community-onset (CO) and hospital-onset (HO) bloodstream infections (BSIs). The objective was to examine the epidemiology of *S. aureus*—MRSA and methicillin-susceptible *S. aureus* (MSSA)—BSIs and to determine the proportion of MRSA BSIs due to USA300.

Methods. From 2007-2013, we used electronic surveillance data to examine the incidence of CO (≤3 days into hospitalization, irrespective of prior healthcare exposure) and HO (>3 days) *S. aureus* BSIs at Stroger Hospital, the major public hospital in Chicago. Available MRSA isolates from 2007-2012 underwent PFGE analysis. We modeled change in BSI incidence using a Poisson regression model.

Results. African-Americans were significantly more likely than others to have a MRSA BSI rather than MSSA BSI (OR = 2.1; 95%CI, 1.6, 2.8, $p < 0.001$); Hispanic ethnicity was negatively associated with MRSA BSI (OR = 0.5; 95%CI, 0.4, 0.8, $p < 0.001$). Younger age was associated with having a USA300 infection ($p = 0.002$).

The incidence of HO-MRSA BSIs significantly declined during the study period ($p = 0.04$). The incidence of HO-MSSA BSIs was stable during the early study period ($p = 0.22$) but declined following 2010 (Figure 1). While the incidence of CO-MSSA BSIs significantly declined over time ($p = 0.04$), the incidence of CO-MRSA BSIs remained unchanged over the 7 year study period ($p = 0.92$) (Figure 2).

88% of MRSA BSI isolates were genotyped. The proportion of genotyped MRSA BSIs due to USA300 was 69%. From Time 1 (2007-09) to Time 2 (2010-12), the proportion of CO-MRSA BSIs due to USA300 MRSA remained stable, 75% vs 77%. For HO-MRSA BSIs, over half (57%) of genotyped strains were USA300 MRSA with a proportion of 60% in Time 1 and 53% in Time 2.

Figure 1. Incidence of Hospital-Onset *Staphylococcus aureus* Bacteremia, 2007-2013

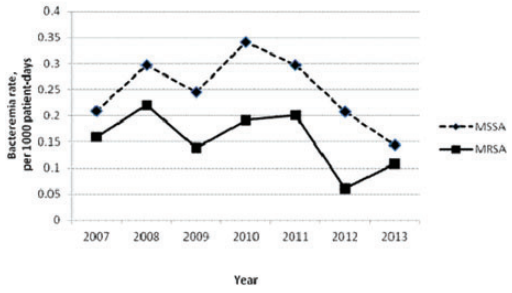
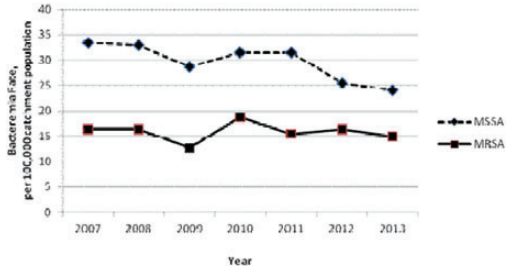


Figure 2. Incidence of Community-Onset *Staphylococcus aureus* Bacteremia, 2007-2013



Conclusion. The incidence of HO-MRSA and HO-MSSA BSIs declined during the study period while the rate of CO-MRSA BSIs was unchanged. Over half of MRSA BSIs were due to USA300 and the proportion of CO and HO MRSA BSIs due to USA300 was stable over time. Our findings suggest that USA300 MRSA is endemic not only in the community but also in certain healthcare settings.

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275. Comparative Genomics of a Population of Human, Animal, and Environmental MRSA Isolates in Ohio

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Background. Methicillin-resistant *Staphylococcus aureus*(MRSA) is a cause of serious infections among humans and animals. In more recent years, MRSA infections have increased in both community and veterinary settings. The primary objective of this study was to demonstrate genotypic similarities and differences among a diverse collection of human, animal, and environmental MRSA isolates.

Methods. This is a descriptive study of human, animal, and environmental MRSA isolates sampled in human and animal hospitals from 2007 to 2010 in Ohio. MRSA isolates were genotyped using pulsed-field gel electrophoresis (PFGE) and staphylococcal cassette chromosome *mec* (SCC*mec*) typing. Genotypic and phenotypic information was assessed for comparison, and descriptive statistics were compiled.

Results. A total of 1284 human, 41 canine, 7 equine, and 254 environmental MRSA isolates were genotyped. Human MRSA isolates carried the SCC*mec* II (50.0%) more than other SCC*mec* elements. The majority of canine MRSA isolates were SCC*mec* II (≥ 80% for all culture sites), while the majority of equine isolates were SCC*mec* IV (≥ 75% for most culture sites). For environmental isolates collected from the human hospital, 49.5% (49/99) were SCC*mec* II and 31.3% (31/99) were SCC*mec* IV. Environmental MRSA isolates collected from the canine hospital were nearly all SCC*mec* II (77/82, 93.9%); whereas, the majority of isolates from the equine hospital were SCC*mec*IV (66/73, 90.4%). PFGE type USA100 and USA300 were the most common among human isolates; alternatively, USA100 and USA500 were the most common among canine and equine isolates, respectively. Multi-drug resistance was highest in environmental isolates collected from the patient hospital (99/99, 100.0%).

Conclusion. Canine and equine MRSA populations had distinct genotypic differences with human strains most common among canine isolates. USA300 (community-associated MRSA) was detected in the healthcare setting. Genotypic environmental MRSA isolate data reflected the distribution of strains circulating in human and animal populations associated with such environments. Future surveillance and infection control research should emphasize understanding of transmission among human, animal, and environmental populations.

Disclosures. **All authors:** No reported disclosures.

276. Molecular Epidemiology of MRSA and VRE Co-colonization among Hospitalized Adults in Detroit

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Background. Co-colonization with methicillin-resistant *S. aureus* (MRSA) and vancomycin-resistant *Enterococcus* (VRE) is a key factor in the emergence of vancomycin-resistant *S. aureus*. Our objective is to describe the molecular epidemiology of MRSA co-colonization through comparison of MRSA *spa* types between co-colonized cases and matched controls.

Methods. We conducted a prospective study among adult inpatients in six hospitals in and around Detroit, Michigan. Cases were defined as individuals with positive cultures for MRSA and VRE within 7 days of one another. Controls with a positive culture for MRSA and not VRE were matched to cases by hospital, infection type, healthcare associated infection, and requirement for intensive care unit (ICU) care. Patient demographics and clinical data were collected by medical record review. *spa* typing was conducted by sequencing of the staphylococcal protein a (spa) gene, and sequences were analyzed using DNAGear. Molecular characteristics were compared between matched study groups using generalized estimating equations.

Results. 113 MRSA isolates were analyzed from 83 MRSA and VRE co-colonized case patients and 30 MRSA-only control patients. Isolates were most frequently identified from acute bacterial skin and skin structure infections (46%) and bloodstream infections (17%). The majority of clinical cultures (76%) occurred within 72 hours of admission. The most common *spa* types were t002 (n = 42; 37%), t008 (n = 33; 29%) or t1094 (n = 12; 11%). The t002 type was significantly more common among co-colonized cases (n = 39; 47%) than among MRSA-only controls (n = 3; 10%) ($p = 0.002$). Conversely, the t008 type was significantly more common among controls (n = 15; 50%) than among cases (n = 22; 22%) ($p < 0.001$).

Conclusion. Patients with MRSA and VRE co-colonization were more likely to be infected with USA100-associated type t002. In contrast, patients with MRSA-only were more likely to be infected with USA300-associated type t008. This difference in molecular epidemiology may represent underlying differences in the medical history of patients at risk for co-colonization.

Disclosures. **E. T. Martin**, NIH/NIAID: Grant Investigator, Grant recipient **M. J. Rybak**, Cubist: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Forest: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Theravance: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Durata: Consultant, Consulting fee; NIH: Investigator, Research grant **K. S. Kaye**, Sage: Grant Investigator and Speaker's Bureau, Grant recipient and Speaker honorarium

277. Molecular Epidemiology of *Staphyloccocus aureus* in Children with Bacteremia

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Background. The molecular epidemiology of *Staphyloccocus aureus* is quickly evolving. The objective of our study was to determine the genetic profiles of *S. aureus* isolates causing bacteremia.

Methods. We performed a retrospective analysis of *S. aureus* isolates causing bacteremia collected from 2010 to 2011. Isolates were characterized using the Identibac S. *aureus* Array Tube platform. This is a unique method that is capable of analyzing the presence of up to 334 *S. aureus* target sequences covering 180 distinct genes and their allelic variants. The genes analyzed include resistance determinants, toxin genes, core variable elements, capsule determinants, and other virulence factors, allowing characterization of the overall genetic background of the bacterial isolate. The genetic profile identified by Identibac allows affiliation of the isolates with clonal complexes (CC) based on a data base maintained in the software.

Results. A total of 121 *S. aureus* isolates were analyzed. Isolates belonged to 17 different CCs. The most common CC was CC8 (35.5%), followed by CC5 (20.6%), CC30 (8.3%) and CC59 (7.4%). Forty-one isolates (33.8%) were methicillin-resistant *S. aureus* (MRSA). MRSA isolates were only associated with CC8 and CC5. The majority of MRSA isolates harbored Panton-Valentine leukocidin (71.8 %) compared to MSSA isolates (28.2 %). The most abundant enterotoxin genes were those of the enterotoxin gene cluster (egc (seg, sei, sem, sen, seo, seu) which were present in 43 % of all isolates. Other common virulence factors identified included the toxic shock syndrome toxin in 9.9% of isolates, the staphylokinase in 11.5%, the hemolysin alpha in 99% and the collagen binding adhesin in 20.6% of isolates. Mup A gene which encodes for mupirocin resistance was present in 2.5 % of isolates and qac gene encoding resistance to quaternary ammonium compound was present in 4.9% of isolates.

Conclusion. We describe a collection of invasive *S. aureus* isolates. Our data suggests that certain clonal complexes, CC8 and CC5 are predominant in bacteremia. Bacteremia was mostly caused by MSSA. The Identibac *S. aureus* Array Tube technology was able to generate comprehensive molecular genotypic information that will allow us to understand the complex epidemiology of *S. aureus.*

Disclosures. **R. Selvarangan**, Alere: Investigator, Research grant

278. High Prevalence of Panton-Valentine Leukocidin in methicillin-susceptible *Staphylococcus aureus* in Camden, NJ

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Background. The Panton-Valentine leukocidin (PVL) is implicated in pathogenesis of *Staphylococcus aureus* (SA) infections including skin/soft tissue infections (SSTIs) and necrotizing pneumonia. *pvl* is extensively described in Community-associated methicillin-resistant SA, especially epidemic clones USA300 and USA400, but is reported less frequently in methicillin-susceptible SA (MSSA). We have noted an increase in severe SSTI by *pvl*-containing MSSA; including strains with USA300 genotype but lacking *mecA*. We prospectively studied prevalence of *pvl* in MSSA in patients at a New Jersey hospital, and further characterized the *pvl* positive MSSA strains.

Methods. We prospectively collected MSSA isolates from diverse specimen sources from a tertiary care hospital in southern New Jersey over a one year period (2013). We tested isolates for *pvl* by PCR using published primers. Prevalence of *pvl* gene among MSSA isolates was correlated with specimen source and antibiotic resistance phenotype.

Results. We collected 134 MSSA isolates from blood (49), wound (44), nasal (14), respiratory (12), body and joint fluid (10), and other (5) sites. Overall 22 isolates had *pvl* (16.6%), including 13 wound, 5 blood, 2 body fluid, and 1 nasal and 1 urine isolates. Highest prevalence of *pvl* was among wound isolates (13/44, 29.5%). Erythromycin resistance (E-R) correlated strongly with *pvl;* 17 of 22 *pvl*-positive isolates were E-R (30% of all E-R isolates; $p < 0.001$). However Clindamycin resistance (C-R) did not correlate with *pvl*; only 2 of 22 *pvl* strains were C-R. 4 of 6 Levofloxacin-Intermediate isolates had *pvl* ($p < 0.01$).

Conclusion. Prevalence of *pvl* is increasing among MSSA from patients at a tertiary care center in southern New Jersey. Prevalence of *pvl* was highest in wound isolates, consistent with the pathophysiologic role of PVL in SSTIs. E-R but not C-R isolates were most likely to have *pvl*. The correlation of non-inducible macrolide resistance with *pvl* in this pool of MSSA isolates is similar to non beta-lactam resistance profiles of USA300 CAMRSA in our region. This is consistent with a hypothesis that *pvl* positive MSSA may evolve from USA300 CAMRSA by loss of *mecA* function via partial or complete deletion, and may explain a regional decline in proportion of CAMRSA in SSTI. Further genetic analysis of this collection of *pvl* positive MSSA is ongoing.

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279. Prevalence and Epidemiology of Mupirocin Resistance Among Those Colonized with Methicillin-resistant *Staphylococcus aureus* in the Community

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Background. Mupirocin ointment is often used to attempt eradication of colonization with methicillin-resistant *Staphylococcus aureus* (MRSA). However, mupirocin resistance, particularly among community-onset MRSA strains, has been increasing. This study sought to describe the prevalence and epidemiology of mupirocin resistance among community-dwelling subjects and their colonized household members.

Methods. Over a three year time period, surveillance cultures for MRSA colonization were obtained from patients presenting to an ambulatory setting with an acute MRSA skin and soft tissue infection (i.e., index case) and their household members. All MRSA isolates obtained from subjects were evaluated for mupirocin minimum inhibitory concentration (MIC) using Etest®. Isolates with high-level mupirocin resistance (MIC >512 µg/ml) were compared to susceptible isolates on the basis of SCCmec type, spa typing and susceptibilities to other commonly tested antimicrobials.

Results. Four hundred thirty-four isolates were included in the analysis. Nineteen (4.4%) isolates demonstrated high-level mupirocin resistance (HLMR). Approximately half of these (47.4%) were isolated from index cases. The results are demonstrated in the table. Clindamycin resistance was seen more commonly among isolates with HLMR(42.1% vs 9.2%; $P < 0.001$). No isolates demonstrated resistance to trimethoprim-sulfamethoxazole. No differences were seen by SCCmec type. The predominant *spa* type seen in both susceptible and HLMR isolates was t008. However, this was more commonly seen in susceptible isolates.

Characteristic	Susceptible N=413	High-level Resistance N=19	P-value
Clindamycin resistance	38 (9.2)	8 (42.1)	<0.001
SCCmec type	235 (56.7)	11 (57.9)	0.91
IV	180 (43.3)	8 (42.1)	0.90
II			
spa type	297 (71.9)	8 (42.1)	0.005
t008	11 (2.7)	1 (5.3)	0.50
t002	11 (2.7)	0 (0)	0.47
t024	45 (10.9)	8 (42.1)	<0.001
other			

Conclusion. HLMR is associated with clindamycin resistance in MRSA surveillance culture isolates. Future studies should determine the rate of development of cross-resistance to other antimicrobials with mupirocin use.

Disclosures. **All authors:** No reported disclosures.

280. Association between acessory gene regulator II expression and mortality among critically ill patients receiving vancomycin for hospital-acquired methicillin-resistant *Staphylococcus aureus* bacteremia

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Background. The polymorphism of the accessory gene regulator (*agr*) of methicillin-resistant *Staphylococcus aureus (MRSA)* is known to play an important role in controlling the production of virulence factors. Notably, infections caused by MRSA with *agr*-II expression are shown to be predictive of vancomycin therapy failure. However, the impact of *agr*-II expression on mortality of patients receiving vancomycin therapy for severe MRSA infections is not well established. The aim of this study was to evaluate the association between *agr*-II expression and 30-day mortality among critically ill patients receiving vancomycin therapy for hospital-acquired MRSA bacteremia.

Methods. A retrospective cohort was performed at a 30-bed general intensive care unit (ICU) of a tertiary hospital in southern Brazil. All cases of documented hospital-acquired MRSA bacteremia treated with vancomycin in the ICU setting between May 2009 and November 2011 were evaluated. Cox regression was performed to evaluate

whether *agr*-II expression (determined by PCR) was associated with 30-day mortality. Covariates included age, presence of immunossuppression, APACHE-II score, initial C-reactive protein (CRP) plasma levels, initial serum creatinine levels, vancomycin minimum inhibitory concentration, vancomycin serum levels and time to effective antibiotic administration.

Results. In total, 21 patients were evaluated during the study period. The prevalence of *agr*-II expression was 38% (8 patients). The median APACHE-II of the study population was 23 (IQR, 19 to 31). The overall cohort mortality was 61% (13 patients). After multivariate analysis, initial plasma CRP ($P = 0.01$), initial serum creatinine ($P = 0.03$) and expression of *agr*-II ($P = 0.02$) were independently associated with the 30-day mortality. Patients receiving vancomycin therapy for bacteremia due to MRSA with *agr*-II expression had their hazard of death increased by 6.6 times (95%CI, 1.2-37.0) when compared with those with bacteremia by MRSA without *agr*-II expression.

Conclusion. Expression of *agr*-II poses risk for mortality in critically ill patients receiving vancomycin for hospital-acquired MRSA bacteremia. Alternative antimicrobial agents including daptomycin and linezolid for treatment of MRSA bacteremia expressing *agr*-II should be considered in this setting.

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281. Regional Changes in Methicillin-Resistant *Staphylococcus aureus* in Purulent Skin and Soft Tissue Infections among Patients Presenting to Canadian Emergency Departments

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Background. Community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) has emerged as a leading cause of purulent skin and soft tissue infections (SSTI) in many areas of the world. The evolving epidemiology of MRSA in SSTIs across Canada is seldom described. This study characterizes the changing prevalence and microbiology of MRSA in patients presenting to emergency departments (EDs) across Canada over half a decade.

Methods. Using a prospective, observational design, we enrolled patients presenting to 27 hospital EDs (spanning 7 provinces) with acute purulent SSTIs over 3 phases: P1 - July 1, 2008 to April 30, 2009; P2 - January 16, 2012 to November 30, 2012; and P3 - April 28, 2013 to March 31, 2014. Participating EDs agreed to collect wound swabs on all patients presenting with purulent SSTIs. Eligible patients were those whose wound cultures grew *S. aureus*. Antimicrobial susceptibility testing by broth microdilution in accordance with CLSI guidelines was undertaken on all isolates. Structured chart audits were undertaken. Simple proportions are reported at site, regional and provincial levels and compared using Chi-squared/Fisher exact test, as appropriate.

Results. A total of 4752 (P1: 1340; P2: 1622; P3: 1790) *S. aureus* positive encounters were recorded over the 3 phases. Accounting for all sites, the overall MRSA prevalence decreased significantly between P1 (31%) and P2 (27%, $p = 0.002$), and remained unchanged in P3 (28%, $p = 0.42$). A similar trend was observed among the 12 sites that participated in all 3 phases (P1 vs P2: $p = 0.004$; P2 vs P3: $p = 0.70$). Among the 18 sites participating in at least two study phases, most (61%) experienced a declining trend in MRSA prevalence, while 28% of them observed an increase (3 Ontario and 2 Alberta sites). City-level analyses revealed variability in the MRSA prevalence. Most cities experienced a decrease in the prevalence. Overall, the highest prevalence was seen in the western provinces of British Columbia (P1: 44%, P2: 66%, P3: 53%), Saskatchewan (P2: 47%, P3: 48%), and Alberta (P1: 48%, P2: 28%, P3: 31%) during all phases, while the lowest prevalence was observed in Quebec (P1: 20%, P2: 19%, P3: 11%).

Conclusion. MRSA epidemiology continues to evolve across Canada. While the overall Canadian prevalence of MRSA in SSTIs remains substantial, it is variable across the country, and appears to be decreasing regionally.

Disclosures. **All authors:** No reported disclosures.

282. Epidemiology of Skin and Soft-Tissue Infections in US Army Trainees at Fort Benning

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Background. Soldiers in training are at high risk for skin and soft-tissue infection (SSTI), especially those caused by methicillin-resistant *Staphylococcus aureus* (MRSA). Robust epidemiological, microbiological, and molecular data are vital to developing prevention strategies. The objective of this investigation was to describe the epidemiology and clinical characteristics of SSTI in a high MRSA setting.

Methods. In July 2012, we initiated a prospective observational cohort study among US Army Infantry trainees at Fort Benning, GA to determine overall and MRSA SSTI incidence and to describe the clinical characteristics of disease. Clinical *S. aureus* isolates underwent molecular characterization, including pulsed-field gel electrophoresis (PFGE).

Results. From July 2012 through July 2013, 25,181 trainees completed 14-week Infantry training. Of those trainees, 846 developed SSTI for an overall rate of 0.04 per 100 person-days. The MRSA SSTI rate was 0.01 per 100 person-days. Rates of SSTI were highest during the summer months. The median interval from training start to clinical presentation for SSTI was 40 (range 0-108) days. The most frequent clinical manifestations were cellulitis (48.7%) and abscess (32.4%) with the majority (65.5%) of infections on the lower extremities. Of the 846 SSTI subjects, 464 clinical specimens were collected, of which 388 (83.6%) were culture-positive for *S. aureus*, with MRSA accounting for 60.1%. Of the 180 MRSA isolates available for analysis, 165 (91.7%) were pulsed-field type USA300.

Conclusion. Skin and soft-tissue infections continue to impose a substantial burden in the trainee population. The epidemiology is dynamic, but USA300 MRSA continues as the predominant SSTI genotype. Effective strategies for SSTI prevention in this and other high-risk settings are critically needed.

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283. Antimicrobial Susceptibility Trends in *Staphylococcus aureus* isolated from Pedatric Patients in Military Treatment Facilities

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Background. *Staphylococcus aureus* (SA) is a ubiquitous pathogen which causes a wide range of infections in children. The ongoing epidemic of methicillin-resistant *Staphylococcus aureus* (MRSA) has led providers to choose alternate therapies such as clindamycin for first-line empiric treatment of both cutaneous and invasive infections. The purpose of this study is to determine annual antimicrobial susceptibility trends among SA isolates from pediatric patients across the Department of Defense (DoD).

Methods. Susceptibility data from SA cultures were identified from military treatment facilities across the DoD. Isolates from pediatric patients (<18 years) obtained between January 1, 2005 and December 31, 2013 were included, regardless of culture type or specimen site. The Mantel-Haenszel x^2 test for linear trends was performed to evaluate changes in susceptibility to 9 commonly utilized antibiotics over the study period.

Results. 41,602 unique isolates from pediatric patients were tested for susceptibility to >1 antimicrobial (Table 1). Changes in oxacillin susceptibility were significant over the study period ($p < 0.001$), with an increase in the percentage of methicillin-sensitive SA (MSSA) isolates from 54.9% to 65.4% over the final 6 years studied (Figure 1). Susceptibility to clindamycin decreased significantly over the study period in the subset of MSSA isolates with no significance in resistance noted in the MRSA isolate subset (Figure 2). Ciprofloxacin susceptibility significantly declined ($p < 0.001$), and among MRSA ciprofloxacin susceptibility declined from 70% to a nadir of 52.4% in 2011, and a subsequent increase to 58.9% in 2013. Susceptibility to all other antibiotics remained stable or increased among MRSA during the study period.

Conclusion. Antimicrobial susceptibility among SA in children has continued to evolve in the post-community acquired-MRSA era. Our data shows a significant decline in methicillin-resistance in SA over the study period and increasing antibiotic resistance in the MSSA isolates. Commonly utilized empiric treatment choices may not be appropriate given these shifts in susceptibility. Continued awareness of susceptibility patterns remains essential in treating pediatric patients with SA infections.

Disclosures. **All authors:** No reported disclosures.

284. Risk Factors for Methicillin Resistant *Staphylococcus aureus* Skin and Soft Tissue Infections in Patients Found to be Colonized When Admitted to an Acute Care Hospital

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Background. MRSA infections are common in patients admitted to US hospitals. Little is known about the impact of asymptomatic MRSA colonization post-discharge in the setting of active MRSA surveillance. This study aimed to determine the risk factors for MRSA SSTI among patient with MRSA nasal colonization detected during an acute care hospital admission

Methods. Retrospective, case-control study of patients admitted to the Audie L. Murphy VA Hospital in San Antonio, Texas. Patients included were ≥18 years old and colonized with MRSA during an acute care hospital admission. Patients on hospice, bone marrow transplants and with MRSA infections upon admission were excluded. We matched 28 patients who developed a MRSA SSTI to 84 controls by

length of follow-up (±10 days, up to 18 months), and collected demographics, known clinical risk factors for MRSA infection and comorbidities. Chi-square and t-test were used for bivariate analysis. A multivariable logistic regression model was used to identify risk factors for MRSA SSTIs post-discharge. P-values <0.05 were considered significant.

Results. Mean age (60.8 years -cases- vs 66.6 years- controls-) and mean Charlson comorbidity score (6.9 vs 6.6) were similar among cases and controls. Factors associated with MRSA SSTIs post-discharge were prior hospital admission within 12 months (19 cases,67.9% vs 33 controls,39.3%), MRSA infection prior to hospital admission (8 cases,28.6% vs 7 controls, 8.3%),history of myocardial infarction (8 cases, 28.6% vs 4 controls, 4.8%), and peripheral vascular disease (8 cases, 28.6% vs 7 controls, 8.3%). Prior antibiotic use was inversely associated with MRSA SSTI (11 cases, 39.3% vs 62 controls, 73.8%). In multivariable analysis, prior hospital admission within 12 months ($p = .006$) and a history of myocardial infarction ($p = .003$) were independently predictive of a MRSA SSTI. Antibiotics three months prior to infection/end of follow up were protective ($p = 0.001$).

Conclusion. Prior hospital admission within 12 months and a history of myocardial infarction are independent risk factors for MRSA SSTIs. Antibiotic use was protective for MRSA infection. Future studies should evaluate these findings as they may be used to design novel preventive interventions.

Disclosures. **J. Cadena**, Cubist Pharmaceuticals: Grant Investigator, Research grant

285. Secular Trends in *Staphylococcus aureus* Bloodstream Infections over Four Decades

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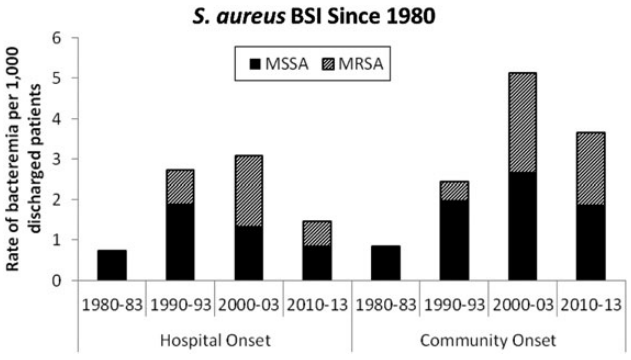
Background. The epidemiology of bloodstream infections due to *Staphylococcus aureus* (SA-BSI) has changed dramatically over the last several decades with the widespread use of intravascular catheters, the emergence and spread of methicillin resistant *S. aureus* (MRSA) and the rise of community-onset infections. We examined secular trends in SA-BSI occurring from 1980 to 2013 with particular focus on MRSA, source of BSI and location of onset.

Methods. Records were reviewed for all patients with SA-BSI who were hospitalized at one academic medical center. Rates of SA-BSI per 1,000 discharged patients were calculated for the first four years of four decades (1980-1983, 1990-1993, 2000-2003 and 2010-2013). Temporal trends were assessed for proportion of SA-BSI due to MRSA and attributed source.

Results. Rates of SA-BSI increased from the 1980-3 study period through the 2000-3 study period however both hospital-onset and community-onset BSIs decreased in the last study period (Figure). In the 1980-3 study period there was only one central line-associated BSI (CLABSI) and two MRSA BSIs. The increase in SA-BSI through 2000-3 was driven by an increase in CLABSI for both hospital-onset and community-onset BSIs; in the 2000-3 period, 75/235 hospital-onset and 166/400 community-onset SA-BSIs (127 of which were dialysis catheter related) were CLABSIs. Hospital-onset SA-BSI decreased by 48% in the 2010-13 period with 51/123 SA-BSI being CLABSIs. Since 2000-3, MRSA has accounted for about half of all SA-BSI although there was a decrease in the proportion of hospital-onset SA-BSI caused by MRSA over the last two study periods, from 57.0% in 2000-3 to 41.5% in 2010-13.



Conclusion. There was an increase in SA-BSI in the first three decades of the study period, in large part due to CLABSIs in and outside the hospital. In the last decade there has been a decrease in SA-BSI, with a marked decrease in hospital-onset infections, including a decrease in CLABSI. While MRSA still causes almost half of all SA-BSI, there was a notable decrease in hospital-onset MRSA in recent years.

Disclosures. **All authors:** No reported disclosures.

286. A Pilot Study of the Acceptability and Feasibility of Self-Collected Pre-Operative *Staphylococcus aureus* Nasal Screening

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Background. Routine pre-operative screening of patients for meticillin-resistant *Staphylococcus aureus* (MRSA) colonisation has been used as a method of reducing post-operative wound infections. As most patients attend pre-operative assessment clinics a number of weeks before their surgical procedure, the results of MRSA screening may not identify recent acquisition. We piloted an investigation of the feasibility and acceptability of a patient-collected nasal swab posted back to the laboratory for analysis.

Methods. 100 patients in a mixed discipline pre-operative assessment clinic were screened for MRSA as per current hospital infection control protocol. They were then issued with a pack including a charcoal swab and information sheet and were advised to return the swab via a pre-paid return envelope. Each pack included a questionnaire regarding ease of use and acceptability of self-collecting the swab at home. The self-collected samples were processed as per routine culture based laboratory methods for *S. aureus* (SA) and MRSA. The clinic taken swabs was processed for MRSA only. The results of both self-taken and nurse-collected screens were collated and compared, and questionnaire data analysed.

Results. A total of 77 packs out of 100 (77%) distributed were returned to the laboratory. 78% of returns were aged below 65 years. MRSA was not isolated from any of the pre-operative assessment clinic swabs or self-collected samples. Meticillin-sensitive SA was isolated from 21/77 (27%). Five returns did not include a questionnaire. 71/72 (99%) of the questionnaire respondents found the instructions easy to understand and all reported that they had managed to collect the samples without difficulty. 97% of patients found the process acceptable and would prefer this to re-attendance to a healthcare facility for further sampling. Informal feedback from pre-operative clinic staff has also been complimentary regarding the scheme.

Conclusion. This preliminary study shows that self-collected nasal screening is acceptable to the majority of patients. The prevalence of MRSA colonisation in our pre-operative population is low, but the detection of MSSA in nearly a third of patients shows that this method may have an acceptable clinical yield. A larger study is required and underway to confirm these findings.

Disclosures. **All authors:** No reported disclosures.

287. Value of Methicillin Resistant *Staphylococcus aureus* Nasal Swab Screening for Predicting Invasive Methicillin Resistant *Staphylococcus aureus* Respiratory Infection in Pediatric Patients with Artificial Airways

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Background. In our 180 bed free-standing children's hospital, all patients admitted to intensive care units or from a nursing facility have a GenXpert MRSA nasal screen. This information is routinely used for isolation purposes, but it has increasingly been used to guide antibiotic usage when patients have a suspected infection. Previous studies have demonstrated that patients with positive MRSA screens are at higher risk for MRSA infection. The objective of this study was to evaluate the predictive value of the MRSA screen result for MRSA infection in patients with suspected respiratory infection as tested by broncheoalveolar lavage (BAL) or tracheal aspirate.

Methods. All patients admitted from January 27, 2009-September 17, 2013 who had both MRSA screening and BAL or tracheal aspirate performed were retrospectively studied. 1336 pairs of screens and cultures were analyzed for correlation of results using descriptive statistics.

Results. There were 196 positive MRSA screens (14.7%). 45 respiratory cultures were positive for MRSA. Of these 45 positive cultures, 13 had negative MRSA screens, while 32 had positive screens. Statistical analyses demonstrated a positive predictive value for the screen of 16.3% and a negative predictive value of 98.9%. Sensitivity of the screen for a positive respiratory culture was 71% and specificity was 87.3%. Relative risk of culture-positive MRSA respiratory infection with respect to positive screen result was 14.8.

Conclusion. Our study demonstrates that the MRSA nasal screen has a high negative predictive value for MRSA infection in pediatric patients with artificial airways. While patients with a positive screen are at significantly higher risk for culture positive infection, the sensitivity and positive predictive value of a positive screen are relatively low. Since patients with a negative MRSA screen have a lower risk of MRSA respiratory infection, this data could help guide clinicians toward earlier narrowing of empiric antibiotic choices in patients with MRSA screen results and pending respiratory cultures. However, clinical judgment should be used, as 29% of patients in our cohort with a culture positive MRSA respiratory infection had a negative screen. Further study is warranted to clarify the implications of these results.

Disclosures. **All authors:** No reported disclosures.

288. Lack of Synergy With Six Blood Isolates of Methicillin-Resistant *Staphylococcus aureus* (Vancomycin MIC of 2) Tested With Combinations of Vancomycin + Gentamicin, Vancomycin + Rifampin and Vancomycin + Cefazolin.

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Background. Vancomycin (V) is the mainstay for treatment of infections caused by MRSA. Yet failures of therapy with V are common. Current guidelines recommend V alone for treatment of most serious infections. Exceptions include prosthetic valve endocarditis and in some instances osteomyelitis and CNS infections where combinations of antibiotics are suggested.

Methods. We used timed kill-curves to test antibiotic combinations used in our center against six isolates of MRSA. These six with V MICs of 2 confirmed by Microscan and E-test were chosen from 15 blood isolates of MRSA saved over three years. We used V and gentamicin (G), V and rifampin (R), two combinations used to treat MRSA, and V and cefazolin (C), a combination recommended in recent publications. Colonies were counted in duplicate at 0, 4, 8, 12 and 24 hour time points. Determinations of synergy, indifference and antagonism were made at the 24 hour time point. Standard definitions requiring 2 log differences in cfu/mL were used.

Results. Results are shown in the following table:

Combination	Synergy	Indifferent	Antagonistic
V + G	0	6	0
V + R	0	5	1
V + C	0	6	0

Antibiotic synergy was not demonstrated with any of the combinations tested. In all but one experiment, the combination was "indifferent," however V + G was more active than V alone for three strains. Although "antagonistic" in only one, V+ R was less active than either drug alone for four of the isolates. Killing with V + C paralleled killing with V alone in all six strains.

Conclusion. We have shown that combining G, R or C with V against six bloodstream isolates of MRSA with V MIC of 2 is not synergistic *in vitro.* These results did show enhanced killing with V + G in three strains and with V + R in one strain. Killing with V + R was slightly worse in three and significantly worse in one of the isolates. These results, although not showing synergy, may support the use of V + G, and, although not showing antagonism, do not support use of V + R.

Disclosures. **P. Schreckenberger**, BioFire: Grant Investigator and Scientific Advisor, Consulting fee and Research grant; bioMerieux: Research Contractor, Research grant; Cepheid: Consultant and Grant Investigator, Consulting fee and Research grant; Cubist: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; Quidel: Scientific Advisor, Consulting fee; Siemens Healthcare: Consultant, Research Contractor and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Becton-Dickinson: Speaker's Bureau, Speaker honorarium; Theravance: Scientific Advisor, Consulting fee; Thermo Fisher: Scientific Advisor, Consulting fee

289. Occurrence of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Surgical Site Infections (SSIs) of Total Knee and Total Hip Arthroplasty (TKA and THA) Procedures within Veterans Health Administration Medical Centers

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Background. TKAs and THAs are typically clean surgeries. Though rare, they can become infected post-surgically. *Staphylococcus aureus* is a common etiologic agent for causing SSI in these surgeries. Infection with MRSA has been contributing to larger percentage of these infections. VA's MRSA Prevention Initiative started early in 2007 and was completely operational by October 2007. During this time, no specific system-wide guidelines for routine pre-operative decolonization practices have been implemented. We analyzed data in association with VA's MRSA Prevention Initiative to see if there was a decrease in MRSA SSIs associated with TKAs and THAs.

Methods. From 2008 through 2012, TKA/THA surgeries done and infections with MRSA in these surgeries have been tracked up to 1-year post surgical implantation of the artificial joint. Poisson regression of combined TKA/THA annual rates was performed for the 5-year period for trend.

Results. From among its 151 medical center sites, VA had 98 which performed one or more TKAs/THAs during the analysis period. 55,454 TKAs/THAs were reported from VAMCs. Of those 55,454, 336 (0.61%) had an SSI within 1 year of the surgery. The table indicates annual rates from the analysis.

	MRSA-associated TKA/THA SSI rates 1 year after implantation		
	mean	95% LCL	95% UCL
*FY2008	0.79%	0.67%	0.94%
FY2009	0.69%	0.61%	0.78%
FY2010	0.60%	0.54%	0.67%
FY2011	0.52%	0.45%	0.60%
FY2012	0.46%	0.37%	0.56%

P=0.0004 for decrease by Poisson regression evaluating all sites annually over time

*FY = Federal Fiscal Year (running from Oct 1 through Sept 30).

Conclusion. Decrease of mean MRSA-associated TKA/THA SSI rates by over 40% was seen between 2008 and 2012, in temporal association with the MRSA National Prevention Initiative.

Disclosures. **All authors:** No reported disclosures.

290. Optimizing clinical outcomes in patients with methicillin-sensitive *Staphylococcus aureus* bacteremia and reported penicillin allergy

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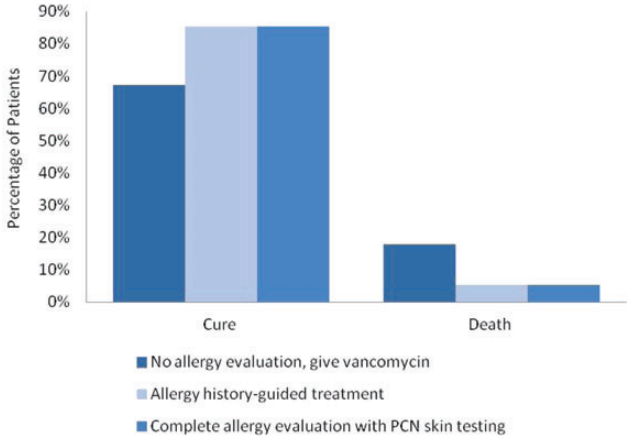
Background. Methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia is a morbid infection with first-line therapies including nafcillin, oxacillin and cefazolin. While these drugs are avoided in patients with true penicillin (PCN) allergy, most such patients are not allergic and could tolerate these medications. We used a decision tree to examine the optimal MSSA treatment strategy for patients with reported PCN allergy.

Methods. We developed a model comparing 3 treatment strategies for patients with MSSA bacteremia and reported PCN allergy: No allergy evaluation, give vancomycin (*Vanc*); Allergy history-guided treatment using cefazolin if reported PCN allergy excluded anaphylactic features (*HX-Cefaz);* and complete allergy evaluation with PCN skin testing, give cefazolin if negative (*ST-Cefaz).* Key literature-based input parameters included the 12-week probability of MSSA recurrence and mortality associated with cefazolin (9.1%, 3.6%) and vancomycin (18.8%, 19.2%), penicillin and cefazolin cross reactivity (2.9%) and proportion of patients who react to cefazolin with a nonanaphylactic PCN allergy history (2.2%). 12-week outcomes included MSSA cure and death; adverse drug reactions (ADRs, toxicity or intolerance); and allergic reactions including those potentially iatrogenic. In sensitivity analyses, we examined the impact of varying uncertain input parameters.

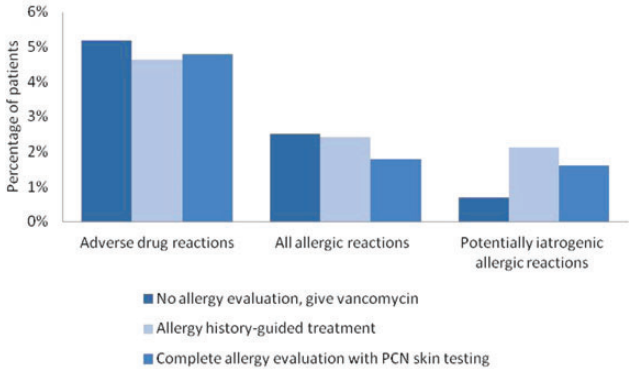
Figure 1: Outcomes associated with 3 treatment strategies for patients with MSSA and reported PCN allergy



Results. *Vanc* resulted in the lowest cure and the highest mortality (Figure 1), and the highest ADRs and allergic reactions (Figure 2); most allergic reactions were not

iatrogenic. Similar numbers of patients are cured with *HX-Cefaz* and *ST-Cefaz*, but *ST-Cefaz* resulted in fewer allergic reactions. *HX-Cefaz* would be preferred to *ST-Cefaz*, leading to the greatest proportion cured and the fewest allergic reactions if <1.6% of patients with a nonanaphylactic PCN allergy react to cefazolin.

Figure 2: Allergic and adverse drug reactions associated with 3 treatment strategies for patients with MSSA and reported PCN allergy



Conclusion. Patients with MSSA bacteremia and a reported PCN allergy have improved outcomes when the allergy is addressed, either by history or skin testing, compared to vancomycin treatment without evaluation. Prospective data on cefazolin reactions in PCN-allergic patients are needed to confirm that full allergy evaluation is preferred over history alone.

Disclosures. **All authors:** No reported disclosures.

291. Efficacy and safety of telavancin in the treatment ofram-positive bloodstream infections in cancer patients

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Background. Gram-positive bacteria are a leading cause of blood stream infections (BSI) in cancer patients. Telavancin is a bactericidal glycopeptide which has not been compared to vancomycin in cancer patients with BSI. We therefore compared the clinical efficacy and safety of telavancin to vancomycin in cancer patients with gram-positive BSI.

Methods. Between March 2011 and May 2013, we enrolled 40 cancer patients (39 evaluable) with uncomplicated Gram-positive BSI who received intravenous telavancin for at least 14 days for S. aureus and 7 days for other Gram-positive cocci. Patients with baseline creatinine clearance (Cr Cl) > 50 ml/minute received a daily dose of 10mg/kg and those with Cr Cl between 30-49 ml/minute received a dose of 7.5 mg/kg. Patients were followed for 1 month after the last dose of study drug. These patients were compared with 39 historical matched control patients (based on underlying disease, type of organism and neutropenia) who were treated with vancomycin.

Results. A total of 78 evaluable patients were analyzed, 39 patients in each group. The most common pathogens causing BSI were Staphylococcus aureus (n = 20), followed by alpha-hemolytic Streptococci (n = 7), Enterococcus (n = 7), coagulase-negative Staphylococcus (n = 4), and beta-hemolytic Streptococci (n = 1). 62% of patients had hematological malignancies and 51% were neutropenic at onset of bacteremia. There was a possible trend towards a better clinical response associated with telavancin compared with vancomycin (89% vs 72%; $p = 0.09$). Microbiological response was similar in both groups (telavancin 92% vs vancomycin 95%; $p = 0.67$). Overall mortality and infectious-related mortality were comparable in both arms. Drug related averse events were similar in both groups (telavancin 26% vs vancomycin 21%; $p = 0.59$). Median creatinine levels and creatinine clearance at baseline, end-of-treatment and last follow-up visits were comparable in both groups.

Conclusion. Treatment with telavancin for gram-positive BSI in cancer patients was generally effective and safe and may provide a useful and convenient alternative to standard vancomycin therapy.

Disclosures. **I. Raad**, Astellas: Grant Investigator, Grant recipient; Pfizer: Consultant, Consulting fee

292. Avoiding time-dependent bias in estimating the attributable cost of healthcare-associated methicillin-resistant *Staphylococcus aureus* infections

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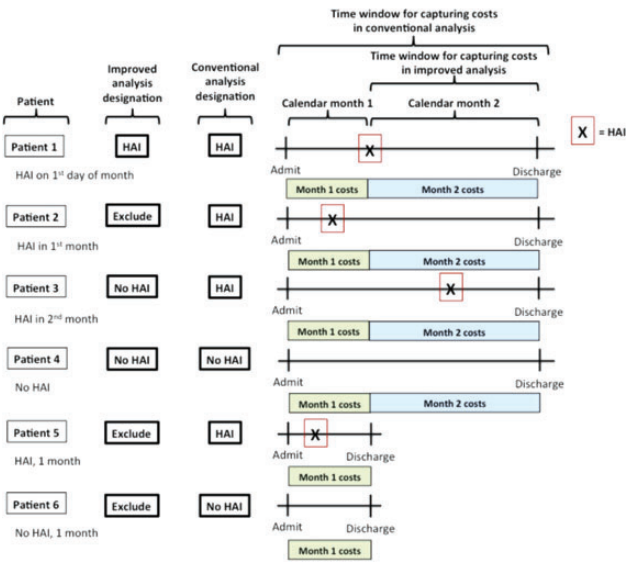
Background. Previous estimates of the impact of healthcare-associated infection (HAI) on healthcare costs have been inflated due to time-dependent bias. In this analysis, we demonstrate the magnitude of this inflation by estimating the healthcare costs attributable to an HAI due to methicillin resistant *Staphylococcus aureus* (MRSA) using a unique dataset in the Department of Veterans Affairs (VA) that allowed us to distinguish between costs that occurred before and after an HAI.

Methods. Data from the VA's activity-based accounting system provides a separate observation for every calendar month during a patient's inpatient stay. In our "improved analysis," we used this data to construct multivariable generalized linear models to compare the healthcare costs occurring after the first calendar month in patients with an MRSA HAI on the first day of a calendar month with those without an MRSA HAI. We compared these results to those from a "conventional analysis" which considered healthcare costs across the patients' entire inpatient stay in those with and without an HAI. Both analyses are described in Figure 1.

Our study cohort consisted of patients with an inpatient admission lasting longer than 48 hours within the VA between October 1, 2007 and November 30, 2010. MRSA HAIs, identified from microbiology reports in the VA electronic medical record, were defined as positive clinical cultures for MRSA between 48 hours after admission and discharge.

Results. The cohort consisted of 121,520 patients (0.08% of whom had an MRSA HAI on the first day of a calendar month) in our improved analysis and 386,794 patients (1.04% of whom had an MRSA HAI) in our conventional analysis. In our improved analysis, estimates of the increase in inpatient costs due to MRSA HAI were \$12,272 ($p < 0.001$) and \$23,733 ($p < 0.001$) for variable and total costs, respectively. In our conventional analysis, estimates of the increase in inpatient costs due to MRSA HAI were more than 40% greater (\$18,003 ($p < 0.001$) and \$33,885 ($p < 0.001$) for variable and total costs, respectively).

Figure 1: Schematic representation of the analyses that estimated the effect of MRSA HAI on inpatient healthcare costs that considered the timing of MRSA HAI during hospitalization (improved analysis) and (b) did not consider the timing of MRSA HAI during hospitalization (conventional analysis).



Note: In the improved analysis, patients were excluded if their inpatient stay did not extend over 2 calendar months (e.g., patients 5 and 6) or if they had an HAI during the 1st calendar month (e.g., patient 2). Of the patients included in the improved analysis, patients with an HAI on the 1st day of the 2nd calendar month were assigned to the MRSA HAI group (e.g., patient 1) and those without an HAI on the 1st day of the 2nd calendar month were assigned to the non-MRSA HAI (e.g., patients 3 and 4). The improved analysis compared costs from the 1st day of the 2nd calendar month and beyond between the MRSA HAI and non-MRSA HAI groups. All 6 types of patients represented in Figure 1 were included in the conventional analysis. Patients with an HAI in the conventional analysis, regardless of the calendar month in which it occurred, were assigned to the MRSA HAI group (e.g., patients 1, 2, 3, and 5) and those without an HAI were assigned to the non-MRSA HAI (e.g., patients 4 and 6). The conventional analysis compared costs across the entire inpatient stay between the MRSA HAI and non-MRSA HAI groups.

Conclusion. This is the first study to account for time-dependent bias in the estimation of incremental per-patient healthcare costs attributable to HAI. We found that failure to account for this bias can lead to substantially inflated estimates.

Disclosures. **All authors:** No reported disclosures.

293. Healthcare-associated methicillin-resistant *Staphylococcus aureus* infections increase the risk of post-dishcarge mortality

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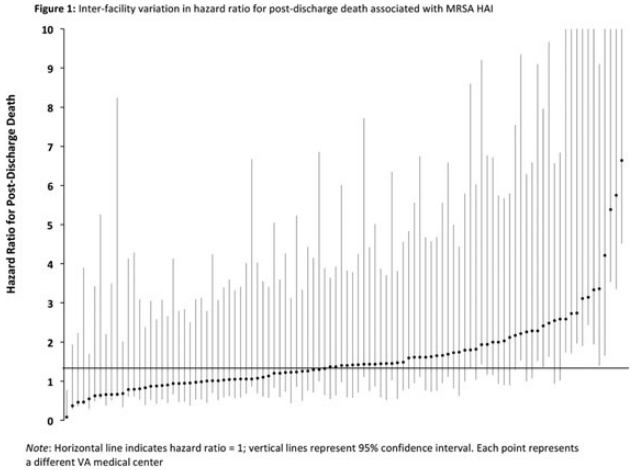
Background. While many studies have estimated the impact of healthcare-associated methicillin resistant *Staphylococcus aureus* (MRSA) infections (MRSA HAIs) on mortality during the initial hospital stay, little is known about the long-term risk of death in these patients. The purpose of this study was to quantify the effect of MRSA HAIs on mortality after discharge from the hospital.

Methods. Our study cohort consisted of patients with an inpatient admission within the US Department of Veterans Affairs (VA) system between October 1, 2007 and November 30, 2010. Of these patients, we identified those with an MRSA HAI from microbiology reports in the VA electronic medical record. MRSA HAIs were defined as positive clinical cultures for MRSA between 48 hours after admission and 48 hours after discharge. Because microbiology data was insufficient to distinguish between MRSA infection and colonization, in a secondary analysis, we categorized MRSA HAIs into bloodstream and non-bloodstream since positive MRSA cultures from blood were most likely infections. We constructed multivariable Cox proportional hazards regressions to assess the impact of MRSA HAIs on post-discharge mortality in the 365 days following discharge using both the full cohort and a propensity score-matched subsample. Finally, we generated a mortality estimate for each of the 123 VA hospitals represented in our data to evaluate inter-facility variability.

Results. In our analysis cohort of 369,743 inpatients, MRSA HAIs were recorded in 3,599 (1.0%) patients. We found that MRSA HAIs resulted in an increased risk of post-discharge mortality both in the full cohort (HR = 1.42, $p < 0.001$) and in the subset of propensity score-matched patients (HR = 1.37, $p < 0.0001$). Similarly, the risk of post-discharge mortality was elevated in patients with MRSA bloodstream HAIs (HR = 1.61, $p < 0.001$ full cohort; HR = 1.72, $p < 0.001$ propensity score-matched subset). In addition, there was considerable variation in estimates across facilities (Figure 1).



Conclusion. We found that MRSA HAIs significantly elevate the long-term risk of mortality. These results underscore the importance of infection prevention efforts in the hospital.

Disclosures. **All authors:** No reported disclosures.

294. A Hierarchical Transmission Model Evaluating the Effectiveness of Hospital Infection Control Strategies

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Background. Although studies have been done to evaluate the efficacy of hospital infection control strategies, results have been inconsistent and interpretation is complicated by variation in design and implementation. Challenges of modeling data from such studies can be met through the development of flexible frameworks that incorporate implementation specific components.

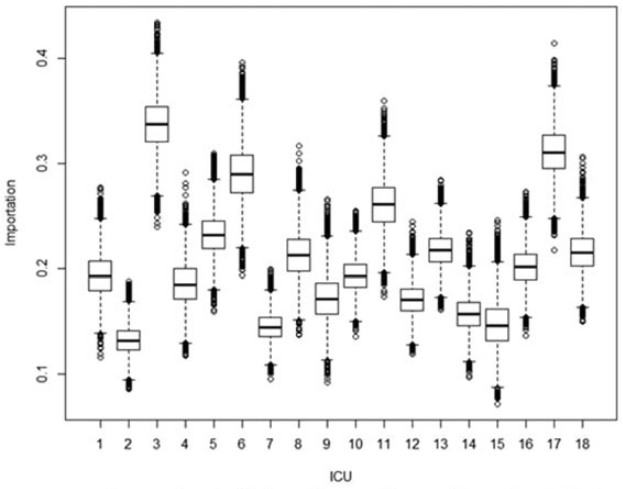

Figure 1: The posterior distribution of importation prevalence of MRSA by ICU, demonstrating the wide variability in importation prevalence between ICUs.

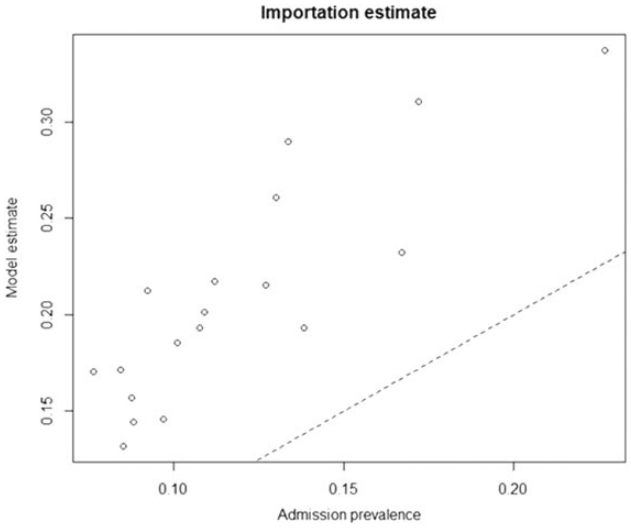

Figure 2: Model importation probability estimates with estimates of admission prevalence, defined to be the proportion of surveillance cultures collected within 2 days of admission that were positive. The slanted dashed line represents equality between the two estimates.

Methods. We developed a hierarchical transmission model based on a Bayesian statistical framework for modeling nosocomial transmission. Markov chain Monte Carlo was used for estimation which allowed for the modeling of missing data and tractability of estimates. Additionally imperfect testing, importation probability and transmission rate were incorporated in the model for parameter estimation. Transmission rates had a common bivariate log-normal distribution for pre- and post-intervention means in the control ICUs, but the post-intervention mean for ICUs in the intervention arm was modified by an additive intervention effect parameter. We retrospectively analyzed data collected from an intervention study including 18 ICUs, 10 of which were assigned to the intervention arm. The study period was from April 2005 to August 2006, during which time 20,945 patients were admitted to an ICU. Surveillance cultures for methicillin-resistant *Staphylococcus aureus* were collected on patients weekly, at admission and at discharge.

Results. The model estimated significant variation in importation across the 18 ICUs (Figure 1) and estimates of importation were consistently higher than those of admission prevalence (Figure 2). The intervention effect parameter estimate was 0.02 with 95% CI [-0.45, 0.49] on the log-scale, suggesting no effect, while estimates of the mean

transmission rate varied little between the pre- and post-intervention periods (Figure 3).

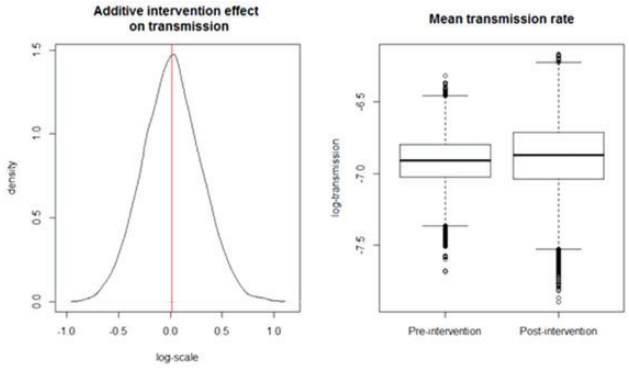

Figure 3: Plot showing the posterior distribution for the intervention effect together with the pre- and post-intervention mean transmission rates.

Conclusion. Modeling importation and transmission did not alter the conclusions of the original study, which showed no intervention effect. Transmission models provide an efficient, flexible framework for parameter estimation, and can be used to analyze infection control interventions. Future work includes incorporating patient-level and ICU-level characteristics, and development of an R package for general use.

Disclosures. **All authors:** No reported disclosures.

295. Excess Length of Stay due to Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococci* Infections at ICUs across the United States

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Background. Understanding the impact of hospital-acquired infections on excess length of stay (LOS) can help to identify variation in practice and opportunities to improve care. However, time-dependent bias, which occurs when the timing of infections is not appropriately taken into account, can inflate the estimates of excess LOS due to HAIs. We used a multistate model to examine the excess ICU LOS after methicillin-resistant *Staphylococcus aureus* (MRSA) and vancoymycin-resistant *enterococci* (VRE) positive clinical cultures.

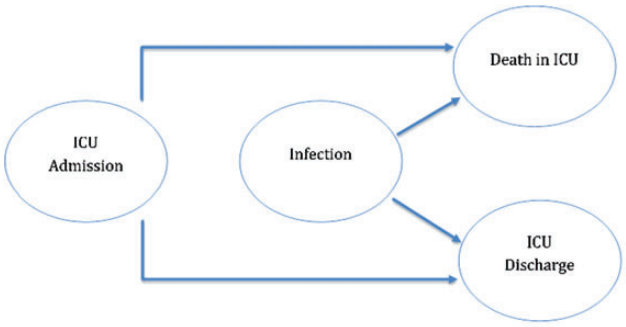

Figure 1: Multistate model showing entry into the Intensive Care Unit, intermediate state of infection and competing endpoints of death and discharge

Methods. We conducted a retrospective study using clinical culture results from 13,278 patients admitted to 18 ICUs in the United States from April 2005 – August 2006. Our multistate model (Figure 1) incorporated an intermediate event, and two endpoints: death and discharge. Because death and discharge are competing events, we modeled them separately to improve our interpretation. We obtained median LOS estimates, interquartile range [IQR] and estimates of excess LOS using the multistate model with 95% Confidence Intervals (CIs) using 1,000 bootstrap samples. Additionally, we examined variation in and associations of excess ICU LOS estimates across the ICUs due to positive MRSA and VRE cultures.

Results. Of patients admitted to ICU, 13.2% died before discharge or ICU transfer. Median ICU LOS [IQR] for those without a positive culture and those with positive MRSA and VRE cultures were 4 days [2, 7], 9 days [4, 20] and 9 days [4, 21], respectively. Multistate model estimates of excess ICU LOS [95% CI] were 3.7 days [2.3, 5.1] and 5.3 days [3.6, 7.5] for MRSA and VRE positive clinical cultures, respectively. Estimates of excess ICU LOS were positively correlated (Figure 2), ranging from -2.0 and 32.0 days and -1.7 and 42.0 days for MRSA and VRE positive clinical cultures, respectively.

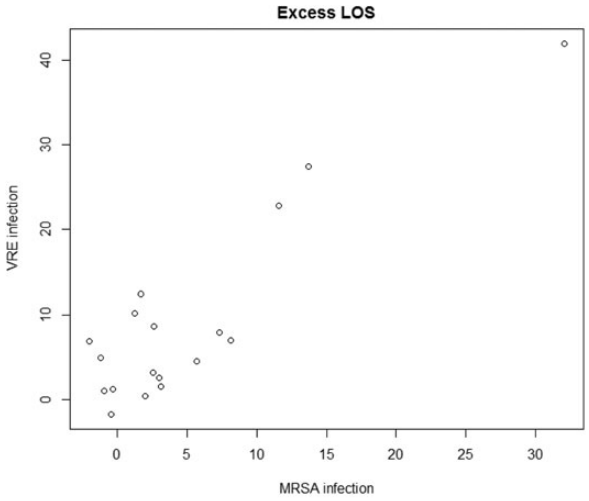

Figure 2: Plot showing the relationship between estimates of excess Length of Stay (LOS) by Intensive Care Unit (ICU) due to methicillin-resistant *staphylococcus aureus* (MRSA) and vancomycin-resistant *enterococci* (VRE) infections.

Conclusion. Overall, excess ICU LOS was longer after positive VRE cultures compared to positive MRSA cultures. Estimated excess ICU LOS were similar to the differences in the median ICU LOS for those with MRSA and VRE positive cultures. There was a positive correlation in excess ICU LOS related to MRSA and VRE infections, suggesting possible ICU-level factors contributing to excess LOS. Future analyses that adjust for confounders are warranted.

Disclosures. **R. E. Nelson**, Roche: Consultant and Grant Investigator, Consulting fee, Research grant and Research support

296. The impact of healthcare-associated methicillin-resistant *Staphylococcus aureus* infections on post-discharge healthcare costs and utilization

Richard E. Nelson, PhD[1]; Makoto Jones, MD, MS[2]; Chuan-Fen Liu, MPH, PhD[3]; Matthew Samore, MD[4]; Martin Evans, MD[5]; Nicholas Graves, PhD[6]; Bruce Lee, MD, MBA[7]; Michael Rubin, MD, PhD[8]; [1]Ideas Center, VA Salt Lake City Health Care System, Salt Lake City, UT; [2]Internal Medicine, University of Utah School of Medicine Division of Epidemiology, Salt Lake City, UT; [3]VA Puget Sound, Seattle, WA; [4]University of Utah School of Medicine, Division of Epidemiology, Salt Lake City, UT; [5]Internal Medicine, University of Kentucky, Lexington, KY; [6]Institute of Health and Biomedical Innovation, Queensland University of Technology, Queensland, Australia; [7]Johns Hopkins Loomberg School of Public Health, Baltimore, MD; [8]Internal Medicine, University of Utah School of Medicine, Salt Lake City, UT

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Background. A number of studies have estimated the cost associated with healthcare-associated methicillin resistant *Staphylococcus aureus* (MRSA) infections (MRSA HAIs) during the primary hospitalization. However, little is known about their impact on post-discharge resource utilization. The purpose of this study was to estimate healthcare costs and utilization attributable to MRSA HAIs after discharge from the hospital.

Methods. Our study cohort consisted of patients with an inpatient admission lasting longer than 48 hours within the US Department of Veterans Affairs (VA) system between October 1, 2007 and November 30, 2010. Of these patients, we identified those with an MRSA HAI from microbiology reports in the VA electronic medical record. MRSA HAIs were defined as positive clinical cultures for MRSA between 48 hours after admission and 48 hours after discharge. We constructed multivariable regression models to assess the impact of MRSA HAIs on post-discharge outpatient, inpatient, and pharmacy costs and utilization in the 365 days following discharge. We used propensity score matching to identify a subset of patients without MRSA HAI who were similar in observable characteristics to those with MRSA HAI.

Results. After applying our inclusion criteria, our cohort included 369,743 inpatients, of whom, 3,599 (1.0%) had MRSA HAIs. Our final analysis sample included 3,592 patients with MRSA HAI who had been matched to 3,592 patients without MRSA HAI. Using generalized linear models, we found that MRSA HAIs resulted in greater pharmacy ($710, $p < 0.0001$) and inpatient costs ($11,044, $p < 0.0001$) during the 365-day post-discharge period. In addition, using logistic and negative binomial regressions, we found that having an MRSA HAI increased the risk of a readmission (OR = 1.396, $p < 0.0001$), the number of prescriptions (IRR = 1.138, $p < 0.0001$), and inpatient days (IRR = 1.204, $p < 0.0001$) but decreased the number of subsequent outpatient encounters (IRR = 0.941, $p = 0.008$).

Conclusion. This study shows that MRSA HAIs are associated with significant post-discharge health care cost and utilization. These findings suggest that financial benefits resulting from infection prevention efforts may extend beyond the initial hospital stay.

Disclosures. **All authors:** No reported disclosures.

297. Trends in *Staphylococcus aureus* (SA) Isolation in 28 US Hospitals, 2009-2013

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Background. Recent data suggest that healthcare-associated invasive methicillin-resistant *S. aureus* (MRSA) infections are declining in the US (JAMA Intern Med 2013;173:1970). However, such infections are the minority of SA disease. Few studies have examined recent trends in epidemiology of SA clinical isolates that include susceptible, community-onset and non-bloodstream isolates. We performed multicenter SA surveillance in 2009, 2011 and 2013.

Methods. We collected SA isolates from July-December in 2009, 2011 and 2013 from a geographically representative sample of US hospitals. 28 centers participated in all 3 surveys, each submitting up to 100 consecutive, unique (1 isolate/patient) clinically-significant SA, with demographic information, during each survey. Susceptibility testing was performed using CLSI methods and *mec*A PCR. Pulsed field gel electrophoresis (PFGE), spa and SCC*mec* typing, and *pvl* detection were performed on all MRSA. We defined as hospital-onset (HO) those SA from cultures obtained >48 h after admission.

Results. A total of 8377 SA isolates were collected (2009:2828, 2011:2767, 2013: 2782). Age distribution of pts was < 5 (6%), 6-20 (10%), 21-64 (59%), and > 65 years (23%), and 55% were male. The most common specimen source was wound/abscess (52%), followed by bloodstream (25%). The % MRSA decreased over time, from 53% of isolates *mec*A + in 2009-2011 to 46% in 2013. Only 15% of SA were HO: among MRSA, the % that were HO decreased from 15-16% in 2009-2011 to 12% in 2013. HO-MRSA accounted for only 5% of all SA clinical isolates in 2013. The USA300 MRSA PFGE type predominated in all three surveys, and by 2013 a single spa type (t008) accounted for 54% of all MRSA, followed by t002 (17.2%), with no other spa type accounting for more than 2% of MRSA. High level mupirocin resistance increased among SA/MRSA from 1.8/2.2% in 2009 to 2.6/3.9% in 2013.

Conclusion. Consistent with reports of declining HO-MRSA infection rates, our microbiology lab-based surveillance reveals that a decreasing proportion of all SA clinical isolates are MRSA or hospital-onset. Rates of resistance to mupirocin, an agent used often in HO-MRSA prevention programs, are rising. Strategies to prevent SA infections beyond HO-MRSA will be needed to substantially impact the burden of SA disease.

Disclosures. **D. J. Diekema**, Forest Labs: Grant Investigator, Research grant

298. Association between Contact Sports and Colonization with Methicillin-Resistant *Staphylococcus aureus* in a Prospective Cohort of Collegiate Athletes

Natalia Jimenez-Truque, PhD, MSCI[1]; Elizabeth Saye, BS[1]; Nicole Soper, MT[1]; Ben Saville, PhD[2]; Isaac Thomsen, MD[1]; Kathryn Edwards, MD, FIDSA[1]; C. Buddy Creech, MD, MPH[1]; [1]Pediatric Infectious Diseases, Vanderbilt University Medical Center, Nashville, TN; [2]Vanderbilt University Medical Center, Nashville, TN

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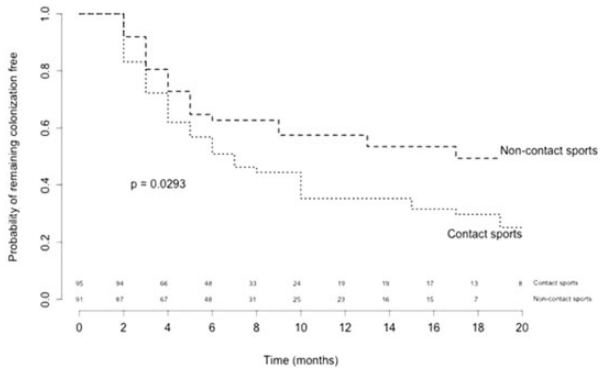
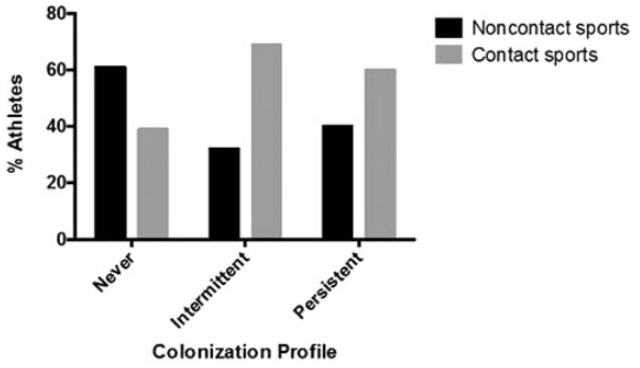
Background. Athletes have higher risk of infection with *Staphylococcus aureus* than the general population. Most studies in athletes have included primarily male contact sports participants and have not assessed staphylococcal carriage, which increases the risk of infection. The natural history of staphylococcal carriage across sports is poorly understood and limits strategies to prevent infections in athletes. We aimed to examine the epidemiology and risk factors of staphylococcal carriage in a cohort of collegiate athletes.



Time to becoming colonized with *S. aureus* in 186 college athletes



Percentage of staphylococcal carrier profiles in athletes

Methods. We enrolled a cohort of 377 varsity collegiate athletes who were followed from August 2008 to April 2010. A baseline, self-administered questionnaire ascertained risk factors for colonization. Nasal and oropharyngeal swabs were obtained at enrollment and monthly thereafter to detect staphylococcal colonization, both with methicillin-susceptible (MSSA) and methicillin-resistant *S. aureus* (MRSA). We used American Academy of Pediatrics definitions of contact and noncontact sports. Secondary outcomes included time to colonization with *S. aureus* and carriage profile (e.g., noncarriers, intermittent carriers, and persistent carriers). A parametric survival model, multinomial mixed models, logistic regression, and multinomial logistic regression were used, as appropriate.

Results. Overall, 224 contact sports and 153 noncontact sports athletes were enrolled. Compared to noncontact sports athletes, those in contact sports had higher risk of carrying *S. aureus* over time. Contact sports participants had higher odds of being colonized with MRSA [odds ratio (OR), 2.36; 95% confidence interval (CI), 1.13-4.93], they tended to carry *S. aureus* for longer periods of time (intermittent carriage OR, 3.60; 95% CI, 2.02-6.40; persistent carriage OR, 2.39; 95% CI, 1.21-4.72), and acquired *S. aureus* more quickly [hazard ratio (HR), 1.61; 95% CI, 1.02-2.55].

Conclusion. Staphylococcal carriage was common in contact sports athletes, particularly for football team members. These findings suggest that efforts to prevent transmission of *S. aureus* among athletes should be focused on contact sports teams.

Disclosures. **K. Edwards**, Novartis: Grant Investigator and Scientific Advisor, Research grant

299. Duration of Colonization with Methicillin-resistant *Staphylococcus aureus* and Determinants of More Rapid Clearance of Colonization

Valerie C. Cluzet, MD[1]; Jeffrey S. Gerber, MD, PhD[2]; Irving Nachamkin, DrPH, MPH[3]; Joshua Metlay, MD, PhD[4]; Theoklis Zaoutis, MD, MSCE[5]; Kathleen G. Julian, MD[6]; David Royer, PhD[7]; Darren R. Linkin, MD, MSCE[8]; Susan E. Coffin, MD, MPH[9]; David J. Margolis, MD, PhD[1]; Judd E. Hollander, MD[1]; Rakesh D. Mistry, MD, MS[10]; Laurence J. Gavin, MD[1]; Pam Tolomeo, MPH[1]; Jacqueleen Wise[1]; Mary K. Wheeler, MBE[11]; Warren Bilker, PhD[5]; Xiaoyan Han, MS[11]; Baofeng Hu[1]; Neil O. Fishman, MD[1]; Ebbing Lautenbach, MD, MPH, MSCE[8]; The CDC Prenvention Epicenters Program[1]; [1]University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; [2]Department of Pediatrics, Division of Infectious Diseases, The Children's Hospital of Philadelphia, Philadelphia, PA; [3]Department of Pathology and Laboratory Medicine, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA; [4]Medicine, Harvard Medical School, Boston, MA; [5]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania, Perelman School of Medicine, Philadelphia, PA; [6]Penn State Hershey Medical Center, Hershey, PA; [7]Lincoln University, Lincoln University, PA; [8]University of Pennsylvania School of Medicine, Philadelphia, PA; [9]Division of Infectious Diseases, The Children's Hospital of Philadelphia, Philadelphia, PA; [10]Children's Hospital Colorado, Aurora, CO; [11]Center for Clinical Epidemiology and Biostatistics, University of Pennsylvania Perelman School of Medicine, Philadelphia, PA

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Background. Factors associated with duration of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization in the community setting are unknown. The objective of this study was to assess the duration of MRSA colonization and factors associated with termination of colonization among subjects presenting with MRSA acute skin and soft tissue infection (SSTI).

Methods. A prospective cohort study was conducted from January 1, 2010 through December 31, 2012 at five academic medical centers. Patients presenting with acute SSTI (i.e., index cases) and their household members were followed with serial surveillance cultures for MRSA colonization every two weeks for six months. Duration of colonization was calculated using a Kaplan-Meier estimate. A Cox proportional hazards regression model was developed to identify factors associated with termination of colonization with MRSA.

Results. Median duration of MRSA colonization among index cases was 36 days (inter-quartile range [IQR] 21-91 days). Fifty-three index cases (19.4%) remained colonized with MRSA at the end of the study period. Factors associated with more rapid

termination of MRSA colonization included: treatment of the MRSA SSTI with clindamycin (adjusted hazard ratio (HR), 1.55; 95% confidence interval (CI), 1.16-2.07; P = 0.003) and non-white race (HR, 1.43; 95% CI, 1.08-1.89; P = 0.01). Neither presence of family members under the age of 18 nor MRSA colonization in household members at study entry were associated with duration of MRSA colonization (HR, 1.17; 95% CI, 0.87-1.56; P = 0.30 and HR, 0.91 95% CI, 0.74-1.10; P = 0.33, respectively).

Conclusion. Among individuals with an acute MRSA SSTI, duration of colonization with MRSA was shorter than has been reported in other studies, due perhaps to a more systematic sampling approach; however, approximately 20% of subjects remained colonized at the end of six months. The association between clindamycin and shorter duration of MRSA colonization may indicate a unique role for this antibiotic in treatment of MRSA SSTI. Interestingly, presence of colonization in a household member was not significantly associated with duration of colonization. Future studies of household decolonization should look at the impact of this on duration of colonization in the index case.

Disclosures. **T. Zaoutis**, Merck: Investigator, Research grant; Merck: Consultant, Consulting fee; Pfizer: Consultant, Consulting fee; Astellas: Consultant, Consulting fee

300. Tracing the Natural History of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Colonization among Residents of a Long Term Veterans' Nursing Home in Pittsburgh, PA

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Background. Residing in long-term care facilities (LTCF) is a risk for MRSA carriage and infection. MRSA colonization rates up to 40% are reported, 3% to 50% of colonizers develop infections. In 2007, VA Pittsburgh Healthcare System (VAPHS) initiated universal screening for MRSA in LTCF patients. This afforded a unique opportunity to examine the natural history and consequences of MRSA carriage in LTCFs. The aims were to assess MRSA colonization and infection over a 6 year period in a VA long term care facility and to identify risk factors for infection among those colonized with MRSA.

Methods. This was an observational retrospective cohort study. Charts of all patients residing at the facility with a surveillance or clinical culture yielding MRSA during FY 2007 through FY 2012 were reviewed. Patients with prior or active staphylococcal infection were excluded. Patients were followed until death, discharge, transfer or up to September 2012.

Results. 359 patients were identified. 41% were MRSA positive on admission and 59% acquired MRSA during their stay at a median of 49 days post admission. Overall 15% acquired MRSA infections-10% of patients that were positive on admission and 18% of new MRSA patients. Factors associated with infection using multivariate analysis included: length of stay [LOS] >3 weeks [OR 8.10 (95% CI 1.9-35.4)], duration of MRSA carriage [1.003/day (1.002-1.005)], dementia [2.66 (1.3-5.3)], skin breakdown [3.98 (2.0-8.0)], female gender [4.73 (1.1-19.8)] and hemodialysis [3.72 (0.9-14.7)]. 14.5% died during the current admission. Mortality was related to age, underlying diseases and MRSA colonization at admission, but not MRSA infection. Use of antibiotics was not associated with MRSA infections or death. The rate of MRSA transmission during this time period averaged 0.89/1,000 bed days of care.

Conclusion. Risk factors significant for MRSA infection are presence of wounds, dementia, hemodialysis, duration of MRSA carriage and prolonged length of stay which would be suitable targets for studies examining benefits of decolonization. The majority of infections in our long-term care facility occurred among those acquiring MRSA colonization after admission, despite an active MRSA prevention program and a low rate of transmission.

Disclosures. **All authors:** No reported disclosures.

301. Risk of Methicillin-Resistant *Staphylococcus aureus* Infection in Patients with Intermittent vs Persistent Nares Colonization

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Background. Prevention of methicillin resistant *Staphylococcus aureus* (MRSA) infection is of concern in healthcare settings. More information is needed about the relationship between MRSA colonization and infection, in order to inform prevention efforts. Among patients followed longitudinally, risk of methicillin sensitive *S. aureus* (MSSA) infection is similar among non-colonized (NC) and intermittently colonized (IC) patients, and higher among persistently colonized (PC) patients. Previous studies of *S. aureus* infection in NC persons vs those with an IC or PC phenotype have not included patients with MRSA colonization, and have been limited to patients on peritoneal dialysis. We compared the incidence of MRSA infection in patients who were screened longitudinally over 41 months, and classified as PC, IC or NC.

Methods. Observational study of 3,873 patients who had > or = 5 MRSA nasal colonization screening tests collected longitudinally from February 20, 2010 through July 26, 2013. Invasive infections were identified using the CDC National Healthcare Safety Network definitions. PC patients had > or = 80% of screening tests positive, NC patients had all negative screening tests. IC patients had > 0 and < 80% of screening tests positive. Kaplan-Meier time-to-event analysis was used to determine the relative risks of infection in PC, IC, and NC patients.

Results. 103 patients developed invasive MRSA infections, 16.3% of PC, 11.3% of IC, and 0.5% of NC patients. PC patients were at higher risk of invasive infection than NC patients, for any given period of time-at-risk (HR 39.2, 95%CI 19.6-78.4, p < 0.001). IC patients were at higher risk than NC patients (HR 23.8, CI 13.8-40.9, p < 0.001). The difference in risk between PC and IC patients was not statistically significant (HR 1.65, CI 0.96-2.84, p = 0.071).

Conclusion. Among the general patient population of this tertiary care medical center, invasive MRSA infection occurred frequently in both persistently and intermittently colonized patients. There was a higher rate of infection in those who were PC when compared with IC individuals, but the difference was not statistically significant. These results suggest that the risk of MRSA infection is similar among persistently colonized and intermittently colonized patients.

Disclosures. **All authors:** No reported disclosures.

302. Methicillin-resistant *S. aureus* (MRSA) and Methicillin-susceptible *S. aureus* (MSSA) Transmission to the Gowns and Gloves of Health Care Workers interacting with Nursing Home (NH) Residents

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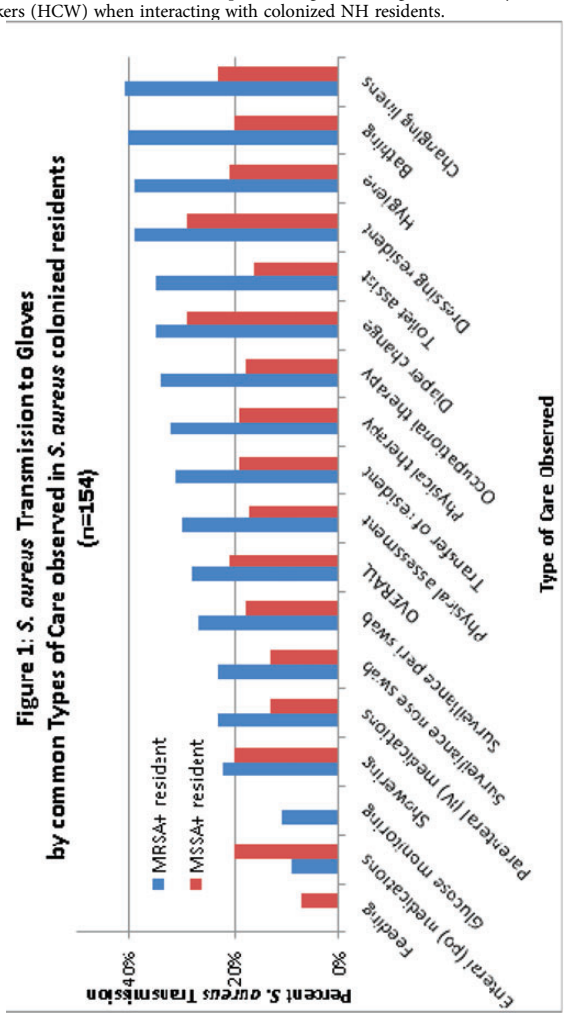
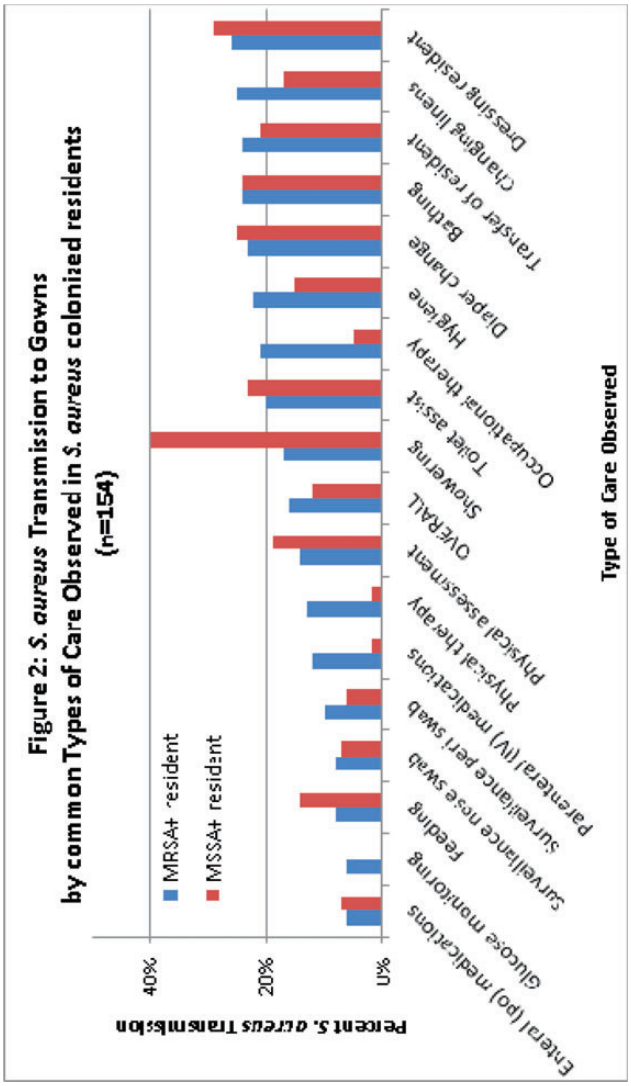
Background. The usefulness of barrier precautions in NHs in unknown. The primary objective of this multi-center study was to estimate the frequency of and risk factors for *S. aureus* transmission to protective gowns and gloves worn by health care workers (HCW) when interacting with colonized NH residents.



Methods. Residents from 14 community NHs in Maryland and Michigan were enrolled and cultured for *S. aureus* at the anterior nares and perirectal skin. HCWs were asked to wear disposable gowns and gloves during a usual care activity (e.g., wound dressing). A research coordinator observed and recorded the type of care

delivered with each activity and swabbed the HCW gown and gloves to test for the transfer of *S. aureus*.



Results. 96 (24%) residents were colonized with MRSA and 58 (15%) with MSSA from 398 enrolled residents. Compared with MSSA colonized residents, MRSA colonized residents were significantly older (80 vs 75 years, $p < 0.01$), more likely to be on antibiotics (14% vs 3%, $p = 0.05$), have a pressure ulcer (24% vs 11%, $p = 0.04$), and have perirectal colonization with *S. aureus* (39% vs 14%, $p < 0.01$). We observed an average of 8.6 care activities per resident. The number and duration of activities did not vary by colonization status; however, the common types of care activities did vary by whether residents were colonized with MRSA or MSSA. For example, transferring the resident was 93% more common care with MRSA colonized residents. Transmission varied by type of care activity from 0% to 41% for gloves and 6% to 26% for gowns (Figures 1 and 2). Transmission to both gloves (28% vs 21%, $p < 0.01$) and gowns (16% vs 12%, $p = 0.03$) was more common during care of MRSA vs MSSA colonized residents.

Conclusion. *S. aureus* transmission to gowns and gloves was common; MRSA transmission was 33% more common than MSSA transmission. This difference could be due to greater burden of *S. aureus* in MRSA colonized residents as suggested by the higher level of perirectal colonization and greater skin breakdown; however, it could also be due to different care activities. To our knowledge, this is the first study to study MRSA transmission by type of care activity in NHs. Our results have substantial implications for infection prevention policy in NHs.

Disclosures. **M. C. Roghmann**, AHRQ: Grant Investigator, Grant recipient and Research grant

303. Comparison of Environmental MRSA Levels on High Touch Surfaces in Contact Isolation and Non-Contact Isolation Patient Rooms: A Veterans Hospital Study

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Background. Nosocomial methicillin-resistant *Staphylococcus aureus* (MRSA) infections in hospitalized patients cause significant morbidity and mortality. Hospital environmental surfaces play an important role in transmission of healthcare-associated MRSA. Evidence suggests that there is a 2-3 percent increased risk of acquisition of MRSA in a patient who occupied a room previously contaminated by MRSA. But the burden of MRSA in non-contact isolation rooms has not been studied well in Veterans hospital settings.

Methods. We identified each contact isolation patient room (occupied by a patient with active MRSA colonization or infection) and non-contact isolation patient room using infection control databases. A total of 5 surfaces were sampled in both the arms (tray table, toilet seat, toilet grab bar, bedrail and call button). The samples were obtained using Rodac contact plates (Hardy Diagnostics, Santa Maria, CA) in a patient room where the patient had at least 2 days of stay. Roll plate technique was used for non-flat surfaces. The contact plates were then incubated at 35-37^{O}C for 48 hours. Deep Pink or mauve colored colonies were identified as MRSA and the total colony counts were recorded. Further, these colonies were confirmed as MRSA by using standard methods. When the colony counts for MRSA were greater than 200 or too numerous to count, they were recorded as 200 to avoid outliers.

Results. We had a total of 23 rooms in the Non-MRSA arm and 39 rooms in the MRSA arm. The total number of colonies identified were 93 (non-MRSA arm) and 1593 (MRSA arm). The average colony count per surface was 0.80 and 8.1 respectively for non-MRSA and MRSA arms.

Conclusion. Non-MRSA rooms have MRSA, but the burden is far lower than MRSA rooms. This may further provide insight into the transmission cycle of MRSA in a hospital setting, especially in closed systems like Veterans hospitals. Further, the non-MRSA rooms may have a role in nosocomial transmission in a hospital environment.

Disclosures. **C. Jinadatha**, Xenex Healthcare Services: Grant Investigator, Research grant

304. Methicillin-resistant *Staphylococcus aureus* in Ohio EMS providers: A statewide cross-sectional study

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) is an organism responsible for varying forms of infection and is considered a major public health threat. Carriage rates of MRSA in hospital personnel has been shown to be higher than the general population. Little research has been done to describe MRSA in emergency medical service (EMS) personnel and no known studies have been performed in Ohio EMS providers. The objective of this study is to use sample weights to determine the statewide nasal carriage prevalence of MRSA among Ohio EMS personnel and the associated risk factors.

Methods. A cross-sectional study was conducted among Ohio EMS personnel randomly sampled from 84 urban and rural agencies. Surveys assessing demographics, occupational history, health, cohabitation status, and hygiene practices were collected with nasal swabs from those who enrolled. Survey weight adjusted analysis was performed (1) to estimate MRSA nasal carriage prevalence of Ohio EMS providers in 2010, and (2) to identify variables associated with MRSA.

Results. MRSA was detected in 4.6% (13/280) EMS personnel sampled. By applying survey weights to account for differential selection, it was estimated that 1,965 Ohio EMS providers were MRSA carriers. After employing the survey weights, factors associated with MRSA carriage were: those who did not practice frequent hand hygiene after glove use (odds ratio [OR], 10.51 [95% Confidence Interval (CI), 2.54 - 43.45]; P< 0.01), living with someone with a recent staphylococcal infection (OR, 9.02 [95% CI, 1.03-78.98]; P = 0.05), and individuals with low frequency of hand washing (OR, 4.20 [95% CI, 1.02 -17.27]; P = 0.05).

Conclusion. The prevalence of MRSA in Ohio EMS personnel is both an occupational hazard and patient safety concern. Implementing methods to reinforce CDC guidelines for proper hygiene could decrease MRSA found in the EMS setting. Previous literature suggests that a reduction in MRSA colonization can lead to decreases in transmission and improved health for both patients and personnel.

Disclosures. **All authors:** No reported disclosures.

305. Changes in antibacterial resistance patterns in *Staphylococcus aureus* strains which are related to microbiologically confirmed nosocomial bacteraemia in a tertiary care educational hospital in Turkey: A perspective through 2001-2013

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Background. In this study it was aimed to evaluate the resistance patterns of microbiologically confirmed nosocomial bacteremia (MCNB) related *S. aureus* strains between 2001-2013 retrospectively.

Methods. Any patient in whom *S. aureus* was isolated in at least one set of blood cultures (Sent to the bacteriology laboratory 72 h after hospital admission) was

considered to have MCNB. Data of antibacterial resistance and hospital admission dates were extracted from hospital patient record database.

Resistance rates between 2000 and 2013

		2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2001-2003	2011-2013	p value
METHICILLIN	Resistance	73.8% 186	70.1% 124	76.7% 89	63.3% 119	55.3% 115	58.8% 124	56.9% 115	60.5% 98	63.3% 88	60.6% 66	57.1% 64	44.1% 41	36.2% 17	73.2% 399	48.4% 122	p<0.001
	Total: N	252	177	116	188	208	211	202	162	139	109	112	93	47	545	252	
LEVOFLOXACİN	Resistance	76.1% 118	76.2% 93	57.8% 67	57.6% 99	51.5% 106	50.0% 99	44.8% 64	63.1% 99	60.4% 81	59.8% 52	52.4% 55	43.2% 38	24.4% 10	70.7% 278	44.0% 103	p<0.001
	Total: N	155	122	116	172	206	198	143	157	134	87	105	88	41	393	234	
GENTAMICIN	Resistance	61.4% 153	61.0% 108	69.0% 80	54.3% 102	48.1% 100	56.5% 118	53.0% 106	59.6% 96	55.8% 77	57.8% 63	50.9% 57	33.7% 31	25.5% 12	62.9% 341	39.8% 100	p<0.001
	Total: N	249	177	116	188	208	209	200	161	138	109	112	92	47	542	251	
ERYTHROMYCIN	Resistance	66.9% 168	61.0% 108	62.9% 73	48.4% 91	33.7% 70	50.5% 100	37.3% 69	48.1% 76	57.2% 79	29.6% 32	29.9% 32	39.8% 37	27.7% 13	64.2% 349	33.2% 82	p<0.001
	Total: N	251	177	116	188	208	198	185	158	138	108	107	93	47	544	247	
CLINDAMYCIN	Resistance	43.4% 109	36.7% 65	50.9% 59	38.0% 71	28.8% 60	38.4% 76	21.7% 41	26.9% 43	33.3% 45	23.1% 25	20.2% 22	29.3% 27	17.0% 8	42.8% 233	23.0% 57	p<0.001
	Total: N	251	177	116	187	208	198	189	160	135	108	109	92	47	544	248	
PENICILLIN	Resistance	92.8% 233	93.2% 165	96.6% 112	93.1% 175	92.3% 192	92.4% 195	93.1% 188	93.8% 152	91.4% 127	90.8% 99	93.8% 105	89.2% 83	78.7% 37	93.8% 510	89.3% 225	p=0.028
	Total: N	251	177	116	188	208	211	202	162	139	109	112	93	47	544	252	

Double or more isolates during each episode were counted as one episode. Blood cultures were performed on Bact/Alert (bioMerieux, Durham, NC). Bacterial identifications were performed by automated API (bioMerieux, Durham, NC). Oxoid antibiotic dics (England) were used to test antibacterial susceptibility by disc diffusion method following the recommendations of CLSI.

Results. Interpreted as described by CLSI. Resistance patterns in the 2001-2003 and 2011-2013 periods were compared by Chi-square test. Results: Oxacillin resistance in 2001 was 73.8% and %36.2 in 2013 (table). When 2001-2003 and 2011-2013 periods were compared, resistance to oxacillin, levofloxacin, gentamicin, erythromycin and clindamycin decreased significantly ($p < 0.05$) (table). No glycopeptide and linezolid resistant strain was isolated during the study period.

Conclusion. There was a steady decrease in the overall *S. aureus* MCNB as well as methicillin resistance rates except 2008-11 which require further investigation. This steady decrease in the resistance rates after the 2003 budget application (which required prior approval of infectious diseases specialist for all extended spectrum antibiotics) and which is probably due to it, suggests that the application may also be useful in decreasing the antimicrobial resistance in at least *S. aureus*.

Disclosures. **All authors:** No reported disclosures.

306. Switch from MRSA PCR to Agar for Nasal Screening Does Not Increase Transmission

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Background. The VA has guidelines to screen inpatients on admission (A), transfer (T), and discharge (D). MRSA infection rates and transmissions have decreased dramatically nationally with a bundle for MRSA, which includes screening, improved infection prevention practices, environmental cleaning and culture change. Screening programs with PCR are expensive, but rapid. Our facility implemented a new screening program with agar (Spectra by Thermo Scientific) with a lab processing time of 24 hours.

Methods. Number of transmissions in our acute care facility (ICU and wards) were compared for 3 months prior to the intervention (period 1, October-December 2012) and 3 months after the intervention (period 2, October-December 2013) using a poisson regression model in Stata There was a wash-out period of 9 months where A and T were tested with PCR and D were tested with agar.

Results. The Incidence Rate Ratio for MRSA transmission was 1.32 (CI 0.67-2.59) for period 2 compared to period 1, t p = 0.42. MRSA admission prevalence was 14% in both periods 1 and 2. Turn-around times for agar tests were also compared to PCR tests. 4777 PCR tests were done in period 1, with a mean turn-around time of 34.9 hours (SD 27.5) compared to 4793 swab tests in period 2 with a mean turn-around time of 58.2 hours (SD 21.0). 19,074 tests were done in 2013 (at a cost for each PCR of $35.00 for reagents, $10 for labor and for each agar $2.60 for reagents and $3.40 for labor) for a potential $724812 cost savings/year (costs including labor $133518 for all agar, $ 858330 for all PCR). Infection rates stayed stable over our time periods.

Conclusion. Increases in MRSA transmissions after change to agar testing were not statistically significant. However, the rate ratio was in a positive direction and warrants continued vigilance. Turn-around time increased from 1 to 2 days (reflecting increase in test time, time to delivery of specimens and our Monday-Saturday daytime lab hours). Potential cost savings are significant. A cost-effectiveness analysis would be of interest.

Disclosures. **K. Gupta**, Paratek: Consultant, Consulting fee

307. Prevalence of *qac A/B* among Methicillin-Resistant *Staphylococcus aureus* (MRSA) Isolates Recovered from Active Surveillance Cultures of the Anterior Nares in the Setting of Chlorhexidine Bathing

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Background. Chlorhexidine (CHG) body washes prevent methicillin-resistant *Staphylococcus aureus* (MRSA) transmission and nosocomial blood stream infections among intensive care unit (ICU) patients. CHG tolerance can be conferred by *qac A/B*resistance genes. The long-term use of CHG bathing may result in the emergence of chlorhexidine-tolerant MRSA strains. The objective was to determine the frequency of *qac A/B* and high-level mupirocin (MUP) resistance among MRSA isolates recovered from active surveillance cultures from the anterior nares. We compared frequencies before and after the introduction of a CHG daily body wash intervention in a surgical intensive care unit.

Methods. Analysis included a random sample of banked MRSA isolates recovered before (2005) and after (2008-2010, 2012) institution of a CHG bathing protocol. PCR was used to detect the presence of *qacA/B.* Disk diffusion with a 200 ug mupirocin disk (Oxoid) was used to detect high level MUP resistance; PCR for detection of *mupA* was performed on all resistant isolates. SCC*mec* typing was performed using a multiplex PCR assay for SCC*mec* types I-V. Power analysis assumed a baseline *qacA/B* prevalence of 1%; to detect an increase in prevalence of 1% per year with a statistical power of 80% 63 samples per year were required.

Results. Sixty-three MRSA isolates per year (out of approximately 250 banked isolates per year), were randomly selected. Of the 315 selected isolates, 30 (9.5%) were *qac A/B* positive and 26 (8.2%) were MUP resistant. There was no significant difference in the prevalence of *qac A/B* positive MRSA isolates before (2005: 4, 6.3%) and after

(2008: 1, 1.5%; 2009: 9, 14%; 2010: 11, 17%; 2012: 5, 8%) use of CHG bathing (p = 0.23).The frequency of MUP resistant isolates per year was: 2005: 6 (9%); 2008: 7 (11%); 2009: 4 (6.3%); 2010: 5 (8%); 2012: 4 (6.3%). For the high-level MUP resistant and/or *qac A*/B positive isolates for which SCC*mec* typing was available (n = 36), SCC*mec*type II (24/36, 66%) was predominant.

Conclusion. Implementation of a daily CHG bathing protocol among surgical ICU patients did not significantly increase the frequency of *qac A/B* genes in MRSA isolates recovered from the anterior nares over a 6 year period. The frequency of high level MUP resistance in these strains also remained stable.

Disclosures. **C. A. Burnham**, Thermofisher Scientific: Consultant, Consulting fee

308. Effect of chlorhexidine bathing and other infection control practices on the Benefits of Universal Glove and Gown (BUGG) Trial: A subgroup-analysis

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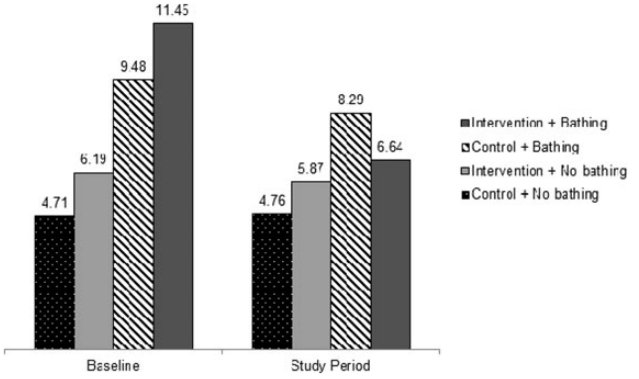
Background. Multiple interventions exist to limit transmission of methicillin-resistant *Staphylococcus aureus* (MRSA). The effect of combining different interventions is not known.

Methods. We conducted a subgroup analysis of the Benefits of Universal Glove and Gown (BUGG) trial to examine the effect of universal gloving and gowning while using other infection control interventions.



Results. Over 20 ICUs and 26,180 patient admissions, the reduction in MRSA transmission observed in BUGG tended to be greater in units also using chlorhexidine bathing (rate difference -1.20, 95% CI -5.02 to 2.63, p-value = 0.18) and was significantly greater in units switching from active surveillance culturing for MRSA (rate difference -8.16, 95% CI -16.42 to 0.01, p-value = 0.05). We found universal glove and gown use worked equally well in academic and non-academic ICUs (p = 0.15).

Conclusion. The reduction in MRSA observed with the universal glove and gown intervention was persistent in units also using chlorhexidine bathing and in academic and non-academic hospitals. Universal glove and gown use appeared to work as well or better in ICUs adopting universal glove and gown after being on active surveillance culturing.

Disclosures. **All authors:** No reported disclosures.

309. Clinical, Psycho-social and Cost Impacts of Performing Active Surveillance to Discontinue MRSA Contact Isolation for Patients Admitted to Medical-surgical Units

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Background. Many healthcare facilities automatically initiate contact isolation whenever known methicillin-resistant *Staphylococcus aureus*-colonized (MRSA+) patients are readmitted, but duration of colonization with MRSA varies. Facilities often lack systemic methods to ensure appropriately timed MRSA screening to discontinue isolation when no longer needed, resulting in continued contact isolation for remote MRSA infections.

Methods. We conducted a process improvement project on 7 medical-surgical units of a 913-bed community-based academic hospital. The project goal was to facilitate MRSA screening of known MRSA+ patients who were readmitted, if their last MRSA+ culture had occurred ≥ 1 year previously, via improved communication between Infection Prevention and nursing and physician staff and flagging of MRSA+ patients eligible for active surveillance. Clearance from isolation required 2 negative nasal MRSA cultures using ChromAgar media. We then conducted a mixed methods, retrospective evaluation of the project to evaluate: (1) percentage of eligible patients screened and cleared; (2) psycho-social evaluation of impact of isolation via a survey of a convenience sample of 32 MRSA+ patients; and (3) cost of the screening program vs cost burden of unnecessary isolation.

Results. During February 2013-March 2014, 269 patients were eligible for MRSA screening, of whom 48 (18%) were unable to complete screening due to discharge or antibiotic use. Of the 221 completing screening, 130 (81%) were found to be no longer colonized. Of 32 patients surveyed, 13 (41%) reported that isolation had affected their hospital stay, and 9 (28%) reported emotional distress resulting from their isolation. Total cost savings of the program were estimated at $101,230/year across the 7 study units. To date, 3 (2%) previously cleared patients have been readmitted with subsequent cultures growing MRSA, requiring re-isolation.

Conclusion. Eighty percent of patients with history of MRSA ≥1 year previously no longer were MRSA-colonized. Our findings suggest that an active surveillance program targeting patients with a distant history of MRSA has the potential to improve patient experience as well as reduce costs.

Disclosures. **All authors:** No reported disclosures.

310. Routine Use of Contact Precautions for MRSA and VRE: Which Way is the Pendulum Swinging?

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Background. Contact Precautions (CP) for preventing transmission of methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE) has been a cornerstone of infection prevention programs. In recent years, however, horizontal interventions such as chlorhexidine gluconate (CHG) bathing and ultraviolet-C (UVC) light disinfection have gained traction, and studies have increasingly suggested that CP may have risks that outweigh its benefits. This study was conducted to assess the present state of CP in U.S. hospitals.

Methods. 751 physician members of the Emerging Infections Network (EIN) who had identified themselves as having interest or involvement in infection prevention/infection control were invited to complete an electronic survey. The survey, which remained open for 4 weeks, contained 8 questions designed to ascertain current practices related to reducing transmission of MRSA and VRE.

Results. 429 members responded to the survey (57.7%). Respondents reported ongoing use of routine CP for MRSA (93%) and VRE (92%). The most widely used trigger for CP for both pathogens was positive clinical culture (97%), followed by pre-existing alert in the electronic record (90%), then positive surveillance culture (76%); practices for discontinuation of isolation varied widely. 81% reported performing MRSA active surveillance testing (AST) and 34% perform VRE AST for specific inpatient populations. 85% perform CHG bathing and 64% perform *S. aureus* decolonization with mupirocin for one or more subsets of inpatients. 23% reported using either hydrogen peroxide vapor or UVC light as means of room disinfection at discharge. Free text responses noted frustration and heterogeneity in the application, practice, and discontinuation of CP.

Conclusion. Routine use of CP for MRSA and VRE remains commonplace, although horizontal interventions such as CHG bathing are increasingly used. Respondents frequently questioned the value of routine CP. The heterogeneity of practices and policies was striking, and may be guided by regulatory pressure. Evidence-based guidelines from professional organizations regarding CP and horizontal interventions are needed.

Disclosures. **All authors:** No reported disclosures.

311. Reducing Nosocomial Infection in the NICU: A report on the first 10 years of our Performance Improvement Journey in Honolulu

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Background. Nosocomial infections are a major problem in Neonatal Intensive Care Units (NICU) that may cause death, disability, increase length of stay, decrease patient satisfaction, utilize medical center resources and generate increased costs. Although, our NICU nosocomial infection rates compared favorably with contemporaneous rates in 2003, we were distressed with sharply defined time limited outbreaks of *P. aeruginosa* (PA), and *S. aureus* (SA) in our crowded open room 60 bed tertiary-care NICU. Our project aim has been to decrease our nosocomial infection in a sustainable manner.

Methods. We began our performance improvement following the Plan-Do-Check-Act cycle and involving many stakeholders. This is a progress report on the first decade of our experience of the ongoing initiative including processes against nosocomial Blood Stream Infections (BSI), SA infections, NEC and Central Line Associated BSI (CLABSI). Universal daily mupirocin ointment to all NICU babies (2004),

hand hygiene initiative (2005), PA environmental reduction initiative (2005), central line insertion bundle (2005), weekly survey and contact isolation for SA (2008), regular scheduled meetings with Infection Control and NICU MD and RN staff (2008), NEC prevention bundle (2008), dwell time limits for IV catheters (2008), comprehensive unit-based safety program (2009), central line maintenance bundle (2011).

Results. Hand Hygiene rose: 60% 2005 to 96% 2012, p <.001, BSI fell from 9.6% admissions, 3.2/1,000 patient days in 2003 to 0.5% admissions, 0.3/1,000 patient-days in 2012. All SA colonization and infections fell after mupirocin p <0.002. NEC in <1500 g. babies declined 11% vs 4% p< 0.03. CLABSI fell from 1.8/1,000 line days 2010 to 0.18/1,000 line days 2012. Major positive attitude changes and professional engagement accompanied these results. A saving of $8,108,790 is estimated from the baseline period of 2003 through 2005 to the entire decade.

Conclusion. We succeeded in reducing all bacteremias, all SA and PA infections, NEC, CLABSI. Our NICU nosocomial Infection rate and NEC rates are now in the lowest quartile of centers reporting to the Vermont Oxford Network.

Disclosures. **All authors:** No reported disclosures.

312. Reduction of Nosocomial Blood Stream Infections (BSI) and Nosocomial Vancomycin-Resistant *Enterococcus faecium* (VRE) Colonisation on an Intensive Care Unit (ICU) after the Introduction of Antiseptic (Octenidine-based) Bathing: An Interrupted Time Series Analysis

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Background. On a 32 bed operative ICU at a university nosocomial VRE cases increased despite enforcement of hand hygiene and environmental disinfection. An intervention consisting in antiseptic bathing with octenidine (Octenisan®, Schülke) was started for control.

Methods. Between January 2012 and April 2014 ICU patients were screened for VRE at admission and twice weekly. Patients with a negative admission screening and a subsequent detection of VRE were defined as nosocomial cases. Intervention started May 2013 and was implemented August 2013. Octenidine based body washes were standardised by the use of new wash clothes for each body region and engaged hand disinfection before contacts at aseptic sites. Active surveillance for BSI and VRE infection and colonisation was performed, and VRE infections were determined according to the Centers for Disease Control and Prevention (CDC) criteria. Positive blood cultures taken after 3 days of admission were defined as nosocomial BSI. In case of skin commensals only the repeated detection in two independent blood cultures was taken as BSI. VRE were typed by PFGE. One-sided Permutation test was used to test the pre- and the post-intervention periods for significance (open source program "R" used).

Results. During the pre-intervention period 100 admitted (61% vanA, 39% vanB) and 113 nosocomial (60% vanA, 40% vanB) VRE cases were detected resulting in mean incidence densities (ID) of admitted and nosocomial cases of 6.6 and 7.53/1,000 patient days, respectively. PFGE analysis revealed three vanA and four vanB clusters with partially differing hyl and esp profiles, as well as unique strains. Post-interventionally, 30 admitted (65% vanA, 35% vanB) and 19 nosocomial (63 % vanA, 37% vanB) cases occurred resulting in mean IDs of 4.13 and 2.61 ($p < 0.001$), respectively. PFGE analysis showed two vanA and one vanB cluster, as well as unique strains. Nosocomial VRE infections were 10 in the pre- and one in the post-intervention period. Incidence densities of BSI pre- and post-intervention were 2.98 and 2.06, respectively ($p = 0.147$).

Conclusion. At admission to surgical ICU a high VRE prevalence was detected. The implementation of universal decolonisation using octenidine in combination with a standardised washing regimen led to a significant reduction of nosocomial VRE and a trend in reduction of BSI.

Disclosures. **All authors:** No reported disclosures.

313. Value of Discontinuation of Contact Precautions (CP) for Methicillin-Resistant *Staphylococcus aureus* (MRSA)

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Background. In hospitals with limited private rooms, CP for patients with a history of MRSA colonization may influence capacity. We assessed outcomes associated with rapid testing and discontinuation of CP for patients with documented clearance.

Methods. We conducted a prospective observational study of PCR-based MRSA screening from June 1, 2012-December 31, 2013 in the Emergency Department (ED) of the Massachusetts General Hospital, Boston, MA. Patients were eligible if they had a history of a MRSA-positive culture, but not more recent than 90d prior to the ED visit. Eligible subjects were enrolled upon screening for nasal colonization with PCR (subject-visit). PCR- subjects had CP discontinued; PCR+ subjects did not. The primary outcome was the proportion of enrolled subjects with CP-discontinuation. For subjects admitted to MGH within 30d of screening, we measured the time from ED arrival to inpatient bed arrival. When subjects were admitted to semi-private rooms and the paired bed remained vacant due to CP-status, we identified idle beds and compared attributable idle bed hours between PCR- and PCR+ subjects. Program costs (i.e., direct testing costs, personnel) minus decreased implementation of CP were estimated and compared to revenue from associated changes in idle bed hours affecting capacity.

Results. There were 2,864 eligible patients; 648 (23%) visits were enrolled. Of these, 65.1% (422/648) were PCR- and MRSA CP were discontinued. Among the 476 admissions, the PCR- (291) and PCR+ (185) admissions had similar mean hours-to-bed arrival (9.1 ± 5.7 vs 9.7 ± 6.4, $p = 0.29$). PCR- subjects had shorter mean idle bed hours compared to PCR+ (28.6 ± 25.2 vs 75.3 ± 70.5, $p < 0.001$). At representative hospital occupancy levels (75-99%), the expected revenues from increased capacity plus averted CP implementation costs exceeded program costs by a ratio of 2:1 (surplus: $181,000 - $271,000).

Conclusion. The majority of subjects were MRSA-negative by PCR and had MRSA CP discontinued. Among admitted subjects, PCR screening for MRSA with real-time removal of CP led to a substantial and significant reduction in idle bed hours. Estimates of program cost were outweighed by decreases in CP implementation costs and increased revenues from increased hospital capacity.

Disclosures. **All authors:** No reported disclosures.

314. When Should Contact Precautions be Discontinued for Patients with Methicillin-Resistant *Staphylococcus aureus* (MRSA)

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Background. When to discontinue contact precautions (CP) for patients (pts) with MRSA remains unresolved and policies vary between hospitals. Our facility considers an MRSA patient positive (+) (and thus remaining in CP) until they have had two active surveillance cultures (ASC) return negative (-) or have undergone successful decolonization therapy.

Methods. From October 2010-March 2014 we prospectively performed admission ASC (and weekly for those with (-) results) on pts known to have been MRSA (+) for at least 1 year to determine the proportion who remained MRSA (+). Characteristics (age, sex, race, hospitalization within the year, presence of a wound or foreign body, receipt of antibiotics, hemodialysis, and residence in a group setting) were collected from a chart review to determine factors associated with persistent carriage.

Results. Over the study period 408 pts with MRSA had an admission ASC done a mean of 1671 days from their first known (+) MRSA culture (range 416 - 5668 days). Ultimately, 82 (20.1%) pts in the cohort had MRSA detected during the study. 68 (16.7%) of 408 had a (+) admission ASC. Of the 339 pts who had a (-) admission ASC, 181 (53.4%) had a second ASC culture and 8 (4.4%) were (+) for MRSA. Of the 173 pts who had two (-) ASC, 6 (3.5%) went on to have a future culture (+) for MRSA.

Increased number of days between first known (+) MRSA culture to admission ASC was associated with a lower risk for having MRSA detected during the study ($p = 0.04$) and having the ASC performed more than 5 years since the first known (+) MRSA culture was associated with the lowest risk (OR 0.45, [0.25-0.79], $p = 0.005$). For example, 18 (12.5%) of 144 pts with an ASC done more than 5 years from their first known (+) MRSA vs 64 (24.2%) of 264 pts with an ASC done 5 years or less from their first known (+) MRSA culture had MRSA detected during the study. Presence of a foreign body significantly increased the risk for having a (+) MRSA culture (OR 1.36 [1.02-1.82], $p = 0.05$) and female sex significantly reduced the risk (OR 0.78 [0.60-1.00], $p = 0.05$).

Conclusion. The proportion of pts with MRSA documented more than a year ago who remained (+) was 20.1% however this significantly decreased over time, particularly after 5 years. Our data also suggest that in the absence of a foreign body and especially among females, CP can be discontinued after one (-) admission ASC.

Disclosures. **C. Salgado**, Wolters Kluwer Health: Editorial Assistance, Licensing agreement or royalty

316. Decolonization of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Carriers in a Surgical Intensive Care Unit (SICU): Success Rate and Risk Factors for Decolonization Failure

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Background. The aim of this study is to evaluate the effect of decolonization therapy using antiseptics on the acquisition of MRSA in a SICU and to identify the risk factors for short-term decolonization failure.

Methods. This study was conducted at a 14-bed SICU over a 23-month period. During a baseline period (January 2012 through November 2012), active surveillance cultures (ASC) for MRSA were performed on nasal swab samples from all SICU patients at admission. Isolation precautions were performed when MRSA was identified. ASC were processed using Chrom-Agar at admission and weekly from August 2012. During an intervention period (December 2012 through November 2013), MRSA decolonization was implemented and ASC were performed twice a week. The MRSA decolonization consisted of a 5-day regimen of nasal mupirocin ointment, chlorhexidine mouth rinse and whole body chlorhexidine bathing. To evaluate the risk factors for short-term decolonization failure, patients who were decolonized for ≥ 3 days were analyzed. Successful decolonization was defined as at least two consecutive negative sets of ASC after decolonization. Segmented regression analysis was used to assess the effect of intervention.

Results. After intervention, the incidence density of MRSA colonization or infection decreased by 27.1% (incidence density, 10.7 vs 7.8 cases per 1,000 patient-days; β, -2.15; 95% CI, -3.49 to -0.80; $P < 0.01$). Of 63 MRSA isolates which underwent susceptibility testing, all isolates remained susceptible to chlorhexidine (MIC_{90}, 4 μg/mL), 11 (17%) were low-level mupirocin resistance (MuR), and no isolates was High-level MuR. Of 46 patients who underwent decolonization for ≥ 3 days, 36 (78%) had successful decolonization. Univariate analysis showed that hospital acquisition of MRSA (OR 12.4, 95% CI 1.77-85.50) and low-level MuR (OR 8.05, 95% CI, 0.92-70.33) were associated with decolonization failure.

Conclusion. Our data support that the use of intranasal mupirocin and chlorhexidine bathing to decrease rates of MRSA infection or colonization. Although high decolonization success rates could be achieved using antiseptic protocols, decolonization may be less successful in patients carrying a mupirocin-resistant MRSA.

Disclosures. **All authors:** No reported disclosures.

317. Clinical effectiveness of mupirocin for preventing *S. aureus* infections in non-surgical settings: A Meta-analysis

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Background. A protective effect of mupirocin has been seen among surgical, nonsurgical and dialysis patients. Our aim is to summarize evidence for mupirocin decolonization for prevention of *S. aureus* infections in non-surgical healthcare settings. The objective was to identify the optimal setting and patient population to implement mupirocin decolonization for prevention of *S. aureus* infections using meta-analytic methods.

Methods. We conducted systematic searches in PubMed, Cochrane Library Databases, Scopus, Web of Science, and ClinicalTrials.gov to identify papers published until 2013 on effectiveness of mupirocin in healthcare settings. Studies were included if they provided data on incidence of *S. aureus* infections. Two investigators independently assessed eligibility of studies and abstracted data with a pilot-tested form. Risk of bias was assessed using the Cochrane tool. The crude odds ratios were pooled (cpOR) using a random-effects model. Heterogeneity was evaluated using the Woolf's test for homogeneity and I^2 statistics.

Results. Of the 12,644 studies identified, 8 randomized controlled trials and 19 quasi-experimental studies met the study inclusion criteria. Mupirocin was observed to reduce the odds of *S. aureus* infections by 70% (cpOR = 0.30, 95%CI 0.23, 0.39) and 60% (cpOR = 0.40, 95%CI 0.27, 0.62) in both dialysis and non-dialysis settings, respectively. Nevertheless, there was highly significant (p = 0.0009) and moderate heterogeneity (I^2 = 46%) among studies. Studies were homogeneous (p > 0.1) when stratified analyses were performed by specific clinical settings. Among the 6 studies that took place in adult intensive care units (ICUs), mupirocin decolonization was associated with a 56% reduction in the odds of *S. aureus* infection (cpOR = 0.44, 95%CI 0.26, 0.73). There was also a protective effect of mupirocin against *S. aureus* exit site infections among patients undergoing peritoneal dialysis (cpOR = 0.23, 95%CI 0.15, 0.36) and against bacteremia among hemodialysis patients (cpOR = 0.15, 95%CI 0.06, 0.36).

Conclusion. Mupirocin decolonization is protective against *S. aureus* infections among both dialysis and adult ICU patient populations. Future studies should target other patient settings such as long-term care facilities.

Disclosures. **All authors:** No reported disclosures.

318. Is the Pulsed Xenon Ultraviolet Light No-Touch Disinfection System Effective on MRSA in the Absence of Manual Cleaning?

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Background. Pulsed xenon ultraviolet no-touch disinfection (PX-UV) devices are widely employed to disinfect surfaces in hospital patient rooms. A truncated manual disinfection followed by PX-UV has been shown to be more effective than manual disinfection alone against methicillin-resistant *Staphylococcus aureus* (MRSA). Mercury-based ultraviolet disinfection has been shown to be effective against MRSA in the absence of any manual disinfection. But the effectiveness of PX-UV disinfection device on MRSA in the absence of any manual disinfection is largely unknown.

Methods. Five high touch surfaces (bedrail, tray table, call button, toilet seat and toilet grab rail) were sampled for aerobic colony counts and MRSA, using Rodac contact plates (Hardy Diagnostics, Santa Monica, CA), before and after pulsed xenon UV disinfection. For non-flat surfaces, roll plate technique was used. The PX-UV was placed and run for 5 minutes each in 3 positions: once on both sides of the bed and once in the bathroom, exposing the above-mentioned high touch surfaces (a total of 15 minutes of PX-UV exposure per room). The plates were then incubated at 35-37^{O}C for 48 hours. For aerobic bacterial counts, individual colonies were counted, and the number was recorded. For MRSA, deep pink or mauve colored colonies were identified as MRSA, and colony counts were recorded. Further, these colonies were confirmed as MRSA by using standard methods. When the colony counts for aerobic bacteria or MRSA were too numerous to count or if the colony counts were greater than 200, the colony count was recorded as 200 to prevent outliers.

Results. We sampled a total of 15 rooms. We found 5747 aerobic bacterial colonies before and 1256 (78% reduction) after PX-UV disinfection. Similarly, we observed 202 MRSA colonies before and 66 (67% reduction) after PX-UV disinfection.

Conclusion. Our results demonstrated that 'no-touch' pulsed xenon UV disinfection system is effective in reducing aerobic bacterial burden and MRSA from the high touch surfaces in a patient room in the absence of any manual cleaning. This information is relevant to understand what happens when environmental management services personnel fail to wipe down a surface.

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319. A discrete event simulation (DES) model of patient flow incorporating infection control policy for vancomycin-resistant *Enterococcus* (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA)

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Background. Infection control policies are critical determinants of patient placement during hospital admission, when patients must be matched to beds based on acuity, service and gender, as well as VRE and MRSA colonization status. We designed and validated a novel DES model of patient flow.

Methods. The model uses a bed-allocation algorithm matching patients to beds in a simulated hospital (Figure). Patients are matched to appropriate beds based on acuity, service, gender and observed colonization status, which may be discordant with their true colonization status, discovered only through diagnostic testing. A data repository of 104,725 historical admissions over a 2-year period was used to populate the model with patients arriving hourly with characteristics drawn from a joint distribution of acuity (12% observation; 68% general; 12% step-down and 8% ICU), service (53% medicine; 47% surgery), gender (49% female) and colonization status (91% non-colonized, 4% VRE, 3% MRSA, 2% MRSA/VRE). Stochastic inputs included: probability distributions of hourly time-varying acuity changes and discharges, published estimates of true colonization, culture and nucleic acid test characteristics, and VRE and MRSA transmission. The model was validated to mean length of stay (LOS, days) and mean occupancy to ensure accurate capture of patient flow, and run over a 5-year period.

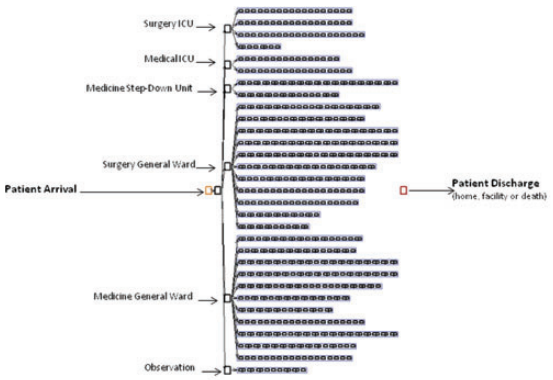

Figure. Overview of modeled hospital. Patients arrive and then are distributed to acuity and service "boxes" u an appropriate bed match can be made. The hospital includes a mix of private (single box) and semi-private be (double box) distributed across intensive care units (ICUs), Step-Down Units, General Wards and Observation.

Results. The model reliably assigned patients to appropriate beds, including when patients experienced changes in acuity or observed colonization status. Mean LOS (± standard deviation) in the data repository was 4.7 ± 5.5d; the model-estimated LOS after five years and >248,000 admissions was 4.9 ± 5.0d. We achieved a valid occupancy of 83.8 ± 4.7% compared to hospital-reported 82.9 ± 1.7%. Other reportable model outcomes include false-cohorting when cohorted patients differ on true colonization status; queues for available resources; and VRE and MRSA transmission under varying surveillance strategies.

Conclusion. DES for modeling patient flow has important applications in infection control. Expansion of the model to incorporate transmission under strategies employing diagnostics to more accurately identify patients with underlying VRE and MRSA colonization will increase its utility to clinicians and policy makers.

Disclosures. **All authors:** No reported disclosures.

320. VRE Colonization and Infection at the NIH Clinical Center (NIHCC)

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Background. Vancomycin-resistant *Enterococcus faecium* (VRE) is a common cause of healthcare-associated infections. In 2009, VRE colonization/infection rates rose on the adult hematology-oncology wards at the NIHCC, prompting initiation of active surveillance cultures in 2009. Whereas colonization/infection rates subsequently declined, they did not return to baseline. We describe a cohort of 333 patients detected between 2007-2013 with VRE colonization or infection.

Methods. Starting in July 2009, perirectal swabs were collected on admission and weekly from non-colonized patients and plated on selective media. In July 2010, swabs were tested by *VanA*/*VanB* PCR (Cepheid), replaced in December 2010 with *VanA* PCR. Patients with PCR+ results were cultured.

Results. Surveillance swabs identified VRE colonization in 65%; clinical cultures identified 35%. Of 215 identified by active surveillance, 24% later grew VRE from clinical cultures.

Among the 215, 65% grew VRE in culture, and 35% had positive PCR, but negative cultures (PCR + /Cx-). Only 30% of PCR + /Cx- patients with subsequent swabs grew VRE from cultures. PCR + /Cx- swabs grew 41 organisms: vancomycin-susceptible *E. faecium*/*faecalis* (27%), vancomycin-resistant *E. faecalis* (5%), *E. gallinarum*/*casseliflavus* (44%), and others (24%). PCR had a positive predictive value of 43%, and 95% of identified organisms were not VRE.

Of 140 with initial positive surveillance cultures, 33% grew VRE from clinical cultures. 32% had ≥3 subsequent negative swabs, but 21% later grew VRE a median of 46 days after the last negative surveillance culture.

Overall, 19% had VRE bacteremia. 44% of all patients died, including 49% initially identified in clinical culture, 72% of those who had VRE bacteremia, 44% identified in surveillance culture and 39% who were PCR + /Cx-.

Conclusion. VRE colonization is tenacious; only 17% of our patients appeared to become decolonized. The low positive predictive value of PCR testing is likely influenced by vancomycin resistance genes in non-VRE bacteria. Mortality in patients with VRE colonization/infection is high, and colonization may be a surrogate marker for underlying disease severity. Understanding the dynamics of VRE colonization is essential for reducing its prevalence.

Disclosures. **All authors:** No reported disclosures.

321. Screening Strategy to Detect Vancomycin-Resistant Enterococci Conversion in Exposed Roommates

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Background. The Ontario Provincial Infectious Diseases Advisory Committee recommends screening VRE roommate contacts on different days, with one taken at minimum of 7 days post exposure (PE). This study aimed to better delineate the risk of conversion, by duration of exposure, and the optimal screening strategy after inadvertent exposure to VRE-positive roommates at a 430 bed community teaching hospital in Toronto, Canada.

Methods. All exposed roommates from December 2004 to March 2014 were screened for VRE at 3 time periods PE, as per protocol: T1 (0-1 day PE), T2 (2-4 days PE), and T3 (5-10 days PE) by rectal swab culture. Screens undertaken ≥11 days PE were grouped as T4. The sensitivity at various time periods for detecting newly colonized roommates were determined and defined as the number of patients who were culture positive at the specific time period(s) divided by the total number of VRE converted patients (from any follow-up period) who were swabbed at the specific time period(s).

Results. Among 377 exposure episodes (367 patients), 253 (67%) had complete follow-up. VRE conversion was detected in 17 of the 253 episodes (7%). The sensitivity at each time period was: T1 = 58%, T2 = 63%, T3 = 75%, and T4 = 78%. Thirteen of the 17 VRE conversions (76%) were detected by 10 days (T3). Testing more than once, with at least one done at T3, achieved a higher sensitivity than testing at T1 alone (T1/T3 combined = 100%, $p = 0.11$ or T2/T3 combined = 100%, $p = 0.24$). Of those with first conversions at T4, none were screened more than once prior to T4 and the median time to positive test was 22 days. Contacts exposed to VRE patients for ≥3 days were significantly more likely to acquire VRE (11%) than those with <72 hours exposure (2.4%, $p = 0.01$). Nonetheless, the conversion rate was significantly higher for those exposed <72 hours compared with the overall prevalence found on admission (2.4% vs 0.17%, $p < 0.001$). All patients were colonized; no infections developed in this cohort.

Conclusion. Roommates exposed to VRE patients are at substantial risk of becoming colonized, with the degree of risk increasing in those exposed for ≥3 days. Our data supports the provincial guidelines of screening exposed roommates at multiple times with at least one taken at 7 days PE.

Disclosures. **All authors:** No reported disclosures.

322. Vancomycin-resistant *Enterococci* with Reduced Daptomycin Susceptibility in Singapore: Prevalence and Associated Factor

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Background. Daptomycin-nonsusceptible *Enterococcus* (DNSE) is an emerging clinical and public health problem. In the United States, DNSE infections with and without prior daptomycin exposure have been reported. In Singapore, daptomycin utilization has increased over the years, but little is known about the epidemiology of DNSE. Our study aims to determine the prevalence of DNSE and understand the factors associated with reduced daptomycin susceptibility.

Methods. We conducted a case-control study in 1600-bed Tan Tock Seng Hospital in Singapore. All vancomycin-resistant *Enterococcus* (VRE) isolates from inpatients from January 1 thru December 31, 2012 were tested for daptomycin susceptibility using the Etest.

Cases were defined as VREs with daptomycin minimum inhibitory concentration (MIC) >= 3 µg/mL [daptomycin reduced susceptible VRE, DRS-VRE], and controls were VREs with daptomycin MIC < 3 µg/mL [daptomycin susceptible VRE, DS-VRE] . Medical records were reviewed for clinical and epidemiological data. To compare the differences in covariates between the groups, odds ratios and 95% confidence intervals were computed. A multiple logistic regression model was used to control for confounding.

Results. None of the 243 VRE-colonized/infected patients had DNSE (MIC >4). About half (135, 55%) had reduced susceptibility to daptomycin (DRS-VRE). None of the DS-VRE and only 3% of DRS-VRE had prior exposure to daptomycin. Patients who had more than 1 movement between wards (OR 0.57, 95% CI 0.33-0.98), a longer duration of cephalosporin exposure (OR 0.941, 95% CI 0.888-0.998), or minocycline resistance (OR 0.49, 95% CI 0.28-0.85), were less likely to have DRS-VRE.

After adjusting for age, gender, comorbidity, hospitalization duration, surgical history, indwelling device use, and duration of aminoglycoside, carbapenem, cephalosporin, daptomycin, fluoroquinolone, penicillin, polymyxin B, and vancomycin use in the past 3 months, more than 1 movement between wards (Adj OR 0.35, 95% CI 0.16-0.74) and minocycline resistance (Adj OR 0.45, 95% CI 0.25-0.84) were independently associated with DRS-VRE.

Conclusion. No DNSE was observed, but 55% of VREs had reduced daptomycin susceptibility. More than 1 movement between wards and minocycline resistance were negatively associated with DRS-VRE. Further research is needed to understand the reasons for these associations.

Disclosures. **All authors:** No reported disclosures.

323. Knowledge, attitudes, and infection prevention practices regarding multidrug-resistant organisms among Emergency Medical Service (EMS) providers

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Background. Little is known about the knowledge, attitudes, and infection prevention practices related to multidrug-resistant organisms (MDRO) among Emergency Medical Service (EMS) providers.

Methods. An electronic survey was sent to a stratified random sample of nationally certified EMS providers between November 2013 and February 2014. The survey included 22 items about hand hygiene, glove use, and environmental disinfection, as well as general knowledge and attitudes pertaining to MDROs. Descriptive statistics were performed.

Results. 5,293 EMS providers received the survey and 516 (9.7%) were returned. Of those, 50.1% were Emergency Medical Technician–Basics (EMT-B) and 34.6% were paramedics. 84.9% reported glove use during patient care. While 95.3% agreed that hand hygiene was necessary regardless of glove use, only 16.1% regularly disinfected their hands prior to glove use and 68.9% did so after glove use. Lack of time, interference with patient care, and low perceived risk of exposure to blood or other body fluids were the most common reasons for non-adherence with hand hygiene. While 85.9% routinely disinfected their medical equipment and stretcher after each patient encounter, less than 60% disinfected the ambulance compartment during a shift, even after visible contamination of the environment. While most had heard of methicillin-resistant *Staphylococcus aureus*, fewer EMT-Bs compared to paramedics were familiar with vancomycin-resistant Enterococcus, *Clostridium difficile*, or multidrug-resistant Gram-negative bacteria and how these organisms are transmitted. Providers reported they would be more likely to use gloves (94.6%), perform hand hygiene (91.2%), and thoroughly disinfect their environment (87.3%) if they knew that a patient had a MDRO. Perceived barriers to such awareness included lack of communication among healthcare personnel and lack of clear documentation in the medical record.

Conclusion. Opportunities exist to improve awareness, knowledge, and practices among EMS providers regarding infection prevention and MDROs through further education and standardization of policies. While non-responder bias may have influenced our survey findings, knowledge and practices are likely to be even poorer in non-responders.

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324. Improved intra-operative Hand Hygiene Compliance

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Background. Hospital acquired infections (HAIs) are a significant issue, impacting 10% of hospitalized patients and hand hygiene (HH) is widely believed to be one of the most important ways of decreasing HAI risk. Numerous studies have found compliance with HH to be low among healthcare workers, with the lowest levels of adherence being associated with limited access to HH while at the bedside.

Methods. Data were collected in the OR of a large teaching hospital in the Northeast. A before and after study design was used and HH events during OR cases were measured. In the pre group (Group 1), wireless data were collected from all the OR wall dispensers in each room (including in/out). An event was captured electronically each time HH was performed. In the post group (Group 2) the primary method for HH was the use of a personal alcohol handrub dispenser that was worn by all non-scrubbed OR personnel during the OR cases.

Results. This study examined the HH practices of non-scrubbed OR staff in a total of 133 case days. There were 71 case days of HH using the wall dispensers (Group 1) and 62 case days using the personal alcohol handrub dispensers (Group 2).

An independent sample t-test for equality of means was run to look for group differences on the outcome variable, the number of HH events per hour during surgical cases. A significant difference ($p < 0.001$) was found in the number of hourly HH events between the two groups. Because the Levene's test for equality of variance was significant, the significance using "unequal variance assumed" of $p < 0.001$ was reported. Group 1 had a mean HH rate of 0.34 uses per hour with a standard deviation of 0.03. Group 2 had a mean HH rate of 5.99 uses per hour with a standard deviation of 1.12. Thus, the data support that OR staff who use a personal HH dispenser completed a significantly higher number of HH events during surgery than those using the wall dispenser for HH.

Conclusion. The findings of this study align with much of the published research regarding HH in the acute care environment. In fact, the rate in Group 1(0.34) is virtually the same as that previously reported for anesthesia providers (0.38) by Koff, et al (2009). These findings provide additional support regarding the importance of having products or systems readily available at the bedside in order to improve healthcare worker HH compliance.

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325. Risk Factors Associated with Multidrug-Resistant Gram-Negative Bacilli Colonization in Wounded Military Personnel Deployed to Iraq and Afghanistan

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Background. Previous studies have shown high rates of colonization and infection with multidrug-resistant gram-negative bacilli (MDR GNB) in patients injured during deployment to Iraq and Afghanistan. Using data from a longitudinal military trauma registry, we evaluated the risk factors associated with MDR GNB colonization.

Methods. Injury circumstances and post-injury management were collected from the Department of Defense Trauma Registry. Antibiotic use, microbiology results, and infection data were collected from the Trauma Infectious Diseases Outcomes Study (TIDOS). MDR GNB colonization was defined as growth of MDR (ESBL production or resistance to 3 or more of: carbapenems, aminoglycosides, fluoroquinolones, or beta-lactams) GNB from active surveillance cultures (groin/axilla) performed within 48 hrs of U.S. admission. Multivariate logistic regression was used to evaluate risk factors associated with colonization. Odds ratios (OR) are presented with 95% confidence intervals.

Results. From June 2009 to May 2012, 2079 deployment-injured patients were admitted to TIDOS-participating U.S. hospitals. Of these patients, 289 (14%) were colonized with a MDR GNB including *E. coli* (74%), *A. baumannii* (15%), *K. pneumoniae* (10%), *E. cloacae* (1%), and *Citrobacter spp.* (< 1%). There was no difference in duration between injury and admission between those with and without colonization (median 5 days in both). In the multivariate model, factors significantly associated with MDR GNB colonization include injury during fighting season (April – September, OR 1.8 [1.4-2.4]), massive blood transfusion (OR 2.7 [1.7-4.2]), fluoroquinolone use post injury (OR 1.8 [1.4-2.5]), and infection prior to U.S. arrival (OR 1.7 [1.1-2.6]). Factors not associated include branch of service, country of injury, mechanism of injury, ICU admission, injury severity score, indwelling orthopedic hardware, cefazolin, or carbapenem use.

Conclusion. Although several factors are associated with higher rates of MDR GNB colonization post deployment-related injury, fluoroquinolone use is the only modifiable one. This finding provides further support for current guidelines which do not recommend routine fluoroquinolone use for post-injury prophylaxis.

Disclosures. **All authors:** No reported disclosures.

326. Antimicrobial co-resistance patterns of gram-negative bacilli isolated from bloodstream infections: a longitudinal epidemiological study from 2002-2011

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Background. Increasing multidrug resistance in gram-negative bacilli (GNB) infections poses a serious threat to public health. Few studies have analyzed co-resistance rates in detail, defined as an antimicrobial susceptibility profile in a subset resistant to one specific antibiotic. The epidemiologic and clinical utility of determining co-resistance rates are analyzed and discussed.

Methods. A 10-year retrospective study from 2001-2011 of bloodstream infections with GNB were analyzed from three hospitals in Greater Vancouver, BC, Canada. Descriptive statistics were calculated for antimicrobial resistance and co-resistance. Statistical analysis further described temporal trends of antimicrobial resistance, correlations of resistance between combinations of antimicrobials, and temporal trends in co-resistance patterns.

Results. The total number of unique blood stream isolates of GNB was 3280. Increasing resistance to individual antimicrobials was observed for *E. coli*, *K. pneumoniae*, *K. oxytoca*, *E. cloacae*, and *P. aeruginosa*. Ciprofloxacin resistance in *E. coli* peaked in 2006 at 40% and subsequently stabilized at 29% in 2011, corresponding to decreasing ciprofloxacin usage after 2007 as assessed by daily defined dose utilization data. High co-resistance rates were observed for ceftriaxone-resistant *E. coli* with ciprofloxacin (73%), ceftriaxone-resistant *K. pneumoniae* with trimethoprim-sulfamethoxazole (83%), ciprofloxacin-resistant *E. cloacae* with ticarcillin-clavulanate (91%), and piperacillin-tazobactam-resistant *P. aeruginosa* with ceftazidime (83%).

Conclusion. Increasing antimicrobial resistance was demonstrated over the study period, and may partially be associated with antimicrobial consumption. The study of co-resistance rates in multidrug resistant GNB provides insight into the epidemiology of resistance pattern development, and can be used as a clinical tool to aid prescribing empiric antimicrobial therapy.

Disclosures. **All authors:** No reported disclosures.

327. Multidrug-Resistant Organisms in Community Hospitals: Initial Trends from the DICON MDRO Biorepository

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Background. Although the majority of Americans receive their healthcare in community hospitals, almost nothing is known about Multidrug-resistant organisms (MDRO) in that setting.

Methods. The DICON MDRO Biorepository is an ongoing resource that prospectively collects clinically well-characterized samples from MDRO-infected patients hospitalized in community hospitals. For this cohort analysis, we analyzed the first 100 subjects enrolled. Data collected at enrollment included demographic information,

previous medical history, social history, culture data, as well as a 90 day follow-up from the time of hospital discharge. Patients under the age of 18 and outpatients were excluded. Data points were collected at the bedside and through a detailed review of each subject's electronic medical record. Standard descriptive statistics were used.

Results. The average patient age was 61.7 (± 17.7); 49 (49%) were women. Seven patients were concurrently infected with more than one MDRO. The three most common MDROs were *C. difficile* (n = 41, 38%), MRSA (n = 41, 38%), and *E. coli* (n = 14, 13%). Multidrug resistant aerobic bacteria caused similar numbers of soft tissue (n = 20, 17%), bloodstream (n = 19, 17%) and urinary tract infections (n = 18, 16%). Co-morbidities such as diabetes (n = 43, 43%), current and previous tobacco use (n = 65, 65%), and BMI >30 (n = 35, 35%) were common. 61 (61%) patients were categorized as having community-onset, community-associated infections; 28 (28%) were classified as hospital-acquired; and 11 (11%) were community-onset, healthcare-associated. 30 (30%) of patients required assistance with more than one ADL upon admission. 5 (5%) patients died and 10 (10%) required admission to the ICU due to infection. The average length of hospitalization was 18 days. For the 66 MDRO-infected patients with complete 90-day follow-up data, 22 (33%) were readmitted to the hospital; 17 (77%) re-admissions were infection related.

Conclusion. Similar to tertiary care centers, *C. difficile* and MRSA were the most common cause of MDRO infections in community hospitals. Over 75% of patients had community-onset infection. Consequences of MDRO infections in community hospitals such as death and readmission were both severe and frequent.

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328. Clinical Impact of Multidrug-Resistant Organisms (MDRO) causing Healthcare-Associated Infections (HAIs) in 10 Colombian cities

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Background. HAIs by Multidrug-resistant Organisms (MDRO) place patients at greater risk of potentially untreatable infections with increased mortality and longer hospital stay. In Colombia, an increased trend of MDRO organisms have been reported in the last five years; however, their association with HAIs remains unascertained. Herein, we describe the clinical impact of MDRO causing HAI using a novel electronic-based tool for surveillance of HAIs.

Methods. A prospective cohort study between July 2012 and June 2013 was conducted in ICU patients from 20 hospitals in the 10 major Colombian cities. A novel electronic tool (*HAI Solutions* software®) was implemented to gather, in real time, the clinical and microbiological data of HAI using CDC definitions. Prevalence by type of HAI, time to development of infection and mortality caused by the three most common bacteria was analyzed among groups during that year.

Results. From 12607 isolates, 1041 (8.3%) met CDC criteria for HAIs; *Klebsiella pneumoniae* (Kpn) was the main isolated bacteria overall (19%), followed by *Pseudomonas aeruginosa* (Pae) with 12% and *Escherichia coli (Eco)* with 11%. Central line-associated bloodstream infection was the most common HAI with Kpn causing 63% of the cases ($p < 0.001$), of which 19% were carbapenem-resistant Kpn. Eco was the first bacteria causing catheter-associated urinary tract infection (41%), of which 14% were carbapenem-resistant. MDR-Pae was the main cause of Ventilator-associated pneumonia after a median of 19 days, in comparison to non MDR-Pae ($p < 0.001$). There was no significant difference in other HAIs for the other MDRO. Of note, 40% of MDR-Pae were re-isolated in a second culture after 15 days of the initial case. Mortality rates were higher for any carbapenem-resistant bacteria vs susceptible isolates: 30% vs 15% for Pae, 28% vs 17 for Kpn and 27% vs 10% for Eco.

Conclusion. This nationwide study reports for the first time, higher mortality rates in HAIs caused by MDRO. These findings highlight the need of implementing strategies to decrease MDRO associated with HAIs in Colombia.

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329. Parsing Multi-Source Microbiology Culture Data in a Regional Health Information Exchange to Describe Patterns of Infection

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Background. In consultation with infection preventionists (IPs), we built an electronic system to parse Health Level 7 version 2 (HL7v2) messages for microbiology culture data sent to a regional health information exchange. The primary purpose of that system was to enable a regional network to deliver alerts when a patient with a history of gram negative rod multi-drug resistant organism (GNRMDRO) is admitted to an emergency department (ED) or hospital. A separate abstract describes the first 12 weeks of GNRMDRO alerts. In building that system, we sought to parse all inbound microbiology culture data (for susceptible as well as resistant organisms), in order to be able to describe bacterial infections and antibiograms across a wide region (27 hospitals). Here we report the results of an initial test of this aspect of the system, for infants 0 to 91 days old.

Methods. We built 1) an HL7v2 correction engine that deals with incorrect microbiology message structure and content. The HL7v2 correction engine parses key data elements needed for epidemiologic analyses: organism, antibiotics tested, minimum inhibitory concentrations, susceptibility interpretation, body source of the culture, and health care facility where drawn. We describe blood and/or urine cultures, for infants 0 to 91 days old, from the first 20 weeks of the new system to parse electronic microbiology culture data.

Results. Seventy-eight infants (42 girls, 36 boys) had at least one positive culture for one or more GNRs (64 urine, 9 blood, 5 infants with both). The majority of the results were *Escherichia coli* (54%), followed by *Klebsiella pneumoniae* (15%), *Enterobacter cloacae* (10%), *Klebsiella oxytoca* (6%), and various others. The age range of the 78 infants was 0 to 91 days. Three of the 78 infants had urine cultures identified as *Enterobacteriaceae* with extended-spectrum beta lactamase (ESBL-E), two with *Escherichia coli* and one with *Klebsiella pneumoniae*. One of these three had a first urine culture that was a GNR but not ESBL-E, followed by a urine culture of ESBL-E three weeks later.

Conclusion. This electronic microbiology parsing system shows promise, in a health information exchange, for describing infection and antibiotic resistance patterns across a region. Most patients with GNRMDRO are adults, but the system is also useful for pediatric data.

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330. Early Implementation of a Regional Electronic Infection Control Network using Parsed Microbiology Culture Data

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Background. In consultation with infection preventionists (IPs), our objective was to build a regional network to deliver alerts when a patient with a history of gram negative rod multi-drug resistant organism (GNRMDRO) is admitted to an emergency department (ED) or hospital. Because most microbiology HL7 messages are not structured in standard Health Level 7 version 2 (HL7v2) format when sent into a health information exchange, a new approach is needed if multi-source electronic culture data are to be used for decision support.

Methods. We built 1) an HL7v2 correction engine that deals with incorrect microbiology message structure and content, 2) decision support to identify superbugs of interest, 3) an admission/discharge/transfer message processor with cross-institutional identity matching to generate alerts upon subsequent ED or inpatient admission, and 4) secure email alerts to the IP(s) at the admitting institution. The HL7v2 correction engine parses key data elements needed for alerts: organism, antibiotics tested, minimum inhibitory concentrations, susceptibility interpretation, body source of the culture, and health care facility where drawn. The five GNRMDRO categories are 1) *Enterobacteriaceae* with extended-spectrum beta lactamase (ESBL-E), 2) carbapenem resistant *Enterobacteriaceae* (CRE), 3) *Pseudomonas aeruginosa* resistant to 3 of 4 antibiotic classes, 4) *Acinetobacter baumannii* resistant to 3 of 4 antibiotic classes, and 5) other.

Results. In the first 12 weeks, email alerts to the IPs were generated for 105 distinct patients (69 with ED visit only, 36 with hospital admission). Five hospital systems were alerted, for 21 distinct hospitals. The GNRMDROs were ESBL-E (84%), CRE (N = 7 [7%]: 6 *Klebsiella pneumoniae*, 1 *Serratia marcescens*), Pseudomonas (5%), Acinetobacter (4%), and other (1%). Body sources were urine (76%), blood (8%), and other (16%) including wound, bronchoalveolar lavage, sputum, or bile. For 26 (25%) of 105 patients, the admitting hospital system was different from the one where the GNRMDRO culture had been drawn.

Conclusion. The amount of cross-over between hospitals – by patients colonized or infected with gram-negative superbugs – is striking. Timely alerts may hasten placement into contact isolation and thereby may help reduce the spread of life-threatening bacteria.

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331. Risk Factors for Vancomycin-resistant *Enterococci* and Carbapenemase-producing Carbapenem-resistant *Enterobacteriaceae* Colonization at admission to a Tertiary-care Center

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Background. Vancomycin-resistant *Enteroccocus* (VRE) and Carbapenemase-producing carbapenem-resistant *Enterobacteriaceae* (CP-CRE) infections are rapidly emerging in Singapore. Colonization often precedes infection. But, prevalence and

factors associated with VRE and CP-CRE colonization remain unknown.

Our study aims to determine the prevalence of VRE and CP-CRE colonization at admission and factors associated with colonization in an adult tertiary-care center in Singapore.

Methods. All new admissions (<48 hours) to 1600 bed Tan Tock Seng Hospital, November 3-7, 2013, were screened for VRE and CP-CRE via rectal swabs using selective culture media. A multiplex PCR with primers targeting bla_{NDM}, bla_{KPC}, $bla_{OXA\text{-}48\text{-}like}$, bla_{IMP} and bla_{IMI} was done on meropenem non-susceptible *Enterobacteriaceae* isolates. Clinical data was obtained from medical records. VRE and CP-CRE colonizers were compared with non-colonizers in case-control studies. To compare differences in covariates between groups, odds ratios and 95% confidence intervals were computed. Multiple logistic regression models were constructed to control for confounding and determine independent factors.

Results. Of 684 patients screened, 13 (1.9%) were colonized with VRE (8 Van A and 5 Van B) and 5 (0.7%) with CP-CRE (2 NDM, 1 KPC, 1 IMP, 1 IMI). Compared to non-colonizers, VRE-colonizers were more likely to have been hospitalized locally in the past 1 year (OR 17.71, 95%CI 2.14-146.68) and exposed to indwelling devices (OR 10.21, 95%CI 2.03-51.31). There was no difference in age, gender, comorbidity, and prior hospitalization overseas. After adjusting for age, gender, and comorbidity, exposure to indwelling devices (Adj OR 9.60, 95%CI 1.45-63.53) was independently associated with VRE colonization. In contrast, CP-CRE colonizers were more likely than non-colonizers to have had a past infection with a multidrug-resistant organism (MDRO) (OR 18.00, 95%CI 2.30-141.17). After adjusting for age, gender, and comorbidity, past MDRO infection (Adj OR 14.20, 95%CI 1.68-119.76) was significantly associated with CP-CRE colonization.

Conclusion. The prevalence of VRE and CP-CRE colonization at admission was low. Prior exposure to indwelling devices was associated with VRE colonization whilst past MDRO infection with CP-CRE colonization. Patients with such exposures should be actively screened at admission.

Disclosures. **All authors:** No reported disclosures.

332. Collateral Benefit of Screening Patients for Methicillin-Resistant *Staphylococcus aureus* at Hospital Admission: Serendipitous Isolation of Patients with Other Multidrug-Resistant Organisms

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Background. Surveillance at hospital admission for gram-positive and gram-negative multidrug-resistant (MDR) organisms (MDROs) is not routinely performed, potentially leaving patients carrying these organisms unrecognized. Veterans Affairs (VA) facilities routinely screen all admissions for methicillin-resistant *Staphylococcus aureus*(MRSA) and place positive patients in Contact Precautions. We assessed how often patients with other MDRO-positive clinical cultures within 30 days following hospital admission might already be in Contact Precautions because of a positive MRSA admission screen.

Methods. MRSA nasal PCR screening and clinical culture results for MDROs were extracted from a nationwide microbiology laboratory database of patients admitted to VA acute care medical facilities from October 2007 through September 2013.

Results. For patients admitted with a positive MRSA screen, the odds ratio of having an MDRO recovered in a clinical culture within 30 days following admission was 4.5 (95% confidence interval [CI] 4.5-4.6) compared to patients without a positive MRSA nasal screen. The odds ratios were 2.3 (95% CI: 2.1-2.4) for vancomycin-resistant *Enterococci*, 2.4 (95% CI: 2.3-2.5) for MDR-*Enterobacteriaceae* (including extended-spectrum β-lactamase producing and carbapenem-resistant bacteria), 2.7 (95% CI: 2.5-2.9) for MDR-*Pseudomonas aeruginosa* (including carbapenem-resistant organisms), and 4.2 (95% CI: 3.7-4.7) for MDR-*Acinetobacter spp.* (including carbapenem-resistant organisms). Twenty-nine to 45% of admissions with MDROs (by species) recovered from clinical cultures within 30 days following admission had positive MRSA nasal screens and could have been in Contact Precautions since admission. This increased to 37% to 55% (by species) if patients with an MDRO in the past year were also included.

Conclusion. Screening for MRSA nasal carriage and isolation of positive patients at hospital admission may provide a collateral benefit for the control of other MDROs.

Disclosures. **All authors:** No reported disclosures.

333. Detection of Carbapenemase-Producing *Aeromonas hydrophila* on Perirectal Surveillance Culture

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Background. *Aeromonas* species are Gram-negative organisms found in aquatic environments. Antibiotic resistance genes have been detected in clinical and environmental isolates, including strains that confer carbapenem resistance. Although rarely reported, *Aeromonas* can acquire bla_{KPC} genes. We describe a patient who had intestinal colonization with bla_{KPC}-carrying *Aeromonas hydrophila* and our use of whole-genome sequencing (WGS) to clarify relatedness to other *Aeromonas* isolates and other bla_{KPC}-carrying organisms in our hospital.

Methods. Surveillance perirectal swabs were inoculated on carbapenem-selective, chromogenic agar. Isolates underwent MALDI-TOF identification; suspected carbapenem-resistant *Enterobacteriaceae* (CRE) underwent bla_{KPC}-PCR testing. WGS was performed on *Aeromonas* isolates. Water and environmental samples were inoculated on MacConkey agar.

Results. Perirectal swabs from two adult patients grew carbapenem-resistant *Aeromonas* spp. within a 3-week period. Both patients occupied the same room at different times, but had no other epidemiological links. MALDI-TOF could not reliably differentiate the isolates to the species level. To investigate possible nosocomial transmission, WGS was performed. WGS identified them as most closely matching *A. hydrophila* and *A. veroni*. Unexpectedly, WGS also identified the presence of a KPC-2 gene on an uncharacterized plasmid within the *A. hydrophila* isolate (retrospectively confirmed by bla_{KPC} PCR); the *A. veroni* isolate contained no bla_{KPC}. The plasmid was not similar to other KPC-carrying isolates identified in our hospital. Environmental cultures were negative for *Aeromonas* spp. or other carbapenem-resistant organisms.

Conclusion. To our knowledge, there are few reports of KPC-carrying *Aeromonas* spp. in clinical settings. The source(s) of our patients' *Aeromonas* isolates is unknown, but WGS confirmed that they were unrelated. As a result of these cases, the standard workup of organisms growing on CRE perirectal surveillance cultures at our institution now includes real-time colony bla_{KPC} PCR on *Aeromonas* and *Enterobacteriaceae*. Hospital surveillance for CRE must consider that non-*Enterobacteriaceae* isolates may serve as hosts of these epidemiologically important carbapenemases.

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334. Emergence of OXA-23-possessing *Acinetobacter baumannii* in Hospitals in New York City

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Background. *Acinetobacter baumannii* is an established nosocomial pathogen in many medical centers worldwide. The spread of multidrug resistant strains of *A. baumannii* has been especially problematic.

Methods. During a three month surveillance study conducted November 2013 – January 2014, all unique patient isolates of *A. baumannii* were gathered from 11 hospitals in New York City. Susceptibility testing was performed by CLSI methods; isolates with a meropenem MIC of ≤ 2 μg/ml were considered susceptible. All isolates were screened by PCR for the presence of carbapenemases. Select isolates underwent genetic fingerprinting using ERIC-2 primers. Findings were compared to a similar surveillance study conducted in 2009.

Results. A total of 158 isolates of *A. baumannii* were gathered from the 11 hospitals. Overall susceptibility rates include: 72% to amikacin, 30% to ciprofloxacin, 94% to polymyxin B, 34 % to ceftazidime, and 31% to meropenem. 58 isolates possessed bla_{OXA23}, two bla_{OXA24}, and one bla_{KPC}.

Nine hospitals participated in a similar surveillance study conducted in 2009. For these 9 hospitals, there was a marked decline in the total number of isolates reported (from 252 in 2009 to 122 in 2013-2014; Table). However, there was a marked increase in the number of isolates carrying $bla_{OXA\text{-}23}$ (from 8 to 48). For these 8 hospitals, the percentage of meropenem-resistant isolates that possessed bla_{OXA23} increased from 5% in 2009 to 58% in 2013-2014.

Genetic fingerprinting of 15 OXA-23-carrying isolates from 8 hospitals revealed that 9 belonged to a single strain.

	Total number of isolates (number with bla_{OXA23})	
	2009	2013-2014
Hospital A	72 (4)	32 (19)
Hospital B	18 (2)	7 (2)
Hospital C	5 (2)	4 (0)
Hospital D	21 (0)	4 (0)
Hospital E	15 (0)	7 (2)
Hospital F	24 (1)	16 (1)
Hospital G	51 (0)	32 (18)
Hospital H	37 (1)	14 (6)
Hospital I	9 (0)	6 (0)
Total	252 (8)	122 (48)

Conclusion. Since 2009, there has been a reduction in the prevalence of carbapenem-resistant *A. baumannii* at hospitals in New York City. However, dissemination of strains carrying bla_{OXA23} has clearly increased in several medical centers.

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335. Infrequent Air Contamination with *Acinetobacter baumannii* Surrounding Known Colonized/Infected patients

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Background. Air sampling during outbreaks has demonstrated a potential for airborne transmission of *Acinetobacter baumannii*. The aim of this study was to assess air contamination with *A. baumannii*in an endemic situation and to examine associated patient factors.

Methods. This study was conducted in seven intensive care units at the University of Maryland Medical Center in Baltimore, Maryland, between May and December 2013. Patients with a culture positive for *A. baumannii* within the previous 5 days were identified. Air surrounding the patient was sampled for one hour, 3 feet from the head of the bed, using the Six-Stage Viable Andersen Cascade Impactor (ACI) (ThermoScientific). RambaCHROM™ Acinetobacter Agar plates were incubated at 37°C in ambient air for 24 hours. Patient factors such as presence of wounds, diarrhea and medical devices and antibiotic therapy were collected.

Results. We sampled the rooms of 12 patients known to be colonized or infected with *A. baumannii.* Two colony forming units of *A.baumannii* were isolated in the air surrounding one patient. (Patient 1 in table). The particles carrying *A. baumannii* were equal to or larger than 7.0 μm in size. *A. baumannii*was not found in the air surrounding the remaining patients. The table shows the characteristics of all patients sampled.

Patient number	Culture Site	MDR	Mechanical Ventilation	Urinary catheter	Central venous catheter	Wound	Diarrhea	Antibiotics
1 *	Sputum Catheter tip	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2	Sputum Peri-anal	Yes	No	Yes	No	No	No	No
3	Sputum	Yes	No	No	No	No	Yes	No
4	Sputum	Yes	Yes	No	No	No	yes	No
5	Sputum	No	Yes	Yes	Yes	No	Yes	Yes
6	Sputum	No	Yes	Yes	Yes	Yes	Yes	Yes
7	Sputum Peri-anal	Yes	Yes	Yes	Yes	No	No	Yes
8	Wound	Yes	No	Yes	Yes	No	No	Yes
9	Sputum peri-anal	Yes	Yes	Yes	Yes	No	No	Yes
10	Sputum	No	Yes	No	Yes	Yes	Yes	Yes
11	Blood	No	Yes	Yes	Yes	No	No	Yes
12	Sputum	No	Yes	Yes	No	No	No	Yes

*= Patient 1 had A. baumannii isolated from the surrounding air.

Conclusion. We found that *A. baumannii in*frequently contaminated the air surrounding patients known to be colonized or infected with *A. baumannii;* many of whom were on a closed ventilation circuit. More studies need to be done to determine which patients are more likely to contaminate the surrounding air.

Disclosures. **All authors:** No reported disclosures.

336. Ambient Air Contamination with *Acinetobacter baumannii*: Longitudinal observations based on the anatomic source of colonization

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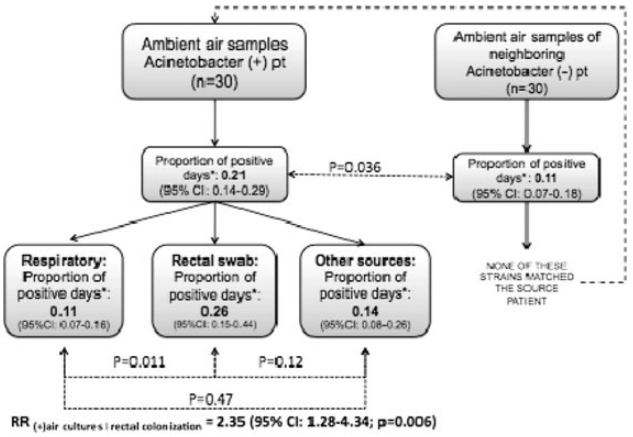
Background. Previously we showed air contamination with *Acinetobacter baumannii* (AB) in a single ICU in 3 separate days. Now we aimed to determine the persistence of air contamination in the rooms occupied by AB(+) patients (pts) while comparing them to the air contamination of their immediate neighboring rooms. We also evaluated the impact of the anatomic source of colonization (e.g., rectum, respiratory) on the degree of air contamination.

Methods. This project was done between March-July 2013 in a large teaching hospital in Miami, FL across 7 adult ICUs. As standard practice, these ICUs perform active surveillance cultures on admission and weekly thereafter (rectum and -if intubated- respiratory tract). Once a new AB(+) patient was identified, daily ambient air surveillances were performed for 10 consecutive days. Open blood agar plates (2-feet from roof) were exchanged daily for the duration of surveillances. Control plates were obtained from adjacent rooms belonging to AB(-) pts. Plates were streaked using a sterile Q-tip, incubated overnight in TSB and plated on MacConkey. AB was determined based on colony color, morphology, and final identification by Vitek II. Air and pts isolates were typed using rep-PCR when available.

Results. During 5-months, 30 AB (+) pts were identified: 17 respiratory (57%), 5 rectal (17%), and 8 (27%) from other sources. A total of 153 air-day samples were obtained. Pts colonized in the rectum had a mean proportion of days with AB in the air of 0.26 compared to 0.11 and 0.14 among respiratory and other sources, respectively (Figure). Thirty adjacent rooms occupied by AB(-) pts were cultured concomitantly (153 air-day samples). The proportion of days that these neighboring rooms were observed as having AB in the air was 0.11 ($p = 0.036$)

There were six cases where both patient and air isolates were available, four of the matching isolates shared >95% similarity between each other, whereas none of the air isolates from the adjacent rooms were closely related with the patient isolates.



Conclusion. Aerosolization of AB seems to be present throughout consecutive days among AB(+) pts and this aerosolization appears to be higher among rectally colonized patients.

Disclosures. **All authors:** No reported disclosures.

337. Nosocomial Transmission of Carbapenem-Resistant *Acinetobacter baumannii* (CRAb) among ICU Patients Detected by CRAb-LAMP

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Background. Nosocomial infections of drug-resistant bacteria are a leading cause of morbidity and mortality worldwide. Carbapenem-resistant *Acinetobacter baumannii* (CRAb) is one of the most important microorganisms in Thailand. The rapid and sensitive detection of this pathogen is required not only for proper therapy but also for infection control measures. However, conventional culture method takes time and has poor sensitivity. We established CRAb-LAMP method for detecting bla_{OXA-23}-positive CRAb, which accounts for approximately 95% of CRAb in Thailand. This method enables direct analysis of clinical specimens, with results available within 40 minutes of sample collection. In this study, we used CRAb-LAMP for active surveillance among ICU patients in Thai hospital and surveyed nosocomial infection.

Methods. The study took place in medical ICU and surgical ICU of Faculty of Medicine Ramathibodi Hospital from December 2013 to February 2014. All the patients who stayed more than 2 days were included and screened for CRAb with LAMP by rectal swab and/or sputum (intubated patient only) on admission, day 7 and discharge. If the either sample showed positive, we defined patient as positive.

Results. Throughout the research period, 794 samples were collected and the sensitivity of LAMP was 100% and its specificity was 88.9%, using the culture method as the gold standard. 334 patients were admitted to the either ICU and 155 (medical ICU: 108, surgical ICU: 47) were eligible in this study. The average length of stay in ICU was 8.9 days. The rate of CRAb-positive on admission was 12.3% (medical ICU: 13.9, surgical ICU: 8.5). The rate of CRAb acquisition was 26.8 per 1,000 patient days (medical ICU: 31.0, surgical ICU: 17.2) and 24.3% (medical ICU: 29.0, surgical ICU: 14.0) of the patients was transmitted during ICU stay.

Conclusion. Active surveillance is important for identifying hidden reservoirs. Our research confirmed that CRAb-LAMP with its high sensitivity and rapidity enabled us to find positive patients early and to investigate the incidence of nosocomial transmission easily. We have started to make appropriate interventions for the CRAb-positive patients from the LAMP result and investigate the efficacy.

Disclosures. **All authors:** No reported disclosures.

338. Prevalence, Mortality and Outcomes of Antibiotic Therapy of Multi-Drug Resistant Acinetobacter baumannii

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Background. This analysis investigates the prevalence, mortality impact, health service utilization and cost of current treatments of multi-drug resistant (MDR) Acinetobacter baumannii (ACB) in the US, identified by the CDC as an urgent and serious threat to public health.

Methods. Hospital costs and utilization were evaluated using the Premier Hospital Database, a large US hospital administrative database containing data elements available in hospital discharge files including diagnoses and procedures categorized according to ICD-9 codes, culture results, antimicrobial susceptibility tests, and antibiotics used to treat infections. Data were extracted for the years 2009-3Q2013. Microbiologic confirmation of Acinetobacter was obtained from 152 hospitals of vrying size. Analyses compared healthcare outcomes in patients with MDR isolates vs non-MDR isolates.

Results. Over the 57-month period, 367 subjects with a primary pneumonia diagnosis and 1,869 with a primary sepsis diagnosis were identified. Unadjusted, al-cause in-hospital mortality among pneumonia patients was 15.46% vs 5.88% for non-MDR patients. Mean (median) length of hospital stay in days (LOS) was 13.4 (9) days vs 10.5 (7) days; hospital costs [mean (median)] were $32,086 ($20,763) vs $24,367 ($13,005); percentage of patients requiring ICU was 47.59% vs 22.55%. Mortality among sepsis/septicemia patients was 21.67% vs 16.91% for non-MDR patients. Mean (and median) LOS was 16.2 (11) days vs 14.8 (9) days; hospital costs [mean (median)] were $43,997 ($26,663) vs $38,494 ($19,974); percentage of patients requiring ICU was 62.81% vs 46.84%. The most frequently used drugs to treat MDR infections were carbapenems (56.02%, tigecycline (26.32%) and colistin (15.03%).

Conclusion. MDR ACB infections incur substantially higher mortality, healthcare resource utilization and costs compared to non-MDR infections. Carbapenems are the most frequently used treatment for MDR ACB, while tigecycline is the most frequently added drug to carbapenem treatment. The value of safe and effective treatments of infections due to Acinetobacter sp. is considerable in view of the additional cost and mortality associated with MDR ACB.

Disclosures. **K. T. Lapensee**, The Medicines Company: Employee, Salary **W. Fan**, The Medicines Company: Employee, Salary **M. Redell**, The Medicines Company: Employee, Salary **M. Dudley**, The Medicines Company: Employee, Salary **J. Loutit**, The Medicines Company: Employee, Salary

339. An International, Multicenter, Retrospective Study of Nosocomial Pneumonia due to *Pseudomonas aeruginosa*

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Background. Nosocomial pneumonia is a prevalent hospital-acquired infection associated with increased morbidity and mortality. The purpose of this study is to describe the clinical characteristics, antibiotic resistance patterns, and outcomes of patients with *Pseudomonas aeruginosa* nosocomial pneumonia.

Methods. Retrospective, hospital-based medical record abstraction. Records were obtained from 10 hospitals throughout the United States and Europe.

Results. Among the 396 patients included in the study, ventilator-associated (50%) was the most common classification followed by hospital-acquired (26%), and healthcare-associated pneumonia (24%). Concomitant bacteremia occurred in 23% of cases and septic shock complicating pneumonia occurred in 63% of patients. Antibiotic resistance was common across all drug classes: aminoglycosides (27%), antipseudomonal (AP) penicillins + β-lactamase inhibitors (29%), AP carbapenems (36%), AP cephalosporins (26%), and ciprofloxacin (34%). Multidrug resistance (MDR) was present in 31% of pneumonia cases. Appropriate initial antibiotic therapy was prescribed in 60% of patients. In-hospital mortality occurred in 42% of patients. In-hospital mortality was significantly greater in patients with an MDR isolate compared to non-MDR isolates (51% vs 33%, $p = 0.001$). The median (IQR) time-to-death was 12 (4, 25) days. Median (IQR) hospital length of stay was 30 (17, 56) days and was significantly longer in survivors compared to nonsurvivors (median 36 vs 27 days, $p = 0.02$).

Conclusion. *Pseudomonas aeruginosa* nosocomial pneumonia is frequently complicated by septic shock and has high in-hospital mortality rate. Antibiotics resistance is common and likely contributes to an unacceptably low rate of initial appropriate antibiotic therapy.

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340. Household (HH) outbreak of ESBL-producing *E. coli* sequence type 131 (ST131) infection with high rate of ST131 intestinal colonization and extensive strain sharing among HH members

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Background. Reasons for the successful global dissemination of multi-drug resistant *E. coli* ST131 are undefined, but may include enhanced transmissibility or ability to colonize the intestine compared to other strains. Accordingly, we assessed the prevalence of ST131 intestinal colonization among HH members of an infant with recurrent urinary tract infections (UTIs) caused by an ESBL-producing, fluoroquinolone (FQ)-resistant ST131 *E. coli* strain.

Methods. *E. coli* was isolated from urine (index patient only) and fecal specimens from all 7 HH members, including the index patient, 3 older siblings, 2 parents, and 1 dog. Isolates were characterized by SNP PCR to detect ST131 and its (ESBL-associated) *H*30-Rx subtype, pulse-field gel electrophoresis to resolve unique strains, and FQ resistance testing.

Results. The index patient, a formerly preterm infant with history of admission to the neonatal intensive care unit presented at 40 days of life with an ESBL-producing *E. coli* UTI. Despite appropriate therapy and no evidence of vesicoureteral reflux or genitourinary abnormalities, she developed three recurrences of ESBL *E. coli* UTI over the next 3 months. During this period, a 2-year-old sister was also diagnosed with ESBL *E. coli* UTI. The index patient's urine isolate represented pulsotype 903 of the FQ-resistant, ESBL-producing *H*30-Rx subclone of *E. coli* ST131. The same ST131 strain was identified in fecal samples from the index patient and 4 of other asymptomatic human HH members at the initial sampling, and from the index patient and 3 other HH members at a second sampling 10 weeks later. In addition, 2 pulsotypes of FQ-susceptible non-ST131 *E. coli* were each shared by two HH members.

Conclusion. In this HH outbreak investigation of ESBL-producing ST131 UTI, clinical and colonizing isolates of ST131 represented the same strain, and nearly all HH members had ST131 intestinal colonization for several months. These findings suggest that ST131 *E. coli* is an efficient and persistent colonizer that can be easily transmitted within HHs, including among children. Strategies to prevent ST131 spread within the community are urgently needed.

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341. Heterogeneous regional distribution of nosocomial infections due to ESBL-producing Enterobacteriaceae in Germany: Data from the German National Reference Center for the Surveillance of Nosocomial Infections (KISS)

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Background. Surveillance systems for hospital infections are reporting increasing rates of extended-spectrum beta-lactamase (ESBL)-positive Enterobacteriaceae in Europe. We aimed to perform a national survey on the trend and regional distribution of nosocomial infections due to ESBL-positive Enterobacteriaceae in German hospitals.

Methods. Data from two components of the German national nosocomial infection surveillance system (KISS) from 2007 to 2012 were used for this analysis. The data derive from intensive care units (ITS-KISS) and surgical departments (OP-KISS). Independent factors determining the proportion of ESBL-positive Enterobacteriaceae among nosocomial infections due to Enterobactiaceae and changes in its regional distribution (broken down into German federal states) were calculated by regression analysis.

Results. From 2007 to 2012, the data showed a significantly growing proportion of ESBL-producing Enterobacteriaceae in surgical site infections ($p = 0.003$), urinary tract infections ($p < 0.001$) and lower respiratory tract infections ($p < 0.001$) due to Enterobacteriaceae. Factors independently associated with a growing proportion were: Thuringia ($p = 0.009$; OR 1.53), North Rhine-Westphalia ($p < 0.001$; OR 1.41) and general surgery ward ($p = 0.002$; OR 1.47).

Conclusion. The proportion of ESBL-positive Enterobacteriaceae from nosocomial infections has significantly increased in Germany over the last six years. Especially hospitals in Central Germany and surgical departments are affected by this development.

Disclosures. **All authors:** No reported disclosures.

342. Epidemiology of *Escherichia coli* Sequence Type 131 in a Veterans Affairs Medical Center

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Background. *Escherichia coli* sequence type 131 (ST131), characterized by fluoroquinolone (FQ) resistance and extended-spectrum β-lactamase production, has emerged as a major health threat. We assessed ST131's prevalence in a Veterans Affairs Medical Center (VAMC), and examined epidemiological and clinical associations.

Methods. From October 12, 2010-April 25, 2011, consecutive *E. coli* isolates from the Minneapolis VAMC clinical microbiology laboratory were characterized for antimicrobial susceptibility and ST131 status. Epidemiological, clinical, and outcomes data from medical record review were assessed for associations with ST131.

Results. Of 311 unique isolates, 61 (19.6%) were ST131. Overall, most isolates were from urine (84%), followed by wounds (13%), respiratory samples (3%), and others (1%). The sole ST131-associated epidemiological factor was long-term care facility (LTCF) exposure (33% for ST131, vs 14% for others; P = .001). Clinically, ST131 was not significantly associated with indicators of severe infection, including SIRS, fever, sepsis, or intensive care unit admission, and was significantly negatively associated with dysuria (10% vs 26%; P = .01). Compared with non-ST131 isolates, ST131 isolates were more likely to be resistant to FQs (85% vs 8%; P < .001), ampicillin (77% vs 34%; P < .001), ampicillin/sulbactam (69% vs 26%; P < .001), gentamicin (36% vs 3%; P < .001), and trimethoprim/sulfamethoxazole (31% vs 17%; P = .02). ST131 also was significantly associated with discordant initial treatment, both overall (63% vs 5%; P < .001) and among patients with evidence of infection (52% vs 5%; P < .001). Despite this, recurrence (clinical and microbiological) and mortality (in hospital and all-cause) were similar between groups.

Conclusion. *E. coli* ST131, which accounted for nearly 20% of unique (by patient) *E. coli* isolates at our VA, was significantly associated with LTCF exposure, extensive antimicrobial resistance, and discordant therapy, but not with more severe infections or worse outcomes. Our findings support that ST131 is a LTCF-associated pathogen, but they challenge the notion that ST131 causes more severe or complicated disease, at least among veterans.

Disclosures. **All authors:** No reported disclosures.

343. Risk Factors for Extended-Spectrum Beta-Lactamase Infection and Evaluation of Carbapenem Use Patterns and Appropriateness in a County Hospital Setting

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Background. Increasing reports of extended-spectrum β-lactamase (ESBL) production among Enterobacteriaceae have resulted in increased usage of carbapenems (CRBs). However, increased utilization of any antibiotic is associated with accelerated bacterial resistance to that antibiotic class. The aim of the present study was to determine: (1) risk factors for infection with ESBL-producing Enterobacteriaceae and (2) patterns and appropriateness of CRB use.

Methods. Patients hospitalized at UCLA-Olive View Medical Center from years 2010-2013 during the months of October to December were evaluated if they received at least 1 dose of CRB therapy during their hospital stay. ESBL infections were characterized as community-acquired, healthcare-associated, or nosocomial. CRB usage was judged as appropriate if it met any of the following: 1) positive ESBL culture, 2) history of prior ESBL culture, 3) Active pseudomonal infection sensitive to CRB, 4) Failure of empiric antibiotics, 5) other appropriate criteria, e.g., necrotizing pancreatitis.

Results. Of 255 total patients, 69 (27%) had an ESBL-positive culture. The majority were isolated from the urinary tract (74%), followed by blood (13%) and wound sites (5%). The majority of ESBL infections were health-care associated (76%), vs community acquired (14%). ESBL-positive patients were more likely to be female (72% vs 46%, p = 0.01), on hemodialysis (HD) (11% vs 7%, p = 0.001), to have a history of previous UTI (57% vs 35%, p = 0.002), or previous ESBL infection (43% vs 22%, p = 0.001) and to have antibiotic exposure in the previous 90 days (68% vs 49%, p = 0.006). Only 1 of 69 (1%) patients with ESBL infection had no documented past medical history.

Only 51% of patients were judged to have received CRBs appropriately. There was no difference between ESBL patients and non-ESBL patients in terms of duration of hospital stay (13 vs 11 days, p = 0.636), ICU admission rate (26% vs 36%, p = 0.135) or in-hospital mortality (9% vs 12%, p = 0.412).

Conclusion. ESBL infection was rare in the absence of specific risk factors (previous UTI, antibiotic exposure, history of ESBL). Data from this study may be used in an evidence-based approach for empiric CRB use to decrease inappropriate usage and bolster antibiotic stewardship efforts.

Disclosures. **All authors:** No reported disclosures.

344. Risk Factors for Infection with *Escherichia coli* among Long-Term Care Facility Residents with Gastrointestinal Tract Colonization with Fluoroquinolone-Resistant *E. coli*

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Background. Infections due to fluoroquinolone-resistant *Escherichia coli* (FQREC) are preceded by gastrointestinal colonization, and are associated with significant morbidity and mortality. Although colonization with FQREC is common among residents of long-term care facilities (LTCFs), risk factors associated with subsequent development of clinical infections in this population remain unclear. The objective of this study was to determine risk factors for developing a clinical infection with *E. coli* in LTCF residents with FQREC gastrointestinal colonization.

Methods. A case-control study was conducted from 2006 to 2008 at three LTCFs within an academic long-term care network. Residents initially colonized with FQREC were followed for 12 months after enrollment, or until discharge or death. Case patients were defined by the presence of a clinical infection with *E. coli*, while control patients were defined as those that did not develop a clinical infection with *E. coli*. A multivariable logistic regression model was developed to identify risk factors for clinical infection with *E. coli* in residents with baseline FQREC colonization.

Results. Over the 3-year study period, 234 participants had baseline colonization with *E. coli*, of which 94 (40%) were colonized with FQREC. Among patients with baseline FQREC colonization, 11 (12%) developed clinical infections with *E. coli* during the study period. Of these, 10 (90%) were due to FQREC. The median time to infection was 131 days (interquartile range, 57-299), with the majority of cases being urinary tract infections (n = 10; 90%). On multivariable analysis, significant risk factors for developing a clinical infection with *E. coli* included the presence of a urinary catheter (OR 11.6; 95% CI 1.87-71.6, $P = 0.008$), diabetes mellitus (OR 6.63; 95% CI, 1.14-38.5, $P = 0.035$), and receipt of trimethoprim-sulfamethoxazole in the 30 days prior to initial sampling up to development of infection (OR 14.6; 95% CI 2.28-93.0, $P = 0.005$).

Conclusion. Development of clinical infections with *E. coli* was relatively common among LTCF residents with baseline colonization with FQREC. Future studies should focus on interventions for timely removal of urinary catheters and judicious use of antibiotics in this vulnerable, medically complex population.

Disclosures. **All authors:** No reported disclosures.

345. Telephone Survey of Infection Control and Antibiotic Stewardship Practices in Long-term Care Facilities in Maryland

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Background. Maryland's population is served by a combination of health care facilities, such as acute care hospitals, long-term care facilities, and home health services. There are rigorous infection surveillance and control programs at acute care facilities but research in long-term care facilities'(LTCFs) are lacking. The purpose of our study is to investigate further the specifics of infection control and antibiotic stewardship programs in long-term care facilities in Maryland.

Methods. All Maryland long-term care facilities are obtained from the administrator for the Maryland Medical Director Association. We contacted each facility's infection control personnel over the phone and administer the survey questions.

Results. There are 231 LTCFs in Maryland. Our telephone survey reached 97 LTCFs but only 88 facilities are included in the analysis as three facilities did not have a designated infection control personnel and six facilities declined participation. Out of 88 facilities, there are 11,793 beds and 207 infection control personnel.

Results

About 95% of facilities have a central line protocol. All facilities surveyed have urinary catheter protocols. 9.5% of facilities use silver impregnated urinary catheters. Most facilities track UTIs and report to the health department in the case of an outbreak. Close to 80% of facilities surveyed stated that they isolate patients with C. diff, MRSA, and VRE but isolation can be only cohort in some facilities.

71% and 84% of facilities already have antibiotic guides and restricted formulary, respectively. About 16% of facilities have antibiotics approval process. 32% of facilities state that they have training for antibiotics prescribing; however, a large percentage, 18.2%, of facilities' infection control personnel did not know whether such training existed.

Conclusion. Antibiotic stewardship programs in LTCFs are still in early development stages despite increasingly resistant organisms. To decrease the transmission and acquisition of nosocomial infections and drug-resistant organisms, not only do we need to have more support and resources for the infection control personnel, but we also need to involve the front line staff's observations and expertise into a comprehensive infection control plan.

Disclosures. **All authors:** No reported disclosures.

346. Longterm carriage of Ciprofloxacin-Resistant *E. Coli* Isolates among Nursing Home (NH) Residents

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Background. With the pervasive use of quinolones, quinolone-resistant gram negative bacteria are increasingly common in NHs. However, there are few estimates of the duration of carriage of resistant strains, the extent colonized individuals carry the same strain at multiple sites, and the proportion of strains shared among residents. We begin to fill these gaps using samples from the Targeted Infection Prevention (TIP) Study.

Methods. We used REP-PCR to type 86 ciprofloxacin-resistant *E. coli* isolates collected during monthly surveillance of 21 individuals with medical devices over a 1 year period in a single NH. Isolates were collected from multiple body sites at each time point and screened for antibiotic susceptibility against ciprofloxacin. REP-PCR amplification was performed on all isolates using $(GTG)_5$-primers; isolates from the same individual were run on the same gel. To check if isolates were shared among individuals, a representative strain from each type was sampled from each individual and run on a single gel. Strains with the identical banding pattern were considered the same.

Results. Most isolates were from the rectum (49%) and the groin (24%). Nine unique REP-PCR-types were observed; 4 individuals (19%) carried at least two genetically unique strains. The median duration of carriage for a single strain was 28 days (range, 1-338 days). One REP -PCR type was found in 7 residents and two among 4 residents; 3 REP-PCR types were found on only one resident suggesting substantial transmission among residents.

Conclusion. Colonized NH residents tended to carry the same ciprofloxacin-resistant *E. coli* strain at multiple body sites and for long periods. 90% of REP -PCR types were found in multiple/at least two individuals suggesting that the risk of transmission of resistant strains of *E. coli* is high in NH.

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347. Antimicrobial Susceptibility of OXA-48, NDM-1 And VIM-4 Carbapenemase-producing Clinical Isolates of *Enterobacteriaceae* From Kuwait Government Hospitals

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Background. Emergence of infections due to multidrug-resistant Enterobacteriaceae presents a significant public health problem worldwide. Treatment alternatives for infections due to carbapenemase-producing Enterobacteriaceae are few and the resistant organisms have the potential for causing serious healthcare epidemics if not promptly detected and contained. The study was conducted to investigate types of carbapenemases-encoded genes and drug resistance among carbapenem-resistant Enterobacteriaceae isolates in 6 government hospitals in Kuwait.

Methods. Enterobacteriaceae isolates resistant to carbapenems were collected over a period of 3 years (2010-2013). Susceptibility testing to 13 commonly used antibiotics was carried out by E test according to the CLSI guidelines. PCR assay was performed for detection of genes encoding ESBLs (bla_{CTX-M}, bla_{SHV} and bla_{TEM}) and carbapenemases (bla_{OXA-48}, bla_{VIM}, bla_{NDM}, bla_{IMP}, bla_{GIM} and bla_{KPC}).

Results. A total of 66 non-duplicated carbapenem-resistant isolates were collected over a period of 3 years. However, only 32/66 (48.5%) carried the carbapenemase resistance genes. Resistance genes analysis showed that 11 isolates carried bla_{OXA-48} gene, 11 carried bla_{VIM-4} gene and 10 carried bla_{NDM-1} gene. 9.1%, 72 and 80 % of bla_{OXA-48}, bla_{VIM-4} and bla_{NDM-1}-carrying Enterobacteriaceae, respectively were resistant to amikacin. 27.3, 18.2 and 40 % of bla_{OXA-48}, bla_{VIM-4} and bla_{NDM-1} carrying isolates, respectively, were resistant to tigecycline and 9.1, 9.1, and 20%, respectively to colistin. Overall, almost 70% of the isolates were resistant to ciprofloxacin and cefepime.

Conclusion. Treatment of carbapenemase-producing Enterobacteriaeae in Kuwait is problematic as some of our isolates are resistant to tigecycline at an unacceptable level and resistance to colistin is emerging.

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348. Rising incidence of carbapenem resistance in health care associated blood stream infections in a tertiary care hospital in Mumbai, India

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Background. A prospective cohort surveillance study was conducted in adult patients admitted to the intensive care unit (ICU) in a tertiary-care hospital in Mumbai, India to determine the incidence rates, microbial etiology and antimicrobial susceptibility of health care associated central line associated blood stream infection (CLABSI).

Methods. All patients admitted to the adult ICU (mixed medical-surgical) during the study period were included. Blood cultures were sent when sepsis was suspected, processed in the BacT Alert 3D system and the VITEK 2 system used for identification and susceptibility testing. CLABSI were defined as per the Centers for Disease Control and Prevention (CDC) definitions.

Results. From January 2010 to December 2013, 20814 adult patients, representing 93751 bed days were enrolled in the study. A total of 8328 central lines were inserted with 50436 central line days. The overall CLABSI rate was 5.67 per 1,000 central line device days (286 cases) and ranged from 5.77 in 2010 to 6.62 per 1,000 central line device days in 2013.

Overall 80 % of all CLABSIs were caused by Gram Negative Bacilli (GNB's); 12 % were caused by Gram positive cocci (GPCs) and 7% were caused by Candida species. *K. pneumoniae*, *A. baumannii* and *P. aeruginosa* were the commonest GNB's. Enterococcus was the commonest GPC (42 % of all GPC), methicillin resistant *S. aureus* (MRSA) contributed to only 12 %. Fourteen percent of enterococcus were vancomycin resistant (VRE). The incidence of ESBL production in GNB increased from 56% in 2010 to 80% in 2013 while the incidence of carbapenem resistance increased from 0% in 2010 to 43% in 2013. Resistance to Beta-lactam plus beta lactamase inhibitor combinations such as piperacillin-tazobactam increased from 14% in 2010 to 70% in 2013. Also ominious was the rise in fluconazole resistance among Candida isolates from 0% in 2010 to 33% in 2013.

Conclusion. This is the largest single centre study of CLABSI from India. Though the incidence rates are superior than those reported from other centers in India, they are inferior to those reported by the national health and safety network of the USA. The increasing incidence of resistance especially carbapenem resistance in gram negative pathogens is of serious concern. Urgent implementation of effective infection control and antimicrobial stewardship strategies is needed.

Disclosures. **All authors:** No reported disclosures.

349. Surveillance of Carbapenem Resistance and the First Case of NDM-7-producing *Klebsiella pneumoniae* in the Philippines

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Background. KPC, NDM, and OXA-48 have spread to virtually every continent, although not every country has been affected. The SMART worldwide surveillance program from 2008-2009 characterized the molecular epidemiology of carbapenem resistant *Klebsiella pneumoniae*, and identified three *K. pneumoniae* ST903 with IMP-26 in the Philippines; no other carbapenemases have been reported in the Philippines.

We sought to characterize recent changes in antibiotic resistance and molecular epidemiology in the Philippines.

Methods. Clinical isolates were collected from the microbiology laboratories of two hospitals in metropolitan Manila, Philippines over 14-months. Bacteria identification and antibiotic susceptibility testing were performed with the VITEK 2. DNA-typing was performed with multilocus sequence typing. Multiplex polymerase chain reaction was used to test for up to seven carbapenemase genes, as previously described.

Results. A total of 364 Enterobacteriaceae were collected, including 19 *Enterobacter* spp., 181 *Escherichia coli*, 135 *Klebsiella* spp., 9 *Proteus mirabilis*, 19 *Salmonella* spp., and 10 other Enterobacteriaceae.

Carbapenem resistance was detected in 2 (1.2%) *E. coli*, and 4 (3.0%) *Klebsiella* spp., but was not found in *Enterobacter* spp. or *P. mirabilis*. A cluster of four patients with

carbapenem-resistant *K. pneumoniae* was identified in a single month, and investigated. Two contained the *bla* $_{NDM-7}$ beta-lactamase gene, and were typed as *K. pneumoniae* ST273. The third had the *bla* $_{VIM}$ gene. None of the seven tested carbapenemase genes were identified in the fourth case.

We also report that carbapenem resistance in the Philippines is rare, but the emergence of NDM-7 should prompt further antibiotic resistance surveillance and implementation of policies to control the spread of antibiotic resistance in this bacterium with outbreak potential.

Conclusion. We report the first two patients with pathogens carrying the *bla* $_{NDM-7}$ gene, and the first patient with a pathogen carrying the *bla* $_{VIM}$ gene in the Philippines. While *K. pneumoniae* ST273 carrying the *bla* $_{NDM-1}$ gene has been described in Italy and the United Kingdom, this is the first report of this sequence type spreading outside Europe.

Disclosures. **All authors:** No reported disclosures.

350. Exposure Investigation and Infection Prevention Measures for a Patient with Confirmed NDM-1 Producing *Klebsiella pneumoniae*

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Background. Carbapenem-resistant Enterobacteriaceae (CRE) producing the New Delhi metallo-beta-lactamase-1 (NDM-1) enzyme is rarely seen in the United States. The first case of NDM-1 CRE at Johns Hopkins Hospital (JHH) was identified in February 2014.

Methods. When a patient's blood cultures grew NDM-1 *Klebsiella pneumoniae* on February 18, 2014, contact precautions and 1:1 nursing were initiated. Education was provided to staff to reinforce compliance with hand hygiene, isolation precautions, and environmental cleaning practices. All patient rooms on the involved units were disinfected using hydrogen-peroxide vapor.

Medical records were reviewed and an exposure investigation was conducted. Exposure criteria included any patient on the same unit as the source patient prior to the initiation of isolation precautions, or any patient occupying a room previously occupied by the source patient.

Using a concentric circle approach, all inpatients meeting the exposure criteria were placed on contact precautions and rectal, urine, sputum, or wound surveillance cultures for CRE were collected per CDC recommendations.

Results. The patient had prior travel history to India, but no healthcare exposure while there and no known history of multidrug-resistant organisms. At JHH, the patient was on two surgical ICUs and one inpatient unit for a total of 27 days prior to the initiation of isolation precautions. 130 patients met criteria for potential exposure. 38 patients who were still inpatients had surveillance cultures obtained. One wound and two rectal cultures grew non-NDM-1 CRE (Figure)..

Table: Hand Hygiene and Environmental Cleaning Results during Potential NDM-1 CRE Exposure

	Hand Hygiene Compliance		Environmental Cleaning Compliance	
	January 2014	February 2014	January 2014	February 2014
ICU A	100%	100%	96%	100%
ICU B	100%	100%	88%	88%
Unit	100%	87%	90%	98%

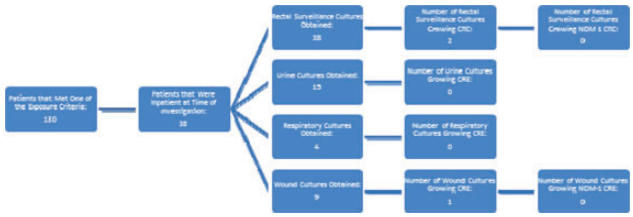

Figure Potentially Exposed Patients and Surveillance Culture Results

Conclusion. NDM-1 producing *Klebsiella pneumoniae* was detected in a patient with prior history of travel to, but no healthcare exposure in, India. Despite 27 days of potential exposure prior to initiation of isolation precautions, no transmissions of NDM-1 CRE occurred, possibly due to excellent hand hygiene and environmental cleaning on the units to which the patient was admitted (Table)

Disclosures. **All authors:** No reported disclosures.

351. NDM-1-producing *Escherichia coli* Isolated from a Case Patient's Environment

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Background. The Oregon Health Authority identified its first New Delhi metallo-β-lactamase-1 (NDM-1)-producing *Escherichia coli* since mandated laboratory reporting for carbapenem-resistant Enterobacteriaceae (CRE) began during 2012. We investigated to determine risk factors, identify the source, and prevent transmission.

Methods. A CRE case is defined as Enterobacteriaceae non-susceptible to all third-generation cephalosporins and ≥1 carbapenem tested. CRE isolates are routinely characterized via Carba NP test and PCR for carbapenemase genes. In addition, this isolate underwent pulsed-field gel electrophoresis (PFGE), strain and plasmid identification, and whole genome sequencing. We conducted laboratory and chart reviews, case and health care provider interviews, contact screenings, site visits, and environmental testing.

Results. In November 2013, testing confirmed a NDM-1 positive, CTX-M-27-producing *E. coli* O25b-ST131 isolated from an outpatient shin wound culture taken from a rural Oregon county resident. Review of regional laboratory reports did not identify other NDM-positive CRE during the preceding year. The case and spouse denied international travel or visitors, and we confirmed only outpatient clinic visits during the previous year. CRE rectal swabs from the resident (N =3) and spouse (N = 1) were negative. Other possible sources such as laboratory error, food contamination, animal shedding, outpatient clinic contamination, or household water contamination were extensively reviewed. Spice (N = 14), nutritional supplement (N = 15), indoor environmental (N = 13), outdoor environmental (N = 18), and vacuum dust (N = 4) samples were collected two months after case confirmation. An NDM-1-producing *E. coli* isolate indistinguishable from the resident's isolate by PFGE was extracted and cultured from a household vacuum dust sample.

Conclusion. Though CRE are associated with exposure to health care in CRE endemic regions, we could not identify any previously described sources in this low-prevalence region. Recovery of a matching strain from a vacuum environmental sample raises concern about the persistence of pathogenic strains in a household environment and an as yet unidentified origin.

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352. Clinical and molecular characteristics of NDM-1 harboring Multi-Drug Resistant Gram Negative Bacteria at Carilion Medical Center

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Background. Carbapenem (C) resistant gram negative bacteria (GNB) have emerged as an important concern as infections by these organisms spread rapidly in hospital settings, are difficult to treat and carry high mortality rates. Among several different types of carbepenemase producing genes, New Delhi Metallo β-lactamase-1 (NDM-1) is a new gene that causes resistance to C antibiotics; GNB also commonly co-harbor Aminoglycoside (A) resistance genes. Both resistance genes can be found commonly on the same plasmid. Infections by NDM-1 harboring GNB are increasingly being reported in US. We are observing an increasing number of multi-drug resistant (MDR) GNB at Carilion Medical Center (CMC) which are resistant to C and A.

Methods. A retrospective study was conducted on a small number of banked specimens (n = 15) of MDR-GNB collected at CMC in 2011-2012. We isolated plasmids of these organisms using Qiagen kits as per the manufacturer's protocol, characterized plasmid profile and performed screening with NDM-1 gene specific primers by using polymerase chain reaction (PCR). Retrospective chart analysis was performed and demographic, clinical and outcome data were collected.

Results. Among 15 MDR-GNB specimens, 10 were *Pseudomonas aeruginosa,* 1 *Enterobacter cloacae,* 1 *Burkholderia cepacia,* 1 *Proteus mirablis,* 1 *Achromobacter xylosoxidans,* 1 *Kleibsiella pneumonia.* Nine of 15 organisms were resistant or

intermediate to Amikacin and 13/15 were resistant to C. These plasmids were larger in size (>23kbp in size) and multiple (2-3) in 5/15 bacteria. NDM-1 gene specific primer PCR with 813 kbp band was positive in 8 of 15 MDR-GNB. Chart analysis was available for 14 patients (pts) only (7 NDM-1 +ve and 7 NDM-1 -ve). Mean age of NDM-1 +ve pts was 65.4 years and NDM-1 -ve pts was 60.8 years. Six of 7 NDM-1 +ve and 3/7 NDM-1 -ve pts were admitted from a healthcare facility. Information regarding foreign travel or contact with foreign pts was unavailable. Five of 7 NDM-1 +ve pts were admitted with acute respiratory failure and 4/7 patients died; 2/7 NDM-1 -ve pts died.

Conclusion. C resistant GNB remain a threat to pts in healthcare settings. NDM-1 gene-present pts have 2.33 times higher relative risk of death than non NDM-1 carrying pts in our study. Resistance to A and C should arouse suspicion to the presence of NDM-1 gene with need for early detection and intervention.

Disclosures. **All authors:** No reported disclosures.

353. Emergence of Carbapenem-Resistant Enterobacteriaceae (CRE) in Orange County, CA and Support for Regional Strategies to Limit Spread

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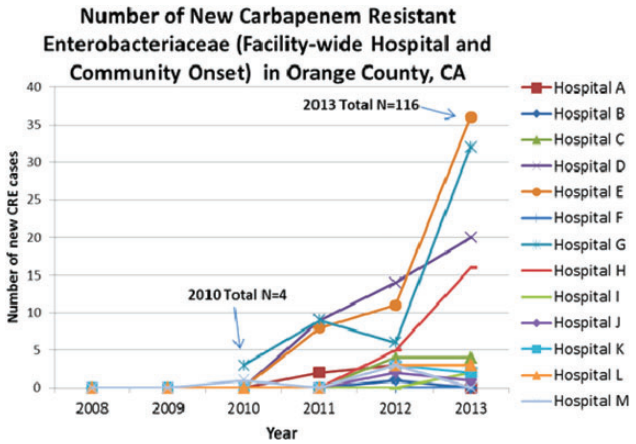
Background. The spread of CRE from eastern to western United States has enabled the study of its emergence in California (CA). We evaluated CRE emergence in Orange County (OC), CA hospitals serving 3.1 million residents and evaluated regional support of infection prevention (IP) programs for containment strategies.

Methods. We conducted a survey (14 questions, 3 data tables) of the 31 hospital IP programs in OC. Questions assessed willingness to adopt strategies to address CRE with responses of "definitely" or "possibly" deemed supportive. Data tables were used to determine the frequency of culture positive CRE patients from 2008-2013.

Results. To date, 14 (52%) IP programs representing 16 hospitals completed the survey (still ongoing). CRE was first detected in 2010 in 12.5% of respondent hospitals. By 2013, 56.3% of hospitals reported CRE cases (Figure). 100% of respondents supported some form of regional collaboration to implement a CRE prevention "bundle". Regarding specific strategies, 100% supported single room and contact precautions for CRE^+ patients and 12.5% had already enacted this. 100% supported active communication regarding CRE^+ status with facilities accepting their patients. 92.8% supported periodic active surveillance of hand hygiene and contact precautions for CRE^+ patient rooms. 85.7% supported daily chlorhexidine bathing of CRE^+ patients (14.3% uncertain), and 12.5% were currently bathing. 64.3% supported (14.3% uncertain, 21.4% against) annual point prevalence screening for CRE in high risk units or patients (e.g., patients admitted from long term care facilities). While 78.6% supported screening roommates of CRE^+ patients, only 42.9% supported screening neighboring rooms.



Conclusion. The swift rise in CRE cases in OC parallels epidemiology seen in other areas where CRE is now endemic. However in OC, CRE is still concentrated in only a few facilities and concerted regional intervention may prevent CRE from becoming endemic. Responding IP programs fully supported regional strategies involving isolating CRE^+ patients and relaying positivity to transferring facilities. However compliance assessment, screening, and decolonization were less well supported and likely influenced by resource and financial requirements.

Disclosures. **All authors:** No reported disclosures.

354. Six Months of Surveillance for Carbapenem-Resistant *Enterobacteriaceae* in Maryland

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Background. Carbapenem-Resistant Enterobacteriaceae (CRE) were recently named one of the top three urgent threats to public health in CDC's 2013 Antimicrobial Resistance Threat Report. The Maryland Department of Health and Mental Hygiene (DHMH) made CRE reportable statewide on November 7, 2013 using a broad surveillance definition

Methods. To make data comparable across states, this analysis was limited to non-duplicate patients and to CRE meeting the CDC's surveillance definition (nonsusceptible to doripenem, imipenem or meropenem by most recent CLSI carbapenem breakpoints and resistant to all third-generation cephalosporins tested).

Results. Maryland laboratories reported 134 CRE between November 7, 2013 and April 30, 2014, representing disease and/or colonization occurring in acute care hospitals, long term acute care hospitals and long term care facilities. The majority of cases (60%) occurred in patients residing in the Baltimore Metro Area (BMA) but rates per 100,000 residents were similar for the BMA (2.94), Southern Maryland (2.83) and the Eastern Shore (2.87) (Figure 1). Residents of the National Capital Region (NCR) and Western Maryland experienced lower rates (1.35 and 0.79 respectively). More than half of cases were isolated from urine but cases were reported from a variety of body sites including sterile sources (Figure 2). Klebsiella pneumoniae was the most frequently reported organism (Figure 3) but cases occurred in 15 separate species of *Enterobacteriaceae*. Most cases (58%) occurred in adults over 65 years of age; another 36% occurred in adults aged 35-64 and the remaining 6% were from adults aged 18-34. No pediatric cases were reported.

Conclusion. Statewide surveillance has shown that CRE is well-established in Maryland. Surveillance data does not differentiate between symptomatic infection and colonization, but it is reasonable to assume that some CRE in urine is colonization only. Given this limitation and recognizing that urine may be a frequent source of transmission, physicians and infection preventionists must carefully consider how to manage CRE in urine. Maryland's antibiotic stewardship efforts must also emphasize reducing unnecessary antibiotic use across healthcare settings to reduce the threat of CRE.

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355. Carbapenem-Resistant Enterobacteriaceae (CRE) Distribution within the Veterans Affairs Healthcare System: 2013

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Background. The Centers for Disease Control and Prevention (CDC) has reported national trends for hospital-acquired infections with CRE. Utilizing the Department of Veteran's Affairs (VA) Healthcare-Associated Infections and Influenza Surveillance System (HAIISS), we sought to describe isolation of CRE among Veterans cared for nationally at inpatient and outpatient VA healthcare settings from January - December 2013.

Methods. We queried the HAIISS Data Warehouse for all isolates of Enterobacteriaceae meeting CDC criteria:

- Nonsusceptible to one of the following carbapenems: doripenem, meropenem, or imipenem AND
- Resistant to all of the following third-generation cephalosporins that were tested: ceftriaxone, cefotaxime, and ceftazidime.

CRE were isolated in VA using standard microbiologic methods. Duplicate isolates were eliminated unless they were isolated in more than one specimen type category.

Results. A total of 528 unique isolates meeting CDC criteria for the one year time period were isolated (table). Klebsiella (64%) and Enterobacter (16%) species were most common. The primary specimen types associated with CRE were urine, respiratory, and blood, with 359 (58%), 102 (16%), and 53 (9%) isolates respectively. The remaining 106 (17%) CRE isolates were from a variety of other specimen types.

[1] MMWR March 8, 2013/62(09);165-170 Vital Signs: Carbapenem-Resistant Enterobacteriaceae

Breakdown of CRE isolates by Genus and U.S. Census region plus Puerto Rico

Bacterial Genus	Northeast	Midwest	South	West	Puerto Rico	Total
Citrobacter	9	2	3	4	3	21
Enterobacter/ Pantoea	12	6	31	20	18	87
Escherichia	2	4	14	4	6	30
Klebsiella/ Raotella	104	36	75	20	101	336

continued.

Bacterial Genus	Northeast	Midwest	South	West	Puerto Rico	Total
Morganella	6	2	1	2	2	13
Proteus	5	9	9	6	0	29
Providencia	0	0	0	1	0	1
Serratia	1	0	3	0	7	11
Total	139	59	136	57	137	528

Conclusion. CRE distribution in VA healthcare settings nationally is similar to that reported by CDC[1], with the largest number of isolates occurring in the Northeast and South. VA did have a higher number of CRE isolates in Puerto Rico compared to that reported by CDC. Consistent with other reports, CRE was isolated most frequently from urine. CRE is emerging as a significant concern in VA.

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356. Epidemiology of Community-Associated Carbapenem-Resistant *Enterobacteriaceae* Identified through the Emerging Infections Program

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Background. Carbapenem-resistant Enterobacteriaceae (CRE) is an emerging public health problem in the United States with acquisition mostly in the inpatient healthcare setting. Other drug-resistant *Enterobacteriaceae* cause community-associated (CA) infections; the spread of CRE in non-healthcare settings could have important public health implications. We analyzed CRE surveillance data to identify CA cases.

Methods. From January 2012-December 2013, 5 Emerging Infections Program (EIP) sites (CO, GA, MN, NY, OR) participated in active laboratory- and population-based CRE surveillance. A CRE case was isolation of *Escherichia coli, Enterobacter* or *Klebsiella spp.* from normally sterile sites or urine that was carbapenem-nonsusceptible (excluding ertapenem) and resistant to all 3rd generation cephalosporins tested. Cases underwent medical record review; a subset of CRE isolates underwent PCR for carbapenemase genes. Cases were classified as CA if they had no hospital admissions, long term care residence or chronic dialysis in the prior year and no indwelling devices in the 2 days before culture; cases with these exposures were considered healthcare-associated (HA).

Results. Of 430 total CRE cases, 414 (representing 329 patients) with known CA/HA status were evaluated. Thirty-nine of 329 (12%) patients had CA CRE. Most CA patients were female (72%); all had CRE isolated from urine only; 44% had a symptomatic UTI; none traveled internationally in the 2 months prior to onset. Both patient groups were similar in age (58 vs 62 years, $p = 0.18$). CA patients had a lower mean Charlson Comorbidity Index (0.90 vs 3.14, $p < 0.0001$) compared to HA patients. CA CRE cases were more likely to be caused by *Enterobacter aerogenes* (40% vs 11%, $p < 0.0001$) and less likely to be caused by *Klebsiella pneumoniae* (30% vs 62%, $p < 0.0001$) than HA cases. Fewer CA CRE isolates were *K. pneumoniae* carbapenemase positive by PCR than HA isolates (2/15, 13%, vs 50/94, 53%, $p = 0.004$).

Conclusion. In-depth review of CRE cases from geographically diverse EIP surveillance sites revealed a few patients did not have major healthcare exposures in the year prior to their CRE culture. It will be important to determine whether these patients have less intensive outpatient or remote inpatient healthcare exposures.

Disclosures. **All authors:** No reported disclosures.

357. Epidemiology of Carbapenem-Resistant Gram-Negative Bacilli in Georgia, Minnesota, and Oregon – 2012

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Background. Carbapenem-resistant Enterobacteriaceae (CRE) and carbapenem-resistant *Acinetobacter* (CRAB) are increasingly reported in the United States and cause infections with high mortality. We initiated a laboratory and population-based surveillance program to describe the epidemiology of CRE and CRAB.

Methods. We defined CRE as *Escherichia coli*, *Enterobacter* spp, or *Klebsiella* spp nonsusceptible to ≥1 carbapenem (excluding ertapenem) and resistant to all 3rd generation cephalosporins tested, and CRAB as *A. baumannii* nonsusceptible to ≥1 carbapenem (excluding ertapenem). CRE and CRAB isolates from sterile sites or urine collected in residents of 3 metropolitan areas in GA, MN, and OR in 2012 were included. Rates were based on 2012 census data. We reviewed patient charts and classified isolates as hospital-onset (HO) (collected >3 days after admission); healthcare-associated, community-onset (HACO) (collected ≤3 days after admission with hospitalization, dialysis, long-term care residence, or surgery in the prior year or with an indwelling device at time of culture); or community-associated (CA) (collected ≤3 days after admission and lacking the above healthcare exposures). Polymerase chain reaction was used to test available CRE for selected carbapenemases.

Results. Of 327 isolates, 213 were CRE (169 patients), 114 were CRAB (100 patients). Most CRE (88%) and CRAB (73%) were from urine; 9% and 25% were from blood respectively. CRE and CRAB incidence (per 100,000 population) was significantly lower in OR (CRE: 0.35, CRAB: 0) and MN (CRE: 1.88, CRAB: 0.12), compared to GA (CRE: 4.58, CRAB: 2.93). Most CRE (72%) and CRAB (62%) isolates were classified as HACO; of these, 49% of CRE and 66% of CRAB were from patients recently in long-term care settings. *K. pneumoniae* carbapenemase was detected in 51% of CRE (*K. pneumoniae* [19/23; 83%], *E. coli* [1/8; 13%], *E. cloacae* [6/9; 67%], *E. aerogenes* [1/13; 8%]); no other carbapenemases were detected.

Conclusion. Most CRE and all CRAB were detected in patients with healthcare exposures. CRE and CRAB incidence varied substantially across surveillance sites. Many CRE meeting our definition do not harbor carbapenemases; whether these organisms pose the same threat as carbapenemase-producing CRE is not known.

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358. Present State of CRE Prevention: What are U.S. Hospitals Doing?

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Background. Carbapenem-resistant Enterobacteriaceae (CRE) have emerged as an immediate threat to hospitalized patients. With limited guidance from the Centers for Disease Control and Prevention (CDC), clinicians often employ interventions recommended for methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE): hand hygiene, contact precautions (CP), environmental disinfection. Some hospitals use targeted active surveillance testing (AST). This study was conducted to assess the present state of interventions to reduce transmission of CRE in U.S. hospitals.

Methods. 751 physician members of the Emerging Infections Network (EIN) who had identified themselves as having interest or involvement in infection prevention were invited to complete an electronic survey. The survey contained 8 questions designed to ascertain current practices related to reducing transmission of CRE.

Results. 429 members responded to the survey (57.7%). 97% reported using CP for CRE. The most widely used trigger for CP was positive clinical culture (97%), followed by pre-existing alert in the electronic record (75%). Practices for discontinuation of CP varied: 38% reported using CP indefinitely once a patient becomes positive; 43% use CP until a patient is cleared, 13% use CP for the specific encounter only and 10% use CP for one year post- positive culture. 18% reported performing CRE AST for a subset of inpatients. Adjunct measures to reduce the risk of transmission such as CHG bathing for any inpatient population and room disinfection using hydrogen peroxide vapor or UVC light were reported to be used by 85% and 23%, respectively.

Conclusion. 97% of respondents use routine CP for CRE; however, practices for the duration of CP are heterogeneous. Though not based upon guidance from CDC, a clearance process for CRE, which results in discontinuation of CP, was used by 43% of respondents. Horizontal interventions such as CHG bathing and UVC light disinfection, while commonly used, are of questionable utility for reducing the risk of CRE transmission. Evidence-based guidelines from professional organizations regarding measures to reducing transmission of CRE are needed.

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359. Epidemiology of Carbapenem-Resistant *Enterobacteriaceae* (CRE) at an Academic Medical Center

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Background. CRE infections have few treatment options and are associated with poor outcomes. Limited data regarding these infections are available from the Southeastern US. This study describes CRE epidemiology at our hospital.

Methods. A retrospective cohort study was conducted of all patients (pts) with a positive clinical culture for CRE from January 2006-December 2013. Data was obtained from chart review. Cultures were categorized as infection or colonization (treated vs not treated by the clinician).

Results. 46 pts had a positive culture for CRE and the rate per 1,000 patient days significantly increased over the study (0.0063 in 2006 vs 0.036 in 2013, $p < 0.001$). Median (med) age was 59, 50% were male, 52% were Caucasian. Med Charlson Comorbidity Index was 5, med number of comorbidities was 3 (hypertension 63%, A 46%, malignancy 20%) and 18 (42%) were receiving immunosuppression. 21 (54%) had antibiotic use within the past 6 months, most commonly a carbapenem (43%), followed by piperacillin/tazobactam (33%) and a cephalosporin (29%). Most (85%) had a history of another multi-drug resistant organism (MDRO), usually VRE or MRSA. 30 (75%) pts had CRE infection. Among these, the urinary tract accounted for 14 (47%), bloodstream for 6 (20%), respiratory tract for 6 (20%), and deep tissue for 4 (13%). Among pts with colonization, urine was the source in 7 (70%) and respiratory in 2 (20%). Overall, *Klebsiella* (54%) was the most common species followed by *Enterobacter* (26%), *Escherichia coli* (11%), *Serratia* (7%), and *Citrobacter* (2%). Med hospital stay was 39 days and med time to positive CRE culture was 16 days. 52% stayed in the ICU a med of 24 days. Overall hospital mortality was 17% (10% in colonized vs 25% in infected pts) but 95% of infected pts experienced morbidity (www.cdc.gov/nchs/data/ice/ice95v1/c28.pdf). Among infected pts who died (6), 3 had urine, 2 had respiratory and 1 had blood as the source of infection. All were treated with appropriate antibiotics.

Conclusion. CRE rates increased at our Southeastern academic hospital. Advanced comorbidity index, history of previous MDRO, lengthy hospital stay and receipt of immunosuppression or broad spectrum antibiotics were common characteristics among pts with CRE. Pts with CRE infection suffered increased morbidity and mortality.

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360. Surveillance for Carbapenemase-Producing Bacteria in the Wake of a Nosocomial Outbreak

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Background. From June 2011 through December 2011, a cluster of KPC-producing *Klebsiella pneumoniae* colonization and infection occurred in the NIH Clinical Center. The Clinical Center has continued monitoring its immunocompromised patient population for carbapenem-resistant *Enterobacteriaceae* (CRE) using active surveillance and periodic environmental sampling.

Methods. From January 2012 through March 2014, perirectal swabs were collected: on admission and weekly in the ICU and other high-risk wards, from patients recently hospitalized at other institutions or transferred out of the ICU, and monthly on all medical-surgical inpatients. Starting September 2013, swabs were collected from all patients admitted to non-behavioral health wards. Swabs were plated onto chromogenic CRE-selective media and incubated at 35°C for 18-24 h; or tested by bla_{KPC} PCR. Environmental surfaces were sampled using moistened gauze pads. Pigmented colonies were identified by MALDI-TOF MS and tested by bla_{KPC} PCR. CRE-colonized patients were isolated with dedicated nursing and 24-hour infection control adherence monitoring. Equipment and rooms were disinfected with bleach, hydrogen peroxide vapor, and/or UV light.

Results. Of 13,762 orders for surveillance swabs, 11,754 swabs from 3,843 patients were collected, an 85% compliance rate, with the gap largely due to patient refusal. Most swabs were cultured (95.8%), with 4.2% tested directly by PCR. Among 15 patients who had newly identified CRE isolates, 11 were KPC +, of whom 1 had acquired the outbreak strain, and 4 isolates had other mechanisms of carbapenem resistance. Since July 2012, no instances of hospital transmission have been detected. Of 343 environmental samples, 12 (4.4%) grew CRE (9 sink drains, 1 faucet aerator, 1 handrail, and 1 medication room surface); all but two were epidemiologically linked to colonized patients.

Conclusion. Stringent infection control measures, including direct observation of hand hygiene compliance and aggressive microbiological surveillance were associated with control of CRE transmission. The relative contributions of healthcare personnel and environmental contamination to the nosocomial spread of CRE remain to be delineated.

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361. Duration of colonization with KPC-producing bacteria at long-term acute care hospitals in Chicago, USA

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Background. *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae (KPC) are endemic in the USA and prevalence is especially high in long-term acute care hospitals (LTACHs). There, vulnerable patients are in close proximity to each other, allowing infections to spread easily. Another important aspect of LTACHs is the high readmission rate which can create a feedback loop, in which readmitted patients re-introduce the pathogen into the facility. Knowledge about the duration of colonization with KPC is essential to identify patients at risk of KPC carriage and to control the spread of KPC in LTACHs.

Methods. Data were collected from November 2011 until June 2013 in four LTACHs in the Chicago region, Illinois. All LTACH patients were screened on admission for KPC and every-other-week point prevalence cultures were taken. All patients with at least one episode of KPC colonization were included in the analyses. The duration of colonization was assessed using a maximum likelihood analysis, which can take into account (false) negative cultures in between positive cultures and can simultaneously assess the sensitivity of the screening test for KPC. Furthermore, we looked at the time between discharge and readmission of patients and assessed the clearance rate in this period, taking interval-censoring into account.

Results. Using data from 625 patients (1065 cultures), the median duration of colonization with KPC was estimated to be 16 months when assuming that negative cultures in between positive cultures were false negative. The corresponding sensitivity was 82%. 242 (re-) admissions were available of 166 patients to assess the duration of colonization after discharge from the LTACH, assuming that patients are 'at risk' of clearance of KPC in this period. In that analysis, the median duration of colonization was 11 months.

Conclusion. About half of the LTACH patients colonized with KPC are still carriers after a year. Colonized patients seem to require isolation or other infection control precautions for a prolonged time.

Disclosures. **All authors:** No reported disclosures.

362. Modeling intrafacility spread of KPC-producing bacteria and impact of cohort strategies in long-term acute care hospitals in the Chicago region, USA

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Background. Nosocomial outbreaks of *Klebsiella pneumoniae* carbapenemase-producing Enterobacteriaceae (KPC) are being reported increasingly. The first recognition of KPC in metropolitan Chicago was in 2007. Prevalence rose rapidly thereafter, especially in long-term acute care hospitals (LTACHs). Using mathematical models we studied the spread of KPCs in LTACHs, determined the transmission capacity of KPC, and investigated the effect of cohorting.

Methods. Data on room occupancy, admission cultures, and every-other-week point prevalence cultures were available from four LTACHs in the Chicago region from June 2012 until June 2013. Three different cohort strategies were adopted at the LTACHs: a pure cohort (all KPC-positive patients on one floor), single rooms for KPC-positive patients, and a mixed cohort (all KPC-positive patients on one floor, supplemented with KPC-negative patients). A data-augmented Markov chain Monte Carlo method with Metropolis-Hastings algorithm was developed to model the transmission process in the LTACHs and to study the effect of different cohort strategies. The transmission process was described by the background transmission rate α (including transmissions independent of the colonization pressure, such as endogenous selection) and the patient-dependent transmission rate β (including transmissions dependent on the colonization pressure: β * ward prevalence).

Results. The average point prevalence of KPC among patients as calculated by the model was 35%. The overall estimates were 0.0022 for α and 0.011 for β. 18% of patients were colonized on admission to the LTACHs and sensitivity of the screening process to detect KPC was 81%. The number of acquisitions per 1,000 patient days was lowest in the LTACHs with a pure cohort ward or private rooms for colonized patients compared to mixed cohort wards.

Conclusion. The prevalence of KPC-producing bacteria in LTACHs is high, primarily due to a high admission prevalence and the resultant impact of high colonization pressure on risk of cross-transmission. Use of a pure cohort or single rooms for KPC-positive patients in LTACHs seemed to limit transmission compared to use of a mixed cohort.

Disclosures. **All authors:** No reported disclosures.

363. Persistence of the *Klebsiella pneumoniae* Sequence Type 258 as the Predominant Clone of Carbapenemase-Producing *Enterobacteriaceae* in Post-Acute Care Facilities in Israel, 2008-2013

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Background. We aimed to study the molecular characteristics and clonal structure of carbapenemase-producing *Enterobacteriaceae*(CPE) in post-acute care facilities (PACF's) in Israel and to analyze the temporal changes that have occurred between 2008 and 2013.

Methods. The prevalence of CPE carriage in PACF's in Israel was determined in two point prevalence national surveys done in 2008 and 2013. The source of CPE acquisition in the 2013 survey was determined based on the National Center of Infection Control database. Surveillance cultures were collected by rectal swabs and were inoculated onto selective media. Isolates were identified by the VITEK-2 system and were tested for the production of carbapenemase by the bla_{KPC}, bla_{NDM} and bla_{OXA-48} –PCR's and by the Carba NP test. Molecular typing was done by PCR for the *pilV-l* gene, designed for a specific allele of the sequence-type (ST)-258 KPC-producing *Klebsiella pneumoniae*(KPC-KP) clone, by BOX-PCR and by MLST.

Results. The prevalence of CPE in the first survey was 184/1,144 (16.1%), all of which were KPC-KP. The prevalence of CPE in the second survey was 127/1,287 (9.9%), of which 113 (89%) were KPC-KP, 9 (7%) were other KPC-producing species and 5 (4%) were NDM- or OXA-48 producing CPE's (n = 1 and 4, respectively). The proportion of the ST-258 clone within the KPC-KP population increased from 120/184 (65%) to 91/113 (80%) in the 2008 and 2013 surveys, respectively. Meanwhile, the proportion of the ST-340 clone within the KPC-KP population decreased from 41/184 (22.5%) to 9/113 (7.9%) in the 2008 and 2013 surveys, respectively. In 83 of the 122 KPC-CPE carriers (68%) identified in the 2013 survey, the source of acquisition was determined to be the PACF itself. All 4 OXA-48 CPE's were acquired either directly or indirectly from patients arriving from the Palestinian Authority or Syria.

Conclusion. Despite the decreased prevalence and the emergence of new types of CPE's in Israel, the ST-258 KPC-KP clone remains the leading culprit of the CPE epidemic in PACF's.

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364. Utility of Carbapenem-Resistant *Enterobacteriaceae* Surveillance Cultures in Predicting Clearance of Colonization

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Background. The Centers for Disease Control and Prevention recommends that institutions in which carbapenem-resistant *Enterobacteriaceae*(CRE) is endemic perform active surveillance testing and maintain contact precautions for CRE-colonized or infected patients, however, does not provide guidance regarding discontinuation of contact precautions for these patients. Here we review our institution's CRE surveillance program to determine the utility of serial screening in predicting clearance of CRE colonization.

Methods. In April 2009, our institution began surveillance perirectal cultures for detection of CRE colonization for high-risk patients and those epidemiologically linked to CRE-infected or colonized patients. All patients with a positive perirectal culture obtained between April 2009 and August 2013 were included in this study. **Results** of follow-up perirectal cultures to assess for ongoing colonization, as well as subsequent clinical isolates, were evaluated. Recurrence of CRE-positivity was defined as a positive perirectal culture or clinical culture, following at least one negative perirectal culture.

Results: During the study period, 142 patients were found to be perirectally colonized with CRE. Fifty-one of 95 (53.7%) patients with at least one follow-up perirectal culture were negative for CRE colonization at the first follow-up culture. After one negative CRE perirectal culture, 24 of 31 patients (77.4%) with a subsequent culture remained negative. After two consecutive negative CRE perirectal cultures, 17 of 20 patients (85.0%) with a subsequent culture remained negative. After three consecutive negative CRE perirectal cultures, six of eight patients (75.0%) remained CRE-negative on all subsequent cultures for the duration of the study. Two patients had recurrence of CRE after at least three consecutive negative cultures.

Conclusion. Our institution's experience with CRE surveillance demonstrates that CRE colonization is prolonged and can be detected intermittently; thus any routine practice of using surveillance cultures to discontinue contact precautions may be associated with an unacceptably high risk of relapse and exposure of other patients to these highly resistant pathogens.

Disclosures. **All authors:** No reported disclosures.

365. Molecular Detection of Multi-Drug Resistant Organism (MDRO) Colonization in a High Risk Patient Population

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Background. Multi-Drug Resistant Organisms (MDROs) present substantial clinical and financial burden to patients and hospitals. Links between MDRO colonization and risk of subsequent infection in high risk patient (pt) populations are not fully characterized. Rapid molecular identification of MDRO could optimize detection, outbreak investigation, and implementation of measures to interrupt transmission.

Methods. Prospective surveillance for nasal and perianal MDRO colonization was instituted over a 3 month period in pts admitted to the Children's National Medical Center oncology (onc) and stem-cell transplant (SCT) wards. MDRO was defined as Methicillin Resistant *Staphylococcus aureus*(MRSA), Vancomycin-Resistant Enterococcus (VRE), Extended-spectrum Beta-lactamase producing gram negatives (ESBL), and Carbapenem-resistant Enterobacteriaceae (CRE). Enrolled subjects were subsequently monitored for 3-6 months for presence of invasive infection and any correlation with colonization. Nasal and perianal E-swabs were simultaneously analyzed using standard culture-based screening methods, as well as Acuitas MDRO GeneTest molecular screen.

Results. Forty-eight pts were enrolled, from whom 42 perianal and 32 nasal swabs were obtained. Using standard culture-based screening methodology, 14/42 (33%) perianal and 0/32 (0%) nasal swabs screened positive for possible MDRO. Acuitas molecular screen and subsquent standard culture and susceptibility test confirmed 4 of these 14 as actual MDRO (4/42;10%); 3 VRE (VanA) and 1 ESBL (CTX-M). Three to six month follow-up revealed no MDRO invasive infections in the study cohort. Non-MDRO invasive infections were identified in 10/48 (21%) subjects due to *Bacillus, Klebsiella (IBL), Micrococcus, Pseudomonas,* rapid growing *Mycobacteria, Staphylococcus aureus,* and *Streptococcus viridans.* Eight of 10 infected subjects were not previously colonized with any pathogen; 1 was colonized with different pathogens, and 1 was both colonized and infected with *Pseudomonas*, but with differing susceptibilities.

Conclusion. Acuitas molecular screen and standard culture accurately identified and excluded MDRO colonization in onc and SCT pts. Colonization with non-MDRO or MDRO pathogens did not predict likelihood or etiology of subsequent invasive infection.

Disclosures. **X. Song**, OpGen Inc.: Grant Investigator, Grant recipient **D. Toal**, OpGen, Inc.: Consultant, Consulting fee **T. Walker**, OpGen Inc.: Employee and Shareholder, Salary **J. Campos**, OpGen Inc.: Grant Investigator, Grant recipient **R. Debiasi**, opgen: Grant Investigator, Grant recipient

366. The Impact of Bathing Hospitalized Dependent Patients with Disposable Washcloths Instead of Traditional Bath Basins on Infection Rates and Skin Condition

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Background. Bath basins are a known reservoir for hospital pathogens. Our objective was to evaluate the impact of use of bath in a bag in place of basins on hospital-acquired infections (HAIs), multi-drug resistant organisms (MDROs) and skin deterioration.

Methods. A prospective, open-label, crossover study in two medical-surgical units was conducted. During each of two 8-month periods on the intervention unit, bath basins were replaced with pre-packaged washcloths; and standard bathing using a bath basin was conducted on the control unit. HAI, MDRO and skin deterioration data were prospectively collected. Bath basins were swabbed of patients who had a culture positive for one of seven MDROs

Results. 2,637 patients were evaluated. There were 7,981 patient days in the intervention group and 8,053 in the control group. 85% of subjects were African-American (mean age 57 years (SD: 17)). 19% of subjects in each group lacked independence with functional status. Over 30% of the study population was diabetic. Patients receiving the washcloth intervention were significantly less likely to experience skin deterioration during stay on the study unit (2.5% intervention group vs 5.5% control group; OR = 0.45; 95% CI: 0.22, 0.88). HAI rates were similar between bathing methods (2.4 per 1,000 patient days in intervention group vs 2.3 per 1,000 patient days in control group; IRR = 1.04; 95% CI 0.55-1.95). The rate of hospital-acquired MDROs was lower in the intervention group (17.4 per 1,000 patient days vs 30.3 in the control group; IRR= 0.66; 95% CI 0.41-1.08). Four patients had similar isolates from both clinical and basin cultures; 2 with MRSA, 1 with carbapenem-resistant *K. pneumoniae* (KPC), and 1 with *A. baumannii* (ACB). *Spa* typing indicated a match between

both pairs of MRSA (t002 and t681, respectively) and MLST identified both KPC isolates as ST258. MLST for ACB isolates determined the two isolates to be unrelated.

Conclusion. Although no impact on HAI acquisition was noted, use of pre-packaged washcloths and elimination of bath basins was associated with notable reductions in skin deterioration and MDRO acquisition (although the latter was not statistically significant). Direct links were demonstrated between MDROs isolated from patients and their basins.

Disclosures. **K. Kaye**, Sage: Grant Investigator and Speaker's Bureau, Grant recipient and Speaker honorarium

367. Effect of Daily Chlorhexidine (CHG) Bathing on Multidrug-resistant Organisms (MDROs) Transmission and Infection at an Intensive Care Unit (ICU)

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Background. Although daily bathing with CHG may prevent the acquisition of Gram positive MDROs (methicillin-resistant *S. aureus* and vancomycin-resistant enterococcus), scant data exists on the impact of this strategy for Gram negative MDROs (carbapenemase-producing *K. pneumoniae*, *P. aeruginosa*, and *Acinetobacter* spp). The aim of this study was to determine whether daily bathing with CHG decreased MDROs acquisition among adult medical-surgical ICU patients

Methods. Since July 2010 an active surveillance protocol to identify asymptomatic colonization by MDROs at ICU admission or weekly during the patient stay, was implemented. In addition a daily bathing with no-rinse 2% CHG-impregnated washcloths was implemented at the end of 2011, reached 100% compliance from January 2012. The **MDROs incoming colonization pressure** and **MDROs acquisition** rate were estimated as the number of isolation of MDROs from surveillance or clinical culture performed less than 48 hours after admittance to the ICU per 1,000 admissions and more than 48 hours after admittance to the ICU per 1,000 patient-days, respectively. Through a prospective before and after study both indicators were compared between Period A: July 2010/December 2011 and Period B: January 2012/December 2013. In all instances non duplicated cases were considered

Results. While there was an 135% increase in the incoming colonization pressure during Period B vs Period A for Gram positive MDROs (92.42 cases per 1,000 admissions vs 39.30 cases per 1,000 admissions; difference 53.12 [95% confidence interval (CI) 1.89 to 8.73]; $p < 0.01$) and a 90% for Gram negative MDROs (33.18 cases per 1,000 admissions vs 17.47 cases per 1,000 admissions; difference 15.71 [95% CI – 5.47 to 36.88]; $p < 0,15$), a significant reduction was observed for the acquisition of Gram positive and Gram negative MDROs (2.40 cases per 1,000 patient-days vs 4.86 cases per 1,000 patient-days; difference –2.46 [95% CI –0.57 to –4.34]; $p < 0.01$; 3.86 cases per 1,000 patient-days vs 7.21 cases per 1,000 patient-days; difference –3.36 [95%CI –1.03 to –5.68]; $p < 0.01$, respectively)

Conclusion. Daily bathing with CHG-impregnated washcloths significantly reduced the risks of acquisition of both Gram positive and negative MDROs, in spite the increase of the incoming colonization pressure rate

Disclosures. **All authors:** No reported disclosures.

368. Community Origin and Mortality in Pneumonia Caused by Carbapenem-Resistant *Klebsiella pneumoniae*

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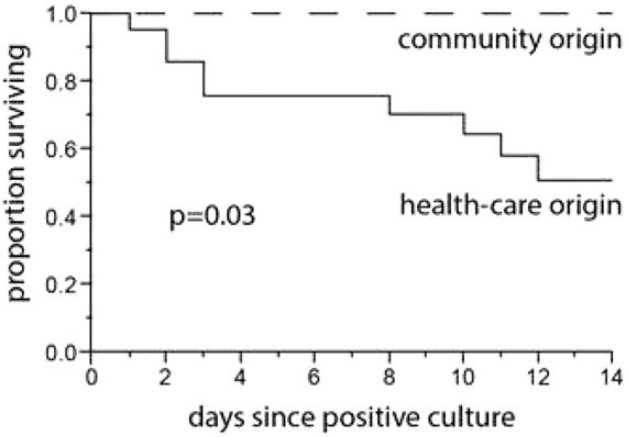
Background. Carbapenem-resistant *Klebsiella pneumoniae* (CRKP) is an increasingly important cause of pneumonia. In order to understand the factors that impact outcomes of CRKP pneumonia, we examined a nested cohort of patients that are enrolled in the prospective Consortium on Resistance against Carbapenems in *K. pneumoniae* (CRaCKle).

Methods. CRaCKle is a prospective multicenter consortium which includes 21 hospitals serving more than 2 million people in the Great Lakes region. All hospitalized patients with CRKP pneumonia were included if their hospitalization began and ended within the study period from December 24, 2011 until October 1, 2013. Each patient was only included once at the time of their first respiratory culture from which CRKP was isolated. Criteria outlined by the American Thoracic Society and the Infectious Diseases Society of America were used to define pneumonia. Severe acute illness was defined as a Pitt bacteremia score ≥ 4.

Results. 29 unique patients with CRKP pneumonia were included; median age was 71 years (IQR 57.5-80 years), median Charlson score was 3 (IQR 2-5), 18 (62%) were female, 16 (55%) were Caucasian, 13 (45%) had chronic obstructive pulmonary disease (COPD), 2 (7%) had bacteremia. 25 (86%) patients were on mechanical ventilation at the time of culture. Eight (28%) patients were admitted from home. Most patients were admitted from long term chronic care (12/29, 41%) or long term acute care (4/29, 14%), 5 (17%) patients were transferred from other hospitals; Median time from admission to first positive culture was 9 days (IQR 6-38 days) in patients admitted from home, vs 7 days (IQR 1-15 days) in all other patients ($p = NS$). None of the 8 patients admitted from home died within 14 days of first positive culture, as compared to 9/21 (43%) of all other patients ($p = 0.03$ by Fisher's Exact). In a multivariable model which adjusted for chronic comorbidities (Charlson comorbidity index) and severe acute illness, community origin remained significantly associated with decreased mortality ($p < 0.01$).



Conclusion. In this nested cohort of hospitalized patients with CRKP pneumonia, community origin prior to admission was associated with improved 14-day survival.

Disclosures. **All authors:** No reported disclosures.

369. Outcomes of Patients with Carbapenem-Resistant *Enterobacteriaceae*

Jillian Raybould, MD[1]; Kelly Carpenter, MD[2]; Nandita Mani, MD[2]; Richard Teran, MPH[3]; Mashashi Waga[4]; Princy N. Kumar, MD[5]; Joseph G. Timpone, MD[6]; [1]Internal Medicine, Georgetown University Hospital, Washington, DC; [2]Georgetown University School of Medicine, Washington, DC; [3]Division of Infectious Diseases and Travel Medicine, Georgetown University Hospital, Washington, DC; [4]Pathology and Laboratory Medicine, Medstar Washington Hospital Center, Washington, DC; [5]Georgetown University Medical Center, Washington, DC; [6]Infectious Diseases, Georgetown University Hospital, Washington, DC

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Background. In an era of increasing antibiotic resistance, the emergence of Carbapenem-Resistant Enterobacteriaceae (CRE) poses a serious threat to public health given the limited treatment options and high mortality rate.

Methods. This is a single center, retrospective, cohort study that evaluated characteristics and outcomes of adult patients hospitalized from July 1, 2010 through June 30, 2013 with their first diagnosis of CRE as confirmed via the Modified Hodge Test.

Results. 27 cases of CRE were identified during the study period. 18 were deemed to have a true infection while 9 were asymptomatic colonizers. *Klebsiella pneumoniae* was the causative organism in all but one case of *Klebsiella oxytoca*. The mean time to CRE diagnosis was 18 days and the mean length of hospital stay was 37 days. 41% of patients were admitted from home, 37% from an outside hospital (OSH), and 22% from a long term care facility. Patients transferred from an OSH had an increased mortality (p 0.0269). Of those admitted from home, 45% were diagnosed with early infection (positive culture in the first 48 hours). Of those with early infection admitted from home, 80% had been hospitalized during the 90 days before CRE diagnosis. Infection was most common in the urine and respiratory tract. Overall mortality rate for patients with an active infection was 44.4%. A higher mortality rate was seen in patients with pulmonary infections (p 0.0003) and patients who had isolation of MDR *Pseudomonas* 6 months prior to CRE (p 0.0172). 81.4% of patients received antibiotics within 90 days prior to CRE diagnosis. The most common antibiotics with activity against gram negatives that patients were exposed to were: piperacillin/tazobactam (37%), fluroquinolones (33.3%), and carbapenems (29.6%). For patients with true infection, 33.3% were given combination therapy with at least 2 of the following: amikacin, colistin, tigecycline, and a carbapenem. 83% of patients who received combination therapy died (p 0.0037). 76.2% of tested isolates were susceptible to colistin, 62.5% to tigecycline, 59.3% to amikacin, and 11.1% to gentamicin.

Conclusion. Infections due to CRE are associated with a prolonged length of stay and result in significant mortality in spite of combination therapy. We observed a particularly high mortality in patients with CRE pneumonia.

Disclosures. **P. N. Kumar**, Janssen: Grant Investigator and Speaker's Bureau, Consulting fee, Grant recipient, Research grant, Research support and Speaker honorarium; GSK: Grant Investigator and Shareholder, Grant recipient, Research grant and Research support; Merck: Grant Investigator and Shareholder, Grant recipient, Research grant and Research support; ViiV Healthcare: Consultant and Speaker's Bureau,

Speaker honorarium; Pfizer: Shareholder, stock shareholder; Johnson and Johnson: Shareholder, stock shareholder; Gilead: Shareholder, stock shareholder

370. The Impact of Early Life Antibiotic Exposure on Childhood Weight Gain

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Background. Antibiotic exposure has been shown to promote weight gain in livestock and has been associated with increased adiposity and altered metabolism in experimental animal models, mediated by alterations in the gut microbiome. Infancy and early childhood represent both an influential period of growth trajectory and a time during which antibiotic exposure is common and often inappropriate. Therefore, we sought to determine the impact of real world, early life antibiotic exposures on childhood weight gain.

Methods. A longitudinal, retrospective study was conducted using a socioeconomically and racially diverse pediatric healthcare network serving > 200,000 children at 31 practices. We included children born between 2001 and 2011 who presented for a preventive health visit in the first 14 days of life and had at least 2 additional visits in the first year. We excluded children born < 35 weeks gestational age; birthweight <2,000 grams or below 5% for gestational age; with chronic medical conditions, prophylactic antibiotic use, or frequent steroid use. Exposures included all systemic antibiotic exposures in the first 6 months of life. The primary outcome was weight through age 8, standardized to WHO/CDC reference populations. A longitudinal mixed effects model was used to assess the association between standardized weight and age by antibiotic exposure interaction, adjusting for sex, race, insurance type, birthweight, preventive health care compliance, household size, birth year, baseline height and primary care practice site. A second analysis, including sets of twins where only one twin had early antibiotic exposure, used a longitudinal mixed effects model to assess the association between paired weight difference and age, adjusting for differences in sex, birthweight, and baseline height.

Results. Of 38,756 children included in the analysis, 5,312 (13.7%) received antibiotics in the first 6 months of life. After adjustment for clinical and demographic variables, antibiotic exposure was associated with a decrease of 0.03 in weight z-score per year ($p < 0.001$). Of 47 sets of twins discordant in early antibiotic use, antibiotic exposure was not associated with a change in weight ($p = 0.59$).

Conclusion. Using data from a large birth cohort, infant antibiotic exposure did not increase early childhood weight gain.

Disclosures. **T. Zaoutis**, Merck: Investigator, Research grant Merck: Consultant, Consulting fee Pfizer: Consultant, Consulting fee Astellas: Consultant, Consulting fee

371. Outcomes of Enterobacter bloodstream infection in hospitalized children

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Outcomes of Enterobacter bloodstream infection in hospitalized children

Background. *Enterobacter spp.* has emerged as a major cause of nosocomial infections in children and adults, and may carry chromosomal *AmpC β*-lactamases that limits the choice of appropriate antibiotics. The antimicrobial treatment strategies for and outcomes of Enterobacter bacteremia in children have not been well described.

Methods. Multicenter, retrospective cohort study of patients ≥18 years admitted with monomicrobial *Enterobacter spp.* bloodstream infection at The Children's Hospital of Philadelphia, Johns Hopkins Children's Medical Center and Mayo Clinic Children's Hospital. Comprehensive chart review was performed to collect clinical and demographic data on all patients. Antibacterial exposure was recorded daily for 30 days and classified by antimicrobial class and whether combination therapy was used. Descriptive analysis included medians for continuous variables and percentages for categorical data.

Results. From January 2002-December 2012, 471 episodes of bacteremia occurred in 411 children [Median age: 1.3 years (IQR: 0.3 – 6.6), male 64%]. Most children had multiple comorbid conditions and outcomes varied by treatment regimen (Table).

¤New requirement of ventilatory support, vasopressors, intensive care admission or relapse of fever during the first 15 days

¦Isolation of Enterobacter spp. 7 days after onset of bacteremia having documented prior clearance

* Combination therapy including an aminoglycoside or quinolone plus the main grouping agent

Baseline characteristics	
≥3 comorbid medical conditions	88%
Presence of immunosuppression	38%
Surgery 1 week prior	20%
Presence of central catheter	82%
Other concomitant infection	26%
ID consultation during first 15 days	41%
Catheter removal	60%
Clinical outcomes by definitive therapy grouping (includes 92% of total episodes)	

	Total	3rd cephalosp		Cefepime		Carbapenem		β-lactam inh		Quinilone	
		Mono	Com*	Mono	Com*	Mon	Com*	Mon	Com*	Mono	Com*
		7%	18%	18%	9%	10%	13%	3%	7%	7%	2%
Clinical worsening¤	14%	9%	17%	12%	12%	15%	19%	17%	12%	16%	12%
Relapse¦	5%	9%	4%	1%	2%	7%	8%	17%	3%	3%	12%
30-day mortality	7%	12%	7%	7%	10%	11%	3%	-	3%	3%	-

Conclusion. *Enterobacter* bacteremia is a severe infection in children. Future studies will compare outcomes by antimicrobial treatment regimen.

Disclosures. **T. Zaoutis**, Merck: Investigator, Research grant Merck: Consultant, Consulting fee Pfizer: Consultant, Consulting fee Astellas: Consultant, Consulting fee

372. Infectious Disease Involvement Decreases Meropenem usage after Hematopoietic Stem Cell Transplantation

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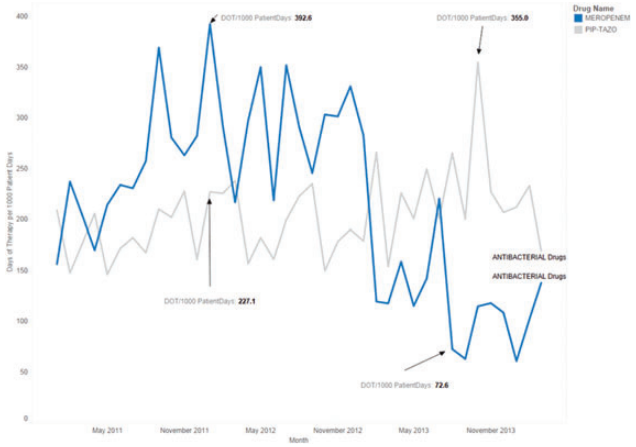
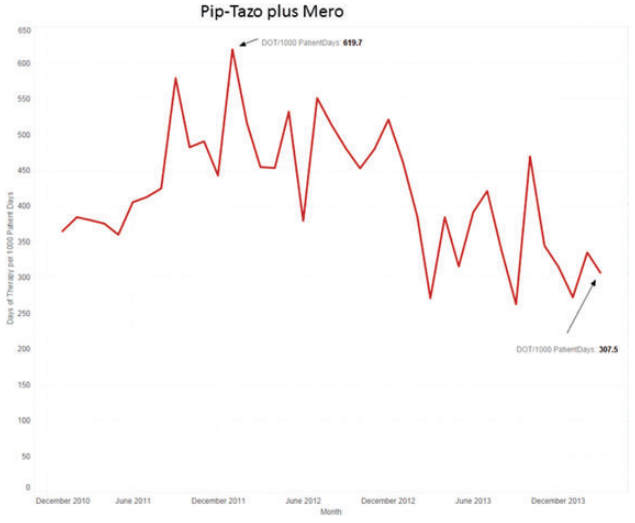
Background. Hematopoietic Stem Cell Transplant recipients (HSCT) are at increased risk for severe infections, and empiric antibiotic choice may be driven anecdotally by single patient experiences in addition to local antibiograms. Knowledge of recent infection patterns may be insufficient to adjust prescribing practices. We report the results of a synchronized collaborative effort between Infectious Diseases and HSCT attendings to decrease meropenem (MERO) use on an HSCT unit.

Methods. Antibiotics prescription practice on HSCT unit before, during and after interventions.



Results. MERO use peaked at 392 days of therapy (DOT) per 1,000 patient-days in October 2011 and remained greater than 300 DOT per 1,000 patient days through

2012. Twice yearly reporting of microbiology data directly to the HSCT team identified an increasing incidence of candidemia in 2012. Interventions included data sharing of recently recovered pathogens, recommendations use MERO then de-escalate to piperacillin-tazobactam (PTZ) with negative cultures, daily huddles between ID and HSCT to de-escalate antibiotics when indicated, and visual display of MERO prescribing patterns in the HSCT unit. Over the following 8 months, MERO use declined to 72 DOT per 1,000 patient-days after which ID/HSCT huddles were decreased in frequency to twice weekly (FIG1). MERO use has remained stable over the ensuing 6 months, averaging 100 DOT per 1,000 patient-days. PTZ use increased modestly from 203 DOT per 1,000 patient-days in October 2011 to a mean of 227 DOT per 1,000 patient-days during the last 6 months. Overall usage of the two antibiotics in the HSCT unit remains lower (peak of 619 in October 2011 to 307 DOT per 1,000 patient-days currently, FIG2).



Conclusion. Multi-prong intervention including education, data sharing, concentrated antibiotic prescribing practices and improved communication resulted in decreased MERO use in the high-risk HSCT population.

Disclosures. **All authors:** No reported disclosures.

373. Development and Application of an Antibiotic Spectrum Index (AbSI) for Benchmarking Antibiotic Selection Patterns Across Hospitals

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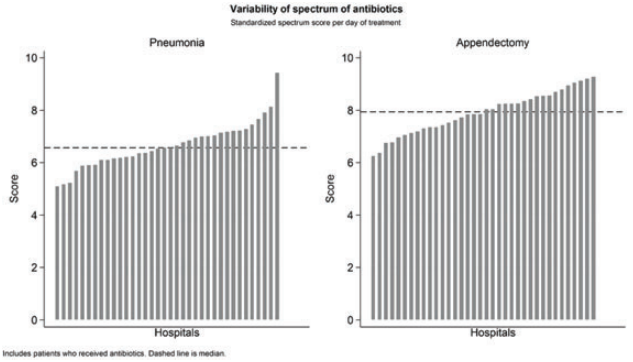
Background. There are few established metrics for comparing antimicrobial use across hospitals. One commonly used metric is days of therapy (DOT) per 1,000 patient days, but this does not measure differences in antibiotic selection patterns, an important influence on antibiotic resistance. We developed a scoring system, the antibiotic spectrum index (AbSI) that ranks antibiotic use based on spectrum of activity to facilitate inter-hospital comparisons in prescribing patterns.

Methods. We classified systemic antibiotics using a score ranking each agent based on spectrum of activity; for each agent the overall score could range from 0-14 points. One point was added to the score for activity against each of the following pathogens: MSSA, MRSA, *E. faecalis*, VRE, *E. coli* and *Klebsiella*, ampC producers, ESBL, Pseudomonas, penicillin-resistant pneumococcus (PRP), *Moraxella and H. influenzae*, Mycoplasma and Chlamydophila, and anaerobes. Drugs considered "last line" agents received an additional point. For example, the vancomycin AbSI = 5 (MSSA, MRSA, *E. faecalis*, PRP, last line). Data was obtained for 36 children's hospitals in 2012 from the Pediatric Health Information System and an aggregate spectrum score (sum of scores of all systemic antibiotics) was calculated for each day of antibiotic therapy for each patient. The standardized spectrum score per day of antibiotic therapy was compared across hospitals, adjusting for patient demographics and severity of illness and stratifying by condition using APR-DRG codes.

Results. Of the 5 conditions accounting for the most overall antibiotic days, AbSI identified low (5.7 and 6.7 for skin/soft tissue infection and pneumonia, respectively), medium (8.0 for appendectomy), and high (10.8 and 14.6 for bone marrow transplant and cystic fibrosis, respectively) index conditions. There was substantial variation in the total aggregate AbSI across hospitals within high use conditions (Figure).



Conclusion. Development and application of an antibiotic spectrum index can objectively classify commonly used agents based on activity against important pathogens. This score facilitates inter-hospital benchmarking and comparisons; follows expected patterns based on illness severity; and can be used to identify important clinical targets for antimicrobial stewardship.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

374. Indication-based Antimicrobial Derestriction: Ceftazidime Derestriction for Febrile Neutropenia

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Background. Febrile neutropenia (FN) is a common condition in children receiving chemotherapy. The University of Chicago Comer Children's Hospital has a rigorous antimicrobial restriction and prior authorization policy overseen by the Antimicrobial Stewardship Program (ASP). Ceftazidime (CTZ), our agent of choice for FN, is restricted. Use requires calling Infectious Diseases (ID) on call for approval, followed by ID calling pharmacy with authorization, leading to a potential delay in order processing.

Recognizing FN as a time-sensitive disease state with a clear indication for CTZ use, we revised the FN clinical pathway, removing the need for prior approval ("derestriction"). Along with derestriction, we implemented prospective CTZ auditing to assess the appropriateness of therapy and adjust therapy as needed.

Methods. To evaluate the change in CTZ use, we collected and aggregated monthly data, before and after derestriction. Information collected includes: indication for CTZ use, time to administration of first dose, number of CTZ days, time to appropriate discontinuation, rate of positive blood cultures, and patient outcomes. Total number of patient-days and ID consults were also collected.

Results. Comparison of the first month after derestriction (January 2014) to the same month the year prior (January 2013) without derestriction, shows no statistical difference in CTZ use (mean of 6 CTZ days/FN patient vs 5 CTZ days/FN patient, [$P = 0.76$]) or the rate of positive blood cultures ($P = 1.0$). There was no statistical difference in the times to administration of the first CTZ dose (mean of 53 minutes vs 54 minutes, [$P = 0.92$]), both less than the goal of <60 minutes. The total number of patient-days (2067 vs 2070, [$P = 0.48$]) and ID consults (71 vs 78, [$P = 0.28$]) remained stable. The number of CTZ approvals for FN appropriately declined to zero after derestriction. No patient deaths occurred during the study period.

Conclusion. Indication-based antibiotic ordering and derestriction can be successfully implemented in an ASP with a historically restriction-based system, without significant change in the appropriate use of the derestricted agent, change in the rate of bloodstream infections or patient outcomes. Future efforts will be directed towards evaluating additional factors affecting time to antibiotic administration.

Disclosures. **All authors:** No reported disclosures.

375. Cost of Antimicrobial Therapy Across US Children's Hospitals

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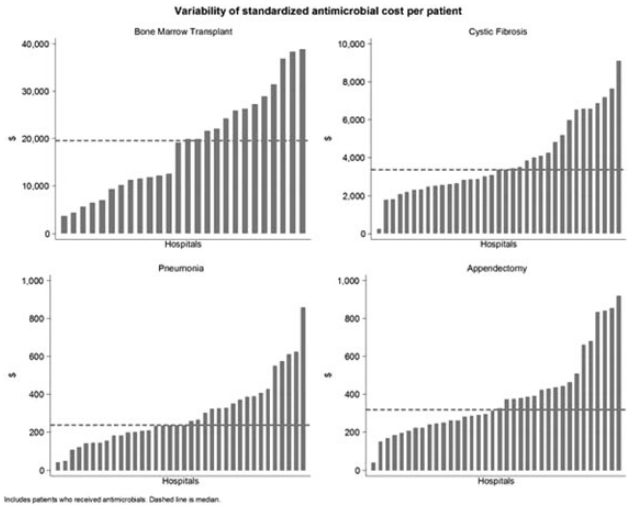
Background. Antimicrobials are among the most commonly used medications for hospitalized children. Antimicrobial stewardship programs (ASPs) have been shown to reduce pharmacy costs through optimization of antimicrobial use. A better understanding of the cost implications of and prescribing patterns for antibiotics may help to target interventions.

Methods. We examined antimicrobial cost for hospitalized children using a database of freestanding children's hospitals. We calculated cost and days of therapy (DOT) for all antimicrobials billed to patients discharged from 36 hospitals during 2012. Standardized cost per patient was compared across hospitals, adjusting for patient demographics and severity of illness and stratifying by condition using APR-DRG codes.

Results. In 2012, $192 million was spent on antimicrobials at 36 hospitals for 599,518 patients. Antimicrobials were 17% of the total pharmacy budget, ranging from 12% to 34% across hospitals. Antibacterials accounted for 73% of total antimicrobial cost (Table). Cost per DOT was two times higher for antifungals and antivirals than for antibacterials. Four of the 5 most expensive drugs (cost/DOT) were antifungals. Collectively, vancomycin, meropenem, piperacillin-tazobactam, and amphotericin B-lipid accounted for > 30% of antimicrobial cost. Bone marrow transplant (11%) and cystic fibrosis (7%) had the highest contribution to total antimicrobial cost. We found wide variation in standardized cost across hospitals when isolating children with specific conditions previously identified as important stewardship targets (Figure).

Table: Antimicrobial cost and DOT by class

	Cost (millions)		DOT		
Class	$	%	n	%	Cost/DOT
Antibacterials	140	73	2,518,344	82	45
Antifungals	38	20	377,352	12	101
Antivirals	14	7	147,470	5	92
Other	1	1	37,233	1	31
	193	100	3,080,399	100	63



Conclusion. Antimicrobials represent a substantial proportion of medication costs in US children's hospitals, and a few specific drugs account for a large proportion of these costs. Costs vary widely across centers even after standardizing by patient demographic and clinical characteristics and isolating specific conditions. Exploring the drivers and outcomes of these differences might reveal important targets for antimicrobial stewardship.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

376. Clinical Impact of an Antimicrobial Stewardship Program on Pediatric Hospitalist Practice, a 5-year Retrospective Analysis

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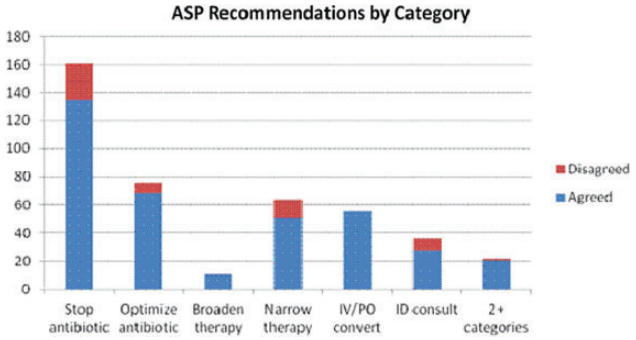
Background. Antimicrobial stewardship programs (ASPs) and the field of hospital medicine are both intended to improve resource use and health outcomes for hospitalized patients. Understanding how these clinical services interact in the hospital setting can inform practice improvement strategies. The objectives of this study were to identify clinical factors associated with ASP intervention among children treated by hospitalists and to determine the impact of ASP interventions on clinical outcomes of children managed by hospitalists.

Methods. This retrospective analysis included ASP reviews of hospitalist patients from a children's hospital system from March 2008 to June 2013. Patient demographics, clinical history, and primary diagnosis were analyzed for association with probability of ASP intervention. Length of hospital stay (LOS) and 30-day readmission were compared between cases of agreement with ASP recommendations and cases of disagreement.

Results. ASP reviewed 2251 hospitalist patients; 356 interventions were made (16% of reviews), and hospitalists agreed with ASP recommendations in 296 cases (87%). The probability of ASP intervention among hospitalist patients decreased during the study period (19% Year 1 vs 10% Year 5, $p < 0.0001$). Ceftriaxone was the most common antibiotic (270/356, 70%) and community-acquired pneumonia was the most common diagnosis (114/356, 32%) associated with ASP intervention. Presence of a co-morbid complex medical condition and infection type were not associated with ASP intervention. The most commonly-recommended intervention was to stop antibiotic therapy; ID consultation had the highest rate of disagreement (Figure 1). There were no differences in LOS or 30-day readmission between cases where hospitalists disagreed with ASP recommendations vs cases when recommendations were followed.



Conclusion. The likelihood of ASP interventions in hospitalist patients decreased over time, suggesting a change in prescribing behavior. Hospitalists usually complied with ASP recommendations, but disagreement was not associated with longer LOS or readmission. These data suggest ASPs and hospitalists are regularly engaged in facilitating a variety of antimicrobial prescribing decisions.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

377. Impact of an Educational Intervention to Improve Antibiotic Prescribing for Nurse Practitioners (NPs) in a Pediatric Urgent Care Centers (UCC)

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Background. Up to 21% of ambulatory pediatric visits result in an antibiotic (abx) prescription and a large portion of these are unnecessary. NP's play a critical role in patient care and are frequent prescribers of abx. It is estimated that 6.8 million yearly ambulatory visits are seen by NP's. No data are available on NPs prescribing for common infections or on antimicrobial stewardship interventions to improve prescribing among NPs. The objective was to determine if educational sessions would reduce inappropriate abx use among NPs in pediatric UCCs.

	Inappropriate Antibiotic Use			Most Common Reason
Diagnosis	Pre	Post	P value	Abx Deemed Inappropriate
Viral Pharyngitis	7/245 (2%)	15/301 (5%)	0.2	Not Indicated (100%)
GAS Pharyngitis	12/55 (22%)	10/107 (9%)	<0.001	Wrong Dose (50%)
UTI	36/38 (95%)	9/46 (19%)	<0.001	Too Narrow (40%)
SSTI	3/34 (9%)	16/94 (17%)	0.25	Too Broad (53%)
AOM	90/397 (23%)	88/428 (21%)	0.46	Too Broad (61%)
Sinusitis	3/9 (33%)	2/11 (18%)	0.44	Too Broad (40%)
Viral URI	21/913 (2%)	3/818 (0.3%)	0.001	Not Indicated (100%)

Methods. Intervention study evaluating NPs abx prescribing patterns at 4 pediatric UCCs following live educational sessions for urinary tract infection (UTI), skin and soft tissue infection (SSTI), pharyngitis, upper respiratory tract infection (URI), otitis media (OM) and sinusitis. ICD9-CM codes were used to identify cases for 2 pre and 3 post intervention months in 2013. Abx appropriateness was based on published guidelines.

Results. A total of 26/43 (60%) NPs in 4 UCCs were enrolled in the study. Median years as an NP was 5 (IQR 3-12 years) with 2 years (IQR 1-5 years) in the UCC setting. The overall rate of inappropriate initial abx use was 10% pre intervention and 8% post intervention ($p = 0.02$). There was a decrease in inappropriate abx use in those who

attended the educational session over those who did not (p <0.01). There was no difference in abx prescribing practice when looking at years as an NP (p 0.4) or years worked in an UCC (p 0.7)

Conclusion. Educational sessions led to improvement in overall inappropriate abx use specifically with UTI, viral URI and GABHS groups. Improvement did not occur in OM, SSTI, sinusitis and viral pharyngitis. Additional stewardship interventions are needed to further reduce unnecessary abx use.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

378. Comparing Antibiotic Prescribing Across Pediatric Ambulatory Settings

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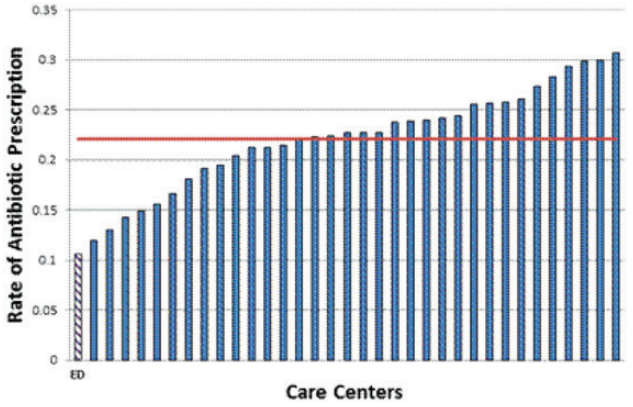
Comparing Antibiotic Prescribing Across Pediatric Ambulatory Settings

Background. While variability in antibiotic prescribing across primary care practices has been previously described, antibiotic prescribing has not been compared across alternate ambulatory sites, including urgent care and Emergency Department settings. Identifying site-specific practice patterns will help to tailor interventions to improve antibiotic prescribing.



Variability of Antibiotic Prescribing Across Practice Sites

Methods. Retrospective cohort study of all non-preventive encounters to a major pediatric Emergency Department (excluding encounters resulting in hospital admission) as well as 35 urban, suburban, and rural primary care and urgent care practices in 2013. Diagnosis codes, antibiotic orders, co-morbid medical conditions, antibiotic allergies, and demographic data were obtained from a comprehensive electronic health record. Center-specific antibiotic prescribing rates were calculated to assess variability and were adjusted for clustering by individual provider.

Results. An antibiotic prescription was given to 22% of 488,388 sick visits in 2013. After adjusting for patient age, sex, race, and insurance type and excluding encounters by patients with chronic conditions, rates of antibiotic prescribing by practice site ranged from 11% to 31% (Figure 1). The Emergency Department had the lowest rate of all ambulatory practices at 11%. ($P < 0.001$ for all comparisons)

Conclusion. Significant variability in antibiotic prescribing occurs across all types of ambulatory pediatric care practices, and is unexplained by patient clinical or demographic factors. Identifying the predictors of and outcomes associated with these prescribing practices should help target interventions to improve patient care.

Disclosures. **All authors:** No reported disclosures.

379. Antimicrobial Stewardship in Pediatrics: Role of Prospective-Audit with Real-Time Feedback

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Background. Antimicrobial stewardship programs (ASPs) are an effective strategy to ensure that antimicrobial (AM) agents are used in accordance with scientific evidence to improve patient outcome, reduce the unnecessary use of AM and costs. We report the impact of the implementation of an ASP on AM use and pharmacy costs among hospitalized children

Methods. In March 2012, active surveillance of AM therapy was implemented Vanderbilt Children's Hospital using Sentri7 (Pharmacy One Source®). Automated rules were developed to identify patients on broad-spectrum antibiotics and antifungals, acyclovir, therapeutic duplication, and with bug-drug mismatches. Dashboards were reviewed by an infectious disease pharmacist and physician, and the primary physician was contacted. Trends of aggregate AM use among hospitalized patients, measured as days of therapy (DoT), 26 months before (January 1, 2010-February 29, 2012) and 19 months after (March 1, 2012-September 30, 2013) the implementation of the program are reported. Antimicrobial use is normalized as DoT/1,000 patient-days (PD). Student's t-test was used to compare continuous variables. Trends of monthly antimicrobial use were analyzed using regression analysis. All tests were 2-tailed at the level of significance of 0.05. Analyses were performed using IBM SPSS software (Version 22; IBM Corp) and R (Version 3.0; R Core Team)

Results. From 2010 monthly average AM (antibiotics, antifungal and antiviral agents) use declined from 697DoT/1,000PD to 592DoT/1,000PD (-15%; $p < 0.01$). Antibiotic monthly use declined by 15% (630DoT/1,000PD to 537DoT/1,000PD, $p < 0.01$). Of these, vancomycin showed the sharpest declined from 113 DoT/1,000PD to 90DoT/1,000PD (-20%; $p < 0.01$). Monthly antifungal and antiviral use declined from 37DoT/1,000PD to 32DoT/1,000 PD (-13%; $p = 0.08$) and 26DoT/1,000PD to 19DoT/1,000 (27%; $p = 0.01$). Antimicrobial and antibiotic costs decreased from $26,006/1,000 PD/year and $16,080/1,000 PD/year (18% and 11% of all pharmacy drug costs) in 2011 to $14,411/1,000 PD/year and 11,154 in 2013, respectively (9%; $p < 0.01$, and 7%; $p < 0.01$ of all pharmacy drug costs)

Conclusion. Implementation of an integrated ASP with prospective audit with real time feedback to prescribers, led to a significant reduction of AM use and cost among hospitalized children

Disclosures. **All authors:** No reported disclosures.

380. Outpatient Parenteral Antibiotic Treatment (OPAT) in Pediatric Medicaid Enrollees

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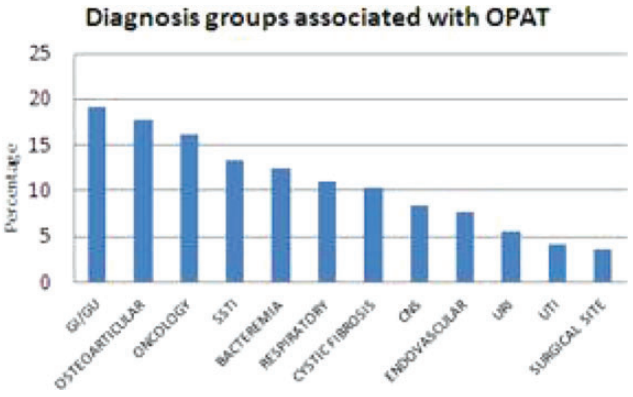
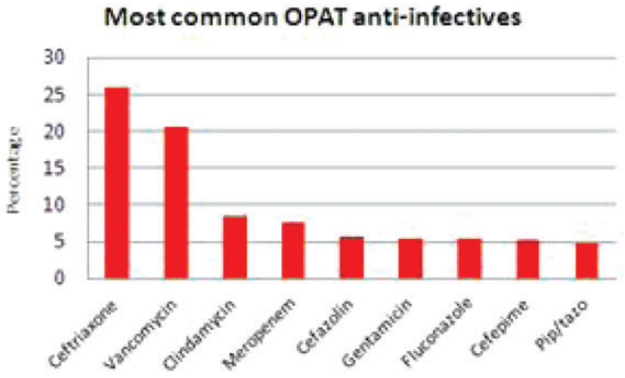
Background. OPAT has been used for nearly 40 years to treat a variety of infections in children. However, evidence demonstrates that OPAT is overused for certain diagnoses (e.g., osteoarticular infections) or antibiotics (e.g., clindamycin) when oral therapy would be appropriate. This may lead to unnecessary costs and complications including emergency department (ED) visits and hospital readmissions. The objective was to describe the diagnoses treated and antimicrobials used for OPAT and the frequency of medical encounters associated with OPAT in a large population of pediatric Medicaid enrollees.

Methods. We analyzed 2009-2011 data from the Truven MarketScan® Medicaid claims database. MarketScan® contains claims data for inpatient and outpatient services, retail prescription drug services, and enrollment information for 6 million Medicaid enrollees from 12 de-identified states. OPAT inclusion criteria required an enrollee to be ≤18 years of age, have an outpatient claim with a healthcare common procedure coding system (HCPCS) code indicating home infusion therapy (S9494, S9497, S9500-504), and either i) a concomitant HCPCS code indicating antibiotic use or ii) a concomitant retail pharmacy fill for an intravenous antibiotic. We defined a medical encounter as a hospital readmission or ED visit occurring during an OPAT episode. We used descriptive statistics to characterize patient demographics, diagnoses, antimicrobials and medical encounters.



Results. We identified 1,373 OPAT episodes for 1,165 patients; 11% of patients had ≥2 episodes. Fifty-four percent of patients were male, and 12% were < 1 year of age. The

most common diagnoses were gastrointestinal conditions (19%) and osteoarticular infections (18%). The most common antimicrobials were ceftriaxone (26%), vancomycin (21%) and clindamycin (9%). Twenty-seven percent of patients had a medical encounter during the OPAT course (13% ED, 14% readmission). Among patients with osteoarticular infections, the most common agent used for OPAT was clindamycin.



Conclusion. For many conditions where OPAT is used, oral therapy could be considered as an alternative. The high rate of medical encounters in this cohort underscores the need for greater scrutiny of pediatric OPAT use through stewardship.

Disclosures. **All authors:** No reported disclosures.

381. Pediatric Antimicrobial Stewardship Program Guideline Implementation within a Larger General Academic Center

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Background. In January 2013 New York University Langone Medical Center (NYULMC) initiated a Pediatric Antimicrobial Stewardship (ASP) program utilizing the prospective Audit and Feedback process. In an effort to standardize therapy and improve quality of care, members of ASP developed evidence-based guidelines for management of common Pediatric infections. Cycles of education and re-education were employed. Antibiograms were developed for each Pediatric Unit and specialty populations.

Methods. Compliance, calculated by the percent of time interventions were accepted, was used as a measure of process change. Outcome data was measured by *Clostridium difficile* (C. diff) rates, Days of Therapy (DOT)/1,000 patient days and resistance patterns of bacteria, specifically *Staphylococcus aureus*, *Enterobacter cloacae*, and *Klebsiella pneumoniae*.

Results. Within the first 12 months of PAS initiation, interventions were suggested in 19% of audited antimicrobials. Among ASP suggested interventions to primary teams, 91% were accepted by the medical team and management was adjusted. The combined Pediatric C. diff rate/1,000 hosptial admissions in the 12 months prior and after initiation of stewardship is 1.02 and 0.36, respectively. Between 2012 and 2013 we observed decrease in DOT for broad spectrum antibiotics meropenem, cefepime and piperacillin-tazobactam and significant decrease in ceftazidime ($p = 0.03$), vancomycin ($p = 0.01$) and gentamicin ($p = 0.025$) use. There was a significant ($p = 0.001$) increase in *S. aureus* susceptibility to amoxicillin-clavulanate, no change in *E.coli* sensitivities, and decrease in *K.pneumonias*ensitivity to ceftriaxone ($p = 0.04$), ceftazidime ($p = 0.03$), cefoxitin ($p = 0.001$) and pipercillin-tazobactam ($p = 0.005$).

Conclusion. Following PAS implementation we observed high rates of compliance and a subsequent reduction in broad spectrum antibiotic use and C.diff rates. The development of guidelines for vancomycin and aminoglycoside use, including high dose extended interval aminoglycosides, may have contributed to the significant decrease in DOT for those antibiotics. We observed a favorable change in *S.aureus* antibiotic profile. The decrease in *K.pneumoniae* sensitivity was not surprising, given similar trends observed at NYULMC and NYC, an 'epicenter' of Klebsiella resistance.

Disclosures. **All authors:** No reported disclosures.

382. Antimicrobial Optimization after Implementation of a Rapid Multiplex PCR Based Diagnostic Test for Positive Blood Cultures at a Children's Hospital

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Background. Rapid multiplex PCR testing was recently FDA-approved for identification of pathogens directly from positive blood cultures (BCx). A potential benefit is more rapid optimization of antimicrobial therapy for bloodstream infection. We recently implemented this testing and examined the effect on antibiotic therapy in hospitalized children.

Methods. In February 2014, we implemented the BioFire Diagnostics FilmArray Blood Culture ID (BCID) panel for the identification of organisms from positive aerobic BCx. We provided formal education to clinicians and a handout with recommended empiric treatment for identified organisms based upon local antibiogram data. Automatic pages with BCID results were sent to the antimicrobial stewardship team on weekdays. We compared antimicrobial usage before and after the implementation in patients with positive BCx from January 1, 2013 to April 30, 2014. BCx positive within 7 days of a previous positive culture with the same organism in the same patient were considered part of the same episode. The primary endpoint was change in antimicrobial therapy (new initiation or discontinuation) within 24 hours of first positive BCx result called to the clinician. Secondary endpoints included antimicrobial discontinuations and initiations.

Results. We identified a total of 744 positive BCx from 384 patients, accounting for 515 infection episodes during the pre-BCID period and 99 BCx in 70 patients, with 77 distinct infections during the BCID time period. BCID was run on 58 cultures in 57 unique patients. An antibiotic change was made within 24 hours of the first blood culture result in 242 of the 515 episodes (47%) in the pre BCID period and in 37 of the 77 episodes (48%) in the BCID period. At least one antibiotic was discontinued in 162 of 515 episodes (31%) in the pre BCID period and in 26 of 77 episodes (34%) in the BCID period. At least one antibiotic was initiated in 185 of 515 episodes (36%) in the pre BCID group compared to 32 of 77 (42%) in the BCID period.

Conclusion. In this early analysis, antimicrobial prescribing was similar for children with bloodstream infection before and after implementation of BCID testing. With improved education and ASP intervention, appropriate antimicrobial therapy may be achieved earlier.

Disclosures. **A. J. Blaschke**, BioFire Diagnostics, LLC: Collaborator and Scientific Advisor, Co-Investigator on NIH grant; BioFire Principal Investigator, Consulting fee and Licensing agreement or royalty

383. Evaluation of Vancomycin Loading Dose in Pediatric Patients

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Background. In adult patients, a loading dose of vancomycin (VAN) has been shown to be safe and effective in improving the likelihood of attaining a desirable initial trough level (10-20 mg/L). Despite many years of experience, the appropriate PK/PD parameter to predict efficacy of VAN dosing in children is uncertain.

Methods. A retrospective analysis of VAN dosing, subsequent trough attainment, and demographic data was completed for pediatric inpatients > 3 months of age who received a VAN loading dose between December 15, 2012-April 1, 2013 and had ≥ 1 recorded steady-state trough level. Only the first course of VAN for each patient was included in the analysis. Patients on VAN prior to admission or with renal dysfunction were excluded.

Patient	Age	Loading Dose (mg/kg)	# Loading Doses Given	Maintenance Dose (mg/kg)	Dosing Interval	Initial VAN Trough	Trough Drawn Before Dose #
1	6 mo	25	1	15	Q 6h	11.2	4
2	4 yr	25	1	15	Q 6h	13.9	4
3	5 mo	25	1	15	Q 6h	9.5	4
4	19 mo	25	1	15	Q 6h	8.3	4
5	24 yr	22	1	11	Q 8h	11.3	4
6	17 yr	18	1	13.6	Q 6h	12.5	6
7	25 yr	27	1	15	Q 8h	11.3	5
8	13 mo	20	1	15	Q 6h	10.5	5
9	2 yr	25	1	14.7	Q 6h	10.2	4
10	23 mo	20	1	15	Q 6h	6.7	4
11	4 yr	20	1	15	Q 8h	11.2	4
12	2yr	25	1	15	Q 6h	12.7	5
13	21 mo	25	1	15	Q 6h	<5	8
14	21 yr	27.8	1	16.7	Q 8h	13	7
15	20 yr	25	1	17.5	Q 12h	5.5	5
16	12 yr	25	1	15	Q 6h	5.4	6
17	21 mo	20	1	15	Q 6h	9.4	5
18	3 yr	25	1	15	Q 6h	23.8	5
19	13 yr	25	1	15	Q 6h	9.4	5

Results. 19 patients were identified for inclusion in the study. Figure 1 shows the dosing strategy and initial trough level for each patient. Initial VAN troughs were obtained after at least 3 maintenances doses in 58% (11/19) patients, and as late as before the 8th dose in 1 patient. All patients received only 1 loading dose. The median loading dose administered was 25 mg/kg (range: 18 – 27.8) with a median maintenance dose of 15 mg/kg every 6 hours. For the entire study population, the initial median trough concentration was 10.9 mg/L (range: <5 – 23.8). 52.5% (10/19) had trough concentrations between 10-20 mg/L and 36.8% (7/19) between 5-10 mg/L. Only 1 patient (5.3%) had an undetectable (<5 mg/L) trough concentration; however, the level was drawn ~45

minutes late. Additionally, 1 patient (5.3%) reported a supratherapeutic trough concentration of 23.8; however, no elevations in serum creatinine were noted. Of those who were initiated on a maintenance dose of 15 mg/kg/dose every 6 hours after the initial loading dose, the initial median trough concentration was 10.4 mg/L (range: <5 – 23.8). No cases of nephrotoxicity were reported.

Conclusion. Use of a loading dose was safe and resulted in achievement of goal initial median trough concentrations of 10 – 20 mg/L in this study population. This may suggest that more aggressive and standardized dosing strategies may benefit pediatric patients in achieving early target trough concentration on VAN therapy.

Disclosures. **All authors:** No reported disclosures.

384. Impact of a New Restriction Policy: Limiting Duration of Therapy of Restricted Antimicrobials to 7 Days in a Pediatric Hospital

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Background. Pediatric Antimicrobial Stewardship Programs (ASPs) are known to reduce antimicrobial (AM) use and hospital costs, and to improve patient (pt) outcomes. Our institution implemented an ASP in 2004 and found significant decreases in AM use. To further optimize AM use, the ASP adopted a defaulted 7 day duration limit to restricted AM orders in November 2011. Treatment beyond 7 days with restricted AMs required re-approval from an ID Attending. Our objective was to determine whether this policy modification decreased overall and prolonged AM use.

Methods. We conducted a retrospective review of restricted antibiotic (ABX) use from one year pre- and two years post-implementation of the 7-day restriction policy. The study was conducted at Alfred I. duPont Hospital for Children. We included carbapenems and MRSA-active ABX (linezolid, daptomycin, and ceftaroline). We excluded vancomycin as it was used as a pilot for this policy. We included all hospitalized pts who received a restricted ABX between November 2010 and November 2013. ABX use was measured using days of therapy (DoT) per 1,000 pt days. The length of therapy (LoT) of each treatment course was compared between the two study periods. Pts who received ABXs for approved indications with prolonged duration (e.g., febrile neutropenia, osteomyelitis) were excluded from the LoT analysis. Data were analyzed using Pearson X^2, X^2 test for trend in proportion and analysis of variance as appropriate.

Results. DoT/1,000 pt days of restricted ABX decreased from 48.5 in the baseline period to 32.7 in year 2 ($p < 0.001$). Carbapenem use decreased significantly from 30.8 to 22.9 by year 2 ($p = 0.03$). Anti-MRSA ABX decreased from 17.7 to 9.8 by year 2 ($p = 0.2$). 477 ABX courses in 304 unique pts were evaluated for LoT. Treatment courses lasting >14 days significantly decreased over the study period ($p < 0.001$). Mean LoT decreased from 5.1 to 3.4 days in year 2 ($p < 0.001$). Unintentional discontinuation of ABX was rare (2 cases) and was not found to result in harm to patients. Pharmacy costs for studied ABX in year 2 were reduced by 57% ($125,156) compared to baseline.

Conclusion. Enhanced restrictions on the duration of ABX therapy with an automatic 7-day order duration contributed to additional reductions in restricted ABX use and costs in an established ASP.

Disclosures. **All authors:** No reported disclosures.

385. Pediatric Antimicrobial Stewardship Programs: A Systematic Review

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Background. Judicious use of antimicrobials is critical to prevent development of resistance and may be enhanced by the activities of antimicrobial stewardship programs (ASPs). While there are many studies of adult ASPs, the clinical and economic outcomes associated with pediatric ASPs have not been well described or reviewed.

Methods. We performed a systematic review using a PubMed search to identify studies with any of the following terms in the title or abstract: "antimicrobial stewardship," "antimicrobial control," "antibiotic control" or "antibiotic stewardship." Studies were further limited to inpatient studies in the United States that contained the terms: "child," "children," "pediatric*," "paediatric*," "newborn," "infant," "neonat*" in the title or abstract. Clinical and economic outcomes from each relevant study were summarized.

Results. Of 71 studies identified, 39 were eliminated based on title. 32 remaining abstracts were reviewed, 23 of which were selected for in-depth review (14 original studies and 9 review articles). Of these, 8 original studies from 4 institutions reported outcomes related to pediatric ASPs. For studies reporting clinical outcomes, 4 studies reported decreased antimicrobial utilization, though the specific metric varied across studies; and 2 studies documented decreases in prescribing errors. Only 2 studies assessed the potential negative impact of ASPs on clinical outcomes; 1 found no difference in mortality or readmission rates after ASP implementation and another found no adverse outcomes among children for whom the ASP recommended no therapy. In terms of economic outcomes, 2 studies reported decreases in antimicrobial drug costs.

Conclusion. Although ASPs have been recommended by IDSA since 2007, only 8 pediatric studies evaluating ASPs from 4 centers have been published. These studies demonstrate reduced antimicrobial utilization, cost and prescribing errors with no apparent negative impact on patient safety. While these findings are promising, the limited evidence-base warrants further investigation. Additionally, there is need for studies focusing on the appropriateness and quality of antimicrobial prescribing practices as well as more formalized economic evaluations.

Disclosures. **All authors:** No reported disclosures.

386. ASP Evaluation of Required Indication for Antimicrobial Orders in a Pediatric Hospital

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Background. Starting in April 2005, as part of our Antimicrobial Stewardship Program (ASP), prescribers were required to select an indication as part of an antimicrobial (AM) order; "other" was an option. In 2011, Centers for Medicare and Medicaid Service (CMS) added "antibiotic orders include an indication for use" as part of its surveyor worksheet. We initiated a daily review of active AM orders with "other" as the indication in April 2012. The goal of this project is to describe our two year experience with this process.

Methods. Our hospital utilizes EPIC (Madison, WI) as our electronic health record (EHR). The on-call ID physician ran a daily report of active AM orders with indication other, reviewed the clinical record, and documented agreement or recommended interventions in the EHR. We performed a retrospective chart review to assess the acceptance of those recommendations.

Results. During the study period, there were 43,384 AM orders, 18% had "other" as the indication. We reviewed 3851 orders with "other" as the listed indication of which 196 (5%) required interventions. There was variability in the acceptance rate by type of intervention:

	Accepted Interventions		Percent Accepted	
Intervention (% of total)	Yes	No	Yes	No
Add Antibiotic (10%)	19	3	86	14
Stop Antibiotic (42%)	67	29	70	30
Modify Therapy (43%)	72	26	73	27
Recommend ID consult (3%)	5	1	83	17
Recommend isolation (3%)	6	0	100	0

Multiple interventions were suggested in 12% of reviews. The recommended intervention was accepted 74% of the time. The acceptance rate was similar in ICU and non-ICU patient care settings.

We noted differences in ordering patterns by AM class. Fluoroquinolones comprised 2% of all AM orders which represented 9% of all indication "other" orders. This class made up 9% of our interventions. Nebulized tobramycin was 0.6% of total AM orders but 2.5% of orders with an "other" indication.

Conclusion. 5% of all AM orders with indication "other" required an intervention, the majority of which were accepted. Some AM classes were overrepresented in the indication "other" orders but had a similar rate of intervention. This offers an opportunity to refine the approved indication list and provide additional prescriber education. In anticipation of a CMS requirement for AM indication, ASPs should carefully select preapproved indications for AMs.

Disclosures. **All authors:** No reported disclosures.

387. The Use of Aerosolized Tobramycin in Children Residing in Pediatric Long Term Care Facilities

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Background. Tobramycin Inhalation Solution (TIS) for chronic suppressive therapy or eradication of *Pseudomonas aeruginosa*is standard for patients with cystic fibrosis. Increasingly, TIS is used off-label to treat other infectious complications of the respiratory tract. Children in pediatric long term care facilities (pLTCFs) have complex comorbid conditions often including respiratory disorders, e.g., bronchopulmonary dysplasia and chronic lung disease. We sought to describe the use of TIS in pLTCFs.

Methods. From October 2013 to March 2014 we reviewed the medical records of all children residing at 3 pLTCFs in the New York metropolitan area to determine if they had received TIS and if so, the indication for treatment. Statistical analyses were completed with Student's t-test or Pearson's chi-square.

Results. During the study period, 8% of residents (25/314) were treated with TIS (10, 8, and 7 were at Site 1, 2, and 3, respectively). The most common indication was tracheitis (n = 10, 40%) followed by "secretion management" (n = 5, 20%). Other indications included atelectasis (n = 2), prophylaxis (n = 2), reactive airway disease (n = 1),

and tracheal colonization (n = 1). No indication was documented for 4 (16%) residents. Most residents (n = 15) were on TIS courses of monthly on-off cycles and 10 received 1 course (range: 4-21 days). Bacterial cultures of the respiratory tract were obtained for 5 (20%) of 25 residents on TIS and were positive for *Serratia marcescens* (n = 2), *P. aeruginosa* (n = 2), and both *S. marescens and P. aeruginosa*(n = 1). Susceptibility testing was available for 4 isolates and all were susceptible to tobramycin. Residents who received TIS were older and more likely to have a tracheostomy and a chronic respiratory disorder (Table).

Table: Characteristics of pLTCF residents who did and did not receive TIS

Characteristics	TIS N=25 (%)	No TIS N=289 (%)	*P*
Mean age, years	10.6	8.2	**0.05**
Male	16 (64)	134 (46)	0.09
Tracheostomy	22 (88)	106 (37)	**<0.01**
Chronic respiratory disorder	19 (76)	156 (54)	**0.03**

Conclusion. Off-label TIS use was observed in all 3 PLTCFs. Further research should determine the efficacy of TIS use in this population and monitor the emergence of multidrug-resistant bacteria in this unique population.

Disclosures. **All authors:** No reported disclosures.

388. Antibiotic Stewardship in the Neonatal Intensive Care Unit (NICU): Metrics Matter!

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Background. Prolonged antibiotic therapy among preterm infants in the NICU is associated with adverse outcomes including death and necrotizing enterocolitis. The optimal metric to measure antibiotic use in the NICU and thus guide stewardship efforts is unknown. The purpose of this study was to apply two different metrics of antibiotic use to a large cohort of NICU infants and compare the results.

Methods. Prospective collection and analysis of all antibiotics provided to every infant admitted to the NICU at Parkland Memorial Hospital, Dallas during a 14 month period (SCOUT study). Pertinent clinical and outcome data were collected. Two different metrics for determining antibiotic use were calculated for all antibiotics: 1) days of therapy (DOT) and 2) number of calendar days (CD) that the antibiotics were administered. DOT was calculated by dividing the dosing interval by 24 hours, then multiplying by the number of doses, summed for each antibiotic. CD was determined by the number of days in which a dose of an antibiotic was administered. For example, a 6-dose course of q8 hour ampicillin begun Monday evening and completed Wednesday morning would equal 2 DOT (8 ÷ 24 x 6 = 2) and 3 CD (Monday, Tuesday, Wednesday = 3).

Results. 1521 infants were admitted during the study period; 364 (24%) received no systemic antibiotics and were excluded. 1157 infants (76%) accounted for 19,788 hospital days and received 1439 separate antibiotic courses. The total volume of antibiotic administered was 9394 by DOT and 5915 by CD. Agent-specific antibiotic use by DOT and CD is shown (table).

Antibiotic	No. of courses	DOT	CD	% difference
All	1439	9394	5915	-37%
Gentamicin	1399	4468	4551	2%
Ampicillin	1233	3579	4417	31%
Oxacillin	181	676	874	23%
Vancomycin	41	249	276	11%
Piperacillin/tazobactam	36	171	195	14%
1st generation cephalosporins	18	10	23	130%
Penicillin	12	69	77	12%
3rd generation cephalosporins	6	10	13	30%
Meropenem	5	26	30	14%
Metronidazole	4	38	42	11%
Other	14	98	115	17%

Conclusion. Antibiotic use in the NICU varies substantially by the metric used. When used to describe a course of antibiotics, CD does not account for the number of agents. When used for specific agents, CD overestimates therapy volume by 13% on average. Our ongoing evaluation of which metric best predicts adverse outcomes is important to guide antibiotic stewardship efforts.

Disclosures. **All authors:** No reported disclosures.

389. Evaluation of Extended-Interval Aminoglycoside Dosing (EIAD) at a Pediatric Institution

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Background. Aminoglycosides (AG) are common antimicrobial agents used for additional gram-negative bacterial coverage in pediatric patients (pts). Conventional dosing of gentamicin (G) and tobramycin (T) is 2.5mg/kg/dose IV q8h based on IBW. Based on pharmacokinetics (PK) and pharmacodynamics, EIAD optimizes antimicrobial activity (maximizing peak to minimum-inhibitory concentration ratio) while minimizing toxicity. We adopted stratified, age-based EIAD dosing recommendations for pediatric patients >3 months (mo)- < 2 years (yr) (Group 1), 2-8 yr (Group 2), and ≥8 yr (Group 3). We describe the safety and efficacy of this dosing strategy.

Methods. Retrospective review of all EIAD orders of G and T from February 1, 2013-July 31, 2013 in pediatric pts >3 mo was performed. Inclusion criteria: pts who received EIAD with 2 serum drug concentrations obtained. Exclusion criteria: neonates <44 weeks corrected gestational age, pregnant women, acute burn injury, estimated creatinine clearance <40mL/minute, cystic fibrosis, dialysis, use for gram-positive synergy or mycobacterial infection. Data collected included age, gender, height, weight (wt), concomitant antimicrobials, baseline renal function, initial dosing regimen and serum concentrations.

Results. 90 EIAD courses in 34 pts were reviewed; 27 courses in 20 pts were included in the analysis. All pts received G. The mean age, wt and AG dose are listed in figure 1. All pts (100%) were receiving a concomitant beta-lactam antibiotic during G therapy. PK parameters were calculated for each course of therapy with associated levels. For the entire study population, mean Ke was 0.3 hr^{-1} ± 0.1, $t_{1/2}$ 2.5 hr ± 0.8, Vd 0.48 L/kg ± 0.1, Cmax 16.9 mcg/mL ± 4.3 and C24hr 0.06 mcg/mL ± 0.12. PK parameters by age group are listed in figure 2. Ke was lower for our study population than reported in the literature except for group 1. For all groups, calculated Vd was much larger than reported in the literature. No cases of nephrotoxicity were identified.

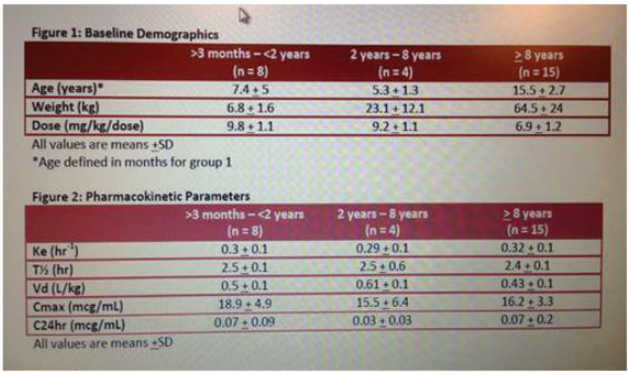

Figure 1: Baseline Demographics

	>3 months – <2 years (n = 8)	2 years – 8 years (n = 4)	≥ 8 years (n = 15)
Age (years)*	7.4 + 5	5.3 + 1.3	15.5 + 2.7
Weight (kg)	6.8 + 1.6	23.1 + 12.1	64.5 + 24
Dose (mg/kg/dose)	9.8 + 1.1	9.2 + 1.1	6.9 + 1.2

All values are means ±SD
*Age defined in months for group 1

Figure 2: Pharmacokinetic Parameters

	>3 months – <2 years (n = 8)	2 years – 8 years (n = 4)	≥ 8 years (n = 15)
Ke (hr^{-1})	0.3 + 0.1	0.29 + 0.1	0.32 + 0.1
T½ (hr)	2.5 + 0.1	2.5 + 0.6	2.4 + 0.1
Vd (L/kg)	0.5 + 0.1	0.61 + 0.1	0.43 + 0.1
Cmax (mcg/mL)	18.9 + 4.9	15.5 + 6.4	16.2 + 3.3
C24hr (mcg/mL)	0.07 + 0.09	0.03 + 0.03	0.07 + 0.2

All values are means ±SD

Conclusion. EIAD appears of be safe in pediatric pts. An age based approach to dosing per wt seems appropriate. Doses of 9.5 mg/kg/dose for those >3 month < 2 year, 8.5 mg/kg/dose for those 2 year- <8 year and 7 mg/kg/dose for those ≥8 year is likely to achieve a Cmax of 15 – 20 mcg/mL with a C24 hour of <1 mcg/mL.

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390. Evaluating Guideline-Recommended Antibiotic Prescribing Practices: *Azithromycin for what?*

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Background. Azithromycin is often prescribed for unclear indications. Our objectives were: 1) to evaluate adherence to published guidelines for respiratory infections, and 2) to determine patterns for azithromycin use among community providers.

Methods. A case-based survey was developed and emailed to members of a statewide registry. Providers chose their preferred management for infections with published treatment guidelines: otitis media, sinusitis, and community acquired pneumonia. After survey completion, participants could request an "answer key" detailing appropriate management of each scenario. A follow-up questionnaire was distributed inquiring whether the exercise had prompted reevaluation of current practices.

Results. We received a 10% response rate and analyzed 163 completed surveys. There was general agreement on half the questions, with ≥ 75% of respondents choosing the recommended antibiotic. The remaining scenarios showed more divided choices. For example, nearly all (97%) agreed to hospitalize a patient with focal pneumonia and low oxygen saturations, but differed in preferred antibiotic regimen, with equal numbers choosing ampicillin alone, ampicillin + azithromycin, or vancomycin - + ceftriaxone. For a 5 year old with 3 days of otalgia, the group was divided between watchful waiting vs treatment with amoxicillin.

In cases where azithromycin was indicated, there was clear agreement from the group on its use. We also observed azithromycin preference in cases of recurrent otitis media and sinusitis. Those who varied from the guidelines to choose azithromycin in one scenario were significantly (28%) more likely to do so in other scenarios ($p < 0.001$).

On the post-survey questionnaire, 26% reported adjusting their practice, 69% reviewed the guidelines, 9% used cases for teaching, and 21% discussed the guidelines with colleagues.

Conclusion. The majority of respondents followed published guidelines, though we did observe variance with more ambiguous cases. When the group did vary from the guidelines, their choices would not likely have adversely affected care. Our results suggest room still exists for improved antibiotic stewardship. Our results and feedback suggest that future guidelines including case-based recommendations or discussions may enhance adherence.

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391. Investigating the Dosage of Vancomycin Necessary for Optimal Exposure In Children

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Session: 45. PK/PD Studies
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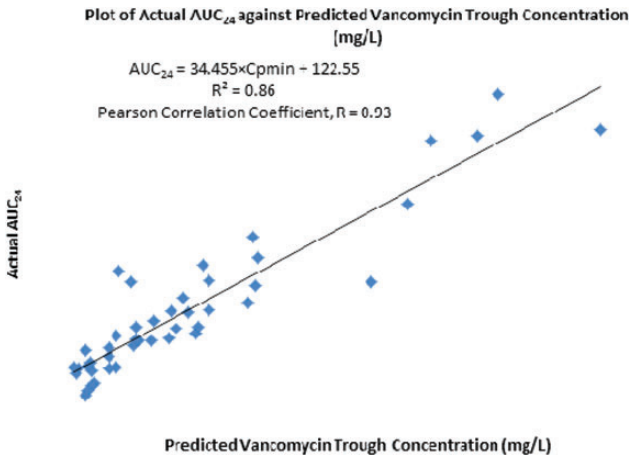
Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) is of serious concern in the management of infectious disease in the hospital and vancomycin has been considered the mainstay in the treatment of MRSA. Clinical trials have shown that optimal clinical outcomes in the management of MRSA using vancomycin were best predicted by a ratio of the area-under-the-concentration-time-curve for 24 hours (AUC_{24}) to the minimum inhibitory concentration (MIC) of ≥400. Concerns were raised over an apparent "MIC creep" for MRSA isolates to vancomycin and there were recommendations to increase the initial dosing regimen for vancomycin in pediatric patients to 60mg/kg/day.

Methods. A retrospective study was conducted in KK Women's and Children's Hospital between January 2012 and December 2013 to investigate the proportion of pediatric patients able to achieve the AUC_{24}/MIC target of ≥400 with the recommended dose of 60mg/kg/day, and the correlation between actual AUC_{24} and true vancomycin trough concentrations.

Results. Of the 44 patients included in the study, only 23 (52.3 %) patients were able to attain an AUC_{24}/MIC ≥400 if the recommended dose of 60mg/kg/day was used. Actual AUC_{24} was found to be positively correlated to true vancomycin trough concentration (Pearson's r = 0.93), with all patients who had trough concentration ≥10mg/L attaining AUC_{24}/MIC ≥400. Heavier patients (≥40kg) were noted to have a higher mean AUC_{24} (p = 0.010). Younger patients (<12 years old) were noted to have a higher dose requirement to achieve the target AUC_{24}/MIC (p = 0.012).



Conclusion. The current dosing recommendation of vancomycin is insufficient to achieve the target AUC_{24}/MIC ≥400. Age and weight may influence the extent of vancomycin exposure when a uniform weight-based dosing is used. The recommended trough concentration in adult population does not correlate with an AUC_{24}/MIC ratio ≥400 in paediatric patients. It is of paramount importance to elucidate the optimal AUC_{24}/MIC target for the paediatric population, before new dosing recommendations can be made.

Disclosures. **All authors:** No reported disclosures.

392. Vancomycin Dosing and Concentrations at a Large University-Affiliated County Hospital

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Background. According to the IDSA guidelines, vancomycin trough concentrations are the most accurate and practical method for therapeutic drug monitoring (TDM).

Methods. As part of a prospective, 3-year, sequential cohort study of a novel Bayesian vancomycin therapeutic drug monitoring (TDM) strategy, to establish the baseline TDM practice we enrolled 83 patients at our tertiary-care, academic, county hospital during the first year from 2012-2013.

Results. Patients were 9 months to 74 years old. The first vancomycin concentration was therapeutic per IDSA guidelines in only 26 (31%) patients, with sampling in 54 (65%) after the 3rd or 4th dose, and before (20%) or after (15%) these doses in the rest. The median sample time after start of therapy was 35 hours (range 8-93 hours). Only 34 (41%) of samples were true troughs drawn within 1 hour before the next planned dose based on the dose interval, and 31 (39%) of 79 were drawn within 1 hour before the next actual dose (4 patients stopped vancomycin). The median true trough was 14.7 mg/L in therapeutic patients and 6.3 mg/L in those that were not therapeutic (p = 0.0008). The median vancomycin dose was 12.5 mg/kg in patients with therapeutic troughs and 13.0 mg/kg in those without (p = 0.88). In 6 (7%) patients with nephrotoxicity, the median vancomycin concentration was 18.1 mg/L vs 11.3 mg/L in patients without renal injury (p = 0.0001).

Conclusion. Measurement of true steady-state vancomycin troughs within one hour of the next dose does not happen for the majority of patients in our hospital setting, biasing interpretation from traditional TDM or nomograms that depend on accurate timing. Therapeutic concentrations cannot be predicted from dosing, and non-therapeutic patients are more likely to be underdosed than overdosed. To prevent underdosing and nephrotoxicity from overdosing, routine use of a TDM approach that can handle sample timing variability, such as a Bayesian algorithm, is strongly justified by our data. Testing of the algorithm is ongoing in years 2 and 3 of our study.

Disclosures. **M. Neely**, Applied Pharmacometrics: Co-founder, Seeking to eventually license a Bayesian dosing software program developed by the Laboratory of Applied Pharmacokinetics, of which I am director

393. Vancomycin Dosing in Obese Patients

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Background. Current guidelines for systemic vancomycin dosing recommended using actual body weight (ABW) regardless of body mass index (BMI). We sought to evaluate the effect of this dosing strategy in obese patients with BMI ≥35.

Methods. Retrospective cohort study of patients ≥18 years old with a BMI ≥35 hospitalized between January 1, 2011 and December 31, 2013 with at least 3 doses of intravenous vancomycin. Inclusion required a normal baseline creatinine clearance (CrCl ≥45 mL/minute) and at least 1 appropriate vancomycin trough measured before the 4thor later dose. Patients were excluded if they received a loading dose or if the maintenance dose was changed before the first trough was measured. We collected data on patient's age, gender, weight (actual, ideal, and dosing), baseline creatinine, calculated CrCl, administered vancomycin dose (including frequency and total daily dose), and vancomycin trough. Linear regression was used to predict the vancomycin trough based on each of these clinical predictors.

Results. The 68 patients identified had a significant positive linear relationship between vancomycin total daily dose (TDD) (mg/kg/day) based on ideal body weight (IBW) and vancomycin trough (p 0.001). The relationship was not significant for vancomycin TDD based on ABW (p 0.072). Other predictors of vancomycin trough included age, gender, and baseline serum creatinine. Multivariable modeling including these predictors, along with vancomycin TDD based on IBW, showed moderate correlation between predicted and actual vancomycin troughs (R^2>0.41). For the average patient in our study, initial doses of 30 mg/kg/day (IBW) predicted vancomycin troughs of 10-15 mcg/mL. To achieve targets of 15-20 mcg/mL, our model suggested that initial doses of 45-60 mg/kg/day (IBW) should be used. Younger patients and male patients were less likely to achieve therapeutic targets without this higher dosing.

Conclusion. For patients with a BMI ≥35, vancomycin dosing based on IBW rather than ABW appears to be more predictive of vancomycin trough, with initial doses of at least 45 mg/kg/day (IBW) more likely to achieve higher vancomycin trough targets. Given the only moderate correlation, it remains important to follow vancomycin troughs and adjust dosing accordingly.

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394. Influence of febrile neutropenia on the pharmacokinetics and dosage requirements of vancomycin

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Background. In recent guidelines, trough serum concentraions of ≥ 15 μg/mL are recommended for vancomycin in severe infections by less-susceptible staphylococcal species such as MRSA. However, optimal doses to attain the trough value in febrile neutropenic (FN) patients are not yet well established.

Methods. To evaluate the influence of neutropenia on the pharmacokinetics and dosage requirements of vancomycin, the trough levels in 8 patients (Goup C; age

59.0 ± 9.1) without neutropenia (≥ 1,000/μL) were compared with those in 7 patients (Group B; age 61.3 ± 12.6) with mild (100 - 1,000/ μL) or in 8 patients (Group A; age 58.5 ± 9.2) with severe (<100/μL) febrile neutropenia using a two-compartment Bayesian pharmacokinetic program. All patients received 2g/day of vancomycin for more than 2 days. Only patients with estimate creatinine clearance (eCCr) more than 70 mL/minute were included in the study.

Results. Increased total clearance and the shorter elimination-half life of vancomycin was observed in patients with neutropenia compared with non-neutropenic patients, and thus, serum vancomycin concentration (SVC) was significantly lower in neutropenic patients [Group A 9.6 ± 1.7, Group B 10.8 ± 2.6, Group C 14.7 ± 1.3, p < 0.01]. Severely neutropenic patients in particular required a higher vancomycin dosage regimen compared with the non-neutropenic patients [Group A 62.2 ±12.5 mg/kg/day vs Group C 40.0 ± 8.1 mg/kg/day, p = 0.007] to attain trough SVC of 15 mg/mL. Significant inverse association was observed between SVC and eCCr in neutropenic, but not in non-neutropenic patients [Group A (p = 0.006), Group B (p = 0.041), Group C patients (p = 0.610)].

Conclusion. Higher initial doses considering the degree of neutropenia and eCCr, and careful monitoring of the serum concentraions thereafter are required for vancomycin in patients with febrile neutropenia.

Disclosures. **All authors:** No reported disclosures.

395. Impact of vancomycin pharmacokinetic/pharmacodynamic data on clinical outcomes of methicillin-resistant *Staphylococcus aureus* bacteremia in children

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Background. Vancomycin is an important antibiotics in treating methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia in the pediatric population. Although studies in adults supported pharmacokinetic/pharmacodynamic (PK/PD) data of area under the curve/minimum inhibitory concentration (AUC/MIC) ≥400, or vancomycin trough concentration (C_{trough}) of 15–20 mcg/mL correlates with favorable clinical outcomes, these remain limited in pediatric patients.

Methods. The study population consisted of hospitalized children < 18 years old with MRSA bacteremia, in whom serum $C_{trough}$of vancomycin was determined from January 2010 to December 2013. Clinical data including demographic profiles, primary sites of infection, underlying diseases, and clinical/microbiological outcomes were retrospectively collected by reviewing medical records. AUC was calculated as daily dose/vancomycin clearance and vancomycin clearance in children was estimated by Burton revised method.

Results. A total of 42 MRSA bacteremia cases were included. The mean age of the study population was 24.6 months (range, 0-17 years) and 62% (26/42) were clinically severe cases requiring an intensive care unit stay, use of mechanical ventilation and/or death with an all-cause 30-day fatality rate of 22.5% (9/40). The vancomycin MIC_{50} and MIC_{90} were 1.0 and 2.0 μg/mL, respectively. Although C_{trough} and AUC/MIC were significantly correlated (Pearson's r = 0.347), the target range of AUC/MIC ≥ 400 or C_{trough} ≥ 15 mcg/mL were initially achieved only in 1 (2.4%) case or 3 (7.1%) cases with the average vancomycin dosage of 37.7 mg/kg/day. Persistent bacteremia at 72 hr after initiation of vancomycin and 30-day fatality were observed more frequently in children with initial C_{trough} <10 mcg/mL compared to those with C_{trough} ≥ 10 mcg/mL [67.9% (19/28) vs 50.0% (2/4), $p = 0.482$; 24.2% (8/33) vs 12.5% (1/8), $p = 0.472$, respectively].

Conclusion. Although few cases with satisfactory PK/PD parameters were included in this study, it was suggested that initial C_{trough} < 10mcg/mL might be associated with persistent bacteremia and higher mortality in serious MRSA bacteremia cases of children. Further study is mandatory for vancomycin dosing information to clarify optimal drug exposure and the impact on clinical outcome in the pediatric population.

Disclosures. **All authors:** No reported disclosures.

396. What is the Best Predictor for Vancomycin Nephrotoxicity?

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Background. The best way to study the association between vancomycin trough (VT) and nephrotoxicity (NT) is not clear. The goal of this study is to explore this association using 3 predictors.

Methods. This is a retrospective, observational cohort study of adult patients who received vancomycin for ≥ 72 hours at the University of Kansas Medical Center between September 7, 2011 and February 7, 2012. The study included both inpatient and outpatient data. NT was defined as: ≥ 50% or ≥ 0.5 mg/dl increase in serum creatinine from baseline on 2 consecutive measurements. Data collected included 3 main predictors: average VT, first VT, VT preceding acute renal failure (VTPARF) and other possible risk factors for NT. We divided the patients into 4 groups (1 to 4): [VT < 10 μg/ml, 10 μg/ml ≤ VT < 15 μg/ml (reference group), 15 μg/ml ≤ VT ≤ 20 μg/ml and VT > 20 μg/ml]. We analyzed the data using average VT and first VT. We also compared the VTPARF to the average VT in patients with no ARF.

Results. The study included 474 patients, 63/474 developed ARF (13.29%). The incidence of ARF in groups (1-4) was: 2/114 (1.75%), 9/180 (5%), 31/122 (25.4%) and 21/49 (42.85%) using the average VT. It was: 17/194 (8.76%), 22/155 (14.19%), 10/66 (15.15%) and 14/42 (33.33%) using the first VT. Compared to reference group (2), ARF incidence was significantly higher in group 3 (p-value = 0.0001), group 4 (p-value = 0.001) by average VT and only in group 4 (p-value = 0.014) by first VT. Among patients with ARF 30/62 (48.39%) had VTPARF ≥ 15 μg/ml vs 119/411 (28.95%) of patients with no acute renal failure using the average VT (p-value = 0.004). ARF incidence was associated with baseline Cr ≥ 1.5 mg/dl (p-value = 0.03). There was a tendency toward increased nephrotoxicity in patients with morbid obesity (p-value = 0.056). There was no observed association with other possible risk factors for NT.

Conclusion. Average VT ≥ 15 μg/ml and first VT > 20 μg/ml are associated with increased NT. Patients with acute renal failure had significantly more VTPARF ≥ 15 μg/ml compared to patients with no ARF (average VT). This study suggests that VT ≥ 15 μg/ml is likely more nephrotoxic than lower levels. The only concomitant risk factor that was associated with NT was baseline Cr ≥ 1.5 mg/dl.

Disclosures. **All authors:** No reported disclosures.

397. Correlation between calculated vancomycin AUC_{0-24}/MIC and acute kidney injury in patients with Methicillin Resistant Staphylococcus Aureus *bacteraemia*

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Background. Higher vancomycin trough levels are associated with increased risk of nephrotoxicity. However clinical data on the correlation between vancomycin pharmacodynamics (PD) parameter AUC_{0-24}/MIC and nephrotoxicity are limited. Our aim was to investigate this relationship further in patients with methicillin resistant *Staphylococcus Aureus*bacteraemia (MRSAB).

Methods. A single centre retrospective observational cohort study involving 127 consecutive MRSAB patients was conducted. Demographics, clinical data and use of concomitant nephrotoxin were retrieved from medical records. Minimum inhibitory concentration (MIC) was obtained using broth microdilution (BMD). Acute kidney injury (AKI) was defined as ≥0.5 mg/L or 50% increase in serum creatinine from baseline on 2 or more consecutive measurements. Classification and regression tree (CART) analysis was performed to identify a vancomycin AUC_{0-24}/MIC threshold for AKI.

Results. AKI was observed in 15.7% of patients (20/127). Clinical characteristics were similar between patients with and without AKI (107/120). The mean vancomycin trough level was 13.8mg/L with higher levels associated with AKI compared to patients with no kidney injury (17.2 mg/L vs 13.1 mg/L; $p = 0.007$). Similar to previous studies the probability of AKI increased when vancomycin trough concentrations were above 15mg/L. A vancomycin AUC_{0-24}/MIC target of > 591 (mg*h/L) was detected by CART analysis; with AKI occurring in 30.3% (10/33) compared to 10.6% (10/94) in patient achieving PD targets above and below 591 respectively ($p = 0.012$). The only other risk factor for AKI on univariate analysis was concomitant use of nephrotoxins (18/20, 90% vs 53/107, 49.5%; $p = 0.001$). On multivariate logistic regression analysis vancomycin PD targets (OR 3.5, 95% CI 1.2-10.2; $p = 0.022$) and concomitant nephrotoxins use (OR 8.35, 95%CI 1.8-38.7; $p = 0.007$) were the only independent predictors of AKI despite age, severity of illness and ICU stay included in the model *a priori*.

Conclusion. AKI is associated with vancomycin PD targets. An increased incidence of AKI is noted with higher AUC_{0-24}/MIC values beyond the currently recommended targets for treatment success.

Disclosures. **All authors:** No reported disclosures.

398. Pharmacokinetics of dalbavancin (DAL) in bone and associated tissues in patients undergoing orthopedic surgical procedures

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Background. DAL is lipoglycopeptide antibiotic which is a highly protein bound (93%) with a long elimination half-life in plasma. DAL exhibits activity against Gram-positive organisms, including MRSA, with an *in vitro* MIC_{90} of 0.06 mg/ml. The objective of this study was to characterize the PK of DAL in bone and associated tissues in patients undergoing joint surgery.

Methods. Adults scheduled for joint surgery (N = 31) were administered 1 g of DAL infused over 30 minutes prior to scheduled surgery. Patients were assigned to 1 of 6 cohorts and had serial plasma PK samples collected up to 45 days post-dose plus 1 bone PK sample collected at 12, 24, 72, 168, 240 or 336 hr post dose. Samples were analyzed for DAL in plasma, synovial fluid, skin, cartilage and

bone using LC-MS/MS. A population PK model was fit to plasma and bone PK data using NONMEM and covariate analysis was performed. Allometry was used to determine the total amount of bone tissue and to estimate the amount of DAL in bone.

Results. DAL concentrations in bone, synovial fluid, synovial tissue, and skin exceeded the DAL MIC_{90} against *S. aureus* of 0.06 mg/mL. DAL concentrations in bone appeared to remain relatively constant for a period of 14 days after a single dose. The mean bone:plasma AUC penetration ratio was 13.9%.

Tissue	Mean concentration±SD (no. of samples) Hour 12	Hour 24	Hour 72	Hour 168	Hour 240	Hour 336
Plasma (mg/mL)	85.3±18.9 (31)	–	–	–	–	15.3±4.1 (31)
Synovium (mg/g)*	25.0±0 (3)	17.9±7.8 (3)	19.5±4.9 (3)	19.2±8.9 (4)	25.0±0 (2)	15.9± 7.9 (3)
Synovial fluid (mg/mL)*	22.9 (1)	27.4±10.8 (4)	19.2±4.9 (3)	11.6±3.3 (2)	13.9±1.0 (3)	6.2±1.7 (2)
Bone (mg/g)	6.3±3.1 (5)	5.0±3.5 (5)	4.6±3.8 (5)	3.8±2.7 (5)	3.7±2.2 (5)	4.1±1.6 (5)
Skin (mg/g)*	19.4±7.9 (2)	12.5±6.5 (3)	13.8±1.4 (2)	15.7±1.0 (2)	21.6 (1)	13.8±2.1 (2)

* Concentrations above the upper limit of quantification are reported as 25 µg/unit

Conclusion. Dalbavancin distributes into bone and associated tissue, including synovium. Bone penetration was 13.9% based upon total drug AUC and the high degree of protein binding suggests that the overall penetration is high relative to free-drug plasma concentrations. This study demonstrates that dalbavancin accumulates in bone and supports further study in patients with osteomyelitis and prosthetic joint infections.

Disclosures. **J. Baldassarre**, Durata Therapeutics: Employee, Salary **S. Van Wart**, Durata Therapeutics: Collaborator, Consulting fee **A. Forrest**, Durata Therapeutic: Consultant, Consulting fee **C. Rubino**, Durata Theraputics: Consultant, Consulting fee **M. Dunne**, Durata Therapeutics: Employee and Shareholder, Salary

399. Urinary NGAL is Elevated in Hospitalized Cystic Fibrosis Patients with Increased Tobramycin Exposure

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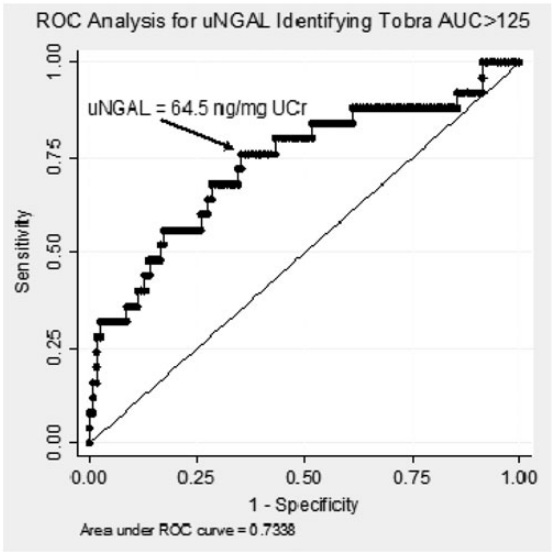
Background. Urinary neutrophil gelatinase-associated lipocalin (uNGAL) is a sensitive marker of kidney injury. It is reabsorbed via the same kidney receptor as tobramycin (tobra) and values could potentially predict changes in drug clearance/exposure during tobra therapy. We examined the relationship between individual tobra pharmacokinetic (PK) parameter estimates and uNGAL values during once daily tobra therapy in CF patients.



Methods. Observational study in CF patients receiving once daily IV tobra for exacerbation of bronchopneumonia from October 2012-January 2014. uNGAL and SCr were measured daily. uNGAL was normalized for urine creatinine (UCr) and natural log transformed for comparisons. Tobra PK parameter estimates ($AUC_{0\text{-}24}$, Cmax, CL) were determined using population model-based Bayesian estimation on days on which tobra levels were obtained (N = 141) using clinical PK software (MW/Pharm). We examined the association of log uNGAL concentrations and PK estimates by ordinary least squares regression accounting for subject clustering while adjusting for the time of day of urine collection and the time between tobra dose and urine sampling. We constructed nonparametric ROC curves to determine the optimal uNGAL cutoff which identifies increased tobra exposure (AUC > 125 mg*h/L). Finally, the slope of each subject's log uNGAL values over therapy was calculated using simple regression and correlated with their median PK parameter estimates.

Results. 29 patients received 44 tobra courses. Median age was 15.3y (IQR 12.5-19.1) and tobra duration was 10 days (range 5-22). Tobra AUC was associated with increased log uNGAL values (beta = .008, p = .04). Cmax (p = .98) and CL (p = .45) were not associated with log uNGAL. The optimal uNGAL cutoff to identify tobra AUC > 125 mg*h/L by Youden's index was 64.5 ng/mg UCr: sensitivity 76%, specificity 65% (Figure). There was a positive correlation between the slope of log uNGAL during therapy and an individual's median tobra AUC (r = .28, p = .07) but not Cmax (p = .60) or CL (p = .80).

Conclusion. Urinary NGAL concentrations are associated with tobramycin exposure (AUC) in patients with CF. Elevated uNGAL may detect increased and supratherapeutic tobramycin exposure and could be used to augment therapeutic drug management in CF patients at risk for renal injury.

Disclosures. **All authors:** No reported disclosures.

400. Beyond the Antibiogram: Using Monte Carlo Analysis to Optimize Institution-Specific Antipseudomonal Therapy

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Background. *Pseudomonas aeruginosa* is the 5th most common pathogen implicated in nosocomial infections with increasing resistance to a limited arsenal of antibiotics. Monte Carlo Simulations (MCS) provide clinicians with an additional tool to guide empiric therapy by determining the probability that an antibiotic regimen will reach a certain pharmacodynamic target to optimize bactericidal activity. This study determined which antibiotic regimens will achieve a goal probability of target attainment (PTA) of 90% against *P. aeruginosa* at our institution.

Methods. This study was a retrospective review of microbiological data from first cultures positive for *P. aeruginosa* at University of Kentucky HealthCare for 2012. Minimum inhibitory concentrations (MICs) for the following antibiotics were analyzed: aztreonam, cefepime, meropenem, and piperacillin/tazobactam administered via intermittent and prolonged infusion, amikacin, gentamicin, and tobramycin. Using MICs from UKHC specific isolates, and pharmacokinetic and pharmacodynamic parameters from previously published studies, a 10,000-subject MCS was run for each antimicrobial regimen to determine PTA.

Results. Two-hundred seventy two isolates were included for analysis. For studied antibiotics against *P. aeruginosa*, the MIC50/MIC90 were 8/8 mcg/mL for amikacin, 8/32 mcg/mL for aztreonam, 4/16 mcg/mL for cefepime, 2/16 mcg/mL for gentamicin, 1/8 mcg/mL for meropenem, 8/128 mcg/mL for piperacillin/tazobactam, and 2/8 mcg/mL for tobramycin. None of the tested β-lactam regimens administered over 30 minutes reached a PTA > 90%. Three-hour infusions of cefepime 2g every 8 hours, meropenem 1g every 8 hours, and meropenem 2g every 8 hours had a PTA of 93%, 92%, and 100%, respectively. Amikacin 25 mg/kg/day had a PTA of 94%.

Conclusion. In patients with kinetics similar to healthy subjects, standard doses of β-lactam antibiotics administered via intermittent infusion do no reach PD targets against *P. aeruginosa* isolates at UK HC. Amikacin 25 mg/kg/day and some prolonged infusions of β-lactams achieved PD targets against *P. aeruginosa*. There are opportunities for further study to examine the clinical application of MCS in designing empiric antimicrobial therapy.

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401. A Phase 1 Study of the Safety, Tolerability, and Pharmacokinetics of the Beta-lactamase inhibitor RPX7009 Alone, Meropenem Alone, and both in Combination (Carbavance) TID for 7 days in Healthy Adult Subjects

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Background. RPX7009 is a novel cyclic boronic acid beta-lactamase inhibitor with potent activity against serine carbapenemases (e.g., KPC). It is being developed in combination with meropenem for the treatment of serious gram-negative infections. This report describes the safety and pharmacokinetic data of the combination after 7 days of TID dosing in humans.

Parameter	RPX7009 1000 mg			Meropenem 1g			RPX7009 2000 mg			Meropenem 2g		
	Alone	Meropenem 1 g		Alone	RPX7009 1000 mg		Alone	Meropenem 2 g		Alone	RPX7009 2000 mg	
	Single (N=5)	First (N=5)	Last (N=5)	Single (N=5)	First (N=5)	Last (N=5)	Single (N=6)	First (N=6)	Last (N=6)	Single (N=24)	First (N=6)	Last (N=6)
C_{max} (mg/L)	21.61 ±8.54	26.61 ±4.80	19.92 ±1.67	18.98 ±3.65	20.19 ±3.97	17.04 ±1.65	51.44 ±15.16	51.86 ±7.26	53.61 ±10.95	42.54 ±15.24	49.85 ±5.03	49.05 ±3.82
AUC (mg·h/L)	77.54 ±15.07	81.11 ±15.96	66.57 ±3.59	59.77 ±12.09	65.83 ±15.35	54.52 ±3.93	159.214	170.442	190.49	150.94a	142.55a	167.71
Half-Life (h)	1.98 ±0.87	1.59 ±0.83	1.06 ±0.16	0.98 ±0.11	1.13 ±0.21	0.84 ±0.09	1.59 ±0.10	1.03 ±0.01	1.57 ±0.24	1.14 ±0.18	1.51 ±0.08	1.07 ±0.18
Vss (L)	21.44 ±5.21	20.23 ±5.20	19.99 ±1.81	21.59 ±5.11	21.08 ±4.50	21.19 ±2.49	21.57 ±9.93	21.84 ±9.50	17.59 ±1.98	22.59 ±2.24	21.74 ±9.03	23.08 ±9.20
Plasma Clearance (L/h)	15.51 ±2.82	12.70 ±2.50	14.55 ±2.05	17.59 ±3.71	15.84 ±3.57	18.4 ±2.24	18.45 ±9.23	12.08 ±2.09	10.42 ±1.85	14.13 ±2.98	14.49 ±2.57	14.77 ±2.84

Methods. Eighty healthy subjects were enrolled into one of 5 cohorts in the single ascending dose phase (250 mg, 1,000 mg, 1,500 mg and 2,000 mg RPX7009 in combination with 1 or 2 g of meropenem). Within each cohort subjects were administered either RPX7009 or meropenem on day 1, then were crossed over to either RPX7009 or meropenem on day 3, then were administered both RPX7009 and meropenem in combination on day 7 followed by 7 days of TID dosing. All infusions were administered over 3 hours. Intensive plasma and urine PK sampling was obtained after dosing and assayed using validated HPLC/MS methods.

Results. Pharmacokinetic parameters, derived using non-compartmental methods, for each drug alone and in combination in the RPX7009/meropenem 1 g/1 g and 2 g/ 2 g cohorts are shown.

No SAEs were observed. One subject who received meropenem 1 g/RPX7009 2 g discontinued early due to an AE of thrombophlebitis. All AEs, except 2 were mild or moderate in severity. Mild nausea was observed only in the subjects who received meropenem 2 g, either alone or in combination.

Conclusion. RPX7009 alone and in combination with 1 or 2g meropenem was safe and well tolerated at all doses tested, with no evidence that the safety profile of meropenem was changed by the addition of RPX7009. There was no accumulation of either RPX7009 or meropenem observed after 7 days of TID dosing. There were no effects of meropenem on the pharmacokinetics of RPX7009 or vice versa. RPX7009 in combination with meropenem is being advanced into patient studies.

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402. Pharmacokinetics of Extended vs Intermittent Intravenous Infusion of Meropenem in Critically Ill Patients Receiving Continuous Veno-Venous Haemofiltration

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Background. In patients receiving continuous veno-venous haemofiltration (CVVH), there is little agreement regarding the most appropriate dosing regimen of meropenem, ranging from 500 mg every 12- 24h to 2,000 mg every 8h. Meropenem is a time-dependent antibiotic and maintaining unbound drug concentrations above the minimum inhibitory concentration (MIC) of pathogen for at least 40% of the dosing interval is required for efficacy. Continuous (i.e., over 24 hours) or extended (EI, i.e., over a prolonged period of time of several hours during the dosing interval) infusions have been proposed to optimize pharmacokinetic/pharmacodynamic (PK/PD) properties, expecting improved clinical outcomes and decreased mortality, but CVVH was generally an exclusion criterion in these studies. The aim of this study was to compare the PK/PD of meropenem during intermittent infusion (II over 0.5 hours) or EI (over 3 hours) in critically ill patients receiving CVVH.

Methods. Patients with severe nosocomial pneumonia and receiving CVVH, were treated prospectively with meropenem 1g every 8 hours either over II (n = 7) or over EI (n = 6). The ultrafiltration flow rate was adjusted to 30-35 ml/kg/hour. At steady state, we calculated the proportion of patients in each group achieving an optimal T > MIC (≥ 40% or 100% of the dosing interval) for 1, 4 and 5 - fold an MIC of 2mg/L which is the European Committee on Antimicrobial Susceptibility Testing (EUCAST) sensitivity breakpoint for *Pseudomonas* spp, *Acinetobacter* spp and Enterobacteriaceae.

Results. Concentrations were: ≥ 40% T ≥ 2 mg/L in 100% of patients for 1 X and 4 X the MIC in both groups and 85.7% vs 100% ($P = 0.34$) for 5 X the MIC in II and EI, respectively; and 100% T ≥ 2 mg/L for II and EI in 100% vs 100%, 42.9% vs 100% ($P = 0.026$) and 28.6% vs 100% ($P = 0.0083$) for 1 X, 4 X and 5 X the MIC, respectively.

Conclusion. In patients with severe nosocomial pneumonia and receiving CVVH with current ultrafiltration flow rates, the optimum regimen of meropenem was 1g infused over 3h every 8h. In this setting, EI offered better PK/PD parameters than II, particularly for a therapeutic goal of 100% T > 4 and 5 - fold an MIC of 2 mg/L.

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403. Ceftolozane/Tazobactam (C/T) Dose Optimization in Patients with End Stage Renal Disease (ESRD) Requiring Hemodialysis (HD) Using Population Pharmacokinetics (pPK) and Monte Carlo Simulations (MCS)

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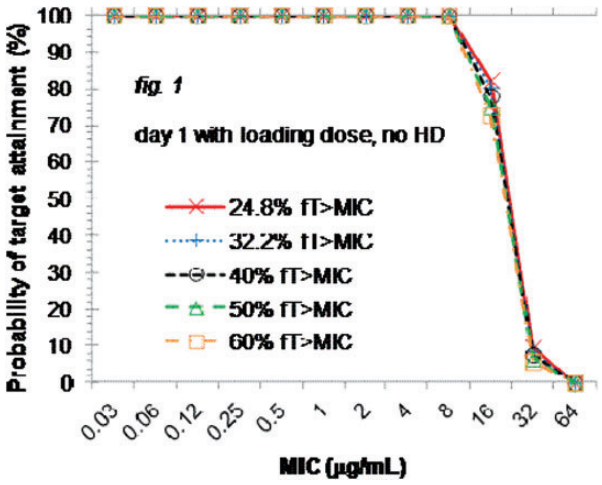
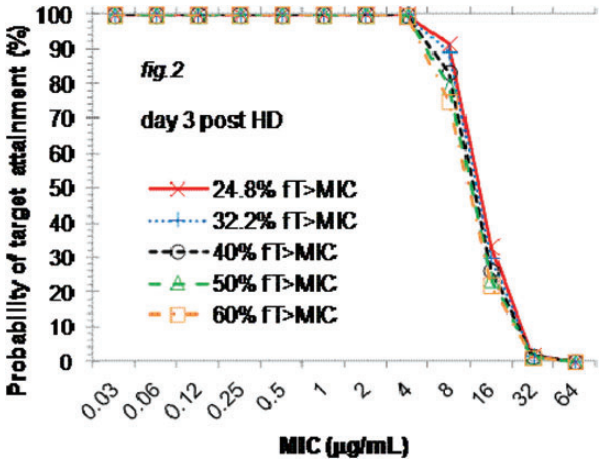
Background. C/T is being developed for treatment of complicated urinary tract infection and intra-abdominal infection. The objective of this study is to characterize the pPK of C/T, determine the probability of target attainment (PTA) of various dosing regimens and identify the optimal dose in subjects with ESRD on HD.

Methods. C/T plasma concentrations from 6 subjects with ESRD following a single dose without HD and a second dose with HD were used to develop a pPK model (Phoenix NLME). MCS was performed (SAS 9.3) to predict individual C/T concentrations in 5,000 subjects to assess the PTA for different dosing regimens and test a range of free-drug time above MIC ($fT > MIC$) targets, including 24.8% for bacteriostasis, 32.2% for bactericidal activity (1-log kill) as well as higher thresholds for bactericidal effects up to 60% $fT > MIC$. MCS used ceftolozane MIC determined with 4 mg/L tazobactam.

Results. A 2-compartment disposition model plus a covariate effect of HD best described the observed C/T plasma concentrations. The key parameter estimates for the final pPK model were: for ceftolozane, clearance (CL) and volume of distribution (Vc) for the central compartment of 0.34 L/hr and 6 L, respectively, with HD increasing CL and Vc by 60- and 4.7-fold, respectively; for tazobactam, CL and Vc of 3.07 L/hr and 11 L, respectively, with HD increasing CL and Vc by 6.6- and 1.5-fold, respectively. PTA exceeded 90% for an MIC up to 8 μg/mL for ceftolozane across all the tested scenarios. Out of all the tested scenarios, the 500 mg/250 mg C/T single loading dose followed by 100 mg/50 mg every 8 hours maintenance dose via 1-hr infusion achieved a >99% PTA against all targets up to an MIC of 8 mg/mL on day 1 (Figure 1) and >97% PTA on all other days without HD. The PTA for bactericidal activity on post HD days was 89% (Figure 2).

Conclusion. Plasma concentrations following C/T infusion in subjects with ESRD on HD can be best described with a 2-compartment disposition model plus a covariate effect of HD on both CL and Vc. In patients with ESRD on HD, a single loading dose of 500 mg/250 mg C/T infused over 1 hour, followed by 100 mg/50 mg every 8 hours infused over 1 hour, preferably at the earliest possible time following completion of each dialysis, achieved a high PTA and was identified as the optimal dose.





Disclosures. **A. Xiao**, Cubist Pharmaceuticals: Employee, Salary **G. Chandorkar**, Cubist Pharmaceuticals: Employee, Salary **G. Krishna**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **E. Hershberger**, Cubist Pharmaceuticals: Employee, Salary

404. Switching from Posaconazole (POSA) Suspension to Tablets in Patients with Hematologic Malignancy Results in Increased Serum Levels but no Hepatotoxicity

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Background. POSA suspension has been used effectively as prophylaxis and as salvage treatment of invasive fungal infections despite concerns of poor bioavailability. Recent studies suggest that the absorption of the new formulation of POSA tablet is minimally affected by food and they attain higher-average concentrations than the suspension in healthy subjects, and are well tolerated. As there are no published data in patients who received sequential POSA suspension and tablets, we reviewed our early experience in order to determine POSA serum level differences and to identify any association between drug exposure and hepatotoxicity.

Methods. We identified patients with hematologic cancer who switched from POSA suspension (400mg twice or 200mg 4 times a day) to tablet (300mg once daily) and had serum level drawn (December 2013-January 2014) in our cancer center. We calculated a median level for each patient when there was more than one level. Hepatotoxicity was defined as CTCAE (Common Terminology Criteria for Adverse Events, Version 4.0) grade 3 or higher. Electronic medical records were retrospectively reviewed for basic demographic, clinical and laboratory data.

Results. We identified 12 such patients. Twenty-one POSA suspension serum levels and 30 tablet levels were included. Target levels for prophylaxis (>700 ng/ml) and treatment (>1,000 ng/ml) were reached in 29 of 30 levels (97%) and 25 of 30 (83%) in patients receiving POSA tablets immediately prior to the time the level was drawn, but in only 12 of 21 (57%) and 5 of 21 (24%) in suspension (Figure 1A). Median POSA concentrations in the tablet group were higher (1910 ng/ml) than those in the suspension (748 ng/ml) group, and was significantly increased in patients who switched from suspension to tablet ($P < 0.01$) (Figure 1B). In 9 patients who had baseline normal liver function, mild asymptomatic increases in liver enzymes (5 patients) were observed after 7 days of treatment and all returned to normal in three weeks without discontinuation. Elevated liver enzymes are unlikely to be associated with drug exposure.

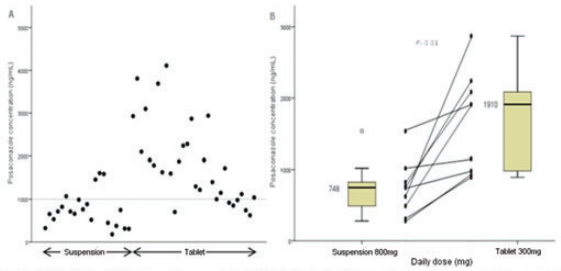

Figure 1. (A) Distribution of all posaconazole concentration. (B) The black line in the box and corresponding concentrations represent the median values. The black line between dots depicts an increased change of median concentration from suspension to tablet for each patient.

Conclusion. Switching from POSA suspension to tablets in patients with hematologic cancer results in increased serum level but no clinically relevant hepatotoxicity.

Disclosures. **D. Kontoyiannis**, Pfizer, Astellas Pharma US, Gilead, and Merck and Co., Inc. Research support, Research support

405. Risk of gentamicin vestibulotoxicity with different dosing regimens: a retrospective cohort study

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Background. Gentamicin is used for the treatment of resistant gram-negative bacterial infections. Studies comparing single-daily dosing (SDD) to multiple-daily dosing (MDD) show similar efficacy and less nephrotoxicity. Less is known about the effects of different dosing regimens on the development of ototoxicity. Among patients referred to our Multidisciplinary Neurotology Clinic (MNC), we compared the impact of SDD vs MDD of gentamicin in patients without acute kidney injury (AKI) on the development of vestibulotoxicity.

Methods. Data was collected for consecutive patients referred to our MNC between 1993 and 2012, including patient demographics, medical co-morbidities, concurrent medications, gentamicin dosing regimen, indications for use, cumulative dose and duration of therapy-to-time of diagnosis of vestibulotoxicity, and presence of AKI, determined by history or 1.5-fold elevation in serum creatinine.

Results. Forty-six patients were identified of whom 19 (43.1%) had no evidence of AKI. Eighteen (94.7%) had imbalance, 10 (52.6%) had oscillopsia (visual blurring with head movement), while only 1 (5.3%) and 2 (10.5%) complained of tinnitus and deafness, respectively. Vestibulotoxicity was confirmed through audiovestibular testing. Twelve patients had received SDD and 5 patients had received MDD; 2 were excluded from analysis because of incomplete dosing documentation. The median cumulative dose resulting in vestibulotoxicity in SDD compared to MDD patients was 4.8g (interquartile range (IQR) = 2.2-8.1g) vs 8.2g (IQR = 6.4-9.4g) ($p = 0.009$) and the median duration of therapy-to-time of diagnosis of vestibulotoxicity was 15d (IQR = 5-22d) vs 34.5d (IQR = 24.3-40.3d) ($p = 0.03$).

Conclusion. In patients referred to our MNC without AKI, gentamicin vestibulotoxicity occurred at a lower cumulative dose and with a shorter duration of therapy if they had received SDD vs MDD. As vestibulotoxicity may result in permanent impairment, including an inability to return to work, prospective safety evaluation for both dosing regimens is warranted.

Disclosures. **All authors:** No reported disclosures.

406. Pharmacokinetic modeling of linezolid dosing regimens for multidrug resistant tuberculosis

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Background. Linezolid (LNZ) is used to treat multidrug-resistant tuberculosis (TB) but use is limited by hematologic and neurologic toxicity that may be decreased with lower doses. We modeled pharmacokinetic (PK) parameters of four treatment regimens.

Methods. We used a two compartment model with nonlinear clearance to generate free LNZ concentration-time profiles for 2,000 virtual patients at steady state for four oral regimens: 600mg daily, 300mg daily, 300mg twice daily (BID), and 600mg 3x/week (wk). Population PK parameters were derived from a mixed group of healthy adults and septic patients. LNZ was modeled with 15 ± 7.1% mean protein binding. We assessed for efficacy: % of dosing interval (%T) >2x minimum inhibitory concentration (MIC), %T >1.2 mg/L (mutant prevention concentration, MPC), and for toxicity: % of patients with trough levels >9.96 mg/L (associated with hematologic toxicity), % T > 3.36 mg/L (associated with neurologic toxicity).

Results. Area under the curve was 85.8 mg*h/L for 300mg BID, 42.3 for 300mg daily, 85.8 for 600mg daily, and 80.6 (0-24 hours), 3.0 (24-48 hours) for 600mg 3x/wk.

Table: Median and Interquartile Range (IQR) for %T with free LNZ concentration > 2xMIC

	MIC							
Regimen	0.06125	0.125	0.25	0.5	1	2	4	8
300 BID	100 (100-100)	100 (100-100)	100 (100-100)	100 (78-100)	82 (48-100)	38 (15-100)	0 (0-62)	0 (0-0)
600 daily	100 (93-100)	100 (79-100)	98 (65-100)	78 (51-100)	57 (37-100)	35 (21-100)	13 (03-51)	0 (0-02)
300 daily	100 (79-100)	98 (65-100)	77 (50-100)	56 (36-100)	35 (21-99)	13 (03-48)	0 (0-17)	0 (0-0)
600 3x/wk (48hrs; Wed-Fri)	69 (46-100)	59 (39-100)	48 (33-100)	38 (25-91)	27 (18-66)	17 (10-40)	05 (1-16)	0 (0-0)

The percent of trough levels > 9.96 mg/L was 20.1% for 300mg BID,18.3% for 600mg daily, 13.8% for 300mg daily, and 11.5% for 600mg 3x/wk (48 hour trough).

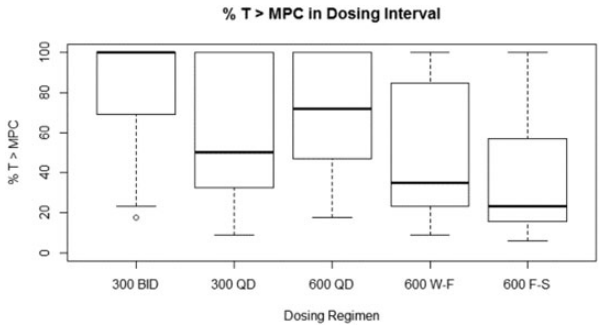

Figure 1. Boxplot of % T with free LNZ concentration > MPC

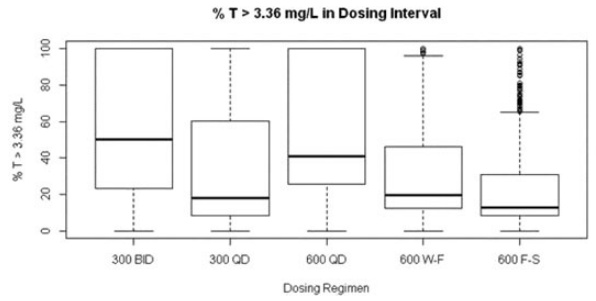

Figure 2. Boxplot of % T with LNZ concentration >3.36 mg/L

Conclusion. Among the low-dose regimens, 300mg daily has similar PK parameters for toxicity and higher parameters for efficacy as 600mg 3x/wk. The standard 600mg daily dose had lower efficacy parameters but improved toxicity parameters compared with 300mg BID. PK and MIC data from patients treated for TB and clinical trials are needed to determine lowest effective dose of LNZ for TB.

Disclosures. **All authors:** No reported disclosures.

407. Impact of methicillin-resistance on mortality, hospital stay and medical cost in patients with *Staphylococcus aureus* bacteremia and endocarditis: A meta-analysis

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) is highly prevalent in hospitals, and recently had emerged in community. Recent published data have shown an inconsistent association between methicillin-resistance and mortality in patients with *S. aureus* bacteremia (SAB). To understand the changing epidemiology of MRSA and the impact of methicillin-resistance on outcomes in adults with *S. aureus*bacteremia (SAB) and endocarditis, we performed a meta-analysis for database published after 2,000.

Methods. We searched studies with SAB or endocarditis using electronic databases such as Ovid-Medline, EMBASE-Medline, and Cochrane Library, as well as five local databases for published studies during the period of January 2000 to September 2011. Two reviewers independently selected cohort studies, which compared in-hospital mortality or SAB-related mortality in adults with MRSA infection to those with methicillin-susceptible *S. aureus* (MSSA).

Results. A total of 2,841 studies have been searched and of them, sixty-two with 17,563 adults were finally selected as eligible. A significant increase in overall mortality associated with MRSA, compared to that with MSSA, was evident with odds ratio (OR) of 1.95 (95% CI, 1.72-2.20, $I^2 = 43\%$; $P < 0.01$). In sixteen studies which reported SAB-related mortality, OR was 2.04 (95% CI, 1 63-2.55). Methicillin-resistance in 13 endocarditis studies increased the risk for mortality, with OR of 2.49 (95% CI, 1.41-4.42). The average length of stay in MRSA group was 10 days longer than that in MSSA (95% CI, 3.36-16.70) Of six that have reported medical costs, two studies were integrated in the analysis resulting in estimated medical costs to be $9,954.58 (95% CI, 8,951.99-10,957.17).

Conclusion. Methicillin-resistance is still associated with increased mortality, hospital stay and medical cost, compared with susceptible one in SAB for published studies since the year of 2000.

Disclosures. **All authors:** No reported disclosures.

408. The Comparison of in-vitro Activity of Daptomycin with Vancomycin and Teicoplanin against Methicillin-Resistant *Staphylococcus aureus* Strains Isolated from Bloodstream Infections

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Background. Methicillin-Resistant *Staphylococcus aureus* (MRSA) is a major problem in the healthcare setting. Bloodstream infections caused by MRSA is an important reason of mortality. Vancomycin and teicoplanin are used for many years in the treatment of MRSA. In contrast, daptomycin is one of the novel options. In this study, in-vitro activity of daptomycin was compared to vancomycin and teicoplanin against MRSA strains isolated from blood cultures.

Methods. The identification of the MRSA isolates was based on conventional microbiological methods and an additional automated identification system (*VITEK® 2*, bioMerieux, France). A total of 200 MRSA clinical isolates were included in the study. Daptomycin, vancomycin, and teicoplanin susceptibility were investigated by E-test (AB bioMerieux, Sweden). E-test was performed according to the instructions of the manufacturer. Susceptibilities of the strains to daptomycin, vancomycin, and teicoplanin were performed using the E-test according to the recommendations of CLSI 2013/EUCAST 2014 and the manufacturer.

Results. The MIC ranges were 0.25-1 µg/ml for daptomycin, 1.5-6 µg/ml for vancomycin, and 2-16 µg/ml for teicoplanin. Daptomycin was found to exhibite a good activity.

Conclusion. According to MIC values, daptomycin seems 6 times more effective than vancomycin and 8-16 times more effective than teicoplanin. With having the lowest MIC values, daptomycin may represent a therapeutic option for the infections caused by MRSA.

Disclosures. **All authors:** No reported disclosures.

409. Efficacy of Vancomycin against Biofilms of Neonatal *Staphylococcus epidermidis* Bloodstream Isolates

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Background. *S. epidermidis* causes nosocomial infections in neonates and critically ill patients, forming biofilms (BF) on surfaces of intravenous catheters. BF development is a major virulence factor, and BF cells are generally more resistant to antibiotics than their corresponding free-living forms. Our objectives were to a) assess the biofilm-producing capacity of *S. epidermidis* bloodstream isolates from neonates and b) evaluate the activity of vancomycin (VAN) against *S. epidermidis* BF.

Methods. BF's of 7 neonatal *S. epidermidis* isolates were produced using 96-well microtiter plates. Following appropriate dilutions from overnight cultures grown in TSB medium, 0.2ml of 10^6 bacteria/mL were used to inoculate microtiter wells. After a 24h-incubation at 37°C, the plates were washed with phosphate-buffered saline solution and stained with 1% safranin solution. BF formation was evaluated spectrophotometrically by optical density (OD) measurement at 595nm. The BF producer strain 35983 RP12 was used as control. BF-producing isolates were then incubated with no antibiotic or with VAN at two-fold dilutions of 0.007-256mg/L for an additional 24h, and bacterial damage (BD) was assessed by XTT reduction assay. BF MIC were determined as >50% BD compared to controls. All isolates were studied 4 times with 5 experimental replicates per condition. Differences were compared by ANOVA with Bonferroni post-test.

Results. Two of seven *S. epidermidis* isolates were strong BF producers (OD > 0.270; SP), whereas the remaining five produced BF of intermediate strength (0.14 < OD < 0.270; IP). Median VAN BF MIC for IP isolates was 32mg/L, the same as that of the control strain (p = ns). Maximum BD for those isolates was 65.6% at 64mg/L. VAN did not reach a BF MIC for SP isolates, as the maximum BD produced was 45% at 128mg/L. Of note, VAN efficacy at higher concentrations tended to decrease (45%-41.1% for SP and 64-60% for IP at 128-256mg/L).

Funded by NeoVanc European Commission program.

Conclusion. Despite the variable BF production among neonatal *S. epidermidis* isolates, high MICs were observed for VAN against mature BF of *S. epidermidis*. Even at very high concentrations, VAN was not totally effective against BF, suggesting difficulty in eradication of *S. epidermidis* BF.

Disclosures. **All authors:** No reported disclosures.

410. Tracking Linezolid Antimicrobial Activity and Resistance in North America: Results from LEADER 2013 Program

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Background. The LEADER Program has monitored the activity of linezolid (LZD) and comparator agents in USA medical centers since 2004. The percent of non-susceptible (NS) Gram-positive (GP) monitored isolates has remained below 1% (range, 0.14-0.45%; 0.17% in 2012).

Methods. In 2013, a total of 7,183 GP pathogens were sampled from 60 medical centers across the USA. Isolates were susceptibility (S) tested by CLSI reference broth microdilution methods. LZD NS isolates were confirmed by repeated reference S testing, with the LZD Etest (bioMerieux, Hazelwood, Missouri) and CLSI disk diffusion methods.

Results. A total of 3,035 *S. aureus* strains were submitted. Methicillin-resistant *S. aureus* (MRSA; 47.9%) varied from 35.1% (Middle Atlantic) to 58.7% (East South Central). Resistance rates among MRSA for many antimicrobial agents were much higher than in MSSA. Examples included the β-lactam agents, levofloxacin (MRSA, 64.2%, MSSA, 11.2%), clindamycin (26.7%, 5.3%), and erythromycin (87.8%, 31.9%). The LZD $MIC_{50/90}$ for *S. aureus* was 1/1 µg/ml (S, 99.9%). There were two LZD NS isolates (MRSA from California and Michigan); both contained *cfr* and L3 mutations. The MIC_{50} and modal MIC for MRSA and MSSA were the same. A total of 580 CoNS isolates exhibited a LZD $MIC_{50/90}$ at 0.5/1 µg/ml (S, 99.5%). The three LZD NS CoNS isolates contained mutations at 23S rRNA and L3 and/or L4. LZD was active against Enterococci with a $MIC_{50/90}$ at 1/1 µg/ml and 99.4% S. All LZD NS enterococci had a G2476T mutation and one also contained a *cfr*. S to LZD for 399 viridans group streptococci (VGS) and 964 β-hemolytic streptococci was 99.7 and 100.0%, respectively. There was one *S. sanguinis* isolate (LZD NS [MIC, 4 µg/ml]), which demonstrated a mutation at the G2576 nucleotide of the 23S rRNA. LZD S for all organisms tested (7,183) was 99.83% with only 12 isolates (6 Enterococci, 2 *S. aureus*,3 *S. epidermidis,* 1 VGS) testing NS.

Conclusion. LZD among USA medical centers demonstrated excellent activity and a sustained S rate of 99.83%. LZD MIC population distributions remain stable without evidence of "MIC creep" among monitored species. These data show no evidence of widespread dissemination of the *cfr* resistance determinant in LEADER Program monitored USA medical centers.

Disclosures. **R. K. Flamm**, Pfizer Inc.: Grant Investigator, Research grant **J. M. Streit**, Pfizer Inc.: Grant Investigator, Research grant **J. E. Ross**, Pfizer Inc.: Grant Investigator, Research grant **R. E. Mendes**, Pfizer Inc.: Grant Investigator, Research grant **R. N. Jones**, Pfizer Inc.: Grant Investigator, Research grant **P. Hogan**, Pfizer Inc.: Employee, Salary

411. Epidemiology and Antimicrobial Susceptibility of Gram-Negative Pathogens Causing Intra-Abdominal Infections in Pediatric Patients in the U.S. – SMART 2010-2013

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Background. Community-associated (CA) and hospital-associated (HA) intra-abdominal infections (IAI) are a major cause of morbidity and, if not properly treated, mortality. The Study for Monitoring Antimicrobial Resistance Trends (SMART) has tracked epidemiology and susceptibility of aerobic gram-negative pathogens (GNP) causing IAI since 2002; this report summarizes the findings for pediatric patients in the U.S. during 2010-2013.

Species (n All†/n HA/n CA)	% of all GNP			AMK - %S			CAZ - %S			ETP - %S			TZP - %S		
	All†	HA	CA	All†	HA	CA	All†	HA	CA	All†	HA	CA	All†	HA	CA
E. coli (142/54/84)	47	41*	55*	98	98	98	95	94	95	99	100	98	96	96	95
P. aeruginosa (39/19/16)	13	15	10	95	89	100	74	79	81	NB	NB	NB	79	84	88
E. cloacae (30/17/12)	10	13	8	97	94	100	74	79	81	90	88	92	73	65	83
K. pneumoniae (24/8/12)	8	6	8	96	88	100	83	75	100	96	88	100	83	75	92
All GNP (300/131/154)				96	96	96	87	82	94	81	82	82	87	85	91

AMK=amikacin, CAZ=ceftazidime, ETP=ertapenem, TZP=piperacillin-tazobactam, S=susceptible, NB=no breakpoint, GNP=gram-negative pathogens.
† Includes isolates without information on length of stay at time of specimen collection; therefore, "n All" does not equal the sum of "n HA" and "n CA".
* Significant difference in prevalence between HA and CA (p<0.05, Fisher exact test)

Methods. 23 U.S. hospitals each collected up to 100 non-selected, consecutive GNP per year, including 300 pediatric GNP in 2010-2013. Organisms were classified as either CA or HA if isolated <48h or ≥48h from admission. Susceptibility and ESBL phenotypes were determined using CLSI broth microdilution.

Results. The table shows the susceptibility of the top 4 species and of all GNP combined (using appropriate CLSI breakpoints and assuming 0% susceptible for species with no breakpoints for any given drug). Only selected agents are shown (one agent per major drug class tested).

Analysis of extended-spectrum β-lactamase (ESBL) phenotypes showed 4%, 6%, and 4% of *E. coli* and 13%, 13%, and 0% of *K. pneumoniae* (albeit with small n's) to be ESBL-positive in all, HA, and CA IAI, respectively.

Conclusion. Although the top 4 species found in HA and CA IAI were identical, the proportion of *E. coli* was significantly different: 41% in HA IAI vs 55% in CA IAI. *P. aeruginosa* and *E. cloacae* tended to be more prevalent in HA IAI. Susceptibility was frequently lower in HA than CA. Of the agents tested, AMK had the highest *in vitro* activity vs all GNP. ETP showed excellent activity vs *Enterobacteriaceae*. Differences in species prevalence and susceptibility between HA and CA pediatric IAI indicate a need for different treatment options for these infections.

Disclosures. **S. Lob**, Merck: Independent Contractor, Consulting fee **R. Badal**, Merck: Independent Contractor, Consulting fee **A. Johnson**, Merck: Independent Contractor, Consulting fee **M. Hackel**, Merck: Independent Contractor, Consulting fee **S. Bouchillon**, Merck: Independent Contractor, Consulting fee **D. Sahm**, Merck:

Independent Contractor, Consulting fee **D. Hoban**, Merck: Independent Contractor, Consulting fee

412. *In vitro* Activity of Key Antimicrobial Agents Against Bacterial Isolates From Intra-abdominal (IAI) and Skin and Wound (SW) Infections: Europe 2004-2013

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Background. IAI and SW infections present major challenges for hospitalized patients. Monitoring the resistance profiles expressed by the causative organisms is important. Therefore, data from the Tigecycline European Surveillance Trial (TEST) program were analyzed for the resistance patterns observed throughout Europe.

Methods. Isolates were collected and tested locally by broth microdilution according to appropriate CLSI guidelines. **Results** of this study were based on isolates tested from 26 European countries from 2004 – 2013.

Results. See table.

Organism (n): IAI/SW	Antimicrobial: Percent Susceptible: IAI/SW[a] TIG	AK	AMP	CFT	LEV	MER	PT	VAN
Acinetobacter spp 163/1546	na/na	66/70	na/na	28/35	50/58	53/70	45/55	na/na
Enterobacter spp 615/2478	96/96	98/98	2/4	53/65	84/89	96/98	68/78	na/na
E. coli 1122/1748	100/100	99/99	38/32	84/76	74/64	99/100	91/90	na/na
ESBL 128/311	100/100	94/96	na/na	na/na	25/22	98/99	74/73	na/na
K. pneumoniae 485/1156	97/96	96/95	2/3	75/67	79/73	95/93	78/76	na/na
ESBL 82/266	94/96	88/88	na/na	4/0	89/34	89/88	32/43	na/na
P. aeruginosa 367/2439	na/na	93/93	na/na	na/na	70/67	65/76	76/75	na/na
S. marcescens 101/861	94/96	99/98	5/4	78/83	93/93	96/99	87/94	na/na
E. faecalis 366/1067	100/100	na/na	98/99	na/na	74/8	na/na	na/na	98/99
E. faecium 381/356	100/100	na/na	21/17	na/na	17/17	na/na	na/na	91/90
S. aureus, MSSA 100/3250	100/100	na/na	na/na	na/na	95/92	na/na	na/na	100/100
S. aureus, MRSA 42/1302	100/100	na/na	na/na	na/na	12/16	na/na	na/na	100/100
S. agalactiae 27/955	100/100	100/100	100/100	100/100	100/98	100/100	na/na	100/100

A na = breakpoints not defined or non-applicable, TIG (tigecycline; FDA breakpoints), AK (amikacin), AMP (ampicillin), CFT (Ceftriaxone), MER (meropenem), LEV (levofloxacin) PT (piperacillin/tazobactam), VAN (vancomycin)

Conclusion. Against *Enterobacteriaceae*, including ESBL-producers, TIG, AK and MER were the most active agents; against gram-positive cocci TIG resistance was not encountered. For *Acinetobacter* spp. all agents demonstrated poor activity; against *P. aeruginosa* AK and PT were the most active agents. Given the propensity of the bacteria associated with IAI and SW infections, continued monitoring of antimicrobial activity in Europe is warranted.

Disclosures. **D. Hoban**, Pfizer: Independent Contractor, Consulting fee **S. Bouchillon**, Pfizer: Independent Contractor, Consulting fee **R. Badal**, Pfizer: Independent Contractor, Consulting fee **D. Sahm**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

413. *In Vitro* Activity of Tigecycline against Commonly-Isolated Pathogens of Skin and Skin Structure Infections in the United States – TEST 2011-2013

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Background. Tigecycline has been approved for the treatment of complicated skin and skin structure infections (SSTIs) in the United States (US) since 2005. Since introduction, tigecycline has shown little development of resistance to common pathogens of SSTIs, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococci (VRE) and extended-spectrum β-lactamase (ESBL) –producing *Enterobacteriaceae*. The Tigecycline Evaluation Surveillance Trial (TEST) has been monitoring the activity of tigecycline and comparators against multiple pathogens collected worldwide since 2004. This study reports on the activity of tigecycline against recent clinical isolates from SSTIs in the US.

Methods. A total of 4,229 clinical isolates from SSTI were collected and identified in 124 cumulative sites in the US in 2011-2013. MICs were determined as specified by CLSI at each site using prepared broth microdilution panels and interpreted according to CLSI guidelines. Susceptibility of tigecycline was interpreted using FDA breakpoints.

Results. The ESBL rates for *Escherichia coli* and *Klebsiella pneumoniae* were 6.2% and 11.6%, respectively. 58.2% of *S. aureus* were methicillin-resistant. Summary MIC data (μg/ml) and %S for tigecycline vs select isolates are shown in the table.

Organism	N	MIC_{50}	MIC_{90}	%S
Acinetobacter baumannii	271	0.25	2	na
Enterobacter spp.	545	0.5	1	96.2
Enterococcus spp.	377	0.06	0.12	99.7
ALL VRE Isolates	61	0.06	0.12	100
Escherichia coli	369	0.12	0.25	99.7
E. coli, ESBL	23	0.12	0.5	100
Klebsiella pneumoniae	268	0.5	1	95.5
K. pneumoniae, ESBL	31	0.5	2	93.6
Pseudomonas aeruginosa	426	8	> 8	na
Serratia marcescens	228	1	2	96.9
S. aureus, MRSA	747	0.12	0.25	100
S. aureus, MSSA	537	0.12	0.12	100

na=No breakpoint available

Conclusion. Tigecycline exhibited excellent *in vitro* activity (93% susceptibility or higher) against major SSTI pathogens from the United States, including resistant phenotypes. MIC_{90} values were 0.12 μg/ml and 0.25 μg/ml for VRE and MRSA, respectively. While MIC_{90} values for ESBL-positive isolates were ≤2 μg/ml, the high rate of ESBL-positive *K. pneumoniae* (11.6%) is cause for concern.

Disclosures. **M. Hackel**, Pfizer: Independent Contractor, Consulting fee **S. Lob**, Pfizer: Independent Contractor, Consulting fee **S. Bouchillon**, Pfizer: Independent Contractor, Consulting fee **D. Sahm**, Pfizer: Independent Contractor, Consulting fee **D. Hoban**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

415. *In Vitro* Potency of Ceftolozane/Tazobactam against *Pseudomonas aeruginosa* Displaying Multidrug Resistance

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Background. Multidrug resistance (MDR) among pathogens, defined as resistance to three or more antimicrobial classes, is an increasingly prevalent event in the management of the infected hospitalized patient. While Enterobacteriaceae with enzyme-mediated resistance and *Acinetobacter* spp. may satisfy this criterion, *P. aeruginosa* (PSA) is a nosocomial pathogen that has a history of intrinsic or developed resistance to many commonly utilized agents. As such, this organism is frequently considered among the most difficult-to-treat MDR pathogens.

Methods. Non duplicate, non urine PSA (n = 973) from 42 US hospitals collected between June 2013 - March 2014 were phenotypically assessed against a variety of antimicrobials using standard CLSI broth microdilution methods. MDR organisms were selected if they displayed resistance to 3 or more of the following classes as represented by resistance to: ciprofloxacin (CIP, MIC ≥4 mg/L), imipenem (IMP, MIC ≥8 mg/L), ceftazidime (CAZ, MIC ≥32 mg/L), piperacillin/tazobactam (TZP, MIC ≥128 mg/L), and tobramycin (TOB, MIC ≥16 mg/L). For comparative purposes, the breakpoint of 8mg/L was used for ceftolozane/tazobactam (TOL/TAZ).

Results. 12% (n = 115) of PSA were determined to be MDR. Rank order susceptibility (MIC_{90}, mg/L) was as follows: colistin 97% (1), TOL/TAZ 86% (32), TOB 51% (128), aztreonam 19% (128), IMP 17% (32), meropenem 16% (32), CIP 13% (32), CAZ 11% (128), cefepime 10% (128), and TZP 9% (512). While the MIC_{90} was 32 for TOL/TAZ, 30% of these organisms had MICs ≤1 mg/L, 24% = 2 mg/L, 26% = 4 mg/L, and 6% = 8 mg/L

Conclusion. In this recent collection of PSA obtained from acute-care hospitals across the US, 12% were MDR based on conventional therapeutic benchmarks. While colistin displayed the highest susceptibility and lowest MIC_{90} value, concerns related to its pharmacodynamic optimization and toxicity make alternative therapies a necessity. TOL/TAZ appears to retain potency against a majority (86%) of these MDR PSA where as other agents tested had %S of 9 -51%. Additional clinical data are needed to delineate the potential effectiveness of TOL/TAZ in the setting of infection with MDR PSA.

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416. Comparing Bacteria Isolated from Patients with Spinal Cord Injury vs All Patients

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Background. Individuals with spinal cord injury or disorder (SCI/D) are at high risk for infections and antimicrobial resistance compared to the general patient population due to factors such as frequent hospitalization, previous antibiotic use, and frequent and chronic use of invasive devices. Increasing resistance of complex infections can result in inadequate empiric prescribing. Thus, the purpose of this project was to evaluate the prevalence and resistance patterns of bacteria isolated from SCI/D patients as compared to a general patient population.

Methods. Microbiology laboratory reports from October 1, 2012-September 30, 2013 for all cultures (inpatient and outpatient) obtained at a Midwestern Veterans Affairs facility were evaluated. Only the first isolate cultured from a single patient was included unless the susceptibility pattern changed. Antimicrobial susceptibility results of individual isolates were compiled into a standardized SCI/D-specific antibiogram and compared to a compiled facility-wide antibiogram using chi-square tests.

Results. A total of 1,716 cultures were evaluated; where 711 were from SCI/D. Frequencies of pathogens isolated in SCI/D and facility-wide were similar; *Escherichia coli* was most frequent, followed by *Staphylococcus aureus*, Enterococcus sp., *Pseudomonas aeruginosa*, and Coagulase-Negative Staphylococcus (CoNS). The *P. aeruginosa* isolates from SCI/D were less susceptible to ciprofloxacin (46.5% vs 58.4%, p = 0.01), meropenem (55.6% vs 69.3%, p = 0.03), and tobramycin (73.6% vs 81.3%, p = 0.04). In SCI/D, *S. aureus* and CoNS isolates were less susceptible to oxacillin, (27.8% vs 50.3%, p < 0.0001 and 21.7% vs 40.3%, p = 0.01, respectively). About three-fourths of Klebsiella sp. ESBLs and *Proteus mirabilis* ESBLs isolates were isolated from SCI/D patients.

Conclusion. Although the frequencies of pathogens isolated were similar, significant differences in susceptibilities were identified for Staphylococcus sp. and *P. aeruginosa*. In addition, the frequency of ESBLs in cultures obtained from patients with SCI/D is worrisome. Differences in susceptibilities suggest that developing an SCI-unit specific antibiogram may be useful in choosing appropriate empiric treatment.

Disclosures. **All authors:** No reported disclosures.

417. Comparison of ESBL rates and susceptibility of *E. coli* from IAI in the USA, Canada, and Mexico 2009-2013

Robert Badal, BS; Sibylle Lob, MD, MPH; Meredith Hackel, PhD, MPH; Samuel Bouchillon, MD; Aaron Johnson, BS; Daryl Hoban, PhD; Dan Sahm, PhD; International Health Management Associates, Inc., Schaumburg, IL

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Background. Extended-spectrum β-lactamase (ESBL) producing *E. coli* are multidrug resistant and pose therapeutic challenges worldwide. This report from the Study for Monitoring Antimicrobial Resistance Trends (SMART) compares ESBL rates and susceptibility of *E. coli* from IAI from the USA, Canada, and Mexico in 2009-2013.

Methods. 44 laboratories (28 USA, 12 Canada, 4 Mexico) each collected up to 100 consecutive gram-negative organisms from IAI each year; 5,183 of 12,421 (42%) were *E. coli*. Susceptibility was determined using CLSI broth microdilution methods and breakpoints. Trends in ESBL rates were assessed with the Cochran-Armitage test.

Results. From 2009-2013, the proportion of ESBL+ *E. coli* showed significant increasing trends in all three countries. Susceptibility of selected drugs in 2013 (values ≥90% are shaded) and ESBL rates from 2009-2013 are shown in the table.

Sensitivity analysis for the USA using only the 13 sites that submitted isolates in all 5 years confirmed the increasing ESBL rates (6, 6, 10, 6, and 14% in the years 2009-2013); however, a similar analysis for Canada did not find a significant trend (in 5 of 12 sites) in part due to a larger drop in 2013 than in the full analysis (9, 8, 11, 19, 10%). All 4 Mexican sites participated in all 5 years.

In 2013, only AMK, ETP and IPM showed %S >90% in all 3 countries against *E. coli*. The much higher ESBL rate in Mexico corresponded to dramatically lower susceptibility rates than North America to most other drugs.

Despite having significantly lower ESBL+ *E. coli* rates than Mexico, the US and Canada must take steps to contain further spread of these organisms, and Mexico itself must continue efforts (such as restricting fluoroquinolone use) to address this situation in which ESBL+ is the predominant phenotype among *E. coli*.

		% Susceptible in 2013									
	n	AMK	SAM	FEP	CTX	FOX	CAZ	ETP	IPM	LVX	TZP
Canada	257	99.2	59.1	90.7	86	93.8	88.7	99.2	99.6	71.6	93.8
USA	548	99.1	49.5	92.5	88.9	91.8	91.4	99.5	99.6	69.3	94.2
Mexico	210	98.6	19.5	42.4	37.6	83.3	42.4	99.1	100	31.4	88.1

	% ESBL+ (total n)				
	2009	2010	2011	2012	2013
Canada*	9% (232)	7% (191)	12% (258)	16% (294)	11% (257)
USA*	6% (551)	7% (614)	9% (552)	6% (602)	12% (548)
Mexico*	40% (193)	65% (236)	55% (207)	61% (238)	59% (210)

AMK=amikacin, SAM=ampicillin-sulbactam, FEP=cefepime, CTX=cefotaxime, FOX=cefoxitin, CAZ=ceftazidime, ETP=ertapenem, IPM=imipenem, LVX=levofloxacin, TZP=piperacillin-tazobactam.
*Significant increasing trend (p<0.05).

Conclusion. *E. coli* ESBL rates were much higher in Mexico, and although all 3 countries showed increasing trends in the full analysis, they appear to be leveling off in Canada and Mexico.

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418. *Antimicrobial Profile of Enterobacteriaceae from North America from 2013*

Brian Johnson, BS[1]; Jack Johnson, MS, MBA[1]; Samuel Bouchillon, MD[1]; Daryl Hoban, PhD[1]; Meredith Hackel, PhD, MPH[1]; Sibylle Lob, MD, MPH[1]; Douglas Biedenbach, BS[1]; Heidi Leister-Tebbe, BS[2]; [1]International Health Management Associates, Inc., Schaumburg, IL; [2]Pfizer Inc., Collegeville, PA

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Background. *Enterobacteriaceae* play an important role in the pathogenesis of hospital infections worldwide. The Tigecycline Evaluation Surveillance Trial (TEST) examines the susceptibility of pathogens isolated from multiple infectious processes from patients in geographically diverse populations. With the increase of antimicrobial resistance, continued surveillance and susceptibility testing of pathogens isolated from patients in North America is essential. The purpose of this report is to examine the susceptibility of selected *Enterobacteriaceae* species isolated from patients in the United States and Canada from 2013.

Methods. 4,010* clinically significant *Enterobacteriaceae* sp. were obtained from patients with a wide spectrum of infections in patients in the United States and Canada. MICs were determined from 30 sites in 2013 using supplied broth microdilution panels. Susceptibility was interpreted according to CLSI guidelines.

Results. The % susceptible for those 4,010 gram-negative bacilli against tigecycline and comparative antimicrobial agents is shown in the following table:

	Drug % Susceptible							
Organism (N)	AK	AC	CPM	CFT	LEVO	MER	PT	TIG
E. aerogenes (272)	99.3	3.7	98.9	77.6	97.4	98.5	86.0	97.4
E. asburiae (102)	100	5.9	100	80.4	97.1	100	91.2	100
E. cloacae (688)	99.9	4.7	95.6	70.4	93.9	98.6	82.1	94.9
E. coli (1232)	99.8	75.1	91.8	86.7	69.6	98.7	96.1	99.7
K. oxytoca (259)	100	87.6	98.1	90.0	95.0	99.2	91.1	98.8
K. pneumoniae (957)	98.6	85.6	90.9	84.1	86.7	95.2	89.7	95.0
S. marcescens (462)	100	1.5	98.7	85.7	91.6	98.1	96.5	96.3

AK=Amikacin, AC=Amoxicillin-Clavulanate, CPM=Cefepime, CFT=Ceftriaxone, LEVO=Levofloxacin, MER=Meropenem PT=Piperacillin-Tazobactam, TIG=Tigecycline

*n's ≤ 15 are not reported

Conclusion. *In vitro* tigecycline, meropenem and amikacin continue to be the most active antimicrobials against all *Enterobacteriaceae*. In the US and Canada the existence of levofloxacin resistant *E. coli* continues to be an issue. Additional monitoring of antimicrobial resistance in hospital pathogens in North America is warranted.

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419. Susceptibility trends for *P. aeruginosa* and *A. baumannii* from IAI in the USA: SMART 2009-2013

Sibylle Lob, MD, MPH; Robert Badal, BS; Samuel Bouchillon, MD; Meredith Hackel, PhD, MPH; Aaron Johnson, BS; Dan Sahm, PhD; Daryl Hoban, PhD; International Health Management Associates, Inc., Schaumburg, IL

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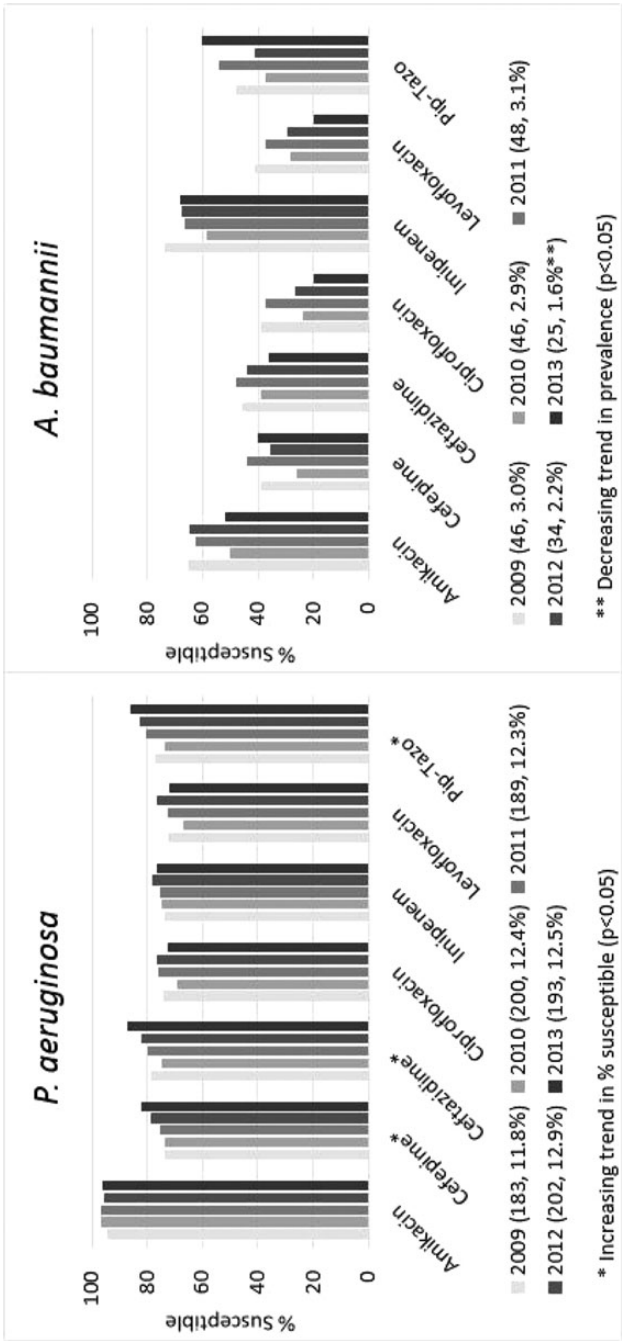
Background. Because of their resistance to many antimicrobials, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* remain pathogens of interest in intra-abdominal infections (IAI), representing approximately 10% and 3%, respectively, of aerobic gram-negative pathogens in IAI globally. This report from the Study for Monitoring Antimicrobial Resistance Trends (SMART) evaluates the susceptibility of *P. aeruginosa* and *A. baumannii* from IAI in the USA between 2009 and 2013.

Methods. 27 US laboratories each collected up to 100 consecutive aerobic or facultative gram-negative isolates from IAI each year. Susceptibility was determined using the CLSI broth microdilution method and breakpoints. Linear trends in susceptibility were assessed with the Cochran-Armitage test.

Results. Susceptibility trends and prevalence of 967 *P. aeruginosa* and 199 *A. baumannii* isolates are shown in the figures. N and % of all gram-negative pathogens are listed in the legend.

A sensitivity analysis was conducted for *P. aeruginosa* susceptibility using only the 12 sites that submitted isolates in all 5 years. The significant increasing trends for ceftazidime and piperacillin-tazobactam were confirmed, the trend for cefepime approached significance ($p = 0.08$), and an additional significant increasing trend was found for levofloxacin ($p = 0.03$).

Conclusion. *P. aeruginosa*'s prevalence was stable at around 12% of gram-negative pathogens isolated from IAI in the USA from 2009 to 2013. Its susceptibility to cefepime, ceftazidime and piperacillin-tazobactam showed statistically significant change ($p < 0.05$), with these drugs demonstrating increasing susceptibility. *A. baumannii*'s prevalence was lower and decreased significantly over the 5 years, but its susceptibility remained stable for all tested drugs between 2009 and 2013. Resistance does not appear to be increasing in these difficult-to-treat IAI pathogens.



Disclosures. **S. Lob**, Merck: Independent Contractor, Consulting fee **R. Badal**, Merck: Independent Contractor, Consulting fee **S. Bouchillon**, Merck: Independent Contractor, Consulting fee **M. Hackel**, Merck: Independent Contractor, Consulting fee **A. Johnson**, Merck: Independent Contractor, Consulting fee **D. Sahm**, Merck: Independent Contractor, Consulting fee **D. Hoban**, Merck: Independent Contractor, Consulting fee

420. Susceptibility of *Enterobacteriaceae* in European and North American Long-term Care Facilities, 2011-2013

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Background. Pathogens in some long-term care (LTC) facilities have been reported to have high antimicrobial resistance with a large proportion of multi-drug resistant (MDR) strains. Using data from the Tigecycline Evaluation and Surveillance Trial (TEST), *Enterobacteriaceae* from LTC settings were compared to other inpatient and outpatient settings in Europe and North America.

Methods. 512 *Enterobacteriaceae* isolates from various specimen sources were collected from LTC facilities, and 27,569 *Enterobacteriaceae* from inpatient and outpatient settings in 15 countries in Europe and North America from 2011 to 2013. MICs were determined at each site using CLSI broth microdilution method and interpreted according to CLSI/FDA guidelines. Isolates were categorized as MDR if resistant to ≥3 drug classes.

Results. MIC_{90} (mcg/ml), % susceptible (%S), and % MDR among *Enterobacteriaceae* from each setting are shown in the table. %S values ≥ 90% are shaded.

Of the species with n >10, *Enterobacter cloacae* had the highest proportion of MDR strains in LTC and inpatient settings (41.4% and 39.8%, respectively), whereas *Citrobacter freundii* had the highest for outpatients (34.7%)

	LTC (n=512)		Inpatients (n=22,155)		Outpatients (n=5,414)	
	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S
Amikacin	8	96.7	4	98.5	4	98.9
Amox-Clav	>32	43.4	>32	45.1	>32	51.7
Ampicillin	>32	11.9	>32	14.3	>32	17.9
Cefepime	>32	83.2	16	89.4	4	92.5
Ceftriaxone	>32	65.4	>32	73.8	32	81.5
Levofloxacin	>8	72.5	>8	81.3	8	82.1
Meropenem	0.25	92.8	0.25	97.2	0.12	97.9
Minocycline	16	78.1	8	81.7	8	84.5
Pip-Tazo	>128	80.1	64	85.2	16	91.3
Tigecycline	2	96.3	1	97.1	1	98.4
% MDR	31.1		25.4*		18.4*	

* Significantly lower than LTC (p<0.05, chi-square test)

Conclusion. A significantly higher proportion of *Enterobacteriaceae* were MDR in LTC settings than in inpatients and outpatients. All study drugs showed lower susceptibility in LTC isolates than in the other two settings. Amikacin, meropenem, and tigecycline were the only drugs studied that showed only minor differences in %S between the three settings. These three agents also demonstrated the highest *in vitro* activity against *Enterobacteriaceae,* with susceptibility >90% in all three settings. Empiric therapy decisions should take into account the high proportion of MDR isolates in LTC settings.

Disclosures. **S. Lob**, Pfizer: Independent Contractor, Consulting fee **B. Johnson**, Pfizer: Independent Contractor, Consulting fee **R. Badal**, Pfizer: Independent Contractor, Consulting fee **M. Hackel**, Pfizer: Independent Contractor, Consulting fee **S. Bouchillon**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

421. Activity of Tigecycline and Comparators Against Lower Respiratory Tract (LRT) Isolates of *Enterobacteriaceae* from North America and Europe: 2009-2013

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Background. *Enterobacteriaceae* play a significant role in LRT infections in at risk patients, especially in the healthcare associated environment. Treatment options are increasingly limited due to increased resistance to cephalosporins and other antimicrobials, thus warranting careful monitoring of resistance trends. The purpose of this study was to determine the *in vitro* activity of Tigecycline and other key antibiotics against LRT isolates of *Enterobacteriaceae* obtained from patients in North American and European hospitals.

Methods. From 2009-2013 8,361 *Enterobacteriaceae* from LRT specimens were obtained from geographically distributed sites as part of the multi-year Tigecycline Evaluation Surveillance Trial (TEST). MICs were determined by the local

laboratory using supplied microdilution panels and interpreted according to CLSI guidelines.

Results.

	Percent Susceptible									
	2009		2010		2011		2012		2013	
	NA[a]	EU[a]	NA	EU	NA	EU	NA	EU	NA	EU
Drug n =	440	601	576	1472	537	1100	943	1683	390	619
Amikacin	98.0	97.5	97.9	97.4	98.3	95.8	98.3	98.5	98.7	99.0
Cefepime	92.7	91.4	93.6	90.0	92.0	86.9	93.4	88.5	90.8	90.6
Ceftriaxone	73.9	72.1	72.1	67.7	75.6	69.7	80.3	71.0	78.2	71.1
Levofloxacin	83.4	84.2	86.6	82.1	84.4	81.4	87.6	83.6	85.4	83.4
Meropenem	96.4	97.2	96.2	98.7	97.8	96.5	97.3	97.0	96.2	97.7
Pip-Tazo[b]	83.4	80.4	85.2	78.9	83.6	79.3	86.2	83.1	88.2	85.0
Tigecycline	98.0	94.7	96.4	96.4	96.8	97.7	96.3	97.0	96.2	97.0

[a]NA: North America, EU: Europe; Pip-Tazo = piperacillin/tazobactam

Conclusion. Tigecycline, amikacin and meropenem consistently demonstrated the highest % susceptibility (> 95%) against LRT isolates of *Enterobacteriaceae* regardless of study year or geographic region. Ceftriaxone was less active against European isolates than against North American isolates overall irrespective of study year possibly due to extended-spectrum β-lactamase prevalence in Europe vs North America. Levofloxacin susceptibility was stable in the mid-80% range over all years. Tigecycline is not indicated for lower respiratory tract infections caused by *Enterobacteriaceae.*

Disclosures. **D. Hoban**, Pfizer: Independent Contractor, Consulting fee **S. Bouchillon**, Pfizer: Independent Contractor, Consulting fee **M. Hackel**, Pfizer: Independent Contractor, Consulting fee **B. Johnson**, Pfizer: Independent Contractor, Consulting fee **R. Badal**, Pfizer: Independent Contractor, Consulting fee **J. Johnson**, Pfizer: Independent Contractor, Consulting fee **S. Hawser**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

422. Antimicrobial Susceptibility Profiles of Key Blood and Respiratory Bacterial Isolates from Africa and the Middle East

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Background. *Enterobacteriaceae*, *P. aeruginosa* and *A. baumannii* can cause serious infections, particularly among hospitalized patients. Each of these organism groups have a propensity to exhibit resistance to many of the drugs used to manage the infections that they cause. Therefore, careful monitoring of the resistance patterns they exhibit is warranted. In this study Tigecycline Evaluation Surveillance Trial (TEST) program data were used to evaluate the *in vitro* activity of several key drugs against blood and respiratory isolates from Africa and the Middle East (AFME).

Methods. A total of 1,591 isolates collected from AFME (Egypt, Morocco, Mauritius, Namibia, South Africa, Tunisia, Israel, Jordan, Lebanon, Oman, Saudi Arabia; 2011-2013) were identified and tested locally by broth microdilution according to CLSI guidelines. All data were collected centrally at IHMA for analysis.

Results. The activities of the various drugs according to specimen source and organism group are provided in the table.

	Enterobacteriaeae(2475)				*P. aeruginosa* (528)				*A. baumannii* (398)			
	Blood (596)		Resp. (386)		Blood (82)		Resp. (162)		Blood (92)		Resp.(139)	
Drug	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}	%S	MIC_{90}
Amikacin	95.6	8	95.1	8	95.1	16	86	32	27.2	> 64	30.9	> 64
Ceftazidime	49.8	> 16	58.0	> 16	64.6	32	71.0	> 16	13.0	32	6.5	> 32
Levofloxacin	73.0	> 8	79	> 8	79.3	> 8	66.7	> 8	18.5	> 8	10.8	> 8
Meropenem	95	0.5	94.8	0.5	81.7	8	69.1	16	14.1	> 16	10.1	> 16
Pip-tazo	80.0	128	81.4	128	73.2	> 128	75.3	64	8.7	> 128	6.5	> 128
Tigecycline	96.8	2	95.3	2	na[a]	na	na	na	na	na	na	na

[a]na: not applicable

Conclusion. Based on percent susceptibility and MIC_{90}'s amikacin, meropenem, and tigecycline were the most active agents against *Enterobacteriaceae*, regardless of specimen source. For *P. aeruginosa* amikacin was the most active with all others having percent susceptibilities near or below 80%. None of the agents had effective activity against *A. baummannii*.. These variations in antimicrobial susceptibilities underscore the need for continued monitoring of resistance trends among these clinical important organism groups encountered in AFME

Disclosures. **M. Renteria**, Pfizer: Independent Contractor, Consulting fee **D. Sahm**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

423. Comparison of pediatric community-acquired, healthcare-associated, and hospital-acquired infections caused by extended-spectrum cephalosporin-resistant *Enterobacteriaceae*

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Background. We compared the clinical, microbiological and molecular characteristics of community-acquired (CA), healthcare-associated (HCA) and hospital-acquired (HA) extended spectrum cephalosporin-resistant (ESC-R) *Enterobacteriaceae* infections identified at a free-standing pediatric hospital.

Methods. ESC-R isolates recovered from urine or other normally sterile site during routine clinical care were prospectively collected from September 2009-September 2013. Targeted organisms were *E. coli* or *K. pneumoniae* not susceptible to 3rd generation cephalosporins, cefepime or carbapenems. Medical record review was performed on infected patients. Infections were categorized as CA (outpatient or < 48 hours after admission from a previously healthy patient without hospitalization in last year), HCA (outpatient or < 48 hours after admission from a patient with chronic conditions or hospitalization in the last year), or HA (>48 hours after admission with no symptoms of infection on admission). ESC-R isolates underwent phenotypic and molecular characterization.

Results. During the study period, 116 ESC-R infections were identified (CA 31%, HCA 56%, HA 13%). HA infections were more likely than CA or HCA infections to involve the blood or peritoneal fluid (40% vs 5%, p =0.001). Among the ESC-R resistance phenotypes, 79 (68%) were ESBL, 34 (29%) were AmpC, and 3 (3%) were carbapenem resistant. Resistance phenotype did not differ between infection categories. Susceptibilities to non-beta-lactam agents were similar between infection categories, except that CA infections were more likely than HCA or HA infections to be susceptible to trimethoprim-sulfamethoxazole (p = 0.007) *E. coli* was the predominant species in all infection categories but there was a higher proportion of *K. pneumoniae* in HCA and HA infections than in CA infections (35% vs 3%, p = 0.04). Among ESC-R *E. coli*, ST131-associated sequence types were more common in CA infections than in HCA and HA infections (40% vs 24%) but this difference was not statistically significant (p = 0.09).

Conclusion. CA ESC-R infections accounted for nearly one-third of ESC-R infections identified in our hospital. CA infections were more likely than HCA or HA infections to involve the urinary tract and be caused by *E. coli*.

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424. Characterization and Profiling of Multi-Drug Resistant (MDR) *Enterobacteriaceae* From Latin America

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Background. *Enterobacteriaceae* species are important pathogens responsible for a wide variety of serious infections. The tendency of these organisms to develop or acquire resistance to key antimicrobials can lead to MDR strains for which the therapeutic choices are limited. Therefore, tracking and profiling MDR strains is an important aspect of any surveillance initiative. In this study data from The Tigecycline Evaluation Surveillance Trial (TEST) program were analyzed to evaluate the profiles and characteristics of MDR populations from Latin America.

Methods. Between 2008 and 2013 8,907 isolates of *Enterobacteriaceae* from Argentina, Brazil, Chile, Colombia, El Salvador, Guatemala, Honduras, Mexico, Panama, and Venezuela were locally collected, identified, and susceptibility tested (broth microdilution) according to CLSI guidelines. The data were centralized at IHMA for analysis of the MDR populations. MDR was defined as resistance to drugs from three or more different antimicrobial classes.

Results. Of the 8,907 *Enterobacteriaceae* isolates 4,077 (45.8%) had a MDR phenotype; of those MDR 77.7% were from inpatients, 21.8% were blood isolates, 18.2% were from urinary tract specimens, 16.4% were from respiratory tract specimens, 7% were from intra-abdominal infections and 8.7% were from wounds. By species, 33.3 % of MDR were *E. coli*, 28.9% were *K. pneumoniae*, 21% were *E. cloacae*, and 9.1% were *S. marcescens*. The individual antimicrobial profiles for all *Enterobacteriaceae* and the MDR population were as follows:

	All Enterobacteriaceae (8907)			MDR (4077)		
Drug	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}
Amikacin	89.95	2	32	79.22	4	64
Cefepime	77.09	≤ 0.5	> 32	52.86	8	> 32
Ceftazidime	0	≤ 8	> 32	0	16	> 32
Levofloxacin	64.12	0.25	> 8	33.87	8	> 8

continued.

	All Enterobacteriaceae (8907)			MDR (4077)		
Drug	%S	MIC_{50}	MIC_{90}	%S	MIC_{50}	MIC_{90}
Meropenem	95	≤ 0.06	0.5	89.38	≤ 0.06	2
Pip-tazo	74.59	4	> 128	48.71	32	> 128
Tigecycline[a]	96.68	0.5	2	93.3	0.5	2

[a]FDA breakpoints used for tigecycline

Conclusion. The MDR rate among *Enterobacteriaceae* is very high in Latin America, especially among inpatient isolates. The MDR phenotype was also prevalent among isolates from the key infection sites. Meropenem and tigecycline were the most active drugs against the MDR population. The critical importance of this phenotype warrants careful and ongoing surveillance.

Disclosures. **M. Renteria**, Pfizer: Independent Contractor, Consulting fee **D. Sahm**, Pfizer: Independent Contractor, Consulting fee **S. Bouchillon**, Pfizer: Independent Contractor, Consulting fee **H. Leister-Tebbe**, Pfizer: Employee, Salary

426. Association between pre-transplant *Staphylococcus aureus* colonisation and post-transplant *S. aureus* infection among cystic fibrosis lung transplant recipients

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Background. Cystic fibrosis (CF) patients are frequently colonized with *Staphylococcus aureus*. However the impact of *S. aureus* colonization on post-transplant outcome among CF patients undergoing lung transplantation is unknown.

Methods. We conducted a 5-year retrospective cohort study of all CF patients undergoing lung transplantation to determine the impact of pre-transplant *S. aureus* infection on the incidence of *S. aureus* infection after transplantation. All patients were followed up to one year after transplantation.

Results. In total, 74 patients with CF underwent lung transplantation at our center. Thirty-seven patients (50%) were colonized with *S. aureus* prior to transplantation, 26 (35%) with MSSA, 6 (8%) with MRSA and 5 (7%) with both MSSA and MRSA. Nineteen (26%) patients had post-transplant *S. aureus* respiratory infections, 10 (14%) of which were pneumonia, 6 (8%) bronchitis and 3 (4%) received therapy without meeting the CDC criteria for respiratory tract infection. In a univariable analysis, pre-transplant *S. aureus* colonization was associated with an increased risk for post-transplant *S. aureus* infection (OR 4.46, 95%CI1.30–15.41; p = 0.01). However, there was no difference in length of ICU or hospital stay. In a multivariable model controlling for age > 30, gender, pre-transplant *Pseudomonas* colonization, pre-transplant *S. aureus* colonization remained independently associated with an increased risk for post-transplant *S. aureus* infection (OR 4.4770, 1.34-16.54; p = 0.01). There was no evidence for a difference in mortality between patients with (2; 5.4%) and those without pre-transplant *S. aureus* colonization (3; 8.1%) (p = 0.64).

Conclusion. Our study suggests that pre-transplant *S. aureus* infection among CF patients undergoing lung transplant increases the risk of post-transplant *S. aureus* infection but does not negatively impact on post transplant one year survival.

Disclosures. **All authors:** No reported disclosures.

427. Low Rates of Vaccination in Listed Kidney Transplant Candidates

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Background. Vaccine preventable infection is associated with high morbidity and mortality in solid organ transplant (SOT) recipients. Vaccination is most effective if it is given pre-transplant, prior to the initiation of chronic immunosuppression. Despite these strong recommendations, there is limited data about pre-transplant vaccination status among listed transplant candidates. We examined vaccination status of patients in our renal transplant program to identify the gaps and to use this information for future protocol to improve the vaccination rates.

Methods. We performed chart review of consecutive patients who were listed as a potential kidney transplant candidate (status 7 or inactive) at Hahnemann University Hospital to evaluate whether or not they had received appropriate vaccinations for pneumococcus, influenza, and tetanus. Hepatitis B was evaluated by the presence or absence of suitable titers of antibodies against hepatitis B virus.

Results. One-hundred two patients were evaluated. Median age of cohort was 52 year-old, 66.7% were receiving dialysis at the time of evaluation. Immunization rates were low with 30.4% having received pneumococcal vaccine, 43% received influenza vaccine, and 9.8% received tetanus vaccine. Patients who received other vaccines i.e., influenza (63.6% vs 5.2%, p < 0.01) and tetanus (25.8% vs 2.8%, p < 0.01) were more likely to receive pneumococcal vaccine. Immunity against hepatitis B virus was found in 41.6% of listed patients and was more likely if the patients were receiving dialysis (70% vs 32.3%, p < 0.01).

Conclusion. In a sequential cohort of patients listed for kidney transplantation, we found that the overall immunization rate of commonly vaccine preventable infection was low. This suggests that, there remains a significant gap between recommendations and actual vaccination rates for this high risk population. To overcome these challenges, we suggest: (1) augmenting current education for both transplant professionals and listed patients, (2) develop quality matrix for appropriate vaccination, (3) simplify vaccination delivery (4) work on resolving financial barriers and (5) to consider infectious disease consultation in early pre-transplant evaluation process.

Disclosures. **All authors:** No reported disclosures.

429. Diagnosis and Treatment of Respiratory Syncytial Virus in Immunocompromised Hosts in Large Midwestern Transplant Centers

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Background. Respiratory syncytial virus (RSV) infection results in significant morbidity and mortality in immunocompromised patients. As the optimal management strategy is unknown, practice varies widely between centers. We sought to assess practice variation in large transplant centers participating in the Midwest Respiratory Virus Consortium (MRVC).

Methods. A survey assessing center characteristics and treatment strategies was sent to Transplant Infectious Disease (TID) physicians at 13 participating centers. In addition, information regarding treatment of other non-influenza, non-RSV respiratory viral infections was obtained.

Results. 11 of 13 centers responded. Multiplex polymerase chain reaction (PCR) was used for diagnosis in 10/11 centers; one center used rapid antigen testing. 8/11 institutions used inhaled ribavirin (RBV) in at least some patient populations. Reasons cited as barriers against use included cost, safety, lack of supporting evidence, and inconvenience. 8/11 centers used oral RBV and 3 stated a specific preference for oral and 3 a preference for inhaled. 4 of 11 used intravenous immunoglobulin (IVIG), often in combination with RBV. In the post-stem cell transplant (SCT) population, patients with lower respiratory tract infection (LRTI) were more likely to be treated than those with upper respiratory tract infection (URTI). Pre-engraftment allo-SCT recipient with URTI would receive RBV in 5/11 centers while LRTI would be treated with RBV in 9/11 centers. 8 centers performed lung transplantation; all used either oral or inhaled RBV for LRTI, 6/8 for URTI. No center routinely treated non-lung solid organ transplant (SOT) recipients with URTI; 7/11 would consider oral or inh RBV in the same group with LRTI. Patients with hematologic malignancy but no HSCT were treated with RBV at a similar frequency (1/11 with URTI, 7/11 with LRTI). 2 of 9 centers in severe cases treated parainfluenza, metapneumovirus or coronavirus with IVIG or RBV.

Conclusion. Treatment of RSV in immunocompromised patients varied greatly between institutions. The presence of such heterogeneity demonstrates the need for further studies defining optimal treatment of RSV in immunocompromised hosts.

Disclosures. **All authors:** No reported disclosures.

430. Patients with Prolonged (>10 days) Neutropenia Displayed Similar IFI Rates Regardless of Hematologic Diagnosis and Chemotherapy Status: A Challenge to Antifungal Prophylaxis Decisions

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Background. Invasive fungal infections (IFI) are a significant source of morbidity and mortality in neutropenic patients. Risk based prophylaxis or pre-emptive therapy are debated clinical approaches. Since 2009, IPC at our tertiary care institution has collected the IFI rate per 1,000 neutropenic patient days. We examine IFI per neutropenic episode by patient characterictics and duration of neutropenia.

Methods. All neutropenic Hematology ward patients were assessed, those with ANC of 0.5 x 10^9/L or less for >10 days were followed prospectively for development of Probable or Definite IFI by the 2008 EORTC criteria. Chart data were collected: demographics, hematologic diagnosis, type of chemotherapeutic regimen, and neutropenic days (NDS), and if an IFI was diagnosed; the fungus, site of culture, and outcome.

Results. There were 277 neutropenic episodes in 180 patients, (mean 26 NDs) identified from January 2009 to December 2010. 'Severe' criteria was met in 177 episodes (63.9%) in 116 patients (mean 37.8 NDs). Twenty (17.2%) of these had IFI with 6 (30%) related deaths.

IFI case patients (21 IFIs) had a mean of 43.9 NDs per episode (4-148 days) . There were 6 cases of aspergillosis, 14 candidiasis, and 1 fungus that failed to grow but resembled coccidiomycosis.

Hematologic Diagnosis	Chemotherapy	Mean Neutropenic Days (range)	IFI per episode of severe neutropenia (%)	*Comment: The "Other" category included aplastic anemia, CLL, CML, lymphoma, HLH, and palliative end stage marrow failure*
AML (n=70)	Induction	28.6 (10-88)	7/70 (10.0)	
	Consolidation	21.9 (10-84)	2/19 (10.5)	
	Re-Induction	38.8 (11-155)	3/19 (15.7%)	
Myelodysplasia (n=15)	n/a	68 (10-420)	2/15 (13.3%)	
ALL (n=14)	Induction	14.6 (11-16)	0/7	
	Re-induction	26 (11-41)	2/7	
Other (n=44)	n/a	52.8 (10-870)	6/44 (13.6%)	

Conclusion. The range of NDs per episode was broader than expected. In all but ALL patients the IFI rate was 10-16% of neutropenic episodes. Our current criteria for antimould prophylaxis (re/induction AML) would have applied to 10 IFI in 89 episodes, with 10 IFI in 69 episodes (all other non ALL patients) planned for prophylaxis under our current rules. Larger studies of the intensity and modifiability of IFI risk in nonacute hematologic diagnoses are needed.

Disclosures. **All authors:** No reported disclosures.

431. Incidence, Burden and Cost Analysis of CMV Reactivation after Use of Anti-Thymocyte Globulin in Resource-Limited Setting

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Background. Cytomegalovirus (CMV) causes a significant morbidity and mortality after kidney transplantation (KT), especially after anti-thymocyte globulin (ATG) use. Despite recommendation, CMV prophylaxis post KT is not always feasible. We aimed to study the incidence, consequences and cost analysis of CMV disease/infection (called reactivation hereafter), after ATG use among KT patients (pts) in resource limited setting.

Methods. Retrospective cohort study of ATG treated KT pts during 2010-2013 at Ramathibodi hospital, Bangkok, Thailand. Data were collected from medical records including type of KT, maintenance immunosuppression, CMV prophylaxis, CMV reactivation, co-infections, cost of inpatient and outpatient post KT and outcome.

Results. Of 30 pts 53%, were female. Pts' median age was 43 (25-68) years old. All were CMV D + /R+. Most (53%) had living related KT. Majority (77%) received ATG as an induction therapy. Combination of mycofenolate/tacrolimus/prednisolone was used in 73%. Rejection occurred in 13 (43%) pts, most (61%) of which were antibody mediated during early post KT. CMV prophylaxis was given only during inpatient stay in 29 (90%) pts with median duration of 13(2-55) days. Outpatient CMV prophylaxis with valganciclovir at a mimimum of 100 day was given in 3 (10%) pts. Incidence of CMV reactivation was 43%, with a median onset of 90 (23-1007) days after KT. None occurred among those receiving outpatient CMV prophylaxis. CMV reactivation associated with significant higher risk of co-infections (P = 0.027). Median duration of follow up was 542 (134-1,348) days. Graft loss was 17%. Survival rate was 97%. Compared with outpatient CMV prophylaxis, the cost of treatment for CMV reactivation was significantly higher for both inpatient cost (P = 0.021), and total cost post KT (P = 0.035).

Conclusion. Incidence of CMV reactivation post KT with ATG use (D + /R+) was high without adequate CMV prophylaxis and viral load monitoring. CMV reactivation associated with significant higher risk of co-infections. Cost analysis showed significant higher cost of treatment for CMV reactivation. CMV prophylaxis should be given in ATG treated pts in resource-limited settings.

Disclosures. **All authors:** No reported disclosures.

432. Pathologic Pyelonephritis In Kidney Transplant Recipients: Bacterial Infection?

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Background. Pyelonephritis (pyelo) in renal transplant recipients (RTxp) is usually treated with antibacterials. Non-bacterial causes such as viral pyelo exist, but histopathologic pyelo without clinical or laboratory features has not been studied.

Methods. Our objective is to characterize RTxp with histopathologic pyelo but without the usual clinical or laboratory features of pyelo. We performed a retrospective chart review of RTxp admitted to Einstein Medical Center Philadelphia from January 1, 2002 to June 30, 2011 with a clinical or pathologic diagnosis of pyelo. Temperature, WBC count, serum creatinine, urine and blood cultures, duration of antibiotics and change in creatinine at discharge were compared. Patients were followed for 1 year to compare rates of readmission, repeat pyelo, rejection, and death. Fisher's exact test and Mann-Whitney test were used to analyze the data.

Results. 6 patients were diagnosed with pyelo by pathologic criteria alone (Path pyelo) (table). 20 patients with clinical pyelo were randomly selected as controls. Median admission creatinines in the two groups were 1.8 mg/dl and 3.3 mg/dl. The higher creatinine in the path pyelo group presumably prompted the renal biopsies (Figure 1). All biopsies were reviewed by 2 pathologists.

The one patient without antibiotics had no recurrent pyelo or rejection. Both groups had similar rates of readmission and recurrent pyelo, suggesting an identical, i.e., bacterial, etiology in both groups (Figure 2). Overall prognosis was benign with only one rejection and no deaths.

Fig 1: Serum Creatinine

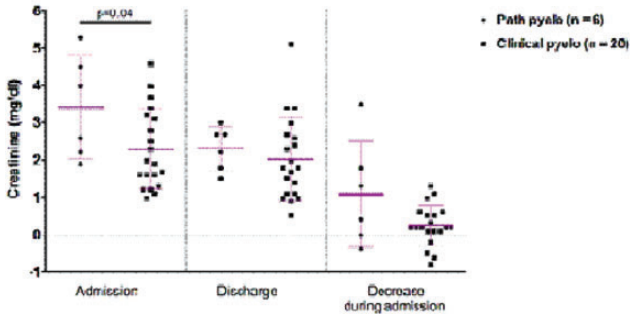
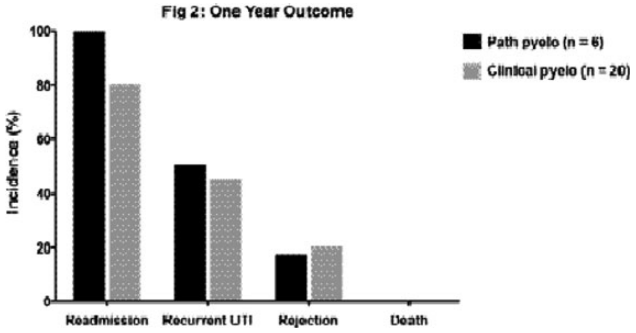


Fig 2: One Year Outcome



Clinical and laboratory data ns=not significant

	Path pyelo (n=6)	Clinical pyelo (n=20)	p value
Urinary symptoms	1*	18	
Abdominal pain	2*,#	15	
Temperature (°C)	<38	38-39	
WBC (10^3/cmm)	5.9 (4-8.3)	9.7 (6.9 -13.2)	
Bacteriuria	1*	20	
Bacteremia	0	5	
Antibiotic Rx	5	20	ns
Rx Duration (Week)	1 (1-1)	2 (2-2)	ns

Endometriosis * Reflux nephropathy, urine with mixed skin flora (ns)

Conclusion. This is a small study with only 6 patients meeting the criteria for pathological pyelonephritis, but this is the first time this rare disease process has been studied. The data is suggestive of a bacterial etiology and benign prognosis, but larger studies are required to further characterize the disease and need for antibiotic therapy.

Disclosures. **All authors:** No reported disclosures.

433. Human Herpesvirus 6 Reactivation, Delirium, and the Effect of Antiviral Prophylaxis Strategies After Cord Blood Transplantation

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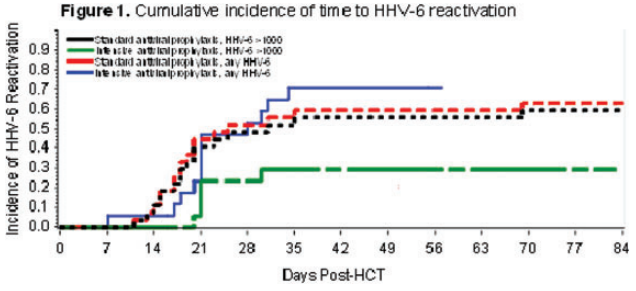
Background. Human herpesvirus 6 (HHV-6) reactivates in the majority of cord blood transplantation (CBT) recipients and is associated with significant morbidity. We previously reported that HHV-6 reactivation after hematopoietic cell transplantation (HCT) is associated with delirium (Zerr et. al. 2011, Blood 117: 5243), but only 21 patients (7%) of the cohort received CBT. Here we examine whether HHV-6 reactivation increases the risk for delirium after CBT and if intensive antiviral prophylaxis can reduce its impact.

Methods. We tested for HHV-6 by twice weekly plasma PCR until day +84 in a prospective cohort of 44 CBT recipients, 34 of whom were assessed for delirium 3 times weekly. Twenty patients were included in our original study (one patient receiving foscarnet was excluded). Antiviral prophylaxis strategies in CMV seropositive patients changed during enrollment from standard prophylaxis (acylcovir 800 mg twice daily) to intensive prophylaxis (ganciclovir 5 mg/kg daily on days -8 to -2 and acyclovir 800 mg three times daily on days 0 to +100) (Milano et. al. 2011, Blood 118: 5689). Delirium was modeled using longitudinal logistic regression with generalized estimating equations, and Cox proportional hazards were used to evaluate risk factors for HHV-6 reactivation.

Results. HHV-6 was detected in 66% of the cohort, and 27% of assessed patients had delirium. Patients with high-level viremia (>1,000 copies/ml, 48%) were more likely to develop delirium (odds ratio [OR], 3.05; 95% confidence interval [CI], 1.03-9; p = >0.043). This relationship was maintained in a series of bivariate models except when adjusting for comorbidity, which was a stronger predictor of delirium. Comorbidity score was not associated with HHV-6 reactivation. Intensive prophylaxis was given to 39% of patients and appeared to reduce risk of high-level viremia (adjusted hazard ratio, 0.28; 95% CI, 0.1-0.76; p = 0.013) (Figure 1). We were unable to analyze the effect of intensive prophylaxis on delirium due to sample size.

Figure 1. Cumulative incidence of time to HHV-6 reactivation



Conclusion. HHV-6 reactivation with high-level viremia after CBT is independently associated with delirium. An intensive antiviral prophylaxis strategy mitigated HHV-6 reactivation, but larger studies are needed to assess this association with outcomes.

Disclosures. **M. Boeckh**, Chimerix, Inc.: Consultant, Research support; Genentech/Roche: Consultant, Research support; Gilead: Consultant, Research support; Clinigen: Consultant, Research support **D. Zerr**, Sage Products: Investigator, Research support; Chimerix, Inc.: Investigator, Research support

434. Prevalence, Risk Factors, and Outcomes of Bacteremia Caused by Carbapenem-resistant Enterobacteriaceae in Neutropenic Patients with Hematologic Malignancies

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Background. Neutropenic patients with hematologic malignancies rely on immediate, active antimicrobial therapy to combat bacterial infections, and thus are uniquely threatened by multidrug-resistant bacteria. Carbapenem-resistant Enterobacteriaceae (CRE) have emerged worldwide and are resistant to nearly all antimicrobial agents, but their impact on neutropenic patients is unknown.

Methods. In order to assess the prevalence, risk factors, and outcomes of CRE bacteremia in neutropenic patients with hematologic malignancies, we reviewed all bloodstream infections (BSIs) from 2008-2012 in this population at New York-Presbyterian Hospital/Weill Cornell and Memorial Sloan-Kettering Cancer Center and conducted a case-control study. For each case of CRE BSI, three controls matched by study site and year were randomly selected among BSIs caused by other pathogens.

Results. CRE caused 4.8% of Gram-negative bacteremias and 2.1% of all BSIs. Of the 42 episodes of CRE bacteremia, 31 (74%) were in patients with acute leukemia, 15 (36%) were in allogeneic stem cell transplant recipients, and 26 (62%) were in patients without prior carbapenem exposure. Independent risk factors for CRE bacteremia were exposure to β-lactam/β-lactamase inhibitors (BL-BLI; odds ratio [OR] = 3.7; $P = 0.01$) and trimethoprim-sulfamethoxazole (TMP-SMX; OR 6.0; $P = 0.007$), glucocorticoid use (OR 5.3; $P = 0.001$), and having a prior culture that grew CRE (OR 19.2; $P = 0.01$). Patients with CRE bacteremia were less likely than controls to receive active empirical therapy (14% vs 56%, $P < 0.001$) and had longer delays until receipt of active therapy (median hours: 52 vs 5, $P < 0.001$). They also had higher 30-day (51% vs 25%, $P = 0.001$) and BSI-related (49% vs 16%, $P < 0.001$) mortality rates, with a median of 3 days from bacteremia onset until death. The six cases of CRE bacteremia that received active empirical therapy had a lower 30-day mortality rate than that of the 36 others that did not (17% vs 58%; $P = 0.09$).

Conclusion. CRE are emerging as lethal causes of bacteremia in neutropenic patients with hematologic malignancies. Exposures to BL-BLI, TMP-SMX, and glucocorticoids and having a prior culture that grew CRE are risk factors for CRE bacteremia in this population. New strategies are needed to shorten the delay until administration of CRE-active agents and mitigate this emerging threat.

Disclosures. **All authors:** No reported disclosures.

435. Epstein-Barr Viral Load and Lymphocyte Subset Number and Function in Pediatric Renal Transplant Patients

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Background. In pediatric renal transplant recipients, persistent EBV viremia is associated with post-transplant lymphoproliferative disease (PTLD), but immune correlates of persistent viremia remain poorly defined. In this study the relationship between circulating lymphocyte subsets and persistent EBV viremia was examined in pediatric renal transplant patients.

Methods. Serial prospectively collected peripheral blood mononuclear cell samples from pediatric renal transplant patients were analyzed for CD4+ T cell subsets including Th1, Th2, Th17, CD4+ and CD8+ effector memory cells, and NK cells by flow cytometry for surface markers and intracellular cytokine staining. Patient demographics and EBV PCR results were extracted from patient records.

Results. 36 samples were obtained from 11 renal transplant patients over six months. Six patients had negative EBV PCR results at all time points. Five patients were EBV PCR positive, one of which was transient, while four remained positive with average PCR viral load of 10,507 copies/ml [range 515-34,710]. The two groups were similar with respect to EBV recipient status, age at transplant, and change in eGFR during the study. Patients with EBV viremia had significantly higher absolute CD4 T cell counts compared to patients without EBV viremia (mean +/- SD, 1629 + /-162 vs 903 + /-82, p = 0.0002). Within CD4 T cells subsets, patients with EBV viremia had a significantly lower percentage of CD4 + CCR4+ Th2 cells compared to those without EBV viremia (mean +/- SD, 3.80 + /-0.80 vs 7.14 + /-0.82, p = 0.019) as well as a significantly lower percentage of IL-4 producing CD4+ cells (0.67 + /-0.075 vs 2.26 + /-0.55, p = 0.002). No difference was seen in CD4+ or CD8+ effector memory, Th1, Th17 or NK cells.

Conclusion. In this cohort, persistent EBV viremia was associated with a statistically greater number of circulating CD4+ T cells, but statistically fewer circulating CD4+ Th2 cells and a blunted IL-4+ response compared to that found in patients without viremia. These results suggest that impairment of Th2 responses may contribute to persistent EBV viremia in pediatric renal transplant recipients.

Disclosures. **All authors:** No reported disclosures.

436. Five Year Cumulative Incidence of Herpes Zoster (HZ) in Autologous Hematopoietic Cell Transplant (HCT) Recipients who Received Long-Term Acyclovir or Valacyclovir Prophylaxis

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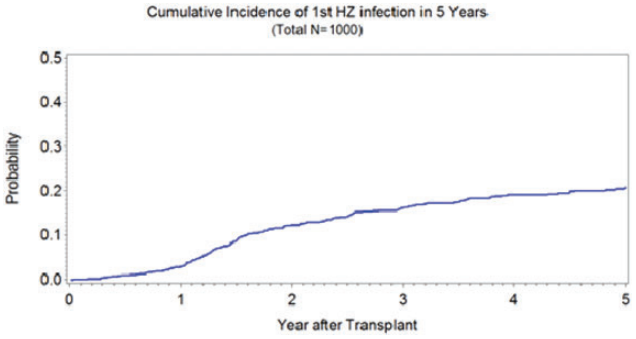
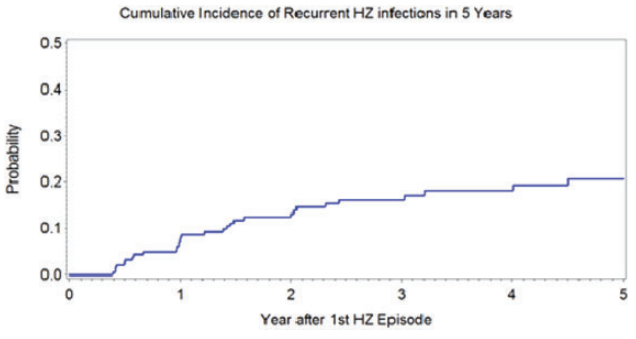
Background. Antiviral prophylaxis with acyclovir/valacyclovir (ACV/VCV) after allogeneic HCT reduces HZ and its complications, but benefits of prophylaxis after autologous HCT are not well described. We determined the incidence of and risk factors for HZ over 5 years in a large cohort of autologous HCT recipients from an era that included ACV/VCV prophylaxis and maintenance chemotherapy for the underlying disease.

Methods. We retrospectively identified 1,000 consecutive varicella zoster virus seropositive autologous HCT recipients from 2002 to 2010. Antiviral prophylaxis was prescribed with ACV 800 mg or VCV 500 mg twice daily for 1 year post-HCT. Cumulative incidence of HZ was evaluated and multivariable Cox regression models were used to evaluate adjusted hazard ratios (aHR) and associated confidence intervals (CI) for the association of ACV/VCV with HZ while adjusted for sex, type of transplant (single vs tandem) and pre-HCT HZ.

Results. Patients were followed for a median of 39.7 months (interquartile range [IQR], 20.7-66.1 months). A total of 192 patients developed at least one HZ episode over 5 years following HCT with an overall cumulative incidence of 0.21 (95% CI, 0.18-0.24) (Figure 1) at a median of 19 months (IQR, 14.4-31.3 months). The majority of patients who developed HZ 157/192 (81.7%) were no longer taking prophylaxis at the time of HZ. A second episode of HZ occurred in 31/192 (16%) of patients at a median of 14.8 months (IQR, 7.1-24.9 months) after the first HZ episode (Figure 2). ACV/VCV had a protective effect against HZ (aHR, 0.61; 95% CI, 0.39-0.95; p = 0.03). Disseminated disease occurred in 18/192 (9.4%) patients during the first HZ episode and 3/31 (9.7%) patients during the second episode of HZ after HCT.





Conclusion. In a large population of autologous HCT recipients who were prescribed one year of ACV/VCV, over 20% of patients developed HZ during 5 years of follow-up, with the majority occurring after completing antiviral prophylaxis. Improved prevention strategies (e.g., an effective vaccine) are needed to provide long-term protection against HZ in high-risk autologous HCT recipients.

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437. Hepatitis E Virus Infection among Solid Organ Transplant recipients at a North American transplant center

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Background. Hepatitis E Virus (HEV) is a leading cause of viral hepatitis worldwide, and is typically associated with flooding and poor sanitation. Recently, HEV infection has been increasingly reported among solid organ transplant (SOT) recipients in industrialized nations. In North America however, cases of HEV infection among SOT recipients remain rare despite a seroprevalence of 15-21%.

Methods. We conducted a retrospective, cross sectional study to investigate HEV infection among SOT recipients at our institution. Post SOT sera collected between 1988 and 2012 were tested for HEV antibody using a PE-2 antigen based ELISA, and for HEV RNA by real time PCR. HEV antibody positive subjects were identified, and pre transplant samples then tested for HEV antibody. Patients with evidence of HEV viremia, HEV IgG seroconversion or IgM positivity were considered recently infected, and serial samples were tested by PCR for evidence of chronic infection.

Results. A total of 314 (176F, 138M) subjects were tested for HEV antibody. Samples were from 274 kidney, 33 lung, 5 cardiac, and 2 liver transplant recipients. Mean age at time of transplant was 45.7 years (range 2Y-80Y), with 17 patients under 18 years of age. Of 314 specimens, 59 (19%) were positive for HEV IgG antibody. Sixteen subjects (5%) demonstrated evidence of recent HEV infection: two (0.6 %) subjects were positive for HEV IgM antibody, four (1%) had evidence of HEV viremia by PCR, and ten (3%) demonstrated HEV antibody sero-conversion after transplantation.

Mean ALT was 55 U/L among recently infected subjects, vs 47 U/L in the rest of the cohort ($p = 0.95$). Elevated ALT (>1.5x ULN) was noted in 46% of recently infected subjects vs 36% in the rest of the cohort ($p = 0.56$). Serial PCR of recently infected subjects yielded no further HEV RNA positive samples.

Conclusion. We report 19% HEV IgG seroprevalence among SOT recipients in our cohort, and evidence of recent infection in 16/314 (5%) of subjects. Four patients (1%) had evidence of active HEV viremia. No association was observed between recent HEV infection and acute hepatitis, and no cases of chronic HEV infection were identified. Further studies are needed to characterize the burden of HEV among SOT recipients in the United States.

Disclosures. **All authors:** No reported disclosures.

438. Genetic Variants Associated with the Development of Clostridium Difficile Infection during Autologous Stemcell Transplantation

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Background. Genetic susceptibility has been thought to contribute to development of infectious diseases in immunocompromised hosts. Clostridium difficile infection (CDI) confers considerable morbidity and mortality during stemcell transplantation (SCT). Unfortunately genes that identify CDI-susceptible SCT recipients have not been well described. We performed a genome wide association study in an effort to determine genetic variants associated with the development of CDI in autologous SCT (ASCT) recipients

Methods. Patients undergoing ASCT for multiple myeloma were genotyped using Illumina's HumanOmni1-Quad v1.0 BeadChip and 1,000, 000 SNPs were tested for association with development of CDI. CDI testing was performed utilizing ELISA for toxin A and B. We then compared baseline clinical characteristics using logistic regression and genetic factors (SNPs) utilizing a false discovery rate (FDR) approach between the two groups. SNPs associated with CDI at FDR of $p < 0.01$ were evaluated.

These SNPs were then incorporated into a logistic regression model combining clinical and genetic factors

Results. 646 pts met study criteria and of these 59.7% were male. Mean Age and GFR were 57.77 ± 9.12 years and 78.30 ± 38.63 ml/minute resp. Fifty-seven (57) pts tested CDI positive and were compared to 589 test-negative controls. Comparison of means± SD between cases and controls for select clinical characteristics were as follows: hemoglobin 10.50 ± 1.45 vs 11.01 ± 1.45 p = 0.019; hematocrit 31.90 ± 4.45 vs 33.35 ± 4.45 p = 0.011; serum albumin 3.59 ±0.58 vs 3.94 ± 0.51 p < 0.001. For the genetic comparison seven SNPs on four genes (FLJ16171,GORASP2,RLBP1L1,ASPH, ATP7B) were associated with CDI at FDR p <0.01. In the combined clinical and genetic model low albumin and three genes RLBP1L1,ASPH,ATP7B were assoc. with CDI

Conclusion. In this study low serum albumin in addition to genes RLBP1L1, ASPH, located on chromosome 8 and ATP7B on chromosome 13 conferred susceptibility to CDI

Disclosures. **S. Apewokin**, T 2 biosystem: Investigator, Research grant; Viracor: Investigator, Research grant

439. Infection Risk in Pediatric Stem Cell Transplant Recipients for Hemophagocytic Lymphohistiocytosis vs Acute Leukemia

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Background. Allogeneic hematopoietic stem cell transplantation (SCT) is often used as definitive therapy for hemophagocytic lymphohistiocytosis (HLH). Data on infectious complications in post-SCT HLH patients are limited, with no analyses comparing their infectious risk to other SCT recipients. This study compares post-SCT infection frequency and mortality rates between pediatric HLH and leukemia patients.

Methods. All HLH SCT patients from 1997 to 2009 were identified from the bone marrow registry at The Children's Hospital of Philadelphia. HLH patients were matched one-to-one to leukemia SCT patients by age and transplant year. Data on demographics, donor source, conditioning regimens, microbiologically-proven infections, and vital status 6 months post-SCT were collected. Multivariate conditional Poisson and logistic/Cox regression models compared infection rate per follow-up days and mortality, respectively.

Results. Eighteen HLH SCT patients (100%) had at least one infection, (median: 2; IQR: 1 to 4). Half of the leukemia SCT recipients had at least 1 infection (median: 1; IQR: 0 to 2). Compared to leukemia patients, HLH patients had a greater incidence of total infections (IRR: 2.47, 95% CI: 1.01 to 6.05; table). After adjusting for sex, conditioning regimen, and antithymocyte or antilymphocyte globulin (ATG/ALG) use, this difference was no longer significant (IRR: 1.69, 95% CI: 0.72 to 3.95). Receipt of ATG/ALG was independently associated with a greater infection rate (IRR: 2.30, 95% CI: 1.10 to 4.81). Mortality rate (HLH 22%, leukemia 28%) and time to death post-SCT did not differ between groups.

Microbiologically Proven Infection

	HLH	Leukemia
	n (%)	
Bacteremia		
Gram Positive	14 (42)	5 (35)
Gram Negative	2 (6)	6 (42)
Candidemia	2 (6)	0
Viral		
Respiratory	9 (27)	2 (14)
Reactivation	6 (18)	1 (7)

Conclusion. HLH SCT recipients have a higher infection rate in the 6 months post-HSCT compared to leukemia patients, a factor associated with pre-transplant ATG/ALG use. It is possible a difference in mortality and infection rates exists beyond the variation in ATG/ALG exposure. Further study of larger cohorts is needed.

Disclosures. **All authors:** No reported disclosures.

440. Incidence and Risk Factors for Pneumococcal Disease in Cancer Patients: A 20 Year Single Center Study at Memorial Sloan-Kettering Cancer Center

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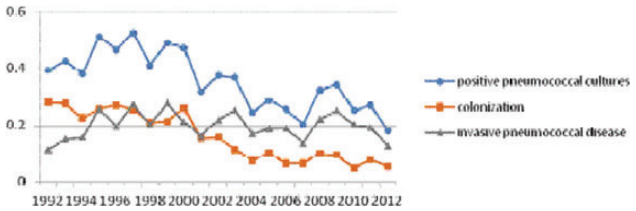
Background. The incidence of invasive pneumococcal disease (IPD) and associated mortality rates are higher in cancer patients compared to the general population. In early 2,000, a protein-polysaccharide conjugate vaccine was introduced for use in children. We sought to examine the impact of its introduction on the incidence of positive pneumococcal cultures (PC) and IPD in a single cancer center.

Methods. Retrospective study at Memorial Sloan-Kettering Cancer Center (MSKCC), a 469 bed acute care facility in New York. Patients with PC for *S. pneumoniae* from 1991-2012 were identified from clinical microbiology records. Cultures were obtained from symptomatic patients at the discretion of the clinicians. IPD was defined as a positive culture from a sterile site (CSF, blood or pleural fluid) or a positive respiratory culture with radiographic signs of pneumonia. All other cases were classified as "colonization." Incidence was calculated per 1,000 inpatient-days and compared between the "early" (1991-2001) vs "late" period (2002-2012). Risk factors for IPD were analyzed via stepwise multivariate logistic regression; all statistical tests were two tailed and $P < 0.05$ was considered statistically significant..

Results. 576 of 1051 (54%) patients with PC had IPD. Serotype 6 was the most frequent (24%); serotype data was only available through 2001.

The PC incidence declined from 0.44 in the early period to 0.28 in the late period ($P = 0.004$) (figure, table). There was also a significant decline in colonization but not IPD rates for the same periods.

Extremes of age (<21, >65) were associated with IPD; penicillin resistance, receipt of chemotherapy and underlying malignancy (hematologic vs solid tumor) was not. Most IPD patients were not vaccinated at MSKCC (93%).



Incidence of pneumococcal disease (per 1,000 patient days)

Incidence and Rate Ratios: Early (1992-2001) vs Late Period (2002-2012)

	PC	Colonization	IPD
Incidence, Early Period*	0.44	0.24	0.19
Incidence, Late Period*	0.28	0.09	0.19
Incidence Rate Ratio (Late/Early Period)	0.64	0.35	1.00
95% CI	0.44-0.84	0.15-0.56	0.62-1.38
P value	0.004	<0.001	0.999

*per 1,000 inpatient-days

Conclusion. The incidence of PC at our center declined after the implementation of conjugate vaccine for childhood immunization. Age <21 or >65 years was associated with IPD.

Incidence of pneumococcal disease (per 1,000 patient days)

Disclosures. **G. A. Papanicolaou**, Pfizer: Grant Investigator, Research grant **A. Kaltsas**, Pfizer: Investigator, Research grant

441. Incidence and Risk Factors for Development of Liver Abscesses in Liver Transplant Recipients with Intra Abdominal Infections - a 10 year retrospective review

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Background. Although intra-abdominal infection (IAI) is a frequent complication after liver transplantation (LT), liver abscesses (LA) appear to be uncommon. There is scarce data regarding LA among liver transplant recipients (LTR). We report on the clinical epidemiology, risk factors, and outcomes of LA in LTR at our institution.

Methods. A retrospective cohort study was performed of all LTs done at Henry Ford Hospital, Detroit Michigan from January 2003 to December 2012. LA was defined

as a parenchymal lesion consistent with an abscess as seen on imaging, together with compatible clinical features. Frequency analysis was performed of all variables using a chi-square test for dichotomous variables and a students't test for continuous variables. A logistic regression for risk factors that could contribute to development of a LA in patients with IAI post-LT was performed. Patients who developed other intra-abdominal infections (OIAI) after transplant (intra-abdominal abscesses or peritonitis) were used as a comparative group.

Results. Of all 986 LTs done from 2003 to 2012 the incidence of IAI was 15.3 per 100 LTRs. The incidence of LA alone was 2.4 per 100 LTRs. The median time from LT to diagnosis of LA was 120 days (IQR: 59-1163). Most (46%) of LAs were polymicrobial infections. Pathogens isolated included: aerobic gram-positive cocci (47.5%), gram-negative (30%), Candida spp. (17.5%), anaerobes (5%). Among LTRs with LA as compared to LTRs with OIAIs, the all-cause mortality was 17% vs 5% (P value 0.03) and liver failure requiring re-transplantation was 13% vs 3% (P value 0.045). Overall 37.5% of LA patients died, developed liver failure requiring re-transplantation or had other serious complications compared to 9% for patients who had OIAI ($P < 0.001$). Logistic regression analysis identified doppler evidence of hepatic artery abnormality (thrombosis, stenosis or rupture) (odds ratio [OR], 10.51; 95% confidence interval [CI], 3.27-33.71) and liver failure due to NASH, Primary sclerosing cholangitis (PSC) or Primary biliary cirrhosis (PBC) (OR, 3.58; 95% CI, 1.27-10.10) as predictors for developing LA compared to OIAI.

Conclusion. In LTRs with IAIs, hepatic artery abnormality and liver failure due to NASH, PSC or PBC are significant risk factors for LA. The development of LA is associated with increased risk of death and re-transplantation.

Disclosures. **All authors:** No reported disclosures.

442. Varicella zoster virus infection after allogeneic hematopoietic cell transplantation in Korean children under relatively short-term acyclovir prophylaxis

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Background. Although the current guideline recommends acyclovir prophylaxis for one year or more after hematopoietic cell transplantation (HCT) to prevent varicella zoster virus (VZV) infection, no epidemiologic data on VZV infection after childhood allogeneic HCT have been reported in Korea. This retrospective study was conducted to characterize VZV infection after allogeneic HCT in a blood and marrow transplantation center where relatively short-term acyclovir prophylaxis has been performed.

Methods. Medical records of 217 consecutive childhood HCT recipients were reviewed, and clinical characteristics were compared between recipients with VZV infection after HCT and those without VZV infection.

Results. In the whole study population, the mean duration of follow-up after HCT was 27.2 ± 16.4 months, and the mean duration of acyclovir prophylaxis was 10.3 ± 4.2 weeks. Thirty-three (15.2%) recipients experienced VZV infection after HCT: 25 cases of herpes zoster and eight cases of chickenpox. VZV infection occurred at a median of 5 months (range: 2-41 months) after HCT, and 72.7% of them occurred within a year after HCT. The most common complication of VZV infection was cutaneous dissemination which occurred in 24.0% of herpes zoster patients. Although one patient experienced severe hepatitis, pneumonitis, acute respiratory distress syndrome and encephalitis accompanied by chickenpox, there was no infection-related death. More recipients with VZV infection were male ($p = 0.012$) and received total body irradiation during pre-transplantation conditioning ($p = 0.003$) compared with recipients without VZV infection. The mean age was higher ($p = 0.001$) and shorter acyclovir prophylaxis was given ($p = 0.003$) in recipients with VZV infection than in those without VZV infection, and there was no VZV infected-patients aged under 5 years.

Conclusion. In Korean children, VZV infection after HCT occurred less frequently compared with previous reports and severe complications were rare despite relatively short-term acyclovir prophylaxis. However, recipients with VZV infection were older and received shorter acyclovir prophylaxis. Therefore, acyclovir prophylaxis after HCT should be performed based on the recipient's age and epidemiology of each country and hospital.

Disclosures. **All authors:** No reported disclosures.

443. Non-Typhoidal *Salmonella* Infections in Cancer Patients

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Background. Non-typhoidal *Salmonella*(NTS) is an important foodborne pathogen resulting in gastroenteritis, bacteremia and subsequent focal infection such as endovascular disease and deep seated infection. Although malignancy is considered as a risk factor of NTS infection, there is limited data describing the clinical characteristics and outcome in cancer patients. The objective of our study is to investigate microbiological, clinical characteristics and outcome of NTS infection among cancer patients.

Methods. From January 2000 to December 2007, we retrospectively reviewed charts of patients with NTS clinical isolates at MD Anderson Cancer Center. We investigated demographics, site of infection, serotype, susceptibility, management and outcomes.

Results. We identified 60 isolates in 45 clinical cases. Median age was 55 (23 – 76) with 3:2 male to female ratio. All had underlying malignancy and 64% had hematological malignancy (45% lymphoma). 27% had neutropenia and 42% had lymphopenia. 60% took antacid, 56% steroids, and 67% chemotherapy within 1 month. Among 60 isolates, 48% were from blood, followed by 22% stool, 18% urine, 5% sputum, and others. Among clinically diagnosed UTI, 57% had anatomical abnormality in urinary tract. Serotype C was the leading pathogen in all isolates (38%), whereas B was most common in blood isolates (41%). Most of the isolates were susceptible (90% to ampicillin, 100% to ceftriaxone and 96% to fluoloquinolones). 29% had severe disease (severe sepsis, septic shock or invasive disease) and among them, 85% received steroids and/or chemotherapy. Only 2% had endovascular disease. 89% received initial active antibiotics. Recurrence within 3 months was seen in 7%, infection related mortality was 4%, and overall mortality was 8%.

Conclusion. Our study is one of the largest case series in cancer patients. The most common malignancy was lymphoma and severe infection occurred in patients receiving immunosuppressive agents. Compared with previous reports in cancer patients, our study showed: 1) higher proportion of severe disease and lower endovascular disease, 2) lower mortality (8% vs 30-40%), perhaps due to earlier initiation of active antibiotics, and 3) more frequent UTI, especially in patients with urologic abnormalities.

Disclosures. **All authors:** No reported disclosures.

444. Incidence, Risk Factors and Outcomes of Delayed-Onset Cytomegalovirus Disease in a Large Retrospective Cohort of Lung Transplant Recipients

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Background. Cytomegalovirus (CMV) disease commonly occurs in lung transplant recipients after stopping anti-CMV prophylaxis. Its epidemiology is not well-studied given difficulties in assembling representative study populations with prolonged follow-up. We hypothesized that delayed-onset CMV disease (> 100 days post-transplant) occurs more commonly than early-onset CMV disease in lung transplant recipients, and is associated with an increased risk of death.

Methods. We assembled a large cohort of lung transplant recipients using 2004 to 2010 ICD-9-CM billing data from 3 Agency for Healthcare Research and Quality (AHRQ) State Inpatient Databases (SID), and identified demographics, comorbidities, CMV disease coded during hospital readmission and inpatient death. We used Cox proportional hazard multivariable analyses to assess for an independent association between delayed-onset CMV disease and death.

Results. In the cohort of 1,528 lung transplant recipients from 12 transplant centers, delayed-onset CMV disease occurred in 13.7% (n = 210) and early-onset CMV disease occurred in 3.3% (n = 51). Delayed-onset CMV pneumonitis was associated with inpatient death > 100 days post-transplant (aHR 1.6, 95% CI 1.1-2.5), after adjusting for transplant failure or rejection (aHR 2.5, 95% CI 1.5-4.1), bacterial pneumonia (aHR 2.8, 95% CI 2.0-3.9), viral pneumonia (aHR 1.5, 95% CI 1.1-2.1), fungal pneumonia (aHR 1.8, 95% CI 1.3-2.3), single lung transplant (aHR 1.3, 95% CI 1.0-1.7) and idiopathic pulmonary fibrosis (aHR 1.4, 95% CI 1.0-1.8).

Conclusion. Delayed-onset CMV disease occurs more commonly than early-onset CMV disease among lung transplant recipients. These results suggest that delayed-onset CMV pneumonitis is associated with an increased risk of death.

Disclosures. **All authors:** No reported disclosures.

445. Epidemiology and Outcomes of *Clostridium difficile* Infections in Heart and Heart-lung Transplant Recipients

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Background. *Clostridium difficile*infection (CDI) is an important cause of diarrhea in transplant recipients, and often complicated by the use of intense immunosuppression and need for antibiotic prophylaxis. We aimed to investigate the epidemiology of CDI in heart and heart-lung transplant (HT) recipients and assessed its impact on outcomes.

Methods. This is a retrospective study of HT recipients from 2000 to 2013. CDI was defined by presence of diarrhea and a positive toxigenic *Clostridium difficile*in stool measured by toxin enzyme immunoassay (EIA) (2000-2006) or polymerase chain reaction (2007-2013). Survival was assessed using Kaplan-Meier method. The hazard ratio (HR) for all-cause mortality was calculated using Cox proportional hazard model.

Results. A total of 322 HT recipients were at risk during the 14-year study period. The median age was 53 years (IQR, 44-60); 66 % were male. During the median follow-up of 49 months (IQR, 19- 95), 27 (8.4%) patients developed CDI after transplant. Of those, six (28.5%) developed CDI within 30 days of transplant, while 21 (71.5%) patients developed CDI beyond 30 days from transplant. Two (7.4%) had hypervirulent

NAP1/BI/027 strain. Six (22%) had at least 1 episode of recurrent CDI. No patient required colectomy or died from CDI. However, patients with CDI had worse overall survival compared to non-CDI patients (log rank test; p < 0.01) **(Figure 1).**In univariate analysis, the predictors of mortality in HT recipients were: CDI anytime after transplant [HR 2.33; 95% CI, 1.14-4.32 (p = 0.02)], female donor [HR 1.83; 95% CI, 1.09-3.03 (p = 0.02)], older donor age per 1 year increase [HR 1.05; 95% CI, 0.99-1.03 (p = 0.09)] and combined heart-lung transplant [HR 2.13; 95% CI, 0.82-4.60 (p = 0.11)].In a multivariate analysis, CDI anytime after transplant remained significantly associated with all-cause mortality [HR 2.23; 95% CI, 1.07-4.27 (p = 0.03)].

Conclusion. CDI is a common cause of diarrhea in HT patients. CDI is significantly associated with, and an independent predictor for, increased mortality after heart transplantation. Efforts to prevent CDI may improve survival of HT recipients.

Disclosures. **All authors:** No reported disclosures.

446. Factors Associated with Hospital Length of Stay among Cancer Patients with Febrile Neutropenia

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Background. Hospital length of stay (LOS) is an important marker of clinical severity and resource consumption in the context of febrile neutropenia (FN). Understanding the factors that increase LOS may increase our knowledge regarding reducing costs and improving the quality of care in FN. Therefore, we conducted this study with the aim of evaluating the factors associated with increased LOS in hospitalized adult cancer patients with FN.

Methods. A prospective cohort study was performed at a single tertiary referral hospital in southern Brazil from October 2009 to August 2011. All adult cancer patients with febrile neutropenia admitted consecutively to the hematology ward were evaluated. A stepwise negative binomial regression was conducted to identify risk factors for prolonged hospital length of stay.

Results. In total, 307 cases of febrile neutropenia (in 169 patients) were evaluated. The overall median hospital length of stay was 16 days (interquartile range 18 days). After multiple negative binomial regression analysis was performed, hematologic neoplasm ($P = 0.003$), high-dose chemotherapy regimens ($P < 0.001$), duration of neutropenia ($P < 0.001$), and bloodstream infection involving Gram-negative multi-drug resistant bacteria ($P = 0.003$) were independently and directly associated with prolonged hospital length of stay in patients with febrile neutropenia.

Conclusion. Hematologic neoplasms, high-dose chemotherapy regimens, prolonged periods of neutropenia, and bloodstream infection by Gram-negative multidrug resistant bacteria increase risk for prolonged hospital length of stay among adult cancer patients with febrile neutropenia.

Disclosures. **All authors:** No reported disclosures.

447. Infectious complication and mortality after Liver Transplantation according to Donor: comparison between Cadaveric and Living Donor Transplantation

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Background. Living donor liver transplantation (LDLT) has been shown to decrease waiting-list mortality and in economic terms, similar overall financial burden to cadaveric donor liver transplantation (CDLT) has been reported. But there are rare studies about infectious complication and mortality after LDLT compared with CDLT. The aim of this study was to evaluate the infectious complication and clinical outcome in LDLT and CDLT group.

Methods. We analyzed the medical records of 148 consecutive liver transplant recipients from May 2010 to march 2014 at Pusan National University Yangsan Hospital, Yangsan Korea.

Results. There were 151 Liver transplantations in 148 patients. Of the 148 patients enrolled, 90 (60.8%) underwent LDLT. Baseline characteristics differed between LDLT vs CDLT group with regard to percentage hepatocellular carcinoma at transplantation (n = 57 vs 12, respectively, p = 0.00) and transplant model for end-stage liver disease (MELD) score (mean = 12.6 vs 26.1, respectively, p = 0.00).

Overall incidence of infectious complications after liver transplantation was 44.5% (64/148) and incidence of infections in CDLT was higher than LDLT group (n = 40, 71.4% vs n = 25, 27.8%, respectively, p = 0.00)

Bacterial infections were the most common infectious complications (n = 55, 85.9%) followed by fungal infections (n = 5, 7.8%), viral infections (n = 3, 4.7%), and tuberculosis (n = 1, 1.6%). Enterococcus spp. (33.3%) were the leading pathogens followed by coagulase-negative staphylococci (17.3%) and E. coli (12.3%). However, the distribution of etiologic agents was not different between CDLT and LDLT group. Intra-abdominal infections (n = 24, 16.4%) were the most common type, which were more frequent in CDLT group (n = 15, 26.8%) than in LDLT group (n = 9, 10.0%) (P = 0.008).

In CDLT group, higher 100-day mortality (n = 16,27.6% vs n = 4, 4.4%, respectively, p = 0.00), longer post operation admission day (mean = 50.9 ± 33.6 days vs 32.13 ± 21.8 days, respectively, p = 0.00) and longer stay of ICU (mean = 23.5 ± 12.7 days vs 10.9 ± 8.9 days, respectively, p = 0.00) were observed.

Conclusion: Our data showed more frequent infectious complication, higher mortality and poor in-hospital outcome in CDLT group than LDLT group. Different in-hospital managing strategies should be considered in CDLT group to reduce infectious complication and mortality.

Disclosures. **All authors:** No reported disclosures.

448. The Epidemiology of *Clostridium difficile* Infection in Liver Transplant Recipients

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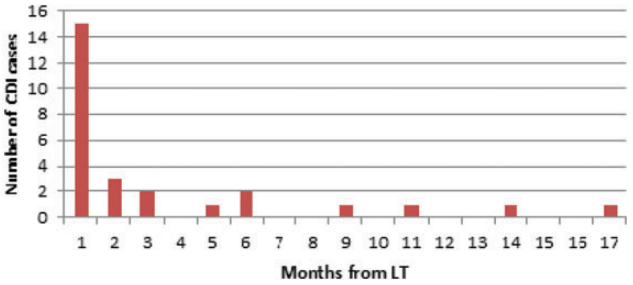
Background. Although *Clostridium difficile* infection (CDI) is common in liver transplant (LT) recipients, the risk factors, clinical manifestations and outcomes for CDI have not been well studied in this population.

Methods. A retrospective study of adults who underwent LT between January 1, 2011-April 4, 2013 at The Mount Sinai Hospital was conducted. Antibiotic exposures from one year prior to LT until one year after LT were reviewed. Clindamycin, fluoroquinolones, piperacillin-tazobactam, 3rd and 4th generation cephalosporins and carbapenems were considered "high-risk" antibiotics. Exclusion criteria were CDI <2 months before LT, prior LT during the study period, death <14 days after LT, and lack of one year follow-up.

Results. There were 214 LT cases during the study period, and 192 patients met inclusion criteria. CDI occurred in 14% (27/192). 56% of the CDI cases occurred within two weeks of LT (figure). Compared to patients without CDI, patients with CDI were more likely to have higher Model for End-Stage Liver Disease (MELD) scores (mean 24.4 vs 19.8, p = 0.04), and liver disease due to either non-alcoholic steatohepatitis (NASH) (5/27 vs 9/165, p = 0.031), or HIV-HCV co-infection (3/27 vs 2/165, p = 0.021). In the year following LT, patients with CDI received more days of high-risk antibiotics (18.3 vs 9.6, p = 0.041), had more hospital admissions (2.7 vs 1.3, p = 0.0006), and spent more days in the hospital (34.1 vs 10.7, p = 0.0001).

At the time of CDI all patients had diarrhea, however, only 7% had a white blood cell count >12, and 26% had fever >38°C. All patients were treated with either metronidazole or oral vancomycin for a mean of 14.9 days. Six (22%) developed CDI relapse, and all were successfully treated. No patients died of CDI after a mean follow-up time of 1.8 years. However, overall survival was significantly lower among those with CDI (78% vs 92%, p = 0.033)



Time from liver transplant (LT) to *Clostridium difficile* infection (CDI)

Conclusion. Risk factors for CDI in LT recipients were higher MELD scores, NASH cirrhosis and HIV-HCV co-infection. CDI was most common in the first two weeks after LT and was infrequently associated with leukocytosis or fever. CDI in LT recipients was associated with lower overall survival.

Disclosures. **All authors:** No reported disclosures.

449. Infections in Recipients of Haploidentical Bone Marrow Transplant: A Modified Prospective Cohort Study

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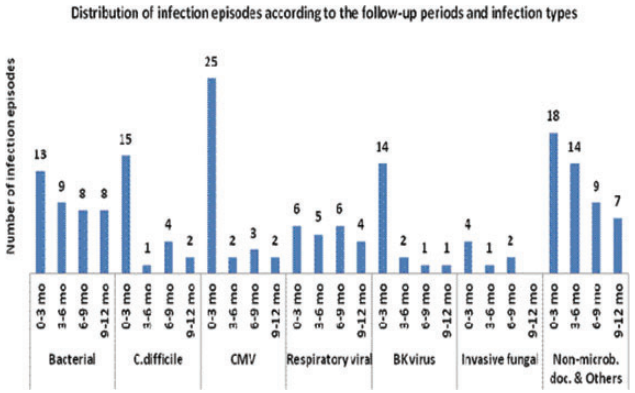
Background. Allogeneic hematopoietic stem cell transplantation (HSCT) from HLA-matched donors cures people with hematological malignancies, but suitable HLA-matched donors are available for a minority. More options are provided with related, haploidentical HSCT (haplo) donors. Our center has pioneered haplo HSCT, especially with use of reduced-intensity (RI) conditioning before bone marrow infusion, and high-dose cyclophosphamide as GVHD prophylaxis. Although low rates of non-relapse mortality (NRM) have been reported, no studies have assessed the epidemiology and outcomes of infections in this unique population.

Methods. A modified prospective cohort study that employed active consent and 3-month windows for data capture (by record review and patient contact) was performed to assess event-driven infectious complications for one year after HSCT. We report details of infections developing in 53 of 162 HSCT recipients enrolled who received haplo HSCT after RI in 2012.

Results. Median age was 60 (range 20-75), with most male (77%) and Caucasian (89%). Non-Hodgkin's lymphoma was the most common underlying disease, followed by AML, with 34% having relapsed or active disease at HSCT. Mortality at 1-year was 30%. 186 infectious events were identified. Per-patient incidence for CMV, bacterial, *Clostridium difficile*, viral respiratory, BK virus, and invasive fungal infections were 43%, 42%, 30%, 26%, 26%, 13%, respectively. Timing and type of infectious events are shown in the Figure. Bacteremia was present in 55% of bacterial infections, mostly with gram-negatives and coagulase-negative Staphylococci. Lower respiratory tract infections were the second most common (26%), followed by GU (13%). While CMV reactivation was common, disease was rare (n = 3). Most common non-microbiologically documented infections were respiratory (61%), and skin (34%).



Conclusion. Despite low (NRM), infections are relatively common, with frequencies highest during the first 3-months. Capture of event data emphasizes the missing microbial cause of many treated respiratory and skin infections. More knowledge of risks will enable development of more tailored screening and prevention algorithms.

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450. Multidrug Resistant Gram Negative Bacteria in a Cohort of Hematopoietic Stem Cell Transplant Recipients

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Background. Bacterial infections are major contributors of morbidity and mortality in hematopoietic stem cell transplant (HSCT) recipients. Little is known about the risks for, or impact of multidrug resistant gram negative (MDRGN) bacterial infections in this population.

Methods. Patients receiving HSCT at Johns Hopkins Hospital between January and December 2012 were consented into a modified, prospective, cohort study to evaluate infectious complications and followed at 3 month intervals. Data relating to underlying disease, transplantation, infections, antimicrobials and complications were collected. Uniquely, the study used standardized definitions to code infectious outcomes. International standard definitions for acquired antimicrobial resistance from the European Society of Clinical Microbiology and Infectious Diseases were used to classify multidrug resistant bacteria. The incidence and type of infections were determined, and outcomes were assessed by risk factor analyses evaluating death, performed by logistic regression.

Results. 162 HSCT recipients were enrolled during the study period. 57% were men 93/162. Most had acute myelogenous leukemia (AML) 44/162 (27%) or lymphoma 41/162 (25%). 73% of grafts were bone marrow 118/162. 53% of donors were mismatched, related (haploidentical) 86/162. 65 patients developed 102 bacterial infections; majority 70/102 (69%) were detected as bacteremia. 36 of 65 patients (55%) developed infections caused by gram-negative bacteria (n = 46). MDRGN organisms were recovered in 21/102 (21%) bacterial infections. E. coli was most common 10/21 (48%). Overall incidence of MDRGN infections was 21/165 (13%). Majority of MDRGN caused bacteremia 15/21(71%). Death occurred in 34/162 (21%) of HSCT recipients. In multivariable logistic regression, only receipt of an allogeneic transplant (OR 3.8, p = 0.047, 95% CI 1.0-13.9) and disease relapse (OR 3.0, p = 0.01, 95% CI 1.3-7.0) were independent predictors of death, with MDRGN infection associated with a non-significant trend (OR 2.2, p = 0.17, 95% CI 0.7-6.6).

Conclusion. MDRGN infections are common after hematopoietic stem cell transplant and frequently involve the bloodstream, with associated trends to poor outcomes. More efforts are needed to better characterize risks and outcomes of MDRGN infections in this population.

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451. Case Finding for Invasive Aspergillosis in Children

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Background. Invasive aspergillosis (IA) continues to pose a serious threat to immunocompromised children. We sought to determine the recent epidemiology of IA and compare the utility of multiple diagnostic strategies for IA case finding.

Methods. A retrospective case series of patients ≤18 years of age with proven, probable or possible IA[1] diagnosed from 2004-2013 was performed at NewYork-Presbyterian Morgan Stanley Children's Hospital, Columbia University Medical Center, New York, NY. Case finding was performed by review of positive cultures and serum galactomannan and by natural language processing to detect relevant pathology findings from autopsy or surgery (e.g., septated hyaline branching, angioinvasion) and from radiographic findings (e.g., halo, air-crescent, nodules).

Results. Twenty-one children were identified by culture (n = 8), galactomannan (n = 10), pathology (n = 14), and/or radiology (19) of whom 13, 4, and 4 cases met criteria for proven, probable, and possible IA, respectively. Natural language processing detected 6 additional cases not detected by either culture or galactomannan. Of the 21 children, 9, 2, and 2 had undergone bone marrow (BM), heart, and liver transplant, respectively, of whom 2 had both BM and solid organ transplant. The remainder were on chemotherapy (n = 5) or had other comorbid conditions including lupus (n = 2). IA rates were 2.8%, 0.9%, and 1.2% in BM, heart, and liver transplant recipients (p = 0.2). The most common sites of infection were lung (n = 12), sinuses (n = 3), and heart (n = 3); 5 patients had multi-site infections. Most (81%) had received antifungal agents within 90 days of IA diagnosis. Prior use of antifungal agents was similar in those with (n = 7/8) and without (10/13) positive cultures. Crude mortality was 67% at 3 months and 86% at 6 months.

Conclusion. In this 10 year study, IA rates appeared to be lower than previously reported, although crude mortality was similar. The use of natural language processing for case finding could improve IA surveillance efforts.

[1]De Pauw B, et al. Clin Infect Dis 2008; 46:1813-21.

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452. Pseudo-Outbreak of Fulminant Toxoplasmosis in Hematopoietic Stem Cell Transplant [HSCT] Recipients

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Background. Fulminant toxoplasmosis is a rare and difficult to diagnose complication after HSCT. Disseminated toxoplasmosis has a reported incidence of 0.1 to 6% in allogeneic transplants and is often fatal.

Methods. We report a cluster of 6 cases of fulminant toxoplasmosis, diagnosed within a 1-year period, at 2 neighboring transplant centers in NYC. Toxoplasmosis was diagnosed by positive serum PCR or at autopsy.

Results. Between December 2012 and September 2013, six patients were diagnosed with fulminant toxoplasmosis at MSKCC (4 cases) and NYPH/Weill Cornell (2 cases). The incidence of cases, preceding this study, was 1-2 cases per year at MSKCC and zero over the prior 5 years at NYP/Weill Cornell. Underlying diagnosis were acute lymphoblastic leukemia (2), acute myeloid leukemia, myeloma, lymphoma and myelodysplastic syndrome (1 each). Patients received ex-vivo T-cell depleted peripheral blood stem cell (TCD-PBSC) allograft (3) or umbilical cord + TCD-PBSC allografts (3). Five patients received anti-thymocyte globulin during their conditioning regimen. Five of 6 patients had positive *Toxoplasma* IgG prior to transplant. All patients presented with fevers prior to developing respiratory failure and death. Median days from transplant to death was 37 days (range 23-135 days). Diagnosis of

toxoplasmosis was made by serum PCR (n = 4 patients, range 45,100-4,900,000 copies/ml) or at autopsy (n = 2 patients). None of the patients were taking prophylaxis with activity against toxoplasma prior to diagnosis. No epidemiologic risk factors to explain the increased incidence were identified.

Conclusion. We report an unexplained cluster of 6 cases of fulminant and fatal toxoplasmosis, occurring within a 1 year period, in TCD and UCB recipients at 2 centers in NYC. No common epidemiologic link was identified. We urge a high index of suspicion for toxoplasmosis, and prompt investigation using toxoplasma serum PCR, for severely immunosuppressed HSCT recipients who are toxoplasma seropositive and present with unexplained fevers.

Disclosures. **All authors:** No reported disclosures.

453. Association of *Clostridium difficile* Infection (CDI) with Excess Mortality after Liver Transplantation (LT) for Hilar Cholangiocarcinoma (CCA)

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Background. LT patients are at higher risk of CDI compared to other hospitalized patients. Since LT patients with CCA often require antibacterial therapy for various infections, they may be at increased risk of CDI. However, the epidemiology, risk factors and impact of CDI in LT recipients with CCA have not been studied. We describe the epidemiology and risk factors for CDI and assess its impact on patient outcomes among LT patients with CCA.

Methods. We conducted a retrospective cohort study of patients who underwent neoadjuvant chemo-radiotherapy followed by LT for CCA during 2004-2013 at a single tertiary referral center.

Results. The population consisted of 124 patients who were followed for median duration of 4.2 years (interquartile range (IQR) 1.5-6.7 years). 15.9% developed CDI within 9.3 years post-transplant (19 episodes in 15 patients).10 (67%) were male. Thirteen (68%) were community-onset CDI. Initial treatment regimen consisted of oral metronidazole in 11 (58%) and oral vancomycin in 8 (42%) episodes. 4 patients developed recurrent CDI. Recurrent CDI was treated with oral metronidazole (50%) and oral vancomycin (50%). No patient died from CDI and none developed toxic megacolon or required surgical intervention. On univariable analysis, LT patients with history of a pre-transplant infection (within 6 months pre-transplant) had lower risk of post-transplant CDI (HR 0.3 (0.1-0.9); P = 0.04). Post-transplant CDI was associated with higher mortality when adjusted for recurrent CCA (HR 4.6 (1.4-15.2); P = 0.01).

Conclusion. CDI is a common infectious complication after LT for CCA, and is associated with a higher risk of mortality. Its prevention, through antimicrobial stewardship, may improve the outcomes of LT patients with CCA.

Disclosures. **All authors:** No reported disclosures.

454. Cytomegalovirus (CMV) Disease after Lung Transplantation (LT) is associated with increased mortality despite Extended Antiviral Prophylaxis

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Background. The duration of anti-CMV after LT varies widely among transplant centers. Because CMV is associated with poor outcome, some centers have extended prophylaxis to reduce the rates of CMV disease. We aimed to assess the epidemiology and outcome of CMV infection in high-risk LT recipients receiving extended (and for some, lifelong) prophylaxis.

Methods. This is a retrospective review of CMV D + /R- and R+ LT recipients during January 2005 to September 2012. Starting in January 2007, valganciclovir prophylaxis was given lifelong for CMV D + /R- and 6 months for R+ LT patients. The risks of CMV infection and disease were assessed for association with the duration of prophylaxis using Cox proportional hazard models. In addition we used similar models to identify risk factors for mortality, including the time-dependent covariates of CMV prophylaxis, CMV infection and disease, and age, sex, and Charlson comorbidity score.

Results. A total of 88 LT patients were at risk of CMV disease, including 32 CMV D + /R-, and 56 R+ LT patients (40 CMV D + /R + ; 16 CMV D-/R+). The median age at LT was 49 (IQR, 51-63) years; 49 (55.7%) were female. The most common indications for LT were chronic obstructive pulmonary disease (n = 27) and idiopathic pulmonary fibrosis (n = 25). CMV infection occurred in 11, while CMV disease occurred in 9 patients. Use and duration of CMV prophylaxis was not significantly associated with mortality. Significant factors for mortality were CMV disease [HR 4.19 (95% CI: 1.67-10.495), p = 0.002], and CMV infection and disease [HR 3.78 (95% CI: 1.73-8.24), p = 0.001]. The associations with these risk factors were not qualitatively impacted by prophylaxis. There was no significant difference in mortality between CMV D + /R- and R+ LT recipients.

Conclusion. CMV infection continues to occur in LT patients despite extended antiviral prophylaxis. It remains to be significantly associated with a higher rate of mortality. Better strategies to improve its prevention may lead to a better outcome among LT recipients.

Disclosures. **All authors:** No reported disclosures.

455. Enterococcal Infections (EI) in Liver Transplant (LT) Recipients- a 9 year retrospective review

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Background. Infections after LT cause significant morbidity and can adversely affect the function of the transplanted organ. Enterococcus faecalis and faecium are pathogens increasingly associated with infections after LT. However, there is scant data available regarding the incidence, risk factors and outcomes of EI in LT recipients.

Methods. This is a cohort study aimed at finding the incidence, risk factors and outcome of EI in LT recipients from years 2004 to 2012 at Henry Ford Hospital in Detroit Michigan. Clinical information including patient demographics, clinical, laboratory, treatment and outcome data was collected. Frequency analysis of all variables using a chi-square test for dichotomous variables and a students' t-test for continuous variables was performed. We also performed a logistic regression for risk factors which could contribute to death with EI.

Results. The incidence of Enterococcal infections in this cohort of 892 LT recipients was 18.3 per 100 (163/892) transplant patients. The median duration of development of EI from the date of transplant was 17 days (mean= 104; range= 1-1460). EI most often presented as urinary tract infections (42%), intrabdominal abscesses (27.6%) and bacteremia (19%). E.faecium (67%) was more common as compared to E.faecalis (33%). Vancomycin resistant *Enterococci*(VRE) was observed in 89/163 (55%) of infections. Among the EI 86.5% were treated for a mean duration of 16 + 19.8 days. Microbiological clearance was achieved in these patients at a mean duration of 4.8 + 7.15 days. A logistic regression revealed previous comorbidities (OR = 4.03), long ICU stay (OR = 1.02), EI occurring less than 1 year after transplant (OR =1.54), presence of concomitant infections (OR = 3.64) and presence of clinical progression or microbiological persistence of infection (OR = 6.36) predicted death in this cohort.

Conclusion. Enterococcal infections are an important cause for morbidity and mortality in liver transplant recipients. Urinary tract is the most common source followed by intraabdominal infections. VRE contributed to half of the EI in this cohort. Death is this cohort was predicted by clinical progression, microbiological persistence, previous comorbidities and presence of coexisting infections.

Disclosures. **All authors:** No reported disclosures.

456. Infectious Myositis Secondary to Multidrug-Resistant Gram Negative Rods in Cancer Patients

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Background. Severe infections caused by multidrug-resistant gram negative rods (MDR-GNRs) are increasing healthcare problem worldwide, especially in immunocompromised patients. Infectious myositis is a primary infection of skeletal muscles, usually secondary to gram-positive bacteria, especially *Staphylococcus aureus*. Although myositis secondary to GNRs are uncommon, several cases secondary to *Escherichia coli* have been reported in cancer patients. The objective of our study is to describe the microbiological and clinical characteristics of infectious myositis secondary to MDR-GNRs in cancer patients.

Methods. From January 2009 to December 2013 we retrospectively reviewed clinical isolates to identify cases of myositis secondary to MDR-GNRs. The diagnosis of infectious myositis was based on clinical presentation (fever and/or pain in the involved muscle), confirmed by compatible radiologic findings and/or muscle biopsy. MDR-GNRs were defined by presence of ESBL or resistance to $\geq$ 3 of 4 groups (3rd-4th generation cephalosporins, carbapenems, piperacillin/tazobactam and/or quinolones). Resistance to carbapenems alone was also criteria for Carbapenem-Resistant Enterobacteriaceae (CRE) and MDR-*Pseudomonas*.

Results. 17 cases of MDR-GNRs myositis were identified. Median age was 56 (10 - 83), with 14:3 male to female ratio. All patients had hematological malignancies (65% AML) and severe neutropenia, with 59% involvement of lower extremities. *E. coli* (47%) was the leading cause, followed by *Klebsiella pneumonia* (24%), *Enterobacter* species (18%), *Pseudomonas aeruginosa* (6%) and *Stenotrophomonas maltophilia* (6%). Among 15 Enterobacteriacea isolates, 27% were CRE and 74% produced ESBL. 88% were diagnosed based on positive blood culture and imaging studies, and the remaining 12% were based on muscle biopsy. 82% received active combination antimicrobial therapy, whereas 18% had active single therapy. None of the patients expired.

Conclusion. Myositis secondary to MDR-GNRs has emerged as a serious problem among neutropenic patients with hematologic malignancy. Awareness of this emerging

infection and causative organisms are essential to ensure early and appropriate therapy, to achieve the best possible clinical outcome.

Disclosures. **All authors:** No reported disclosures.

457. *Actinomyces* Infection in Hematologic and Solid Cancer Patients at the University of Texas MD Anderson Cancer Center in 1998-2014

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Background. *Actinomyces* species are common human commensal flora that become pathogenic only under certain conditions. Characteristics and treatment of actinomycosis in cancer patients have not been well described. A descriptive analysis of the disease in this population is presented herein.

Methods. *Actinomyces*-positive cultures for any source were identified at The University of Texas MD Anderson Cancer Center microbiology laboratory from 1998 to 2014. A retrospective review of the patients' medical records was carried out, and case definitions were created to classify the infection as proven, probable, or possible based on clinical presentation, culture site, and pathologic findings. Patient characteristics were collected, including known risk factors for actinomycosis noted in the literature.

Results. We identified a total of 156 cases of actinomycosis after excluding 582 contaminants. The patients' median age was 58 years. According to our definitions, 14 (9%) of the cases were proven, 60 (38%) were probable, and 82 (53%) were possible. Most of the patients (66%) had solid tumors, whereas 21% had hematologic malignancies and 12% had no cancer diagnosis. The presentations by anatomical site were the thorax (45%), abdomen-pelvis (29%), and face-neck (20%). Other patient characteristics are listed in the table. In terms of treatment, aminopenicillins were used most frequently (71%) followed by tetracyclines (37%). The mean duration of treatment was 6 weeks, and 74% of the cases responded to therapy.

Variable	Patients (%)
History of local trauma or surgery (at the site of infection)	52
Lymphopenia (<1,000 cells/mm^3)	40
Radiation therapy	34
Steroid use (within 1 month)	8

Conclusion. Actinomycosis in cancer patients has a variety of presentations, with the thorax being the most common site of infection. Disruption of mucosal barriers is an important factor in the pathogenesis of the infection as evidenced by the high number of patients with a history of local trauma/surgery and radiation therapy. Penicillins continue to be the most used antibiotics, with a good success rate. Diagnosis is complicated by frequent colonization by *Actinomyces* spp., necessitating a high level of clinical suspicion for an early diagnosis.

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458. Enterococcal Infections (EI) in Kidney Transplant (KT) Recipients – a Four Year Retrospective Review

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Background. Enterococcus spp. has emerged as an important nosocomial pathogen. The epidemiology and outcomes of Enterococcal infections (EI) in kidney transplant (KT) recipients is poorly defined. We describe the incidence, clinical epidemiology and outcomes of EI in KT recipients at our institution.

Methods. A retrospective cohort study was done of EI in patients who received a KT between 2009 and 2012 at Henry Ford Hospital, Detroit Michigan. Clinical information including demographics, clinical, laboratory, treatment and outcome data were collected. Frequency analysis was performed using chi-square test for dichotomous variables and student's t-test for continuous variables. Logistic regression analysis was done of risk factors that could contribute to adverse outcomes resulting from EI namely, clinical failure, graft loss or death. Clinical failure was defined as lack of clinical resolution of infection or microbiological eradication after ≥ 7 days of specific antibiotic therapy.

Results. The incidence of Enterococcus isolated in our cohort of 478 KT recipients, followed up for a minimum of 1 year after KT, was 16.1 per 100 (77/478). Of the isolates 47% were E. faecalis, 28% E. faecium and 42% vancomycin-resistant enterococci. In 10/77 (13%) patients the enterococci represented colonization and were not treated. EI in the remaining 67 patients developed at a median of 30 days after KT (mean: 113.04 days; range: 5-1362). Of the EIs 78% (52/67) were UTIs and 16% were intra-abdominal infections. The mean duration of antibiotic therapy for EIs was 18.0 ±13 days. Clinical failure occurred in 34% of patients with EIs. There was 1 graft failure, and 6 deaths of which 1 was attributable to Enterococcal bacteremia. Logistic regression analysis revealed that pre-transplant antibiotic use was predictive of adverse outcomes after EI (OR = 5.05, CI = (.94, 27.21), p = .042).

Conclusion. EIs especially UTIs are common after KT, but mortality and graft loss is rare. VRE was isolated in half the EIs, necessitating VRE-specific antibiotic treatment. Clinical failure occurred in about third of patients with EIs and was associated with pre-KT antibiotic exposure.

Disclosures. **All authors:** No reported disclosures.

459. Clinical Characteristics and Outcomes of West Nile Neuroinvasive Disease in Immunocompromised Hosts: A case-Control Study

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Background. Westnile neuroinvasive disease (WND) can result in significant morbidity and mortality even in immunocompetent hosts. The clinical features and outcomes in immunocompromised hosts have not been very well described

Methods. A case control study was performed involving patients receiving cancer care in our institution. All patients with a positive IgM or IgG in CSF were indentified as cases and randomly matched to three test-negative controls. Clinical presentations, outcomes, lab parameters, csf profiles and radiological studies were compared between the two groups

Results. Seven cases and tewnty-one controls met inclusion criteria. The underlying reason for immudeficiency for the cases was Multiple Myeloma in five patients HIV in one patient and renal transplant in another. The most common clinical symptom for the WND cases was fever in five patients (71%) whereas this was present in only nine (52%) of contols. Incidences of cranial nerve palsies, focal motor weakness and reflex abnormalities were not different between the two groups. CSF chemistry profiles was normal in the WN cases whereas CSF protienachia was more common four (19%) in the test-negative controls. CSF WBC was elevated in three (42%) of cases and twelve (57%) controls. Radiological studies were abnormal on three cases and 10 controls (two controls did not have studies) Death within ninety days occured in two (29%) cases compared to two controls (9.5 %)

Conclusion. WND presentation in immunocompromised hosts is similar to other CNS disorders and is often not associated with abnormal CSF profile or radiological imaging. Clinicians should maintain a high index of suspicion and a low threshold for CSF sampling in such patients

Disclosures. **S. Apewokin**, T 2 biosystem: Investigator, Research grant Viracor: Investigator, Research grant

460. Bacteremic vs Non-bacteremic Febrile Episodes in Children with Cancer: Prospective Multicenter Study in 5 Centers in Israel

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Background. There are significant differences among the centers in etiology of bacteremia during febrile episodes in children with cancer; and trend of increase in Gram negative bacteria has been observed. The objectives of the study were to characterize and compare bacteremic and non-bacteremic febrile episodes in children with malignancies.

Methods. Data from all episodes of fever in children (0-18 years old) with solid tumors (ST) or hematological malignancies (HM) in 5 Israeli hospitals were prospectively collected during 2008-2009, including: demographical, clinical, laboratory, microbiological information, treatment and outcome. For coagulase-negative staphylococci (CONS), only 2 consecutive cultures were considered positive.

Results. There were 863 episodes of fever in 232 children; 511 (60%) with ST; 352 (40%) HM; 135 (16%) episodes with 166 bacteria isolated from blood. Among them Gram positive bacteria 123 (74%), including CONS 61 (37%), *Staphylococcus aureus* and *Streptococcus viridians* 16 (10%) each, others 30 (17%); Gram negative bacteria including *E.coli* 12 (7%), *Klebsiella* spp. 8 (5%), *Enterobacter* spp. 7 (4%), *Pseudomonas* spp. 5 (3%), others 11 (7%).

Bacteremia was more frequent in the presence of Hickman catheter, 40/150 (27%) or PICC lines, 15/56 (29%) vs PORT-A-CATH, 80/622 (13%) ($p < 0.001$); when absolute neutrophil count (ANC) <100/mm^3 (80/378 (21%), vs ANC 100-499/mm^3 (29/211 (14%) or ANC >500/mm^3 (26/244 (11%) ($p < 0.001$); and in patients with most intensive treatments (including AML, JMML, some relapse protocols) 32/132 (24%) vs less

intensive treatments 103/579 (15%) ($p = 0.01$). The following parameters were significantly different in bacteremic vs non-bacteremic episodes: duration of fever, duration of neutropenia and CRP ($p < 0.05$ each). Mortality was 8/135 (6%) in bacteremic vs 2/714 (0.3%) in non-bacteremic ($p < 0.001$) episodes.

Conclusion. Gram positive pathogens remain the predominant cause of bacteremia in children with solid or hematological malignancies in Israel. Bacteremia is significantly more frequent following intensive chemotherapy, in the presence of Hickman or PICC line as compared to PORT-A-CATH; during deep neutropenia <100/mm^3, and it is associated with increased mortality.

Disclosures. **All authors:** No reported disclosures.

461. *Clostridium difficile* Infection and Mortality in Lung Transplant Recipients: A Single-Center Retrospective Cohort Study

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Background. *Clostridium difficile* infection (CDI) is a common cause of nosocomial diarrhea. It can result in severe complications and death, especially among immunocompromised hosts. We conducted a single-center, retrospective cohort study to characterize CDI in lung transplant (LT) recipients (R).

Methods. The transplant database was reviewed for all adult LT (including heart-LT) performed between 2002 to 2011. CDI was defined by the presence of diarrhea and a positive stool test for toxigenic *Clostridium difficile* (enzyme immunoassay [EIA] for *C. difficile* toxins A and B from 2002 to June 2007 followed by polymerase chain reaction (PCR) from July 2007 onwards), or colonoscopic or histopathologic findings of pseudomembranous colitis.

Results. Fifteen of 91 LTR developed at least one CDI episode, with a total of 19 CDI episodes. The cumulative incidence of CDI was 9%, 11% and 18% at 6 months, 1 and 3 years post-transplantation respectively. Median time to diagnosis of first CDI episode was 164 days (interquartile range: 75 to 562 days) after LT. 80% (12 of 15) of LTR who developed CDI had received induction immunosuppression with OKT-3 or thymoglobulin. All but one patient was receiving a gastric acid-suppressing agent at the time of CDI diagnosis. 71% (10 of 14) were on a proton-pump inhibitor, and 29% (4 of 14) were on a H2-receptor blocker. All were receiving chronic antibiotic prophylaxis: 15 (100%) were on trimethoprim-sulfamethoxazole for *Pneumocystis jiroveci* prophylaxis; 9 (60%) were on azithromycin for bronchiolitis obliterans syndrome prophylaxis. LTR who developed CDI had a higher hazard of mortality after diagnosis (HR: 3.73; 95% CI (1.82-7.66); *p*-value <0.01), and only 26% (4 of 15) of LTR were alive at the conclusion of the study.

Conclusion. CDI is associated with increased mortality in LTR. LTR have many risk factors that predispose them to development of CDI. Strategies to decrease the risk of CDI are needed to improve survival in this patient population.

Disclosures. **All authors:** No reported disclosures.

462. Impact of Pre-transplant LVAD Therapy on Survival and Infectious Complications in Heart Transplant Recipients

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Background. Heart failure has become a major epidemic affecting more than 23 million people worldwide. Approximately 550,000 new cases of heart failure are diagnosed annually in the United States. Orthotropic heart transplantation provides the greatest survival benefit for advanced heart failure. However, the demand for donor hearts far exceeds organ supply. Therefore, implantable left ventricular assist devices (LVADs) are increasingly being used as a bridge to transplantation and often as destination myocardial surrogate therapy. The objective was to analyze the rate of infectious complications and overall survival in heart transplant recipients with and without prior LVAD therapy.

Methods. We retrospectively reviewed medical records of all heart transplant recipients from January 2007 to June 2013 at 3 Mayo Clinic sites (Rochester, Arizona and Florida). Patients were excluded if: 1) their LVAD was not a Heartmate II device, 2) they had more than one device prior to transplant, 3) if they had a total artificial heart or RVAD implanted, and 4) if the patient died less than 6 months after transplant.Data including patient demographics, comorbid conditions, details of heart transplantation, infectious complications and survival was compared between patients who received LVAD therapy prior to transplant to those who did not.

Results. Overall, 296 patients were eligible for the study. Of these, 65 (22%) patients had received LVAD therapy prior to heart transplant. Majority of the patients were males (70%) and Caucasian (79%). The two groups were similar in terms of demographics and co-morbid conditions. The presence of pre-transplant LVAD did not have any significant effect on time to first infection after transplant (Hazard Ratio: 1.066, 95% CI [0.664 to 1.714], $p = 0.79$). The rate of post-transplant infections was 1.35 for those who received an LVAD and 1.31 for those who did not, $p = 0.91$. Similarly, no difference was seen between the two groups in terms of patient's survival (HR of 0.484, 95% CI [0.112 to 2.081], $p = 0.33$)

Conclusion. The presence of an LVAD prior to heart transplant does not increase rate of infection post-heart transplant and does not adversely affect survival in these patients.

Disclosures. **All authors:** No reported disclosures.

463. Incidence of Candidemia In Pediatric Liver Transplant Patients

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Background. In adult liver transplant recipients, candidemia is of significant concern in the post transplant period. Prophylaxis is recommended in adult high-risk patients, such as those with prolonged operative time, retransplantation or high-volume transfusion requirement. There are limited data on the incidence of candidemia in pediatric liver transplant recipients. We aimed to describe the incidence of candidemia in the 30 days post-liver transplant and frequency of perioperative antifungal therapy at a large pediatric institution.

Methods. All liver transplant patients from 2000 to 2011 at the Children's Hospital of Philadelphia were retrospectively reviewed. Data on perioperative antifungal therapy and blood culture results were collected. Patients were followed for 30 days post-transplant to evaluate for the onset of candidemia.

Results. 134 patients underwent liver transplantation over the 12-year study period. Candidemia was diagnosed in the first 30 days post transplant in 10 (7.1%) patients. Rates of candidemia varied with each three-year period with the lowest rate being in the last three years of the study (Table). Perioperative antifungal therapy was infrequently used. Rates increased between the periods of 2000 to 2002 and 2003 to 2005 but then remained stable (Table).

Table: Rates of candidemia and perioperative antifungal therapy by 3 year time periods

	Liver transplant patients	Candidemia (n, %)	Perioperative antifungal therapy (n, %)
2000-02	30	2, 6.7%	2, 6.7%
2003-05	24	4, 16.6%	3, 12.5%
2006-08	35	3, 8.6%	4, 11.4%
2009-11	45	1, 2.2%	5, 11.1%
Total	134	10, 7.4%	14, 10.4%

Conclusion. The incidence of candidemia among pediatric liver transplant patients appears to have decreased over time in this single center cohort. The overall rate of perioperative antifungal therapy remained low and did not increase in accordance with the decrease in candidemia. Further investigation in multicenter cohorts is warranted to determine sources for decreasing candidemia rates such as improved infection control practices and operating room factors.

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464. BK Virus Genetic Changes in Pediatric Kidney Transplant Patients with Prolonged BK Viral Load

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Background. BK virus (BKV) is a prominent post-transplant infection for pediatric kidney transplant patients. We do not know what differentiates the patient that manifests BK nephropathy or prolonged BK viral load from the patient who does not. Little is known about genetic changes in the entire genome, which encodes five proteins: agnoprotein, VP1-3, Large T and small t antigen. The overall aim of this study is to identify specific BKV strains (genetic variants) from pediatric kidney transplant patients that would predict higher risk of BKV disease.

Methods. To detect specific BKV strains, we sequenced the entire BK genome. Long range inverse PCR with four primer sets was used to amplify the full BK genome and next generation sequencing was performed using the Ion Torrent™ Personal Genome Machine. Longitudinal plasma samples were sequenced from 6 pediatric kidney transplant patients. BK viral load ranged from 10^3 to 10^6 during the sampling period.

Results. In the table, amino acid substitutions accounting for ≥ 95% of the populationare listed for each BK protein. For an individual patient, the same high frequency amino acid substitutions were consistently found in multiple longitudinal blood samples (average 3 samples/patient). Patients with prolonged and sustained high BK viral load by PCR with or without BK nephropathy were more often associated with amino acid substitutions in the Large T antigen compared to the other proteins. Few significant genetic changes were identified overall.

Patient	LT	VP1	VP2	Outcome	BK+ Duration
1	Q668 E L5F	S77R	-	BKN BK VL 10^4	14m
2	-		-	BKN BK VL 10^3	9m
3	S405C S1421C D241E	-	-	Persistent BK viral load	9m, now resolved
4	T592A		-	Persistent BK viral load	3m, now resolved
5			T341A	Persistent BK viral load BK VL < 10^3	6m
6	D241E			BKN BK VL 10^3	84m

BKN–BK nephropathy; BK VL–BK viral load; m-months

Conclusion. Using next generation sequencing, genetic changes resulting in amino acid subsititutions can be detected throughout the entire BK virus genome but appear to concentrate in the Large T antigen in pediatric kidney transplant patients who have persistent BK viral load with or without BK nephropathy. Large T antigen is known to be important in polyomavirus replication. Genetic changes in BK virus appear to remain stable, without any significant new genetic changes appearing over time.

Disclosures. **All authors:** No reported disclosures.

465. Systemic Ribavirin Therapy for Respiratory Syncytial Virus Infections in Pediatric Solid Organ Transplant Patients: A single hospital experience over 3 RSV seasons

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Session: 47. Transplant Infectious Diseases
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Background. Respiratory Syncytial Virus (RSV) is the most common cause of lower respiratory tract infection in children and supportive care remains the mainstay of therapy. Immunocompromised patients are more severely affected by RSV infection, but approved treatment options remain limited. Systemic Ribavirin treatment for RSV infections has been previously described in lung transplant recipients, but its use in in pediatric solid organ transplant (SOT) patients has not been well defined. Given the large volume of pediatric SOT patients at our center, we retrospectively analyzed the use of systemic ribavirin for RSV infections in this patient population.

Methods. We reviewed medical records for all pediatric transplant patients who had positive RSV antigen and/or PCR testing from October 2011 to April 2014. Patient characteristics, use and dosage of Ribavirin from pharmacy records, immunosuppresive therapy, co-infections, clinical and laboratory changes were evaluated.

Results. Fifteen patients who were RSV positive received eighteen courses of Ribavirin; one patient also received IV Ribavirin for compassionate. Eight patients who were RSV positive were not treated. Patient transplant types and demographics are provided in Figures 1 and 2. The oral Ribavirin dose ranged from 15-20mg/kg/day, given for a range of 5-14 day courses. Treatment had to be stopped in one patient due to pancytopenia. Additional outcome measures for PICU admission, oxygen requirement, need for mechanical ventilation showed no significant difference between the two groups. One patient in each group received Palivizumab for RSV prophylaxis per consensus guidelines.

Ribavirin was well tolerated in our pediatric SOT transplant patients with RSV infection without severe side effects. There were missed opportunities to provide RSV prophylaxis for these high risk patients. Larger prospective studies are needed to better describe oral Ribavirin as a potential treatment for RSV in this patient population.

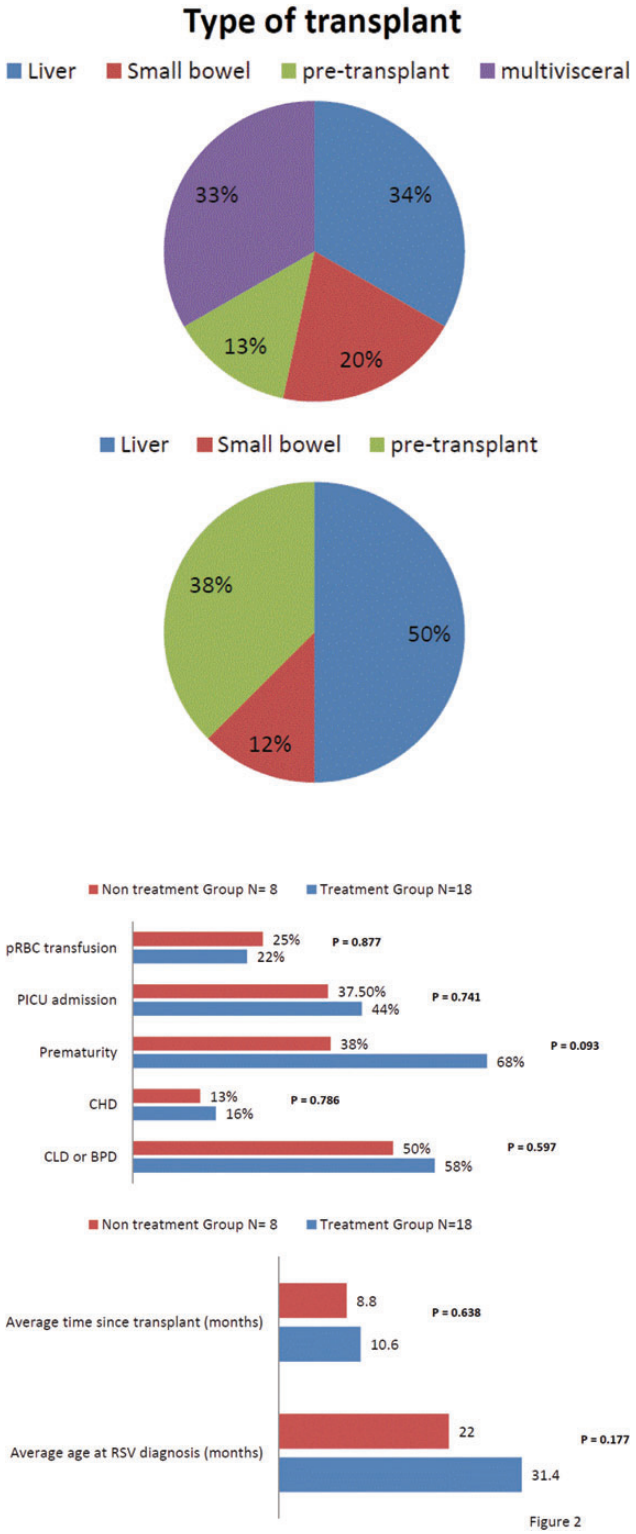

Figure 2

Conclusion. This is the first larger study of systemic ribavirin use for RSV in pediatric SOT patients.

Disclosures. **All authors:** No reported disclosures.

466. Skin lesions in febrile neutropenic patients

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Session: 47. Transplant Infectious Diseases
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Background. Rashes in febrile neutropenic patients present an important problem in differential diagnosis for their physicians. In these patients, rashes may be the first and only evidence of a serious and life-threatening infection. In this study, we aimed to retrospectively report the etiology of skin lesions in febrile neutropenic patients with hematologic malignancies.

Methods. In our study, hospitalized febrile neutropenic patients with hematologic malignancy, aplastic anemia, or bone marrow transplantation were included. Patient files were screened retrospectively and patients with skin lesions during febrile neutropenic episodes were selected. Patients with febrile neutropenia were initiated an antipseudomonal beta-lactam therapy according to IDSA guidelines. Skin lesions of these patients during febrile neutropenic episode, consulted and evaluated with infectious disease and dermatology specialists

Results. A total of 50 patients were included in our study. Twenty six (52%) of the patients were male and the average age was 45.8 (± 15), respectively. The most common underlying disease was acute myeloid leukemia with 29 (48%) patients. The most frequently observed type of lesion was maculopapular eruption (40%) whilst it was followed by erythematous necrotic nodule (18%). The most common cause of skin lesions were infections and drug eruptions with 26 (52%) and 16 (32%) patients, respectively. Ecthyma gangrenosum in 8 patients, skin involvement of oppurtunistic fungal infections in 7 patients and herpes labialis in 5 patients were most common causes of skin lesions in infection group. In 16 (32%) patients the skin lesions were found to be related to drugs; piperacillin/tazobactam, co-trimaxazol and etoposid were the most common cause of drug related skin lesions. Of the patients, 6 patients died during or soon after the development of skin lesions and in 5 of 6 patients, the skin lesions were found to be related with infectious causes.

Conclusion. Infections were found to be the most common cause of skin lesions in febrile neutropenic patients.

Disclosures. **All authors:** No reported disclosures.

467. Analysis of Clinical and Economical Outcomes of Fidaxomicin Use for *Clostridium difficile* infections

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Session: 48. Treatment of Antimicrobial Resistant Infections
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Background. *Clostridium difficile* infections (CDI) result in considerable morbidity and mortality. With more than 336,000 CDI cases reported in 2009 and the emergence of the hypervirulent NAP1/BI/027 *C. difficile* strain, there is great incentive to identify effective antimicrobial treatment options. Fidaxomicin is a novel agent with bactericidal activity against *C. difficile*, and its use may help achieve CDI resolution and prevent recurrence. The purpose of this study was to examine the use of fidaxomicin at the St. Vincent Indianapolis Hospital and to assess the clinical and economic benefits its use provides.

Methods. This retrospective matched cohort study evaluated patients with CDI who received fidaxomicin or vancomycin from March 2012-October 2013. Each adult participant who had received fidaxomicin was matched and compared to two participants who had received vancomycin. Participants were excluded if they had received either medication for less than two days and/or were pregnant during treatment. The primary objective was clinical efficacy, defined by cure or clinical improvement of CDI at discharge and neither a record of death nor readmission to a St. Vincent Health hospital thirty days post discharge. Secondary objectives included length of total hospital stay, length of hospital stay after initiation of CDI treatment, number of readmissions, number of readmissions related to CDI, adverse events, presence/development of CDI sequelae, and actual variable direct and total hospital costs.

Results. Twenty-six fidaxomicin patients met inclusion criteria and were matched to 46 vancomycin patients. Both cohorts were statistically similar at baseline in all areas except probiotic use (62% fidaxomicin vs 15% vancomycin, $p < 0.001$). There was no significant difference in clinical efficacy rates between the two cohorts (46% fidaxomicin vs 50% vancomycin, $p = 0.809$). Patients in the fidaxomicin cohort were found to have a longer average length of stay (22.5 days vs 13.8 days, $p = 0.015$). Other secondary outcomes were not significantly different.

Conclusion. Fidaxomicin did not show a difference in our composite outcome when compared to vancomycin in our patient population receiving therapy for CDI.

Disclosures. **M. Bochan**, Cubist Pharmaceuticals: Speaker's Bureau, Speaker honorarium

468. RBX2660 (microbiota suspension) for Recurrent *C. difficile* Infection: 60-Day Interim Analysis of the PUNCH-CD Phase 2 Safety Study

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Background. There is increasing recognition that fecal transplant (FT) is an effective treatment for recurrent *C. difficile* infection (CDI). However, donor screening and product preparation can be burdensome. Despite promising efficacy results, safety data are limited. We report on a 60-day interim analysis of the first prospective open-label multi-center safety study of a next generation microbiota restoration therapy that has been standardized and manufactured under controlled conditions.

Methods. Patients with recurrent CDI, defined as at least 3 CDI episodes or at least 2 severe episodes resulting in hospitalization, were enrolled. All patients received treatment with RBX2660 (microbiota suspension) administered via enema. A second treatment was permitted if CDI recurred in < 8 weeks after the first treatment. Follow-up was at 7, 30 and 60 days and 3 and 6 months after the last treatment. The primary objective was the product-related adverse events (AEs). A secondary objective was CDI resolution.

Results. Of the 40 patients enrolled at 11 centers in the US, 34 patients (mean age 66.8 years, 67.6% female) received at least one treatment. Thirty-one patients were included in a 60-day interim analysis. A total of 158 AEs were elicited in 29 patients. AEs were predominantly mild to moderate and included flatulence, belching, constipation, and occasional bouts of diarrhea. There were 9 serious AEs reported in 6 patients (3 recurrent CDI ≤ 8 weeks days post-treatment, all of which required hospitalization; 1 case of pneumonia; 1 pelvic fracture; 1 stab wound; 1 chronic obstructive pulmonary disease; 1 pulmonary edema and 1 respiratory failure). None of the serious AEs was related to RBX2660 or its administration. Efficacy of RBX2660 defined as the absence of CDI at 8 weeks after the last dose was 87.1%.

Conclusion. RBX2660 was well-tolerated and demonstrated satisfactory safety in a 60-day interim analysis of the first prospective multi-center study of a next generation standardized, commercially prepared microbiota restoration therapy for recurrent CDI.

Disclosures. **E. Dubberke**, Rebiotix: Consultant and Investigator, Consulting fee and Research support; Sanofi Pasteur: Consultant and Investigator, Consulting fee and Grant recipient; Merck: Consultant and Grant Investigator, Consulting fee and Research support; Cubist: Consultant and Investigator, Consulting fee and Research support **R. Orenstein**, ReBiotix: Investigator and Scientific Advisor, Consulting fee and Research support; Merck: Consultant and Investigator, Research support **P. Mariani**, Rebiotix: Investigator, Research support **K. Mullane**, Rebiotix: Research Contractor, Research support; Astellas Pharma US Inc.: Research Contractor and Speaker's Bureau, Research support; Ason Pharmaceuticals: Research Contractor, Research support; Chimerix: Research Contractor and Scientific Advisor, Research support; Cubist/Optimer: Research Contractor and Scientific Advisor, Consulting fee and Research grant; Merck Sharp and Dohme Corp: Research Contractor and Scientific Advisor, Consulting fee and Research support; ViroPharma: Research Contractor, Research support; Pfizer: Research Contractor, Research support **M. K. Sobcinski**, Rebiotix Inc.: Employee, Salary

469. The Relationship between Vancomycin Minimum Inhibitory Concentrations (MICs) and Treatment Failure among Patients with Methicillin-Resistant *Staphylococcus aureus* Blood Stream Infections (MRSA-BSI) at the University of Connecticut Health Center (UCHC)

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Background. MRSA-BSI has been associated with mortality rates of 20-30%. In recent publications, many factors have been associated with increased risks of treatment failure, including vancomycin MIC >1 μg/ml. Over the past few years, we have observed a substantial increase in the prevalence of MRSA with vancomycin MICs of 2 μg/ml. The purpose of our study is to compare the treatment outcomes of patients with MRSA-BSIs caused by MRSA strains with vancomycin MICs of 1 μg/mL vs 2 μg/mL.

Methods. This is an ongoing retrospective observational cohort study of adult patients with MRSA-BSIs that occurred between January 2008-November 2013. Patients were included in the cohort if they were treated with vancomycin for >3 days and had at least 1 serum vancomycin level obtained during therapy. The primary outcome is treatment failure defined as: a composite of 30-day mortality; persistent bacteremia for ≥ 5 days; or clinical nonresponse. Previous published studies using this composite endpoint have reported treatment failure rates of 39% to 53%. Therefore, we used an anticipated difference in treatment failure rate of 25%. An adequate sample size (based on α error of 0.05 and β error of 80%) would be 102 patients in order to achieve adequate power.

Results. Thus far data have been collected and evaluated for a total of 33 patients; vancomycin MICs were 1 μg/mL and 2 μg/mL for 16 and 17 patients, respectively. The median ages were 59 (range 23-92) and 57 years (range 21-85) respectively. There were 11 male and 5 female patients in the MIC ≤1 μg/ml group compared to 8 male and 9 female patients in the MIC ≥2 μg/ml group. Treatment failure was higher in the MIC ≥2 μg/ml group (10/17 = 64.7%) compared to the MIC ≤1 μg/ml group (6/16 = 37.5%). Treatment failure was predominantly related to higher numbers of patients with persistent bacteremia in the MIC ≥2 μg/ml group (7/17 = 41.2%) compared to the MIC ≤1 μg/ml group (3/16 = 18.8%). There were 6 patients in the MIC ≥2 μg/ml group who required ICU level of care as compared to 3 patients in the MIC ≤1 μg/ml group.

Conclusion. A preliminary analysis of data from 33 patients has already revealed a numerical trend towards higher prevalence of treatment failure driven by persistent bacteremia for the patients who had MRSA-BSIs caused by strains with vancomycin MIC ≥2 μg/ml.

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470. Oritavancin Activity Against Gram-positive Clinical Isolates Responsible for Documented Skin and Skin Structure Infections in USA and European Hospitals (2012-2013)

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Background. Oritavancin (ORI) is under regulatory review in the USA and Europe for the treatment of acute bacterial skin and skin structure infections (SSSI) caused by Gram-positive pathogens. The ORI activity was assessed against contemporary isolates causing SSSI.

Methods. 8,428 isolates from documented SSSI were collected from 27 sites in the USA and 34 sites in Europe, Israel and Turkey as part of the SENTRY Antimicrobial Surveillance Program (2012-2013). Bacteria were identified by standard algorithms and MALDI-TOF. Susceptibility testing was performed by CLSI methods (M07-A9); interpretation of MIC results used CLSI (2014) and EUCAST (2014) criteria

Results. ORI had $MIC_{50/90}$ values of 0.03/0.06 µg/ml against *S. aureus*, which were ≥8-fold lower than those obtained for vancomycin (VAN; $MIC_{50/90}$, 1/1 µg/ml), daptomycin (DAP; $MIC_{50/90}$, 0.25/0.5 µg/ml) or linezolid (LZD; $MIC_{50/90}$, 1/1 µg/ml). These agents had equivalent $MIC_{50/90}$ values against methicillin-susceptible (MSSA) and -resistant *S. aureus* (MRSA). ORI $MIC_{50/90}$ values against coagulase-negative staphylococci (CoNS; $MIC_{50/90}$, 0.03/0.06 µg/ml) were ≥8-fold lower than comparators. VanA-phenotype *E. faecalis* had ORI MIC values ($MIC_{50/90}$, 0.25/0.5 µg/ml) 16-fold higher than those obtained for VAN-susceptible isolates ($MIC_{50/90}$, 0.015/0.03 µg/ml); nevertheless, ORI was ≥2-fold more active than DAP ($MIC_{50/90}$, 0.5/1 µg/ml) or LZD ($MIC_{50/90}$, 1/1 µg/ml) against VanA *E. faecalis*. ORI ($MIC_{50/90}$, 0.004/0.008 µg/ml) had equivalent MIC values against VanB and VAN-susceptible *E. faecium* and higher MIC values ($MIC_{50/90}$, 0.03/0.12 µg/ml) against VanA strains. However, ORI MIC values against VanA *E. faecium* were 8- to -64 lower than active (100% susceptible) comparators (DAP, $MIC_{50/90}$, 2/4 µg/ml; and LZD, $MIC_{50/90}$, 1/1 µg/ml). ORI had potent activity against *S. pyogenes* ($MIC_{50/90}$, 0.03/0.12 µg/ml), *S. agalactiae* ($MIC_{50/90}$, 0.03/0.06 µg/ml) and the *S. anginosus* group ($MIC_{50/90}$, 0.008/0.015 µg/ml), with slightly higher MIC results against *S. dysgalactiae* ($MIC_{50/90}$, 0.06/0.25 µg/ml).

Conclusion. ORI had potent activity *in vitro* against this contemporary collection of Gram-positive isolates causing SSSI. These results benchmark ORI activity prior to becoming clinically available.

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471. Antimicrobial Activity and Spectrum of Ceftaroline Tested Against Bacterial Isolates Causing Skin and Skin Structure Infections (SSSI) in United States (USA) Medical Centers

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Session: 48. Treatment of Antimicrobial Resistant Infections
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Background. Ceftaroline (CPT), the active form of CPT fosamil, is a broad-spectrum cephalosporin with bactericidal activity against Gram-positive (GP) organisms, including methicillin-resistant (R) *S. aureus* (MRSA), and common Gram-negative organisms, including wildtype Enterobacteriaceae (ENT).

Methods. 8,446 isolates were consecutively collected from patients with SSSI in 149 USA medical centers in 2013. Strains were tested for susceptibility (S) by CLSI broth microdilution against CPT and comparators.

Results. 51.0% of *S. aureus* isolates were MRSA. CPT was very active against methicillin-S *S. aureus* (MSSA; MIC_{90}, 0.25 µg/mL) and MRSA (MIC_{90}, 1 µg/mL). Against MSSA, CPT was 16-, 4- and 4-fold more active than ceftriaxone (CRO), linezolid (LZD) and vancomycin (VAN), respectively; and 17.2% of MSSA were clindamycin (CLI)-R (5.0% constitutive [Con-R] and 12.2% inducible [Ind-R]). MRSA showed high R rates to levofloxacin (LEV; 57.7%) and CLI (25.8%; 17.7% Con-R and 8.1% Ind-R). CPT inhibited all β-haemolytic streptococci (βHS) at ≤0.03 µg/mL (MIC_{90}, ≤0.015 µg/mL), and it was at least 64- and 32-fold more active than LZD and VAN, respectively. CPT was slightly more active against group A compared to other βHS groups. Viridans group streptococci (VGS) were very S to CPT ($MIC_{50/90}$, 0.03/0.06 mg/ml), while 93.0 and 98.8% of strains were PEN-S ($MIC_{50/90}$, ≤0.06/0.25 µg/mL) and CRO-S ($MIC_{50/90}$, 0.25/0.5 µg/mL), respectively. CPT inhibited 81.8% of ENT at ≤0.5 µg/mL. CPT exhibited good activity against non-ESBL-phenotype strains of *Klebsiella* spp. and *E. coli* (MIC_{90}, 0.25 µg/mL for both), but limited activity against ESBL-producing and/or CRO-R strains.

	Cumulative % inhibited at CPT MIC (µg/mL):									
Organism (n)	**≤0.015**	**0.03**	**0.06**	**0.12**	**0.25**	**0.5**	**1**	**2**	**4**	**8**
S. aureus (5182)	<0.1	0.1	0.2	3.7	47.4	73.8	99.4	100.0	-	-
MSSA (2540)	0.1	0.1	0.3	7.5	95.1	100.0		-	-	-
MRSA (2642)	-	-	-	0.2	1.6	48.6	98.8	100.0	-	-
βHS (746)	95.3	100.0	--	-	-	-	-	-	-	-
VGS (172)	40.1	83.7	98.8	99.4	99.4	100.0	-	-	-	-
Enterobacteriaceae (2346)	0.3	4.0	28.7	57.6	72.9	81.8	87.2	88.9	90.1	91.2
E. coli (655)	0.9	9.0	42.9	70.7	80.8	87.2	89.2	90.1	91.0	91.9
non-ESBL (582)	1.0	10.1	48.3	79.6	90.4	96.7	99.0	99.8	100.0	
ESBL (73)	-	-	-	-	4.1	11.0	11.0	12.3	19.2	27.4
Klebsiella spp. (482)	0.2	2.1	29.5	60.2	78.6	84.2	87.1	88.2	88.8	89.8
non-ESBL (420)	0.2	2.4	33.8	69.0	90.2	96.7	99.3	99.8	99.8	99.8
ESBL (62)	-	-	-	-	-	-	4.8	9.7	14.5	22.6

Conclusion. CPT was active against GP and ENT pathogens recently isolated from SSSI in USA medical centers, including MRSA (0.0% R). CPT spectrum against GP was similar to that of LZD and VAN; against ENT, CPT had a spectrum comparable to CRO. CPT appears to be a valuable option for treatment of SSSI, including those caused by MRSA.

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472. Ceftaroline-induced Neutropenia: Two Case Reports

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Session: 48. Treatment of Antimicrobial Resistant Infections
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Background. Neutropenia is a known adverse effect of the cephalosporin antibiotic class, however it has not been well described with ceftaroline – a 5th generation cephalosporin with activity against methicillin-resistant *Staphylococcus aureus* (MRSA). We describe two cases in which patients experienced neutropenia while receiving ceftaroline for MRSA infections.

Methods. The first patient was a 33 year-old male with a history of intravenous drug use who developed MRSA tricuspid and mitral valve endocarditis with a vancomycin MIC of 2 mcg/mL and daptomycin MIC of 1 mcg/mL. After blood cultures remained positive with vancomycin, antibiotics were changed to ceftaroline 600 mg every 8 hours and daptomycin 8 mg/kg daily. After 32 days of therapy, the ANC decreased to 140/µL and ceftaroline and daptomycin were discontinued. With filgrastim, his ANC recovered after 7 days.

The second patient was a 37 year-old female admitted for severe gastroparesis and diabetes, found to have MRSA bacteremia with a vancomycin MIC of 2 mcg/mL. She was treated with vancomycin and then switched to daptomycin as blood cultures remained positive for 14 days. She was found to have a renal abscess and pyelonephritis but no other metastatic foci and was discharged on daptomycin. She was readmitted with CPK elevation > 1,000 mg/dL and peripheral eosinophilia thought to be due to daptomycin and was switched to ceftaroline 600 mg every 12 hours. After 20 days of inpatient and outpatient treatment, she was re-admitted with back pain and found to have an MRI consistent with septic arthritis of L3-L4 at which time vancomycin was added and ceftaroline increased to 600 mg every 8 hours. After 15 days of combination therapy, her ANC decreased to 1,000/µL (WBC of 2,900/µL). Ceftaroline was discontinued and 7 days later, her ANC and WBC normalized. She continued vancomycin monotherapy.

Results. Using the Naranjo scale, the likelihood of ceftaroline causing neutropenia in case 1 was possible (score of 4) and in case 2 was probable (score of 7).

Conclusion. In both of these patients, long courses of high dose ceftaroline were used to treat complicated MRSA infections. Patients should be closely monitored for neutropenia while receiving ceftaroline, particularly those receiving treatment with every 8 hour dosing for longer than 14 days.

Disclosures. **All authors:** No reported disclosures.

473. Comparison of MicroScan System Prompt and Turbidity Methods for Measuring Vancomycin Minimum inhibitory concentration (MIC) against Methicillin-resistant *Staphylococcus aureus* (MRSA) with MIC of 2ug/ml, the Clinical Implications and economic impact of using alternative antimicrobial agents to vancomycin for MRSA with possible MIC of 2ug/ml

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Background. Vancomycin remains the mainstay of therapy for Invasive MRSA infections. IDSA guideline recommends an alternative antibiotic in patients with vancomycin MIC of 2ug/ml. There is considerable variability of MIC results depending on the method used. MicroScan method is the most commonly used in the US. Usually MicroScan report values higher than broth microdilution method and this can lead to use of alternative agents.

Methods. A single-center study comparing MicroScan Prompt method vs MicroScan Turbidity method. We collected 21 MRSA isolates from sterile sites with Vancomycin MIC of 2ug/ml measured by Prompt method. The accuracy of MIC was confirmed by repeating the Prompt method. Same isolates were tested by Turbidity method and compared with CLSI standard Broth microdilution (BMD) method. In addition, we identified 56 patients over 9 months with invasive MRSA infections with vancomycin MIC of 2 measured by prompt method and its impact on prescribing an alternative agent.

Results. Only 52.2% of MRSA isolate were 2ug/ml when Prompt method was repeated. Turbidity method by MicroScan and BMD method showed only 9.5% of MRSA isolate were 2ug/ml. MicroScan Turbidity and BMD method correlated with each other 100%. MicroScan Prompt method overcalled vancomycin MIC in 90% of MRSA isolates. Among 56 patients with invasive MRSA infection, 86% of the patients had their antibiotics changed due to MIC of 2(n= 48 of 56). Antibiotics were changed to Daptomycin (72.9%), Ceftaroline (18.7%), Clindamycin (4.1%), Linezolid (2%) and Telavancin (2%). The prices of these antibiotics in comparison to Vancomycin in

multiples of Vancomycin price are Daptomycin 27, Ceftaroline 11, Clindamycin 0.3, Linezolid 25 and Telavancin 18. The average increase in cost was 16.2 times of the Vancomycin price.

Conclusion. The MicroScan Turbidity can be a cost effective method to measure vancomycin MIC and comparable to the standard BMD method. MicroScan Prompt method over calculates the Vancomycin MIC, results in overprescribing of alternative antimicrobial agents to vancomycin, increase the healthcare associated cost and risks increase of antimicrobial resistance which defies important goal in antimicrobial stewardship.

Disclosures. **All authors:** No reported disclosures.

474. Ceftaroline Salvage Therapy for MRSA Bacteremia Following Vancomycin Failure

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia (MRSAB) is associated with significant morbidity and mortality. Vancomycin (VAN) is the drug of choice for MRSAB, optimization of VAN dosing is challenging in the setting of an elevated MIC (>1-2mcg/ml). Daptomycin (DAP) is an alternative for MRSAB, however DAP MICs tend to be elevated among patients with elevated VAN MICs or that failed VAN, increasing the risk for DAP failure. Ceftaroline (CFT) is active against MRSA and may be considered in the management of MRSAB as well. We summarize our experience with CFT as salvage therapy (ST) for MRSAB and the correlation observed between elevated VAN MIC and/or VAN failure and DAP MIC.

Methods. All adult patients that received CFT ST for MRSAB following VAN failure and/or in the setting of elevated VAN MIC (>1-2 mcg/ml) between August 31, 2012 to April 30, 2014 were included. Patients were evaluated for clearance and duration of positive blood cultures, MIC data, ST regimen, and VAN duration. MIC methodology included: VAN (Vitek-2); DAP (Etest); CFT (agar dilution).

Results. Six MRSAB patients initially treated with VAN received CFT ST. All patients received prior or concomitant DAP with CFT. Five of 6 patients received an additional anti-MRSA antibiotic. Median VAN duration was 9 days and median total duration of positive blood cultures was 8.5 days. 83.3% (N = 5) of patients grew MRSA isolates with a VAN MIC of 1-2 mcg/ml, 3 of these isolates were DAP non-susceptible (NS). An additional MRSA isolate found to be DAP NS occurred in a patient that received 25 days VAN, and was reported to have had an elevated VAN MIC based on outside hospital cultures that could not be confirmed. All isolates were susceptible to CFT (MIC of 0.5-1 mcg/ml). One patient died prior to documented clearance of blood cultures, the remaining 5 survived and cleared blood cultures within 2-3 days following CFT.

Conclusion. CFT in combination with an additional agent is effective as ST for MRSAB, resulting in blood culture clearance within 2-3 days. MRSA isolates with elevated VAN MIC values and patients with prolonged courses of VAN exhibited elevated DAP MIC values. CFT may be preferred over DAP for MRSAB following VAN failure and/or an elevated VAN MIC given the prevalence of elevated DAP MICs.

Disclosures. **J. Pisano**, Pfizer: Grant Investigator, Research grant

475. Telavancin (TLV) *In vitro* Activity Tested Against a USA Collection of Methicillin-resistant *Staphylococcus aureus* (MRSA), Including a Multidrug-resistant (MDR) Subset (2011-2013)

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Background. The broth microdilution (BMD) method for telavancin (TLV) was recently revised by the FDA and CLSI. This study assessed the TLV activity using a revised BMD (rBMD) method, following the CLSI guidelines for water-insoluble agents. Polysorbate-80 was added in the test medium. This rBMD method was deemed necessary for greater accuracy and reproducibility of TLV MIC results.

Methods. 9,610 *S. aureus*collected from 28 USA sites were included. Susceptibility testing was performed based on CLSI guidelines (M07-A9 and M100-S24). MIC interpretation was guided by FDA (TLV) and CLSI (2014) criteria. MRSA resistant to ≥3 drug classes were defined as MDR.

Results. TLV had MIC_{50}, MIC_{90} and MIC_{100} of 0.03, 0.06 and 0.12 µg/mL, respectively, against methicillin-susceptible, MRSA, non-MDR and MDR subsets. MRSA with vancomycin (VAN) MIC = 2 µg/mL had TLV MIC_{50} (0.06 µg/mL) 2-fold higher than those MRSA with VAN MIC at ≤1 µg/mL. These TLV MIC_{50} results were equivalent to those noted for MRSA categorized by the daptomycin (DAP) MICs. However, TLV had MIC_{90} and MIC_{100} results of 0.06 and 0.12 µg/mL, respectively, regardless of MRSA subset. VAN ($MIC_{50/90}$, 1/1 µg/mL), DAP ($MIC_{50/90}$, 0.25/0.5 µg/mL) and linezolid ($MIC_{50/90}$, 1/1 µg/mL) were active against MDR (≥99.7% susceptible); however, TLV had MICs 8- to 32-fold lower than these comparators.

S. aureus (no. tested)	MIC (µg/mL) 50%	90%	Number (cumulative %) inhibited at MIC (µg/mL) ≤0.015	0.03	0.06	0.12
All (9,610)	0.03	0.06	364 (3.8)	6210 (68.4)	3012 (99.8)	24 (100.0)
MSSA (4,959)	0.03	0.03	242 (4.9)	3272 (70.9)	1437 (99.8)	8 (100.0)
MRSA (4,651)	0.03	0.06	122 (2.6)	2938 (65.8)	1575 (99.7)	16 (100.0)
VAN ≤1 µg/mL (4,561)	0.03	0.06	119 (2.6)	2930 (66.8)	1502 (99.8)	10 (100.0)
VAN = 2 µg/mL (90)	0.06	0.06	3 (3.3)	8 (12.2)	73 (93.3)	6 (100.0)
DAP ≤0.5 µg/mL (4,607)	0.03	0.06	122 (2.6)	2928 (66.2)	1545 (99.7)	12 (100.0)
DAP = 1-2 µg/mL (43)	0.06	0.06	0 (0.0)	9 (20.9)	30 (90.7)	4 (100.0)
MDR (1,371)	0.03	0.06	37 (2.7)	749 (57.3)	574 (99.2)	11 (100.0)
Non-MDR (3,280)	0.03	0.06	85 (2.6)	2189 (69.3)	1001 (99.8)	5 (100.0)

Conclusion. TLV had potent activity against *S. aureus*, including less susceptible and MDR subsets, inhibiting all *S. aureus* at ≤0.12 µg/mL, the FDA breakpoint for susceptibility. These results establish the new benchmark for TLV activity.

Disclosures. **R. E. Mendes**, Theravance: Grant Investigator, Research grant **H. S. Sader**, Theravance: Grant Investigator, Research grant **R. K. Flamm**, Theravance: Grant Investigator, Research grant **D. J. Farrell**, Theravance: Grant Investigator, Research grant **R. N. Jones**, Theravance: Grant Investigator, Research grant

476. Heterogeneous Vancomycin-Intermediate Coagulase-Negative Staphylococci in Neonates: Does treatment with Linezolid improve outcomes?

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Background. Heterogeneous vancomycin-intermediate coagulase-negative staphylococci (HCoNS) are emerging pathogens in neonates with central-line associated bloodstream infections (CLABSI). We aimed to compare clinical outcomes of neonates with HCoNS treated with vancomycin vs linezolid.

Methods. Retrospective cohort study of patients with a central line, ≥ 1 positive blood culture for HCoNS and treated with vancomycin or linezolid (2009-2014), from a level III neonatal intensive care unit. Study outcomes were: CLABSI duration, 7-day and 30-day mortality, thrombocytopenia, early CLABSI recurrence (≤ 2 weeks after first negative blood culture) and late recurrence (> 2 weeks after first negative blood culture). χ^2 was done for categorical variables and student t-test for continuous variables.

Results. Eighty nine patients were included; 62.9% (n = 56) were treated with vancomycin and 37.1% (n = 33) with linezolid. Vancomycin blood levels were done in 54/56 patients; 70.4% reached therapeutic levels during CLABSI treatment. Of all patients, 51.7% were males and 88.8% born < 37 weeks. Median gestational age was $27^{3/7}$ weeks and median birth weight was 805 g. All patients had similar underlying medical diagnoses; 54% with gastrointestinal conditions before CLABSI onset. Risk factors and clinical manifestations of CLABSI did not differ between groups. One third of patients required inotropes for hemodynamic instability and 19% developed necrotizing enterocolitis during or shortly after CLABSI. Median age at CLABSI was 15 days (2-97). *S.epidermidis* was causative in 96.6% of cases. Blood culture became negative within 48h of central line removal in 38% of patients. Statistically significant differences between patients treated with vancomycin vs linezolid included 30-day all-cause mortality (16.1% vs 27.3% respectively, p = 0.019) and late CLABSI recurrence (66.7% vs 0%, p = 0.024). All patients with late recurrences had initially been treated with vancomycin; half had ≥ 2 late recurrences. No significant difference was found for duration of CLABSI, thrombocytopenia, early recurrence, time-to-death or 7-day all-cause mortality.

Conclusion. In our study, vancomycin was as effective as linezolid for treatment of CLABSI caused by HCoNS in neonates. Additionally, we found that linezolid may prevent late CLABSI recurrence.

Disclosures. **All authors:** No reported disclosures.

477. In vitro Synergy Testing of Daptomycin with Beta-lactams, Gentamicin, Rifampin and Tigecycline against Daptomycin Non-Susceptible Enterococci

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Background. Combination therapy is an important consideration for treatment of daptomycin (DAP) non susceptible *Enterococcus*(DNSE) infections. There are limited *in vitro* or *in vivo* data regarding possible synergy between DAP with other antimicrobials against DNSE.

Methods. *In vitro* synergy testing of DAP with eight antimicrobials [ampicillin (AMP), cefazolin (CFZ), ceftriaxone (CRO), ceftaroline (CTL), ertapenem (ERT), gentamicin (GEN), rifampin (RIF), tigecycline (TGC)] was performed using time-kill assays against 9 unique isolates of DNSE [DAP MIC 24 - >256 ug/mL, determined by broth microdilution]. Change in colony-forming units per ml (CFU/ml) over 24-h antimicrobial exposures for DAP alone or in combination were evaluated by kill curve. Synergy was defined as ≥ 2 $\log_{10}$ reduction in CFU/ml at 24 h with the combination, as compared to DAP or the test antimicrobial alone. Two different DAP concentrations were tested: 0.5X the DAP MIC for each isolate; and 180 ug/ml, the maximal achievable serum DAP concentration (Cmax) corresponding to a DAP dose of 12 mg/kg/day. All other agents were tested at their respective Cmax, based on routine dosing.

Results. Two *E. faecalis* and 7 *E. faecium* were tested. AMP, CTL, ERT showed the greatest synergy with DAP against DNSE (Figure 1). Figure 2 shows the change in CFU/mL after 24-h antimicrobial exposures for test antimicrobial alone or in combination with DAP (at Cmax) for 2 isolates that displayed growth after 24 h incubation at the DAP Cmax. For 7 isolates that did not grow under these conditions, DAP (at Cmax) in combination with TGC and RIF displayed antagonism for 2 and 5 isolates, respectively. No trends were noted in results between *E. faecalis* and *E. faecium,* nor between isolates with high-level resistance (>256 µg/mL) and lower DAP MICs.

Figure 1: Synergy results for testing daptomycin with various antimicrobials at 0.5x the daptomycin MIC of 9 DNSE isolates

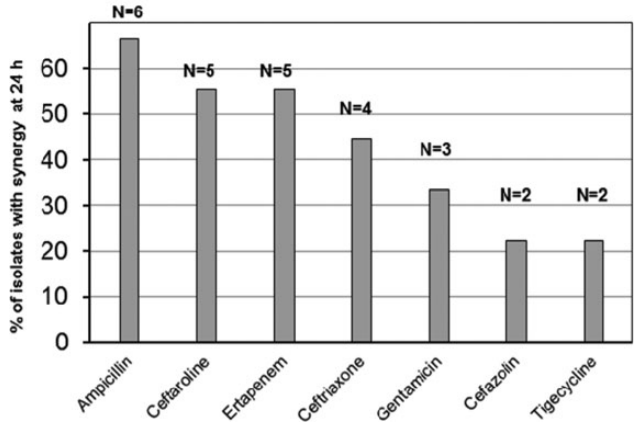
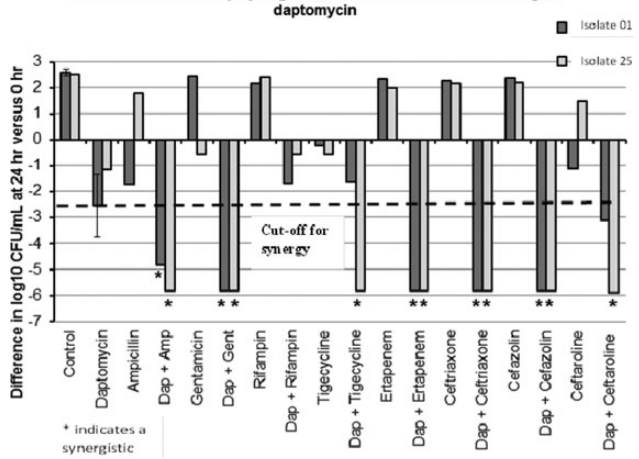


Figure 2: Interaction of daptomycin with various antimicrobials for 2 DNSE isolates that displayed growth over 24h incubation in 180 ug/ml daptomycin



Conclusion. Time-kill assays revealed synergy for the DAP-AMP combination in 6/7 DNSE isolates at 0.5X the DAP MIC and for both DNSE isolates that grew at the DAP Cmax. DAP also had synergy with all 5 beta-lactams tested and GEN against 22-56% of DNSE isolates. Since combinations of DAP with antimicrobials may display indifference or antagonism, further studies are needed to determine the potential usefulness of combinations of DAP with other agents for treatment of DNSE infections.

Disclosures. **R. M. Humphries**, Affinity Biosensors: Investigator, Research support

478. Daptomycin Susceptible vs Nonsusceptible *Enterococcus faecium* Bacteremias: Comparison of Clinical and Microbiological Outcomes

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Background. Daptomycin nonsusceptibility is reportedly emerging in all targeted gram-positive pathogens including *Enterococcus faecium.* Reported rates of daptomycin nonsusceptible *E. faecium* (DNSEF) isolates have ranged from 0.6% to 19.1%. Currently, there is limited data regarding the management and outcomes of daptomycin nonsusceptible enterococcal infections. The objective of this study is to expand current knowledge and to compare clinical and microbiological outcomes between patients with daptomycin susceptible *E. faecium* (DSEF) and DNSEF bacteremias.

Methods. A microbiology report of patients with positive blood cultures for *Enterococcus* species between September 2008 and October 2013 was generated. Electronic medical records were reviewed and data was collected from patients meeting the selection criteria. Patients of at least 18 years of age with blood cultures positive for *E. faecium* were eligible for inclusion. Identification and susceptibility testing was performed by the hospital laboratory using an automated microbiology system (Microscan Walkway®). Primary endpoints included clinical and microbiologic response rates. Secondary endpoints included hospital length of stay and 30-day mortality from index culture, and in-hospital mortality.

Results. Overall, 60 patients were evaluated; 35 were included in the DSEF group and 25 were included in the DNSEF group. In the evaluable patients, microbiological clearance was observed in 27 of 27 (100%) for the DSEF group and 21 of 21 (100%) in the DNSEF group (p = 1.00). Clinical cure was observed in 25 of 35 (71.4%) and 14 of 25 (56%) patients in the DSEF and DNSEF groups, respectively (p= 0.28). Median length of stay from the index culture in the DSEF and DNSEF groups were 11.7 and 12.4 days respectively (p = 0.78). As compared to DSEF bacteremias, DNSEF bacteremias had higher rates of 30-day mortality (44.0% vs 31.4%, p = 0.42) and overall in-hospital mortality (52.0% vs 34.2%, p = 0.19).

Conclusion. Bacteremias caused by DNSEF may be associated with worse clinical outcomes, including lower rates of clinical cure and higher rates of mortality.

Disclosures. **All authors:** No reported disclosures.

479. Clinical outcomes in patients with extended-spectrum-beta-lactamase-producing (ESBL) *Enterobacteriaceae* bloodstream infections (ESB) treated with carbapenems (CP) and non-carbapenems (NC)

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Background. CP is considered the drug of choice for treating serious infections caused by ESBL producers. Recent data suggest that alternative agents like beta-lactam/beta-lactam inhibitor combinations with in vitro activity such as piperacillin-tazobactam (PT) may have efficacy in treating ESB.

Methods. This 4 year retrospective observational cohort study compared CP to NC for treatment of ESB in adult patients at a community hospital from January 2010 to December 2013. Data were collected from electronic medical records, microbiology, and pharmacy databases. Primary outcomes include clinical response (CR), clinical relapse (RL), and in-hospital mortality (MO). Secondary outcomes include hospital length of stay (HL), ICU length of stay (IL), number of days to reach clinical improvement (DC), and ICU readmission (IR). Other outcomes include adverse drug events (AE) and duration of therapy (DT). MICs were determined by automated susceptibility testing methods. Patients were excluded from analysis if < 18 years of age, treatment < 24 hours, and severe neutropenia (<500/mm^3).

Results. 47 patients with documented ESB were identified with 43 evaluable for analysis. 20 patients were treated with CP for DT 5.5 ± 3.9 days (d). 23 patients were treated with NC for DT 5.7 ± 7.4 d. 78.3% patients in NC group were treated with PT (n = 18) while 8.6% patients in NC group were treated with levofloxacin (n = 2). 88.9% isolates from PT group had MIC < 8 mg/L (n = 16) and 90% isolates from CP group had MIC < 1 mg/L (n = 18). Majority of ESB were due to *E. coli* (n = 30) followed by *K. pneumoniae* (n = 11). 4 patients had mixed polymicrobial bacteremia. Most common source was urinary tract (n = 25) followed by biliary/GI tract (n = 9). Mean APACHE II scores (17 ± 5.8 vs 20.3 ± 9.5), age (72.7 ± 11.7 vs 71.8 ± 14 years) and comorbidities were similar between CP and NC. Mean IL was shorter (1.4 ± 0.6 vs 4.6 ± 4.6 d), MO was lower (5% vs 26%), and CR was higher in CP group (85% vs 60.9%). However, mean HL, DC, and RL were similar between both groups (8.1 ± 5.9 vs 10.6 ± 16.3 d, 2.9 ± 1.9 vs 3.7 ± 4.7 d, and 5% vs 4.3%, respectively). Neither IR nor AE were observed in CP group but 2 of each occurred with NC group.

Conclusion. MO is lower and CR is higher with CP compared to NC for treating ESB. The role for PT as alternative therapy for ESB remains controversial and warrants further studies.

Disclosures. **All authors:** No reported disclosures.

480. Development of Resistance to Group 2 Carbapenems in *Pseudomonas aeruginosa* isolates in a Long-term Acute Care Hospital in Metropolitan Detroit

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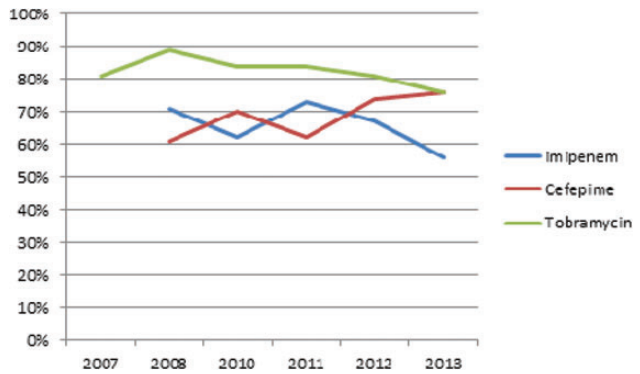
Background. Resistance of *Pseudomonas aeruginosa* (PA) isolates to imipenem and meropenem (Group 2 carbapenems) has been well documented in acute care hospitals. Literature review suggests a decrease in susceptibility of PA to imipenem and meropenem in these acute care hospitals is associated with an indiscriminate use of group 2 carbapenems as formulary antibiotics. However, there is limited research on the development of resistance to carbapenem antibiotics in PA isolates in long term acute care hospitals (LTACHs). The aim of this study is to analyze the change in susceptibility pattern of *Pseudomonas aeruginosa* to various antibiotics in a long term acute care hospital in Metropolitan Detroit from 2007 to 2013.

Methods. Minimum Inhibitory Concentrations (MICs) of various antimicrobials including imipenem, cefepime and tobramycin to PA was retrieved from the microbiology database from 2007 to 2013 at an LTACH in Detroit. The only carbapenems used as formulary antibiotics at this LTACH over all these years were group 2 carbapenems (imipenem and meropenem). Unique blood and urine isolates were included for analysis. Linear graphs were plotted to indicate the trend. Chi square test was used to calculate the p value.

Results. A decrease in susceptibility to imipenem was observed in PA isolates during the study period. The susceptibility of PA to imipenem decreased from 71% in 2008 (n= 140) to 56% in 2013 (p = .006, O.R= 1.975, 95% C.I 1.208, 3.230). However, there was not a significant change in susceptibility pattern for other antibiotics (graph).



Susceptibility trends of PA over time

Conclusion. Resistance to group 2 carbapenems in LTACHs is a cause of concern as these are recommended for severe nosocomial infection caused by *Pseudomonas aeruginosa*. This may exert selection pressure that can lead to collateral damage i.e., resistance to prescribed antibiotics as well as other antimicrobial agents. Also, as a result of resistance to group 2 carbapenems, LTACHs may have to use toxic agents like amikacin and colistin as an empiric choice for PA infection. Therefore, there is an urgent need to make group 1 carbapenems (Ertapenem) available in these LTACHs and include them as formulary antibiotics along with group 2 carbapenems. Also, de-escalation to ertapenem is recommended when clinically appropriate.

Disclosures. **All authors:** No reported disclosures.

481. Successful Treatment of Multi-drug Resistant *Acinetobacter baumannii* Ventilator-Associated Pneumonia with a Novel Colistin and Fusidic Acid Combination Therapy

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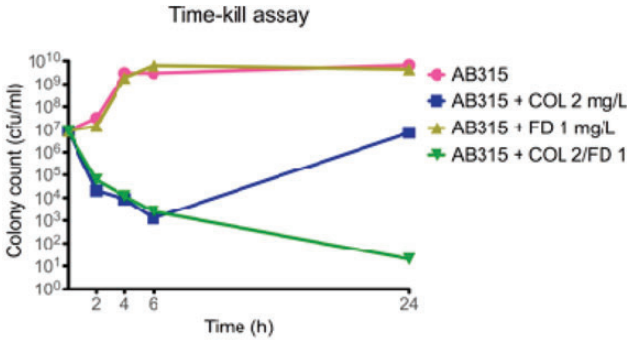
Background. The treatment of *Acinetobacter baumannii* infections is increasingly challenging due to the success of multi-drug resistant (MDRAB) strains and the lack of new compounds in development. Combination therapies are increasingly employed although there is little data on the clinical efficacy and outcome of unorthodox regimens.

Here we describe successful treatment of a MDRAB ventilator-associated pneumonia (VAP) in a 19-year-old trauma patient with colistin and fusidic acid following identification of potent antimicrobial synergy *in vitro*.

Methods. *Acinetobacter baumannii* isolated from endotracheal aspirates on day 15 was found to be resistant to all agents tested with the exception of colistin (MIC 0.25 mg/l). Potential synergy between colistin and fusidic acid was identified in a double disc diffusion test and investigated further in microtitre checkerboard assays and a time-kill study using susceptible clinical breakpoint concentrations of colistin (2 mg/l) and fusidic acid (1 mg/l; for *Staphylococcus spp*). The patient was treated with intravenous colistimethate sodium (Colomycin) 2 million units 8 hourly and fusidic acid 500mg 8 hourly for a total of 16 days.

Results. The MDRAB isolate was identified as a member of the UK OXA-23 clone 1 lineage by molecular typing. Synergy between colistin and fusidic acid *in vitro* was confirmed with a FICI of 0.5 and SBPI of 17 in checkerboard assays and an 8 log fold reduction in viable counts using the combination in time-kill studies (figure).

Clinical response was rapid, with improvement in both systemic and biochemical markers of infection within 48 hours. Clinical cure and microbiological eradication was achieved after 16 days of treatment with surveillance cultures for MDRAB remaining consistently negative.



Time-kill assay. COL 2mg/l – 8x MIC colistin sulfate. FD 1mg/l – 0.004x MIC fusidic acid.

Conclusion. The combination of colistin and fusidic acid was identified as a highly active therapy for the treatment of MDRAB VAP. The regimen was well tolerated, efficacious and led to sustained microbiological and clinical cure. Further studies to determine and refine the role of colistin/fusidic acid therapy in the treatment of MDR Gram-negative infections are warranted.

Disclosures. **All authors:** No reported disclosures.

482. Intrathecal Colistin Therapy to Treat Multidrug Resistant Gram Negative Central Nervous System Infection

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Background. *Acinetobacter baumannii* has emerged as an important multidrug-resistant(MDR) healthcare-associated pathogen. Meningitis caused by these MDR pathogen is a real challenge to treat in critical care units.

Methods. A 52 years old lady admitted in ITU following road traffic accident with fracture of paranasal sinuses,CSF rhiorrhea and altered sensorium. She was intubated and mechanically ventilated. He was otherwise stable but On 6th day there was few febrile spike.TLC was 22800(N90%), increased ET secretion, X-ray chest showed right lower opacity. Considering a case of ventilator associated pneumonia(VAP) emperical antibiotic started (inj Meropenem @1gm iv tds) after sending ET suction for gram stain and culture.

Results. Gram stain: Plenty pus cells, Gram negative coccobacilli, likely *Acinetobacter sp*-fair number. Considering Acinetobacter VAP inj colistin added with the existing regime @ 9 MU loading then 3 MU tds. Next day C/S report: *Acinetobacter baumannii* sensitive to colistin (MIC<0.5) but resistant to meropenem (MIC>16). Antibiotic combination therapy continued and patient became afebrile after 48 hours.

On 11th day patient again developed febrile spikes with drowsiness and neck rigidity. Lumbar puncture was done, CSF cloudy, Cell count-460(92% neutrophils), protein 78mg/dl, sugar 31mg/dl, all of which suggestive of bacterial meningitis. Gram stain: few gram negative coccobacilli. Considering a case of Acinetobacter meningitis, intrathecal colistin started @ 10mg/day, along with iv colistin and inj meropenem stopped. Culture grew same *Acinetobacter sp* with same antibiotic sensitivity. Treatment continued and within next couple of days patient became afebrile again, ventilator weaned off and extubated on day 17. The treatment continued for a period of two weeks with intermitten screening culture of CSF, until it became microbiologically negative. The period was otherwise uneventful except one episode of UTI caused by Proteus mirabilis which needed oral antibiotic therapy with levofloxacin. She was discharged on 27th day.

Conclusion. Patients with CNS infection by MDR Acinetobacter isolates susceptible to colistin may benefit from adjunct intrathecal colistin therapy, along with IV colistin as colistin can not achieve adequate CNS penetration after iv administration.

Disclosures. **All authors:** No reported disclosures.

483. Carbapenemase-Resistant *Enterobacteraciae* Bacteremia associated with Disseminated Strongyloidiasis: Successful Treatment with Subcutaneous Veterinary Ivermectin and Intravenous Polymyxin B and Tigecycline

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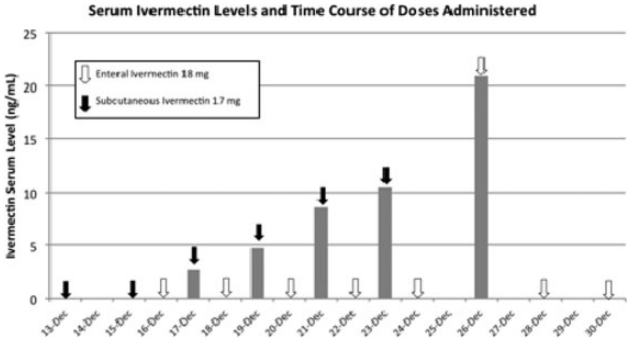
Background. In patients with severe, disseminated strongyloidiasis, case reports have described treatment with veterinary subcutaneous ivermectin with relative success. However, mortality with concomitant bacteremia is very high, reported up to 87%.

Methods. We describe a 70 year-old woman originally from Jamaica admitted with cervical myelopathy with severe C2 through C7 stenosis treated with multiple courses of high dose steroids and spinal fusion. She had a complicated hospital course including a post-operative wound infection. During this time, it was noted she had increasing gastrointestinal dysmotility and malabsorption with increasing feeding tube residuals. She was found to have carbapenemase-resistant *Klebsiella pneumoniae* (CR-Kp) bacteremia and pneumonia and was treated with intravenous polymyxin B and tigecycline for 17 days. After 9 days of treatment for the CR-Kp infection, she developed worsening hypotension requiring vasopressor support. She continued to have very high residual feeding tube output and underwent endoscopy. The pathology revealed diffuse *Strongyloides stercoralis*. She was placed on total parenteral nutrition and it was determined that she would not be able to adequately absorb oral ivermectin. An emergency IND was filed to the FDA requesting use of subcutaneous veterinary ivermectin. The parenteral ivermectin was obtained from a tractor supply store. With IRB approval and informed consent obtained, the patient received ivermectin 200 mcg/kg (17 mg) in 2 divided syringes subcutaneously every 48 hours.

Results. Monitoring of gastrointestinal aspirate samples demonstrated cleared parasite burden and the patient was ultimately discharged to hospice. Of note, she developed increased AST and ALT > 5 times the upper limit of normal which resolved upon discontinuation of ivermectin.



Conclusion. Several studies suggest that *S. stercoralis* can remain dormant for more than 30 years and corticosteroids may induce active infection. Disseminated strongyloidiasis has been associated with concomitant gram-negative bacteremia thought to be due to filariform larvae burrowing through the intestinal mucosa. With increasing rates of CRE, concomitant bacteremia with multi-drug resistant organisms furthers the complexity of *Strongyloides* infection.

Disclosures. **All authors:** No reported disclosures.

485. Colistin Nephrotoxicity in Critically Ill Patients after Implementation of a New Dosing Strategy

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Background. Intravenous colistin is increasingly used to treat multidrug-resistant Gram-negative infections. Highly variable nephrotoxicity rates were reported by recent studies. Recent PK/PD studies propose a loading dose and a maintenance dose equation for better efficacy; and data are scarce for renal toxicity of such regimens. This study aimed to evaluate incidence and risk factors for nephrotoxicity associated with colistin after implementation of a new dosing regimen including a loading dose.

Methods. A prospective observational study was conducted among adult patients who received at least 48 hours of intravenous colistin from December 1, 2012 to January 1, 2014 at medical and surgical intensive care unit (ICU)s in a university hospital. Severity of acute kidney injury (AKI) was defined by RIFLE (risk, injury, failure, loss, and end-stage kidney disease) criteria.

Results. Fifty-nine patients met the inclusion criteria, and 31 (52.5%) developed nephrotoxicity. The APACHE-II score at colistin initiation was > 15 in 81% of patients. The median time to nephrotoxicity was 7 days (range, 3 to 18). Patients with AKI were in Risk (10.2%), Injury (16.9%), Failure (25.4%) and no patients had long-term kidney failure or required hemodialysis after their course of colistin therapy. A logistic regression model identified three predictors of colistin-associated nephrotoxicity; age (odds ratio [OR], 1.04; 95% confidence interval [CI], 1.01 to 1.08), the number of days that estimated target plasma concentrations of colistin were ≥ 3.5 mg/L in the first week of therapy (OR, 2.4; 95% CI, 1.25 to 4.47), and baseline creatinine (OR, 0.2; 95% CI, 0.07 to 0.60). Colistin nephrotoxicity was not related to the duration of therapy, total cumulative or average daily dose. Thirty-day all-cause mortality rates were similar among patients who developed nephrotoxicity and those who did not (58.1% vs 46.4 %, respectively; p = 0.53).

Conclusion. In this cohort of severely ill ICU patients, colistin led to a relatively high rate of nephrotoxicity (52.5%). Further studies are needed to identify the optimal dose for both efficacy and safety. Monitoring colistin plasma concentrations may be a useful strategy for prevention of AKI.

Disclosures. **All authors:** No reported disclosures.

486. Meropenem and Piperacillin-tazobactam have Comparable Outcomes in Treatment of Bloodstream Infections Caused by Extended Spectrum Beta-lactamase Producing *E.coli and Klebsiellae*

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Background. Widespread use of carbapenems for treatment of infections caused by extended-spectrum β-lactamase (ESBL) producing Gram-negative bacilli has contributed to increasing carbapenem resistance. Despite some studies suggesting that β-lactam/β-lactamase inhibitor (BLBLI) combination antibiotics are non-inferior to carbapenems, their use has been limited by concerns of clinical efficacy.

We compared outcomes between patients treated with BLBLIs and carbapenems for bloodstream infection (BSI) caused by ceftriaxone non-susceptible *E coli* and *Klebsiella spp.*, in an institution with a relative high incidence of ESBL-producing isolates.

Methods. The study was conducted in the Singapore National University Hospital, a tertiary referral hospital with approximately 1,000 beds. All adult patients with a BSI caused by E. coli or Klebsiella spp. which were confirmed as third generation cephalosporin non-susceptible, but piperacillin-tazobactam and meropenem susceptible between May 2012 to May 2013 were included. Data recorded include demographic information, co-morbidities, presence of any devices, antibiotic therapy within 30 days of BSI and outcomes including subsequent isolation of carbapenem resistant organisms or Clostridium difficile, relapsed BSI and dates of discharge or death.

Results. During the study period there were 92 BSIs that fulfilled the microbiological inclusion criteria. 79 (85.9%) were caused by E. coli and 13 (14.1%) by K. pneumoniae. The patients had a median age of 74.5 years [range 23-100]. 53.3% were female. For patients given definitive monotherapy with either a carbapenem (n = 23) or a BLBLI (n = 24), 7 and 30 day mortality was similar in both groups (8.7% vs 8.3%, p = 1.0 and 17.4% vs 8.3%, p = 0.42 respectively). There were no significant differences in subsequent isolation of carbapenem resistant organisms (4.3% vs 4.2%, p = 1.0), C. difficile infection (13.0% vs 8.3%, p = 0.67) or relapsed BSI (0% vs 2%, p = 0.23).

Conclusion. BLBLIs appear to have a similar efficacy to carbapemens in treatment of susceptible ESBL E.coli and K.pneumoniae bloodstream infections. Larger randomized clinical trials are needed especially in this era of carbapenem resistance.

Disclosures. **All authors:** No reported disclosures.

487. Infections Caused by Enterobacteriaceae Species following Cardiac Surgery: Impact of Polymyxin Resistance on Treatment Outcomes

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Background. Mediastinitis is one of the dreaded complications post cardiac surgery resulting in high mortality rates (10% to 47%) and increased length of hospital stay and hospital costs. Thus far, no studies have described the management or outcomes of postoperative mediastinitis infections caused by carbapenem-resistant *Enterobacteriaceae*(CRE) resistant to polymyxins.

Methods. We conducted a single center, retrospective study of cardiac surgery patients who developed mediastinitis due to CRE infections from December, 2010 to March, 2014. Patients were grouped according to whether they were susceptible (MIC ≤ 2 μg/mL) or resistant (MIC ≥ 4 μg/mL) to polymyxin. Electronic medical records were reviewed for pertinent clinical and microbiological data; all isolates underwent PCR testing for the presence of the bla_{KPC} gene. The primary outcome measure was 60 day mortality and secondary outcomes included antibiotic related length of stay (LOS_{AR}) and duration of hospitalization.

Results. In the 33 patients who developed a CRE infection during the study period, all isolates tested positive for bla_{KPC-2}. Twenty patients (61%) were isolated with *Klebsiella pneumoniae* and 13 (39%) with *Enterobacter* species. Patients were empirically started on combination (n = 30, 91%) therapy; for targeted therapy, 10 (30%) were treated with double coverage, 14 (42%) triple coverage and 9 (27%) with four or more antibiotics. Fifteen (45%) patients were infected with polymyxin resistant strains (MIC range, 4 to ≥16 μg/mL); 18 (55%) were infected with polymyxin susceptible strains (MIC range, ≤0.5 to 2 μg/mL). Patients with a polymyxin resistant infection had a significantly higher mortality at 60 days compared to patients with a polymyxin susceptible infection (53% vs 11%, p = 0.02). No significant difference in median LOS_{AR} was detected between groups (42 days [IQR, 28-54] vs 30 days [IQR, 16-44], p = 0.12). In addition, the length of hospitalization between groups was not significant (70 days [IQR, 48-83] vs 56 days [IQR, 40-67], p = 0.11).

Conclusion. Polymyxin resistance adversely impacts patient outcomes with CRE mediastinitis infections. Further research is needed to identify optimal treatment strategies to reduce mortality associated with multi-drug resistant mediastinitis infections.

Disclosures. **A. Forrest**, Durata Therapeutic: Consultant, Consulting fee

488. Treatment Outcomes in Patients with Extended-Spectrum Beta-lactamase Producing Organisms

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Background. Extended Spectrum Beta-Lactamase (ESBL) producing organisms are associated with significant morbidity and mortality. In 2010, the Clinical and Laboratory Standards Institute (CLSI) lowered the breakpoints for most cephalosporins. This change was made in part because minimum inhibitory concentrations were thought to be more predictive of outcomes than the presence of an ESBL enzyme per se. Our institution implemented these interpretative criteria in April 2011 but continued to perform ESBL testing for quality assurance purposes without reporting the results to clinicians. Therefore, we sought to evaluate the impact of the change in ESBL reporting on treatment outcomes, prescribing patterns, and cost savings.

Methods. Patients with blood cultures positive for ESBL-producing *Enterobacteriaecae* from January 2007 to December 2009 (i.e., PRE) were compared to patients from April 2011 to December 2013 (i.e., POST).

Results. We identified 80 patients with ESBL-producing *Enterobacteriaecae*, with 38 patients (41 isolates) in the PRE group and 42 patients (43 isolates) in the POST group. Baseline characteristics were similar between groups. The organisms identified in both groups were *E.coli* (64%), *K.pneumoniae*(23%), *E.cloacae*(7%), and others (6%). The recurrence rate in the PRE and POST (12% and 7%, p = 0.2), the length of stay (median 19 vs 13 days, p = 0.1) and 30-day all-cause mortality (32% vs 19%, p = 0.3) were not statistically significantly different between both groups. 80% (34) of patients in both groups were treated with carbapenems; 58% (20) of these patients had isolates which were also susceptible or susceptible dose-dependent to cefepime based on the new CLSI criteria. Approximately $400 per patient would have been saved if cefepime had been used instead.

Conclusion. The change in ESBL reporting was not associated with a statistically significant change in treatment outcomes or prescribing patterns or drug costs. This may have implications for improved stewardship.

Disclosures. **S. Butler-Wu**, Thermo Fisher Scientific: Scientific Advisor, Salary

489. Accuracy of Clinicians' Empiric Treatment Choices for Resistant Gram-Negative Uropathogens

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Background. Emergence of multi-drug resistant uropathogens (MDR UTI) is making treatment of UTI more challenging. We sought to evaluate the accuracy of empiric therapy for gram-negative MDR UTI and the utility of prior culture data in improving accuracy.

Methods. We performed a retrospective review of electronic health record for treatment of MDR UTI from 3 VA facilities from 2010-2013. MDR UTI was defined as a clinician diagnosed infection resulting in therapy for a gram-negative uropathogen resistant to 3 or more classes of antibiotics. Previous culture data and antimicrobial use were captured from inpatient and outpatient settings.

Results. Among 111 episodes of MDR UTI treated by clinicians, 58 (52.2%) empiric therapy choices were active against the pathogen. 81 had prior microbiologic data available for a gram negative organism within the last 2 years, with 69% within the last 6 months. 46/81 (56%) patients received empiric therapy concordant with prior available culture data whereas 35/81 (44%) received discordant therapy. When empiric therapy was concordant with prior culture data (even if current MDR UTI was not the same organism), the antibiotic covered the uropathogen in 36/46 (78%) events. If therapy was discordant from previous microbiology, 12/35 (34%) empiric therapy choices were active (OR 6.9; 95% CI 2.6;18.6, p < .001). Empiric therapy was equally as likely to be active when concordant with recent (within 6 months) or remote (2 years) culture data (75.8% vs 84.6%, p = .70 Fishers). Genitourinary (GU)-directed agents (nitrofurantoin or sulfa; OR 18.0, 95% CI 5.4;59.1, p <.001) or broad-spectrum agents (carbapenems, 4thgen cephalosporins; OR 33.1, 95% CI 8.6;127.1, p <.001) were more likely to be active than fluoroquinolones and earlier generation cephalosporins.

Conclusion: Only half of empiric therapy choices were active against MDR UTI. Choosing an agent concordant with previous susceptibility data significantly increased the chance of activity for the current MDR UTI, even if the previous uropathogen was a different species and the data was remote. Either GU-directed or broad therapy choices were more likely to be active than other regimens. Accuracy of empiric therapy could be improved using these simple rules.

Disclosures. **K. Gupta**, Paratek: Consultant, Consulting fee

490. High Dose Tigecycline for the Treatment of Multi-Drug Resistant Gram Negative Urinary Tract Infections

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Background. Tigecycline is a glycylcycline derived from the tetracycline antibiotics with potent bacteriostatic activity against gram negative, gram positive, and anaerobic organisms. With only 15 to 22 percent of tigecycline excreted unchanged in the urine with a standard dose of 50 mg every 12 hours, clinicians have debated the use of tigecycline for the treatment of multi-drug resistant urinary tract infections (MDR UTIs) based on concerns about inadequate drug concentrations in the urine. Therefore, higher doses of tigecycline (100 mg every 12 hours) may be warranted to achieve higher urinary concentrations as the drug displays linear pharmacokinetics. The purpose of this study is to evaluate clinical outcomes using high-dose tigecycline for the treatment of MDR UTIs.

Methods. A retrospective review was conducted on adult patients who received high dose tigecycline (100 mg every 12 hours) for the treatment of MDR UTIs between 2012 and 2013. Data was collected and analyzed to compare treatment success and failure rates, time to treatment success, length of hospital stay, incidence of *Clostridium-difficile* associated diarrhea, and incidence of nausea and vomiting.

Results. Of the 107 patients with UTIs who were administered tigecycline, 7 patients were treated with high dose tigecycline. Twenty-eight percent of the patients were male with a median age of 58 years (range 30 – 79). The UTIs were most commonly caused by extended spectrum beta-lactamase Enterobacteriaceae (71%) followed by *Klebsiella pneumoniae* carbapenamases (43%). Overall, 86% and 14% of the patients who were treated with high dose tigecycline were found to have treatment success and treatment failure, respectively. Nausea and vomiting occurred in only 1 patient without the need for discontinuation of therapy.

Conclusion. Although the sample size was small, high dose tigecycline appears to be an alternative for the treatment of MDR UTIs. However, larger, prospective studies are warranted to further characterize this relationship.

Disclosures. **All authors:** No reported disclosures.

491. Comparative Effectiveness of Single vs Combination Antibiotic Prophylaxis for TRUS-biopsy

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Background. Single agent prophylaxis with fluoroquinolones (FQ) or cephalosporins (drugs of choice) or trimethoprim-sulfamethoxazole or aminoglycosides (alternatives) is recommended prior to transrectal ultrasound guided prostate biopsy (TRUS-biopsy). However increasing FQ resistance (FQ-R) has led to a rise in post-biopsy infections. We sought to compare the rate of infectious related complications in patients receiving ciprofloxacin vs alternative regimens such as ciprofloxacin plus a cephalosporin or a non-FQ regimen for TRUS-biopsy prophylaxis.

Methods. A total of 487 men who underwent a TRUS-biopsy at VA Boston Healthcare System between 2011-2013 were retrospectively evaluated for infections within 30 days, including symptomatic urinary tract infection (UTI) with fever, bacteremia, or sepsis. Men undergoing concurrent procedures or lacking documentation of prophylaxis compliance were excluded. Electronic records were used to extract outcome data from the national VA healthcare system, including outpatient and urgent care visits.

Results. Of 455 men evaluated, there were 25 infections (5.5%), with sepsis occurring in 2.4%, UTI in 1.5% and bacteremia in 0.4% of patients. *E. coli* was the most common urine (89%) and blood pathogen (92%), with FQ-R rates of 88% and 91% respectively. Ciprofloxacin alone was associated with significantly more infections than ciprofloxacin plus an additional agent (p = 0.019). Intramuscular gentamicin alone was also significantly associated with a higher infection rate compared to all other regimens (p = 0.014). Ciprofloxacin plus cefpodoxime was the most common combination regimen. Any combination was highly protective, with a 75% reduction in infection rate compared to ciprofloxacin or gentamicin alone (OR 0.25, 95% CI 0.06; 0.77, p = 0.01). Diabetes, immunosuppression, hospitalization within prior year, and UTI within the previous 6 months were not associated with post-biopsy infection risk.

Conclusion. The overall incidence of post TRUS-biopsy infection in this cohort was higher than previous reports. The findings suggest that ciprofloxacin or gentamicin alone are inferior regimens compared to a combination regimen. The preferred combination likely depends on local susceptibility data.

Disclosures. **K. Gupta**, Paratek: Consultant, Consulting fee

492. Complicated Intra-abdominal Infection (cIAI) and 30-day Hospital Readmission

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Background. Patients with cIAI may be at increased risk of poor health outcomes post-hospital discharge. Our objective was to quantify the association between cIAI and 30-day hospital readmission.

Methods. This was a retrospective cohort study of adult patients (age >18 years) with cIAI admitted to Oregon Health and Science University (OHSU) between January 1, 2010–June 30, 2013. Included patients must have had a diagnosis code consistent with cIAI, a procedure code for surgical intervention, and been discharged alive. We excluded patients with non-cIAI infectious diagnoses codes during the index admission, chronic liver disease, or those receiving peritoneal dialysis. We defined 30-day hospital readmission as readmission to OHSU within 30 days of discharge. Potential risk factors of readmission included demographics (e.g., age, sex, body mass index), comorbid illnesses (e.g., peptic ulcer disease, diabetes, cancer) and length of stay. Antibiotic exposures of interest included receipt of anaerobic coverage ≥72 hours, vancomycin for ≥72 hours, and monotherapy vs combination therapy. We calculated the incidence of 30-day readmission among patients with cIAI and used bivariable analysis to identify potential predictors of 30-day readmission among these patients. We used multivariable logistic regression to identify independent risk factors for readmission within 30 days.

Results. Among 259 patients with cIAI who were discharged alive, 171 patients (66%) met our inclusion criteria. Incidence of 30-day readmission was 45.6% and median (interquartile range) time to readmission was 10 (4-17) days. Total hospital length of stay > 14 days during the index admission was significantly associated with 30-day hospital readmission; odds ratio: 2.35, 95% confidence interval: 1.11 to 4.96. No other variables were identified as risk factors or had protective effects.

Conclusion. Patients with cIAI were frequently readmitted to the hospital within 30 days of discharge and often following extended hospital stays. Given the lack of significant predictors to identify patients at increased risk of readmission, improvements in care for extended admissions should be considered, along with an additional emphasis on prevention of cIAI to reduce these poor outcomes.

Disclosures. **J. P. Furuno**, Cubist Pharmaceuticals: Grant Investigator, Research grant and Research support **B. N. Noble**, Cubist Pharmaceuticals: Grant Investigator, Research support **M. R. Elman**, Cubist Pharmaceuticals: Grant Investigator, Research support **J. C. Mcgregor**, Cubist Pharmaceuticals: Grant Investigator, Research grant and Research support.

493. Differences in Potency and Categorical Agreement between Colistin and Polymyxin B When Testing 15,377 Strains Collected Worldwide

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Background. Two polymyxin agents, colistin (COL) and polymyxin B (PB), are available for clinical use worldwide and clinical laboratories may not be able to susceptibility test both compounds appropriately. We evaluated the correlation between COL and PB MIC values on a large collection of Gram-negative bacilli (GNB) within the spectrum of the polymyxins.

Methods. 15,377 clinical GNB, including *P. aeruginosa* (PSA; 3,821), *Acinetobacter* spp. (ASP; 1,068), *Klebsiella* spp. (KSP; 4,177) and *E. coil* (EC; 6,311) were tested for susceptibility against COL and PB by CLSI broth microdilution methods using commercial (Sensitrite®) dry-form panels. The isolates were collected worldwide in 2013.

Organisms (no.)	PB more potent than COL by (% of strains):			Same MIC	COL more potent than P	
	≥3 dilutions	2 dilutions	1 dilution	value	1 dilution	2 dilutions
P. aeruginosa (3,821)	-	<0.1	2.9	**85.4**	11.6	<0.1
Acinetobacter spp. (1,068)	-	0.8	18.8	**75.1**	5.1	<0.1
Klebsiella spp. (4,177)	<0.1	<0.1	2.5	**41.2**	55.0	1.1
E. coil (6,311)	-	-	1.0	**44.8**	53.2	0.9
All (15,377)	<0.1	<0.1	3.1	**56.1**	40.0	0.7

a. Categorical agreement between polymyxin B and colistin according to CLSI breakpoint criteria.
b. NA, not applicable due to the lack of breakpoint criteria for polymyxin B by either CLSI or EUCAST.

Results. Percentages of strains inhibited at ≤2 µg/ml of COL/PB were 99.8/99.8% for PSA, 97.2/97.9% for ASP, 95.8/95.9% for KSP and 99.6/99.6% for EC. Among PSA and ASP, COL and PB MIC values were within +/- one doubling dilution for >99.0% of strains, and identical MIC values were observed for 85.4% of PSA and 75.1% of ASP. When CLSI breakpoints were applied, categorical agreement (CA) was 99.8% for PSA and 98.9% for ASP (Table). Among KSP and EC, 55.0 and 53.2% of strains displayed a COL MIC one dilution lower than PB. However, differences in potency varied according to the degree of polymyxin susceptibility. Among KSP, percentages of strains with COL MIC ≥1 dilution lower/identical/ ≥ 1 dilution higher compared to PB were 58.5/39.9/1.6% for isolates with COL MIC ≤2 µg/ml, and 2.9/72.9/24.1% for isolates with COL MIC ≥4 µg/ml, respectively. If a susceptible/resistant breakpoint of ≤2/ ≥ 4 µg/ml were applied for both COL and PB (similar to ASP), CA would be 99.8% for KSP and >99.9% for EC.

Conclusion. There was a good correlation between COL and PB MIC values and ≥98.9% CA when testing PSA and ASP. Against KSP and EC, COL exhibited slightly greater potency than PB against isolates with lower MIC values (≤2 µg/ml) for both compounds, while PB was slightly more potent than COL against strains with decreased susceptibility (MIC, ≥4 µg/ml) to the polymyxins.

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494. Excellent Safety and Tolerability of Colistin in Septic Neonates. A Retrospective Study from a Neonatal and a Pediatric Cardiac Surgical Unit in India

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Background. There is paucity of data about safety, tolerability and efficacy of colistin in neonatal sepsis. Hence this study was conducted two separate neonatal and pediatric cardiac surgical intensive care units in a tertiary care hospital in Mumbai, India.

Methods. This is a retrospective study in which the case records of all neonates aged less than 1 month who received colistin for at least 5 days in the years 2011-2013 were included. Data including age, sex, gestational age, birth weight, risk factors for sepsis, age at initiation of colistin, dose and duration of therapy, companion drugs, indication for treatment (definitive/ empirical) and outcomes was abstracted and analyzed. Therapy was considered empirical when cultures were negative and definitive when peripheral blood cultures or endotracheal cultures (in the setting of health care associated pneumonia) were positive.

Results. A total of 32 neonates were administered colistin during the study period (3 in 2011, 12 in 2012 and 17 in 2013). Fifteen were term babies and seventeen were preterm. Risk factors for sepsis included prematurity in seventeen and surgery for congenital heart disease in the rest. The mean gestational age of the preterm babies was 30 weeks (range 24-36) and the mean birth weight was 2 kg (range 660 gms-3.5 kg). The average post natal age at starting colistin was 13 days (range 5-30 days) and average duration of therapy was 13 days (range 5-22 days). The most common companion drug was meropenem (25/32 babies) and median dose of colistin was 6 mg/kg/day (range 4-12 mg/kg/day). Therapy was empirical in 15/32 patients and definite in 17/32 (blood stream infection in 12 and pneumonia in 5). Of the patients who were culture positive, eight had infection with carbapenem resistant strains of klebsiella (4), acinetobacter (2) and pseudomonas (2). Only 2 babies died; both having infection with carbapenem resistant strains. Adverse effects including rise in serum creatinine or neurotoxicity were seen in none.

Conclusion. The study demonstrates excellent safety of colistin even in extremely low birth weight babies. The clinical outcomes were excellent though documented infection with carbapenem resistant strains was seen in only 25% (8/32) of study subjects and use was empirical in around 50%.

Disclosures. **All authors:** No reported disclosures.

653. Implementation of PCV7/PCV13 in Israel Had a Significant Impact on both Pneumococcal and Non-Pneumococcal Complex Otitis Media (OM) Rates

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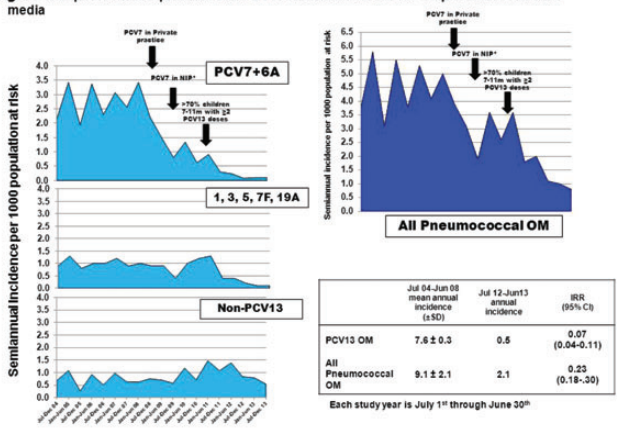
Background. Pre-licensure and post implementation pneumococcal conjugate vaccine (PCV) studies have demonstrated that PCV impact on recurrent, non-responsive and chronic OM cases (complex-OM; COMP-OM) was significantly larger (up to 40%) than when all-cause OM or first OM were measured. COMP-OM is frequently caused by non-pneumococcal pathogens, often forming biofilm, in which non-typable *Haemophilus influenzae* (NTHi) is the most frequent. We assessed the impact of PCV7/PCV13 introduction on all-cause COMP-OM enriched OM episodes, as well as specifically pneumococcal, NTHi and culture-negative episodes.

Methods. These were previously described (Dagan et al, 49th IDSA, Abstr. 1344, 2012). The surveillance period was July 2004 through December 2013. PCV7 was introduced to the National Immunization Program (NIP; with catch-up) in July 2009 and has been gradually replaced by PCV13 since November 2010.

Results. Overall, 6,250 OM episodes for which information was available, were submitted for culture. ≥1 factors associated with COMP-OM were present in 2685/3996 (67%) children: 2165/3331 (65%) in culture-positive children and 520/665 (78%) in culture-negative patients. Incidences (per 1,000 children <2 years) of PCV7 -+6A serotypes, serotypes 1, 3, 5, 7F, 19A, non-PCV13 serotypes and overall

pneumococcal OM by 6 month-intervals and rate reduction calculations are shown in Figure 1. Incidences of NTHi, culture-negative and all-cause OM as well as rate reduction calculations are shown in Figure 2.

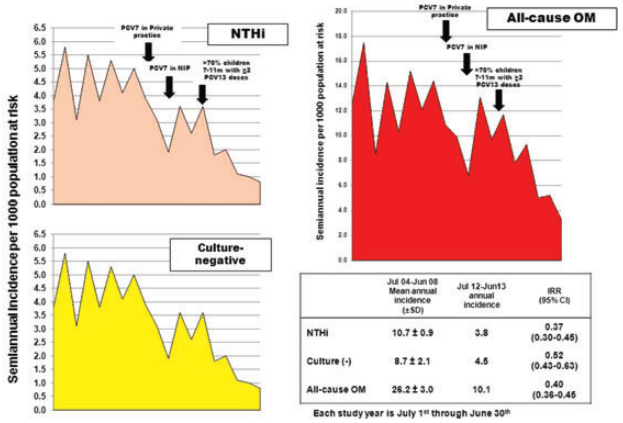
Figure 1: Impact of the sequential PCV7/PCV13 introduction to the NIP on pneumococcal otitis media



	Jul 04-Jun 08 mean annual incidence (±SD)	Jul 12-Jun13 annual incidence	IRR (95% CI)
PCV13 OM	7.6 ± 0.3	0.5	0.07 (0.04-0.11)
All Pneumococcal OM	9.1 ± 2.1	2.1	0.23 (0.18-.30)

* NIP = National Immunization Program (PCV given at 2, 4, 12m of age; PCV7 started July 2009 with a catch-up project; PCV13 started gradually November 2010, with no catch-up)

Figure 2: Impact of the sequential PCV7/PCV13 introduction to the NIP on nontypeable *H. influenzae* (NTHi), Culture-negative and all-cause OM incidence



	Jul 04-Jun 08 Mean annual incidence (±SD)	Jul 12-Jun13 annual incidence	IRR (95% CI)
NTHi	10.7 ± 0.9	3.8	0.37 (0.30-0.45)
Culture (-)	8.7 ± 2.1	4.5	0.52 (0.43-0.63)
All-cause OM	26.2 ± 3.0	10.1	0.40 (0.36-0.45

Conclusion. All OM cases, including pneumococcal, NTHi and culture-negative episodes enriched with COMP-OM were markedly reduced in children <2 years after PCV7/PCV13 introduction.

Disclosures. **R. Dagan**, Pfizer: Consultant, Grant Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; MSD: Consultant, Grant Investigator and Scientific Advisor, Consulting fee and Research grant; GSK: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium **E. Leibovitz**, Pfizer: Speaker's Bureau, Speaker honorarium

654. Local persistence of vaccine-targeted pneumococcal serotypes as causes of disease in adults

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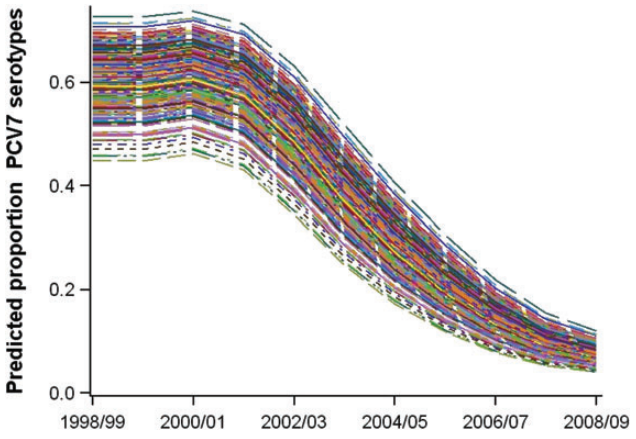
Background. Because vaccination of children with pneumococcal conjugate vaccines (PCVs) has had a strong indirect effect on adults, it is unclear whether direct immunization of adults with the same vaccine would impact disease rates. We hypothesized that communities with high population densities or low vaccine uptake among children might maintain PCV-targeted serotypes at a higher proportion.

Methods. Data on invasive pneumococcal disease (IPD) cases were collected as part of the Active Bacterial Core surveillance system for Connecticut (1998-2009). Data on PCV7 uptake by census-tract were obtained from the Connecticut Immunization Registry and Tracking System. In each census tract and year, we estimated the proportion of all IPD cases that were caused by PCV7 serotypes. Binomial regression models were used to evaluate factors associated with having a higher proportion of disease cases caused by PCV7 serotypes. Covariates included year, census tract-level information on population density, percent of residents that were black or Hispanic, household size, income, and pediatric vaccine uptake. Spatial random effects were estimated with radial smoothing

Results. Following the introduction of PCV7 in children, the proportion of disease cases in adults caused by PCV7 serotypes declined by 36% per year. However, PCV7 serotypes were significantly more common in census tracts with high population densities and large Hispanic populations. The community-level differences in serotype distribution were apparent before PCV7 introduction (predicted 45-72% of IPD cases caused by vaccine serotype in 1998/99) (figure). By 2008/2009, PCV7 serotypes accounted for a small fraction of IPD cases in all communities but continued to comprise a greater fraction of disease cases in high density communities (high of 12% vs low of 4%) (figure). There was no association between serotype distribution and vaccine uptake.



Conclusion. Serotype distributions vary significantly with community characteristics. However, in a population with high levels of pediatric vaccine uptake, the residual burden of PCV serotypes is small in all communities within several years after vaccine introduction.

Disclosures. **D. Weinberger**, Pfizer: Investigator initiated research grant, Research grant; Merck: Consultant, Consulting fee

655. Regional Differences in Pediatric Invasive Pneumococcal Disease (IPD) Rates in Tennessee (TN)

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Background. Although pediatric IPD rates for TN have been reported, regional differences within TN have not been examined. We aimed to determine pediatric IPD rates in TN regions before and after PCV13 introduction (2010).

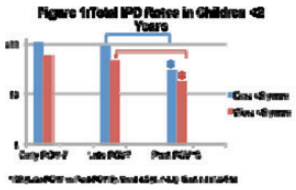
Annual IPD RATE per 100,000 EARLY-PCV7 ERA	East <2 yrs	West <2 yrs	IRR (95% CI)	East 2-18 yrs	West 2-18 yrs	IRR (95% CI)
EARLY-PCV7 ERA						
PCV7	**33.8**	**18.9**	**1.8 (1.0-2.3)***	2.6	3.7	1.4 (0.8-2.4)
PCV13	**23.5**	**11.4**	**2.1 (1.0-3.9)***	1.3	1.4	1.1 (0.4-2.5)
Non-PCV	29.4	19.7	1.5 (0.8-2.5)	1.7	1.7	1.0 (0.5-2.1)
Not-typed	**19.1**	**7.5**	**2.6 (1.2-5.4)***	**1.9**	**0.5**	**3.5 (1.4-9.0)***
Total	**106**	**57.5**	**1.8 (1.4-2.5)***	**6.1**	**8.7**	**1.4 (1.0-2.0)***
LATE-PCV7 ERA						
PCV7	1.1	1.2	0.9 (0.02-9.4)	**0.9**	**0.3**	**3.6 (1.1-12)***
PCV13	**33.3**	**19.1**	**2.3 (1.5-3.5)***	2.3	2.7	0.9 (0.5-1.5)
Not-typed	**17.8**	**8.1**	**2.2 (1.1-4.2)***	**1.8**	**0.8**	**2.2 (1.0-4.7)***
Non-PCV	**27.7**	**16.4**	**1.7 (1.0-2.8)***	2.3	1.9	1.2 (0.6-2.1)
Total	**91.0**	**44.8**	**2.0 (1.5-2.7)***	7.4	5.7	1.3 (0.9-1.8)
POST-PCV13 ERA						
PCV7	0	0	NA	0.3	0	NA
PCV13	5.3	3.6	1.5 (0.1-9.0)	1.3	0.9	1.4 (0.3-5.0)
Not-typed	5.3	0.7	7.4 (0.4-434)	0.7	0.4	1.8 (0.2-1.0)
Non-PCV	18.7	13.1	1.4 (0.5-3.6)	1.3	2.1	0.6 (0.2-1.8)
Total	29.4	17.4	1.7 (0.8-3.6)	3.6	3.4	1.1 (0.5-2.1)

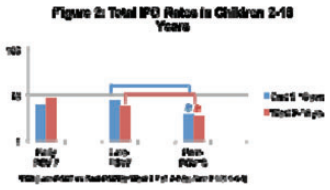
*CI excludes 1 indicating significant differences

Methods. Active population and laboratory-based surveillance identified IPD cases from 11 TN counties from 2001-2012. Counties were separated into East (2)

and West (9). For each case, trained nurses collected clinical data, and the isolates were sent to CDC for serotyping. IPD incidence was calculated using U.S. census data and was expressed per 100,000 person-years. Groups were stratified by age: <2 and 2-18 years (yrs). Incidence rates were calculated for 3 time periods: Early-PCV7 (2001-2004), Late-PCV7 (2005-2009), and Post-PCV13 (2011-2012). The transition year 2010 was excluded and incidence rate ratios (IRR) were calculated to compare East and West TN IPD rates.

Results. The table shows IPD rates by serotype, region, age group, and time period. Figures 1 and 2 illustrate the decline in IPD rates by time period and region.





Conclusion. Overall IPD rates Post-PCV13 decreased in all regions and age groups. IPD rates among children were significantly higher in East TN during the Early-PCV7 and Late-PCV7 period; however, those regional disparities were eliminated in the Post-PCV13 era.

Disclosures. **A. De St. Maurice**, Pfizer: Grant Investigator, Research grant **C. G. Grijalva**, Pfizer: Consultant and Grant Investigator, Consulting fee and Research grant **C. Fonnesbeck**, Pfizer: Grant Investigator, Research grant **W. Schaffner**, Pfizer, GlaxoSmithKline, Dynavax: Limited consulting fee, Consulting fee; Merck and Sanofi Pasteur: Data safety monitoring board, Board membership benefits **N. Halasa**, Pfizer: Grant Investigator, Salary

656. Immunogenicity and Safety Evaluation of a New Syringe Presentation of Reduced Antigen Content Diphtheria-Tetanus-Acellular Pertussis Vaccine in Healthy Adolescents: Results from a Randomized Trial

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Background. GlaxoSmithKline Vaccines' reduced antigen content diphtheria-tetanus-acellular pertussis vaccine (dTpa), indicated for booster vaccination in children, adolescents and adults, has been licensed in >70 countries worldwide. It has been available as a single dose vial or a prefilled disposable syringe without a needle. The syringe presentation was recently replaced by a prefilled syringe with tip cap and plunger stopper manufactured with different components. The present study compared the immunogenicity and safety of dTpa in the new and previous syringe presentations.

Table. Seroprotection/seropositivity rates, booster response rates, GMCs and adjusted GMC ratios for dTpa antibodies 1 month after booster vaccination (per-protocol immunogenicity cohort)

Antigen (cut-off)	Group	% ≥ cut-off (95% CI)	Booster response, % (95% CI)	GMC, IU or EU (95% CI)	Adjusted GMC ratio dTpa-previous/dTpa-new (95% CI)
D (0.1 IU/mL)	dTpa-new	99.7 (98.3–100)	80.1 (75.3–84.3)	6.8 (6.2–7.5)	0.96 (0.85–1.09)
	dTpa-previous	100 (98.9–100)	79.0 (74.1–83.3)	6.5 (5.9–7.1)	
T (0.1 IU/mL)	dTpa-new	100 (98.9–100)	82.9 (78.3–86.8)	18.9 (17.3–20.7)	0.97 (0.86–1.10)
	dTpa-previous	100 (98.9–100)	84.6 (80.2–88.4)	18.5 (16.9–20.3)	
PT (5 EU/mL)	dTpa-new	99.4 (97.7–99.9)	94.0 (90.8–96.4)	140.2 (126.0–156.1)	0.92 (0.82–1.04)
	dTpa-previous	99.1 (97.3–99.8)	92.8 (89.3–95.4)	125.9 (112.7–140.7)	
FHA (5 EU/mL)	dTpa-new	100 (98.9–100)	97.1 (94.6–98.7)	1080.2 (995.2–1172.5)	0.92 (0.83–1.03)
	dTpa-previous	100 (98.9–100)	96.5 (93.8–98.2)	1013.7 (940.0–1093.2)	
PRN (5 EU/mL)	dTpa-new	100 (98.9–100)	98.1 (96.0–99.3)	652.4 (572.1–743.9)	0.98 (0.85–1.13)
	dTpa-previous	100 (98.8–100)	99.7 (98.3–100)	619.2 (546.0–702.2)	

% ≥cut-off, % of subjects with post-booster antibody concentration ≥ specified cut-off; **booster response for D and T**, for initially seronegative subjects, post-booster antibody concentrations ≥0.4 IU/mL, for initially seropositive subjects, a ≥4-fold increase in antibody concentration from pre- to post-booster; **booster response for PT, FHA and PRN**, for initially seronegative subjects, post-booster antibody concentrations ≥20 EU/mL, for initially seropositive subjects with pre-booster concentration <20 EU/mL or ≥20 EU/mL, a ≥4-fold or ≥2-fold increase, respectively, in antibody concentration from pre- to post-booster; **adjusted GMC**, GMC obtained from an ANCOVA model adjusted for pre-booster concentration and number of previous DT(P)/dT(pa) doses; **IU**, international unit; **EU**, ELISA unit.

Methods. Phase IV, randomized, controlled, single-blind, multicenter, parallel-group study in Mexico and Chile (NCT01362322). Healthy adolescents aged 10–15 years who had previously received 5 or 6 doses of DTP-combination vaccines, were randomized (1:1) to receive a dTpa booster in the new (dTpa-new, N = 335) or previous (dTpa-previous, N = 336) syringe presentation. Antibodies against diphtheria (D), tetanus (T) and pertussis antigens (pertussis toxoid [PT], filamentous hemagglutinin [FHA] and pertactin [PRN]) were measured pre- and 1 month post-booster. Non-inferiority of dTpa-new vs dTpa-previous was shown if the upper limits (ULs) of the 95% confidence intervals (CIs) for the post-booster geometric mean concentration (GMC) ratios (dTpa-previous/dTpa-new) for antibodies to the 5 dTpa antigens were ≤1.5 (primary objective). Solicited and unsolicited symptoms were recorded for 4 and 31 days post-booster, respectively. Serious adverse events (SAEs) were recorded up to study end.

Results. The per-protocol immunogenicity cohort comprised 321 dTpa-new and 319 dTpa-previous subjects. Non-inferiority of dTpa-new vs dTpa-previous was shown for all antigens (range of ULs of 95% CIs for GMC ratios: 1.03–1.13; Table). One month post-booster, immune responses were in similar ranges for all antigens in both groups (Table).

Solicited and unsolicited symptoms were reported at similar rates in both groups, with no large swelling reactions (diameter >100 mm). One SAE (injury, not assessed as vaccine-related) was reported in the dTpa-new group.

Conclusion. Changing the syringe presentation did not impact the immunogenicity and safety profiles of dTpa in adolescents.

Disclosures. **K. Abarca**, GSK: Grant Investigator, Consulting fee, Research support and Speaker honorarium **A. Lepetic**, GSK: Employee, Salary and Stock options as a part of my job agrement **K. Hardt**, GSK: Employee and Shareholder, Salary **G. Jayadeva**, GSK: Employee and Shareholder, Salary **S. Kuriyakose**, GlaxoSmithKline Pharmaceuticals: Employee, Salary **H. H. Han**, GSK: Employee and Shareholder, Salary **N. Pavia-Ruz**, GSK: Investigator, Research support

657. Estimates of Pertussis Vaccine Effectiveness in Air Force Pediatric Dependents Seen at Military Treatment Facilities

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Background. The United States Air Force School of Aerospace Medicine Epidemiology Consult Service identified an increase in reported cases of pertussis from 2011-2013. Infants and young children are most commonly affected by pertussis and suffer the severest health consequences from the infection. Vaccination compliance is critical for reduction of pertussis cases; however, the current acellular pertussis vaccine may not provide sufficient protection from infection. This study examined pediatric pertussis vaccine effectiveness (VE) for Air Force dependents less than 12 years of age.

Methods. We conducted a test-negative, case-control study among Air Force pediatric dependents seen at military treatment facilities from 2011-2013, comparing cases with a positive pertussis test result and/or culture to controls who received the same lab tests with a negative result. Twelve years (2002-2013) of historical pertussis vaccination data were examined for all cases and controls. Our study population was categorized by age group and vaccination status based on the Centers for Disease Control and Prevention recommended pertussis vaccination schedule. VE was calculated with respect to vaccination status and pertussis lab results.

Results. We compared 27 pertussis laboratory positive cases with 974 pertussis laboratory negative controls, 2 months old to < 12 years old. Comparing completely vaccinated to non-vaccinated patients, overall VE was 78.26%. Among children 2 months to < 6 years old, the VE was 94.23%. VE was highest amongst those 15 months old to < 6 years old (97.55%). Children 6 years old to < 12 years had the lowest VE (48.48%). Comparing partially vaccinated patients to non-vaccinated patients yielded 64.24% overall VE.

Conclusion. Pertussis vaccination was effective at preventing laboratory confirmed pertussis among our Air Force pediatric dependent population, with highest protection among completely vaccinated, young children. We found pertussis VE varied by age groups. Our overall calculated pertussis VE corroborates other pertussis VE studies looking at similar age groups.

Disclosures. **All authors:** No reported disclosures.

658. Assessment of Knowledge, Awareness, and Attitudes Towards Pertussis and Pertussis Immunization Strategies in Post-Partum Mothers

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Background. Given increases in the incidence of pertussis, protective strategies for young infants are used (cocooning, maternal immunization), but there is limited data regarding two key areas for implementation - knowledge of pertussis in pregnant women, and their willingness to participate in various preventative campaigns. With increasing rates of pertussis in Manitoba and anticipating future public health needs should Manitoba move toward a maternal immunization strategy, we surveyed postpartum women on their knowledge and beliefs of infant pertussis and prevention strategies.

Methods. Women were interviewed at the two obstetrical centers in Winnipeg. A survey was developed using the Health Belief Model, assessing knowledge level about pertussis, beliefs and attitudes towards pertussis immunizations, and willingness to participate in two protective strategies (third-trimester or mother only postpartum immunization). There was then an educational portion about pertussis and follow-up questions to determine whether this had changed their views.

Results. Of 143 women surveyed over 8 months, 67% had a moderate knowledge score regarding pertussis and its risks; 55% of participants considered Tdap (tetanus-diphtheria-acellular pertussis) to be safe. Only 5% of women reported having discussed pertussis with their physician during their pregnancy.

Fifty-seven percent of participants would have agreed to receive Tdap immediately post-partum, and 65% would consider Tdap in the third trimester of a subsequent pregnancy. There was a significant link between pertussis knowledge levels and intent to vaccinate ($p < 0.001$). Of 29 participants who disagreed with both protective strategies, 45% stated they would consider them after receiving the education about pertussis.

Conclusion. A significant proportion of post-partum women had limited knowledge of infant pertussis disease; however prevention strategies were acceptable to a majority of surveyed women. A consideration to improve uptake of either strategy in Manitoba would be to increase the target population's knowledge and awareness of the significance of infant pertussis and the risks associated with pertussis infection, as well as the safety profile of the vaccine.

Disclosures. **All authors:** No reported disclosures.

659. A comparison of local determinants of vaccine hesitancy in Botswana and the Dominican Republic, two middle-income countries

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Background. Vaccine acceptance is a critical component of sustainable immunization programs. Despite significant research into determinants of vaccine acceptance in developed countries, less is known about those in middle-income countries such as societal norms, trust in the healthcare system and government, and sources of vaccine information including the media. This study explores knowledge and attitudes regarding vaccines and vaccine-preventable diseases (VPD) among caregivers and immunization providers in Botswana and the Dominican Republic (DR), two middle-income countries with expanding immunization programs, to understand local determinants of vaccine hesitancy.

Methods. We conducted focus groups with 33 providers and 22 caregivers in Gaborone, Botswana and 37 providers and 59 caregivers in the DR. Focus groups were conducted in the participants' native language, digitally recorded and transcribed. Transcripts were translated into English, coded in qualitative data analysis software (NVivo 10), and analyzed for common themes.

Results. Botswana's vaccination rates are >99.5% (based on DTP3). Respondents reported high vaccine acceptance due to societal norms, trust in the healthcare system and knowledge about vaccines. In the DR, vaccination rates are 85% (based on DTP3). Respondents reported knowledge about vaccines and VPD was the major promoter of vaccine acceptance. Participants did not express the same level of trust in the government and healthcare system as was expressed in Botswana, and did not view vaccination as a societal norm. In both countries, the majority of vaccine communication is from healthcare workers and, for providers, is from medical literature. Negative information from popular media is regarded with skepticism.

Conclusion. Knowledge of vaccines and VPD were key promoters of vaccine acceptance in both Botswana and the DR. Participants from Botswana were also significantly influenced by societal norms and a high level of trust in the healthcare system and government, which may affect vaccination rates. In settings such as the DR, where societal norms and trust of the healthcare system are not primary drivers of vaccine acceptance, public health efforts should consider local promoters of vaccine acceptance.

Disclosures. **All authors:** No reported disclosures.

660. The effect of immunization on measles incidence in the Democratic Republic of Congo

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Background. Measles continues to be one of the largest causes of vaccine-preventable disease mortality among children under five, despite the fact that a safe and efficacious vaccine is readily available. While global vaccination coverage has improved tremendously, measles outbreaks persist throughout sub-Saharan Africa. Since 2010, the Democratic Republic of Congo (DRC) has seen a resurgence of measles outbreaks, mainly attributed to severe deficiencies in Routine Immunization (RI) at the Health Zone level, where only 22% of reported vaccine coverage rates reach higher than 90%.

Methods. We used available data from the 2010-2013 IDSR system for measles suspected cases counts reported weekly by health zone to investigate the decline in measles incidence post-immunization (by health zone) with one dose of measles containing vaccine (MCV1) with and without the addition of Supplementary Immunization Activities (SIAs). The impact of measles immunization by health zone was modeled with poisson regression, using vaccination coverage levels from two years prior.

Results. At the provincial level, median incidence ranged from 0.67 to 7.67 per 100,000 in 2010, while the median incidence ranged from 0.96 to 273.8 per 100,000 in 2012. In 2013, median incidence ranged from 5.79 to 322.61 per 100,000. Furthermore, multivariate modeling at the health zone level showed that each 1% increase in MCV1 coverage was associated with a .79% decrease in incidence. The addition of an SIA in a health zone was associated with a 2.34% increase in incidence.

Conclusion. Our results highlight the fact that measles in DRC is highly susceptible to immunization programs, particularly mass campaigns. Repeated occurrences of large-scale outbreaks in DRC suggest that vaccination coverage rates are grossly overestimated and signify the importance of the re-evaluation of measles virus dynamics and prevention and control strategies.

Disclosures. **All authors:** No reported disclosures.

661. Initiation and Completion of the Hepatitis A Vaccine Series among a Privately Insured US Pediatric Population

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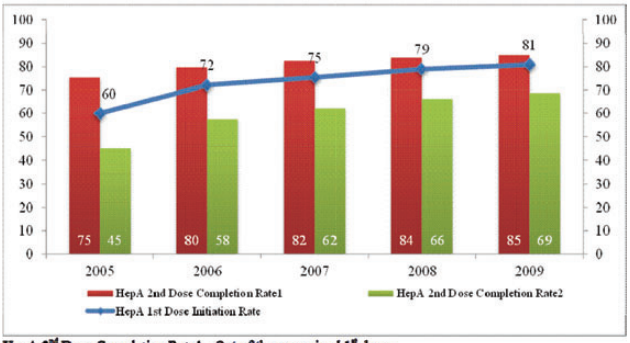
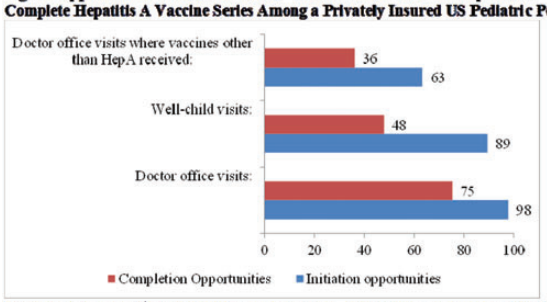
Background. In May 2006, ACIP recommended routine Hepatitis A (HepA) vaccination of all children aged 12 to 23 months, with 2 doses separated by 6 to 18 months, regardless of risk category or geographic location. We assessed HepA vaccine series initiation (first dose) and completion rates (first and second dose) and identified potential missed opportunities for HepA vaccination in the years following this recommendation.

Fig 1: Initiation & Completion of Hepatitis A Vaccine Series Among a Privately Insured US Pediatric Population



HepA 2nd Dose Completion Rate1 - Out of those received 1st dose;
HepA 2nd Dose Completion Rate2 - Out of total study population

Fig 2: Opportunities Missed to Either Initiate First Dose of Hepatitis A Vaccine or Complete Hepatitis A Vaccine Series Among a Privately Insured US Pediatric Population



Hepatitis A Vaccine 1st Dose Initiation Opportunities - Children after 1 year of age that did not receive their first dose of the Hepatitis A vaccine but did have at least one doctor office visit during the 3 and1/2 year follow-up period.
Hepatitis A Vaccine 2nd Dose Completion Opportunities - Children after 6 months of the first dose of Hepatitis A vaccine that did not receive their second dose of Hepatitis A but did have at least one doctor office visit during the 3 and 1/2 year follow-up period.
Doctor office visits - These visits also include well-child visits and visit where children received another vaccination but not HepA.

Methods. We conducted a retrospective, observational study using the MarketScan® Commercial Claims Database. The study population was comprised of children born between years 2005 and 2009 that were continuously enrolled for at least 31/2 years from the date of birth. Multivariate analyses were performed to understand factors associated with HepA vaccine series initiation and completion.

Results. There were 202,513 eligible children included in this study. HepA series initiation increased from 60% in the 2005 birth cohort to 81% for the 2009 birth cohort (Figure 1). Series completion among those who had a first HepA dose increased from 75% to 85% for the 2005 and 2009 cohorts, respectively. Among the 26% of children not receiving their first dose of HepA vaccination, 63% had ≥ 1 visit where they received another vaccination but not HepA, 89% had ≥ 1 well-child visit and 98% had ≥ 1 doctor office visit. Among the 13% of children who did not complete the HepA vaccine series after at least 6 months from the first dose, 36% had ≥ 1 visit where they received another vaccination but not HepA, 48% had ≥ 1 well-child visit and 75% had ≥ 1 doctor office visits (Figure 2).

Children were more likely to initiate and complete the HepA vaccine series if they were from more recent birth cohorts, from states with a HepA vaccination recommendation prior to the ACIP universal recommendation, from states with daycare/school entry requirements, were enrolled in an HMO health plan, or had pediatricians as primary providers.

Conclusion. In this study, approximately one in every four children remained unvaccinated against HepA. Although the HepA vaccine series initiation and completion improved from 2005 to 2009, vaccine coverage has stabilized in recent years. It is important for providers to identify every opportunity for HepA vaccination, to assure that children get protection from this vaccine-preventable disease.

Disclosures. **T. Weiss**, Merck: Employee, Salary **D. Zhang**, Merck: Employee, Salary **N. N. Borse**, Merck: Consultant, Consulting fee **E. Walter**, Merck: Collaborator, Consultant and Investigator, Consulting fee

662. Missed opportunities for influenza vaccination among inpatients with influenza

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Background. Visits to a tertiary care institution may represent opportunities for influenza vaccination. The aim of this study was to identify missed opportunities in pediatric inpatients with influenza and to explore which visits are best to target for vaccination.

Methods. We conducted a retrospective chart review of inpatients with PCR-confirmed influenza admitted to Children's Hospital Colorado from 2010-2014. Medical records were reviewed for patient demographics, prior visit type and characteristics. Missed opportunities for influenza vaccination were defined as prior visits for which the influenza vaccine was available in an underimmunized patient. Bivariable relationships were examined using chi-square tests.

Results. We identified 352 inpatients with influenza. Of these, 309 (88%) were >6 months of age at diagnosis. 6 encounters were excluded due to repeat hospitalizations. 92/303 patients (30.4%) were completely vaccinated. 40 patients with unknown vaccination status were excluded from subsequent analyses. 30% (79/263) of patients had ≥1 missed opportunity for influenza vaccination. Of those with a missed opportunity, 33% (26/79) had one visit, 67% (53/79) had ≥2 visits. The median number of missed opportunity visits was 3 (range: 1-11). There were 246 missed opportunity visits; most were to specialty clinics (54%), followed by ED/Urgent Care (20%). 76% experienced their initial missed opportunity prior to the influenza season. 65% (51/79) had missed opportunities at "sick visits".

170/263 (64 %) of patients were considered high risk. 76% of high risk patients vs 24% not at high risk had a missed opportunity visit ($p = 0.01$). Patients with a metabolic syndrome or seizure disorder were more likely to have a missed opportunity visit ($p < 0.02$ for both).

Conclusion. Nearly one third of inpatients with influenza had a missed opportunity for vaccination, the majority of whom were considered high risk for severe complications. Most visits occurred prior to the onset of the influenza season, but when vaccine was available. Subspecialty outpatient visits provide an excellent opportunity for influenza vaccination, as a means to target high risk patients, and because they represent the highest proportion of missed opportunities for vaccination.

Disclosures. **All authors:** No reported disclosures.

663. Physician Electronic Best Practice Alerts vs Nursing and Pharmacist-Driven Screening and Ordering: Which System Delivers More Inpatient Influenza Vaccines?

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Background. Influenza vaccine is recommended annually for children >6 months of age. Primary care clinics are the traditional setting for vaccination, but hospital admissions also create an opportunity to immunize. Thus, the Centers for Medicare and Medicaid Services (CMS) includes inpatient influenza immunization as a process measure. Hospitals must create effective systems to screen and vaccinate inpatients whenever possible.

Many electronic healthcare records (EHR) include best practice alerts (BPA) to increase provider compliance with evidence-based care and quality measures. However, as the number of clinical decision alerts increases, physician (MD) "alert fatigue" may lead to alert override.

In 2009, we added an influenza vaccine BPA for all inpatients. The BPA suggested that the MD screen the patient for vaccination, but it was not mandatory. In November 2011, we changed to a mandatory multi-disciplinary screening system. Within the admission orders, the MD must decide if the child has a vaccine contraindication. If none exists, the MD orders "vaccination based on RN screening." The RN then asks the parent "Has your child received an influenza vaccine this year? If not, would you like one?" If the parent answers "Yes," an internal EHR alert triggers the pharmacist to order age-appropriate vaccine which the RN administers prior to discharge.

We sought to determine if this system improved the number and rate of vaccines given.

Methods. We obtained the number of inpatient vaccine doses given from September 1, 2008 through the current season, and the number of distinct patients discharged per season. During the 2009-10 season, some patients required 2 separate vaccines (H1N1 and seasonal influenza) per national recommendations. We counted these as one "vaccination encounter"(VE) rather than 2 doses. We compared the number and rate of VEs from September 1, 2008 – November 6, 2011 (BPA only), and November 7, 2011 – April 13, 2014 (multi-disciplinary).

Results. Over 6 seasons, 1,117 VEs occurred. With BPA alone, 359 VEs occurred over 3 seasons (mean rate= 3.45% of hospital discharges, range 2.03-3.71%). With the new system, 758 VEs occurred over 3 seasons (mean rate= 7.36%, range 6.09-10.07%), a 111% VE increase and 114% rate increase ($p < 0.001$).

Conclusion. A mandatory, multi-disciplinary system for inpatient influenza vaccine screening and ordering is superior to BPA alone.

Disclosures. **All authors:** No reported disclosures.

664. Influenza Vaccination in Chronically Ill Children: Taking a Closer Look at LAIV

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Background. Children with underlying chronic conditions are sub-optimally vaccinated against influenza, even if influenza vaccines (IV) are publicly funded. Since 2012, the province of Quebec has recommended live-attenuated IV (LAIV) as the preferred vaccine for children with non-immunocompromising conditions. For a second consecutive year, an influenza vaccination clinic was set up in our pediatric tertiary care hospital. We aimed to compare this clinic's results to last year's and evaluate patients' preference for LAIV vs trivalent inactivated IV (TIV).

Methods. Between October 15 and December 24 of each year (2012 and 2013), a vaccination clinic was opened weekdays during working hours and staffed with vaccine nurses. TIV and LAIV were available. Parents were asked to fill a pre-piloted questionnaire. Descriptive statistics were used.

Results. During both years, we reached 630 patients with chronic illnesses accounting for 9% of the total outpatient visits for that time of year. In 2013, 264 (44%) were between 2 and 9 years, 257 (43%) were aged 9 to 18 years and 75 (13%) of vaccinated patients were immunosuppressed. Of the 623 participants for whom the information was available, 378 (61%) had received their IV in the previous year and in 49% (172/348), had received it in our vaccination clinic. For 122 of 603 parents who answered (20%), the presence of this vaccination clinic was instrumental in their child receiving their IV.

In 2012, 437 of 588 patients aged 2 years and over (74%) were vaccinated with LAIV, compared to 348 of 512 (68%) this year ($p = 0.02$). These represented 79% of LAIV eligible children ($n = 442$). Of 360 patients previously vaccinated, 103 (29%) had received LAIV the year before and 88% chose to be vaccinated again with LAIV this year. LAIV was preferred by caregivers ($n = 341$) because it was perceived as less painful (49%), no needle was involved (41%) and in 42% because of their physician's recommendation. Additionally, 487 household members were vaccinated in 2013.

Conclusion. Yearly influenza vaccination coverage in children with chronic illnesses can be improved with a vaccination clinic on site at a tertiary centre. Household members are also reached through this strategy. When LAIV is not contra-indicated, it remains caregivers' and patients' preferred vaccine.

Disclosures. **All authors:** No reported disclosures.

665. Polymorphism of cytokines and killer immunoglobulin-like receptor (KIR) gene in children with Bacille Calmette-Guérin lymphadenitis

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Background. Bacille Calmette-Guérin (BCG) lymphadenitis is relatively common local adverse reaction after BCG vaccination, and the risk factors were known as the

inoculation skill, the strain or amount of BCG, and an age at immunization. The association of the immune state and BCG adverse reactions has been mainly focused on severe adverse reaction. There were limited reports on the influence of immune regulatory genotypes on the BCG lymphadenitis.

Methods. A total of 42 children with BCG lymphadenitis and 56 healthy control children were enrolled. Detection of single nucleotide polymorphism located in the interferon-gamma (IFN-γ), tumor necrosis factor (TNF)-α, interleukin (IL)-1α, IL-4, IL-10 and killer immunoglobulin-like receptor (KIR) gene were performed by PCR with sequence-specific priming (PCR-SSP). Also, we compared this result with previously known data of 159 healthy Korean population.

Results. There were no differences in age, sex, and BCG vaccine type between children with BCG lymphadenitis and control. No statistically significant differences were observed between two groups for the frequency of TNF-α (-308), IFN-γ (-5644), IL-1α (-889), IL-10 (-819,-1082) genotypes, however, a significant differences in the frequency of TNF-α-238*G/A genotype was found ($p < 0.03$, OR = 5.4). The frequency of genotypes of IL-4-590*C/T was significantly higher in children with BCG lymphadenitis than those in healthy Korean population ($p < 0.04$, OR = 2.2). Polymorphism of KIR gene did not exhibit significant association with BCG lymphadenitis.

Conclusion. A frequent high producer TNF-α-238*G/A and/or IL-4-590*C/T may be one of the genetic factors responsible for BCG lymphadenitis. Our result suggests that this cytokine gene polymorphisms may be associated with host susceptibility to BCG lymphadenitis.

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666. Bronchiolitis in Indigenous Infants: a Review of Incidence and Risk Factors in Canada, the United States (US), Australia and New Zealand

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Background. Health outcomes of indigenous populations are often different than those of non-indigenous peoples in the same country. Bronchiolitis, usually due to Respiratory Syncytial Virus (RSV), is the most common cause of hospitalization in infancy; we performed a systematic review to determine the incidence of and risk factors for bronchiolitis in indigenous children in four English speaking affluent countries (Canada, US, New Zealand, Australia).

Methods. An electronic search of Medline for English language literature for the years 1966 to 2012 was conducted. MeSH headings used were:[bronchiolitis]; [respiratory tract infection]; [Respiratory Syncytial Virus infection] combined with each of the following MeSH terms: [Inuit]; [Indians, North American]; and [Oceanic Ancestry Group]. The search was repeated using the MeSH terms [bronchiolitis]; [respiratory tract infection]; [Respiratory Syncytial Virus infection] and the text terms "Aboriginal" and "Indigenous". Any article describing incidence in children <5 years using a population denominator was eligible. No methodologic or quality criteria were applied.

Results. 403 articles were identified; 52 were included. Review of the reference lists of these papers identified 6 additional papers. Illness outcomes were hospitalization (classified as RSV or bronchiolitis or pneumonia or any respiratory), outpatient care, emergency room visit or mortality. Most studies (75%) were retrospective and based on secondary data. >90% of studies compared illness rates to a non-indigenous population. All studies found higher illness rates in indigenous children than in the reference population; rates ranged from 1.3 to 20 times higher. Risk factors identified were age < 2 months, household crowding, prenatal tobacco use, wood stove, poor air quality, remote residence, low birth weight, low cord blood anti-RSV antibody, and protective factors were breastfeeding and indoor plumbing.

Conclusion. Indigenous infants are at higher risk for bronchiolitis requiring medical care than non-indigenous infants despite these countries' high standard of living. Many identified risk factors are preventable.

Disclosures. **All authors:** No reported disclosures.

667. The Timing of Hepatitis B virus Vaccination Does Not Influence Seropositivity Rates of Pediatric Liver Transplantation Recipients

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Background. Hepatitis B virus (HBV) infection poses a significant threat to children who have undergone solid organ transplantation. Therefore, completion of the HBV vaccine series is strongly recommended prior to transplantation. However, pediatric transplant recipients in Japan often fail to complete the full series prior to transplantation due to time constraints caused by the lack of a universal HBV vaccination program. Patients often complete the series as a combination of vaccines administered pre and post transplantation. We aimed to determine whether the timing of HBV vaccine influences the serostatus of patients post liver transplant and also evaluate factors that influence serostatus in the largest number of cases.

Methods. Patients were enrolled after informed consent before and after LT then followed prospectively. HBV vaccines were administered at least 2 weeks prior to LT and ≥1 year after LT if patients' liver function was stable. We collected information on patients who completed a total three doses of HBV vaccine. Serum antibody titers for HBs antibody were investigated and ≥10mIU/ml was considered positive. We compared the demographics and vaccine schedules of patients based on their HBs antibody positivity.

Results. Serological analyses for HBV were performed on 50 patients (median age 4.3 years, underlying disease; biliary atresia 34, metabolic disorder 7, fulminant hepatitis 5, other 4) who received a total of three doses of the HBV vaccine and were positive in 60.0% (30/60). There were no meaningful associations with serostatus in age, sex, body weight, underlying disorders, concentration of immunosuppressants, time between test and each immunization and blood tests. The seropositivity rate did not differ according to the timing of 3 doses of HBV vaccination administered pre/post LT (3/0, n = 7, 57.1%, 2/1; n = 8; 62.5%, 1/2; n = 7; 57.1%, 0/3; n = 28; 60.7%).

Conclusion. Pediatric liver transplant recipients achieved a seropositivity rate of approximately 60% after three doses of HBV vaccine regardless of when the doses were administered. Further HBV vaccine strategies are necessary to protect from HBV infection in children who experienced LT.

Disclosures. **All authors:** No reported disclosures.

668. The Effectiveness of Beta-lactam Monotherapy, Beta-lactam and Macrolide Combination Therapy or Fluoroquinolone Monotherapy in Patients Hospitalized with Community-Acquired Pneumonia: a Cluster-Randomized Cross-Over Trial

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Background. Optimal empirical treatment for community-acquired pneumonia is unknown. We compared empirical treatment strategies of beta-lactam monotherapy (BL), beta-lactam/macrolide combination (BLM) and fluoroquinolone monotherapy (FQL) in hospitalized community-acquired pneumonia (CAP).

Methods. A cluster-randomized cross-over trial was performed in seven Dutch hospitals. CAP patients initially admitted to a non-ICU ward and treated with antibiotics were eligible, independent of antibiotics chosen. Deviations for medical reasons were allowed and were considered per protocol treatment. The primary endpoint was 90-day mortality, with a non-inferiority margin of 3%. Secondary endpoints were time to oral treatment and length of stay. Intention-to-treat (ITT), per-protocol (PP) and on-treatment (OT) analyses were performed. All analyses were adjusted for cluster-period effects and confounders.

Results. Of 3,325 eligible patients, 656, 739 and 888 patients were included in the BL, BLM and FQL periods, respectively. Protocol adherence was 94%, 88%, and 93%, and 71%, 73% and 80% of patients received the preferred antibiotic class in the respective periods. Baseline characteristics did not differ between study periods. Crude 90-day mortality rates were 9.0% (n = 59), 11.1% (n = 82), and 8.8% (n = 78) in the BL, BLM, and FQL periods, respectively. BL was non-inferior to BLM and FQL for day-90 mortality, except for FQL in OT analysis compared to FQL (Figure 1). Median (IQR) length of stay was 6 (4-8), 6 (4-10) and 6 (4-8) for BL, BLM and FQL, respectively. BLM was associated with a longer length of stay (Figure 2). Median (IQR) duration of IV treatment was 4 (3-5), 4 (3-5) and 3 (0-4) in the respective periods. FQL was associated with a shorter duration of IV treatment (Figure 3), however, this did not result in a shorter length of stay.

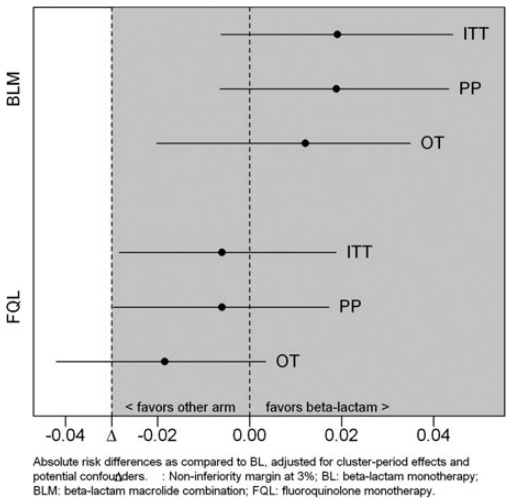

Figure 1. absolute risk differences in 90-day mortality

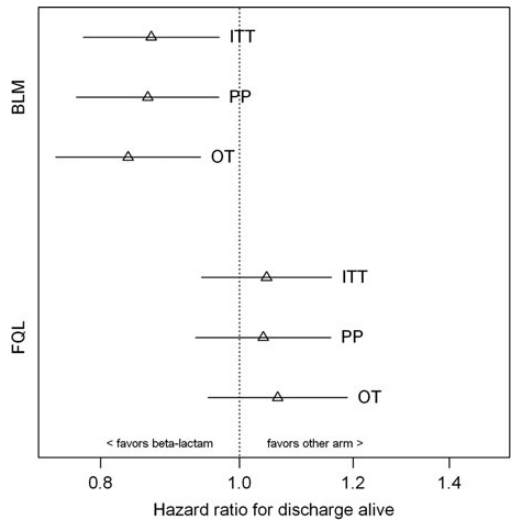

Figure 2. hazard ratios for length of stay

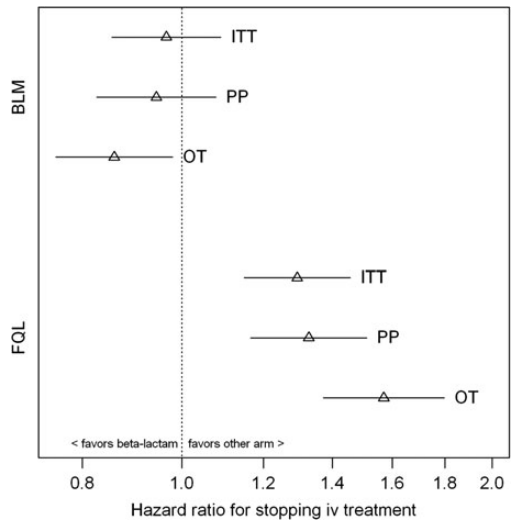

Figure 3. hazard ratios for time to oral treatment

Conclusion. A strategy of preferred empirical treatment with BL for patients hospitalized with CAP to non-ICU wards was non-inferior to BLM or FQL strategies for 90-day mortality. BLM was associated with a longer length of stay, and FQL with a shorter duration of IV treatment.

Disclosures. **All authors:** No reported disclosures.

669. DRIP – *Drug Resistance In Pneumonia*: Derivation and Prospective Multi-center Validation of a Scoring Model to Predict Drug-Resistant Pathogens

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Background. Predicting risk for community-acquired pneumonia due to drug-resistant pathogens (CAP-DRP) is challenging. Healthcare-associated pneumonia (HCAP) criteria have limited predictive value. However, a more accurate model has not yet been validated in a U.S. cohort.

Methods. In a retrospective derivation cohort of 200 culture-positive CAP and HCAP cases, previously identified risk factors for CAP-DRP were analyzed by logistic regression. A novel prediction tool, the DRIP score, was derived from 10 of these factors, weighted according to AOR (Table 1). A validation cohort of 200 culture-positive cases was identified prospectively at four U.S. centers (May 2013 - May 2014). The performance of DRIP, HCAP and other prediction models was evaluated in this group (Table 2).

Results. In the derivation group CAP-DRP prevalence was 26%. Prior antibiotic use (60 days) (AOR 7.3, $p < 0.01$), tube feeding (AOR 25.6 $p = 0.02$), long term care (AOR 4.1 $p = 0.05$), and prior CAP-DRP (AOR 7.2 $p = 0.079$) were associated with CAP-DRP. The DRIP score best differentiated high and low risk at a threshold of ≥4 points with a PPV of 73.1, NPV 90.5, accuracy of 86% and AUROC of 0.844. This was superior to HCAP (AUROC 0.604, accuracy 72%), and all other predictive models (Figure 1). In the validation cohort, DRIP was again most predictive: AUROC of 0.831, PPV 67.1, NPV 85.5, accuracy 78.5% (Figure 2). CAP-DRP prevalence was 34.5%. Compared to HCAP, the DRIP model would reduce over treatment by 46% with similar rates of under treatment.

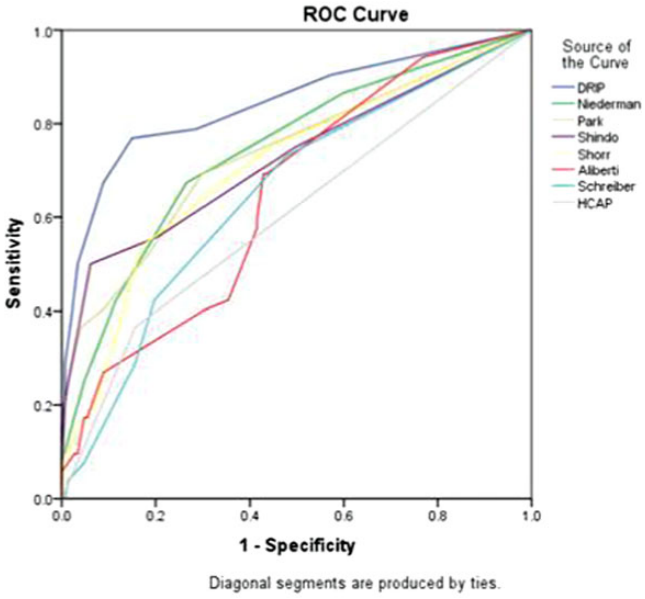

Figure 1. Derivation cohort

Figure 2: Validation cohort

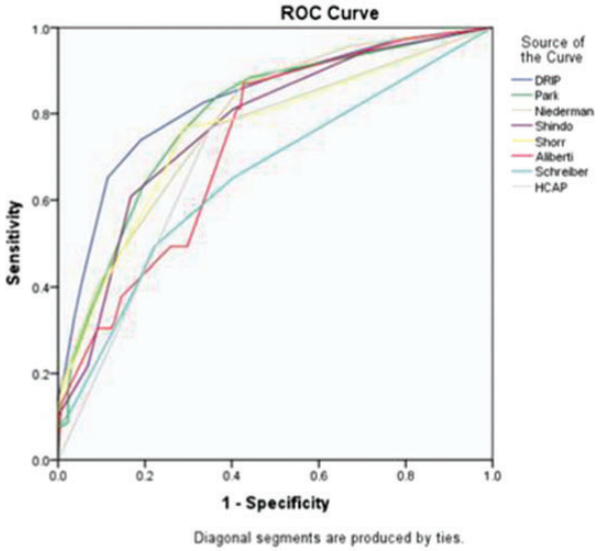

Table 1: DRIP Score

	Points
Antibiotic use <60 d	2
Long term care	2
Tube feeding	2
Prior CAP-DRP (1 yr)	2
Hospitalization <60 d	1
Chronic pulmonary disease	1
Poor functional status	1
Gastric acid suppression	1
Wound care	1
MRSA colonization (1 yr)	1

Table 2: Validation Cohort, n=200

Model	Sens %	Spec %	PPV %	NPV %	AUROC	Accuracy %
DRIP	73.9	80.9	67.1	85.5	0.83	78.5
HCAP	76.8	64.9	53.5	84.2	0.71	69.0
Schreiber	49.3	77.9	54.0	74.5	0.66	68.0
Shorr	79.7	54.2	47.8	83.5	0.75	67.0
Niederman	86.9	57.3	51.7	89.3	0.79	67.5
Shindo	81.2	59.5	51.4	85.7	0.77	67.0
Aliberti	87.0	55.7	50.8	89.0	0.73	66.5
Park	75.4	71.8	58.4	84.7	0.79	73.0

Conclusion. In this prospective multi-center U.S. study, the DRIP score was more predictive of CAP-DRP than HCAP and other models and has potential to decrease antibiotic over-utilization. Further validation is needed.

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670. Trends and Microbiology of Infective Endocarditis in Children during 2000-2010 in United States

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Background. Infective endocarditis (IE) is rare in children. We studied the incidence, trend and microbiology of IE in children over the past 11 years using Nationwide Inpatient Sample (NIS) database. NIS database is the largest all-payer inpatient care database in the United States containing data on more than 8 million hospital stays from over 1,000 hospitals.

Methods. Using data from NIS database from 2000 to 2010, hospital admissions with primary discharge diagnosis of IE in children aged ≤19 years old were studied. Incidence was calculated based on total number of children in respective years from US Census. Children with underlying congenital heart defects (ventricular septal defect, hypoplastic left heart etc.) as well as other acquired heart conditions (rheumatic heart disease, cardiac transplant) were identified. Microbiological causative agents were identified from the discharge diagnosis. Linear regression was used to assess trend of incidence of IE admissions over time.

Results. There was a total of 3,840 (95% CI: 3,395-4,285) admissions with IE with an overall incidence of 4.25 per million children. 27.2% were ≤5years, 16.6% were 6-10 years and 56.2% were ≥11 years old. 52.2% had an underlying heart disease. Overall 30.2% of cases were culture negative. Of those with culture-positive IE, *Streptococcus* species was most common (40.1%) followed by *Staphylococcus aureus* (36.6%). 26% of the culture- positive IE were due to viridans streptococci group (VSG). VSG was most common in those with underlying heart disease (32.9%) and *Staphylococcus aureus* was most common in those without heart disease (47.0%). The incidence of IE was stable over the study period ($p = 0.4$ for trend). Among those with positive cultures, there was a significant decline in proportion of *Staphylococcus aureus* IE (slope -1.9; $p = 0.01$) and a trend towards increase in proportion of VSG IE (slope +1.4; $p = 0.1$). The overall mortality of IE was 2.8%. Among culture-positive patients Staphylococcal IE had the highest mortality (5.0%).

Conclusion. The incidence of IE in children has remained unchanged in the US over the last 11 years. However, the microorganisms causing IE seem to be changing with significant decrease in *Staphylococcus aureus* among culture-positive patients. Overall, Streptococcus spp was the most common cause of culture-positive IE.

Disclosures. **All authors:** No reported disclosures.

671. Greater Hospital-Complexity and Case-Volume are Associated with Lower Mortality among Patients with *Staphylococcus aureus* Bacteremia

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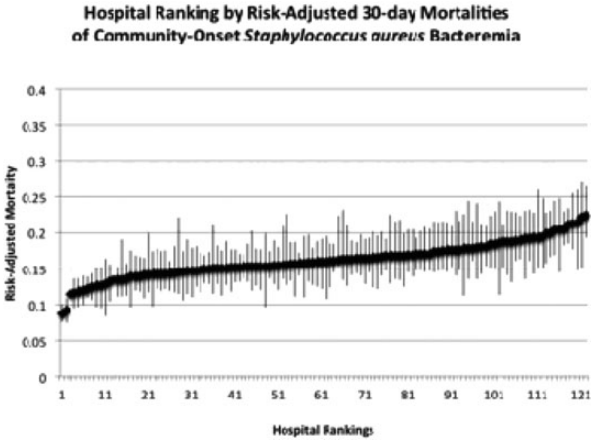
Background. Prior studies have examined hospital-level variation in outcomes for patients hospitalized with common non-infectious conditions, such as myocardial infarction and heart failure. However, little is known about hospital-level variation in outcomes for serious infections. We used a nationwide microbiology database in Veterans Affairs (VA) Healthcare System to quantify hospital-level variation in *Staphylococcus aureus* bacteremia (SAB) outcomes, and to explore associations between outcomes and hospital characteristics.

Methods. This was a retrospective cohort study of patients admitted to VA hospitals with first episode of community-onset SAB (positive culture within 48 hours of admission) between 2003 and 2010. Patient characteristics and all-cause 30-day mortality were obtained from VA databases; hospital characteristics were from VA organizational surveys. We used hierarchical logistic regression to calculate risk-adjusted mortality for each hospital, and to evaluate associations between hospital characteristics and patient-level mortality. Patient-level variables included demographics, comorbidities, year of admission, prior hospitalization, methicillin susceptibility of culture isolate, vital signs, and laboratory tests at the time of admission.

Results: Analyses included 27,380 patients in 122 hospitals. Overall crude mortality was 16.0%, and ranged from 6.8% to 30.2% across hospitals. After adjusting for patient characteristics (i.e., "case-mix") hospital-level mortality ranged from 8.8% to 22.4% (Figure). Mortality was lower among patients admitted to hospitals with larger case volumes [>60/year vs <15/year: OR 0.70 (0.56-0.86)], higher ICU complexity [complex ICU vs no ICU: OR 0.47 (0.24-0.93)], and academic affiliations [OR: 0.70 (0.53-0.94)]. Hospital characteristics were more strongly associated with patient mortality than was methicillin susceptibility of the isolate (MRSA vs MSSA: OR 1.13 (1.05-1.21).



Conclusion. Greater hospital-complexity, case-volume, and academic affiliation are associated with lower mortality among patients with SAB. Further study is needed to identify modifiable hospital characteristics and to direct quality-improvement efforts.

Disclosures. **All authors:** No reported disclosures.

672. Staphylococcus aureus Bacteremia in Hospitalized Children

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Background. *Staphylococcus aureus* is a common cause of bacteremia in adults and children. There are published adult guidelines for *S. aureus* bacteremia management, but there are limited comparative effectiveness data to inform pediatric treatment guidelines. Describing the clinical characteristics and outcomes of pediatric inpatients with *S. aureus* bacteremia is necessary to prioritize future comparative effectiveness studies.

Methods. An observational cohort of children >2 months and <19 years was assembled using Premier Perspective™ Database, a nationally representative administrative database of billing and microbiology data. All incident admissions between 2009 and 2012 with lab-confirmed *S. aureus* bacteremia were included. Outside facility transfer patients were excluded. Admissions with a positive blood culture in the first 3 days were considered community-onset (CO); those beyond 3 days were considered healthcare-onset (HO). Two infectious diseases physicians independently reviewed

all ICD-9 codes per admission to determine the source of bacteremia; subsequent reviewer discussion adjudicated disagreements. Wilcoxon rank-sum and Chi squared tests were used to compare medians and proportions, respectively.

Results. There were 414 patients with *S. aureus* bacteremia; median age was 6.5 years (IQR: 1 to 13 years). Patients were more frequently white (n = 218, 53%), male (n = 261, 63%) and had CO infection (n= 368, 89%). Length of stay (LOS) after onset of bacteremia was longer for patients with HO (HO: 14 days, IQR: 5 to 28 vs CO: 5 days, IQR: 3 to 9; p <0.001). The source of bacteremia was determined in 346 patients (84%) and was most commonly a bone/joint (HO: n = 14, 30%; CO: n = 140, 38%), skin/soft tissue (HO: n = 8, 17%; CO: n = 71, 19%), or pneumonia (HO: n = 5, 11%; CO: n = 40, 11%). The HO case fatality rate was higher than for CO (11% vs 2%, p = 0.0038).

Conclusion. This is the first large, multi-center study of pediatric *S. aureus* bacteremia. CO bacteremia was more common, but HO bacteremia patients had longer LOS and higher case fatality rates. Future analyses will explore the impact of treatment strategies on patient outcomes.

Disclosures. **All authors:** No reported disclosures.

673. Comparative Effectiveness of Vancomycin vs Early Daptomycin for MRSA Bacteremia with Vancomycin MIC >1 mg/L: A Multicenter Evaluation

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Background. Evidence suggests that vancomycin has reduced effectiveness in MRSA bacteremia with higher vancomycin MIC values (> 1 mg/L). However, clinical studies comparing vancomycin to alternative therapy in these patients are limited.

Methods. We conducted a retrospective, nationwide, multicenter, matched (by age, bacteremia type, severity of illness, ID consult and institution), cohort study that compared daptomycin vs vancomycin among adult patients with MRSA bacteremia with high vancomycin MICs (1.5-2 mg/L). The primary outcome was composite failure, defined as having: 60-day all-cause mortality, 7-day clinical or microbiological failure, failure at end of therapy, and/or 30-day BSI relapse. Secondary outcomes included early bacteremia clearance by day 4 without recurrence and acute kidney injury (AKI). Stratified treatment-outcomes analyses by key baseline covariates were performed.

Results. One hundred seventy patients from 11 United States institutions were included. The median daptomycin dose was 6 mg/kg (interquartile, IQ, range, 6-8 mg/kg). Daptomycin was dosed >8 mg/kg in 26% (22/85). All patients had vancomycin troughs of at least 10 mg/L (median 17.5 mg/L; IQ range, 14.0-22.0 mg/L). Vancomycin troughs were >15 mg/L in 71% (60/85). The primary composite endpoint did not vary between the daptomycin and vancomycin groups (31% vs 39%, respectively, P = 0.259). Both end of therapy failure and acute kidney injury were significantly lower in the daptomycin relative to the vancomycin group (11% vs 24%, respectively, P = 0.025, and 9% vs 23%, respectively, P = 0.043). In the stratified analyses, daptomycin demonstrated a higher rate of bacteremia clearance by day 4 than vancomycin (94% vs 56%, respectively, P = 0.035) among immunocompromised patients (n = 26).

Conclusion. Results from this multicenter study provide real-world comparative data on the outcomes with daptomycin vs vancomycin in adult patients with MRSA bacteremia with vancomycin MIC 1.5-2 mg/L. As with all observational studies, these findings should be interpreted cautiously.

Disclosures. **P. Moise**, Cubist: Employee and Shareholder, Salary **D. Culshaw**, Cubist: Employee and Shareholder, Salary **K. Lamp**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **T. Lodise**, Cubist Pharmaceuticals: Consultant, Consulting fee

674. Comparison of the Microbiology and Antibiotic Treatment between Diabetic and Non-Diabetic Patients Hospitalized with Acute Bacterial Skin and Skin Structure Infection

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Background. Diabetics with certain complicated skin infections are at increased risk for gram-negative pathogens; however, the microbiology of uncomplicated infections such as cellulitis and cutaneous abscess has not been well-described. The purpose of this study was to evaluate the microbiology and antibiotic treatment of diabetics hospitalized for cellulitis or abscess.

Methods. This was a secondary analysis of two published cohorts of patients hospitalized for otherwise uncomplicated cellulitis or abscess where complicated infections such as osteomyelitis or infected diabetic ulcers were excluded. The microbiology and antibiotic utilization were compared among diabetics and non-diabetics. Broad gram-negative therapy was defined as use of fluoroquinolones, β-lactamase inhibitor combinations, carbapenems, 2nd-5thgeneration cephalosporins, or aminoglycosides. Logistic regression was performed to identify factors associated with use of broad gram-negative therapy.

Results. Of 770 patients with cellulitis or abscess, 167 (22%) had diabetes mellitus. Diabetics were more likely to have cellulitis as the presenting infection (67% vs 56% of cases, p = .008). Of cases with a positive culture, an aerobic gram-positive organism was isolated in 92% of diabetics and 93% of non-diabetics (p = .79). Aerobic gram-negative organisms were isolated in 6% of diabetics and 11% of non-diabetics (p = .26). These comparisons were similar when stratified by cellulitis vs abscess. Despite the similar microbiology, diabetics were more likely to be treated with broad gram-negative therapy (45% vs 33% of cases, p = .003). By logistic regression, diabetes mellitus was independently associated with use of broad gram-negative therapy (OR 1.69, 95%CI 1.15 – 2.49).

Conclusion. Compared with non-diabetics, diabetics hospitalized with cellulitis or abscess were not more likely to have gram-negative pathogens; however, they were more likely to be treated with broad gram-negative therapy. Although a limitation of this type of analysis is that most cases of ABSSSI do not involve positive cultures, these findings suggest diabetics with otherwise uncomplicated cellulitis or abscess do not need broad gram-negative therapy.

Disclosures. **All authors:** No reported disclosures.

675. Outcomes of Acute Bacterial Skin and Skin Structure Infections (ABSSSI) by vancomycin dosing regimen and vancomycin trough serum concentrations in the DISCOVER Program

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Background. Dalbavancin is a lipoglycopeptide antibiotic with activity against Gram-positive pathogens and a long half-life allowing for weekly dosing. DISCOVER 1 and 2 were identically designed clinical trials of dalbavancin vs vancomycin (VAN) with option to switch to oral linezolid for the treatment of ABSSSI. We evaluated outcomes of ABSSSI in patients treated with VAN by dosing regimen utilized and serum trough concentrations for VAN.

Methods. Both trials were double-blind, double dummy, pharmacist-unblinded randomized trials in which patients with ABSSSI were randomized to receive dalbavancin 1g IV on Day 1 and 500 mg IV on Day 8 or VAN 1g (or 15mg/kg) IV every 12 hours (q12h) for at least 3 days with an option to switch to oral linezolid 600 mg q12h to complete 10-14 days of therapy. The primary endpoint was measured at 48-72 hours of therapy with success requiring cessation of spread of the infection and absence of fever. Secondary endpoints included clinical status at the end of therapy. Outcomes by fixed vs weight-based dosing regimens of VAN and outcomes by serum VAN trough concentrations were analyzed.

Results. Please see Tables 1 and 2.

Table 1: Efficacy by fixed* vs weight-based dosing regimen of vancomycin

Efficacy Outcomes	Fixed-Dose Regimen	Weight-based Regimen
48-72 hour outcomes		
Success	349/441 (79.1)	172/210 (81.9)
Failure	92/441 (20.9)	38/210 (18.1)
Difference (95% CI)	-2.8, (-9.0, 4.0)	
Clinical Success at EOT		
Success	383/441 (86.8)	179/210 (85.2)
Failure	58/441 (13.2)	31/210 (14.8)
Difference (95% CI)	1.6 (-3.9, 7.8)	

*1 gram intravenously twice daily

Conclusion. Clinical response rates for patients with ABSSSI were similar in patients treated with a fixed-dose regimen or weight-based dosing regimen of vancomycin. No association was observed between serum vancomycin trough concentrations and efficacy outcomes at the 48-72 hour time point or at EOT.

Disclosures. **S. Puttagunta**, Durata Therapeutics: Employee and Shareholder, Salary **M. Wilcox**, Durata Therapeutics: Scientific Advisor, Consulting fee **G. Talbot**, Durata Therapeutics: Consultant, Scientific Advisor and Shareholder, Consulting fee **M. Dunne**, Durata Therapeutics: Employee and Shareholder, Salary

Table 2: Efficacy by serum trough vancomycin concentrations

	VAN concentration ≤10 µg/mL	VAN concentration > 10 µg/mL
48-72 hour outcomes		
Success	79/95 (83.2)	78/94 (83.0)
Failure	16/95 (16.8)	16/94 (17.0)
Difference (95% CI)	0.2 (-10.7, 11.1)	
Clinical success at EOT		
Success	83/95 (87.4)	82/94 (87.2)
Failure	12/95 (12.6)	12/94 (12.8)
Difference (95% CI)	0.2 (-9.7, 10.0)	

676. Efficacy and Safety of Tedizolid and Linezolid in IV Drug Users in a Pooled Phase 3 Population of Patients with Acute Bacterial Skin and Skin Structure Infection (ABSSSI)

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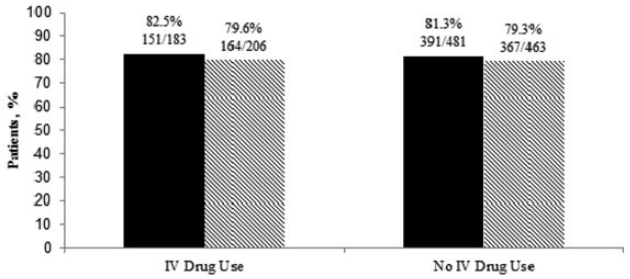
Background. Tedizolid (TZD) is a novel oxazolidinone antibacterial with potent activity against a wide range of Gram-positive pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA). Two Phase 3 clinical trials demonstrated noninferior efficacy of TZD (200 mg daily for 6 days) to linezolid (LZD) (600 mg twice daily for 10 days) for treating ABSSSI. Since ABSSSI are common in IV drug users, this analysis compares the efficacy and safety of TZD in IV and non-IV drug users.

Methods. The primary endpoint was early clinical response (≥ 20% reduction from baseline in lesion area at 48–72 h after end of therapy); a secondary efficacy endpoint was the investigator assessment of clinical response at the posttherapy evaluation (PTE, 7 to 14 days after

last dose of study drug). An analysis of the pooled Phase 3 population (N = 1333; TZD, n = 664; LZD, n = 669) compared efficacy and safety of TZD vs LZD in IV and non-IV drug users. Safety assessments included liver function tests and adverse events (AE).

Fig. 1. **Early Clinical Response at 48–72 Hour Visit by IV Drug Use (ITT Population). Tedizolid (solid bar); Linezolid (striped bar).**



ITT, Intent to Treat

Fig. 2. **Investigator-Assessed Clinical Response at PTE by IV Drug Use (CE-PTE Population). Tedizolid (solid bar); Linezolid (striped bar)**

Results. IV drug users comprised 27.6% (183/664) of the TZD and 30.8% (206/669) of the LZD treatment arms. Wound infections were the most common type of ABSSSI in IV drug users (50.8% and 53.4% in TZD and LZD groups, respectively), whereas cellulitis/erysipelas was most common in non-users (54.5% and 57.5%, respectively). In both treatment groups, the most common baseline pathogen in IV drug users was *S. aureus* (73.6% and 76.5% for TZD and LZD, respectively). For both treatment groups, early clinical response at the 48–72 h visit and investigator-assessed clinical response rates at the PTE was similar in IV and non-IV drug users (Figure 1, Figure 2). Overall AE rates were similar in IV and non-IV drug users (46.2% for TZD vs 41.5% for LZD, 47.8% vs 41.2%, respectively). Changes in lab parameters including liver function tests were also similar.

CE-PTE, Clinically Evaluable-Posttherapy Evaluation.

Conclusion. In patients treated with TZD or LZD in the ESTABLISH-1 and -2 Phase 3 clinical trials, the efficacy and safety profile was similar between IV and non-IV drug users.

Disclosures. **C. De Anda**, Cubits: Employee and Shareholder, Salary **E. Fang**, Trius/Cubist: Employee, Salary **A. Das**, Cubist: Consultant, Consulting fee; Cempra: Consultant, Consulting fee; Cerexa: Consultant, Consulting fee; Nabriva: Consultant, Consulting fee; Paratek: Consultant, Consulting fee; Trius: Consultant, Consulting fee; Achaogen: Consultant, Consulting fee; Durata: Consultant, Consulting fee **P. Prokocimer**, Cubist: Employee and Shareholder, Salary

677. Distinct microbial species in acute and chronic wounds in community-recruited injection drug users: Antimicrobial sensitivity more common than not

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Background. This study aimed to characterize the microbial population of acute and chronic wounds among injection drug users (IDUs) frequenting the mobile, community-based Baltimore Needle Exchange Program (BNEP)

Methods. Acute (duration <8 weeks) and chronic wounds (duration ≥8 weeks) in clients of the BNEP were cleaned and debrided prior to sampling for aerobic and anaerobic culture. Cultures were processed using standard microbiologic procedures for aerobes and anaerobes, and routine antimicrobial sensitivity testing was performed. Statistical analysis included t-tests and logistic regression.

Results. Fifty wounds from 35 participants were cultured. Of these, 52% were chronic wounds and 48% were acute wounds. Rates of methicillin-sensitive *Staphylococcus aureus* and methicillin-resistant *S. aureus* (MRSA) were equivalent, 36%. *Pseudomonas aeruginosa* was the most common gram-negative organism overall and was present in chronic wounds exclusively (27%). *P. aeruginosa* isolates were highly antibiotic-sensitive with only one isolate showing resistance to piperacillin. *Escherichia coli* was the second most common gram-negative organism (12%), and isolates were also highly antibiotic sensitive. Four of six *E. coli* isolates were resistant to only ampicillin and trimethoprim/sulfamethoxazole (67%), and two of six isolates were pan-sensitive (33%). Chronic wounds were more common in African Americans (OR 4.25, 95% CI 1.25–14.50), and more often had anaerobic bacteria (OR 4.38, 95% CI 1.03–18.56). Women had greater risk of MRSA-positive cultures (OR 6.50, 95% CI 1.38–30.68). MRSA was not seen preferentially in one wound type vs the other.

Conclusion. Highly antibiotic-sensitive gram-negative bacteria were seen in this population, suggesting that this community-based sample of individuals may have limited historical interactions with the health care system. There are also differences in cultivatable wound microbiome by race, gender and wound type among IDUs that warrant additional investigation. The potential implications of these differences regarding microbial wound communities may inform treatment and prevention efforts.

Disclosures. **All authors:** No reported disclosures.

678. Ceftaroline vs Vancomycin in Treatment for Skin and Soft Tissue Infections (SSTI) in Obese Patients

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Background. A prior study to evaluate the safety and efficacy of ceftaroline vs vancomycin plus aztreonam in SSTI demonstrated that clinical cure rates were similar for ceftaroline compared with vancomycin plus aztreonam. The majority of the patient population in the study had Body Mass Index (BMI) < 30. There is very little data on the efficacy of ceftaroline in patients with BMI>30. We conducted a study to compare the efficacy and safety of ceftaroline in a population with normal BMI compared with those with BMI > 30.

Methods. Retrospective study of patients admitted to Vidant Medical Center from May to September of 2013 with the diagnosis of SSTI and who were treated with ceftaroline. Patients' BMIs were calculated, and duration of treatment and adverse effects were noted. We also examined vancomycin use in patients with SSTI from May to September of 2011 and 2012 in order to compare the efficacy and safety between

vancomycin and ceftaroline. Student's t-test and Fisher's exact test were used to assess differences in categorical values. P values <0.05 were considered statistically significant.

Results. Of total 244 patients, 134 received ceftaroline and 110 received vancomycin with or without gram-negative coverage therapy. Baseline characteristics of the treatment groups were comparable. Among 134 patients in the ceftaroline group, 84 patients (62.7%) had BMI > 30. Clinical improvement were similar between patients with BMI<30 and BMI>30 (96% vs 95.2%). Among 110 patients treated with vancomycin, there were 85 patients (77.3%) with BMI > 30. When compared with vancomycin in patients with BMI > 30, clinical cure rate was similar for those treated with ceftaroline (95.2% vs 97.6%). However, there was a higher rate of acute kidney injury in patients with BMI > 30 who were treated with vancomycin (7.06% vs 0%, $p = 0.028$).

Conclusion. Ceftaroline therapy was associated with similar clinical cure rates in both normal (BMI <30) as well as among obese (BMI>30) patients when compared with vancomycin with or without gram-negative coverage combination therapy. The medication was well tolerated and had minimal side effects in all patients. In obese patients, vancomycin was associated with a higher incidence of acute renal injury as compared with ceftaroline.

Disclosures. **P. Cook**, Gilead (investigator), Pfizer (investigator), Merck (investigator and speakers' bureau, Forest (Speaker honorarium)

679. Ceftaroline Fosamil (CPT-F) for the Treatment of Acute Bacterial Skin and Skin Structure Infections (ABSSSIs) in Obese Patients

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Background. Obesity rates are increasing in the US and the treatment of ABSSSI in these patients is often challenging. CPT-F is approved for the treatment of ABSSSI and community-acquired bacterial pneumonia in the US, and for similar indications in the EU. CAPTURE is a multicenter retrospective study evaluating patients (pts) treated with CPT-F in the US. Data on the treatment of obese pts with CPT-F for ABSSSI are presented.

Methods. Data were collected at participating centers by randomly ordered chart review between September 2011 and February 2014 which included demographics, disease characteristics, antibiotic use, pathogens, location of care, and clinical response. Obesity was defined as a body mass index ≥ 30 kg/m^2. Pts with a clinical outcome determined were evaluable.

Results. Of evaluable pts treated for ABSSSI, 883/1735 (51%) were obese. The mean age was 58.5 years (SD ± 15.8), 49% were male, 53% had diabetes and 39% were morbidly obese (BMI ≥ 40 kg/m^2). Infection types included deep/extensive cellulitis (67%), major abscesses (15%), and infected ulcers (13%). The most common infection sites were the leg/thigh (59%) and foot (24%). Most pts, 807 (91%), were treated in a general hospital ward. Pathogens were recovered in 47% of pts, most commonly MRSA (20%) and MSSA (11%). MRSA and MSSA were isolated mainly from the ABSSSI site (> 96%), also from blood (< 9%) or both ABSSSI and blood (< 7%). Other antibiotics were used prior to CPT-F therapy in 80% of pts, most commonly vancomycin (53%) and piperacillin-tazobactam (24%). Concurrent antibiotics were used in 33% of pts, most commonly clindamycin (19%) and vancomycin (13%). The mean duration of CPT-F therapy was 5.8 days (SD ± 4.2). Clinical success was 91% in obese pts overall, and 90% in the morbidly obese. In pts with diabetes, clinical success was 89%. Clinical success for CPT-F monotherapy was 92% and for concurrent therapy, was 89%. In patients with MRSA and MSSA, clinical success rates were 88% and 93%, respectively.

Conclusion. In obese pts, clinical success with CPT-F therapy was high, including pts with diabetes. These data support the use of CPT-F as a treatment option for ABSSSI in pts with obesity, including those with diabetes.

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680. Predictors of Recurrent *Staphylococcus aureus* Skin Infection After Treatment: Host, Behavioral, and Pathogen Level Factors

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Background. Many patients suffer from recurrent *Staphylococcus aureus* infections, however, there are few longitudinal data examining predictors of recurrences and few data holistically incorporating the competing host, behavioral, and pathogen factors that may contribute to recurrent infections.

Methods. We longitudinally studied adults and children with *S. aureus* skin infections in Los Angeles and Chicago. We surveyed subjects and their household contacts for *S. aureus*body colonization, household fomite contamination, behavioral and clinical factors at months 0, 3, and 6. Using repeated measures modeling, we examined host, pathogen, behavior, and clinical factors associated with recurrent skin infection.

Results. Among 330 index subjects, 182 (55%) were infected with an isolate of the USA300 genetic background. Thirty nine percent reported a recurrent skin infection by 3 and 51% by month 6. Among 588 household contacts, 10% reported a skin infection by month 3 and 13% by month 6. Among index subjects, subsequent skin infection was associated with (P <0.05) Los Angeles site, diabetes, hospitalization in the prior 3 months, skin infection in the prior 12 months, cephalexin use in the prior 12 months, household fomite contamination with *S. aureus*, and household fomite contamination with MRSA; infection was inversely associated with contact sports participation. In the multivariate model, independent predictors of subsequent skin infection in index patients were hospitalization in the prior 3 months and household fomite contamination with MRSA; contact sports participation in the prior 3 months was inversely associated. Among household contacts, independent predictors of subsequent skin infection were Chicago site, antibiotic exposure in the prior 12 months, and skin infection in the prior 3 months.

Conclusion. In our longitudinal study of patients discharged after *S. aureus* infection, recurrence rates were very high. Patients were more likely to suffer recurrence if household fomites were MRSA contaminated. We found no pathogen or colonization-level factors associated with recurrent infection. *S. aureus* prevention efforts may need to focus on decontamination of household fomites to prevent recurrent infections.

Disclosures. **All authors:** No reported disclosures.

681. Microscopically Diagnosed Necrotizing Fasciitis: A Series of 29 Patients —Can We Depend on the Macroscopic Findings?

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Background. Necrotizing fasciitis (NF) is one of the life threatening infections which need early diagnosis and treatment for a better prognosis. The mortality rate was 10 to 40% in some reports. We perform exploratory incision along the Infectious Disease Society of America (IDSA) guideline if NF is suspected. However, the indication of surgical debridement usually depends on the macroscopic findings by surgeons. The aim of this study was to validate surgical decisions by macroscopic findings.

Methods. We retrospectively researched the medical records of NF cases from June 2002 to October 2013 of a tertiary care hospital in Chiba, Japan. Cases were defined as NF if histopathology demonstrated both necrosis of fascia and polymorphonuclear infiltrate. All patients were categorized into two groups: debridement NF and non-debridement NF. Demographics, clinical characteristics, the focal skin sign category and laboratory risk indicator for necrotizing fasciitis (LRINEC) score were compared in both group. The focal skin sign was divided to following three categories: stage 1 (early) - tenderness, erythema, swelling and warmth; stage 2 (intermediate) - blister or bullae, skin fluctuance and skin induration; stage 3 (late) - hemorrhagic bullae, skin anesthesia, crepitus and skin necrosis.

Results. All 29 patients meeting histopathologic criteria for NF were included. Debridement was performed in 22 patients and not indicated in 7 patients because they had no macroscopic NF findings at exploratory incision. The mortality rate was 27.3% in debridement group and 42.9% in non-debridement group (p = 0.64). Gram stains were positive with 77.3% in debridement group and 42.9% in non-debridement group (p = 0.16). Mean time from onset to diagnosis was 3.6 days in debridement group and 1.6 days in non-debridement group (p = 0.09). Cases with LRINEC score > 6 (intermediate - high risk) were only 52.6% in debridement group, and all patients in non-debridement group were LRINEC score < 6 (low risk) (p = 0.08).

Conclusion. The mortality rate in histopathologically diagnosed NF patients was almost same as previous reports, even though debridement was not performed for the patients without macroscopic fascia finding. And no significant difference was noted in the mortality between debridement and non-debridement group.

Disclosures. **All authors:** No reported disclosures.

682. Microbiology and Antibiotic Treatment among Injection Drug Users and Non-Injection Drug Users Hospitalized with Acute Bacterial Skin and Skin Structure Infection

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Background. Injection drug use is a common risk factor for acute bacterial skin and skin structure infections (ABSSSI) that may influence antibiotic prescribing

patterns. The objective of this study was to compare the microbiology and antibiotic treatment of injection drug users and non-injection drug users hospitalized for ABSSSI.

Methods. This was a secondary analysis of two published cohorts of patients hospitalized for cellulitis or cutaneous abscess. Injection drug use was defined as documentation of last use within 6 months prior to hospitalization. Microbiology and antibiotic utilization were compared among patients with and without injection drug use. Antibiotics with broad anaerobic activity were defined as β-lactamase inhibitor combinations, clindamycin, carbapenems, and metronidazole.

Results. Of 770 patients hospitalized for ABSSSI, 126 (16%) were injection drug users. Compared with non-injection drug users, injection drug users were more likely to have an abscess as the presenting infection (83% vs 34% of cases, $p < .001$). Injection drug users were also younger (median age 43 vs 51 years, $p < .001$) and more likely to have upper extremity involvement (18% vs 9%, $p = .005$), multiple sites of infection (10% vs 5%, $p = .02$), HIV infection (10% vs 2%, $p < .001$), and a prior skin infection (31% vs 22%, $p = .03$). In cases where a microorganism was cultured, streptococcal species (50% vs 27%, $p < .001$) and anaerobes (29% vs 8%, $p < .001$) were more common among injection drug users, while *Staphylococcus aureus*was less common (52% vs 67%, $p = .02$). These findings were similar when limiting the analysis to cases involving an abscess. Injection drug users were treated with antibiotics with broad anaerobic activity more frequently than non-injection drug users (69% vs 60%, $p = .048$), particularly with β-lactamase inhibitor combinations (52% vs 41%, $p = .02$).

Conclusion. Compared with non-injection drug users, ABSSSI in injection drug users are more likely to involve streptococcal species and anaerobes and less likely to involve *S. aureus*. Injection drug users are more likely to be treated with β-lactamase inhibitor combinations; however, whether such broad-spectrum therapy is necessary should be further evaluated.

Disclosures. **All authors:** No reported disclosures.

683. Intravenous Immunoglobulin as a Potential Marker for Toxic Shock Syndrome Secondary to Necrotizing Fasciitis: A Large Database Analysis of Outcomes at US Academic Medical Centers

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Background. Necrotizing fasciitis (NF) is a rare, rapidly progressing, severe subtype of necrotizing skin and soft-tissue infection (NSSTI) that in 30-50% of cases presents with toxic shock syndrome (TSS). Intravenous immune globulin (IVIG) has been recommended for TSS, but level-1 evidence is lacking. However, IVIG administration might be used to identify likely cases of NF-related TSS among patients with NSSTIs that otherwise require vasopressor support for shock.

Methods. An administrative database of 110 academic medical centers containing individual charges related to drugs and days of therapy was queried for adult cases with an International Classification of Diseases-Version 9 (ICD-9) diagnostic code for NF, Gas or Fournier's Gangrene and at least 1 ICD-9 procedure code for surgical debridement between October 2010 and February 2014. Cases were dichotomized based on use of IVIG. Analyses were restricted to cases with vasopressor dependent shock in the major and extreme categories of the *3M* All Patients Refined Diagnoses Related Group Severity of Illness (SOI) scale. The primary outcome was in-hospital mortality and secondary outcomes were mean duration on vasopressors and mean direct hospital costs.

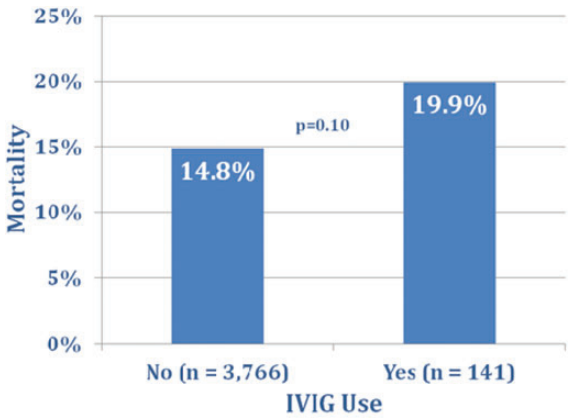

Figure 1: Mortality by intravenous immunoglobulin (IVIG) use among patients with necrotizing skin and soft-tissue infections. Analysis was restricted to those with high Severity of illness (All Patients Revised-Diagnosis Related Groups Severity of Illness Score of Major and Extreme) in vasopressor-dependent shock that underwent at least one debridement or amputation procedure.

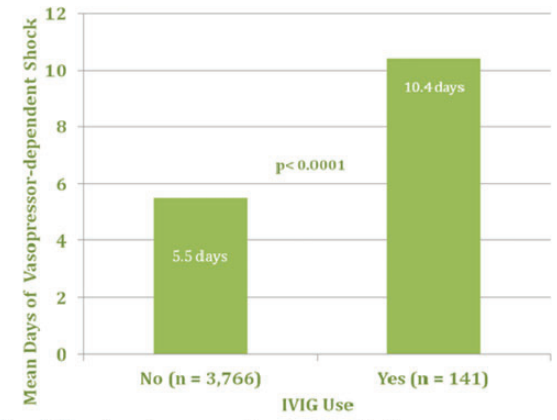

Figure 2: Mean days of vasopressor-dependent shock by intravenous immunoglobulin (IVIG) use among patients with necrotizing skin and soft-tissue infections. Analysis was restricted to those with high Severity of illness (All Patients Revised-Diagnosis Related Groups Severity of Illness Score of Major and Extreme) in vasopressor-dependent shock that underwent at least one debridement or amputation procedure.

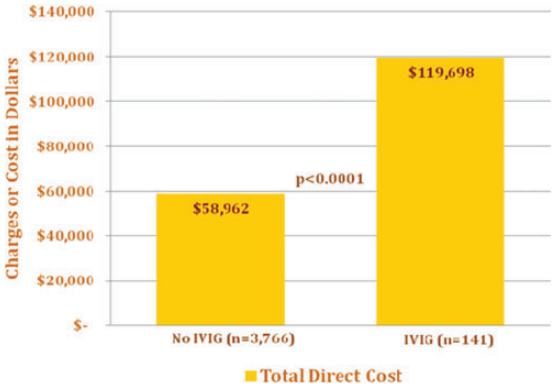

Figure 3. Mean direct healthcare costs by intravenous immunoglobulin (IVIG) use among patients with necrotizing skin and soft-tissue infections. Analysis was restricted to those with high Severity of illness (All Patients Revised-Diagnosis Related Groups Severity of Illness Score of Major and Extreme) in vasopressor-dependent shock that underwent at least one debridement or amputation procedure.

Results. Of 4221 adults with NSSTIs, vasopressor dependent shock and undergoing surgical debridement, only 147 (3.5%) received IVIG. Among those in the major and extreme categories of SOI, in-hospital mortality was higher in the IVIG group at 19.9% (28/141) than in the non-IVIG group at 14.8% (558/3766) but the difference was not significant ($p = 0.10$). IVIG patients remained on vasopressors longer (10.4 ± 9.5 days vs 5.5 ± 7.5 days; $p < 0.0001$). Direct healthcare costs were twice as high in the IVIG group at $\$119,698 \pm \$118,232$/case ($p < 0.0001$).

Conclusion. Use of IVIG in cases of NSSTIs with vasopressor dependent shock is rare. This likely reflects both the small proportion of these cases that meet criteria for NF-related TSS, as well as inconsistent use of this still controversial intervention. Adult cases of NSSTI with vasopressor dependent shock that received IVIG stayed in shock longer and bore higher healthcare costs. IVIG administration identifies a very sick subpopulation of NSSTIs associated with shock.

Disclosures. **All authors:** No reported disclosures.

684. A Festering Affliction: Etiology and Clinical Manifestations of Thorn-Associated Infections

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Background. Cacti of multiple varieties are frequently encountered in the desert southwest, including the greater Phoenix metropolitan area; thus, cactus and thorn injuries are frequent reasons for patients seeking medical attention. Nocardia, atypical

mycobacteria, and fungi are cited in the differential diagnoses of thorn injuries, but their relative frequency is unknown.

Methods. We conducted a retrospective chart review of patients who sustained thorn injuries from cacti or undifferentiated thorns between 2001 – 2009 in order to summarize the nature of resulting infections and the offending pathogens.

Results. We reviewed 1,945 patient medical records with confirmed (C-cactus) and potential (P-cactus) cactus and thorn (confirmed [C-thorn], potential [P-thorn]) injuries and identified 1,043 patients presenting with findings related to, or suggestive of, such an injury. Within this group, 706 (68%) and 77 (7%) patients had C-cactus and P-cactus injuries, while 218 (21%) and 42 (4%) had C-thorn and P-thorn injuries, respectively. Among 1,043 patients, 54 (5%) had positive cultures: 27 (50%) C-cactus, 12 (22%) P-cactus, 8 (15%) C-thorn and 7 (13%) P-thorn. Among these 54, 32 (59%) were male, median age was 63 years, and 94% were Caucasian. Thirty-eight (70%) injuries occurred in the upper and 15 (28%) occurred in the lower extremities. The most common organisms identified were *S. aureus* (29, 44%) and coagulase negative *Staphylococcus* (12, 18%). Other pathogens included *Streptococcus* sp. (6, 9%), *Propionibacterium* sp. (4, 6%), *Pseudomonas* sp. (2, 3%), *Actinomyces* sp. (1, 2%), *Nocardia* sp. (4, 6%), and *Mycobacteria* sp. (4, 6%). Forty-two (78%) specimens grew single agents; 12 (22%) were polymicrobial. No specific microorganisms were unique to cactus vs unspecified thorn injuries. We did not find Coccidioides, *Sporothrix*, or molds. Although most cases developed cellulitis (20, 37%), others manifested as soft tissue abscesses (9, 17%), osteomyelitis (2, 4%) and septic bursitis (2, 4%). Initial presentation was to the Emergency Department (43%), a subspecialty practice (22%), or a primary care office (17%).

Conclusion. Our detailed review indicates that typical cutaneous microorganisms (rather than pathogens residing on cacti or thorns) cause the majority of such infections resulting from cactus or thorn injuries.

Disclosures. **All authors:** No reported disclosures.

685. Time to Onset and Duration of Adverse Events in Patients with Acute Bacterial Skin and Skin Structure Infections Treated with Oritavancin – The SOLO Studies

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Background. Oritavancin (ORI) is a lipoglycopeptide antibiotic characterized by rapid, concentration dependent bactericidal activity against Gram-positive bacteria including methicillin-resistant Staphylococcus aureus (MRSA), and by a long terminal half-life (245 hours) which allows for single dose treatment. The objective of this analysis is to evaluate the time to onset and duration of adverse events (AEs) in two phase 3 studies (SOLO I and II) in patients with Acute Bacterial Skin and Skin Structure Infections (ABSSSI).

Methods. The SOLO studies were global, multi-center, randomized, double-blind studies with identical design evaluating single dose IV ORI (1200 mg) vs IV vancomycin(VAN, 1 g or 15 mg/kg, every 12 hours for 7 to 10 days) in adults with ABSSSI. Safety assessments included vital signs, ECG, safety laboratory analysis and occurrence of AEs and serious AEs (SAEs). An extended safety follow up assessment was conducted at Day 60 (+ 7days).

Results. A total of 976 and 983 patients received ORI and VAN, respectively. The overall incidences of AE, SAE and AE leading to study drug discontinuation were similar between ORI (55.3%, 5.8% and 3.7%) and VAN (56.9%, 5.9% and 4.2%) treatments. Median time to onset and durations of AEs in both groups were the same (2 days and 3 days, respectively). The majority of AEs occurred within the first three days of the study (64.8% in ORI, 66.2% in VAN). The incidences of AE onset and AE duration by time intervals as outlined in Figures 1 and 2 were similar between treatment groups.

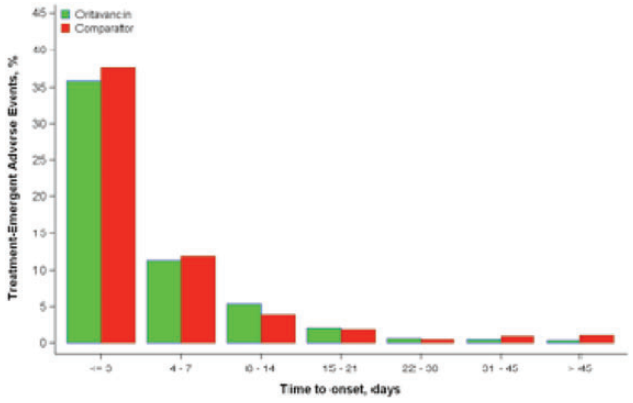

Figure 1. Time to Onset of Adverse Events by Time Interval

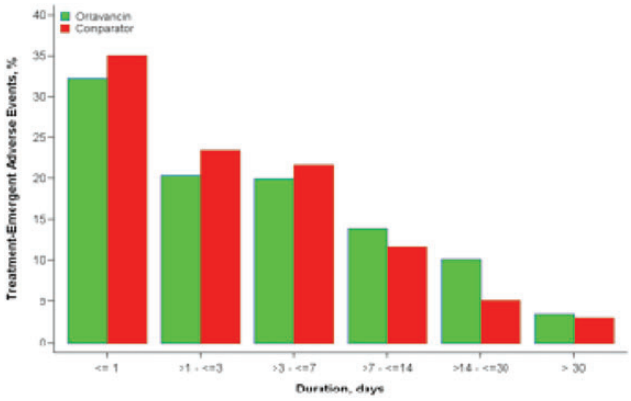

Figure 2. Duration of Adverse Events by Time Interval

Conclusion. The long terminal half-life of ORI does not prolong time to onset or duration of AEs. Single IV dose of 1200 mg ORI was well tolerated in ABSSSI patients.

Disclosures. **R. Corey**, The Medicines Company: Investigator, Grant recipient **W. O'riordan**, The Medicines Company: Investigator, Grant recipient **N. Huang**, The Medicines Company: Consultant, Salary **H. Jiang**, The Medicines Company: Employee, Salary **S. Good**, The Medicines Company: Employee, Salary **P. Giordano**, The Medicines Company: Investigator, Grant recipient **M. Wikler**, The Medicines Company: Employee, Salary

686. A Fishmonger's Tale

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Background. Fish are vectors of several zoonoses that can pose serious health problem in the immunocompromised patients. The clinical manifestation is often cutaneous and occurs at the site of inoculation. However, bacteremia and deep-seated infection have been described. We report a case of *Pseudomonas aeruginosa* causing ecthyma gangrenosum in an immunosuppressed patient after fish handling and review the literature of previously reported cases of fish handling infection.

Methods. We retrospectively reviewed the literature of all cases of infection among fishmongers utilizing the PubMed database from 1990 to present. A comparative analysis was performed to explore the risk factors, bacterial pathogens, treatment, and outcomes.

Results. Thirty-eight cases of infections acquired through fish handling were identified. The median age was 58 years. The most common underlying medical conditions were diabetes mellitus (DM), alcoholism, and rheumatic heart disease (RHD). The most common bacteria involved were *Streptococcus iniae* (11 cases), *Vibrio vulnificus* (7 cases), and *Mycobacterium marinum* (7 cases). Other pathogens reported were *Erysipelothrix rhusiopathiae*, *Aeromonas hydrophila*, *Vibrio damsela*, *Proteus vulgaris*, *Morganella morganii, Lactococcus garvieae, Mycobacterium abscessus, Streptococcus halichoeri*, and in our case *Pseudomonas aeruginosa*. Cellulitis was the most common manifestation but necrotizing fasciitis, tenosynovitis, osteomyelitis, endocarditis, and septic shock have been documented. Beta-lactam agents such as penicillin, or ampicillin-sulbactam were often prescribed for streptococcal infection while anti-mycobacterial agents such as rifampin, ethambutol, and clarithromycin were often used for *M. marinum* infection. Four cases of death were reported, representing a mortality of 11%.

Conclusion. Chronic medical conditions such as DM, alcoholism, and RHD can predispose patients to infection, particularly among fishmongers. These infections pose significant morbidity and mortality in the immunocompromised hosts if not recognized early. Thus, a thorough history, including occupational and recreational exposure, is essential to prompt the clinician to consider these atypical zoonotic pathogens in the differential diagnoses and provide the appropriate management.

Disclosures. **All authors:** No reported disclosures.

687. Localized Hypertrichosis After Infectious Rash ("HAIR") in Adults: A Report of 5 Cases

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Background. Localized excess hair growth or hypertrichosis has been associated with a variety of factors, inluding repeated skin trauma, periphery of burns and insect bites. Review of English language literature in the past 50 years revealed only a single report of localized HAIR, an infant with recent chicken pox. I, herein, report localized HAIR in 5 adults with a recent diagnosis of skin and soft tissue infection (SSTI).

Methods. Localized HAIR was defined as excessive growth of hair in a circumscribed area of skin previously involved with an infection. All patients had been evaluated and treated by an infectious disease consultant (FAM) during the period 2004-2012.

Results. Five cases of localized HAIR were analyzed; all had been recently hospitalized and seen in consultation for evaluation and treatment of an SSTI. Patient age ranged from 39-71 years (mean 49 years). There were 3 (60%) women and 2 (40%) men; 3 (60%) were white and 2 (40%) were African-American. Three (60%) cases involved the upper extremities (2 in the forearm, 1 in the hand), and 2 (40%) cases involved the lower extremities. Septic thrombophlebitis and olecranon bursitis were diagnosed in 1 patient each; no obvious source of infection was found in the remaining patients. The 2 patients with lower extremity SSTI had pre-existing chronic lower extremity edema. Comorbidities also included diabetes in 2 (40%) patients, and traumatic asplenia in 1 (20%) patient. Diagnosis of localized HAIR was made 6-12 weeks following the implicated SSTI. All patients were considered to have fully recovered from their SSTIs with return to baseline health at the time of the diagnosis of localized HAIR, which they frequently considered unsightly. Based on the benign nature of non-infectious-related localized hypertrichosis and its usual resolution with time, all patients were reassured. One patient had complete resolution of localized HAIR when seen 3 years later.

Conclusion. Localized HAIR is one of the potential sequelae of SSTIs. However, aside from its potential esthetic concerns, it appears to have no health consequences, does not require further evaluation and patients should be reassured accordingly.

Disclosures. **All authors:** No reported disclosures.

688. The Effect of Preoperative Vancomycin on Bacteria Isolation from Operative Cultures

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Background. Antibiotics are often initiated early in hospital stay for patients with musculoskeletal infections (MSKI). Surgical cultures may not be obtained for several days. Previous authors have shown that a single dose of perioperative antibiotics is not associated with a larger percentage of negative cultures in cases of prosthetic joint infection. The effect of multiple days of antibiotics on culture has been studied in small samples of patients with vertebral osteomyelitis with varying results. The purpose of this study is to evaluate the effect of preoperative vancomycin on the isolation of bacteria from intraoperative samples.

Methods. This is a prospective observational cohort of adult patients referred to the MSKI consultation service between July 1, 2012 and March 6, 2014 at an urban public safety net hospital. The primary outcome was the isolation of bacteria from operative samples. The number of days of preoperative vancomycin was calculated for each operative sample. Culture results were stratified into 2 groups: those who received no antibiotics and those who received ≥2 days of vancomycin in the 14 days prior to culture. The chi-squared test was used to determine if the number of days of vancomycin was associated with isolation of bacteria.

Results. 308 operative cultures were eligible for inclusion; 254 cultures were obtained with no preoperative antibiotics while 54 cultures were obtained after ≥2 days of vancomycin. The percentage of cultures from which *S. aureus,* coagulase-negative *Staphylococcus*, *Streptococcus* species, and *Enterococcus* species were isolated did not differ between patients who received 0 vs ≥2 days of vancomycin (table).

Preoperative days of vancomycin and isolation of bacteria from operative cultures.

Bacteria	0 days n=254	≥2 days n=55	P
S. aureus	42.5%	49.1%	NS
Coagulase-negative *Staphylococcus*	19.3%	23.4%	NS
Streptococcus sp.	26.0%	38.2%	NS
Enterococcus sp.	8.3%	9.1%	NS
Culture negative	18.3%	14.3%	NS

Conclusion. In conclusion, this study found no reduction in the growth of bacteria after ≥2 days of preoperative vancomycin. A larger sample size is needed to determine if increasing days of preoperative vancomycin affects culture yield.

Disclosures. **All authors:** No reported disclosures.

689. Enhanced Detection of *Staphylococcus aureus* Colonization in Patients Undergoing Total Joint Arthroplasty

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Background. Prosthetic joint infections (PJI) often result in multiple surgeries and long-term antibiotic administration, along with substantially increased healthcare costs. Due to the catastrophic nature of these infections and the increasing number of patients undergoing total joint arthroplasty (TJA), attention has turned to the development of prevention strategies for PJI. Studies have shown that colonization with *S. aureus* is a risk factor for surgical site infection, but few data are available on *S. aureus* colonization in patients undergoing TJA. This study sought to determine which anatomic site(s) are most frequently colonized with *S. aureus* in patients undergoing TJA, and to evaluate the utility of a preoperative questionnaire to predict *S. aureus* colonization.

Methods. A cross-sectional study was performed on patients undergoing TJA at an academic medical center. A questionnaire assessing medical history and potential risk factors for *S. aureus* colonization was administered at a routine preoperative visit. Patients were cultured for *S. aureus* in the nares, oropharynx (OP), axilla, groin and the proposed surgical site.

Results. Sixty six of the 232 patients in the study (28%) were found to be colonized with *S. aureus*, including 19 patients (8%) colonized with MRSA. The nares, OP and groin were the most common sites of colonization; detecting 80%, 36% and 15% of the colonized patients respectively. None of the variables assessed in the questionnaire were found to be significantly associated with *S. aureus* colonization, although having a household member with a history of *S. aureus* approached significance ($p = 0.08$).

Conclusion. *S. aureus* colonization is common in patients undergoing TJA, and the MRSA colonization rate of 8% is relatively high compared with other study populations. Sampled together, the nares and OP had a sensitivity of 92%, which increased to 97% when the groin site culture was added, indicating these as optimal screening sites. Awareness of *S. aureus* colonization status may assist with infection prevention strategies, including the use of decolonization protocols and adjustment of perioperative antimicrobial regimens. An infection risk assessment questionnaire was not helpful in predicting *S. aureus* colonization.

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690. 16s rRNA Gene PCR: An Unreliable Tool for the Diagnosis of Prosthetic Joint Infections (PJI)

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Background. Negative routine cultures often occur with prosthetic joint infections (PJI) despite overt signs of infection. 16s rRNA gene polymerase chain reaction (PCR) has been proposed as a diagnostic tool to help identify causative organisms among those with culture negative PJI.

Methods. Joint fluid, tissue or bone was collected from patients with PJI who were admitted to Barnes-Jewish Hospital between September 15, 2012 and April 15, 2013. PJI was defined per IDSA guidelines. Patients were considered to be culture negative or positive based on the results of routine microbiological cultures after 48 hours of incubation. DNA was extracted from samples using the MoBio Bacteremia Kit. Full length amplification of the 16S rRNA gene was performed, and PCR products were visualized using agarose gel electrophoresis. If a PCR product was present, it was sequenced and compared to GenBank and RDP to assign an organism identification per CLSI standards. Control samples were performed with each run.

Results. We collected 54 samples from 42 unique patients with culture-negative PJI including 28 (51.9%) hip, 18 (33.3%) knee, 7 (13.0%) shoulder, and 1 (1.9%) ankle samples. Sample types included tissue (31, 57.4%), fluid (13, 24.1%), and bone (10, 18.5%). *Staphylococcus aureus*-specific PCR was negative in all patients with culture negative PJI. 16s rRNA gene PCR was also negative in all patients with culture negative PJI. Samples were collected from 35 patients with culture positive PJI including 18 (51.4%) hip and 17 (48.6%) knee samples. Sample types included 25 (71.4%) tissue, 8 (22.9%) fluid, and 2 (5.7%) bone. *S. aureus* was isolated in 21 routine cultures. *S.* aureus-specific PCR correctly identified 12 (57.1%) of samples with *S. aureus* and incorrectly identified 1 sample. 16s rRNA gene PCR correctly identified 3 samples with *S. aureus* and 2 samples with *Streptococcus spp*. Two polymicrobial cultures were identified as mixed; 4 monomicrobial cultures were identified as mixed. Among those with positive cultures for *S. aureus,* PCR was more likely to be positive from tissue samples than all other tissue types ($p = .03$). **Conclusion:** 16s rRNA gene PCR proved to be unreliable diagnostic tool among patients with culture positive or negative PJI.

Conclusion: 16s rRNA gene PCR proved to be an unreliable diagnostic tool for patients with culture positive and negative PJI.

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691. Rifampin in the Treatment of Staphylococcal Prosthetic Joint Infections

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Background. Rifampin is widely utilized in treatment of prosthetic joint infections (PJI) with retained hardware caused by Staphylococcal species. However, there is little data regarding clinical outcomes.

Methods. We conducted a retrospective cohort study of patients with coagulase-negative Staphylococcus (CoNS), methicillin-sensitive (MSSA) and -resistant *Staphylococcus aureus* (MRSA) PJI who were treated with adjunctive rifampin therapy after admission to a large tertiary care hospital from July 2005 to June 2010. The epidemiology, clinical outcomes, and risk factors for failure were examined. Treatment success was defined as no further readmissions for PJI within 1 year of the index hospitalization.

Results. A total of 237 patients with MRSA (56), MSSA (69), or CoNS (112) PJI were identified during the study period. Sixty-eight patients (29%) were discharged with rifampin combination therapy. Amongst patients treated with rifampin, MSSA was isolated in 30% and MRSA isolated in 25%. Partial exchange and debridement and implant retention (DAIR) was completed in 63% of all patients. Vancomycin was the most commonly prescribed IV antibiotic (48, 71%), followed by oxacillin (9, 13%). Concurrent therapy with daptomycin (2, 2.9%) or ceftriaxone (4, 5.9%) was rarely used. Antibiotic duration averaged 51 days (range 30-106, ± 14.6). Abnormal laboratories were common (53, 78%); however, only 18 (26.5%) required a change in antibiotic therapy. The most common side effect necessitating change was rash (9, 13.2%). Significant drug-drug interactions (1) and liver toxicity (2) were rare. Three patients (4%) were lost to follow up. Complications of antibiotic use caused 9% of all readmissions and 25% of the cohort was readmitted for infection (16, 25%). Rifampin use was not associated with decreased readmission for infection (MSSA, $p = 0.4$; MRSA $p = 0.5$; CoNS, $p = 0.7$).

Conclusion. Rifampin has been utilized as adjunctive treatment of staphylococcal PJI in cases of retained hardware. Although well tolerated in the study population, rifampin did not reduce the risk for PJI-related readmission compared to those who did not receive rifampin.

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692. Prognostic Value of Inflammatory Markers during Treatment of Prosthetic Joint Infections

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Background. The role of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) in predicting outcome of prosthetic joint infections (PJI), treated with a 2-stage exchange, has been inconclusive. We evaluated the utility of ESR and CRP and their improvement during treatment in predicting cure at the time of the second stage surgery in adults with PJI treated with a 2-stage approach.

Methods. We conducted a case-control study of adult patients seen at the University of Kansas Medical Center with PJI between January 1, 2003 and June 30, 2013, treated with a 2-stage exchange. Cases had documented treatment failure defined as (1) one positive culture growing the same original organism; (2) two positive cultures growing a different organism; (3) one positive culture growing a new organism with histopathology showing acute inflammation (>5 WBC/high power field) or (4) gross purulence at re-implantation. Controls were patients who did not meet criteria for treatment failure. Serial ESR and CRP were recorded.

Results. A total of 71 patients were enrolled. The mean age was 60 years; 52% were male. Among our patients, 22.5% were smokers, 28% had diabetes mellitus, 10% were immunosuppressed, and 32% had other co-morbidities (peripheral vascular disease, rheumatoid arthritis, liver disease). The mean time between implant and infection was 1922 days. The indication for implantation was osteoarthritis in 64% and post-traumatic causes in 21%. The most common organism isolated was *Staphylococcus aureus* (34%), followed by coagulase-negative Staphylococcus (30%). Five out of 71 patients (7%) failed treatment. There was a trend towards higher CRP value among patients who failed treatment (mean CRP 11.35 vs 4.23 mg/dL, p-value 0.056). There was no difference in mean ESR, change in ESR or change in CRP between the 2 groups. No other predictors of treatment failure were identified.

Conclusion. CRP values prior to prosthetic joint reimplantation might predict treatment failure in patients with PJI.

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693. Comparison of the 2011 Musculoskeletal Infection Society (MSIS), the 2013 International Consensus Meeting (ICM) and the Infectious Diseases Society of America (IDSA) Diagnostic Criteria for Prosthetic Joint Infection (PJI)

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Background. Previously, we compared the 2011 MSIS and IDSA diagnostic criteria, finding a very high degree of agreement for case classification. In 2013, the ICM diagnostic criteria were released as a modification to the MSIS criteria, with the major change being removal of periprosthetic purulence as a minor criterion. Herein, we are presenting a comparison of the three diagnostic criteria.

Methods. The medical records of patients evaluated at Mayo Clinic Rochester for knee or hip prosthetic failure from 1997-2012 were reviewed and patients were classified as having PJI and aseptic failure (AF) by the MSIS, ICM and IDSA diagnostic criteria.

Results. A total of 423 subjects were studied, 29 (6.9%) with hip and 394 (93.1%) with knee prostheses. Among these, 79 (18.7%), 81 (19.1%) and 81 (19.1%) were classified as PJI by MSIS, IDSA and ICM criteria, respectively. There was disagreement between MSIS and IDSA criteria in 4 cases (1 AF and 3 PJI cases by IDSA criteria, $p = 0.3$).

There was disagreement between ICM and MSIS criteria in 6 cases ($p = 0.4$), with 2 classified as PJI by MSIS and AF by ICM criteria. Both were classified as PJI by IDSA criteria and clinically managed as infections. The other 4 were classified as AF by MSIS and PJI by ICM criteria. Three of these were classified as AF and 1 as PJI by IDSA criteria, and all 4 were managed as non-infected cases; none had evidence of infection on follow up.

There was disagreement between ICM and IDSA criteria in 8 cases ($p = 1$), with 4 classified as PJI by IDSA but AF by ICM criteria. Two were classified as PJI by MSIS (and managed as infections) and 2 as AF by MSIS (one managed as an infection and the other as non-infected with no evidence of infection on follow up). Among the 4 cases classified as AF cases by IDSA criteria and PJI by ICM criteria, 3 were classified as AF by MSIS criteria (2 managed as non-infected cases, with no infection on follow up, and 1 managed as an infection), and 1 was classified PJI by MSIS criteria (and managed as infection).

Conclusion. Although no statistically significant difference was found across the three classification systems, overall there was less discordance between the IDSA and MSIS classification systems than between the ICM and the other two classification systems. The finding of periprosthetic purulence appears to be an important criterion for PJI diagnosis.

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694. Bone and joint infection due to bacteria producing Extended Broad Spectrum Beta lactamase

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Background. Bone and joint infection due to bacteria producing Extended Broad Spectrum Beta lactamase (ESBL) are rare but rising nowadays. Data on this disease are scarce and outcome is not well known. We present a cohort of 43 cases.

Methods. Multicentric retrospective cohort of consecutive cases of bone and joint infection due to ESBL producing microorganism identified from the charts of the microbiology laboratory. Case definition needs at least one per operative sample positive to ESBL producing microorganism and a medical and surgical management for a bone and joint infection. We collected from the medical charts: epidemiologic characteristics, disease history, management and outcome.

Results. Fourty three bone and joint infections due to ESBL producing microorganisms were identified, 34 were men, mean age was 56 years old, 10 were immunosuppressed. Ten patients recently travelled in foreign countries. The infection was hematogenous in only 1 case. Type of infection were: articular device (n = 28), osteitis (n = 7), arthritis (n = 7). In 23 cases it was not the first surgery on the site. Eleven infections were considered as acute. Most frequent involved bacteria were *Enterobacter spp.* (n = 14), *Escherichia coli* (n = 13), *Klebsiella spp.* (n = 13), *Proteus spp.* (n = 4). Infections were polymicrobial in 27 cases, one was associated with bacteriemia. Carbapenem was the antibiotic prescription in39 cases. Switch or extraction of the device was performed in 16 cases. Outcome was defavourable in 20 cases: septic failure with new indication for surgery and two deaths.

Conclusion. Bone and joint infections due to ESBL producing microorganisms occur in patients with important co morbidities and a history of surgery; their outcome is frequently severe.

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695. Bone and Joint Infections in Children in the Era of Community-Acquired Meticillin- Resistant *S. aureus*

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Background. Osteoarticular infections (OAI) are common in children, and community-acquired meticillin resistant *S. aureus* (CA-MRSA) is the leading cause in some countries. The aim of this study was to evaluate epidemiological data, clinical and microbiological features and outcome of OAI with serial C-reactive protein (CRP) monitoring.

Materials and Methods. A prospective study was conducted between December 2011 and December 2013. Forty patients were included. The course of illness was monitored using the erythrocyte sedimentation rate (ESR) and serum CRP. Main outcome measure was full recovery and no recurrence nor sequelae for at least 3 months after hospital discharge.

Results. 40 patients (p) completed the study: 20p (50%) had arthritis, 17 (43%) osteomyelitis, and 3 (7%) osteoarthrithis. Median (Md) age was 90 months (range: 3-186). The most common site of infection was the hip (12 p -30%), followed by the knee (9 p -22%). Md CRP value upon admission was 50 mg/l (range: 26.3-86.5) which normalized within Md of 7 days (range: 1-60). Md ESR level was 75 (range: 50-102) and normalized within Md of 28 days (range: 14-30). Bacterial cultures were positive in 30 p (75%): CA-MRSA was found in 19p, Meticillin-sensitive *S aureus* in 6 p, and others in 5 p. Cultures were negative in 10 p (25%). Md duration of intravenous treatment was 7 days (range: 5-10). Md treatment duration was 28 days (range: 21-40); Md hospital stay was 7 days (range: 3 to 10). The patients were followed for a Md of 12 months, during which 1 p relapsed and 4 had sequelae. Analyzing patients with CA-MRSA separately, initial CRP was higher (Md 76 vs 50, $p< 0.02$), normalization occurred later (Md 14 days vs 7 days, $p< 0.03$), and duration of treatment (Md 32 vs 23, $p < 0.004$) as well as hospital stay (Md 9 vs 7, $p= 0.12$) were longer. Surgical drainage was necessary in all patients. Sequelae were present in 3 patients and 1 relapsed.

Conclusion. CA-MRSA was the leading cause of osteoarticular infections and was associated with higher CRP on admission, later normalization, and longer treatment duration. Complications, drainage requirement, and sequelae were most common in those patients.

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696. Relative Contribution of Blood and Bone Cultures in the Microbiologic Diagnosis of *Staphylococcus aureus* Osteomyelitis in Children

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Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) USA300 is a predominant cause of community-acquired (CA) invasive infections in the United States. Optimal treatment of *S. aureus* osteomyelitis requires its isolation from blood or bone cultures for determination of antimicrobial susceptibility. We determined the contribution of blood and bone cultures in the microbiologic diagnosis of osteomyelitis in the era of CA-MRSA infections.

Methods. Isolates and patients were identified from a prospective *S. aureus* surveillance study. The database was searched from April 2012–March 2014 for patients with the diagnosis of osteomyelitis. Medical records were reviewed and data entered on standardized forms. Statistical analyses were performed with STATA 12.

Results. MSSA and MRSA infection occurred in 70 (59.3%) and 48 (40.7%) children ($n = 118$), respectively. MRSA osteomyelitis was associated with intraosseous/subperiosteal abscess ($p = 0.009$) and/or pyomyositis/myositis ($p = 0.02$). Blood cultures (BC) were performed in 111 of 118 (94%) patients and were positive in 61% (68/111). In 33.8% (23/68) of cases, a BC was the only source that that yielded *S. aureus*. Bacteremia did not differ between MRSA (62%) vs MSSA (60.6%) osteomyelitis. Surgery was performed in 75.4% (89/118) of patients. Intra-operative cultures were positive in 93.3% (83/89) of cases and in 50.6% (42/83) it was the only positive culture. A bone biopsy was performed by interventional radiology (IR) in 12% of patients (14/118). The IR culture was positive in 78.6% (11/14) of cases and in 36.3% (4/11) it was the only positive culture. In 43 of 50 patients (86%) with a negative BC, bone culture (surgical or IR) led to a change in antibiotic management.

Conclusion. Since 2012 most cases of *S. aureus* osteomyelitis were caused by MSSA, continuing with a shift in epidemiology at our institution which started in 2007. The majority of patients were bacteremic, however, a bone culture (surgical or IR) played a significant role in the diagnosis and treatment of patients with negative BC. IR bone cultures may be positive for *S.aureus* when BCs are negative, allowing for appropriate antibiotic treatment of osteomyelitis in the era of CA-MRSA infections.

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697. Treatment and Outcome of Culture-negative Osteomyelitis in Children

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Background. Treatment of acute hematogenous osteomyelitis (AHO) is controversial with regard to length of therapy and intravenous to oral therapy switch. Previous studies have reported changing from intravenous to oral therapy after only 3 days in patients with an identified pathogen. However, there is little data on the treatment and outcomes for culture-negative AHO especially in an era of methicillin-resistant *Staphylococcus aureus* (MRSA).

Methods. Cases of AHO admitted to our pediatric hospital from 2008-2013 were retrospectively reviewed. Clinical and laboratory data collected included age, gender, symptoms prior to admission, culture results, complete blood counts, erythrocyte sedimentation rates (ESR) and C-reactive proteins (CRP). Medical and surgical treatment regimens, as well as outcomes, were also recorded.

Results. There were 93 children admitted with AHO including 49 with methicillin-susceptible *S. aureus* (MSSA), 16 with MRSA, and 16 with negative blood and/or bone cultures diagnosed by imaging and a compatible clinical and laboratory picture. There were no significant differences between culture-negative and culture-positive children with regard to age (7.6 vs 8.2 years), preceding trauma (25% vs 24%), presenting symptoms of fever (75% vs 79%), pain (100% vs 96%), swelling (44% vs 57%) and erythema (38% vs 40%), and maximum CRP (12.3 vs 16.2 mg/dL) and ESR (73.4 vs 76.9 mm/hr). Of 77 children with culture-positive AHO, 19 had concomitant septic arthritis while none of the 16 culture-negative children did ($p = 0.036$). Eleven children (68.8%) with negative cultures were transitioned to oral antibiotic therapy in ≤ 7 days compared to 35 (45.5%) with positive cultures ($p = 0.90$). Nine of 11 were sent home on cephalexin to complete therapy; the other 2 received linezolid and clindamycin. Thirteen of these 16 were not treated for MRSA. Mean length of treatment was 40.7 days for culture-negative children vs 37.2 days for those with positive cultures ($p = 0.26$). Of 14 patients seen in follow-up, all but one had complete resolution of their symptoms.

Conclusion. Culture-negative AHO has a similar clinical presentation to culture-positive disease. In areas where MRSA is infrequent, early switch to an MSSA oral regimen appears safe and effective with close follow up and avoids the added expense and toxicity of MRSA coverage.

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698. Optimal Duration of Antibiotic Therapy in Patients with Hematogenous Vertebral Osteomyelitis Who Undergo and Do Not Undergo Surgical Debridement

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Background. Surgery is frequently performed in patients with hematogenous vertebral osteomyelitis (HVO) for resolution of significant spinal cord compression, prevention or correction of spinal instability, management of severe pain, and drainage of abscesses. The aim of the study is to evaluate the optimal duration of antibiotic therapy in patients with HVO who undergo and do not undergo surgical debridement.

Methods. We conducted a retrospective chart review of adult patients (≥16 years of age) with HVO from five tertiary care hospitals over a 7-year period. HVO was defined as both radiographic evidence of vertebral osteomyelitis and microbiologic demonstration of bacterial pathogens either from the site of infection itself (e.g., abscess, intervertebral disc, or vertebral bone) or the blood.

Results. Of the 333 patients with microbiologically diagnosed HVO, 143 (41.9%) underwent surgery and 190 (58.1%) did not undergo surgery. Compared with no surgery group, surgery group was more likely to have neurologic deficit (22.4% [32/143] vs 11.6% [22/190]; $P = 0.008$) and epidural involvement (66.9% [95/142] vs 42.9% [79/188]; $P < 0.001$). Of the 333 study patients, 28 died before completing antimicrobial therapy for their infection (8 [5.6%] in the surgery group and 20 [10.5%] in no surgery group; $P = 0.11$). Of remaining 305 patients, 27 (8.9%) experienced recurrence within 12-month post-treatment follow-up. Among no surgery group, recurrence was more common in patients treated with <8 weeks of antibiotic therapy than in those treated with >8 weeks of therapy (23.7% [14/59] vs 6.3% [7/111]; $P = 0.001$). However, this association was not evident among surgery group (9.1% [4/44] vs 2.2% [2/91]; $P = 0.09$). Multivariate analysis indicated that end stage renal disease (OR, 6.28; 95% CI, 1.46–26.91), <8 weeks of antibiotic treatment (OR, 4.85; 95% CI, 2.01–11.70), no surgical debridement (OR, 2.72; 95% CI, 1.02–7.29), and MRSA (OR, 2.38; 95% CI, 1.01–5.65) were independently associated with recurrence.

Conclusion. Prolonged antibiotic therapy of >8 weeks was beneficial in patients who did not undergo surgical debridement, but this association was not evident in patients who underwent surgical debridement.

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699. Long Term Outcome of Pyogenic Vertebral Osteomyelitis: A Cohort Study of 260 Patients

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Background. The long term outcome of patients with pyogenic vertebral osteomyelitis (PVO) has not been assessed.

Methods. We conducted a retrospective cohort study to describe the long term outcome of PVO and to assess risk factors for treatment failure in patients evaluated at our institution between 1994 and 2002. Patients were followed until July 1, 2013.

Results. Two hundred and sixty patients with PVO were included in this study. Twenty seven percent (70) of patients developed their infection following an invasive spinal procedure. Staphylococcus aureus accounted for 40% (103) of infections. Forty nine percent (128) of patients underwent spinal surgery as part of their initial therapy. The median duration of parenteral antimicrobial therapy was 42 days (IQR: 38-53). The estimated 2, 5 and 10 year cumulative probability of treatment failure free survival was 72%, 69% and 69%. Seventy five percent of patients that developed treatment failure did so within 4.7 months of diagnosis. Residual neurological defects and persistent back pain were seen in 16% and 32% of patients respectively. In a multivariate analysis, longer duration of symptoms prior to diagnosis and having an infection with S. aureus were associated with increased risk of treatment failure.

Conclusion. Increasing duration of symptoms and infection with *S. aureus* were associated with treatment failure in patients with PVO. Most treatment failures occurred early after initiation of treatment. PVO is associated with a high 2 year failure rate. Persistent neurological deficits and back pain are common after therapy.

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700. A cohort of pneumococcal bone and joint infections in adult patients

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Background. Pneumococcal bone and joint infection is a rare disease. No recent series are available since the vaccination coverage is encouraged. We present clinical and biological characteristics and outcome of a cohort of 62 cases of pneumococcal bone and joint infection.

Methods. We report a retrospective, multicenter study in France and Switzerland in 7 reference centers for complex osteoarticular infections. Case was defined by suggestive clinical and radiological signs and microbiological identification requiring at least one isolate of *Streptococcus pneumonia* in deep sample (bone and joint and/or blood culture). Informations were collected with a standard data questionnaire.

Results. We present 62 cases, mean age: 65.1 years old (29-93) and sex ratio of 0.5.

Twenty-seven patients (43.5%) presented risk factors: immunosuppressive therapy (n = 12), diabetes mellitus (n = 11), alcoholism (n = 10), asplenia (n = 5). One vaccinated patient had an infection with 6A serotype not included in the vaccine. Localizations were peripheral joints (n = 51), vertebral osteomyelitis (n = 13) and both for 4 cases. Orthopaedic prosthesis was involved in 25 (40.3%) patients. Another concomitant localization was diagnosed in 23 patients: pneumonia (n = 16), meningitis (n = 3), sinusitis (n = 2), otitis (n = 2), endocarditis (n = 1). Fourty seven patients had acute symptoms (<1 month). Upon diagnosis 45 patients (72.6%) were febrile, mean CRP level was 233.7 mg/L (6.4-609). Blood cultures were positive in 38 cases. Antibiotic treatment included Amoxicilline for 32 patients, rifampicin for 21 patients and anti pneumococcal fluoroquinolone for 13. All prosthetic joint infections required surgery. Four (6.0%) treatment failures were diagnosed: 2 early deaths due to acute sepsis, 1 recurrence probably due to poor compliance and 1 chronic infection with a prosthetic joint infection. The outcome is excellent when sepsis is controlled, but its prevention could be easily improved in most of cases by vaccination.

Conclusion. Pneumococcal bone and joint infections is a rare but severe infection in adults. Clinical spectrum is wide and often acute with a previous or concomitant deep airways infection.

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701. Acute Bacterial Arthritis: How Long Should You Wait for Culture Results?

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Background. Synovial fluid cultures are important in the diagnosis and appropriate treatment of acute bacterial arthritis. However, there is limited data on time to positivity, and hence, the optimal incubation period for joint aspirates is unknown.

Methods. We reviewed the charts of 94 adults who had monoarthritis less than two weeks prior to admission. Patients with disseminated gonococcal disease and the results of repeat synovial fluid cultures from the same admission were excluded. Subjects with at least one of the following were considered high-risk: $\geq$ 80 years old, rheumatoid arthritis, diabetes mellitus, malignancy, chemotherapy or immunosuppressant therapy, joint prosthesis in the affected joint, peripheral leukopenia, human immunodeficiency virus infection, and a history of crystal-induced arthropathy. The positivity rate and time to positivity of synovial fluid in combined agar plate and broth culture were calculated.

Results. The overall positivity rate was 22.3% (21 of 94). None of the 21 low-risk patients had a positive culture result. Twenty one of 73 (28.7%) high-risk subjects showed growth, with a mean time to positivity of 36.7 ± 27.1 hours. While half of these turned positive within a day of incubation, growth was detected up to 90 hours. The positivity rates did not differ significantly (P = 0.23) between those who received antibiotics prior to arthrocentesis (8 of 26, 30.8%) and those who did not (13 of 68, 19.1%). There was also no significant difference (P = 0.90) in the rates between those who had crystals detected in the synovial fluid (6 of 26, 23.1%) and those who had none (14 of 64, 21.9%). Diabetic subjects were more likely (P = 0.0001) to have a positive culture result than nondiabetic subjects (RR = 7.4). Four of seven patients with an HIV infection grew bacteria from their synovial fluid, three of which were MRSA.

Conclusion. In patients with acute monoarthritis, waiting for culture results until the fourth day of incubation, and maybe even later, is reasonable. This is especially true for high-risk patients. The presence of crystals in itself, even in the absence of bacterial growth after 24 hours, should not trigger the discontinuation of antibiotic treatment.

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702. A Bone of Contention for Culture Selection

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Background. Osteomyelitis (OM) is a serious infection with high morbidity that poses a significant clinical challenge. Diagnostic tests have varying sensitivity and specificity, and treatment is often prolonged with combination therapy. Many factors play a role in the choice of antibiotic therapy, and how much bone culture results contribute to management is an unsettled issue.

Methods. A retrospective review of bone biopsy microbiology results from June 2013 to January 2014 was done at an 802-bed academic medical center. Only patients that had a bone culture performed for a clinical suspicion of OM based on radiographic studies were included in this study. Demographic information, comorbidities, co-existing microbiology results, and antibiotic selection were collected for each patient from their electronic medical record.

Results. 90 patients had bone biopsies performed for a clinical suspicion of OM. Patients had a mean age of 60.6 years ranging from 22 – 91 years and were predominantly male (63.3%, n = 57). 65.5% (n = 59) had positive bone biopsy culture results. Superficial wound cultures were performed on 48% (n = 43) patients; 79% (n = 34) of which were positive. A third of the patients (33%, n = 30) had both positive bone biopsy and wound cultures, 16 (53%) of which grew identical organisms while 14 (47%) showed mixed flora, but had at least one organism identical to the bone biopsy culture. Antibiotic therapies were adjusted in 60% (n = 54) of patients based on bone biopsy results.

Conclusion. The majority of our patients' antibiotic coverage was altered following bone biopsy culture results. Bone biopsy proved to be critical in the therapeutic management of osteomyelitis. Further study is needed to complete comparative analysis for outcomes in patients whose treatment was affected by the bone biopsy vs patients in which it was not.

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703. Osteoarticular Tuberculosis in an Inner City University Medical Center: Epidemiology and Outcomes

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Background. Osteoarticular tuberculosis (TB) is an uncommon form of extra-pulmonary TB and the diagnosis challenging. The goal of our study was to obtain a better

understanding of the epidemiology and outcome of this infection in our inner-city patient population.

Methods. We retrospectively reviewed the records of patients treated for osteoarticular TB at University Hospital in Newark, NJ from 2000-2012. Microbiology laboratory records were used to identify patients with positive bone/joint cultures for *Mycobacterium tuberculosis* (MTB). Specimen source, organisms isolated, MTB PCR results, and susceptibilities were recorded. The following data was extracted from the electronic medical record of case patients: demographics, comorbid conditions, history of active or latent TB, site of infection, symptoms and duration, surgical procedures, imaging studies, ESR, CRP, histopathology, anti-TB regimen, duration of therapy and outcomes.

Results. There were 24 patients with musculoskeletal specimens positive for MTB representing 4.2% of all positive MTB specimens. 20 infections were extra-spinal (83%) with foot/ankle most frequent (21%); 8 were spinal. Osteomyelitis was present in 17; 9 had joint involvement; 10 abscess formation. Pain (92%), swelling (50%) and weight loss (21%) were the most frequent presenting symptoms; fever occurred in only 8%. Mean duration of symptoms was 5.9 mos; mean age 38 years. 71% of patients were men. The majority of patients were immigrants (75%). Prior history of pulmonary TB was present in 5 patients; 7 were diagnosed with pulmonary TB concomitantly; 8 had bacterial infection. Comorbid conditions included HIV, IVDU, and HCV. Mean ESR was 55; CRP 55. Mean time to culture diagnosis was 45 days. 19 MTB isolates were fully susceptible; 4 had 1-drug resistance; 2 had 3-drug resistance; 1 had multidrug resistance. All patients initially received 4 anti-TB drugs. 75% of patients required surgery; 2 patients amputation. 9 patients were cured, 6 improved, 2 failed, 1 died, 6 were lost to follow up.

Conclusion. Osteoarticular TB in our patient population is uncommon and occurs most frequently in immigrant men. The spine and foot/ankle are the most common sites of infection. Diagnosis is often delayed and outcomes variable. A high index of suspicion is needed to establish a timely diagnosis and provide appropriate therapy.

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704. *Mycobacterium bovis* vertebral osteomyelitis due to intravesical Bacillus Calmette-Guérin (BCG): A rare complication of a common therapy

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Background. Intravesical Bacillus Calmette-Guérin (BCG) is a well known and effective therapy for bladder carcinoma. Complications from BCG are very uncommon. Vertebral osteomyelitis secondary to BCG is exceedingly rare.

Methods. We report a case of vertebral osteomyelitis due to *Mycobacterium bovis* following intravesical BCG therapy. We then present a review of all the reported cases of BCG-induced vertebral osteomyelitis.

Results. The patient is a seventy-nine year old male with history of bladder cancer for which he had transurethral resection done. This was followed by intravesical therapy with BCG. A month after his last BCG treatment, he started developing low back pain. A computerized tomographic (CT) scan of the lower back showed a lytic lesion at the level of the twelfth thoracic (T12) and first lumbar (L1) vertebrae. Patient's back pain progressively worsened and he subsequently developed right sided foot drop. A CT myelogram showed significant destruction of the T12 and L1 vertebral bodies and severe spinal canal stenosis at the T12-L1 level. The patient underwent T8-L4 posterior arthrodesis and T12-L1 corpectomies. Cultures from the spine grew *Mycobacterium bovis*, which as expected, was resistant to pyrazinamide and sensitive to all other first line antimycobacterial agents. Patient did well in the postoperative period and was discharged on triple therapy with isoniazid, rifampin and ethambutol, which he is scheduled to receive for a twelve month course.

A review of the English literature revealed a total of sixteen cases of vertebral osteomyelitis due to *M. bovis* secondary to intravesical BCG therapy. All the patients were male, with an age range from 64 to 94 years, with a mean of 75 years. The time from last BCG treatment to onset of symptoms ranged from two weeks to eleven years, with a mean of 28 months. Most of the patients underwent percutaneous or open drainage, along with antimicrobial therapy. The most frequently used combination was isoniazid, rifampin and ethambutol, for twelve months.

Conclusion. Vertebral osteomyelitis due to *Mycobacterium bovis* is a very rare complication of intravesical BCG therapy. A combination of surgical debridement and prolonged antibiotic therapy offer a favorable prognosis.

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705. Correlation of Radiologic Tests in the Diagnosis of Brucellosis with Osteoarticular Involvement

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Correlation of Radiologic Tests in the Diagnosis of Brucellosis with Osteoarticular Involvement

Background. The most common complication of brucellosis is musculoskeletal system involvement. Bone and joint involvement in brucellosis may present as mainly sacroiliitis and spondylitis. In this study, we aimed to evaluate the correlation of plain X-rays, bone scintigraphy, and contrast-enhanced magnetic resonance imaging in the diagnosis of osteoarticular involvement of brucellosis.

Methods. Patients older than 18 years old, who followed up, diagnosed with brucellosis disease and decided to get treatment in Cukurova University, Faculty of Medicine, Infectious Diseases and Clinical Microbiology clinic and outpatient clinic between May 2009 and November 2010 were included in the patient group.

Results. Average age of 86 patients with brucellosis diagnosis were 40.86 ± 18.4 and there were 38 (44,2%) males and 48 (55,8%) females in this group. Spondylitis and sacroiliitis have been described in the same ratio, 22.1% (n = 19). Sacroiliitis were unilateral in 13 and bilateral in six patients. Sacroiliac involvement was detected in 28.9% of men and 16.6% of women (p = 0,270). Eight patients (42.1%) had both sacroiliitis and spondylitis. Pathological involvement was determined in Tc99m bone scintigraphy in only three of 19 patients (15.8%) with sacroiliitis in plain X-rays. One patient with normal bone scintigraphy had bilateral sacroiliitis in MRI. Two patients with normal bone scintigraphy had bilateral spondylitis in MRI. Seven patients had findings of spondylodisciitis in both bone scintigraphy and MRI.

Conclusion. Our findings suggest that there may be inconsistency between plain X-ray, bone scintigraphy and MRI. Sensitivity of bone scintigraphy is low at brucellar sacroiliitis and false negative results were seen when compared to MRI in spondiliitis cases. As a result, spondylitis can be accidentally underdiagnosed by the bone scintigraphy, which is used for screening osteoarticular involvement.

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706. Minocycline-Induced Cutaneous Hyperpigmentation in an Orthopedic Patient Population

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Background. Patients on chronic minocycline suppression for orthopedic infections at a single institution were studied for development of minocycline-induced cutaneous hyperpigmentation and analysis of risk factors.

Methods. This is a retrospective cohort study of Mayo Clinic patients with hardware or non-hardware associated chronic orthopedic infections treated with long term minocycline suppression between 2002 and 2011. Long term minocycline suppression was defined as daily minocycline use for ≥ 3 months. Electronic medical records were reviewed for details pertaining to the relevant orthopedic infection, minocycline treatment course, development of hyperpigmentation if applicable, and dermatologic and clinical considerations. Cox proportional hazards model was used to evaluate specific dermatologic and clinical factors, including co-morbidities and concurrent medications.

Results. Of 291 patients, 53.6% developed hyperpigmentation, 87.8% of which was type II, which appeared most commonly in the lower extremities (74.5%), upper extremities (43.8%), and face (38.0%). Mean duration of suppression prior to hyperpigmentation was 549.08 days with a mean cumulative dosage of 107.26 g.

Notable risk factors for development of hyperpigmentation included a previous smoking history vs a history of never-smoking (RR 1.4, p = 0.039) or actively smoking (RR 2.5, p = 0.0027) at the time of minocycline initiation. Patients with knee prostheses were also at increased risk compared to those without a knee prosthesis (RR2.1, p < 0.0001). A daily dose of 300 mg was associated with higher risk as compared to dosages of 200 (RR 30.8, p = 0.0281) or 100 mg (RR 120.0, p =0.0079).

Use of calcium channel (RR 1.48, p = 0.037) or beta blockers (RR 1.38, p = 0.0448) was associated with increased risk. Patients with vitamin D deficiency (RR 6.82, p = 0.0039), hematologic malignancies (RR2.67, p = 0.0410), or benign prostatic hypertrophy (RR2.31, p = 0.0046) were also at increased risk.

Conclusion. Minocycline-induced cutaneous hyperpigmentation is common with long term use in orthopedic infection patients. Higher daily doses of minocycline were strongly associated with increased risk of hyperpigmentation.

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707. Rapid Identification of Pathogens Causing Septic Arthritis using FilmArray®

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Background. Septic arthritis (SA) is a common and serious infection in children and can cause significant orthopedic morbidity. Bacteria are most often implicated, but routine cultures are frequently negative, because of prior antibiotics or delayed evaluation of joint fluid (JF). As such, children are treated with broad-spectrum antibiotics. A rapid molecular test that can identify the common bacteria causing joint infection could improve patient care.

Methods. The FilmArray® (FA) Blood Culture ID (BCID) System (BioFire Diagnostics, Inc., Salt Lake City, UT) performs nucleic acid purification and multiplex PCR to identify 22 bacterial pathogens in approx. 1 hour. The BCID system is approved only for use with positive blood cultures. Testing was performed on archived JF samples collected from children <18 years old with clinical signs and symptoms of SA at Primary Children's Hospital (UT) from October 2012 to April 2014. FA identification was compared to conventional culture.

Results. JF from 28 children with SA were evaluated. A bacteria was identified by culture (blood and/or JF) in 14 (50%) children, (JF-11 (39%), Blood-8 (29%)). By FA testing, a bacteria was identified in 14 (50%) JF. Of the 14 culture-identified pathogens, 13 (93%) were contained on the FA BCID panel, of which 11 (85%) were identified by FA testing of JF. 8 children had *S. aureus* identified by culture and 6 were identified by PCR of JF. Those not identified by the FA were identified by blood culture only. In addition, FA identified 3 additional pathogens in culture-negative JF; *Haemophilus influenzae* type a- 2 and *H. influenzae* type b- 1 (Table).

Pathogen	Blood/JF Culture	JF by FA testing
S. aureus	8 (7MSSA/1 MRSA)	6 (5 MSSA/1 MRSA)
Salmonella spp	1	1
H. influenzae	0	3 (type a-2, type b-1)
S. pyogenes	2	2
S. pneumoniae	1	1
E. faecalis	1	1
*S. moliniformis**	1	0
No Pathogen Identified	14	14

*Not included in FA BCIP panel

Conclusion. The FA BCID System is a novel tool for the rapid identification of bacterial pathogens. Our study demonstrates the potential utility of this system for the direct identification of pathogens from JF specimens. Rapid identification of pathogens from JF, including samples that are ultimately culture-negative, has the potential to improve the medical management of patients with septic arthritis.

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708. Risk Factors for Infections after Open Fractures - Opportunities for Improving Prophylactic Antimicrobial Therapy

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Background. Open fractures (OF) are frequently associated with infections. This result in prolonged hospital stays, repeated surgeries and chronic disabilities. The osteomyelitis, related to open fractures with hardware in place, are frequently caused by organisms resistant to the recommended antibiotic prophylaxis.

Methods. A retrospective medical record review of hospitalized-patients, ≥18 years diagnosed with open fracture from December 2011-July 2012 at Palmetto Health Richland, a Level 1 Trauma Center in Columbia, SC. The aim is to compare open fractures by infection status (infected, not infected) and determine factors associated with increasing and mitigating infection, particularly to determine the efficacy of our current antibiotic prophylaxis guidelines.

Results. 80 patients with OF were included. The average age at injury was 38.5 years. The majority were male (75%) and nonwhite (56%). Motor vehicular collision was the most frequent cause of injury (41%). 14 patients developed osteomyelitis. Compared to those who did not develop infection, individuals who developed an infection were more likely to have a tibia/fibula fracture (57% vs 22% p = .03), grade IIIb fracture (19% vs 7% p <.001), visible wound contamination (64% vs 23%, p = .002) and previous hardware (21% vs 5%, p = .03). Compared to those who did not develop infection, those with infection were taken to the operating room sooner (mean 8 hours vs 26 hours, p =.03) and had placement of hardware sooner (mean 8 hours vs 26 hours, p = .02). There was no difference in the duration of prophylactic antibiotics. Compared with other prophylactic antibiotic combinations, individuals who developed an infection were more likely to receive peri-operative gentamicin (64% vs 26%, p =.006) along with cefazolin (100% vs 77%, p =.04). The average time to developing an infection was 54 days. Gram negative (GN) rods were the most common organism isolated. Individuals with infections required an average of 4 additional surgical procedures (range 2-10).

Conclusion. Grade III B open fractures of the lower extremity with visible contamination were more likely to develop osteomyelitis after initial surgery. Findings suggest that more effective GN antimicrobial coverage should be included in the initial peri-operative period for high risk patients.

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709. Clinical Epidemiology of Obligate Anaerobic Infections in Military Trauma Patients from Iraq and Afghanistan

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Background. Combat-related injured patients have historically been noted to have decreasing rates of obligate anaerobic wound infections after the first week following injury, reaching nadir after day 20. This study defines the epidemiology, and outcomes of infection with obligate anaerobes among US military patients injured in Iraq and Afghanistan.

Methods. Utilizing the Trauma Infectious Disease Outcome Study (TIDOS) population between June 2009 and May 2013, all patients with obligate anaerobic bacteria were compiled. Clinical information (demographics, injury data, outcomes) associated with obligate anaerobes was evaluated.

Results. 69 patients with 84 unique isolates were evaluated. 51 (74%) injuries were due to explosive device blasts, 8 (12%) to gunshot wounds (GSW) and 87% of patients were initially hospitalized in Afghanistan, 96% required hospitalization in the ICU. The median time from injury to positive culture was13 days (IQR 7,27).The majority of the isolates (74%) were from wounds and primarily *Bacteroides* spp. (table). 18 (26%) patients had multiple different species of obligate anaerobes recovered. 8 infected patients had the same organism isolated on repeat culture (>7 days apart) despite active antimicrobial being provided. Five (7.2%) patients died during initial hospitalization, but there was no attributable mortality related to infections with obligate anaerobes.

	Total	Intra-abdominal	Upper Ext	Pelvic	Lower Ext	Other*
# of isolates (# of patients)	84 (61)	12 (7)	6 (5)	16 (13)	37 (31)	13 (11)
ISS** median (min-max)	21 (4-66)	24 (12-50)	22 (17-33)	27 (12-38)	18 (4-66)	21 (4-43)
Days injury to culture	13 (1-401)	12 (3-47)	8 (5-50)	11 (5-95)	15 (3-401)	7 (1-238)
B. fragilis	15 (16)	1 (1)	0	4 (4)	9 (9)	1
B. non-fragilis	16 (16)	4 (4)	0	7 (7)	5 (5)	0
F. magna	9 (14)	0	0	2 (2)	7 (7)	2 (2)
Clostridium spp.	16 (14)	1 (1)	6 (5)	1 (1)	6 (5)	2 (1)
P. acnes	9 (9)	0	0	0	4 (4)	5 (5)
Other	19 (15)	6 (4)	0	2 (2)	6 (6)	4 (3)

*Blood, Respiratory, Head wound, CSF
**ISS-Injury Severity Score

Conclusion. Obligate anaerobes can be isolated from war wounds more than 2 weeks after injury, which is later than previously noted. The majority of war wounds with anaerobic infection were caused by *Bacteroides* spp.

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710. Retrospective Observational Study of Etiology of Bloodstream Infections Requiring Hospitalization in Adult Sickle Cell Disease

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Session: 101. Bacteremia: Epidemiology of Bloodstream Infections
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Background. Bacterial infections in sickle cell disease (SCD) children are predominantly due to encapsulated organism. There is paucity of information on the frequency of bloodstream infections (BSI) with these organisms in adults with SCD. We hypothesized that majority of BSI in adult SCD is associated with long term central venous access and Staphylococcal species is the major pathogen.

Methods. Blood cultures with isolation of any organism from January 1, 2007 to December 31, 2011 were cross matched with individuals 18 years and older, followed at Louisiana Health Sciences Center, Shreveport Sickle cell clinic. Retrospective chart review of hospitalization episode associated with each positive blood culture was tabulated and analyzed.

Results. 149 episodes of care with BSI in 58 unique subjects followed at sickle cell clinic were identified between 2007- 2011. All were Afro-American; 34(58.6%) female and 24(41.3%) male. 41(70%) had SS, 8(13.7%) with Sickle beta-thalassemia and SC disease each and 1(1.7%) had sickle cell trait. 282 blood samples had isolation of one or more organisms (109 mono-microbial) and 197 unique organisms were identified. Coagulase negative Staphylococci (97) was the most common organism followed by *Staphylococcus aureus* (24), Corynebacterium species (15) and Candida (11). Three Non-tubercular Mycobacteria and one Salmonella Group B was isolated and there were no samples with isolation of Pneumococcus or Hemophilus. 104 of 143 (72.7%) episodes of hospitalization associated with positive blood culture occurred in subjects with indwelling long term central venous access leading to access catheter removal in 40 (38.4%), antibiotic salvage attempt in 14(13.5%). 38(36.5%) were deemed contaminants by treating physician and 11 (10.5%) positive culture results were attributed to non-catheter source of infection or unascertainable at time of discharge.

Conclusion. In adults with SCD, hospitalizations associated with positive blood cultures are predominantly due to Staphylococcal species. 51.9% of hospitalization episodes in individuals with long term catheter access and positive blood culture were attributed to catheter as source of infection.

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711. Clinical epidemiology of patients with blood stream infection in a nationwide institution of Rheumatology in Japan

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Background. Patients suffered from autoimmune diseases, who take combined immunosuppressive agents, were faced with multiple immune deficiency and organ impairments due to autoimmune diseases. However clinical epidemiology of blood stream infection is still unknown among them.

Methods. This study design was a retrospective chart review. Tokyo Women's Medical University (TWMU) Institute of Rheumatology (IOR) is one of the largest institute with rheumatoid arthritis (RA) in Japan, and more than 6,000 patients per year admitted to our institute. All episodes of positive blood culture in adult patients who visit or admit to IOR, 18 years of age or older, were evaluated from April 2010 to January 2014. Information on the patient's age, sex, underlying disease (RA or non-RA), immunosuppressive agents used, dose of steroid, persistent bacteremia, clinical outcomes and newly ascertained underlying diseases were collected. One set of positive blood culture yielding Coagulase-Negative Staphylococci, Bacillus sp. were defined as contamination. Persistent bacteremia was defined as at least two positive blood cultures for same organism obtained on different calendar days. Data were compared using Wilcoxon's rank test or Fisher's exact test in appropriate. The p value < 0.05 was considered statistical significant. Statistical analyses were performed JMP ver.11 for Mac OS X.

Results. During study period, 1064 sets of blood culture were performed. 78 (7.3%) sets of blood culture from 47 patients (RA group; n = 19, non-RA group; n = 28) were enrolled. The most frequently yield organism was *E.coli* (38%) in Gram-negative rods (GNR), *S.aureus* (38%) in Gram-positive cocci (GPC). The mean age was 65 (26-85) years old. In uniivariate analysis, no significant differences were found in mortality rate in 30 days, use of immunosuppressive agents, prophylactic oral TMP-SMX. However patients with persistent bacteremia was tend to be higher in non-RA group (15.8% in RA group and 43.5% in non-RA group, $p = 0.09$).

Conclusion. To our knowledge, this is the first English report of clinical epidemiology of blood culture among patients with autoimmune diseases including RA. Our results suggests that Non-RA patients may develop complication (i.e., abscess) due to persistent bacteremia. Further investigation with sufficient number of cases is needed.

Disclosures. **All authors:** No reported disclosures.

712. Gram-negative associated Ventricular Assist Device infections

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Background. Ventricular assist devices (VADs) are increasingly utilized for patients with end-stage heart failure. Infections are among the most common associated complications. Gram -negative (GN) organisms have been increasingly implicated. We sought to classify GN VAD infections, analyze risk factors and correlate outcomes with these infections.

Methods. We retrospectively reviewed our experience in a tertiary center from 2005-2013. Infections were classified as VAD specific (VAD-S), VAD related (VAD-R) and non-VAD (N-VAD) related. Demographics, co-morbidities, cultures and outcomes were analyzed with Fisher's exact test and other methods.

Results. 436 VAD devices were placed during the study period, 77 (18%) GN infections were identified: VAD-S and VAD-R 37(48%), N-VAD 40(52%). Mean age 69.5 years (20-75), 50 (64.9%) males, DM in 34 (44%). In addition to VAD, 44 (57%) had intra- aortic balloon pump (IABP), 55 (71%) permanent pacemaker (PPM). Mediastinal exploration (ME) done in 35 (45%), 21 (60%) had ME once. *Pseudomonas aeruginosa* (PA) in 34 (44%), *Klebsiella pneumoniae* (KP) 32(41%) and *Escherichia coli* (EC) 19 (25%). Orthotopic heart transplant (OHT) done in 22 (28%). Overall 37 (48%) pts expired.

In VAD-S and VAD-R, 13 (35%) had driveline infections (DRI) of which 15 (40%) were PA, 10 (27%) had bacteremia (BC) of which 7 (29%) had PA and 14 (38%) had DRI and BC of which 4 (11%) had PA. ME done in 19 (51%). OHT done in 10 (27%). Eighteen (49%) expired. Age was not significantly associated with risk of infection. IABP pts had lower BC rates (p= <0.01) and >1 ME was associated with higher wound infections ($p = 0.018$). Pts without BC received more OHT ($p = 0.007$).

In N-VAD, 36 (90%) had pneumonia, 38(95%) UTI and 5 (12%) *C.difficile* colitis. Pneumonia was caused by KP and PA in 7 (13%), UTI was caused by EC in 10 (26%). OHT done in 12(30%). Nineteen (47%) expired. Respiratory infections were more prevalent in younger (<50 years) (p= 0.04), non DM ($p = 0.03$) and those with ME (p= 0.069). DM and females had more UTI (p =< 0.01and $p = 0.004$).The rate of discharge from the hospital was higher in OHT ($p = <0.01$).

Conclusion. GN VAD infection is associated with a significant mortality including in pts with N-VAD. ME increased risk of infection. OHT pts had a higher rate of discharge from hospital.

Disclosures. **All authors:** No reported disclosures.

713. Short vs Long Courses of Antibiotic Treatment in Adults with Uncomplicated Gram-negative Bacteremia in a Tertiary Inistituition

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Background. Widespread use of antimicrobials has been associated with emergence of multi-drug resistant gram-negative bacteria and superinfections such as *Clostridium difficile*. Shortening of antimicrobial treatment duration is an approach adopted by most antimicrobial stewardship programs to reduce antimicrobial use. Although emerging evidence has advocated the use of short-course treatment in a variety of infections, the evidence in bloodstream infections remains poor. Therefore, this study aims to describe and compare the clinical outcomes of short-course (SC) and long-course (LC) antibiotic therapy.

Methods. A retrospective exploratory cohort study was conducted between April 2011 to December 2012 in adults (≥21 years-old) with uncomplicated bacteremia caused by *E. coli, Klebsiella spp.* and *Proteus spp*. The exclusion criteria were as follows: 1) immunocompromised patients; 2) presence of gram-negative bacteria found resistant to initial empiric antibiotics; 3) presence of deep-seated bacterial infections; 4) presence of concurrent infections and 5) <48 hours of antibiotic use. The study subjects were categorized into 2 groups based on the duration of antibiotic prescribed: short-course (≤10 days) and long-course (>10 days). The clinical outcomes (i.e., mortality, clinical failure, microbiological failure and bacteremia relapse), presence of *C. difficile* associated diarrhea and emergence of resistant isolates in subsequent infections were evaluated.

Results. A total of 337 patients with 344 independent episodes of gram-negative bacteremia were evaluated; 36 and 308 episodes were from SC and LC group respectively. LC antibiotics appeared not to have conferred clinical advantages whereas SC antibiotics did not compromise the overall treatment if source control was sufficiently achieved. Two cases of mortality and 2 cases of bacteremia relapse were observed in LC group vs 1 mortality case in SC. Emergence of resistant isolates, including Carbapenemase-resistant enterobacteriaceae, and *C. difficile* associated diarrhoea were present in 7 and 3 patients respectively in the LC group but none in the SC group.

Conclusion. SC antibiotics appeared not to have compromised treatment efficacy and may be considered in patients with adequate source control and evident clinical improvement.

Disclosures. **All authors:** No reported disclosures.

714. Gram Negative Bacteremia: Are Shorter Courses of Antimicrobial Therapy Feasible?

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Background. The optimal duration of bloodstream infections due to gram negative bacteremia has been poorly defined. The objective of this study was to determine if short courses of antimicrobial therapy were non-inferior to intermediate and long courses of antimicrobial therapy for gram negative bacteremia.

Methods. A retrospective, single-center, chart-review was performed on patients with a documented gram negative bacteremia from August 2006 to November 2013. Patients meeting eligibility criteria were placed in the short-course, intermediate-course, and long-course treatment groups if their duration of antimicrobial therapy was less than or equal to 7 days, between 8 to 14 days, or greater than 14 days, respectively. Data collected included age, gender, source of bacteremia, infecting organism, duration of therapy, and time to defervesence. The primary outcome was the achievement of a clinical response at the end of therapy. Secondary outcomes included achievement of microbiological cure at the end of therapy, and association of clinical response in each group with the causative organism, source of bacteremia, and time to defervesence.

Results. Of 368 cases of gram-negative bacteremia, 178 cases met eligibility criteria. Median age was 64 years with 67% females. Median SAPS II (Simplified Acute Physiology Score) was 33 points. The most common infecting pathogen was *Escherichia coli* (46%), followed by *Klebsiella pneumoniae* (22%). The most common source of bacteremia was the urinary tract (53%), followed by indwelling catheters (14%). Clinical response rates at the end of therapy were 78.6%, 89.0%, and 80.6% for the short-course, intermediate-course, and long-course treatment groups, respectively (P = 0.202). Microbiological cure rates at the end of therapy were 83.3%, 89.0%, and 91.7% for the short-course, intermediate-course, and long-course treatment groups, respectively (P = 0.690). Logistic regression analysis did not reveal any association of clinical response in each group with infecting organism (P = 0.350), source of bacteremia (P = 0.502), or time to defervesence (P = 0.561).

Conclusion. Short-course therapy for gram-negative bacteremia appears to achieve similar clinical response rates and microbiological cure rates compared with intermediate- and long-course therapy.

Disclosures. **All authors:** No reported disclosures.

715. Impact of Fluoroquinolone Resistance on Community-Onset Gram-Negative Bloodstream Infections

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Background. There has been a disconcerting increase in fluoroquinolone resistance (FQ-R) rates among gram-negative bloodstream isolates. FQ-R isolates are often resistant to other antimicrobial agents, limiting options for intravenous to oral switch. This retrospective cohort study examines the hypothesis that FQ-R is associated with longer hospitalization in patients with gram-negative bloodstream infections (BSI).

Methods. Hospitalized adults with first episodes of community-onset gram-negative BSI from January 1, 2010 to December 31, 2012 at Palmetto Health Richland and Baptist Hospitals in Columbia, South Carolina were identified. Multivariate linear regression was used to examine risk factors for prolonged duration of hospitalization among survivors.

Results. Among 474 unique patients, 384 (81%) and 90 (19%) had BSI due to fluoroquinolone-susceptible (FQ-S) and FQ-R gram-negative bacilli, respectively. Overall, median age was 66 (interquartile range 52-79) years and 189 (40%) were men. Compared to patients with BSI due to FQ-S bloodstream isolates, those with FQ-R isolates were more likely to be men (53% vs 37% P = 0.004), have a Pitt bacteremia score ≥4 (31% vs 21% P = 0.03), and receive inappropriate empirical antimicrobial therapy (26% vs 3% P < 0.001). In univariate analysis, mean duration of hospitalization was longer in patients with FQ-R as compared to FQ-S isolates (11.6 vs 9.3 days, parameter estimate 2.28, 95% confidence intervals [CI] 0.21, 4.35; P = 0.03). However, after adjustments in multivariate model, FQ-R was not independently associated with prolonged hospital stay (table).

Risk factors for prolonged hospitalization in bloodstream infection

Variable	Parameter estimate	95% CI	P-value
Male gender	0.45	-1.13, 2.03	0.58
Non-urinary source	2.42	0.87, 3.98	0.002
Pitt score (per point)	1.52	1.11, 1.93	<0.001
FQ-R	0.50	-1.59, 2.60	0.64
Inappropriate therapy	3.62	0.40, 6.83	0.03

Conclusion. FQ-R appears to be a marker for high acute severity of illness and inappropriate empirical antimicrobial therapy, both of which are associated with prolonged hospital stay following BSI. Rapid identification of FQ-R bloodstream isolates could improve empirical antimicrobial therapy and patient outcomes.

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716. Risk Factors for Resistance to Beta-lactam/Beta-lactamase Inhibitors and Carbapenems in *Bacteroides spp*. Bacteremia

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Background. *Bacteroides* resistant to β-lactam/β-lactamase inhibitors (βL/βLI) and carbapenems are being increasingly recognized but the prevalence and risk factors are unknown. The purpose of this study is to determine the prevalence of *Bacteroides* resistant to βL/βLIs and carbapenems and identify potential risk factors for the development of resistance to these agents.

Methods. We conducted a single center case-control study of patients with *Bacteroides* bacteremia from January 1, 2010 to August 31, 2013 at a 1,000-bed tertiary medical center. Cases were defined as patients with *Bacteroides* bacteremia resistant to carbapenems and/or βL-βLIs. Cases were matched 1:3 to bacteremic patients with susceptible isolates by year of positive blood culture. We determined the prevalence of *Bacteroides* in the blood resistant or intermediate to βL/βLI and/or carbapenems, risk factors for resistance, and patient outcomes. Cases and controls were compared using Chi square and Wilcoxan rank sum tests. Logistic regression was performed to assess independent predicators of resistance.

Results. 159 unique patients with *Bacteroides* bacteremia were identified. 26 (16%) patients had *Bacteroides* isolates resistant or intermediate to βL/βLI and/or carbapenems. Amoxicillin/clavulanate was the most common agent to which isolates were resistant or intermediate (11.5%), followed by ertapenem (7.0%) and piperacillin-tazobactam (6.8%). 101 patients were included in the case-control analysis. Duration of therapy with a βL/βLI prior to infection was an independent predictor of resistance (OR 1.25; 95% CI 1.08-2.31). More patients with resistant *Bacteroides* died prior to discharge (37.5% vs 4.0%; p = <0.001) than patients with susceptible organisms.

Conclusion. We found higher resistance rates among *Bacteroides* than what has been reported previously. Duration of exposure to βL/βLI was the only independent risk factor for resistance, supporting judicious use of these agents. There was higher mortality with resistant *Bacteroides*, which is likely confounded by a sicker cohort with a higher percentage in the intensive care unit and longer hospital stay prior to first positive culture.

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717. Clinical characteristics and outcome of metallo-β-lactamase-producing *Enterobacter cloacae* bacteremia at a tertiary care cancer center in Japan

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Background. Recent reports suggest that metallo-β-lactamase (MBL)-producing *Enterobacter cloacae* increases as a pathogen of healthcare-associated infections in Japan. Bacteremia caused by MBL-producing *E. cloacae* is a major concern due to the resistance to most β-lactams including carbapenems. However, little is known about MBL-producing *E. cloacae* bacteremia in patients with cancer. The aim of this study is to examine the clinical characteristics, outcome, and risk factors of MBL-producing *E. cloacae* bacteremia.

Methods. A retrospective cohort study in patients with *E. cloacae* bacteremia was conducted at an 800-bed tertiary-care cancer center in Japan, from April 2011 through March 2014. Isolates demonstrating intermediate or resistant to third generation cephalosporins or carbapenems were screened and confirmed. We reviewed demographics, comorbidities, and other clinical characteristics. Mortality and risk factors of MBL-producing *E. cloacae* bacteremia were also assessed.

Results. During the study period, 44 cases were diagnosed with *E. cloacae* bacteremia. The incidence of healthcare-facility onset *E. cloacae* bacteremia was 0.57 per 10,000 patient-days. MBL-producing *E. cloacae* were detected in 11 cases (25%). After screening of MBL-producing strains, PCR analyses were carried out for 5 of 11 isolates, all of which were IMP-1 type beta-lactamase. Among bacteremic patients with MBL-producing *E. cloacae*, inappropriate empirical antimicrobial therapies were likely to be selected compared to those with MBL-non-producing *E. cloacae* (90.9% vs 54.5%, P = 0.067). However, 30-day all-cause mortality between two groups was not different (9.1% vs 12.1%, P = 1.0). Factors associated with the development of MBL-producing *E. cloacae* bacteremia were prior antimicrobial use (adjusted odds ratio [aOR], 9.25; 95% confidence interval [CI], 1.27-67.4; P = 0.028) and no history of recent surgery (aOR, 13.8; 95% CI, 1.16-164; P = 0.033).

Conclusion. The frequency of MBL-producing *E. cloacae* bacteremia was high among *E. cloacae* bacteremia. Prior antimicrobial use and no history of recent surgery

were associated with MBL-producing *E. cloacae* bacteremia. Mortality was not different regardless of antimicrobial therapies and type of resistance.

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718. Predictors of Hospital Mortality Among Septic ICU Patients With *Acinetobacter spp*. Bacteremia: A Cohort Study

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Background. Inappropriate empiric antibiotic therapy (IEA) increases mortality in severe infections. Carbapenem resistance among *Acinetobacter spp*. challenges a clinician's ability to choose appropriate coverage. We hypothesized that among septic ICU patients with *Acinetobacter spp*. bacteremia (Ac-BSI), patients with carbapenem-resistant *Acinetobacter spp*. (CRAc) are at high risk for IEA, and that IEA is a predictor of hospital death.

Methods. We conducted a single-center retrospective cohort study, 2002-2012, of adult septic ICU patients with Ac-BSI at Barnes-Jewish Hospital, a 1200-bed urban teaching hospital. IEA was defined as exposure to initially prescribed antibiotics not active against the pathogen based on *in vitro* susceptibility testing, and having no exposure to appropriate antimicrobial treatment within 24 hours of drawing positive culture. We compared patients who died to those who survived, and derived logistic regression models to identify predictors of hospital mortality and of IEA. Proportions and odds ratios (OR) with 95% confidence intervals (CI) are presented for categorical variables, and median values with interquartile ranges (IQR) for continuous variables.

Results. Out of 131 patients with Ac-BSI, 65 (49.6%) died (non-survivors, NS) before discharge. NS were older than survivors (S) (63 [51, 76] vs 56 [45, 66] years, $p = 0.014$), and had a higher APACHE II (24 [19, 31] vs 18 [13, 22], $p < 0.001$) and Charlson (5 [2, 8] vs 3 [1, 6], $p = 0.009$) scores. NS were also more likely than S to have hospital-acquired Ac-BSI (72.3% vs 50.0%, $p = 0.009$), and prior antibiotics (75.4% vs 57.6%, $p = 0.031$) as risk factors for a healthcare-associated infection, as well as to require pressors (75.4% vs 42.4%, $p < 0.001$) and mechanical ventilation (75.4% vs 53.0%, $p = 0.008$). Both CRAc (69.2% vs 47.0%, $p = 0.010$) and IEA (83.1% vs 59.1%, $p = 0.002$) were more frequent among NS than S. In logistic regressions, IEA emerged as an independent predictor of hospital death (OR 3.58, 95% CI 1.28-9.98), while CRAc was the single strongest predictor of IEA (OR 50.38, 95% CI 13.49-188.17).

Conclusion. Among septic ICU patients with Ac-BSI, IEA predicts mortality. Carbapenem resistance appears to mediate the relationship between IEA and mortality.

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719. A Rare Variant of Lemierre's Syndrome – Fusobacterium necrophorum Sepsis from Gynecological Origin

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Background. Lemierre's syndrome is a rare, potentially severe disorder consisting of septic emboli from an internal jugular vein thrombus after oropharyngeal infection. There are a few case reports illustrating a variant of Lemierre's syndrome with the female genital tract being the source.

Methods. Case report and review of the literature. A 19 year-old female presented with abdominal pain, nausea, vomiting and fever. The patient denied any sexually transmitted diseases or recent pregnancy. Besides severe pallor, no other focal signs were present on examination. Her laboratory values revealed severe microcytic anemia, thrombocytosis and leukocytosis with neutrophilic predominance. There were no signs of hemolysis. Abdominal and chest computerized tomography showed pelvic thrombophlebitis and ascites as well as "septic" pulmonary emboli. Admission blood cultures grew Fusobacterium necrophorum on day three. As there was no evidence of infection or thrombophlebitis in the head and neck region, a more detailed sexual history was taken by a female medical resident and the patient revealed she was recently pregnant and had an abortion (not done by a medical professional). Keeping in mind her recent history of septic abortion and Fusobacterium sp. being a common commensal of the female genitourinary tract, a diagnosis of Lemierre's syndrome was made. The patient improved with ampicillin/sulbactam. As our patient had extensive thrombosis extending to inferior vena cava with septic emboli, she was started on anticoagulation.

Results. Lemierre's syndrome is a rare, well described entity that usually follows infection of oropharyngeal structures associated with thrombus formation in adjacent veins and septic emboli to the lungs. Though oropharyngeal structures are the most common source, Fusobacterium sp. can originate from the female genitourinary tract and may have similar clinical picture with the exception of the site of thrombosis and presenting complaints.

Conclusion. This case report illustrates a pelvic variant of Lemierre's syndrome.

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720. Clinical Features and Risk Factors for Mortality of *Stenotrophomonas maltophilia* Bacteremia in Patients with Hematologic Malignancies

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Background. *S. maltophilia* is an important nosocomial pathogen, mainly in immunocompromised patients, and is associated with high mortality. However, data regarding clinical features and risk factors for mortality of *S. maltophilia* bacteremia in patients with hematologic malignancies are limited.

Methods. We conducted a retrospective analysis of *S. maltophilia* bacteremia in patients with hematologic malignancies who were treated at Samsung Medical Center, in South Korea, from 2000 to 2012.

Results. During a 13 year period, we identified 101 adult patients with *S. maltophilia* bacteremia. The median age of the patients was 57 years (IQR, 45–64 years), 87 cases (86.1%) were hospital-acquired, and 25 cases (24.8%) had polymicrobial bacteremia.The most common underlying hematologic malignancy was acute myeloid leukemia (61 [60.4%] of 101) and twenty patients (19.8%) underwent stem cell transplantation. 83.2% of the patients had profound neutropenia and the median duration of neutropenia before the onset of bacteremia onset was 16 days (IQR, 10-26 days). 81 patients (80.2%) received prior antibiotic therapy during the previous month with carbapenem and, in 73 patients (72.3%), breakthrough bacteremia developed during carbapenem treatment. Catheter related infection (59.4%) and pneumonia (30.7%) were the most frequent primary sources of bacteremia. The 14-day mortality rate was 40.6% (41 of 101) and 65 patients (64.4%) received appropriate definitive antimicrobial therapy. Multivariate analysis demonstrated that the independent risk factors for 14-day mortality were pneumonia (OR, 18.76; 95% CI, 3.29-107.06; $P = 0.001$), septic shock (OR, 15.84; 95% CI, 2.25-111.55; $P = 0.006$), while appropriate definitive antimicrobial therapy was found to be a protective factor for 14-day mortality (OR, 0.06; 95% CI, 0.01-0.40; $P = 0.004$).

Conclusion. Physicians should consider *S. maltophilia* as the causative organism in hematologic malignancy patients, particularly those with the presence of prolonged neutropenia and carbapenem exposure. Although mortality rates were high, appropriate antibiotic therapy may improve the outcome of *S. maltophilia* bacteremia in patients with hematologic malignancies.

Disclosures. **All authors:** No reported disclosures.

721. Decreasing Prevalence of Vancomycin-Heteroresistance (hVISA) among Methicillin-Resistant *Staphylococcus aureus* (MRSA) Blood Isolates over 10 years: Potential Impact of Vancomycin Treatment Guidelines

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Session: 103. Bacteremia: Staphylococcal Bacteremia
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Background. Vancomycin treatment guidelines, which advocate a 10-15 mg/L trough level for *S. aureus* bacteremia (SAB), may impact the incidence of hVISA and VISA among clinical MRSA isolates.

Trends of vancomycin (V) MIC, hVISA and VISA prevalence among MRSA blood isolates over 10 years: n (%)

	Study year				
	2002-3 (n=186)	2005-6 (n=179)	2008-9 (n=164)	2010-12 (n=199)	p^a
V MIC (Etest)[b]	1.78± 0.39	1.81±0.47	1.68±0.26	1.55±0.29	<0.0001[c]
MIC ≥2 mg/L	93 (50.0)	82 (45.3)	58 (35.4)	38 (19.1)	<0.0001
hVISA	18 (9.7)	10 (5.6)	5 (3.0)	4 (2.0)	0.0003
VISA	4 (2.2)	2 (1.1)	0	5 (2.5)	1.0

a: Extended Mantel-Haenszel chi square for linear trend; b: mean±SD; c: 2010-12 vs each other period; 0.01 2008-9 vs 2005-6 and 0.004 vs 2010-12 (ANOVA with post hoc Bonferroni analysis).

Methods. Standardized screening of MRSA blood isolates saved from 2002-2012 for hVISA and VISA on BHI agar supplemented with vancomycin 3 and 4 mg/L, respectively (previously shown to be the best screening method based on correlation with population analysis profile). One isolate was selected from each patient and trends were analyzed over time.

Results. We encountered 1231 patients with SAB, MRSA accounted for 729 (59.2%). Screening for hVISA was possible for 728 isolates (one isolate could not be recovered for testing). Vancomycin MIC (Etest) was stable between 2002 and 2009 but decreased in 2010-12 (table). The incidence of isolates with vancomycin MIC ≥2mg/L and heteroresistance steadily decreased whereas the changes in VISA prevalence was not significant.

Conclusion. Standardized screening using BHI agar supplemented with vancomycin revealed a steadily decreasing incidence of hVISA and isolates with vancomycin MIC ≥2mg/L. The reasons for these trends are uncertain but adherence to updated vancomycin treatment guidelines which advocate for high vancomycin trough levels may suppress the development of less susceptible progeny. VISA remains rare.

Disclosures. **All authors:** No reported disclosures.

722. Infectious Diseases Consultation Increases Adherence with Quality of Care Indicators for Management of *Staphylococcus aureus* Bacteremia

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Background. Adherence to evidence-based quality of care indicators in treatment of *Staphylococcus aureus* bacteremia (SAB) has been shown to improve clinical outcomes. We studied the effect of Infectious Diseases (ID) consultation on adherence to established quality of care indicators for management of SAB.

Methods. Using a retrospective study design, we conducted chart reviews on all patients who were managed for SAB at Vidant Medical Center and affiliated community hospitals during a one-year period (November 2012 to November 2013). Subjects were divided into two groups: those who received ID consultations and those who did not. Information on demographics, quality-of-care indicators, and clinical outcomes were obtained. Fisher's exact test and chi square analysis were used to assess differences in the two groups with $p < 0.05$ denoting statistical significance.

Results. Of 182 patients with SAB, 84 patients (mean age 51, 59.5% male, 47.6% Caucasian) had ID consultation and 98 (mean age 56, 60.4% male, 38.7% Caucasian) did not receive ID consultation. Methicillin-sensitive *Staphylococcus aureus* (MSSA) were identified in 55.9% of patients in ID consultation and 61.2% in non-ID consultation group ($p = 0.56$). As compared to the non-ID consultation group, patients in the ID consultation group were more likely to have repeat blood cultures within 96 hours (86.9% vs 69.3%, $p = 0.008$), have an echocardiogram (92.8% vs 62.2%, $p < 0.0001$), and receive appropriate antibiotics in terms of duration and choice (100%, vs 76.5%, $p < 0.0001$). Also, patients in the ID consultation group were more likely to have early de-escalation (within 24 hours) to nafcillin or cefazolin (from vancomycin or daptomycin) in cases of MSSA bacteremia (89.3% vs 71.6%, $p = 0.03$). Recurrences of bacteremia within 90 days were similar in both groups (73.8% vs 69.3%, $p = 0.2$). There was a trend towards decreased all-cause mortality during the initial admission in ID consultation group (9.5% vs 20.4%, $p = 0.06$).

Conclusion. ID consultation increases adherence with evidence-based quality of care indicators, leads to more appropriate antimicrobial therapy, and can improve patient outcomes during management of SAB. Clinicians should consider getting ID consultation for all patients with SAB.

Disclosures. **P. Cook**, Gilead (investigator), Pfizer (investigator), Merck (investigator and speakers' bureau), Forest (Speaker honorarium)

723. Community vs Hospital Acquired *Staphylococcus aureus* Bacteremia in A Canadian Tertiary Care Center: A Retrospective Chart Review, 2010-2012

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Background. Staphylococcus aureus (SA) bloodstream infections (BSI) are a significant cause of morbidity and mortality. The objective of this study is to compare rates of MRSA and MSSA bacteremia in our hospital over time and to describe the characteristics of community-acquired (CA) and healthcare associated (HA) BSI admitted to hospital over a two year period.

Methods. This study took place at a 739-bed inpatient tertiary care center in Edmonton, Canada. All patients who had a blood culture positive for SA between January 1, 2010 and December 31, 2012 and were admitted to the University of Alberta Hospital were included. Information was extracted from paper charts. Data analysis was performed using IBM SPSS 22.

Results. A total of 342 separate episodes of SA BSI were reviewed. Of the 342 episodes, 198 were admitted to medical services (57.8%) and 149 (43.5%) required ICU admission. The mean age was 60.6 years (+/- 17.6 years, range 18-99 years). More men than women were affected (237, 69.3%). Fifty four percent (54.3%, 186) of SA BSI were CA. Rates of BSI did not change over time, except in the last quarter of 2012, HA-MRSA rates fell. Thirty-day mortality was similar (CA 24.2%, 45; HA 19.2%, 30). Greater 120-day mortality was seen in the CA group (60, 32.3% vs 41, 26.2%). In 305 (89.1%) cases, infection source was identified. Main sources of CA BSI were skin and soft tissue infections (37, 12%), endocarditis (26, 8.5%), and pneumonia/aspiration (29, 9.5%). Main sources of HA BSI were central access (47, 15.4%), pneumonia/aspiration (20, 6.6%) and post-operative infections (30, 9.8%). Age and sex distributions, mean duration of bacteremia and the mean vancomycin mean inhibitory concentration were the same in both groups. On average, patients with HA bacteremia stayed one day longer in the ICU (5.9 vs 6.8, range 0-72) and 1.6 days longer in hospital overall (35.1 days vs 33.5 days, range 1-745 days).

Conclusion. To our knowledge very few studies have examined differences in CA and HA SA BSI. Our study suggests the geographical place of onset is not determined by age, sex or resistance pattern and does not affect mortality. The main difference between the two entities is the source of infection. Soft tissue infections are the predominant source in community acquired SA bacteremia whereas central catheters are the predominant source in hospital acquired SA BSI.

Disclosures. **All authors:** No reported disclosures.

724. Vancomycin Minimum Inhibitory Concentration Does Not Predict Death, Recurrence or Readmission in Patients with *Staphylococcus aureus* Bacteremia in a Safety-Net Hospital

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Background. *Staphylococcus aureus* (*S. aureus*) bacteremia (SAB) is a leading cause of bloodstream infections and results in tremendous health and financial burden. Prior studies examining the impact of the vancomycin minimum inhibitory concentration (MIC) on outcomes in patients with SAB have methodological and statistical limitations. The goal of this study was to determine whether increased vancomycin MIC is associated with higher risk for 90 day readmission, recurrence of disease or mortality in patients with SAB.

Methods. This was a prospective cohort study of all adult patients with SAB presenting to San Francisco General Hospital, the San Francisco County hospital, from 2008-2012. Subjects were identified by a hospital-wide infection surveillance system. The main predictor was vancomycin MIC, dichotomized as less than 2 mcg/mL or equal to 2 mcg/mL. The primary outcome was death within 90 days. Secondary outcomes were readmission or recurrence of disease within 90 days. Covariates included methicillin resistance, age, race, gender, severity of illness, co-morbidities, source of infection, injection drug use and all antibiotics administered over the study period with activity against *Staphylococcus aureus*. A survival analysis with a Cox proportional hazards model was used to estimate 90-day outcomes.

Results. Of 437 unique first time cases of SAB, 23 patients were excluded for incomplete data, leaving 414 individuals with SAB for the final analysis. Eighty-two (19.8%) patients had a vancomycin MIC = 2 mcg/mL. 60 subjects (14.5%) died, 124 (30.0%) were re-admitted and 10 (2.4%) had recurrence of SAB within 90 days. Multivariate regression showed equivalent risk of death (HR = 1.00, 95% CI (0.52, 1.91)), readmission (HR = 1.19, 95% CI (0.77, 1.85)) and recurrence (HR = 5.72 (95% CI (0.27, 123.56)) of SAB at 90 days for MIC < 2 vs MIC = 2.

Conclusion. In this prospective cohort study, in which antibiotic treatment course and length of hospital stay were comprehensively measured and loss to follow-up was minimized, vancomycin MIC was not predictive of mortality, disease recurrence or readmission at 90 days in the treatment of SAB.

Disclosures. **D. Deck**, Forest Pharmaceuticals: speaker, Speaker honorarium; Merck: speaker, Speaker honorarium

725. *Staphylococcus aureus* Bacteremia in Children: A Retrospective Review at a Tertiary Care Hospital

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Background. While *Staphylococcus aureus* bacteremia (SAB) is associated with high morbidity and mortality in adults, less is known about this condition in children.

The objective of this study was to describe the characteristics, source, treatment and outcomes of children with SAB in an era when *methicillin-resistant Staphylococcus aureus*(MRSA) rates are increasing.

Methods. All children presenting to the Hospital for Sick Children, Toronto, between April 1, 2007 and April 1, 2010 with ≥1 positive blood culture for *Staphylococcus aureus* were included in the study. Charts were retrospectively reviewed as part of a multicenter study on SAB management in adults and children. SAB that developed after 48 hours was considered hospital acquired.

Results. A total of 147 children with a median age of 3 years (IQR 0,9) were included; 51% were male. Eight (5%) patients were not admitted to hospital and are not known to have received therapy. Almost all isolates (n = 142) were methicillin-sensitive *Staphylococcus aureus*. The most common source was a central line (n = 72, 49%), and 14 (19%) of these patients had a second site affected. Most central line infections were hospital acquired (n = 47, 65%, p < 0.001) and the line was removed in only 43% of cases (n = 31).

Other sources included osteomyelitis and septic arthritis (n = 39), pneumonia/empyema (n = 19), cellulitis (n = 12), surgical site infection (n = 11), infective endocarditis (n = 4), urinary tract infection (n = 1) and staphylococcus scalded skin syndrome (n = 1). Overall, 25% had more than one site affected.

The median antibiotic treatment duration was 23 days (IQR 14, 42). Thirty-five patients (24%) received less than 1 week of IV therapy and did not present back to this hospital with treatment failure. Treatment varied widely depending on the source of infection and the admitting service. A total of five patients died, but only one was felt to be related to *Staphylococcus aureus*.

Conclusion. SAB in children differs significantly from adults in terms of both morbidity and mortality and extrapolating treatment decisions based on adult literature may lead to inappropriate prolonged antibiotic exposure. There is significant variability in the treatment of pediatric SAB and prospective trials are needed to guide management.

Disclosures. **All authors:** No reported disclosures.

726. Readmission rate associated with *Staphylococcus aureus* bacteremia

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Background. *Staphylococcus aureus* bacteremia (SAB) is one of the most common blood stream infections resulting in significant mortality and morbidity. The objective of the study was to evaluate outcomes in patients with SAB.

Methods. We conducted a retrospective chart review of the patients who were admitted to the hospital in 2013, whose blood culture was positive of *S. aureus*. Outcomes evaluated were mortality, follow up blood cultures, length of stay (LOS), rate of readmission due to another SAB, and all-cause 30-and 60-day readmission rates. Statistical analyses were performed with SPSS software and Microsoft Excel software, with continuous and nominal data evaluated with the student t-test and the X^2 test, respectively.

Results. One hundred seven patients were identified to have 119 inpatient encounters associated with SAB. Mortality during index hospital stay was 18%. Among the survivors, 25% didn't have confirmatory negative culture obtained prior to discharge. Length of stay (LOS) was significantly shorter in patients who didn't have negative blood culture compared to patients who had negative culture (5.2 days vs 14.9 days, P < 0.0001). Eleven percent of patients had readmissions with another SAB during the study period. All-cause 30- and 60-day readmission rates were 26% and 39%, respectively. Fifty seven percent of 60 days readmissions were due to an infection and 17 % was secondary to primary SAB, such as allergic reaction to antibiotic, acute kidney injury, intravascular line issues, and/or opportunistic infections. Overall, readmissions associated with infections accounted for 75% of 60 day readmissions. Among the survivors, Methicillin Resistant *S. aureus* (MRSA) group had higher rate of readmissions in 60 days compared to Methicillin Susceptible *S. aureus* (MSSA) group (50% vs 26%, P = 0.028).

Conclusion. In patients who had index admission for SAB, readmission rate with another SAB was 11%. All-cause readmission rates were 26% and 39%, respectively in 30 days and 60 days, and up to 75% of 60 days readmissions were related to the primary SAB.

Disclosures. **All authors:** No reported disclosures.

727. Evaluating the Impact of Socioeconomic Status on Clinical Presentation in Patients with *Staphylococcus aureus* Bacteremia

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Background. *Staphylococcus aureus* bacteremia (SAB) is a leading cause of bloodstream infections, carrying high rates of morbidity and mortality. Limited research exists on the impact of socioeconomic status (SES) on complications and severity of illness at the time of initial presentation in patients with SAB.

Methods. This was a prospective cohort study of all adult patients with a first presentation of SAB presenting to San Francisco General Hospital, the San Francisco County hospital, from 2008-2012. Subjects were identified by a comprehensive infection control surveillance system. Primary predictors were homelessness, percent of individuals under the federal poverty limit (POV) or median household income (MHI) within each patient's reported zip code. Primary outcomes were intensive care unit (ICU) admission, meeting systemic inflammatory response syndrome (SIRS) criteria on admission, and diagnosis of vertebral osteomyelitis or endocarditis. Multivariate logistic regression controlling for HIV status, age, race, gender, injection drug use and the Charlson comorbidity index was used to assess the impact of SES on primary outcomes.

Results. There were 437 unique individuals with first presentations of SAB, of which 406 had homelessness data and 398 had a reported zip code, median income and poverty data. 94 (23.2%) of individuals were homeless. In separate logistic regression models, MHI and POV were not associated with ICU admission, but homelessness was protective against admission to the ICU (OR 0.39, 95% CI (0.19, 0.80)). No variables were predictive of meeting SIRS criteria on admission. MHI, POV and homelessness were not associated with diagnoses of vertebral osteomyelitis/discitis or endocarditis. Post-hoc Cox proportional hazard modeling revealed no association between homelessness and mortality, readmission or SAB recurrence at 90 days.

Conclusion. In an ethnically and economically diverse safety-net population, in patients presenting with SAB, lower neighborhood SES was not associated with complications at presentation including endocarditis, vertebral osteomyelitis/discitis, ICU admission and meeting SIRS criteria. Homelessness was protective against ICU admission, suggesting SES may impact triage decision-making.

Disclosures. **D. Deck**, Forest Pharmaceuticals: speaker, Speaker honorarium; Merck: speaker, Speaker honorarium

728. Evaluation of Empirical Regimens Including Antistaphylococcal Betalactam Antibiotics vs Vancomycin Monotherapy on Outcomes of Patients with Methicillin-Susceptible *Staphylococcus aureus* (MSSA) Bacteremia

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Background. Little is known about the outcomes of patients who are initiated on vancomycin as empiric monotherapy relative to antistaphyloccal BL therapy for MSSA BSIs. The purpose of this study was to evaluate outcomes of patients with MSSA BSIs who were treated with vancomycin monotherapy empirically compared to those who also received an antistaphylococcal BL.

Study Results

Variable	Vancomycin monotherapy (N=20)	Empiric BL (N=75)	P-Value
Demographics			
Male	55%	69.1%	0.23
Intensive Care Unit	55%	47.2%	0.55
Age, mean±SD	53.2±14.5	54.9±15.7	0.67
BL allergy	25%	3.6%	0.005
Acute Physiology and Chronic Health Evaluation II (APACHE II), mean±SD	19.9±10.3	21.4±10.0	0.55
Charlson Index, mean±SD	4.4 ± 2.8	4.3 ±3.1	0.9
Primary Outcome			
Clinical failure	35%	23.6%	0.33
30-day mortality	20%	16.3%	0.71
BSI 7 days	20%	7.2%	0.11

Factors Related to Clinical Failure	
Variable	**Odds Ratio [95% Confidence Interval])**
Vancomycin monotherapy	2.98 [0.78-11.38]
Age	1.05 [0.99-1.12]
APACHE II	1.12 [1.03-1.21]
Charlson Index	0.94 [0.71-1.24]

On multivariate analysis, only APACHE-II score was associated with clinical failure.

Methods. This was a single-center retrospective study of patients with MSSA BSIs from April 2008-December 2013. Inclusion criteria were: receipt of ≥48 hours of empiric therapy; ≥1 positive blood culture with MSSA; first positive culture drawn within 24 hours of starting empiric antibiotics. Exclusion criteria consisted of: use of anti-

MRSA therapy for concomitant infection; polymicrobial BSI; use of other agents active against MSSA. The primary endpoint was clinical failure, a composite of 30-day mortality and persistent BSI ≥7 days. Logistic regression was performed to determine factors associated with the endpoint.

Results. 339 charts of patients with *S. aureus* BSI were screened and 75 of these patients were included in the final analysis.

Conclusion. This study does not show a significantly increased risk of clinical failure in patients who are treated with vancomycin monotherapy empirically. The lack of significant differences between groups may be due to insufficient power to detect a difference; therefore, a larger study evaluating the influence of empiric antibiotic choice for MSSA BSI is warranted.

Disclosures. **J. Gallagher**, Cubist: Consultant, Consulting fee; Optimer: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium; Astellas: Speaker's Bureau, Speaker honorarium; Forest: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium; Pfizer: Scientific Advisor, Consulting fee

729. Activity of Ceftaroline and Comparator Agents Tested against *Staphylococcus aureus* from Patients with Bacteremia in United States (USA) Medical Centers (2009-2013)

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Background. Ceftaroline (CPT), the active metabolite of the prodrug CPT fosamil, is the first cephalosporin with potent activity against methicillin-susceptible (MSSA) and -resistant *S. aureus*(MRSA). CPT is approved for treatment of community-acquired penumonia and acute bacterial skin infections.

Methods. 4,426 *S. aureus*isolates from the AWARE CPT surveillance program were derived from patients with bacteremia in 2009-2013. Isolates were collected in 150 medical centers distributed through all 9 USA Census regions, and tested for susceptibility (S) against CPT and comparators by the CLSI broth microdilution method. S interpretations were determined per CLSI criteria.

Results. 45.5% of isolates were MRSA. CPT ($MIC_{50/90}$, 0.25/1 µg/mL) inhibited 97.9 and 100.0% of *S. aureus* at ≤1 and ≤2 µg/mL, respectively (Table). Daptomycin (DAP; $MIC_{50/90}$, 0.25/0.5 µg/mL), linezolid (LZD; $MIC_{50/90}$, 1/2 µg/mL) and vancomycin (VAN; $MIC_{50/90}$, 1/1 µg/mL) were active against ≥99.8% of isolates. S rates for erythromycin ($MIC_{50/90}$, >16/ > 16 µg/mL), clindamycin (CLI; $MIC_{50/90}$, ≤0.25/ > 2 µg/mL) and levofloxacin (LEV; $MIC_{50/90}$, ≤0.5/ > 4 µg/mL) were 42.5, 80.8 and 59.2%, respectively. Against MSSA, CPT ($MIC_{50/90}$, 0.25/0.25 µg/mL; 100.0% S) was 16-, 4- and 4-fold more active than ceftriaxone ($MIC_{50/90}$, 4/4 µg/mL), LZD ($MIC_{50/90}$, 1/2 µg/mL) and VAN ($MIC_{50/90}$, 1/1 µg/mL), respectively, and slightly more potent than DAP ($MIC_{50/90}$, 0.25/0.5 µg/mL). Among MRSA, 95.4 and 100.0% of strains were inhibited at ≤1 and ≤2 µg/mL of CPT, respectively. 35.8% and 75.4% of MRSA were resistant to CLI and LEV, respectively. 99.7% of MRSA strains were DAP-S ($MIC_{50/90}$, 0.25/0.5 µg/mL), and LZD ($MIC_{50/90}$, 1/2 µg/mL) and VAN ($MIC_{50/90}$, 1/1 µg/mL) were active against >99.9% of MRSA strains.

Organism (no.)	No. of isolates (cum. % inhibited at CPT MIC (µg/mL) of: ≤0.06	0.12	0.25	0.5	1	2
S. aureus (4,426)	13 (0.3)	222 (5.3)	2,105 (52.9)	1,113 (78.0)	880 (97.9)	93 (100.0)
MSSA (2,413)	13 (0.5)	221 (9.7)	2,067 (95.4)	111 (>99.9)	1 (100.0)	–
MRSA (2,013)	0 (0.0)	1 (0.0)	38 (1.9)	1,002 (51.7)	879 (95.4)	93 (100.0)

Conclusion. Our results demonstrate the potent in vitro activity of CPT when tested against a large collection of contemporary (2008-2013) *S. aureus*isolates causing bacteremias in USA hospitals.

Disclosures. **H. S. Sader**, Forest: Grant Investigator, Research grant **D. J. Farrell**, Forest: Grant Investigator, Research grant **R. K. Flamm**, Forest: Grant Investigator, Research grant **R. N. Jones**, Forest: Grant Investigator, Research grant

730. A Retrospective Comparison of Self – Administered Ceftriaxone vs Cefazolin for Methicillin-Susceptible Staphylococcus Aureus Bacteremia in an Outpatient Antibiotic Therapy Setting.

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Background. MSSA bacteremia is a common cause of community-acquired and hospital-acquired infections with significant morbidity and mortality. Ceftriaxone is a third generation cephalosporin with activity against gram positive and gram negative aerobic bacteria including MSSA. It is well tolerated and offers significant cost reduction with its once daily dosing in the outpatient setting. Although it is not considered the antimicrobial agent of choice for MSSA infections, its pharmacokinetic profile and presumed activity against MSSA make it an option for long term antibiotic administration. There are, however, few published data documenting its efficacy in the treatment of significant MSSA bacteremia.

Methods. We conducted a retrospective cohort study of patients with MSSA bacteremia at the Outpatient Parenteral Antimicrobial Therapy (OPAT) Clinic at Parkland Hospital from January 2011 to December 2013 that were treated with either self-administered cefazolin or ceftriaxone as the definitive treatment. We collected demographic, clinical outcome data, and adverse events. Successful treatment (clinical improvement, no 90 day readmission, no recurrence of bacteremia) was compared after the completion of the two antibiotics.

Results. In total, 65 patients were seen at the OPAT clinic for MSSA bacteremia. 23 (35%) received cefazolin and 23 (35%) received ceftriaxone. Mean duration of treatment was 33 days. All patients received nafcillin or cefazolin in the hospital prior to initiating definitive therapy outpatient. Most common etiologies of the bacteremia included osteomyelitis (56%), skin soft tissue infection (15%), line related infection (15%), and endocarditis (13%). 90 day readmission rate was similar (3 of 23 [13% for cefazolin and 4 of 23 [17%] for ceftriaxone). Treatment success were similar after the completion of antibiotics (20 of 23 [87%] for cefazolin vs 19 of 23 [83%] for ceftriaxone). None of the patients from both group had adverse effects requiring discontinuation.

Conclusion. In this comparison of ceftriaxone vs cefazolin for MSSA bacteremia, there was no difference in treatment success after completion of antibiotics. Ceftriaxone is therefore an acceptable alternative to Cefazolin for MSSA bacteremia in the outpatient setting.

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731. Utility of Ceftaroline in the Treatment of Persistent Bacteremia and Deep-Seated Infections

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Background. Ceftaroline fosamil is an advanced generation cephalosporin with anti-MRSA activity. Currently, there are only a few limited agents (vancomycin, daptomycin, and linezolid) available for the treatment of serious MRSA infections. We report eleven patient cases of using ceftaroline in the treatment of persistent, complicated MRSA bacteremia and deep-seated infections.

Methods. This IRB approved study evaluated adult inpatients from January 2012 - September 2013 with persistent MRSA bacteremia prior to the initiation of ceftaroline. All patients were identified from the UK Center for Clinical and Translational Science Enterprise Data Trust. Information collected included demographics, antibiotic usage, culture and sensitivity results, and treatment outcomes. Patients were monitored for clinical response and resolution of bacteremia. Susceptibility was performed using the Phoenix Testing System or E-test.

Results. There were a total of 11 patients (3 females and 8 males) with an average age of 46 years (range of 25-71). The majority of the patients had endocarditis (7/11). MRSA bacteremia ranged from 3 to 14 days prior to ceftaroline initiation. Ceftaroline was used in combination with vancomycin with or without rifampin (N = 4), daptomycin (N = 4), or linezolid (N = 1). Three strains were daptomycin non-susceptible (MICs ranged from 3 -6 mcg/ml), 10 cases had vancomycin MICs > 1.5, one case had a hetero-resistant vancomycin isolate, and one case had ceftaroline non-susceptible isolate. With the addition of ceftaroline, bacteremia resolved within 1-7 days. Seven patients were treated successfully. However, one patient expired from complications of septic embolism leading to pulmonary hemorrhage and 3 patients expired after withdrawal of care.

Conclusion. Ceftaroline was safe and effective in clearing bacteremia in these patients with persistent MRSA infections that were resistant to other antibiotics. It is an alternative agent used in these difficult to treat multi-drug resistant serious infections where there are limited antimicrobial agents available.

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732. Predictors of Cardiac Implantable Electronic Device Infection in Patients with Staphylococcus Aureus Bacteremia

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Background. Staphylococcus aureus bacteremia (SAB) is commonly associated with cardiac implantable electronic device infection (CIED-I). This usually requires explantation of the device. In cases of SAB in the presence of CIED that is not

obviously infected (after examination of the pocket and transesophageal echocardiogram), decision about device removal is less clear. Predicting CIED-I in those cases would be helpful.

Methods. This case-control study included all adults admitted to the University of Kansas Medical Center with SAB in the presence of a CIED between January 1, 2007 and December 31, 2012, using ICD 9 codes, CIED registry, and microbiology database. Cases had device infection evidenced by pocket infection or CIED related endocarditis; controls did not, over a 12 weeks follow up period. Clinical predictors of CIED-I were evaluated using logistic regression. Mortality was evaluated at 30 and 365 days.

Results. We identified 64 patients with CIED who had 70 separate episodes of SAB during the study period. Of all 70 episodes of SAB, 74.3% were in males, 74.3% were in white, and mean age was 65.3 years. MRSA accounted for 48.6% of SAB. There were 31 episodes involving the device (44.3%, cases) and 39 SAB without CIED-I (55.7%, controls). On univariate analysis, factors associated with increased risk of device infection included fever (Odds ratio [OR] 5.65, 95% confidence interval [CI] [1.45-22.04], p-value 0.011), persistent bacteremia at 72h (OR 2.89, CI [0.97- 8.60], p-value 0.052), and tachycardia (OR 2.41, CI [0.82- 7.10], p-value 0.098). Factors associated with decreased risk of device infection included end stage renal disease (ESRD) (OR 0.24, CI [0.07 - 0.81], p-value 0.029) and immunosuppression in the past 3 months (OR 0.23, CI [0.05- 1.16], p-value 0.096). On multivariate analysis only fever remained significantly associated with device infection (OR 6.58, CI [1.20-36.04]). Mortality at 30 and 365 days was not significantly different between cases and controls.

Conclusion. Fever, tachycardia and persistent bacteremia were associated with increased risk of CIED-I among patient with SAB, while ESRD and immunosuppression were protective on univariate analysis. Only fever remained significantly associated with CIED-I on multivariate analysis.

Disclosures. **All authors:** No reported disclosures.

733. Vancomycin-Resistant Enterococcus (VRE*) faecium* Bloodstream Infections and Mortality

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Background. Enterococci are the third most common cause of healthcare-associated bloodstream infections, and VRE infections, particularly those caused by *Enterococcus faecium*, are associated with increased morbidity, mortality, length of stay and cost due to antibiotic resistance to several antimicrobial agents.

Methods. A retrospective review of electronic medical records from January 2010 to December 2013 of VRE *faecium* bloodstream infections (BSI) at single 900 bed teaching hospital in Detroit. Patients identified through microbiology records. Demographics, comorbidities, and therapeutic antibiotic regimens used were evaluated to assess risk factors and outcome.

Results. A total of 159 cases of VRE *E. faecium* BSI were identified. Mean age was 62 years with 54% male. Fifty percent of bacteremia cases occurred in ICU, 31% in wards, 18% in ED. Common sources of infection were catheter-related (44%), intra-abdominal (35%), urinary tract (11%). Isolates were hospital-acquired (64%) and health-care associated (35%). Common underlying comorbidities were AKI (54%), immunosuppression (47%), CKD (40%), diabetes (35%), malignancy (34.5%), dialysis (31%) and liver disease (27%). Endocarditis occurred in 6%. Patients received the following treatments: daptomycin (D) 38%, linezolid (L) 23%, combination of D followed by L 27%, or no therapy 11%. Ninety-day mortality was 44%. There was a difference in location onset (ICU 61% vs 40%), infection origin (hospital-acquired 74% vs 56%), source of infection (intra-abdominal 44% vs 27%) and comorbidities between the expired and non-expired group. Hematologic malignancies were 37% in expired vs 10% in survived, cirrhosis 37% vs 19%, dialysis 43% vs 21%. There was no difference between age, gender or choice of antibiotic use. In the patients who expired, 39% received D, 19% L, 20% combination of both, 20% received no therapy. In survival group, 37% received D, 26% L, 37% both D and L, 4.5% no therapy.

Conclusion. Mortality in VRE *faecium* bloodstream infections was more common in patients with severe underlying disease, ICU onset, hospital-acquired infection, intra-abdominal source and receipt of ineffective antibiotics.

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734. Pneumococcal Bacteremia in Cancer Patients: A Case Series

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Background. One of the major causes of morbidity and mortality in cancer patients is infection. Gram-positive bacteremias now represent 40 to 50% of all bacteremic episodes in neutropenic cancer patients. However, pneumococcal bacteremia is uncommon in cancer patients including those who are neutropenic. Resistance to commonly used antibiotics is expected in our population due to heavy exposure to prophylactic and empiric use of fluoroquinolones and beta lactams.

Methods. We reviewed the records of patients with documented *Streptococcus pneumoniae* bacteremia at the Moffitt Cancer Center between June 2003 and January 2013. The study population was identified by positive blood cultures obtained from the Microbiology Laboratory over the same period of time.

Results. During the study period, 27 episodes of *Streptococcus pneumoniae* bacteremia occurred, and were analyzed. Of the 27 patients, 15 were males (56%) with a mean age of 55 years (range: 22-78 years). Most of the patients (78%) received empirical antibiotic treatment as soon as bacteremia was clinically suspected on the basis of fever. Ten (37%) cases were resistant to Ceftriaxone, 11 (41%) were resistant to Penicillin, and 13 (48%) were resistant to Levofloxacin. Seven (26%) patients were neutropenic (PMN < 1500/uL) at the onset of the bacteremia. Thirteen (59%) had a hematologic malignancies and 11 (41%) had a solid tumor. Four (15%) patients had COPD, 3 (11%) had asthma and 1 (4%) had pulmonary fibrosis. One patient did not receive any empirical treatment, deteriorated and died within 24 hours after onset of the initial symptoms. Overall, 3 (11%) patients died during their hospital stay.

Conclusion. Although pneumococcal bacteremia remains rare in cancer patients including those with neutropenia, resistance to commonly used antibiotics is higher than expected. Our study illustrates the difficulty of choosing empiric antibiotics for patients with suspected pneumococcal bacteremia with such a high level of resistance.

Disclosures. **All authors:** No reported disclosures.

735. Nutritionally Variant Streptococci Bacteremia in Cancer Patients: A Relatively Benign Occurrence

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Background. Nutritionally Variant Streptococci (Abiotrophia and Granulicatella) are found normally in the oropharynx, genitourinary tract, and intestinal tract. NVS are typically associated with endocarditis in immunocompetent patients and bacteremia in immunosuppressed patients. Chemotherapy-induced mucositis and neutropenia have previously been identified as risk factors in cancer patients. In this study we investigated the clinical characteristics of NVS bacteremia in cancer patients and identified risk factors and mortality rates associated with these infections.

Methods. We retrospectively reviewed all cases of NVS bacteremia occurring from June 1999 to April 2014 at H. Lee Moffitt Cancer Center and Research Institute. We collected data regarding baseline demographics and clinical characteristics such as age, sex, underlying malignancy, neutropenic status, duration of neutropenia, treatment, and outcome.

Results. Thirteen patients were identified with positive NVS blood stream infection. Ten patients (77%) had hematologic malignancies. Seven patients (54%) were neutropenic with an average duration of 14 days. The median age was 60 years. There was no gender predilection. Seven patients had mucositis at the time of diagnosis. One patient had gingivitis with dental abscess. None of the patients developed infective endocarditis. Most patients were on empiric antimicrobial therapy with ciprofloxacin, levofloxacin or piperacillin/tazobactam at the time of breakthrough bacteremia. Almost all patients received vancomycin as definitive treatment. All the patients had transient bacteremia with an average duration of positive blood cultures of 1 day. The 30 day mortality rate was 16.67%. Mortality was not attributable to NVS bacteremia.

Conclusion. NVS should be considered as a possible agent of gram positive bacteremia in cancer patients with neutropenia and a breach in oral or gastrointestinal mucosa, especially chemotherapy-induced mucositis or gingivitis. We recommend against routine removal of the central venous catheters given the benign course of NVS bacteremia, rapid clearance from blood, and likely oral or GI tract source of the pathogen. NVS bacteremia did not contribute to the mortality of patients in our study.

Disclosures. **All authors:** No reported disclosures.

736. Clinical characteristics of invasive Group G Streptococcal diseases in a tertiary care hospital in Japan over 12 years: Comparison with invasive non-Group G streptococcal diseases

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Background. Invasive streptococcal diseases are associated with significant morbidity and mortality. Group A streprococci (GAS) and Group B streptococci (GBS) have been considered as the main pathogens. Recently, the reports on invasive Group G streptococcal (GGS) diseases have increased worldwide. The reports on the detailed clinical epidemiological information are quite limited.

Methods. Patients diagnosed with invasive streptococcal diseases at NCGM from January 2002 to January 2014 were identified retrospectively. Invasive streptococcal diseases were defined as isolation of organisms from normally sterile sites. Clinical characteristics and laboratory findings were obtained from medical records and those of invasive GGS diseases were compared with invasive non-GGS (NGGS) diseases.

Results. Fifty four patients with invasive GGS diseases (GGS group) and 69 with NGGS (NGGS group) were identified. NGGS consists of 17 (24.6%) GAS and 52 (75.4%) GBS. The isolation of organisms was mainly from blood culture (n = 114, 92.7%). The mean age of GGS group was significantly higher than NGGS group (table, Figure 1). Clinical characteristics of two groups are summerized in table and figures. In-hospital mortality did not differ between two groups (0% vs 4.3%, p = 0.26). No penicillin or cephalosporin resistance was observed in either group. NGGS isolates were more resistant to levofloxacin as compared to GGS isolates (n = 13 [18.8%] vs n = 0 [0%], p = 0.001). Cellulitis, especially at lower limb, were more frequent among GGS group than NGGS (Figure 2).

Clinical characteristics of GGS and NGGS patients

Variable	GGS, no. (%)	NGGS, no. (%)	P value (GGS vs NGGS)
Age	75.6±14.8	58.9±20.9	<0.001
Male	34 (63%)	35 (51%)	0.20
Impaired consciousness	23 (43%)	12 (20%)	0.01
Diabetes mellitus	9 (16%)	13 (6%)	0.82
Cardiovascular disease	29 (54%)	25 (36%)	0.07
Malignacy	18 (33%)	17 (25%)	0.32

Figure 1. Rates of patients with invasive GGS and NGGS diseases

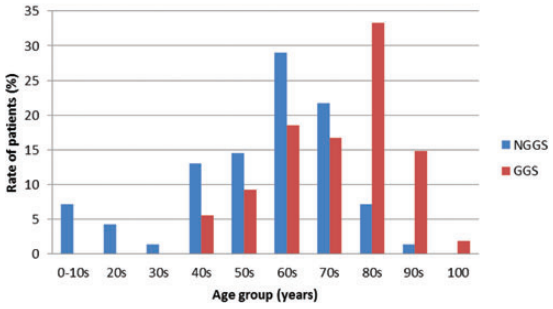
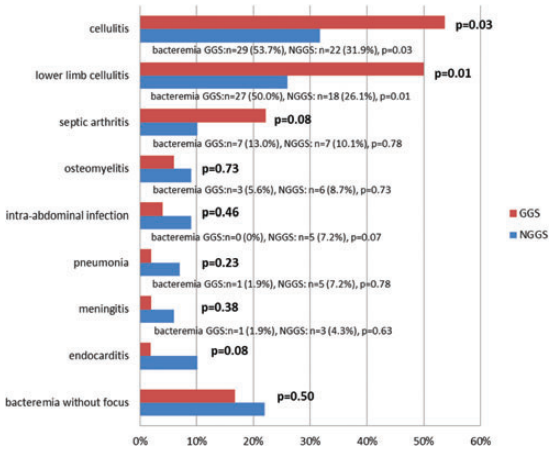


Figure 2. Infectious clinical syndromes



Conclusion. GGS is more likely to be associated with the cellulitis in elderly population with the underlying diseases. An aging society is coming worldwide in future. It is important that primary physicians and ER doctors recognize the clincal characteristics of the invasive GGS disease, which are distict from NGGS disease. This is a report for the world from Japan which aging goes ahead through.

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737. The Impact of Obesity and Diabetes on the Risk and Outcomes of Invasive Group A *Streptococcus* Infections in Adults, Active Bacterial Core Surveillance (2010-2012)

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Background. With limited prevention strategies, identifying prognostic factors for invasive group A *Streptococcus* (iGAS) infections is important. Obesity and diabetes have been linked to increased risk of skin and soft tissue infections (SSTIs)–common manifestations of iGAS. We analyzed iGAS incidence and outcomes in obese vs normal weight persons and diabetics vs non-diabetics.

Methods. We identified 2010-2012 community-onset cases of iGAS among non-pregnant adults from select counties at 10 US Active Bacterial Core surveillance sites. Cases are defined by isolation of GAS from a normally sterile site or from a wound in a patient with necrotizing fasciitis or streptococcal toxic shock syndrome in a resident of the surveillance area. Patient demographics, height, weight and clinical data were obtained from medical records. We used height and weight to calculate body mass index (BMI) or imputed BMI for missing values, categorizing patients into normal weight (BMI 18.5- < 25.0), overweight (25.0- < 30.0), obese grades 1-2 (30.0- < 40.0) and obese grade 3 (≥40.0). Through Poisson regression, we estimated iGAS incidence by BMI category and diabetes status after controlling for sex, age, race and other underlying conditions using ABCs catchment area population estimates from the 2011 Behavioral Risk Factor Surveillance System survey for denominators. Multivariable logistic regression was used to compare risk of death by BMI category and diabetes status.

Results. There were 2135 iGAS cases. Diabetes [relative risk (RR)= 3.0, 95% confidence interval (CI)= (2.3-3.9)] and grade 3 obesity among non-diabetics (RR= 2.8, 95%CI= 2.3-3.4) were associated with an increased risk of iGAS. Neither obesity nor diabetes was associated with increased risk of death. SSTIs, with the lowest case fatality ratio (1.9%) among all infection types, were more common in obese and diabetic persons compared to normal weight (p < 0.001) and non-diabetic (p = 0.001) persons, respectively.

Conclusion. Diabetes and extreme obesity in non-diabetics were independent risk factors for iGAS. SSTIs, which tend to be less severe than other infection types, seem to be driving the increased risk. Efforts to prevent and treat obesity and diabetes may help reduce the occurrence of iGAS.

Disclosures. **All authors:** No reported disclosures.

738. The Increasing Threat of Group B *Streptococcus* Infection in Adults

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Background. Group B Streptococcus (GBS) is not just the primary cause of sepsis in neonates anymore. It is also becoming an increasingly important cause of morbidity and mortality in adults. The rise of GBS infections globally is not new and has been reported over the past few decades. However with the marked increase of cardiovascular disease and diabetes over the last several years, which are both serious risk factors for GBS infection, along with fewer antibiotics being available for treatment due to growing antimicrobial resistance, the rise in cases could grow exponentially. This study aims to better understand the current rates, risk factors, outcomes, and resistance patterns of GBS bacteremia.

Methods. This is a retrospective study using electronic medical records of non-pregnant patients >16 years of age with positive *Streptococcus agalactiae* bloodstream infections collected from the Inova Health system in Northern Virginia from 2011-2013.

Results. 113 cases of positive *Streptococcus agalactiae* were identified from 2011-2013, with 21% (24/113) of them being recurrent cases. The average number of

episodes per year was 38. The average age of patients was 63.9 years with a range of ages 18-94, of which 59% (67/113) were male, and 41% (46/113) were female. In 66% of cases, the infection source was without focus. The remaining cases had infectious sources associated with pneumonia, cellulitis, osteomyelitis, septic arthritis, infective endocarditis, and pyelonephritis, and 7% of patients presented with septic shock. The most common co-morbidities included hypertension, diabetes mellitus, and coronary artery disease. Mortality rate in this group was 15% (17/113) and the most common resistant antibiotics included tetracycline (61%), erythromycin (39%), clindamycin (31%), azithromycin (31%), and clarithromycin (31%).

Conclusion. GBS infections continue to rise, particularly in patients with significant co-morbidities leading to recurrent infections, amputations, or even death. Antibiotic resistance is increasing, and currently there are only a few options available for treatment. Therefore, it is imperative that more attention be placed on the prevention and treatment of GBS infections.

Disclosures. **All authors:** No reported disclosures.

739. Outcomes and pharmacoeconomic analysis of a home intravenous antibiotic infusion program in veterans

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Background. The implementation of outpatient parenteral antimicrobial therapy (OPAT) programs has increased due to the benefits of reduced cost with equivalent clinical outcomes compared to inpatient care. The purpose of this study is to evaluate the outcomes, both efficacy and adverse effects, of our program. Secondarily, a pharmacoeconomic analysis was performed to compare costs of the program to inpatient hosiptal care or rehabilitation.

Methods. This study is a retrospective chart review of 98 courses of OPAT between April 2011 and July 2013 to determine success rate and risk factors for failure. Clinical failures were defined as readmission during therapy, readmission within 3 months after discontinuation, or death. Failure due to adverse drug event (ADE) was defined as premature discontinuation, antibiotic switch, or readmission due to ADE. Baseline characteristics and program specific data were analyzed to determine variables that may affect outcome. Statistically significant variables were built into a multivariate logistic regression model to determine factors predictive of OPAT failure. A pharmacoeconomic analysis of this program was performed using billing records.

Results. Overall there were 43 failures (43.9%) and 55 successes (56.1%). Of the total failures, 27.9% were due to ADE, 25.6% to therapy failure, 34.9% to comorbidities, and 11.6% to miscellaneous causes. In the multivariate analysis, shorter duration of therapy was associated with a higher chance of failure ($p = 0.0003$). Eosinophilia was also a predictor of failure ($p = 0.0026$). The total cost of the program was $610,344. When compared to inpatient or rehabilitation care during the same period, the cost savings was $10,201,386 or $2,657,531, respectively.

Conclusion. OPAT is becoming an increasingly important option that is safe and effective for managing patients who require long-term use of intravenous antimicrobials. In our study, patients tolerated OPAT well, with a low number of failures due to ADE. Eosinophilia and shorter duration of treatment were associated with higher rates of failure. The clinical outcomes and cost savings of our program demonstrate that OPAT can be a viable alternative to long-term inpatient antimicrobial therapy.

Disclosures. **All authors:** No reported disclosures.

740. Hospital Avoidance Utilizing an ID Supervised OPAT Program

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Background. Evaluate the effectiveness of an infectious disease physician managed outpatient antibiotic therapy (OPAT) program.

Methods. A retrospective chart review of 3754 patients from August 2011 through July 2013 who received intravenous OPAT through our program. Patients were either initiated in the hospital (HI) or in the office (OI).

Results. 3754 patients were initiated or continued on IV antibiotics for 3 days or longer in the outpatient setting after evaluation by an infectious disease (ID) specialist. Evaluated therapy was delivered exclusively in the outpatient setting. The age of patients ranged from 2-99 years old (average 60). Predominant diagnoses were (Bone/Joint) B/J: 30.1%, (Skin/Soft Tissue) S/ST: 25%, Abscess: 15.2%, UTI: 10.1%. Most common antibiotics were Ertapenem: 26.7%, Daptomycin: 25%, Ceftriaxone: 24.7 %, Vancomycin: 24.5%. 524 patients required at least 2 antibiotics during therapy. Duration of therapy for specific diagnoses: B/J: 34.7 days, S/ST: 14.22 days, UTI: 11.8 days, Abscess: 22.9 days. Outcomes were defined as success, modified success and failure. Success was defined as cure without relapse or admission due to primary infectious diagnosis. Modified success was defined as success with line complications or adverse drug reactions but without hospital admission. Failure was defined as relapse within 30 days of therapy completion or hospitalization due to progression of primary infection or treatment complication.

Failures were seen in 200 patients (5.33%), with 91 relapses (2.42%), 66 primary infection progressions (1.76%), and 43 admissions due to therapeutic complications (1.15%). Relapses were more commonly seen in OI and primary infection progressions in HI patients. Overall cure rates were 94.67%. Total number of patients requiring hospitalization after admission to our program was 109 (2.9%).

Conclusion. An ID physician supervised OPAT program is safe, efficient, and cost effective. With the continued push for alternatives to inpatient care, it becomes increasingly important for ID physicians to play a role in outpatient care to optimize outcomes, reduce hospital utilization, minimize complications, and maximize cost containment. This program will meet the needs of patients, payers, and healthcare facilities as healthcare reform continues.

Disclosures. **R. Petrak**, HHI Infusion: Board Member, Consulting fee **R. Fliegelman**, HHI Infusion: Shareholder, Dividends

741. Management of Hepatitis C Among Infectious Diseases Physicians: Current Practice and Opinions

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Background. Hepatitis C (HCV) is a prevalent cause of morbidity and mortality. Updated screening guidelines, public awareness campaigns, and new direct-acting antiviral agents are likely to increase the number of patients seeking HCV care. Infectious diseases (ID) physicians have been identified as a group well suited to manage HCV, but the current and anticipated role of ID physicians has not been sufficiently evaluated.

Methods. Adult ID physicians were surveyed regarding their opinions and current practices related to HCV care through the Emerging Infections Network (EIN) via a 10-question survey.

Results. Of 1,172 EIN members in the U.S., Canada, and Puerto Rico, 550 (47%) responded. Most (71%) responded that ID physicians should evaluate and/or treat all HCV infections with gastroenterology/hepatology support, while a minority (25%) responded that ID physicians should only evaluate and/or treat patients with mild-moderate liver fibrosis or HIV co-infection. Overall, 54% of respondents currently evaluate and/or treat HCV infection in some capacity, either as HCV mono-infection (40%) and/or HIV/HCV co-infection (47%). Fifty-two percent of physicians who do not currently evaluate and/or treat HCV mono-infection indicated interest in doing so in the future. Factors influencing this decision include clinical capacity/infrastructure, interferon-free regimens for all genotypes, and training/experience. Respondents who do not plan to evaluate and/or treat HCV mono-infection in the future (27%) most commonly cited insufficient capacity/infrastructure, lack of desire, and inadequate training/experience as their rationale. Most ID physicians (61%) did not feel that graduate medical education prepared them to evaluate and/or treat HCV, and members indicated a need for a broad range of training resources.

Conclusion. More than 90% of respondents believe that ID physicians should be active in HCV management. The majority of ID physicians who wish to manage HCV mono-infection already provide this service, although many may increase this area of their practice. Expanding graduate medical education, emphasizing continuing medical education, and developing novel management paradigms will be necessary to optimize HCV care in the future.

Disclosures. **All authors:** No reported disclosures.

742. Evaluation of Anti-Tuberculosis Medication Errors at an Urban University Hospital

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Background. Combination therapy with Isoniazid, a Rifamycin, Pyrazinamide and Ethambutol is the standard of care for active tuberculosis (TB) treatment. Errors in medication administration could lead to inadvertent underdosing and resistance development, or significant side effects with overdosing. Given the recent nationwide focus on medication errors we attempted to establish the incidence of TB medication errors at University Hospital in Newark, NJ, a community with a relatively high prevalence of TB compared with the rest of the United States.

Methods. A retrospective review of anti-TB medications prescribed during admissions between July 2010 - June 2013 was conducted at University Hospital in Newark, NJ. Data was compared to the 2003 CDC guidelines for TB management. Medication errors were classified as improper drug regimen, incorrect dosing, incorrect medication adjustment for kidney and liver dysfunction and errors associated with concomitant highly active anti-retroviral therapy (HAART) use. We also categorized errors by consulting and admitting service at time of initiation.

Results. A total of 72 admissions withsuspected, active TB were reviewed during the study period. 42 admissions (58%) had at least one error. Of the 63 total errors identified, the most common errors involved incorrect dosing of pyrazinamide (45%) followed by Ethambutol (25%). Of the 19 patients on concomitant HAART therapy, 37% were dosed incorrectly. Of the three patients in our study with creatinine clearance < 30 ml/minute, not one had appropriate renal dosing. Medication error rate was not significantly different whether the patient had an Infectious Disease (ID) consult (63.6%), a Pulmonology consult (57.4%), or both (61.3%).

Conclusion. TB medication error rates are high among inpatients with suspected active TB despite frequent practice exposure. While this is the first recent study to evaluate inpatient anti-TB medication errors, our findings are consistent with those seen in studies of HIV medication errors at this institution and nationwide. The development of certain interventions, such as EMR reminders or mandatory pharmacist consults, could potentially reduce this error rate in the future.

Disclosures. **All authors:** No reported disclosures.

743. Development of a smartphone-based physician decision tool for common pediatric infectious conditions

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Session: 105. Clinical Practice Issues
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Background. Smartphones have emerged as important consumer and business devices for physicians. However, little empiric evidence exists regarding physicians' use of smartphone apps for clinical purposes. We sought to determine the feasibility of developing and implementing a smartphone-based app for managing febrile infants <60 days old and community-acquired pneumonia (CAP) and to evaluate trends in utilization of this app after release.

Figure 1: Users and use of app over time

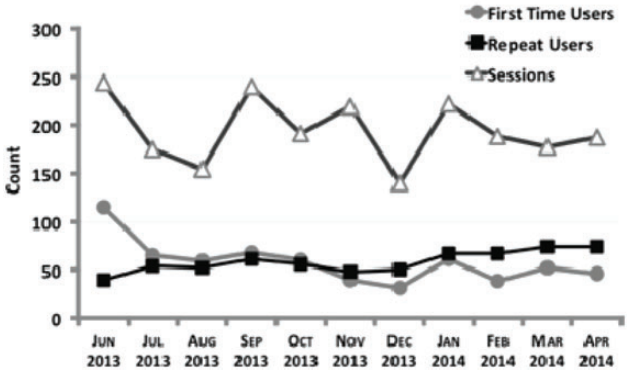
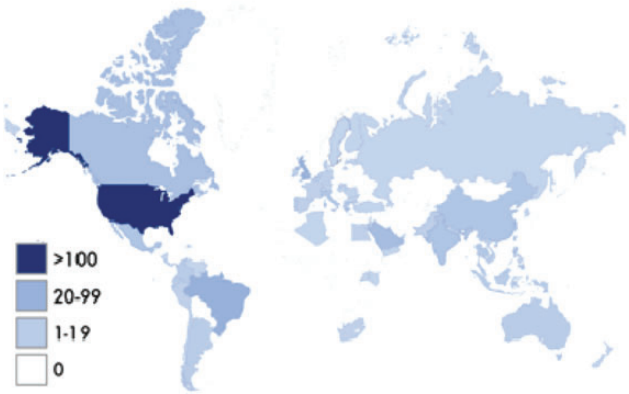


Figure 2: Total number of downloads by country



Methods. We identified select pediatric conditions among existing guidelines at our hospital for inclusion in the app. An initial search for private software developers was conducted. After discussing the project with these potential partners, formal bids were submitted to us. Based on cost, design values, project vision, and availability, we selected an appropriate developer. Wireframes (visually simplified schematics) were created and submitted to the developer to guide app creation. We selected a cohort of beta testers from volunteers at our hospital. Betas (or "draft" versions) were distributed to our testers via TestFlight. Based on testers' feedback, the app was revised. The app was released worldwide in Apple's iTunes App Store in June 2013; available as a free download. We collected download data from Apple's developer portal and usage data using embedded analytics code from Apsalar.

Results. Since release, the app has been downloaded 744 times and used 2,137 times (Figure 1). The app was most downloaded in its first month, representing 22% of total downloads. The app was most popular in the US (47% of total downloads) followed by Brazil, the United Kingdom, and Saudi Arabia (Figure 2). Users average 2 sessions per month; the average session length is 33.6 seconds. Users most frequently accessed information for CAP, specifically antibiotic choices for inpatient treatment of complicated pneumonia (194 uses) and guidance for diagnostic radiology (124 uses) and laboratory (121 uses) choices. A checklist for assessing HSV risk was the most commonly accessed (94 uses) component of the febrile infant guideline.

Conclusion. Smartphone apps represent a mechanism for worldwide dissemination of evidence-based recommendations.

Disclosures. **J. G. Newland**, Pfizer: Grant Investigator, Grant recipient

744. Apps for ID: A Regularly Updated Database of iPhone and iPad Apps for Infectious Disease Physicians

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Background. Smartphone and tablet apps are an important tool for infectious disease physicians, hospital epidemiologists, and infection preventionists. However, discovering and evaluating infectious disease-related apps is difficult. The app store changes too quickly for manual systematic review of apps by experts to be practical, and we are not aware of any regularly-updated, high-quality resources listing relevant apps.

Methods. We have created a searchable database of all apps in the Apple App Store, where iPhone and iPad apps are sold. By searching this database with a pre-programmed query, we systematically generated a list of infectious disease-related apps sorted by relevance. This list of apps was then manually curated to remove any irrelevant apps.

The curated app list is automatically and systematically updated each month to include new apps, and is then published on a public website: http://purl.org/geco/id-apps. It is searchable and allows physicians, nurses, and other domain experts to post their own reviews of listed apps.

Results. Out of more than 1,100,000 apps in the Apple App Store, our query identified 2,654 apps sorted by relevance. 14 out of 20 infectious disease-specific apps previously identified by Moodley et al. were listed in the top 200 results from our database. In the top 30 results, 2 were not relevant to infectious diseases and 1 was not in English; these were manually removed. The top 3 apps included *Infections* (antimicrobial prescribing guidelines), *CDC Antibiotic Guidelines*, and *Infection Control Pocketbook*.

Conclusion. We created a list of infectious disease apps for physicians that will be kept up-to-date through an automatic process. This service will allow physicians to more easily find phone and tablet apps related to infectious diseases.

Disclosures. **All authors:** No reported disclosures.

745. Risk of Peripheral Blood Eosinophilia and Hypersensitivity Reactions among Patients Receiving Outpatient Parenteral Antibiotics

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Background. Drug-induced peripheral eosinophilia (EOS) complicates antimicrobial therapy, though little is known about its frequency and implications. Using a population of monitored outpatients on parenteral antibiotics, we aimed to determine the frequency of drug-induced EOS and risk of subsequent hypersensitivity reactions (HSR).

Methods. We evaluated a prospective cohort from the Outpatient Parenteral Antimicrobial Therapy program consisting of discharged inpatients evaluated by Infectious Disease consultants beginning therapy from September 1, 2012-December 31, 2013 and monitored during prescribed intravenous antibiotic therapy (>2 weeks) with at least one differential blood count. We considered whether age or gender was associated with EOS, defined as an absolute eosinophil count (AEC) ≥500/mL. We examined the association of EOS with subsequent sign of HSR, including: documented rash; liver injury (new ALT > 100U/L); and renal injury (CrCL increase >0.5mg/dL or 50% of baseline). Relative risk was calculated from binomial regression with a log link

accounting for periods before and after onset of EOS, defined as 5 days before EOS detection.

Results. Of the 824 patients, 60% were male with median age 60y and median duration of therapy 41d (IQR: 31-45d). Of these, 210 (25%) developed EOS with a median peak AEC of 726/mL (IQR: 594-990/mL, range: 500-8,610/mL). Occurrence of EOS was associated with greater age (median: 64y vs 59y, p<0.001), but not gender (p>0.25). There were subsequent signs of HSR in 65/210 (31%) of patients with EOS, including rash (N = 32), renal injury (N = 31), and liver injury (N = 13). Once patients develop EOS, compared to patients who never develop EOS, they are at increased risk of developing rash (15.2% vs 6.0%, p < 0.001; RR 3.2, 95% CI 2.0,5.0;) and possibly renal injury (14.8% vs 10.1%, p = 0.08; RR 1.8, 95%CI 1.2, 2.7), but not liver injury (6.2% vs 6.7%, p > 0.5; RR 1.05, 95%CI 0.58, 1.9).

Conclusion. Eosinophilia is a common complication of extended parenteral antimicrobial therapy. A majority of patients with EOS do not develop signs of an HSR. However, EOS confers an over 3-fold risk of developing a rash and may increase the risk of renal injury. Further studies are needed to examine whether patients with EOS have a greater risk of renal or liver injury.

Disclosures. **All authors:** No reported disclosures.

746. Tolerability of Cephalosporins and Carbapenems in Patients with Reported Penicillin Allergies in a Real World Setting

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Background. Practitioners have historically avoided cephalosporins and carbapenems in penicillin allergic patients. Despite recent literature suggesting a lower cross-sensitivity than originally reported; practitioners continue to avoid cephalosporins and carbapenems in this patient population. The purpose of this study is to evaluate the tolerability of cephalosporins and carbapenems in patients with reported penicillin allergies in a real world setting.

Methods. A retrospective study was performed using de-identified information from patient medical records. Patients were excluded if a cephalosporin or carbapenem allergy was reported prior to receiving the antibiotic, an unspecified beta-lactam allergy was listed, or a medication to treat an allergic reaction (steroids, diphenhydramine, or IM epinephrine), were received two hours prior to receiving the antibiotic. Cross-reactions were determined if the antibiotic was discontinued and either received a medication to treat an allergic reaction or an allergy was added to their patient profile.

Results. Five hundred patients were included (n = 480 Cephalosporins, n= 20 Carbapenems) and 20 met the reaction criteria resulting in a prevalence of 4% cross-sensitivity for all included patients, and 4.2% (n = 20) for cephalosporins and 0% (n = 0) for carbapenems. Reported penicillin allergy severity and the rate of reaction were found to be statistically significant (p value 0.035). When the variables gender, antibiotic received, and age were held at fixed values, andthe prior penicillin allergy reaction was listed as severe the odds ratio for another reaction was 6.6 (p-value 0.032, 95% CI 1.17-37.66) and 5.9 for mild (p-value 0.021, 95% CI 1.31-26.95).

Conclusion. Despite the limitations of a de-identified, retrospective study the results show a low cross-reactivity prevalence rate and the limited reactions that occur were mild in nature. Giving a cephalosporin or carbapenem to patients with reported penicillin allergies appears to be well tolerated in a real world setting.

Disclosures. **All authors:** No reported disclosures.

747. Implementation of weight-based blood culture collection in pediatric hematology/oncology patients

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Background. Several studies have shown that collecting larger blood volumes improves bacteremia detection in children. In this study, we assessed existing blood culture practices for hematology/oncology patients in a pediatric hospital, and through a multidisciplinary approach formulated institutional guidelines to optimize blood volume and minimize frequency of blood draws for blood culture.

Methods. We assessed frequency and volume of blood culture sets, patient weights, and culture results for routine blood cultures from pediatric hematology/oncology patients over six months at Lucile Packard Children's Hospital. We then implemented weight-based blood culture collection criteria and defined the frequency of follow-up testing to one culture set at 24 hours after presentation, unless otherwise indicated. The guidelines were re-enforced through educational activities with nursing staff and treating physicians. The efficacy of the intervention was monitored over the following four months.

Results. During the pre-intervention period, patients were undergoing daily draws regardless of prior blood culture results and 35% of blood culture sets did not meet weight-based criteria. Cultures on Day 1 captured nearly all patients with true pathogens, while positivity on subsequent days was frequently due to contaminants. After the intervention, the average number of follow-up cultures for the unit decreased from 131.5/month to 66.3/month, whereas the average number of cultures on the day of presentation (Day 1) did not change (62.2 vs 56.8/month). The proportion of positives that likely represent skin microbiota contaminants also decreased. Additionally, blood culture sets with sufficient volumes based on weight-based criteria increased from 65% in the month before the intervention to 85% in the following year.

Conclusion. One-time weight-based blood culture is sufficient for recovery of blood cultures with true pathogens in a pediatric hematology/oncology population. Evidence-based institutional policy was able to achieve optimized blood volume and minimized frequency of blood culture.

Disclosures. **All authors:** No reported disclosures.

748. Outpatient Parenteral Antimicrobial Therapy (OPAT) with Continuous Infusions by Elastomeric Infusion Devices in Japan, as an Effective Tool for Better Antimicrobial Stewardship

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Background. Once-daily antimicrobials such as ceftriaxone are frequently used for OPAT in many countries, however those agents tend to be overused due to their convenience. Our infectious diseases team implemented the new OPAT project with continuous infusion by elastomeric infusion devices in July 2012 and has expanded it with support of homecare services. The aim of this study is to review our project at Kameda Medical Center after 22 months of operation.

Methods. We retrospectively collected data about age, sex, diagnosis, organisms, types of OPAT (hospital OPAT or homecare OPAT), antimicrobials, treatment duration, bed-days saved, outcome, readmission rate and estimated cost reductions of all patients who were treated by OPAT with continuous infusions from July 2012 to April 2014.

Results. 20 patients were treated by OPAT with continuous infusions by elastomeric infusion devices during the study term. The median age was 62 years (range 15-82). 15 patients (75%) were treated by hospital OPAT, and 5 (25%) treated by homecare OPAT. The most common diagnosis was osteomyelitis (35%), followed by soft tissue infection (20%). The prevalence of bacteremia was 60%. The most commonly targeted organism was methicillin-sensitive *Staphylococcus aureus* (55%). Cefazolin was used most frequently (60%), followed by Penicillin G (15%). The median OPAT days was 15 (range 4-29 days). Total bed days saved was 311. Peripheral inserted central catheter (PICC) was inserted for all patients and only one had to change PICC during the treatment. Only one patient discontinued OPAT due to leukocytopenia. 18 patients were cured and 2 were improved. No patient needed readmission. The estimated medical cost reduction was about 2.6 million yen, that is approximately 25 thousand US dollars.

Conclusion. Our OPAT project with continuous infusions by elastomeric infusion devices successfully used first-line narrow spectrum antimicrobials for outpatients, which avoids prescribing unnecessary once-daily antimicrobials with broader spectrum. Our experience shows OPAT with continuous infusion is safe and feasible practice not only for efficient bed utilizations and medical cost savings but also for better antimicrobial stewardship.

Disclosures. **All authors:** No reported disclosures.

749. Validation of the Problem List for Real-Time Identification of Patients with Pneumonia for Stewardship Intervention

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Background. In-hospital stewardship interventions require identifying at-risk patients at the point of care. Patients with pneumonia (PNA) are often targeted for stewardship interventions. One way to identify patients with PNA in real-time is to use the electronic problem list (PL), a clinician-maintained list of a patient's medical issues that resides within the electronic health record. The reliability of the PL for identifying patients with PNA is unknown. This study had two objectives: 1. Determine the reliability of the PL for detecting patients with PNA. 2. Assess the potential benefit of in-hospital stewardship interventions for PNA patients.

Methods. All data were collected at the Ohio State University. To assess the reliability of the PL we calculated the percentage of patients with PNA on their PL who fit a clinical definition of PNA, and, separately, the percentage of patients with a primary discharge diagnosis of PNA who had PNA on their PL. Two infectious diseases

physicians reviewed each of these cases to determine whether a stewardship intervention could have been made. Potential interventions were categorized into empiric antibiotic choice, duration of therapy, or targeted therapy.

Results. Among consecutive patients with PNA on their PL, 79% (70/89) met CDC criteria for PNA. Figure 1 details those who did not. Of 53 patients with a primary discharge diagnosis of PNA, 28 (53%) had PNA on their PL during hospitalization. These 53 patients were further categorized as having community-acquired PNA (CAP) or healthcare associated PNA (HCAP). Overall, a stewardship intervention could have been made in 48% of those with CAP and 64% of those with HCAP. The intervention category most commonly identified was duration of therapy for HCAP and empiric therapy for CAP (Figure 2).

Figure 1: Cases not meeting the standard definition for pneumonia

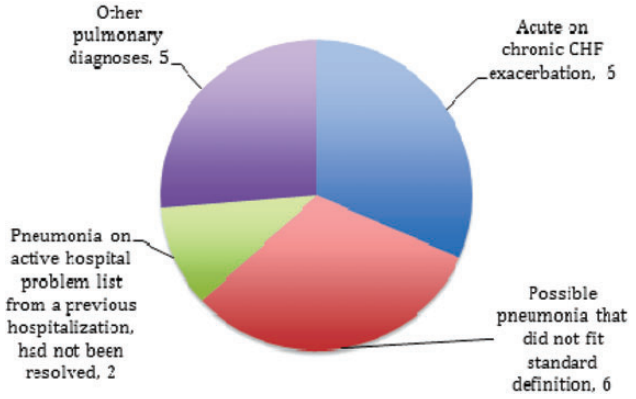
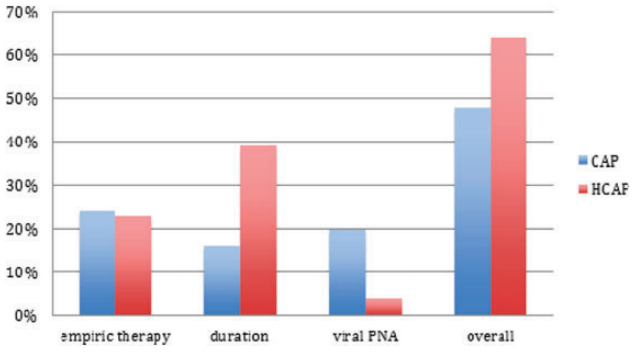


Figure 2: Potential stewardship interventions



Conclusion. We found that patients with PNA on their PL had clinically significant PNA in over 75% of cases. However, among those patients discharged with a diagnosis of PNA only about half had PNA documented on their PL. The lack of PL sensitivity for capturing PNA patients suggests a need to improve PL quality prior to using it for real-time interventions. Our study also demonstrates many potential opportunities for real-time stewardship intervention for patients with PNA.

Disclosures. **All authors:** No reported disclosures.

750. Effectiveness, Safety, and Impact on Healthcare Decongestion by a Busy Canadian Infusion Centre for Outpatient Parenteral Antimicrobial Therapy

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Background. Outpatient Parenteral Antimicrobial Therapy (OPAT) provides intravenous (IV) antibiotic therapy to patients in an ambulatory setting. Typically OPAT is overseen by Emergency Room (ER) physicians. However, in 2011 a standalone infusion center was created to decongest the Surrey Memorial Hospital ER, the second busiest in Canada. The infusion centre is staffed by infectious diseases (ID) specialists who oversee care with a multidisciplinary care team. This study describes and evaluates the infusion center with respect to safety, efficacy, antibiotic de-escalation, and ability to decongest the ER.

Methods. This retrospective observational study evaluated patients treated at the infusion centre between October 1, 2012 and September 30, 2013. Six hundred patients registered in the infusion centre were randomly selected. For subjects meeting inclusion and exclusion criteria, medical records were reviewed for demographics, clinical information, microbiology, antibiotic usage, and outcomes. Treatment success was defined as improvement in referral condition at end of therapy without relapse or hospital admission within 30 days of discharge.

Results. During the study period, 1900 patients were referred to the infusion centre. Of the 600 patients, 523 met inclusion and exclusion criteria. The most common sites of infection were skin and soft tissue (44.8%), urinary tract (16.3%), and oral/ear-nose-throat (9.0%). Mean duration of therapy at the infusion centre was 6.1 days; resulting in 3456 patient-days diverted from ER and inpatient beds. In addition, 39.1% of episodes had discontinuation or oral step down of their antibiotic regimen. Of the 503 episodes with outcome data, treatment success was found in 414 episodes (82.3%). Mortality rate was 0.6%. Adverse drug reaction rate was 7.8/1,000 OPAT patient-days, with no *C. difficile* or serious IV line complications.

Conclusion. The infusion centre model of OPAT is a safe and effective means of delivering IV antibiotics. It has shown significant impact on ER decongestion and potentially reduced unnecessary hospital admissions, which may lead to significant cost savings. In addition, antibiotic stewardship was achieved with early de-escalation of antibiotics.

Disclosures. **All authors:** No reported disclosures.

751. Outpatient Parenteral Antimicrobial Therapy (OPAT) Outcomes at a Tertiary Care Hospital

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Background. The practice of OPAT became widespread with demonstration of its safety in selected patients. However, with concerted efforts to reduce hospital lengths of stay, there is currently no selection for OPAT. Virtually every patient is a potential candidate for OPAT. Data on OPAT outcomes with unselected patients are very limited. The purpose of this study was to evaluate clinical outcomes and complications in an unselected cohort of patients treated with OPAT at a tertiary care hospital.

Methods. All OPAT courses at Cleveland Clinic over one calendar year were identified from the institution's OPAT registry. For each treatment course, outcomes at the end of the treatment course were abstracted through review of the electronic medical record. ED visits and hospital readmissions while on OPAT were enumerated. A successful clinical outcome was defined as cure, successful suppression or improvement at the end of therapy.

Results. From January 1, 2013 to January 1, 2014, 3162 OPAT courses were administered at Cleveland Clinic. The total number of OPAT days was 69545. The treatment sites were home (62%), facilities (34%), dialysis centers (3%) and infusion centers (<1%). The vascular access device was a PICC in 2340 instances (74%). The treatment outcome was undefined in 655 (21%) courses because of early termination of treatment. The outcomes in the remaining 2507 OPAT courses were as follows: clinical cure 1450 (58%), improved 326 (13%), successfully suppressed 231 (9%), failed therapy 24 (1%) and unknown 476 (19%). About 15% of OPAT courses were complicated by at least one ED visit and 21% were interrupted by rehospitalization, the latter occurring a mean of 16 days after discharge from hospital.

Conclusion. Among all patients discharged from hospital on OPAT from a tertiary care hospital, at least 80% of patients who complete the treatment course have a successful clinical outcome. ED visits and hospital readmission are common.

Disclosures. **N. Shrestha**, Forest: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; The Medicines Company: Scientific Advisor, Consulting fee **S. J. Rehm**, Pfizer: Scientific Advisor, Consulting fee; Merck: Scientific Advisor, Consulting fee

752. Assessment of Aminoglycoside Dosing at a Large Academic Medical Center

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Background. Intravenous aminoglycoside (AG) dosing is complex and highly individualized based on indication, patient's age, and renal function. Protocols available at study site guide dosing of AGs. This study assesses adherence to current protocols and investigates efforts needed to optimize AG dosing.

Methods. 100 consecutive patients who received AG (gentamicin, tobramycin, or amikacin) from July-August 2013 were included. Patients were excluded if AG given for peri-operative prophylaxis, non-TB mycobacterium, or received AG immediately prior to admission. Dosing was classified as optimal if in accordance with dosing protocols. Dosing weight included actual body weight, unless obese, then adjusted body weight was used. Peak, trough, and random levels and associated dose adjustments

were assessed. AG-induced nephrotoxicity per RIFLE criteria was evaluated in patients receiving ≥5 days therapy.

Results. Of 100 patients, 40% received gentamicin, 35% tobramycin, and 25% amikacin. 57% of orders occurred in an ICU setting. Most common infections were sepsis (50%), respiratory (16%), and intra-abdominal (9%). Median duration was 1 day (IQR 1-2.25). Majority of orders (48%) used traditional interval. Total of 62 orders were adherent to protocol for both dose and frequency. 35% of orders contained doses not according to protocol (14% of doses above and 21% of doses below protocol), while 2% contained non-protocol frequency and 1% contained frequency plus dose not according to protocol. 93% of doses higher than protocol were in obese patients. A total of 67 levels were ordered for 35 patients, with a majority (63%) being random levels. Of peak and trough levels, 38% and 65% were within therapeutic range. Dose adjustments occurred in 4 orders, 75% were deemed appropriate. Of 11 patients assessed for AG-induced nephrotoxicity, one (9%) met criteria. Thirty-three (68%) of 49 of traditional interval orders were eligible for extended interval dosing.

Conclusion. More than one-third of AG orders were non-adherent to available protocols. Majority of orders higher than protocol occurred in obese patients. AG-induced nephrotoxicity was rare. Investigation of clinical decision support to optimize initial AG dosing to achieve PK-PD targets is warranted.

Disclosures. **N. Shrestha**, Forest: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; The Medicines Company: Scientific Advisor, Consulting fee

753. Does Electronic Medication Reconciliation at Hospital Discharge Curb Distracted Prescribing for Outpatient Parenteral Antibiotic Therapy? A Pilot Study

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Background. Medication errors at hospital discharge are an important safety issue that can affect Outpatient Parenteral Antibiotic Therapy (OPAT) outcomes. Electronic medication reconciliation is a process to correct discrepancies at healthcare transitions. This study takes a novel approach of measuring types and prevalence of intravenous (IV) antibiotic errors at hospital discharge before and after the implementation of a mandatory electronic discharge medication reconciliation tool (EDMRT). This study was approved by Tufts Medical Center IRB.

Methods. A retrospective study at tertiary hospital where residents order discharge medications. One hundred pre-EDMRT and 100 post-EDMRT subjects were recruited at random from Tufts Medical Center's clinical OPAT program. Using infectious disease (ID) recommendations as gold standard, we compared each antibiotic listed in ID consultants' notes to the hospital discharge orders and defined any discrepancy as an error i.e., the outcome of interest. After generating crude odds ratio of discharge with antibiotic error in the post-EDMRT era compared to the pre-EDMRT era, multivariable regression was performed to account for potential confounding: day of discharge (weekend vs weekday), average years of practice by prescriber, type of inpatient service (medicine vs surgery) and total number of medications per subject.

Results. Prevalence of intravenous antibiotic errors decreased from 30 errors among 100 pre-EDMRT subjects to 15 errors among 100 post-EDMRT subjects. Dosages were the most common error type. Adjusted odds ratios (OR) of discharge with intravenous antibiotic error in the post-EDMRT era 0.39 (95% CI: 0.18, 0.87, $p = 0.021$) respectively compared to the pre-EDMRT era. Adjusted OR was nearly identical to crude OR (0.41). Number of discharge medications was associated with increased OR of discharge error, suggesting an underlying mechanism of "distracted prescribing".

Conclusion. Prevalence of antibiotic errors was significantly lower in the post-EDMRT era. Electronic medication reconciliation may be important to curb distracted prescribing. Our outcomes demonstrate the value of an OPAT program, which caught and addressed these errors in real-time as patients were discharged.

Disclosures. **All authors:** No reported disclosures.

754. Improving antibiotic delivery in the ICU

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Background. Surviving sepsis campaign issued a recommendation at Level 1B to administer antimicrobials within 1h in septic shock and, at 1C to septic patients without shock. The landmark paper by Kumar et al demonstrated that each hour of delay in antimicrobial administration over the ensuing 6 hrs was associated with an average decrease in survival of 7.6%.In a pilot study conducted at CCF ICU we identified that the delivery of antibiotics to septic patients was suboptimal (Average 3.2hrs, median 2.4hrs) The purpose of this study was to identify barriers to the delivery of first dose of antibiotics in the Cleveland Clinic Florida (CCF) ICU and implement measures to improve the antibiotic delivery.

Methods. We reviewed all the first dose orders placed in the intensive care units (ICUs) for 2 months between 2012 and 2013. We identified the current barriers to antibiotic delivery and implemented an educational intervention addressing these and stressing the importance of early antibiotic delivery.Data was then collected post intervention. Pre-operative prophylactic antibiotics were excluded.

Results. There were two major barriers identified in our ICUs for antibiotic delivery: 1) Delay in the antibiotic pick up from the pyxis and 2) Delay in the antibiotic pick up to administration to the patient. The average time from antibiotic order to administration to the patient in the ICUs, preintervention was 1.8 hrs (obtained over 3 months in 2012 and 2013). The median time for pharmacy authorization and release was 4 mins. The median time from pharmacy release to pick up from the pyxis was 1.00 hour. After the intervention the median time from pharmacy release to pick up dropped to 10 mins and the average time from antibiotic order to administration to the patient dropped to 1.3 hours ($P = 0.02$ CI 0.84 to 0.07)

Conclusion. Through dedicated educational intervention and collaboration with pharmacy and ICU nursing staff teams, we were able to decrease the time to pyxis pick up by 50 mins. Based on previous studies this simple educational intervention and team collaboration, could translate to decrease in mortality in septic patients in our ICUs.

Disclosures. **All authors:** No reported disclosures.

755. Comparison of Outpatient Antimicrobial Therapy (OPAT) in a Physician Office Infusion Center (POIC) vs Traditional Home Health Care (HHC)

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Background. OPAT allows patients (pts) with moderate to severe infections who do not require hospitalization to complete treatment using a POIC or traditional HHC. Safety and efficacy in both settings has previously been reported. Objective parameters in both settings as well as hospital (hosp) readmissions were evaluated based on location of care.

Methods. Medical records of 3 Infectious Disease (ID) practices for pts treated with OPAT from October 1 to December 31, 2013 were reviewed. Data extracted were demographics, diagnosis, comorbidities, antimicrobial usage, length of therapy (LOT), pathogens, laboratory monitoring, follow-up visits with ID physician, and 30-day hospital admission rates. Significant differences were determined using Chi square or Fisher's exact test ($p \leq 0.05$, significant).

Results. 172 pts in the POIC group were compared to 23 pts in the HHC group. The most frequent diagnosis in POIC was skin and soft tissue infections (SSTIs), (51%), respiratory (7%) and intra-abdominal (7%) infections; in HHC was SSTI (39%), osteomyelitis (22%) and septic arthritis (13%). Overall LOT was 24 and 26 days for the POIC and HHC group, respectively. Predominant antibiotics in POIC vs HHC pts were vancomycin (34% vs 26%), ceftriaxone (23% vs 39%) and cefazolin (20% vs 17%). Polymicrobial pathogens were reported for 11/99 pts in the POIC group and 3/18 in the HHC group. Laboratory monitoring was performed as ordered for 95% of POIC pts in contrast to 67% of HHC pts ($p < 0.001$). 96% of POIC pts complied with scheduled follow-up physician visits as opposed to 53% of HHC pts ($p < 0.001$). Hosp admissions within 30 days of OPAT initiation were reported for 12 POIC (7%) compared to 4 pts in the HHC group (17%) ($p = 0.03$). POIC admits included 5 worsening infections (3%), 2 catheter complications (1%), 2 drug-related adverse events (1%) and 3 conditions unrelated to infection (2%). In contrast, the HHC group had one worsening infection (4%), 2 unrelated to infection (9%) and one endocarditis patient (4%) was admitted with dehydration who eventually expired due to multi-organ system failure.

Conclusion. OPAT through POIC offers a closely supervised setting with significantly higher compliance of laboratory monitoring and follow-up physician visits accompanied by a significantly lower 30-day hospital admission rate compared to the HHC setting.

Disclosures. **J. S. Adams**, Diatherix Laboratories: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium

756. Emergency Department Visits During Outpatient Parenteral Antimicrobial Therapy (OPAT) Administered at Home

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Background. Although administration of OPAT at home is now common practice, there is a paucity of data on the frequency of emergency department (ED) visits during such treatment. The purpose of this study was to describe ED visits while on OPAT at home.

Methods. All OPAT courses carried out at home for patients at Cleveland Clinic over one calendar year were identified from the institution's OPAT registry. For each treatment course ED visits that occurred while on OPAT were sought in the electronic medical record.

Results. From January 1, 2013 to January 1, 2014, 1950 OPAT courses were carried out at home for 1464 patients, for a total of 43908 OPAT days. Mean patient age was 55 years. The vascular access device was a PICC in 1514 instances (78%). Of 257 ED visits, 117 (39%) were for OPAT-related complications (2.66 visits per 1,000 OPAT days). 98 (5%) OPAT courses had at least one ED visit for an OPAT-related problem, with a median time to first visit of 9 days after hospital discharge. Of the 117 OPAT-related ED visits, 17 (15%) were for antimicrobial adverse events (0.39 per 1,000 OPAT days) and 100 (85%) for vascular access complications (2.28 per 1,000 OPAT days). Five (30%) of 17 visits for antimicrobial adverse events and 20 (20%) of 100 ED visits for vascular access complications resulted in hospitalization.

Conclusion. About one in 20 patients receiving OPAT at home has at least one ED visit for an OPAT-related complication during the course of treatment. The majority of these ED visits do not result in hospitalization.

Disclosures. **N. Shrestha**, Forest: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; The Medicines Company: Scientific Advisor, Consulting fee **S. J. Rehm**, Pfizer: Scientific Advisor, Consulting fee; Merck: Scientific Advisor, Consulting fee

757. Comparison of Nephrotoxicity in Outpatient Parenteral Antimicrobial Therapy (OPAT) Patients Receiving Beta-lactams or Vancomycin

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Background. Outpatient parenteral antimicrobial therapy (OPAT) programs are growing as a cost-effective, safe, and practical way to treat patients with complicated infections outside of the hospital. The guidelines for therapeutic monitoring of vancomycin state that there is minimal difference in incidence of toxicity between vancomycin and beta-lactams. However, there are few studies describing the use of vancomycin in the OPAT setting.

Methods. Retrospective chart review was conducted of patients enrolled in the OPAT program who received vancomycin or a beta-lactam for an orthopedic or neurosurgical indication between 2008 and 2010. Inclusion criteria included patients 18 years or older with an intended treatment duration of at least two weeks. Exclusion criteria were patients who received both vancomycin and a beta-lactam.

Results. 267 patients were included. The median age was 53.7 (range 20.1-87.5) years in the beta-lactam group (n = 146) and 57.7 (range 20.4-86.8) years in the vancomycin group (n = 121). The anticipated duration of therapy was roughly equivalent (37 vs 38 days), as was the length of stay prior to discharge (7 vs 6 days). There was no significant difference in OPAT treatment setting, site of infection or comorbidities between the vancomycin and beta-lactam groups. Nephrotoxicity occurred more frequently in the vancomycin group than the beta-lactam group (13% vs 3%, $p = 0.001$). Patients with a body mass index (BMI) > 30 did not experience higher rates of vancomycin induced nephrotoxicity than those with a BMI < 30. In patients who experienced OPAT nephrotoxicity on vancomycin, there was no difference in the number of patients with prior kidney injury vs those without a history of kidney injury.

Conclusion. Rates of nephrotoxity were significantly higher in patients receiving vancomycin compared to patients receiving beta-lactams in the outpatient setting. The study was limited by sample size but further research should include identifying inpatient risk factors that correlate to development of nephrotoxicity in OPAT.

Disclosures. **All authors:** No reported disclosures.

758. Treatment Complications During Outpatient Parenteral Antimicrobial Therapy (OPAT) Administered at Home

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Background. OPAT is commonly administered at home. Such treatment has potential for the occurrence of antimicrobial adverse events (AEs) and vascular access complications that require clinical intervention. The purpose of this study was to examine adverse events and complications that occur during the course of OPAT at home.

Methods. All OPAT courses carried out at home for patients at Cleveland Clinic over one calendar year were identified from the institution's OPAT registry. AEs and vascular access complications that occurred during the treatment course were abstracted from the electronic medical record. Only AEs or complications that triggered a clinical intervention were included.

Results. From January 1, 2013 to January 1, 2014, 1464 patients received at 1950 OPAT courses at home, for a total of 43908 OPAT days of treatment. Mean patient age was 55 years. The most commonly prescribed antimicrobials were vancomycin (30% of courses), piperacillin-tazobactam (11%) and ceftriaxone (10%). 157 OPAT courses (8%) had at least one antimicrobial AE. A total of 216 antimicrobial AEs (4.92 per 1,000 OPAT days) were noted. The most common of these was a rash (25% of all AEs noted), followed by diarrhea (14%). The first antimicrobial AE occurred a median of 9.5 days after starting therapy. The vascular access device was a PICC in 1514 instances (78%). 176 OPAT courses (9%) had at least one vascular access complication. A total of 213 vascular access complications were noted in 176 OPAT courses. The first antimicrobial AE occurred a median of 10 days after starting therapy. The most common complication was occlusion (49%), followed by accidental dislodgement (14%). Thrombosis and line infection occurred in 15 (0.8%) and 7 (0.4%) of OPAT courses, respectively, at rates of 0.34 and 0.16 per 1,000 OPAT days.

Conclusion. During OPAT at home, 8% and 9% of OPAT courses, respectively, have at least one antimicrobial AE or vascular access complication requiring clinical intervention.

Disclosures. **N. Shrestha**, Forest: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; The Medicines Company: Scientific Advisor, Consulting fee **S. J. Rehm**, Pfizer: Scientific Advisor, Consulting fee; Merck: Scientific Advisor, Consulting fee

759. Patient-Captured Digital Images to Assess Post-operative Wounds for Infection: a pediatric ambulatory surgery cohort study

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Background. Digital images are being used with increasing frequency for remote clinical assessment. Given the need for post-discharge assessment of many surgical patients, digital images might become a tool to assess wounds for surgical site infections (SSI), particularly for patients who have undergone ambulatory surgical procedures and/or lack easy access to medical care.

Methods. We administered structured parental interviews 30 to 45 days after ambulatory surgery cases performed within a pediatric healthcare network over a 13-month period. Parental report of sending a digital image of their child's wound triggered a structured review of the electronic health record (EHR) for the presence of an image within the child's EHR and whether an action was taken by a clinician in response to the image.

Results. Of 4513 interviewed parents, 124 (2.7%) reported sending a clinician a digital image of their child's wound. The EHR of 94 (75.8%) of these patients contained a reference to a digital image, and only half (62 of 124) of EHR records contained an image file. Most of the digital images present in the EHR were sent after urologic (n = 61, 64.9%) and plastic surgery (n = 13, 13.8%). Images were taken a median of 5 days (IQR 10 days) after surgery. Of the 94 patients with an EHR reference to a digital image, most (n = 80, 85.1%) did not trigger an immediate action. Some patients, however, were given an appointment for an unscheduled follow-up visit (n = 7; 7.4%) or prescribed an antibiotic without an appointment (n = 4; 4.3%). One of the 94 patients with an EHR reference of a digital image ultimately met National Healthcare Safety Network criteria for an SSI. Most (57 of 62, 91.9%) of the digital images present within the EHR had been received by email.

Conclusion. Digital images are being sent by patients and used by clinicians for the remote assessment of surgical wounds. Future prospective studies should address the impact of this practice on patient care and the diagnosis of surgical site infections.

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760. Piperacillin/Tazobactam-Induced Adverse Drug Events in Pediatric Patients on Outpatient Parenteral Antimicrobial Therapy (OPAT)

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Background. Piperacillin/tazobactam is an ureidopenicillin (piperacillin) combined with a ß-lactamase inhibitor (tazobactam). We have noted an increased rate of suspected piperacillin/tazobactam-related adverse drug events (ADEs) compared to other antibiotics in patients on Outpatient Parenteral Antimicrobial Therapy (OPAT). We sought to compare ADEs in patients who received piperacillin/tazobactam vs other antibacterial agents.

Methods. Patients (< 18 years of age) who received antibacterial agents as OPAT from January 2010-December 2012 were included. Data collected included demographics, clinical features and ADEs documented during therapy (including abnormal signs/symptoms and abnormal lab values) and considered to be antibiotic-related if there was no other explanation along with resolution of symptoms or normalization of lab values upon discontinuation of the antibiotic.

Results. 106 patients (age range 2 months-17.9 years; median 10.5 years; 61 males) met inclusion criteria. 38 patients received piperacillin/tazobactam vs 68 patients received other antibacterial agents. The most common diagnoses treated with OPAT were perforated appendicitis (29%), pneumonia (18%), and osteomyelitis (13%). Of those who received piperacillin/tazobactam, 15 patients (39%) developed ADEs [most commonly fever (73%), transaminitis (67%), leukopenia (67%), neutropenia (67%), rising ESR and CRP (67%)] abdominal pain (40%), rash (20%), and vomiting (20%)], vs 3 patients (4%) who received other antibacterial agents ($p = <0.001$). 80% of patients had ADEs that included a constellation (3 or more) of clinical and laboratory features with a median time-to-ADEs of 17 days (range 7-23). 67% of patients with ADEs were hospitalized with a median length of stay of 4 days.

Conclusion. Patients receiving piperacillin/tazobactam in OPAT had a significantly increased risk of ADEs compared to other antibacterial agents. These events often manifested with a constellation of clinical findings that frequently were thought to be related to the primary diagnosis rather than ADEs, and often resulted in re-hospitalization and a change or cessation of therapy.

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761. A Comparison of Outpatient Parenteral (OP) Antibiotic Therapy (AT) Outcomes: Physician Office and Home Based Therapy

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Background. The use of OPAT has become a standard modality for patients requiring long term intravenous antibiotics. The delivery of OPAT can be at home or at an OP infusion center (IC). We reviewed outcomes in patients receiving OPAT at one IC (The PIIC Center) and at home.

Methods. A database reviewing outcomes for patients (N = 117 IC, N = 48 home) cared for by the authors in these settings was created with variables reviewed including: demographics, comorbidities, diagnosis, antimicrobials used and duration, type of access, referral site, adverse events, and outcomes. Success was defined as lack of relapse, emergency room (ER) visit, or readmission during OPAT and within 30 days of OPAT discharge. Modified success was defined as resolution of the original infection but with the development of another related infection (e.g., *C. difficile* or peripheral inserted catheter (PICC) infection) or a line complication (e.g., PICC thrombosis) not requiring ER visits or readmission.

Results. The baseline characteristics in both groups were similar with patients having 6.8 comorbidities per person. The most common diagnoses indicating use of OPAT were: skin, soft tissue, bone and joint, abscess, and urinary tract infections. Patients receiving OPAT at home were more likely to receive PICC lines (82% vs 21%) and have a longer duration of treatment (25 days vs 14 days) compared to patients receiving OPAT at the IC. Home OPAT patients often had issues with access (38% vs 8%) and had a 27% failure rate compared to 7% at the IC.

Conclusion. OPAT provided by the office based IC had better outcomes compared with OPAT provided at home.

Disclosures. **D. O'neill**, The PIIC Center: Owner, Salary **V. Kak**, Cubist: Speaker's Bureau, Speaker honorarium **D. Trimble**, The PIIC Center: Employee, Salary

762. Outpatient Parenteral Antimicrobial Therapy (OPAT) Treatment Center as Part of Integrated Care Delivery – Single-Center Experience from the First Three Years of Operation

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Background. To describe and evaluate the clinical experience of delivering outpatient antimicrobial therapy (OPAT) at the St. Vincent Outpatient Treatment Center (OTC) which, in partnership with Infectious Disease of Indiana, offers a unique model in its integrated care delivery, staffing, and monitoring practices.

Methods. A retrospective cohort from the first 3 years of OTC operation (January 2010 – December 2012) was assessed to describe patient characteristics, clinical characteristics, and outcome of hospital admission during OPAT treatment. The sample included those treated with antibiotics most frequently used by patients seen in the OTC - ceftriaxone, daptomycin, or ertapenem. Those on other antimicrobial therapy were excluded.

Results. Of 2,684 OPAT patients, 51% were male and the cohort had a mean age of 52 years. Most patients had commercial insurance (57%), followed by Medicare (29%), self-pay (9%), and Medicaid (4%). Patients were either diverted to OPAT from hospitalization (N = 1735, 65%) or initiated on OPAT, avoiding hospitalization (N = 949, 35%). The two groups differed modestly, most notably in age with means of 51 for OPAT post-hospital and 54 for OPAT only ($p < 0.001$). OPAT was delivered at the OTC (57%), self-administered (33%), or at an external site (9%). Antibiotic use was 39% daptomycin, 35% ertapenem, and 26% ceftriaxone. Diagnoses for which OPAT was prescribed included skin and soft tissue (50%); bone and joint (17%); intra-abdominal (7%); genitourinary (7%); sepsis, pulmonary/respiratory, device-related, endovascular, ear-nose-throat or other infection (5% or less each). Overall, there were 81 hospital admissions from OPAT (3.1%). Admissions were similar for both OPAT post-hospital and only groups (3.3% vs 2.5%, $p = 0.24$) and ranged from 1.6% for genitourinary to 11.1% for endovascular diagnoses. The average treatment duration, including any intervening hospitalization was 17 days, 17.5 and 15.8 days for the post-hospital and OPAT only groups respectively.

Conclusion. Once daily IV antibiotics are the most common therapies in this OPAT model. The unique model at the St. Vincent OTC demonstrates a type of care integration that potentially diverts patients to OPAT in order to reduce the number and length of hospitalizations required by patients.

Disclosures. **M. Bochan**, Merck and Co., Inc.: Investigator, Research support **A. Sung**, Merck and Co., Inc.: Research Contractor, Salary **S. Marcella**, Merck and Co., Inc.: Employee, Salary **Y. Xie**, Merck and Co.: Employee, Salary

763. Low Hospital Admission Rates Following Physician Office Infusion Center (POIC)-Based Outpatient Treatment with Intravenous Antibiotics (IVABs)

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Background. Current Centers for Medicare and Medicaid Services 30-day hospital (hosp) readmissions for all medical discharges are 16.1%, with many of these preventable. Outpatient antibiotic therapy (OPAT) has proven beneficial for patient (pt) safety and quality of care, however, little is known about hosp admissions following OPAT in a POIC. A recent study indicated a readmission rate of 26% for all OPAT settings. Our study investigates 30-day unplanned hosp admissions of pts treated with IVABs only through an Infectious Disease (ID) POIC.

Methods. 600 pts were retrospectively evaluated from centralized databases; 60 random pts from each of 10 POICs from January 1 to June 30, 2013. Pt demographics, diagnosis, comorbidities, drug therapy, emergency department (ED) visits and hosp admissions within 30 days of OPAT initiation. Comparison of unplanned admissions was done by Fisher's exact test. Risk factors for hosp admissions were assessed using odds ratios (OR).

Results. Altogether, 41 of 600 pts (6.8%) had unplanned admissions to the hosp within 30 days of receiving OPAT. Readmissions for previously hospitalized occurred in 32/404 pts (8%) and 9/196 pts (5%) were admitted following POIC-initiated OPAT ($p = 0.39$). For all admissions, 24 (59%) were for worsening infection, 3 (7%) for device-related issues, 5 (12%) for new or unrelated infections and 9 (22%) for reasons unrelated to infection. ED visits were reported for 38/600 pts (6.3%) with 40% resulting in hospitalization. Frequent diagnoses reported in pts admitted were bacteremia (27%), intra-abdominal (20%) and skin and skin structure infections (15%) with a mean length of treatment of 12, 14, and 11 days, respectively. Risk factors analyzed for hosp admissions were co-morbidities ≥ 3 (26/41pts; OR 9.1), prior 6 month hosp admissions (23/41; OR 6.7), age ≥ 60 years (22/41 pts; OR 6.08), obesity (12/41pts; OR 2.2), bacteremia (11/41 pts; OR 1.9), malignancy (10/41pts; OR 1.7), and diabetes (10/41pts; OR 1.7).

Conclusion. POIC-based OPAT following hosp discharge resulted in lower hosp readmission rates than indicated in current data. POIC-based OPAT without previous hospitalization resulted in even fewer hosp admissions. OPAT by an ID physician in an office-based setting provides highly effective, high quality therapy, leading to a reduction in costly hosp admissions and readmissions.

Disclosures. **F. S. Alvarado**, Pfizer: Speaker's Bureau, Speaker honorarium **H. B. Baker**, Cubist: Speaker's Bureau, Speaker honorarium

764. Risk Factors for Failure of Outpatient Parenteral Antimicrobial Therapy (OPAT) in the Management of *Staphylococcus aureus* Bacteremia (SAB)

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Background. *Staphylococcus aureus* bacteremia (SAB) requires prolonged intravenous antibiotic courses. Outpatient parenteral antimicrobial therapy (OPAT) is commonly used to complete these courses of therapy. While OPAT is generally considered safe and effective, treatment failures occur. We hypothesized that specific risk factors for treatment failure exist among our patient population.

Methods. To identify factors associated with treatment failure, a retrospective review of all patients receiving OPAT for SAB between January 2011-September 2013 at a large, tertiary-care Veterans Affairs (VA) medical center was conducted. Treatment failure was defined as incomplete therapy, therapy extension, infection relapse, or hospital admission or surgical intervention within 60 days of therapy completion. Chi-square and Student's t-test were used to analyze differences between those failing therapy and those who did not; multivariate logistic regression analysis was used to identify risk factors associated with treatment failure.

Results. Of 118 SAB patients treated with OPAT, 101 met inclusion criteria. Treatment failure occurred in 36 (35.6%) patients. In multivariate analysis, heart failure (OR 3.67; CI 1.13 – 12.0), previous OPAT (OR 14.1; CI 2.02 – 97.8), immunosuppression (OR 10.5; CI 1.74 – 63.3), and treatment with daptomycin (OR 9.56; CI 1.89 – 48.4) were independently associated with treatment failure. No statistically significant differences in failure rates were identified between OPAT settings: rates for home vs skilled nursing facility (SNF) vs the VA community living center (CLC) were 37%, 43%, and 24% respectively ($p = 0.33$).

Conclusion. In a high complexity veteran patient population, OPAT failure rates for SAB were consistent with those previously reported in the literature. Specific health factors were however associated with higher rates of failure. A nonsignificant trend toward lower failure rates was seen among OPAT patients in the CLC, a VA long-term-care facility possessing its own infectious diseases consultation service. Given the morbidity and cost of SAB treatment failures, similar analyses may benefit other large OPAT programs in order to prospectively optimize the local selection of patients and settings in which successful treatment will most likely occur.

Disclosures. **All authors:** No reported disclosures.

765. Impact of a Hospital Based Antibiotic Stewardship Team on Prescribing Fluroquinolones at a Long Term Care Facility

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Background. Overuse of fluroquinolones (FQ) in a long term care facility (LTCF) is associated with bacterial resistance and an increase incidence of *Clostridium difficile* infection (CDI). A hospital based antibiotic stewardship team (H-AST) has had an impact on decreasing the use of FQs in a hospital setting, but there is limited data on the impact of a hospital based team providing educational initiatives at an off-site LTCF.

Methods. A relationship was established between a H-AST and 520 bed LTCF. The H-AST focused on decreasing FQ use in asymptomatic bacteriuria (AB), skin soft tissue infections (SSTI), and respiratory tract infections (RTI). Interventions performed included: distribution of a LTCF specific UTI antibiogram, medical staff in-services, and family member education on the risk of antibiotic overuse. Baseline data was collected monthly from July 2012-March 2013 and intervention data was collected from July 2013-March 2014 and compared quarterly. FQ use was measured in defined daily doses per 1,000 patient days (DDD/1,000 PD). The relative percentage of FQ use compared to total antibiotic use (FQ DDD/Total antibiotic DDD) was also determined. Pearson's chi-squared test was performed. Rates of CDI, AB, SSTI, and RTI (cases/1,000 PD) were collected during the baseline and intervention period.

Results. During the 9 months prior to intervention, FQ quarterly use increased 51.4% (10.3 to 15.6 DDD/1,000 PD). Post intervention FQ use decreased 51.9% (15.8 to 7.6 DDD/1,000 PD). The relative percentage of FQ use compared to total antibiotic use decreased 6% from baseline (23% to 17%) $p = <0.05$. Ciprofloxacin had the greatest decline in DDD from baseline $p = <0.05$. CDI rates decreased by 7.6% in the intervention period. Infection rates of AB and RTIs decreased by 10.5% and 25% respectively and treatment rates of SSTIs increased by 11% when compared to baseline data.

Conclusion. The H-AST decreased FQ use by over 50% and significantly decreased FQ use relative to total antibiotic use at the LTCF by utilizing mainly educational initiatives. This significant decrease in FQ usage may also have an impact on antibacterial resistance rates and CDI in the future.

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766. Clinical Features and Outcome of Patients with Middle East Respiratory Syndrome-Coronavirus (MERS-CoV) Infection

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Background. The number of laboratory confirmed cases of Middle East Respiratory Syndrome-Corona Virus is increasing and has been associated with high mortality rate. Our aim is to describe clinical features and outcome of patients infected with MERS CoV in a tertiary hospital outbreak in Jeddah, Saudi Arabia.

Methods. We reviewed the medical records of 30 patients with confirmed MERS CoV infections during hospital outbreak between April 7 until April 30, 2014. We followed WHO definitions for confirmed MERS CoV infection.

Results. A total of 30 patients were diagnosed with confirmed MERS CoV infection. 16 patients were health care workers. The mean age was 43 years (SD 16.5). Seventeen patients were male (54.8%). Majority of patients N = 20 (66.7%) were symptomatic on presentation. Fever was the most presenting symptoms N = 20 (66.7%) followed by cough N = 18 (60%). Although only 10 patients (35.7%) reported shortness of breath on presentation, 27 patients (93.1%) had abnormal chest xary. In terms of laboratory findings, 13 patients (54.2%) had lymphopenia on presentation. Significant number of patients developed progressive respiratory disease; 9 patients (30%) required mechanical ventilation and 12 patients (38.7%) required ICU admission.

Conclusion. Fever and abnormal chest x ray were the most common clinical features in patients with MERS CoV infection. Significant number of MERS CoV patient's required mechanical ventilation and ICU admission.

Disclosures. **All authors:** No reported disclosures.

767. Association of Mortality with Leukocyte Distribution in Crimean-Congo Hemorrhagic Fever: Twelve Years Experience in A Retrospective Case Control Study

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Background. Crimean-Congo hemorrhagic fever (CCHF) is a life threatening illness. In this study we aimed to detect the effect of the leukocyte, lymphocyte and monocyte levels on the survival. To our knowledge this is first study analyzing the relationship between mortality and leukocyte distrubition.

Methods. A total of 220 patients were evaluated between 2002 and 2013 years retrospectively. Demographic, clinic and laboratory parameters of the fatal and non-fatal patients were compared statistically.

Results. The mean age of the patients was 50.21 ± 17.07 years (15-85) and the mortality rate was 16.4%. The most frequent symptoms were fever (88.2%), lack of appetite (79. %) and myalgia (75%). Of the 220 patients 29.5% had hemorrhages and 11.4% had somnolence. Most of the patients (75%) were working in animal husbandry and 63.6% had tick bite history. Mean duration of symptoms after tick bite was 3.87 ± 3.06 days. Mean hospitalization time (6.42 ± 3.06 days) was significantly shorter in fatal cases ($p < 0.001$). Univariate analysis revealed that hemorrhages (66,7 %), somnolence (47.2%), petechia 36.1% and ecchymoses 38.9% were significantly higher in fatal cases ($p < 0.001$). In multivariate analysis; somnolence, hemorrhages and diarrhea were independent factors for mortality (OR:36.5, OR:12.4 and OR: 5.9, respectively). In comparison of the first and third admission-day laboratory values, increase of leukocytes (WBC), lymphocytes and monocytes were significant in non-fatal cases ($p < 0.001$). ROC curve analysis revealed that if the first day WBC count was $\geq 2950/mm^3$, mortality rate could be predicted with 62.1% sensitivity and 33.1% specifity. In consideration of mean hospitalisation length in fatal cases (4.3 days), third-admission day leukocyte distributions were analyzed between the two groups. It was found that, increases of the neutrophils and decreases of the monocytes were independent risk factors in mortality. Although decreases of lymphocytes were significant in univariate analysis, there was no difference in multivariate analysis.

Conclusion. The depletion of monocyte and lymphocyte counts and the increase of neutrophils were correlated with poor outcome. This result suggests the importance of mononuclear immune response for survival in CCHF.

Disclosures. **All authors:** No reported disclosures.

768. Host Gene Polymorphisms and Susceptibility to Viral Enteropathogens in Children Living in The Gambia and Kenya

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Background. The Global Enteric Multicenter Study (GEMS) is a prospective case control study to determine pathogen specific diarrheal disease burden among children <5 years of age in Africa and Asia. Using samples from children in The Gambia and

Kenya, we conducted a gene candidate study that examined the association of the host DNA single nucleotide polymorphisms (SNPs) and specific viral enteropathogens rotavirus and norovirus causing diarrhea.

Methods. Stool specimens from moderate to severe diarrhea cases and their age, sex and area matched controls were examined for the presence of enteropathogens and host DNA SNPs (N = 144) in 26 genes that code for host proteins involved in pathogen attachment, inflammation, innate and acquired immune responses to enteropathogens. We analyzed the distribution of SNPs and compared cases vs controls according to enteropathogens identified. Comparisons were made using SNPSTATs software following the dominant model. Logistic regression model was used to adjust for potential confounders including site and age.

Results. Microbiological and genotype data were available in 1,164 subjects. In The Gambia, diarrhea due to norovirus was associated with SNP in *C3orf23* (69% vs 36%, OR = 4.0, CI = 1.1.5-13.7, P = 0.03), SNPs in *IL12B* (67% vs 32%, OR = 4.2, CI = 1.19-15, P = 0.025) and a SNP in *MBL* (29% vs 58%, OR = 0.3, CI = 0.08-0.9, P = 0.045) and diarrhea from rotavirus was associated with SNPs in *CD180* (88% vs 49%, OR = 8, CI = 1.66-35, P = 0.003). In Kenya, diarrhea from norovirus was associated with a SNP in *C3orf23* (71% vs 23%, OR = 8, CI = 1.4-42, P = 0.013), and SNPs in *LPLUNC* (50% vs15%, OR = 6, CI = 1.5-21, P = 0.012) and diarrhea from rotavirus was associated with *LPLUNC* (61% vs 40%, OR = 2.5, CI = 1.2-5.3, P = 0.011).

Conclusion. Distinct SNPs were associated with pathogen specific viral diarrhea in children under 5 years of age living in two African countries.

Disclosures. **All authors:** No reported disclosures.

769. Short Duration of Antimicrobial Treatment for Acute Cholangitis with Bacteremia due to Gram-negative Bacilli after the Publication of the Updated Tokyo Guidelines 2013 (TG13)

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Background. The optimal duration for acute cholangitis with bacteremia is unclear. We had treated all acute cholangitis cases with bacteremia at least for two weeks. However, TG13 recommended minimum duration of 2 weeks only when bacteremia with Gram-positive cocci is present. We have implemented shorter duration of antimicrobial treatment for acute cholangitis with bacteremia due to gram-negative bacilli since May 2013. The aim of this study was to validate our modified practice.

Methods. We collected the clinical information of all patients diagnosed as acute cholangitis with bacteremia from July 2012 to March 2014 using the electronic medical record at Kameda Medical Center. TG13 diagnostic criteria were used to confirm the diagnosis of acute cholangitis. The patients who had gram-positive bacteremia, biliary tract malignancies, complication of cholecystitis or hepatic abscesses, and did not receive endoscopic-retrograde cholangiopancreatography were excluded. Baseline characteristics of the patients, Pitt bacteremia score, TG13 severity index, the duration of antimicrobial treatment, 30-day mortality, and recurrence rate within 3 months were retrospectively compared before and after May 2013.

Results. A total of 224 episodes of acute cholangitis were treated during the study term and 96 fulfilled the case definitions. 42 episodes were treated before and 54 were treated after May 2013. There were no significant differences in baseline characteristics, Pitt bacteremia score and TG13 severity index. The duration of antimicrobial treatment was shorter (15.2 days vs 10.0 days; P < 0.001) in the patients treated after May 2013. 30-day mortality and recurrence rate did not significantly differ (5.1%, vs 0%; P = 0.17, 13.3% vs 3.3%; P = 0.19).

Conclusion. Our study suggests shorter duration of antimicrobial therapy seems adequate in treating acute cholangitis with bacteremia due to gram-negative bacilli once source of infection is controlled.

Disclosures. **All authors:** No reported disclosures.

770. Intra-abdominal Infections in Africa and The Middle East; A Systematic Review and Meta-analysis

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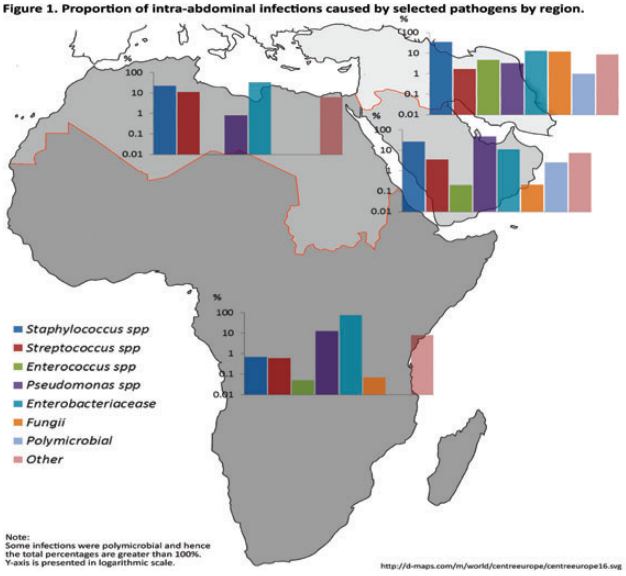
Background. Understanding the epidemiology of the intra-abdominal infections (IAIs) is important for clinical decision making. This was a systematic review and meta-analysis of IAIs studies in adults in Africa and Middle East (AFME) region.

Methods. PubMed and Medline-Plus were searched in September 2013 using prespecified keywords. Non-AFME, case reports, reviews, editorials and study protocols were excluded. Weighted averages with 95% confidence intervals were calculated and data were analyzed using Microsoft Excel and SAS 9.4 (SAS Institute, Cary, NC).

Results. A total of 220 IAI papers were included (47,796 individuals; 4,798 isolates). Complications were reported in 86 studies, severity of infection in 38 studies and mode of acquisition in 173 studies. Overall, 44.1% (37.7-50.5%) of IAI were caused by Gram-positive bacteria, 42.4% (35.0-49.8%) by Gram-negative bacteria and 7.1% (6.3-8.0%) were caused by fungi. Polymicrobial infection was documented in only 1.2% or IAIs. Regional prevalence of selected pathogens causing IAI in AFME is shown in Figure 1. Complicated IAI constituted 38.3% of IAIs in which the presence of complications was reported. The proportion of complicated IAI increased significantly over time (r= 0.33, $P < 0.01$). Furthermore, the proportion of IAIs caused by Gram-negative bacteria increased (r= 0.32, P< 0.01), while those caused by Gram-positive bacteria decreased (r= 0.45, $P < 0.001$) over time. Patients with complicated IAIs were significantly younger than those with uncomplicated IAIs (34.5 vs 38.3 years, $P < 0.02$), whereas patients with hospital-acquired IAIs were significantly older than those with community-acquired IAIs (43.5 vs 35.2 years, $P < 0.001$). Average length of hospital stay was 18.5 days for patients with peritonitis, 5.2 for appendicitis and 3.1 for surgical site infection ($P < 0.01$). The most commonly used antimicrobial agents were cephalosporins (31.8%), followed by extended-spectrum penicillins (29.4%), aminoglycosides (26.5%) and metronidazole (24.5%). Overall attributable mortality, which was reported in 45 studies, was relatively low at 4.1% (1.6-6.6%).

Figure 1. Proportion of intra-abdominal infections caused by selected pathogens by region.



Conclusion. Gram-negative bacteria are increasingly important causes of IAI in AFME with decreasing contribution of Gram-positive bacteria.

Disclosures. **All authors:** No reported disclosures.

771. Can Human Bocavirus mRNA Detection Differentiate Acute Infection from Viral Shedding?

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Background. Human Bocavirus (HBoV), a DNA virus in the family Parvoviridae, is frequently detected in patients with acute respiratory disease. However, it is also prevalent in asymptomatic children, thus its pathogenicity is unclear. We hypothesized that spliced viral capsid mRNA produced during active replication (i.e., pathogenic period) may be a better marker for acute infection than HBoV genomic DNA, which can be shed for weeks to months (i.e., non-pathogenic period) and may thus be less specific for acute disease. We compared prevalence of capsid mRNA and DNA in children with community-acquired pneumonia (CAP) and controls as part of the CDC Etiology of Pneumonia in the Community (EPIC) study.

Methods. We enrolled hospitalized children <18 years with CAP (January 2010-June 2012) and controls (February 2011-June 2012) at the Utah site of the EPIC study; nasopharyngeal/oropharyngeal (NP/OP) specimens were obtained. HBoV mRNA and genomic DNA were quantified from NP/OP specimens. A spliced transcript for HBoV1-4 VP1/VP2 was targeted for mRNA detection.

Results. We obtained NP/OP samples from 812 children with CAP (median age 2.2 years; interquartile age [IQR] 1.0-6.2) and 337 controls (median age 5.8 years; IQR

2.8-11). HBoV DNA was detected in 114/812 (14.0%) cases and 30/337 (8.9%) controls (odds ratio [OR] 1.7; 95% CI 1.1-2.5); HBoV mRNA was detected in 21/812 (2.6%) cases and 2/337 (0.6%) controls (OR 4.4; 1.1-19). Following adjustment for age, enrollment month, and detection of other respiratory viruses, HBoV DNA was associated with CAP (adjusted OR [aOR] 2.0; 1.2-3.2) but mRNA had a stronger association (aOR 7.9; 1.7-36). When the analysis was restricted to children in whom no other viral or bacterial pathogens were detected, the association with DNA detection was similar (OR 2.2; 1.2-4.0; 25/140 cases, 22/240 controls), while the association of HBoV mRNA detection with CAP increased (OR 14.5; 1.8-117; 8/140 cases, 1/240 controls).

Conclusion. Detection of HBoV by spliced capsid mRNA was strongly associated with CAP in children while genomic DNA was associated, even after adjusting for age, season, and respiratory pathogen co-detection. HBoV mRNA detection may be a marker of acute, infection and could be a useful diagnostic test.

Disclosures. **R. Schlaberg**, Epoch Biosciences: Collaborator, Research reagents

772. Risk Factors Associated with Pneumonia Co-infection in Children under 5 Years of Age Presenting to a Diarrheal Hospital in Dhaka, Bangladesh, 1996 to 2007

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Background. Worldwide, pneumonia and diarrhea are the top causes of mortality in children under 5 years of age. The mucosal immune system is common to both respiratory and gastrointestinal tracts, and there is epidemiological evidence that infection of one may predispose to infection of the other. Our aim was to determine the risk factors for concurrent presentation of diarrhea and pneumonia.

Methods. We used prospectively collected data from the Diarrheal Disease Surveillance System of the Dhaka Hospital in Bangladesh to identify children under 60 months of age who presented with signs and symptoms of pneumonia, defined as a patient who satisfied all three criteria: 1) History of cough with diarrhea, 2) an abnormal lung exam on admission, and 3) tachypnea on admission. We compared the characteristics of those with pneumonia against a control group who did not satisfy any of the above criteria, matched for month and year of admission at a ratio of 1:3.

Results. For the years 1996-2007, out of total 14,628 diarrheal patients under age 5 surveyed, there were 607 (4%) patients who satisfied criteria for pneumonia. Of those with pneumonia, 26 (4%) died, compared with only 2 (0.1%) of those with diarrhea only. Cases with pneumonia also had a longer hospital stay (mean (SD), 84 (97) hrs vs 25 (41) hrs in controls). A pathogen was detected in the stool of 4536 (31%) of all patients, including 353 (58%) of those with pneumonia. In a multivariable logistic regression model comparing cases (n = 607) with controls (n = 1808), including socio-demographic and behavioral factors, we found that concurrent pneumonia was associated with severe acute malnutrition, younger age, less maternal education, lower family income, and lack of current breastfeeding. Entry of individual pathogens into the model identified rotavirus as negatively associated with pneumonia.

Conclusion. We demonstrate that malnutrition, young age, lack of breastfeeding, poor education status, and lower family income are independent risk factors associated with concurrent pneumonia in young children presenting with diarrhea in Bangladesh.

Disclosures. **All authors:** No reported disclosures.

773. Viral Etiology in Hospitalized Children Less than Two Years of Age with Lower Respiratory Infections in Amman, Jordan

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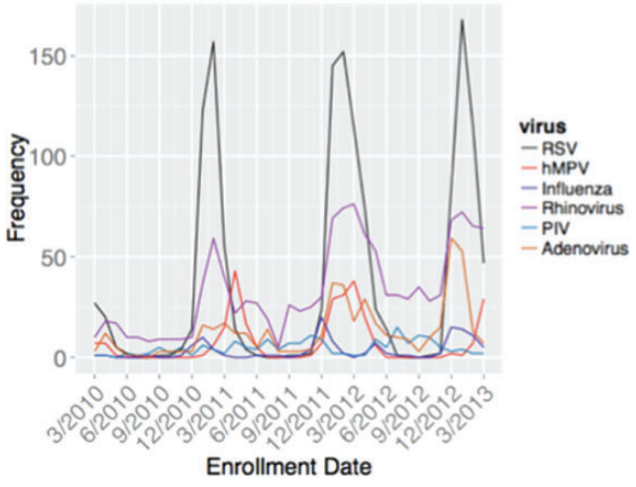
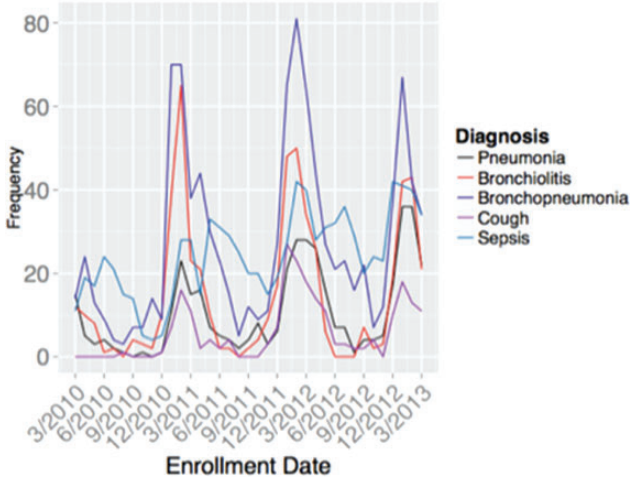
Background. Acute lower respiratory infections (ALRI) are a leading cause of death in children, but the role that viruses play in their etiology in Jordan and the Middle East is poorly characterized.

Methods. A prospective 3-year, year-round viral surveillance in children <2 years of age admitted with respiratory symptoms and/or fever at the Al-Bashir government hospital from March 16, 2010-March 31, 2013 was conducted. Clinical and demographic data were collected. Nasal/throat swabs were obtained and were tested by real-time RT-PCR for respiratory syncytial virus (RSV), metapneumovirus (MPV), rhinovirus (HRV), influenza, and parainfluenza viruses 1, 2, and 3 (PIV1-3) and MERs-CoV.

Results. 3169 children were enrolled, virus detected in 81%. Mean age 3.5 months, 60% male. Most common ALRI diagnoses were bronchopneumonia (32%), bronchiolitis (17%), and pneumonia (12%). 284 (9%) were admitted to the ICU and only 31 (1%) died. The table describes clinical presentation and viruses by these diagnoses. MERS-CoV was not detected. The figures display the frequency of viruses and diagnoses over time, respectively.

	Pneumonia N=394	Broncho-pneumonia N=1020	Bronchiolitis N=547	Total Cohort N=3169
Age (mean)	2.4 months	7.9 months	3.4 months	3.5 months
Sex (male)	220 (56%)	604 (59%)	362 (66%)	1913 (60%)
Vitamin D level (median)	11.7 ng/mL	20.6ng/mL	17.9ng/mL	16.5 ng/mL
No PMH	342 (87%)	863 (85%)	519 (95%)	2848 (90%)
Cough	358 (91%)	945 (93%)	526 (96%)	2366 (75%)
Wheezing	250 (63%)	735 (72%)	483 (88%)	1757 (55%)
Fever	201 (51%)	716 (70%)	173 (32%)	1763 (56%)
Abnormal chest x-ray	381/390 (98%)	980/1009 (97%)	512/540 (95%)	2077/2963 (70%)
Oxygen Use	209 (53%)	279 (28%)	215 (40%)	1013 (32%)
MV	26 (7%)	37 (4%)	21 (4%)	111 (4%)
ICU	80 (20%)	53 (5%)	32 (6%)	284 (9%)
Death	10 (3%)	4 (0.003%)	1 (0.002%)	31 (1%)
Virus				
RSV	225 (57%)	476 (47%)	374 (68%)	1397 (44%)
HRV	153 (39%)	374 (37%)	215 (39%)	1238 (39%)
MPV	37 (9%)	123(12%)	56 (10%)	273 (9%)
Influenza	14 (4%)	50 (5%)	14 (3%)	123 (4%)
PIV	17 (4%)	68 (7%)	23 (4%)	175 (6%)
Adenovirus	68 (17%)	175 (15%)	62 (11%)	475 (15%)





Conclusion. Viruses play a major role in ALRI in Jordanian children. Pneumonia was associated with higher morbidity and mortality; those children were younger, had lower vitamin D levels, and were more likely to require oxygen.

Disclosures. **All authors:** No reported disclosures.

774. Non-invasive pneumococcal pneumonia has its own and distinct serotype distribution in Portugal

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Background. *Streptococcus pneumoniae* is the main etiological agent of pneumonia. Numerous studies have addressed the serotype distribution of invasive pneumococcal disease (IPD) due to the availability of conjugate vaccines targeting the capsular polysaccharides. However, there is more limited information on the serotypes causing non-invasive pneumococcal pneumonia (NIPP). Our aim was to characterize pneumococci causing NIPP in adults, in order to determine recent changes in serotype prevalence and antimicrobial resistance, the potential coverage of pneumococcal vaccines and to compare the results with IPD.

Methods. Serotypes and antimicrobial susceptibility profiles of a sample of 1300 isolates recovered from adult patients (≥18 years) between 1999 and 2011 (13 years, 100 randomly selected isolates/year) were determined.

Results. Overall, the most frequent serotypes were 3 (18%), 11A (7%), 19F (7%), 19A (5%), 14 (4%), 22F (4%), 23F (4%) and 9N (4%). There were significant changes in the proportion of isolates expressing vaccine serotypes, namely there was a steady decline of the serotypes included in the 7-valent conjugate vaccine from 31% (1999-2003) to 11% (2011). Taking together the most recent study years (2009-2011), the potential coverage of the 13-valent conjugate vaccine was 44% and of the 23-valent polysaccharide vaccine was 66%. Erythromycin resistance increased in the study period, reaching 18% in 2011.

Conclusion. The serotype distribution found in NIPP differed from the one found in IPD, with only two common serotypes among the ones responsible for half of each presentation – serotypes 3 and 19A. Serotypes found to be enriched in NIPP relative to IPD (6A, 11A, 15C, 19F and 23B) had been previously suggested to have a lower invasive disease potential. In spite of these differences, the overall prevalence of resistant isolates was similar in NIPP and in IPD.

Disclosures. **J. Melo-Cristino**, Pfizer: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Gilead: Speaker's Bureau, Speaker honorarium **M. Ramirez**, Pfizer: Speaker's Bureau, Speaker honorarium; GlaxoSmithKline: Consultant, Consulting fee

775. Nosocomial Influenza (NI) in cancer patients during a high activity season in Mexico City

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Background. NI constitutes a serious risk among patients with immunodeficiency. Vaccination of health-care workers (HCW) and infection control measures compliance is the cornerstone for the prevention of NI. We present a cluster of patients with cancer and NI during a high activity season in Mexico (winter 2013-14).

Methods. Patients and HCW with influenza-like illness (ILI) from Instituto Nacional de Cancerologia in Mexico City (126-bed, teaching, referral cancer hospital for adult patients) are regularly evaluated by the Infectious Diseases Department. Those with high suspicion of ILI are tested for influenza by rtPCR. Patients who developed ILI between January 1, 2014 and March 31, 2014 and tested positive to influenza were included, and those who had been in-hospital >= 48 hr were considered as nosocomial. We studied patients characteristics, hospital length of stay, neoplasia related variables and respiratory tract infection (RTI) symptoms, clinical course and outcomes.

Results. Between January and March, 2014, 100 patients (tested: 97) and 53 (tested: 48) HCW were evaluated with ILI. 62 patients were admitted because of ILI, and 6 (8.8%) developed ILI while in-hospital. Of the 68 admitted patients, 34 (50%) were positive to influenza (AH1N1: 28, H3N2: 6). Four and 2 patients with NI were positive to AH1N1 and H3N2, respectively. Two had leukemia, 2 lymphoma, 1 aplastic anemia and 1 breast cancer; 5 (83.3%) were male. Four (66%) received chemotherapy within 30 days of the onset of symptoms; 5 (83%) had lymphopenia and 1 (16%) had < 500 neutrophils. All were treated with oseltamivir, 3 patients for 10 days and 1 for 15 days, because of shedding and/or persistence of symptoms. Two (33.3%) patients were on mechanical ventilation, both died, 1 of influenza and 1 with septic shock, both positive to H1N1.

Conclusion. NI accounted for 17.6% of the confirmed influenza patients admitted to the hospital, mostly, with hematological neoplasia. Attributable mortality rate was 33.3%, similar to that observed for community-acquired influenza. Most cases were related to AH1N1, as was reported for North America during this last influenza season.

Disclosures. **All authors:** No reported disclosures.

776. Acinetobacter baumannii ventilator acquired pneumonia in a high density unit of North India

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Background. *Acinetobacter baumannii* (AB) is responsible for 8-10% cases of late ventilator acquired pneumonia in the ICU.

Methods. Prospective study of all AB– VAP cases admitted to the Medical High Density Unit (HDU) from 1 March 2010 to 31 March 2011.

Results. Of 50 cases, 33 were males and 17 females. Mean age was 42.8± 17.1 years (range = 15-88 years). Thirty seven cases were referred to our hospital from a primary health center (mean stay = 5.5 ± 1.2 days). AB-VAP occurred after 11.5 ± 4.3 days in-hospital. Underlying conditions were; diabetes mellitus in 34%, essential hypertension in 36%, immunosuppressive therapy in 8% and coronary artery disease in 4%. Risk factors for AB-VAP were; neurological disorders in 36%; severe sepsis in 16%; organophosphorous poisoning in 10% and diabetic ketoacidosis and acute kidney failure in 6% each. The mortality rate was 52%. Antibiotic resistance pattern of AB showed that 82% isolates were multi-drug resistant and 58% carbapenem resistant. Chi square analysis revealed that carbapenem resistance in AB-VAP isolates correlated to mortality. Upon multivariate analysis, survivors (n = 24) differed from non-survivors (n = 26) in a shorter length of stay at the primary level hospital, a significantly shorter duration of HDU stay and total length of stay at this hospital and lower SOFA score at time of culture positivity. On comparing the time period that invasive catheters were retained in these patients of AB-VAP, shorter retention times of central venous catheters, urinary catheters and endotracheal tubes was observed in survivors.

Conclusion. AB-VAP in the medical HDU, has a high mortality rate. Risk factors for mortality are a prolonged period of stay in primary level hospitals, increased retention time of invasive catheters and endotracheal tubes and the presence of carbapenem resistance in the AB isolates

Disclosures. **All authors:** No reported disclosures.

777. Cost of Treating Patients with Pneumococcal Community-Acquired Pneumonia (CAP) in French Hospitals: Interim Results of the Prospective PNEUMOCOST Study

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Background. Documenting the economic burden of CAP is essential to define efficient vaccination strategies. PNEUMOCOST study was designed to estimate the cost of treatment in the French context.

Methods. A prospective, multi-centric, observational study including patients hospitalized for a pneumococcal CAP involved 40 centers. Five hundred and fifty patients were expected to be enrolled from October 2011 to April 2014. All enrolled patients are followed over a 6 month period. Interim results on patients' profiles and initial hospitalization are presented. Inclusion criteria: adult age >18, CAP confirmed at admission by X-ray, *S. pneumoniae* confirmed with microbiological sampling. Informed consent was required. Exclusion criteria: pregnancy, patients included in clinical trials, patients with prior 48 h admission for another cause, patients unable to answer to follow-up questionnaire over six months.

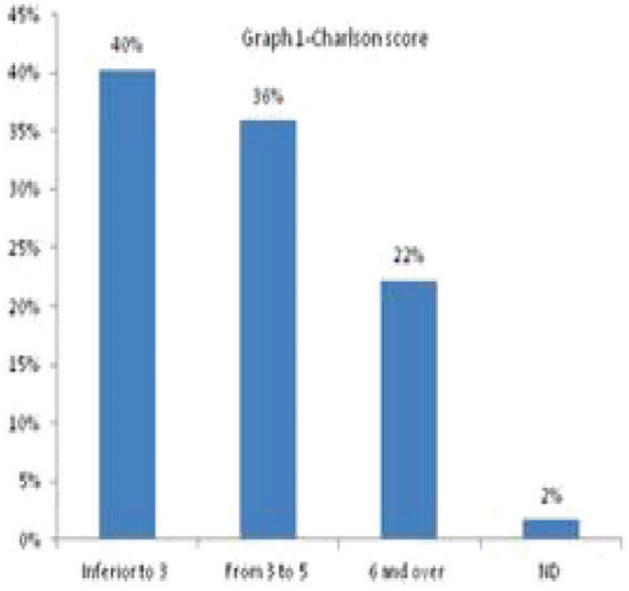
Results. Patients characteristics: 455 patients with validated clinical data; 54.6% of patients were men, average age 63 years (Min: 19; Max: 96); 77.3% of patients were 50 +. *S. pneumoniae* was identified through urinary antigen detection (UAD) alone in 44% of cases; altogether, 73.4% UAD were performed, blood

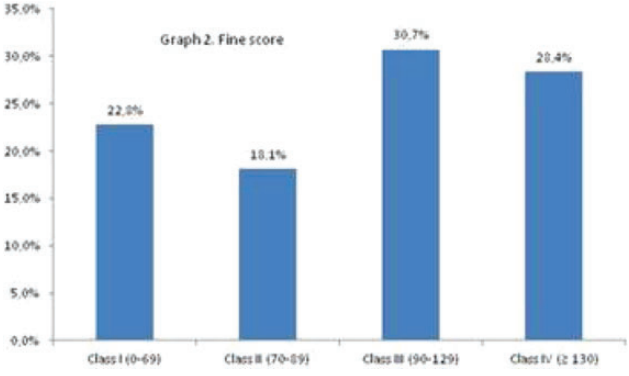
cultures in 37.4%, other tests were mainly sputum culture. The table displays antibiotic sensitivity.

	Table 1- Antibiotic sensitivity		
	Penicillin G	Amoxicillin	3G Cephalosporins
# cases	231	236	238
High sensitivity	78.4%	91.1%	95.0%
Intermediate sensitivity	21.2%	8.1%	4.6%
Resistance	0.4%	0.8%	0.4%

Average length of stay (LOS) was 13.8 days (SD 14.8). LOS increased with the Charlson score, from 10.5 days for score 0 to 17.4 for scores ≥6. Rate of admission in a resuscitation unit increased with the Port score, from 14% for Class 1 to 49% to Class 4. Surprisingly, inpatient mortality rate was low (1.8%; n = 8 patients). Average cost of stay from a payer's perspective was € 6,962 (SD € 6,933). The distribution of cost was skewed: 25% of stays represented 56% of total costs of all stays.

Charlson and Port scores of enrolled patients are displayed in Graphs 1 and 2.





Conclusion. PNEUMOCOST is the largest French cohort of patients hospitalized for pneumococcal CAP to date. Initial results confirm the high economic impact of the disease. Follow-up data should increase this burden.

Disclosures. **C. Chidiac**, Pfizer: Board Member, Consulting fee **H. Laurichesse**, Pfizer: Board Member, Consulting fee **J. Gaillat**, Pfizer: Board Member, Consulting fee **P. Petitpretz**, Pfizer: Board Member, Consulting fee **G. De Pouvourville**, Pfizer: Board Member, Consultant and Grant Investigator, Consulting fee and Research grant

778. Influenza-like Illness in Korean Soldiers, 2011-2013: Comparison between military and community population

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Background. To better understand respiratory illness in Korean military, we have been performing sentinel surveillance of influenza-like illness (ILI) in Korean soldiers since 2011.

Methods. Between 41st week of 2011 and 30th week of 2013, The Armed Force Medical Command has collected patient number with ILI and total patient number examined from selected infirmary of 10 sentinel surveillance sites every week. Case definition of ILI was fever higher than 38°C with cough or sore throat. The change of ILI in military population was compared between ILI in community population and patient number admitted to military hospitals with influenza related illness.

Results. During influenza epidemic period in community (53rd week of 2011 - 18th week of 2012) in 2011-12, the incidence rate of ILI in military population was 18.7-76.4 cases per 1,000 patients - week. Within same period, the rate of ILI in military was 1.6-7.6 times higher than ILI in community. In 2012-13 season of influenza epidemic period in community (2nd week of 2013 - 16th week of 2013), incidence rate of ILI in military population was 18.1-39.1 cases per 1,000 patients-week. Within same period, the rate of ILI in military was 1.6-6.7 times higher than ILI in community. Especially in 19-30th week of 2013 in 2012-13, after the end of influenza epidemic, the incidence rate of ILI in military population was 10.6 - 22.8 times higher than community population. From total ILI cases, the ILI rate in recruits was 35-60% during influenza epidemic season, but increase to 78% after 19th week of 2013. During influenza epidemic season, hospitalization rate due to influenza related illness was 4.0 -40.8 cases per 10,000 patients-week in 2011-12, and 1.1-8.0 cases per 10,000 patients-week in 2012 - 13.

Conclusion. In 2011-12, ILI activity was higher during influenza epidemic period than non-epidemic period in military population, but in 2012-13, ILI activity peaked in non-epidemic period of influenza. Our surveillance suggests that the ILI in military population could be rapidly increase with other reparatory virus, unlike in community population where seasonality of ILI is influenced by influenza virus.

Disclosures. **All authors:** No reported disclosures.

779. Viral Pathogen Detection by Metagenomics and Panviral PCR in Children with Pneumonia with no Identifiable Etiology: Preliminary Results from the CDC Etiology of Pneumonia in the Community (EPIC) Study

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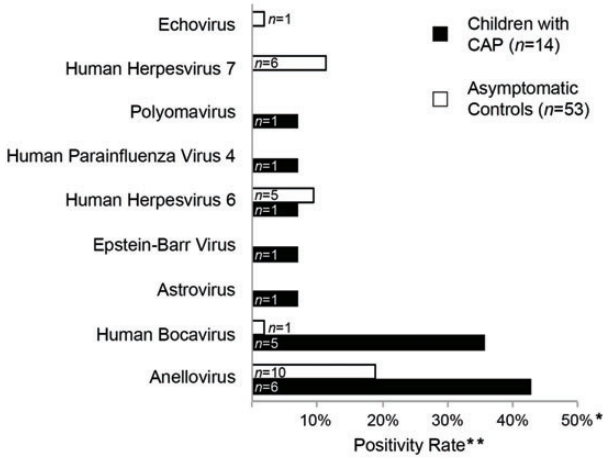
Background. Community-acquired pneumonia (CAP) is a leading cause of pediatric hospitalization. Consistent with previous studies, no pathogen was identified in 19% of children hospitalized with clinical and radiographic CAP in the CDC EPIC study despite comprehensive viral and bacterial diagnostic testing. Pathogen identification is a critical step for appropriate antimicrobial use. Here we applied two broad pathogen detection approaches, RNA-Seq-based metagenomics and a panviral family/genus PCR panel, to identify unrecognized pathogens in children with CAP of no identifiable etiology. Age and season-matched children served as controls.

Methods. We obtained nasopharyngeal/oropharyngeal (NP/OP) swabs from hospitalized children <5 years with CAP and controls enrolled at the Utah site of the EPIC study. Patients included in this analysis had negative results by blood culture, whole blood PCR, pleural fluid culture and PCR, NP/OP PCR for viruses and atypical bacteria, and paired serologies for selected viruses. Total RNA was subjected to metagenomics (mean 12 million sequencing reads/sample) and viral sequences identified with a custom data analysis pipeline. Total nucleic acid was also tested by panviral family/genus conventional PCR for detection of 19 viral genera and family with known and potentially novel viral pathogens.

Results. We studied 14 hospitalized children <5 years with CAP (median age 1.8 years; interquartile range [IQR] 1.1-2.7) and 53 controls (median age 1.7 years; IQR 0.8-3.4). Viruses were identified in 9/14 (53%) children with CAP and in 21/53 (40%) controls (figure). Human bocavirus (HBoV) was detected significantly more frequently in children with CAP (odds ratio 21; 95% CI 2-206).



* Numbers do not add up to 100% due to viral co-detection

** Panviral genus/family PCR panel targets viruses of the following groups: adenovirus, alphavirus, anellovirus, arenavirus, astrovirus, bornavirus, bunyavirus, calicivirus, circovirus, coronavirus, enterovirus, flavivirus, herpesvirus, influenza virus, paramyxovirus, parvovirus, polyomavirus, reovirus, and rhabdovirus

Conclusion. Two broad pathogen detection approaches identified human viruses in >50% of children with CAP of previously unrecognized etiology. However, most viruses, including anellovirus and herpes viruses were also prevalent among controls making their role uncertain. HBoV detection was associated with CAP. In addition to pathogen detection, metagenomics allows for genome sequencing, phylogenetic analyses, and identification of entirely unexpected viruses. Further analysis on a larger sample is underway.

Disclosures. **All authors:** No reported disclosures.

780. Clinical Characteristics And Outcomes among Children with Neurological Disorders Hospitalized with Community-acquired Pneumonia (CAP) in the Etiology of Pneumonia in the Community (EPIC) Study

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Background. Although children with neurological disorders are vulnerable to complications from respiratory infection, CAP epidemiology among these children is poorly understood.

Methods. Children <18 years hospitalized with clinical and radiographic CAP were enrolled in the CDC EPIC study in Memphis, Nashville, and Salt Lake City. Children residing in a chronic care facility and those with recent hospitalization, tracheostomy, or severe immunosuppression were excluded due to healthcare exposure. Neurological disorders were defined as cerebral palsy, spinal cord abnormalities, epilepsy, Down syndrome, developmental delay, and chromosomal and other disorders with primary neurological manifestation. We compared children with neurological disorders to those with other non-neurological co-morbidities and with children with no co-morbidities.

Results. From January 2010-June 2012, 2358 children with CAP were enrolled; 279 (12%) had a neurological disorder (54% with another co-morbidity), 968 (41%) had non-neurological co-morbidities only, and 1,111 (47%) had no co-morbidities. Children with neurological disorders were older, had longer hospital and intensive care unit (ICU) length of stay (LOS), and more ICU admissions, than children without neurological disorders; there were no differences in the proportion mechanically ventilated.

Variable*	Group 1 Neurological disorder n=279	Group 2 Non-neurological co-morbidity n=968	Group 3 No co-morbidity n=1111	p-value Group 1 vs 2	p-value Group 1 vs 3
Median age in years (interquartile range)	5.9 (1.7-9.8)	2.8 (1.3-6.2)	1.8 (0.8-4.6)	<0.01	<0.01
Congenital heart disease	95 (34)	104 (11)	-	<0.01	-
Asthma	83 (30)	696 (72)	-	<0.01	-
Hospital LOS >3 days	153 (55)	316 (33)	357 (32)	<0.01	<0.01
ICU admission	102 (37)	186 (19)	209 (19)	<0.01	<0.01
ICU LOS >3 days	49/102 (48)	66/186 (35)	86/209 (41)	<0.01	<0.01
Invasive mechanical ventilation	34/102 (33)	52/186 (28)	79/209 (38)	0.12	0.11
Death	1 (0.4)	0 (0)	2 (0.2)	-	-

*Values are No. (%) unless otherwise specified

Conclusion. When hospitalized with CAP, children with neurological disorders had a more severe course of illness, in terms of ICU admission and LOS, in comparison with children without neurological disorders, which may be independent of respiratory failure alone.

Disclosures. **K. Edwards**, Novartis: Grant Investigator and Scientific Advisor, Research grant

781. Rhinovirus in Children Hospitalized with Community Acquired Pneumonia: Insights from the Centers for Disease Control and Prevention (CDC) Etiology of Pneumonia in the Community (EPIC) Study

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Background. Human rhinoviruses (HRV) are frequently detected in both children with respiratory symptoms and asymptomatic children. Thus, the relevance of HRV detection in children with pneumonia remains unclear. Some data suggest that HRV-C is associated with severe disease. We studied the association between HRV species and viral load among children hospitalized with radiographically-confirmed pneumonia and asymptomatic children (controls).

Methods. Molecular testing for HRV and 12 other respiratory viruses was performed on naso-/oro-pharyngeal swabs from children <18 years hospitalized with pneumonia (January 2010-June 2012) and a convenience sample of children without pneumonia (February 2011-June 2012) enrolled at the Utah site of the CDC's EPIC study. HRV speciation was by amplifying and sequencing the VP4/VP2 regions of the HRV genome and comparing sequences to HRV strains in GenBank. HRV load (RNA copies/mL) was determined using standard curves from quantified HRV RNA transcripts normalized with human RNase P gene (specimen control).

Results. HRV detection was similar among children with pneumonia and controls, (166/853, 20% vs 38/226, 18%; $p = 0.18$). The majority of HRV detections were single detections, however co-detection with another respiratory virus was more frequent among children with pneumonia than controls (41% vs 11%; $p < 0.01$). HRV-C was more commonly detected in children with pneumonia than controls (Table). HRV viral load was significantly higher among children with pneumonia compared with controls (median 6.9 vs 5.9 $\log_{10}$ copies/mL; $p < 0.001$). However, while median viral loads for HRV-B (7.0 vs 6.1 $\log_{10}$ copies/mL; $p = 0.5$) and HRV-C (6.8 vs 6.4 $\log_{10}$ copies/mL; $p = 0.4$) were similar in children with pneumonia compared with controls, HRV-A viral load was higher in children with pneumonia (7.0 vs 5.9 $\log_{10}$ copies/mL; $p < 0.001$).

Conclusion. HRV was commonly detected among children with pneumonia and controls, though children with pneumonia had higher viral loads. HRV-C, but not other species, was associated with pneumonia. These data suggest that HRV species and viral load may play a role in the development of pneumonia in children.

	Children with pneumonia (n=166)	Asymptomatic children (n=38)	P
HRV-A	60 (36%)	19 (50%)	NS
HRV-B	13 (8%)	6 (16%)	NS
HRV-C	84 (51%)	9 (24%)	0.003
Non-typeable	9 (5%)	4 (10%)	NS

Disclosures. **K. Edwards**, Novartis: Grant Investigator and Scientific Advisor, Research grant

782. The efficacy of anaerobe specific antibiotics in patients with aspiration pneumonia

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Background. IDSA/ATS guidelines state that anaerobic coverage is indicated only for aspiration pneumonia in patients with a history of loss of consciousness as a result of alcohol/drug overdose or after seizures in patients with concomitant gingival disease or esophageal motility disorders. Despite this, clinicians often add anaerobic coverage in patients without these risk factors. Given the paucity of studies on anaerobe specific antibiotics in aspiration pneumonia, we assessed their efficacy by comparing patients treated with and without anaerobe specific antibiotics.

Methods. A single-center retrospective cohort study that compared a group of aspiration pneumonia patients treated with anaerobe specific antibiotics to a group of patients without anaerobe specific antibiotics. All medical records with a discharge diagnosis of aspiration pneumonia were reviewed. Inclusion criteria were the presence of risk factors for aspiration as well as imaging findings consistent with pneumonia. Main outcomes included length of stay, inpatient mortality, and need for change in antibiotics.

Results. 636 patients with a diagnosis code of aspiration pneumonia were identified. 390 patients met all inclusion criteria. 279 patients received initial anaerobe specific coverage while 111 did not. Apache II and PORT scores were similar (10.5 ± 4.6 vs 10.5 ± 4.4) and (110 ± 30 vs 108 ± 32) respectively. No significant differences in length of stay (10.5 vs 11.5 days ($p = 0.29$), or mortality (13% vs 18%, $p = 0.20$) were detected. A change in antibiotics occurred more often in patients initially treated without anaerobic coverage (24% vs 38% $p < .01$).

Conclusion. In this retrospective study of patients hospitalized with aspiration pneumonia, no difference in mortality or length of stay were detected between patients initially treated with anaerobe specific antibiotics and those without, however patients not receiving initial anaerobic coverage were more likely to have a change in antibiotics. Prospective studies on the role of anaerobe specific antibiotics in aspiration pneumonia are needed.

Disclosures. **All authors:** No reported disclosures.

783. Detection of Respiratory Viruses in Sputum from Adults Using Automated Multiplex Polymerase Chain Reaction (PCR)

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Background. Respiratory tract infections (RTI) frequently cause hospital admissions among adults. Diagnostic viral RT-PCR of nose and throat swabs (NTS) is useful for patient care by allowing better antibiotic management, timely antiviral use and appropriate patient isolation. Previously, we found that the addition of sputum RT-PCR testing improves the diagnostic yield for respiratory viruses. However, automated RT-PCR systems are not amenable to utilizing sputum due to its viscous nature. Thus, we evaluated a simple method of processing sputum for use in the fully automated FilmArray Respiratory Viral Panel RT-PCR assay (FilmArray).

Methods. Archived sputum and NTS samples collected in the winters of 2008-2012 from hospitalized adults with RTI were used. From this collection, a random subset of sputum samples previously positive for viruses (Flu A, Flu B, RSV A, coronaviruses OC43 and 229E, human metapneumovirus (HMPV), parainfluenza viruses 1-3 and rhinovirus) by manual RNA extraction and uniplex real-time RT-PCR were selected. A sterile cotton tip swab was dunked in the sputum followed by swirling in 700 uL of sterile water (dunk method) and tested by FilmArray. In addition, quantitative RT-PCR was performed on dunked sputum and NTS samples for Flu A, RSV, OC43 and HMPV.

Results. Virus was identified in 31% of 965 illnesses using uniplex RT-PCR. The addition of sputum RT-PCR significantly increased the diagnostic yield compared to NTS alone (302/965 [31%] vs 197/965 [20%]; $p = .0001$). Sputum was the only sample positive for 105 subjects, including 35% (22/64) of influenza cases. Of 108 randomly selected sputa previously positive by uniplex PCR, 99 (92%) were also positive by FilmArray using the dunk method. Quantitative RT-PCR revealed significantly higher mean viral loads in dunked sputum compared to NTS samples for Flu A, RSV and HMPV ($p = 0.0001$, $p = 0.006$, $p = 0.011$).

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Conclusion. The dunk method is a simple and practical method for processing sputum for use in a fully automated PCR system with a yield of 92% compared to manual extraction and uniplex RT-PCR. The higher viral load in sputum may allow detection when the NTS viral load is below the limits of detection. Testing of sputum may be particularly important in patients with lower respiratory tract disease during influenza season.

Disclosures. **A. Falsey**, Regeneron: Consultant, Consulting fee; Hologic: Consultant, Consulting fee; Sanofi Pasteur: Research Contractor, Research grant; AstraZeneca: Research Contractor, Research grant; ADMA Biologic Inc.: Research Contractor, Research grant **E. Walsh**, Clearpath Incorporated: Consultant, Consulting fee; Alios Biopharma: Consultant, Consulting fee

784. Acute respiratory infections and *Streptococcus pneumoniae* Carriage

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Background. Bacterial pneumonia and otitis media often follow influenza and other upper respiratory viral infections. *Streptococcus pneumoniae* (SP) is one of the most frequent culprits. While animal models suggest influenza enhances SP transmission and growth and that SP may increase influenza morbidity, there is limited evidence in human populations. We estimated the prevalence of SP among adults and children with acute respiratory illness (ARI) with and without laboratory confirmed influenza, to gain insight into the interaction between SP and influenza.

Methods. The Household Influenza Vaccine Effectiveness (HIVE) Study actively monitored ARI among 290 households with at least 2 children during the 2013-2014 influenza season. In addition to clinical data and specimens collected for viral testing, HIVE participants 2 years-old and older with ARI from 166 households provided oropharyngeal swabs for bacterial studies. Samples were screened by real-time PCR (RT-PCR) for the presence of influenza and 10 other respiratory viruses, and, in a blinded way, for the presence and relative abundance of SP by RT-PCR amplifying the *lytA* gene. SP serotypes were determined using multiplex PCR.

Results. 332 subjects reported illness at least once, for a total of 519 illnesses. SP was found in the oropharynx of 118 different subjects (35.5%), corresponding to 148 illnesses (28.5%): 34/241 (14%) in adults and 114/278 (41%) in children ($p < 0.001$). Subjects carrying SP were younger (on average 13.8 years-old vs 25.2, $p < 0.001$), and were more commonly infected with influenza (8.7% vs 5.9%, $p = 0.24$) than subjects without SP, although not significantly. This was particularly true for children under 17 (9% of SP carriers had influenza, vs 4.7% of non-carriers, $p = 0.10$). Relative abundance of SP was higher in SP carrying children than adults ($p < 0.001$), but did not differ by influenza infection. Results of other respiratory viruses and serotypes are pending.

Conclusion. SP oropharyngeal colonization was frequent in a household population with members suffering from ARI. Colonization rates and relative abundance of SP were higher in children. We found a tendency towards a higher rate of SP carriage among subjects with influenza, especially in the children, suggesting an association between SP colonization and viral infection.

Disclosures. **All authors:** No reported disclosures.

785. The Effect of Temperature, Humidity, Wind Speed, and UV-Light on the Recovery of Aerosolized Influenza Virus

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Background. Transmission efficacy of Influenza in aerosols is dependent on environmental factors such as temperature, relative humidity (RH), air flow, and UV-light. We studied the impact of these factors on the recovery of an aerosolized wild-type Influenza virus.

Methods. Influenza A virus (A/WS/33 H1N1) was aerosolized via nebulizer (droplet nuclei) and airbrush (droplet nuclei/droplet mix). Virus was collected through a mannequin head into a breathing bag of an artificial lung system filled with virus transport media. During emission virus was exposed to varying environmental conditions: (1) indoor (20°C; 40%RH); (2) winter (6°C; 35%RH); and (3) summer (34°C; 77%RH). Within each condition, directed air flow (low: 137 feet/second, high: 154 feet/second) and exposure to UV-C light (low dose: 18W; high dose: 36W) was applied. Quantitative virus detection was performed via plaque assay in MDCK cell cultures.

Results. With indoor set as standard, winter reduced virus recovery by 44% ($p = 0.01$) in droplet nuclei and increased recovery, though not significantly (12%, $p = 0.58$) in droplet nuclei/droplet mix. Summer decreased recovery by 64% in droplet nuclei ($p = 0.0001$) and 11% in droplet nuclei/droplet mix ($p = 0.67$). Within each condition, increased air flow led to a reduction in droplet nuclei ($p < 0.0001$). There was indication that increased air flow may improve recovery across all conditions for droplet nuclei/droplet mix ($p = 0.09$). Application of low dose UV-C resulted in a >98% reduction for droplet nuclei across all conditions ($p < 0.0001$). For droplet nuclei/droplet mix, low dose UV-C had no effect across all conditions ($p = 0.35$), but high dose UV-C decreased droplet nuclei/droplet mix ($p = 0.0019$).

Conclusion. Indoor conditions most effectively supported the potential for airborne Influenza transmission by small particles (droplet nuclei). However, winter shifted virus recovery to large particles making droplet transmission more likely. Summer decreased both, small and large particles. Within each condition, directed airflow reduced small particle collection by dilution, while increasing larger particle recovery by acceleration towards the collection point. UV-C light reduced virus recovery with the smallest impact observed in large particles.

Disclosures. **All authors:** No reported disclosures.

786. Decreasing Exposure to Radiation for Pediatric Complicated Pneumonia: Replacing Computed Tomography with Ultrasound

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Background. Several studies suggest the use of chest ultrasound (US) as an equal alternative to computed tomography (CT) scans for diagnosis and to guide treatment for complicated pneumonia, thereby decreasing exposure to radiation. Within the four year period of this study, a complicated pneumonia algorithm was initiated (April 2013), which specifies preference for chest US over chest CT scan.

The goal of this study was to evaluate the impact on illness and hospital course given a change in radiographic evaluation.

Figure 1. Positive Culture/PCR Results (n=118)

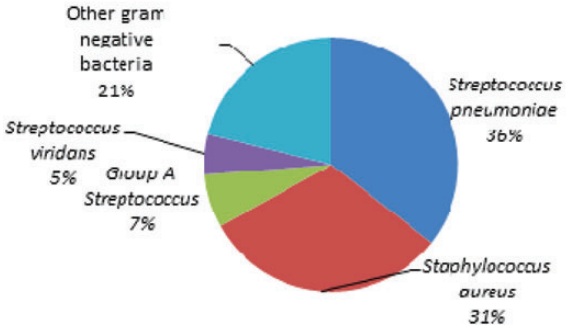
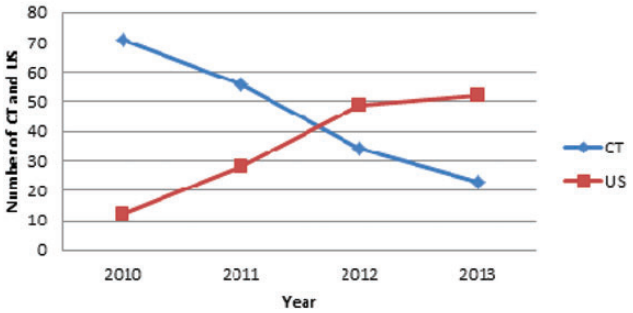


Figure 2: Chest CT and US over Time



Methods. This is a single-center, retrospective study of patients hospitalized during 2010-2014 with diagnosis of complicated pneumonia. Patients included were identified by diagnosis code for pneumonia and an additional qualifier: chest CT, chest US, or pleural culture. Then, each case was manually reviewed to ensure it met the diagnosis by clinical definition. Baseline demographics and variables were collected for the study population. The following variables were compared pre- and post-algorithm implementation: intensive care unit (ICU) admission rates, ICU length of stay (LOS), hospital LOS, days with a chest tube, rate of chest tube insertion, complications (necrotizing pneumonia, pneumothorax, abscess, and return to OR after chest tube insertion), and number of antibiotics received.

Results. The total number of patients included in the study was 296, 49% being male, with a median age of 5.4 years. Median length of stay was 9 days and 43% of cases were admitted to the ICU. Figure 1 shows the distribution of bacteria identified. We found that the number of ordered chest CTs decreased with a corresponding rise of chest USs during the study period (Figure 2). There was a statistically significant decrease in the number of patients who received a chest CT scan and increase in patients who received a chest US ($p < 0.0001$) after the implementation of the algorithm. There was no significant difference seen in any of the other variables.

Conclusion. The introduction of an algorithm for the management of complicated pneumonia at our institution combined with an effort among physicians to change practice, led to significant reduction in chest CT use and increase in chest US use. This change in practice reduced radiation exposure to children.

Disclosures. **All authors:** No reported disclosures.

787. Respiratory Pathogen Detection in Cases of Severe Acute Respiratory Illness (SARI) Among Hospitalized Patients at Two Metro-Area Hospitals, Minnesota, 2013-2014

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Background. In the United States, surveillance of non-influenza severe acute respiratory illness (SARI) is not well established. The Minnesota Department of Health (MDH) is conducting pilot hospital-based surveillance to characterize SARI in adults and children year-round.

Methods. SARI surveillance was implemented two hospitals (one pediatric, one general). Residual upper respiratory specimens, collected for diagnostic testing, were submitted to the MDH-Public Health Laboratory from December 2013 to February 2014. Specimens were tested for 22 viral and bacterial pathogens by real-time PCR. Admission records, including history and physical, were reviewed to identify patients meeting SARI case definition (cough, shortness of breath, or difficulty breathing, with or without fever), and medical records were reviewed to obtain demographic and clinical data on patients with submitted specimens.

Results. Of known hospitalizations, 1,232 specimens were submitted. Pediatrics median age was 2.9 years (range X – xx); adult median age was 45.3 years (range xx-xx). There were no detections of enterovirus, influenza B, coronavirus 229E, Bordetella, *Legionella pneumophila,* or mycoplasma all other detections are presented in the table. 204 (19%) pediatric patients had >1 pathogen detected compared to 2 (2%) adult patients ($p < 0.01$). The most common pediatric co-detection was RSV and rhinovirus (xx/204).

	Pediatrics (n=1087) No. (%)	Adults (n=138) No. (%)	p-value
Any pathogen detected	780 (71)	48 (35)	<0.001
RSV	454 (42)	6 (4)	<0.001
Rhinovirus	156 (14)	2 (1)	<0.001
Adenovirus	98 (9)	2 (1)	0.002
Influenza A	63 (6)	31 (22)	<0.001
Chlamydophila pneumonia	3 (<1)	0	NS
Coronavirus HKU1	53 (5)	0	0.008
Coronavirus NL63	38 (4)	3 (2)	NS
Coronavirus OC43	33 (3)	0	0.038
hMPV	45 (4)	2 (1)	NS
Parainfluenza 1	22 (2)	1 (1)	NS
Parainfluenza 2	13 (1)	0	NS
Parainfluenza 3	2 (<1)	0	NS
Parainfluenza 4	2 (<1)	0	NS

NS=not significant; hMPV=human metapneumovirus

Conclusion. MDH established a pilot surveillance effort for SARI at two hospitals. Pediatric patients were more likely than adults to have a pathogen detected and to have > 1 pathogen detected. Data are helpful to inform the development of prevention and therapeutic interventions for respiratory infections.

Disclosures. **All authors:** No reported disclosures.

788. Are Clinical Prediction Scores in Community-Acquired Pneumonia Equally Reliable Across Various Etiologic Categories?

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Background. Clinical prediction rules purport to determine, at the time of presentation for community-acquired pneumonia (CAP), which patients (pts) will require

ICU admission or die within 30 days. Our goal in the present study was to determine whether the scores are equally reliable in different etiologic subgroups of CAP (i.e., bacterial, viral, undetermined, etc.).

Methods. In this prospective study, we calculated PSI, SMART-COP, IDSA/ATS minor (mATS) criteria, and CURB-65 as predictors of ICU admission and 30 day mortality in pts hospitalized for CAP at the VA Medical Center, Houston. Bacterial CAP (BCAP) was defined as the isolation of a respiratory pathogen from an adequate sputum sample or blood, or urinary antigen tests. Viral CAP (VCAP was determined by nasopharyngeal PCR. Pts in whom an infectious etiology was presumed despite negative microbiologic studies were classified as "etiology unknown."

Results. Of 191 pts with CAP, 23 (12.0%) required ICU admission, 30 day mortality was 7.8% (15/191). Point estimates of sensitivity and area under the receiver-operator-characteristic curve (ROC) as predictors of ICU admission are shown in Tables. The sensitivity of each scoring systems was significantly greater for BCAP compared to CAP of unknown etiology ($P < 0.05$). AUROC for each scoring systems was greater for BCAP than for VCAP and unknown. The same relationship was observed for 30 day mortality.

Etiology	PSI > 3	SMART-COP > 2	mATS > 2	CURB-65 > 2
BCAP	100	89	78	44
VCAP	33	33	67	0
All infected	84	77	69	30
Unknown	50	40	10	20

Sensitivity (%) for Predicting ICU Admission

Etiology	PSI	SMART-COP	mATS	CURB-65
BCAP	0.80 (0.65-0.95)	0.88 (0.72-1.00)	0.87 (0.72-1.00)	0.67 (0.47-0.88)
VCAP	0.42 (0.15-0.69)	0.52 (0.08-0.96)	0.58 (0.17-0.99)	0.54 (0.19-0.90)
All infected	0.72 (0.56-0.87)	0.80 (0.64-0.96)	0.79 (0.64-0.85)	0.66 (0.49-0.82)
Unknown	0.50 (0.31-0.69)	0.64 (0.45-0.82)	0.61 (0.43-0.78)	0.58 (0.41-0.75)

AUROC (95% CI) as a Predictor of ICU Admission

Conclusion. The sensitivity of each index performed significantly better in pts with BCAP vs VCAP or CAP of unknown etiology. Sensitivity is more important clinically than AUROC because the consequences of failing to admit to an ICU a patient who requires that level puts the patient at risk for mortality. The high false negative of the scores in viral and CAP of unknown etiology limit their reliability in predicting outcomes.

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789. Outpatient Antiviral Prescribing Practices among Providers in the U.S. Influenza Incidence Surveillance Project, 2009–2014

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Background. Prescribing practices for influenza antiviral agents vary widely and under-prescribing is common. Few data regarding antiviral prescribing practices exist from outpatient settings.

Methods. During 5 influenza seasons (November–March) from 2009–2014, 129 outpatient providers participating in the Influenza Incidence Surveillance Project (IISP) collected respiratory specimens and clinical data for patients of all ages with onset of influenza-like illness (ILI; defined as fever with cough or sore throat) within 7 days. Specimens were tested for influenza using RT-PCR. We evaluated factors associated with antiviral prescribing practices.

Results. Among 8,832 patients with ILI, 1,568 (18%) were prescribed antivirals. In the age groups for whom outpatient antiviral treatment is recommended, 107 (9%) children <2 years and 49 (23%) adults >65 years received an antiviral prescription. Prescribing practices varied by season, from 11% of ILI patients receiving a prescription in 2011-2012, to 23% in 2012-2013. Patients who received prescriptions were more likely to be seen in clinics that received private vs public funding (20% vs 13%, $p < 0.001$). Patients deemed by the provider to have moderate or severe illness were more likely to receive an antiviral prescription than patients deemed to have mild illness (28% vs 15%, $p < 0.001$). Median time from illness onset to visit date among persons treated and not treated was 1 day (IQR 1–2 days) and 2 days (IQR 1–3 days), respectively ($p < 0.001$). Of 5,910 (67%) patients who presented for care <2 days from illness onset; 22% received antiviral prescriptions compared with 9% who presented after 2 days ($p < 0.001$). Among 6,272 patients with rapid influenza testing performed, patients with a positive result were more likely to receive antiviral prescriptions than those with negative tests (51% vs 9%, $p < 0.001$). Similarly, influenza detection by RT-PCR (unknown to treating provider) was associated with a higher frequency of antiviral prescriptions (37% vs 8%, $p < 0.001$).

Conclusion. Influenza antivirals were prescribed infrequently for outpatients with ILI, including among high-risk age groups for whom antivirals are recommended. Understanding factors associated with outpatient antiviral prescribing is important for communicating antiviral treatment recommendations.

Disclosures. **All authors:** No reported disclosures.

790. Predictors of Influenza Infection in Older Adults Presenting to Emergency Departments (EDs) in Toronto, Canada

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Background. Diagnosis of influenza in the elderly may be complicated by atypical presentations. We compared the characteristics of community-dwelling adults aged ≥60 years presenting to EDs during the 2011/2012 and 2012/2013 influenza seasons.

Methods. We identified patients presenting to six EDs with influenza-compatible symptoms. Clinical characteristics, medical history and demographics were collected by patient interview, chart review and from vaccine providers. NP swabs were tested for flu using PCR. We modeled predictors of flu using multivariable logistic regression models that compared cases to test negative controls.

Results. Of 1318 participants, 151 (11%) had flu (98 AH3N2, 12 AH1N1, 4 A(not subtyped), 37 B). In multivariable models, factors associated with flu were cough (A: OR 4.00, 95%CI 1.67-9.60; B: OR 10.4, 95%CI 2.35-45.8), feverishness and/or $T \geq 37.2^0C$ (A: OR 3.81, 95%CI 2.22-6.54; B: 2.36, 95%CI 1.02-5.47), symptom duration of 2-5d (A: OR 2.15, 95%CI 1.35-3.43; B: OR 2.27, 95%CI 1.05-4.94) and level of flu in the community (A: OR 1.04, 95%CI 1.00-1.07; B: OR 1.13, 95%CI 1.08-1.19). The CDC ILI definition identified 47 (31%) flu cases. Additional factors associated with flu A included having any respiratory symptom (OR 2.29, 95%CI 1.22-4.23), working with children (OR 12.3, 95%CI 2.50-60.7), recent exposure to ILI (OR 1.74, 95%CI 1.08-2.83) and older age (OR 1.03, 95%CI 1.00-1.05). Confusion was associated with flu B among those not frail at baseline. As age increased, cough was more predictive of flu A and B.

Characteristics of participants with no flu, flu A and flu B (n=1318)

	No Flu n=1167	(%)	Flu A n=114	(%)	Flu B n=37	(%)
Cough	649	(56)	*107	(94)	*35	(95)
Feverishness/T >=37.2^{0}C	463	(40)	*89	(78)	*26	(70)
Symptom onset 2-5 days prior	320	(27)	*60	(53)	*21	(58)
Any respiratory symptom	556	(48)	*97	(85)	22	(59)
Any systemic symptom	1064	(91)	*113	(99)	36	(97)
Confusion	257	(22)	34	(30)	12	(32)
Exposure to person with ILI	275	(24)	*53	(46)	11	(30)
Influenza vaccination	766	(66)	80	(71)	20	(56)
Working with children	14	(1)	5	(4)	0	(0)
Age(yrs), median	76 (IQR 16)		77 (IQR 16)		78 (IQR 17)	
% Positive flu tests, all labs, median	21 (IQR 15)		*29 (IQR 13)		26 (IQR 13)	

*p<0.05 when compared against no flu

Conclusion. Cough and fever are as predictive of flu in the elderly as in younger adults but standard case definitions miss most patients. Adding epidemiological factors may be helpful for flu diagnoses.

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791. Does Smoking Increase the Risk for Respiratory Illness or Isolation of Respiratory Viral Pathogens among Healthcare Personnel Using Facial Protective Equipment in Outpatient Healthcare Settings?

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Background. Healthcare personnel (HCP) in outpatient and other settings may be at risk for an acute respiratory illness (ARI). Smoking may increase the risk of ARI. It is unknown if HCP who smoke and use appropriate facial protective equipment (FPE) in outpatient healthcare settings are at greater risk of ARI than non-smokers who also use FPE. The Respiratory Protection Effectiveness Clinical Trial (ResPECT) studies the effectiveness of medical masks and N95 respirators for preventing ARI in outpatient HCP. Our objective is to determine if HCP who smoke are more likely to have a respiratory viral pathogen (RVP) isolated from nasal/throat swabs.

Methods. At study enrollment, HCPs were asked about current smoking history and pre-existing respiratory conditions. In addition, nasal and throat swabs were obtained during the study period. All participants had at least 2 random/asymptomatic swabs collected. When an HCP reported ARI symptoms, swabs were obtained. For the 2012-2013 influenza season the respiratory viral pathogens (RVPs) were identified using RT-PCR/ ESIMS (PLEX-ID, Abbott) from these specimens and the absolute proportions and types of RVPs isolated were compared between smokers and non-smokers.

Results. Of the 1077 HCPs enrolled in 2012-2013, 1069 (99.3%) responded to the pre-study survey question concerning smoking status; 93(8.7%) smoked.

A total of 2630 swabs were collected: 630 (24%) were from symptomatic HCPs at the time of collection. Among 464 HCPs, 47% of smokers and 43% of non-smokers had at least 1 swab obtained when symptomatic with an ARI. RVPs were isolated from 271 (10.3 %) of 2630 swabs (28% symptomatic and 72% asymptomatic). Smokers were not more likely to report symptoms of an ARI or to have a RVP isolated (table).

Respiratory Viral Pathogens Isolated by Smoking Status

Pathogen	Smoker	Non-smoker
	N=93	N=976
Adenovirus	0 (0%)	7 (0.27%)
Coronavirus	6 (0.23%)	98 (3.73%)
Influenza A	1 (0.04%)	37 (1.41%)
Influenza B	0 (0%)	23 (0.87%)
Metapneumovirus	0 (0%)	5 (0.19%)
Parainfluenza	2 (0.08%)	3 (0.11)
Respiratory syncytial virus	2 (0.1%)	26 (0.99%)
Rhinovirus	7 (0.27%)	54 (2.05%)
Totals	18 (19.3%)	253 (25.9%)

**Differences not statistically significant*

Conclusion. HCP who smoke represented only a small percentage of ResPECT participants. Prior research suggests that smoking is associated with a higher risk of bacterial/respiratory tract infection. Among HCP who smoke and use FPE in outpatient settings there was not a higher risk of acute respiratory illness or isolation of respiratory viral pathogens, perhaps demonstrating the effectiveness of FPE.

Disclosures. **All authors:** No reported disclosures.

792. Predictors of viral pneumonia in patients with community-acquired pneumonia

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Background. Viruses are increasingly detected as major causes of community-acquired pneumonia (CAP), and early antiviral therapy affects the outcome. However, few studies were performed about the clinical predictors of viral pneumonia. In this study, we investigated the clinical predictor of viral pneumonia in patients with CAP, which are helpful for considering diagnostic tests for respiratory viruses and early empirical antiviral therapy.

Methods. We retrospectively identified all adult patients (≥ 18 years old) with CAP who were tested by polymerase chain reaction (PCR) test for respiratory virus at two teaching hospitals between October 2010 and May 2013. Demographic and clinical data were collected by reviewing the Electronic Medical Records of the patients.

Results. During the study period, 333 patients with CAP who were tested by respiratory virus PCR were identified. Viral pneumonia (n = 53) was associated with rhinorrhea, higher lymphocyte fraction in white blood cells, lower serum creatinine and ground-glass opacity (GGO) in radiography, compared to non-viral pneumonia (n = 256) ($p < 0.05$ each). In multivariate analysis, rhinorrhea (HR 2.78; 95% CI, 1.23-6.29) and GGO (HR 3.83; 95% CI, 1.97-7.43) were revealed as independent risk factors for viral pneumonia in patients with CAP. The sensitivity, specificity, positive and negative predictive value (PPV and NPV) of rhinorrhea were 21%, 91%, 32% and 85%: The sensitivity, specificity, PPV and NPV of GGO were and 41%, 84%, 35% and 87%, respectively.

Conclusion. Clinical predictors have low sensitivity to viral pneumonia. However, high specificity and PPV of rhinorrhea and GGO suggest that these can be useful indicators for empirical antiviral therapy.

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793. Incidence of Cardiovascular Events in Patients with Influenza Pneumonia or Pneumonia Due to Other Etiologies

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Background. Cardiovascular diseases, influenza, and pneumonia are leading causes of morbidity and mortality worldwide. Cardiovascular events (CVE) are common during the clinical course of pneumonia. Investigators have documented an increased incidence of cardiovascular events and associated mortality during the influenza season as well. However it is unknown as to if these associations are due to all-cause pneumonia or influenza-specific pneumonia. The Community-Acquired Pneumonia Organization (CAPO) is an international observational study that assesses the management of hospitalized patients with community-acquired pneumonia (CAP). Using the centralized CAPO database we decided to conduct this study with the aim to compare the incidence of cardiovascular events in patients with pneumonia due to influenza or pneumonia due to other etiologies.

Methods. This was a secondary analysis of the CAPO study database. Influenza was identified via PCR. Patients with CAP were classified into two groups: CAPFlu (+) or CAPFlu (-) based on influenza PCR results. The following CVE were recorded during hospitalization: arrhythmias, congestive heart failure, acute myocardial infarction and pulmonary embolism. Fisher's exact test was used to compare cardiovascular events.

Results. A total of 800 patients with CAP were included in the study. Of the 112 CAPFlu (+) patients, 14 (13%) had a CVE, while of the 688 CAPFlu (-) patients, 77 (11%) had a CVE ($p = 0.75$). New serious arrhythmia and acute worsening of a long-term arrhythmia combined were the most frequent CVE in both groups [9% CAPFlu (+) vs 5% CAPFlu (-)].

Conclusion. This study indicates that there is no difference in the incidence of cardiovascular events in patients with pneumonia due to influenza or pneumonia due to other etiologies. The inflammatory response to pneumonia is the primary driver for CVE, regardless of etiology.

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794. Socioeconomic and racial disparities associated with pandemic and seasonal influenza among children

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Background. Previous research suggests socioeconomic disparities related to both individual and community characteristics in the risk of infection during novel H1N1 pandemic influenza. This case-control study examined whether similar disparities exist during seasonal influenza.

Methods. We compared cases of laboratory-confirmed influenza (LCI) to influenza-negative controls among a cohort of children <18 years old who presented to a large metropolitan pediatric network with a respiratory illness during consecutive respiratory seasons from 2005 to 2013 and the periods of activity for 2009 novel H1N1 pandemic influenza. We limited analyses to all children who resided in Philadelphia County and had respiratory viral testing performed. Subjects were geocoded to a neighborhood (defined as minor civil division.) Generalized estimating equations evaluated associations between individual and community risk factors and LCI while adjusting for neighborhood clustering. Model parameters were used to calculate risk profiles for seasonal vs pandemic influenza.

Results. Among the 16,464 children who had a respiratory viral test performed, 1,975 (12.0%) had LCI (21 % for pandemic and 11.5% for seasonal LCI). Within the 1,422 seasonal influenza cases, risk of LCI was independently associated with Asian (OR 1.43, 95% CI 1.06, 1.95) and black (OR 1.30, 95% CI 1.05, 1.60) race and age ≥ 5 years (OR 3.03, 95% CI 2.69, 3.42) while lower risk was associated with residence in a high-income neighborhood (0.8, 95% CI 0.7, 0.9). The predicted probability of influenza was highest (25%) among Asian children ≥5 years old living in mid-level income neighborhoods. In contrast, the predicted probability (56%) for pandemic influenza was highest among children >5 years old on Medicaid but lived in neighborhoods with low poverty rates

Conclusion. In contrast to pandemic influenza cases, racial but not socioeconomic disparities exist in the risk for seasonal influenza while residence in high income neighborhoods may be protective. This suggests that individual and community-level factors influence disease risk differently during pandemic compared to seasonal influenza. These findings may have important implications for prevention efforts and pandemic preparedness.

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795. Comparison of respiratory viral shedding with culture and PCR based method in persons with hematologic malignancy

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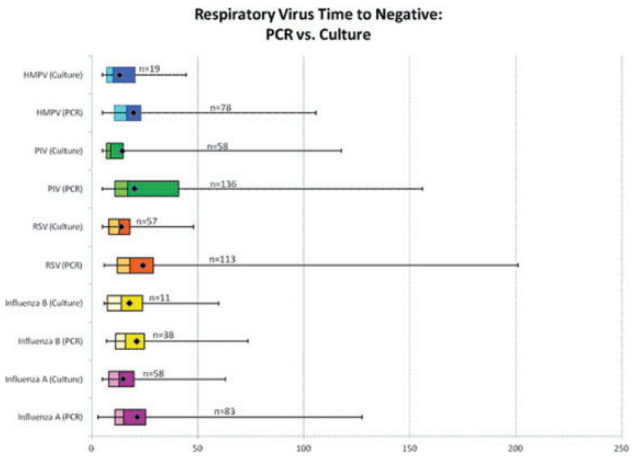
Background. Community respiratory viruses (CRV) are a leading cause of infection related morbidity and mortality for patients undergoing cancer treatment. Molecular based testing (PCR) is a faster, more sensitive diagnostic method than culture. PCR does not differentiate between active viral replication and resolved infection, thus making test of cure and isolation policies for CRV-positive patients unclear. The goal of this analysis was to compare duration of CRV shedding as detected by culture and PCR for patients with hematologic malignancy.

Methods. Results of respiratory virus tests from two study periods, January 2009-September 2011 (culture) and September 2011-April 2013 (PCR) were reviewed for patients with hematologic malignancy [hematopoietic stem cell transplant, leukemia, lymphoma, and pediatric oncology]. Patients were included if tested positive for influenza A, influenza B, parainfluenza (PIV), human metapneumovirus (HMPV), and/or respiratory syncytial virus (RSV), and if first re-tested within 5-30 days after initial diagnosis. The patients' symptoms at time of each re-test were also reviewed.

Results. This study included 651 CRV infection episodes; 203 detected by culture and 448 by PCR.

The figure shows the median and range of shedding for each virus. The median length of shedding by culture and PCR respectively is as follows, influenza A: 13 vs 15; influenza B: 14 vs 16; RSV:13 vs 18; PIV: 9 vs 17; HMPV 10 vs 16.5. Of the 72 (16%) PCR-positive patients who shed virus for >30 days, most (74%) were non-influenza viruses. There was no correlation between symptoms at time of test and result of test. Patients with ALC< 200 at time of retesting were more likely to still shed the virus (table).

Viral shedding



Symptoms at repeat test

Result	Count	% fever	% cough	% rhinorrhea	% sinus congestion	% LRI	% ALC<= 200
+	186	6.5%	56.5%	41.9%	12.4%	14.0%	11.80%
-	262	4.6%	33.6%	20.6%	7.3%	3.4%	3.10%

Conclusion. For our cohort of immunosuppressed patients, longer shedding was seen with PCR than culture. Shedding of influenza viruses was similar across both methods, seldom lasting > 1 month. Overall, shedding >1 month was rare, and seen most with RSV and PIV. Symptom based assessment of viral shedding is unreliable. Our findings should help guide infection control practices for CRV in high risk patients.

Disclosures. **All authors:** No reported disclosures.

796. Transmission of Human Rhinovirus Genotypes among Childcare Attendees

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Background. Human rhinovirus (HRV) is the most common cause of respiratory illness in children. HRVs are genetically diverse and classified into three clades: HRV-A, B, and C. No previous studies have analyzed HRV transmission in a childcare setting.

Methods. Between February 2006 and May 2009, children enrolled at three childcare facilities on a military base in Washington State between the ages of five weeks to 30 months were monitored for respiratory illness. Up to 71% of children in each classroom were enrolled. Mid-nasal swabs were collected at the time of respiratory illness and weekly until symptoms resolved and from a subset of asymptomatic children at enrollment. Samples were tested for HRV by real-time reverse transcriptase polymerase chain reaction. Sequencing was conducted targeting the 5' non-coding region.

Results. HRV was detected in 360 samples from 160 children during 250 illnesses and from 74 of 141 swabs from 127 asymptomatic subjects. Of these, 289 (67%) specimens were successfully sequenced, including 66 unique genotypes. HRV-A, HRV-B, and HRV-C were detected in 170, 15, and 104 samples, respectively. Up to five distinct genotypes circulated in a single classroom during a two-week period. We observed HRV genotype clustering in individual classrooms. One HRV-A genotype was detected in 25 patients located in nine classrooms over 107 days. This HRV-A genotype circulated among four (44%) study participants in one room over 15 days, three (27%) participants in a second room over seven days, and three (17%) participants in a third room over three days. Within 14 days of initial detection, a separate HRV-A genotype was detected in seven (30%) enrollees located in a fourth room. Four days after initial detection, a HRV-C genotype was detected in four (44%) children in a fifth room. A different HRV-C genotype was found in three (15%) participants in the third room within a two-day period.

Conclusion. HRV-A and C were the most common species detected in symptomatic childcare attendees. Diverse HRV genotypes circulated within childcare facilities, clustering in individual classrooms during short time periods. Infection control and prevention should target these settings to reduce transmission.

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797. Viral co-infections in hospitalized patients with respiratory tract infections

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Background. Improvement in molecular technologies in the past ten years allow us to simultaneously test respiratory viruses such as human rhinovirus (HRV), respiratory syncytial virus (RSV), influenza A virus (FluA), parainfluenza virus-1 (PIV-1), parainfluenza virus-3 (PIV-3), human coronavirus-OC43 (HCoV-OC43), human coronavirus-229E (HCoV-229E), adenoviruses (AdV) and a panel of newly discovered viruses such as human metapneumovirus (hMPV), HCoV -NL63, human bocavirus (Boca), human polyomavirus KI (KIV) and human polyomavirus WU (WUV). The simultaneous detection of a broad spectrum of viruses allows the identification of viral co-infection in upper respiratory infections (URTI) and lower respiratory tract infections (LRTI). In this study establishing a link between viral co-infections and an increase in disease severity can be thought-provoking.

Methods. The aim of this study is to investigate the role of viral co-infection in patients with respiratory tract infections (RTI) by using real time PCR techniques.

Results. In total, 934 hospitalised patients aged between 3 days and 80 years were screened over a three years period, from September 2010 to September 2013. Among the 351 patients diagnosed with viral infections, HRV was detected in 41.9%, FluA virus in 15.1% and RSV in 13.1%. Viral co-infection was detected in 49 patients (14%) with HRV being the most common virus associated with co-infection (26 patients or 7.4%), followed by AdV (14 patients or 4%) and HCoV-OC43 (12 patients or 3.4%). It was interesting to note that three patients had three viral co-infections. Among the 49 co-infected patients viral co-infections were common among those aged less than 1 year of age (20 patients or 40.8%). Thirty two patients or 65.3% were admitted to wards and (17 patients or 34.7%) to ICU or PICU. Furthermore, among the virally co-infected patients LRTI was the most frequent reason for hospitalization (38 patients or 77.6%).

Conclusion. Simultaneous testing of respiratory viruses by real-time PCR is a suitable tool for the detection and evaluating the role of viral co-infections in respiratory tract infections. The data of this study established a link between viral co-infections and an increase in disease severity.

Disclosures. **All authors:** No reported disclosures.

798. Hospitalization due to Respiratory Syncytial Virus (RSV) and Influenza Infection in Adult Patients: a Retrospective Cohort Study

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Background. A better understanding of the characteristics and outcomes of adult patients hospitalized with RSV as compared to influenza infection is needed.

Methods. We conducted a retrospective cohort study of adult patients admitted to four hospitals in Toronto, Canada, between September 2012 and June 2013 with RSV or influenza infection diagnosed by RT-PCR. Main outcomes were hospital length of stay (LOS), need for intensive care (ICU) or mechanical ventilation (MV), and all-cause mortality. Chi-square and Fisher's exact test were used for analysis.

Results. 86 patients with RSV and 231 with influenza were included. Median age was 74y in RSV and 73y in influenza patients. Patients with RSV had more underlying illness (P = 0.03) with a trend toward greater underlying cardiac disease (P = 0.054), but no difference in rates of underlying lung disease, malignancy or immunosuppression. Most common symptoms and signs in both groups were cough, dyspnea, sputum production, fever, weakness and wheezing. 56% of influenza and 50% of RSV patients met CDC criteria, and 12% of influenza and 16% of RSV patients met PHAC criteria for influenza-like illness. Dyspnea, sputum production, weakness and wheezing were all more common in RSV patients (P = <0.01 for all). There were no significant differences in main outcomes, or overall lower respiratory tract or cardiovascular complications. CHF exacerbation was more common in RSV patients (P = 0.01). Mean and median hospital LOS was 11 and 6 days for both groups. 15% with RSV and 13% with influenza required ICU care, and 9% in both groups required MV. 6% with RSV and 9% with influenza died during hospitalization. Need for MV and ICU were associated with mortality in both groups (P = 0.01). More co-pathogens were identified in RSV patients (11/86 vs 14/231, p = 0.048), with greater associated mortality in influenza patients. 78% of RSV and 72% of influenza patients were treated with antibiotics.

Conclusion. Adults hospitalized with RSV or influenza infection experience similar hospital LOS, need for ICU and MV, and mortality. While presenting signs and symptoms are nonspecific, patients with RSV have greater dyspnea, sputum production, weakness and wheezing. Patients with RSV and influenza often receive antibiotics. There is need for development of RSV vaccines and treatments for adults.

Disclosures. **All authors:** No reported disclosures.

799. Linezolid vs Vancomycin in the Treatment of Nosocomial Pneumonia: A Cost-effectiveness Analysis Incorporating Results from the ZEPHyR Trial

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Background. Existing cost-effectiveness analyses comparing linezolid and vancomycin for the treatment of a variety of pneumonias utilize data from trials which are controversial. This study examines the cost-effectiveness of vancomycin vs linezolid in the treatment of nosocomial pneumonias incorporating results from a recent prospective, double-blind, multicenter, controlled trial in adults with methicillin-resistant *Staphylococcus aureus* nosocomial pneumonia.

Methods. A decision analytic model was created examining the cost-effectiveness of utilizing linezolid vs vancomycin for treatment of nosocomial pneumonia from a payer perspective with a lifetime time horizon. Publicly available cost, efficacy, and utility data was used to populate relevant model variables. The primary outcome measure was incremental cost-per quality-adjusted life year (QALY) with secondary analyses on incremental cost-per life saved and the budget impact to the United States healthcare system. A probabilistic sensitivity analysis varied parameters in a hypothetical cohort of 10,000 patients and univariate sensitivity analyses assessed the impact of model uncertainties and robustness of our conclusions.

Results. Results indicated the lifetime cost per QALY increased 3% ($205,761 vs $212,138) by utilizing linezolid vs vancomycin for nosocomial pneumonia. The incremental cost per QALY by utilizing linezolid over vancomycin was $56,917. Our model predicted an incremental cost-per life saved of $491,106 with linezolid utilization. Vancomycin dominated linezolid in the subset of patients with documented MRSA. The incremental cost of utilizing linezolid as the preferred treatment option if no mortality benefit exists between agents was $6,378 per patient. Variations in all-cause 60-day mortality rates had the potential to impact results. Results of a Monte Carlo simulation demonstrated linezolid had a 69.9% chance to be cost-effective at our willingness-to-pay threshold.

Conclusion. Empiric utilization of linezolid may be a cost-effective alternative to vancomycin; however, results were highly dependent on outcome data which remains controversial. Results provide a multi-factorial framework to facilitate discussions when evaluating antimicrobial therapy for nosocomial pneumonia.

Disclosures. **All authors:** No reported disclosures.

800. Infectious pulmonary complications following allogeneic hematopoietic stem cell transplantation at a high-volume, academic, transplant center

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Background. Infectious pulmonary complications (IPC) cause significant morbidity and mortality following allogeneic hematopoietic stem cell transplantation (HSCT). Diagnostic chest imaging and microbiologic testing are essential tools for evaluating IPCs in the posttransplant setting.

Methods. A retrospective chart review was performed on an established cohort of 94 patients who underwent allogeneic HSCT at MSKCC between September 4, 2009 and August 4, 2011. A pulmonary complication was defined as incident clinically-relevant abnormal parenchymal findings identified on diagnostic imaging from the start of pretransplant conditioning until up to 3 years posttransplantation. An IPC was considered to be infectious (proven, probable or possible) based on the results of standard evaluation of respiratory and other specimens, as well as clinical interpretation. Relationships between transplant factors, IPC diagnoses and clinical outcomes were evaluated using logistic regression.

Results. Over 3 years, 62/94 (66%) of subjects developed at least one posttransplant IPC. 55/62 (89%) occurred during the first year, of which 33 (60%) occurred during the first month after HSCT. Nearly half of subjects (33) had undergone ablative preparative conditioning. 44 (73%) of IPCs were considered bacterial, 15 (24%) viral and 3 (5%) fungal in origin. 13 (21%) diagnoses were proven, with identification of specific viral (HHV6, respiratory viruses), bacterial (Legionella, Klebsiella, Pseudomonas spp), or fungal (Aspergillus) organisms in lower respiratory tract specimens. 28 (45%) of IPC diagnoses were considered probable, and 21 (33.9%) were non-specific. Multivariate analysis demonstrated that a pulmonary complication more than doubled the risk of death from any cause [OR 2.6 (1.1-6.9) 95% CI; p = 0.046].

Conclusion. This study demonstrates a high incidence of post-transplant IPCs at an academic transplant center. The minority carried a specific diagnosis, thereby limiting targeted intervention in the majority of cases. Importantly, pulmonary complications were associated with a significant increase in overall mortality following HSCT. Recognition and effective management of these complications are important in order to optimize overall care of these patients and their subsequent clinical outcomes.

Disclosures. **All authors:** No reported disclosures.

801. Molecular Epidemiological Characteristics of *Klebsiella pneumoniae* Associated with Bacteremia among Patients with Pneumonia

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Background. Some important virulence factors have been elucidated among *Klebsiella pneumoniae* infections. We investigated the relationship between virulence factors and molecular epidemiological factors, and assessed the risk factors for bacteremic pneumonia (BP) due to *K. pneumoniae*.

Methods. From April 2004 through April 2012, a total of 68 *K. pneumoniae* isolates from patients with pneumonia (23 from BP and 45 from non-bacteremic pneumonia [NBP]) were collected from ten medical institutions in Japan. Additionally, ten K2-positive strains which were isolated more than 30 years ago were included in this study. These isolates were characterized using multilocus sequence typing (MLST), and characteristics of their virulence factors such as hypermucoviscosity phenotype, RmpA, and aerobactin production between BP and NBP were examined.

Results. MLST analysis was performed with the 68 isolates from patients with pneumonia, and some sequence type (ST) groups were defined as genetic lineages (GLs), which were groups of STs in which allele profiles had at least 5 loci in common on the basis of the profile of primary founders or subgroup founders in a population snapshot determined by eBURST. GL65s were significantly more prevalent among patients with BP (21.7%) than those with NBP (4.4%). K2-positive strains were classified into GL14 and GL65, depending on the virulence factors. The *rmpA* and gene for aerobactin were all positive among the GL65-K2 strains and all negative among the GL14-K2 strains. In multivariate analysis, the independent risk factors for bacteremia included GL65 (adjusted odds ratio [AOR], 15.96; 95% confidence interval [CI], 2.03–125.47) as well as neoplastic disease (AOR, 7.83; 95% CI, 1.86–33.00) and hypoalbuminemia (AOR, 4.25; 95% CI, 1.03–17.47).

Conclusion. GL65 was more prevalent among patients with BP, and was associated with the virulence factors of *K. pneumoniae*.

Disclosures. **All authors:** No reported disclosures.

802. The Cost of a Measles Outbreak in 2013, New York City, United States

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Background. Although measles was declared eliminated from the United States in 2,000, importations continue to occur. In March 2013, an intentionally unvaccinated adolescent with measles returned to New York City (NYC) from the United Kingdom, leading to an outbreak of 58 cases. We examined the cost to the NYC Department of Health and Mental Hygiene (DOHMH) to respond to and contain the outbreak.

Methods. Direct costs were calculated as the sum of inputs (immunoglobulin/vaccine, courier/travel, postage, advertising, laboratory testing) and personnel time. Personnel time cost was calculated as hourly wage x routine business hours worked plus paid overtime and fringe. The incremental cost was calculated as total direct costs minus salary and fringe paid to DOHMH staff during routine business hours. In-kind costs (uncompensated hours worked by DOHMH-funded staff and salaries of DOHMH staff funded by outside agencies), overhead, and costs to outside medical facilities and patients were not included.

Results. Direct costs were $394,447 ($62,101 inputs, $332,346 compensated personnel time). The incremental cost was $73,134 (19% of total direct costs). DOHMH-funded staff (n = 75) worked 9,337 hours (8,667 routine business hours, 324 paid overtime, 346 uncompensated). DOHMH staff funded by outside agencies (n = 12) worked 716 hours. Activities included case/contact investigations (5,861 hours, 58%), administrative activities (445 hours, 4%), laboratory work (2,765 hours, 28%), and community outreach (981 hours, 10%). Among all staff, 68% performed duties related to their routine job description.

Conclusion. Response and containment of this outbreak required assistance from a large number of staff, of whom one-third performed duties outside of their routine job description. This emphasizes the importance of a robust and flexible public health infrastructure to facilitate redirection of personnel. These cost figures likely underestimate the total cost, as they do not account for in-kind costs or costs to medical facilities, outside agencies, patients, and society. The significant burden and impact of measles outbreaks as well as other public health emergencies, underscore the importance of continued support and resources for public health departments.

Disclosures. **All authors:** No reported disclosures.

803. Direct Costs and Duration of Hospitalization of Patients Hospitalized with Community Acquired Pneumonia: a Nationwide Retrospective Claims Database Analysis

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Background. Community-acquired pneumonia (CAP) is one of the most common acute infections requiring hospital admission resulting in a substantial clinical and economic burden. While several studies have reported the cost for hospitalized CAP, there have been few studies using a national dataset to estimate the age-and type of care specific costs of hospitalized CAP.

Methods. A retrospective study of claims data from a nationwide Dutch database (covering 16.7M inhabitants) was conducted. From this database (DBC information system), patients with at least one claim with a final diagnosis of CAP between January 2008 and December 2011 were selected. The main outcome measures were the direct hospitalization costs and the duration of hospitalization of CAP, both stratified by age and severity. Severity was defined based on the type of care received ("ICU" [i.e., inpatient CAP admitted for at least one night to the ICU], "general ward" [i.e., inpatient CAP only admitted at the general ward] or "outpatient" [i.e., ED and policlinic visits without an overnight stay and therefore not counted as hospitalization days]). For this study the population was divided into the following age-groups: 0-9; 10-17; 18-49; 50-64; 65-74; 75-84; ≥85 years.

Results. In total, 196,554 CAP cases were included in the analysis. Of these 123,673 (63%) were hospitalized for 1 or more nights of which 5.9% (n= 7,265) spend at least one night on the ICU. In total, these 123,673 patients spend 828,356 days in the hospital of which 51,745 (6.2%) were spend on the ICU. The total costs related to all CAP episodes during these 4 years was €714M, resulting in a mean cost of €3,631 euro per episode. Mean costs were highly dependent on age and type of care with costs ranging from €482 for 0-9 year olds treated outpatient up to €14,402 for 50-64 year olds admitted to the ICU. The mean duration of hospitalization of ICU patients and general ward patients was 15.2 days and 6.2 days, respectively. ICU patients spend 44% of their total admission time on the ICU (i.e., 6.7 days).

Conclusion. The financial burden of hospitalized CAP is high and varies significantly depending on age and the severity of the CAP. Effective interventions to prevent pneumonia could result in large cost savings.

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804. Epidemiology and Molecular Characteristics of *Mycoplasma pneumoniae* (Mp) during an Outbreak of Mp-Associated Stevens-Johnson Syndrome, Colorado, 2013

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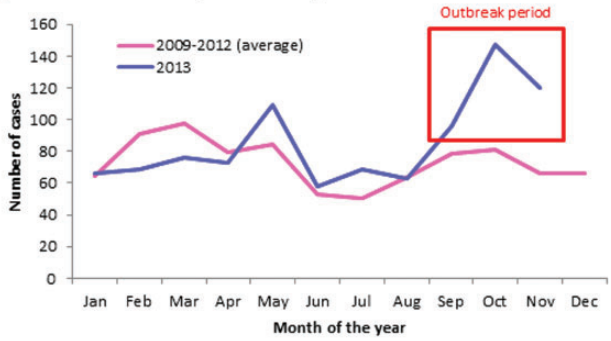
Background. In fall 2013, a novel outbreak of 5 cases of *Mycoplasma pneumoniae* (Mp)-associated Stevens-Johnson syndrome (SJS) among pediatric patients was identified at Hospital A, Colorado. Mp is a leading cause of community acquired pneumonia in children and young adults, but subsequent development of SJS, a severe, immune-mediated mucocutaneous disorder, is rare. We investigated the epidemiology of Mp in the community and the molecular characteristics of Mp strains in SJS and non-SJS patients to understand why this outbreak occurred.

Methods. We used ICD-9 codes to identify pneumonia cases (etiology unspecified: 482.9, 486; Mp-specific 483.0) among patients aged 5–21 years at Hospital A from 2009–2013. We collected available Mp-positive specimens from 5 Colorado hospitals and 4 referral laboratories. Quantitative PCR was used to confirm Mp. Subtyping by multilocus variable-number tandem-repeat analysis (MLVA) for differences at 4 genomic loci and macrolide resistance testing were performed on confirmed Mp-positive specimens.

Results. Pneumonia cases peaked in October, 2013 coinciding with the period of the SJS outbreak (September–November 2013; figure). Mp was confirmed in specimens from 4 SJS patients and 42 non-SJS patients (table). MLVA subtyping showed three different strains among SJS patients, all of which also occurred among non-SJS patients. Three SJS patients (75%) had 3 of 4 matching loci in their MLVA pattern (3-X-6-2) compared with 11 (26%) non-SJS patients, although this trend did not reach statistical significance. Macrolide resistance was identified in 7% of all strains.

Figure: Pneumonia cases by month of the year



Data from Hospital A, patients aged 5-21. Pneumonia cases based on ICD-9 codes 482.9, 483.0, 486.

Results of laboratory testing

		SJS patients, n = 4 n (%)	Non-SJS patients, n = 42 n (%)
Collection dates, 2013		Sep–Nov	Jan–Dec
Macrolide testing			
Susceptible		4 (100)	37 (88)
Resistant		0	3 (7)
MLVA type			
3-5-6-2	3-X-6-2	1 (25)	8 (19)
3-6-6-2		2 (50)	3 (7)
4-5-7-2		1 (25)	26 (62)

Conclusion. A heavy community burden of Mp disease likely contributed to the increase in Mp-associated SJS cases seen at Hospital A. The trend toward MLVA pattern 3-X-6-2 raises the possibility that strain features may influence the development of SJS, although the small sample sizes limited interpretation. Clinicians should be aware of the relationship between Mp and SJS.

Disclosures. **C. C. Robinson**, Biofire Diagnostics Inc.: Scientific Advisor, Consulting fee

805. Predictors of 30-day hospital readmission in patients with community-onset pneumonia

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Background. Predictors of hospital readmission after community-onset pneumonia are not well characterized. The aim was to compare characteristics of readmitted vs non-readmitted patients to identify predictors of 30-day readmission in a cohort of patients with an index hospitalization for community-onset pneumonia.

Methods. Retrospective evaluation of adults admitted to a 624-bed U.S. academic medical center with an ICD-9 diagnosis code of pneumonia from January 2010-December 2011. All patients had a new or progressive infiltrate on chest imaging and at least two of: hypo/hyperthermia, WBC <4k or >12k, or respiratory symptoms (e.g., cough, shortness of breath). Chi-squared, Student's t-test, and Mann-Whitney U were used for univariate analysis. Variables with a $p < 0.1$ in univariate analysis were candidates for the stepwise multivariate logistic regression to identify factors independently associated with readmission.

Results. 508 patients included with 19.3% (98/508) experiencing 30-day readmission. Baseline characteristics at index hospitalization for the readmitted/non-readmitted groups were the following: median age: 66.5y/65y ($p = 0.77$); CURB-65 score >2: 33.7%/12.2% ($p < 0.001$); ICU admission: 7.1%/6.6% ($p = 0.85$); WBC: 12.9K/12.3K ($p = 0.48$); immunocompromised status: 19.4%/9% ($p = 0.003$); MRSA colonization: 12.2%/3.7% ($p = 0.001$); HCAP: 63.3%/44.9% ($p = 0.001$); aspiration risk: 26.5%/18.8% ($p = 0.086$) COPD: 33.7%/26.3% ($p = 0.145$); heart failure: 21.4%/15.4% ($p = 0.15$); diabetes 30.6%/26.8% ($p = 0.45$); hemodialysis 12.2%/3.7% ($p = 0.001$); antibiotic use in the last 90 days: 41.8%/28.9% ($p = 0.013$); median number of hospitalized days in the last 180 days: 4/0 ($p < 0.001$). In the final multivariate model, primary viral pneumonia was protective for 30d hospital readmission OR = 0.115 [95%CI 0.01-0.96] and four variables were independently associated with readmission: MRSA colonization, OR = 3.13 [95%CI 1.33-7.38]; hemodialysis, OR = 2.56 [95%CI 1.07-6.13]; CURB-65 score >2 OR = 3.58 [95%CI 2.05-6.24]; immunocompromised status, OR = 2.71 [95%CI 1.39-5.32].

Conclusion. Independent predictors of 30-day readmission in multivariate analysis are typically not modifiable; preventive interventions should be focused on these four patient populations to decrease hospital readmission.

Disclosures. **M. E. Rupp**, 3M: Consultant and Grant Investigator, Consulting fee and Research grant

806. Causes of Early and Late Mortality Following Invasive Pneumococcal Disease in Hull and East Yorkshire, 2007-2009

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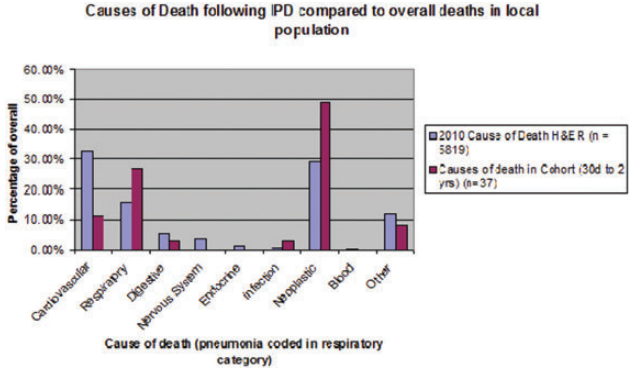
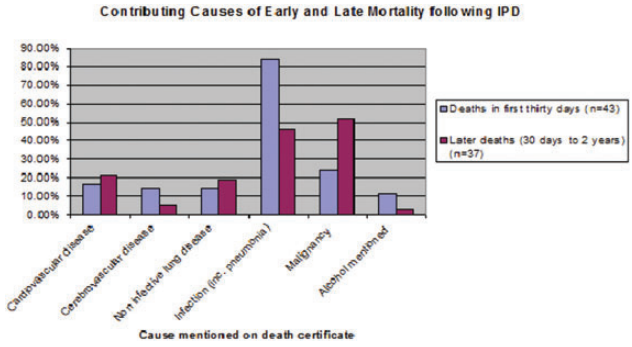
Background. Although considered an acute illness, evidence suggests increased long term mortality following invasive pneumococcal disease (IPD). There is a lack of evidence regarding the underlying causes, but work in pneumonia suggests an increase in cardiovascular deaths. We conducted a retrospective cohort study to examine the causes of death in the two years following IPD.

Methods. All adult cases of IPD presenting to Hull and East Yorkshire Hospitals (1400 bed teaching hospital), 2007 to 2009 were identified via the Department of Microbiology's electronic-database. Medical records were reviewed and death certificates obtained for patients who died within 2 years of an episode of IPD. Causes of death within 30 days (early) were compared to those between 30 days and 2 years (late). Late deaths were compared to causes of death in our local population (N = 5819) in 2010.



Results. 207 patients (50.7% male, mean age 64.9) were included. Most patients (80%) had pneumonia. Mortality at 30 days following IPD was 20.8% (n = 43) and 38.6% (n = 80) by 2 years. Within 30 days, infection was the primary cause of death in 60.5% and contributed to 83.72%. Infection remained an important cause of late death, being the primary cause in 24.3% and contributory in 45.9%. Of late deaths due to infection, 89% were due to respiratory infection. Malignancy was the primary cause of most late deaths (48.6%). A higher proportion of deaths between 30 days and 2 years were caused by respiratory disease (including respiratory infection) and malignancy compared to overall deaths locally (27.0% vs 15.7% and 48.6% vs 29.0%, respectively), but less were due to cardiovascular disease (10.8% vs 32.6%).



Conclusion. The majority of early deaths following IPD are due to infection, which remained an important primary and contributory cause of death during follow-up. Respiratory diseases (including pneumonia) were responsible for a greater proportion of late deaths compared to the general population. This work does not support the hypothesis that IPD increases late cardiovascular deaths with the majority of non-infective deaths being due to malignancy. Whether late deaths can be prevented by intervention (e.g., conjugate vaccine) after the IPD episode is unclear, but should be explored.

Disclosures. **All authors:** No reported disclosures.

807. Relationship between Respiratory Virus Infection and Pneumococcal Colonization in Children

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Background. Respiratory viruses and pneumococcus act in synergy during the course of respiratory illness, but the pathogenesis is not fully understood. The purpose of this study is to evaluate the association of respiratory virus infections and pneumococcal colonization in children, and to find out affecting factor in their relationship.

Methods. From May 2009 to June 2010, 1,367 nasopharyngeal aspirates were collected from children who visited Seoul National University Children's Hospital for acute respiratory symptoms. 12 respiratory viruses (influenza virus A, B; parainfluenza virus 1, 2, 3; respiratory synctytial virus (RSV) A, B; adenovirus; rhinovirus A/B; metapneumovirus; human coronavirus 229E/NL63, OC43/HKU1) were determined by multiplex RT-PCR. *S. pneumoniae* was isolated using conventional culture methods. Demographics of affected children, characteristics and the impact of pneumococcal carriage on respiratory virus infection were assessed.

Results. Among the 1,367 nasopharyngeal aspirates, 228 isolates (16.7%) of *S. pneumoniae* were recovered, and 834 respiratory viruses from 731 (53.5%) nasopharyngeal aspirates were detected. The most common respiratory viruses were as follows: rhinovirus (30.2%), RSV A (17.4%), adenovirus (11.4%), and influenza virus A (11.2%). The pneumococcal carriage rate was higher among those with respiratory virus than those without respiratory virus isolated [21.3% (156/731) vs 11.3% (72/636), $P < 0.001$)]. Among 12 respiratory viruses tested, influenza A (OR 3.00, 95% CI 1.75-5.14), influenza B (OR 2.73, 95% CI 1.16-6.47), RSV A (OR 2.38, 95% CI 1.56-3.63), RSV B (OR 2.90, 95% CI 1.31-6.41), and rhinovirus A/B (OR 1.96, 95% CI 1.37-2.80) were associated with higher likelihood of pneumococcal carriage.

Conclusion. Pneumococcal carriage rate was higher in children of whom respiratory viruses were isolated, especially in influenza virus A and B, RSV A and B, and rhinovirus A/B.

Disclosures. **H. J. Lee**, National Research Foundation of Korea: Investigator, Research grant

808. Outcomes of Older Adults with Sepsis at Admission to an Intensive Care Unit

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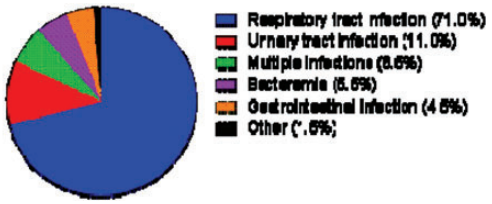
Background. Prior studies have shown that older adults with sepsis have high in-hospital mortality rates; however, less is known about mortality in patients who survive hospitalization. The primary aims of this study were to 1) assess the association of sepsis at ICU admission with clinical outcomes (mortality and decline in functional status) after ICU discharge, and 2) identify other predictors associated with increased mortality and decline in functional status in adults age 60 or older admitted to an ICU.

Methods. Prospective cohort study of 309 patients 60 years or older admitted to a medical ICU. Sepsis was defined as 2 of 4 criteria for SIRS: (Temp >38.3 or <36°C, HR > 90 beats/minute, RR > 20 breaths/minute or PaCO2 < 32 mmHg 4, WBC > 12,000 or <4,000 cells/mm^3) plus an infection within 2 calendar days before or after admission. Infections were identified using CDC/NHSN definitions for health-care associated infections. The main outcome measure was time to death within 1 year of ICU admission. The secondary outcome measure was decline in functional status, defined as change in a count of activities of daily living (ADL) from baseline to 1 month after ICU discharge. A Cox proportional hazards model was developed to evaluate sepsis as a predictor for mortality. Multiple linear regression was used to assess factors associated with decline in functional status.

Results. Of the 309 patients, 196 (63%) were defined as having sepsis. Sites of infections are shown in Figure 1. When adjusting for baseline admission covariates, sepsis had a significant impact on survival (hazard ratio [HR] 1.80, 95% confidence interval [CI] 1.28-2.52, p = <0.001); however, after adjusting for baseline admission and process covariates (antibiotics and vasopressor use within 48 hrs), the impact of sepsis on survival became non-significant (HR 1.26, CI 0.87-1.84, p = 0.22). Having sepsis was associated with a decline in ADLs from baseline to 1 month post ICU discharge after adjusting for clinically relevant co-variates (parameter estimate 0.787, standard error 0.385, p= 0.04).

Figure1. Categories of Documented Infections (n=200)



Conclusion. This study suggests that use of antibiotics and vasopressors may be associated with a decrease in mortality when treating older adults with sepsis and that sepsis may be associated with a greater decline in functional status compared to those admitted to an ICU without sepsis

Disclosures. **All authors:** No reported disclosures.

809. Contemporary Experience with Ceftaroline Fosamil for the Treatment of Community-acquired Bacterial Pneumonia

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Background. Community-acquired bacterial pneumonia (CABP) is a serious infection in many patients. Ceftaroline fosamil (CPT-F) is approved for the treatment of CABP and acute bacterial skin and skin structure infections in the US, and for similar indications in the EU. CAPTURE is a multicenter registry study describing patients treated with CPT-F in the US.

Methods. Data were collected at participating centers by randomly ordered chart review between September 2011 and February 2014, which included demographics, disease characteristics, antibiotic use, location of care, and clinical response. Evaluable patients (pts) were those with a clinical outcome determined.

Results. 649 pts were evaluable. Demographics and co-morbidities are presented in the table. On diagnosis 81% of pts had 2 or more signs and symptoms; most common were dyspnea (76%), cough (65%), abnormal auscultatory findings (63%), and sputum production (46%). At initiation of CPT-F treatment, 35% were located in an intensive care unit (ICU). 84% received prior antibiotics; most commonly ceftriaxone (35%), vancomycin (31%), azithromycin (27%) and levofloxacin (26%). The mean duration of CPT-F therapy was 6.1 days (SD ± 3.8). Concurrent antibiotics were used in 64% and included azithromycin (23%), levofloxacin (17%) and vancomycin (8%). Overall clinical success was 83%; 73% in the ICU and 88% in the ward. Clinical success with CPT-F monotherapy was 84%, and with concurrent therapy, 83%. Clinical success was 85% for CPT-F as first line therapy and 83% as 2nd line therapy. CPT-F was discontinued in 8 (1%) pts due to an adverse event. The majority of pts were discharged to home (60%) or to another healthcare facility (35%).

Demographics and Co-morbidities	Pts (N=649) n (%)
Males, Females	315 (49) 334 (51)
Age, years, mean (SD), range	63.4 (17.5) 18–99
Pts with co-morbidities	514 (79)
Structural lung disease	276 (43)
Smoking	223 (34)
Gastroesophageal reflux	146 (22)
Prior pneumonia	159 (24)
Congestive heart failure	134 (21)
Cerebrovascular accident	53 (8)
Alcoholism	54 (8)

Conclusion. Contemporary clinical use of CPT-F for treating CABP show high rates of clinical success including pts in the ICU. CAPTURE data support the use of CPT-F as an important antibiotic for treatment of complicated CABP.

Disclosures. **L. B. Johnson**, Forest Laboratories: Investigator, Research support **C. M. Cannon**, Forest Laboratories: Investigator and Speaker's Bureau, Research support and Speaker honorarium **L. E. Johnson**, Forest Laboratories: Investigator, Research support **S. Wallace**, Forest Laboratories: Shareholder, have owned approximately $25,000 in stock in Forest Laboratories, purchased long before any involvement with this project **A. Jandourek**, Cerexa Inc.: Employee, Salary **H. D. Friedland**, Forest Laboratories: Employee and Shareholder, Salary

810. Antibiotic Treatment Patterns and Outcomes Following Outpatient Treatment of Community-Acquired Bacterial Pneumonia: A US Cohort Study

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Background. Antibiotic drugs are the standard treatment for community-acquired bacterial pneumonia (CABP) but are associated with the development of bacterial resistance and side-effects. This study estimates the rate of adverse events, hospitalizations and treatment failure following outpatient treatment with antibiotics, and compares them by type of antibiotic administered.

Methods. CABP episodes were identified in the Truven database between January 1, 2007 and December 31, 2012 in patients 18 years of age or older with a pneumonia diagnosis and treated with monotherapy beta-lactam (BL), fluoroquinolone (FQ), or macrolide (M) preceded by both ≥30 days free of institutional care and ≥90 days free of antibiotic use. The effects of monotherapies BL vs M and FQ vs M on risk of adverse events, pneumonia-related hospital visits and treatment failure within 30 days of CABP episode were estimated after adjusting for pre-treatment demographics, health care resource use and costs using multivariate regression models. Treatment failure was defined as switch in drug class ≥ 6 days after initial CABP treatment.

Results. Out of a total of 441,820 CABP patients, 84% were initiated with the following monotherapies: BL (N = 36,702), FQ (165,768) and M (N = 169,335). Comparing the three cohorts revealed that patients receiving FQ therapy were the oldest while BL treated patients were the sickest. FQ vs M initiation was associated with an increased risk of an adverse event (OR = 1.23, 95% CI: 1.20-1.25), increased 30-day odds of pneumonia-related hospital visits (OR = 1.83, 95% CI: 1.69-1.98) and a reduced 30-days odds of treatment failure (OR = 0.90, 95% CI: 0.87-0.94). BL vs M initiation was associated with an increased risk of an adverse event (OR = 1.26, 95% CI: 1.23-1.31), increased 30-day odds of pneumonia-related hospital visits (OR = 1.72, 95% CI: 1.53-1.93) and an increased 30-days odds of treatment failure (OR = 1.27, 95% CI: 1.20-1.35).

Conclusion. Compared to initiating outpatient CABP treatment with M monotherapy, initiation with FQ or BL monotherapy was associated with a significantly increased risk of an adverse event and pneumonia-related hospital visit. The risk of treatment failure was reduced with FQ but increased with BL. Thus, treatments are needed that are both effective and have few side effects.

Disclosures. **S. Eapen**, Cempra, Inc.: Consultant, Research support **C. Llop**, Cempra, Inc.: Consultant, Research support **E. Tuttle**, Cempra, Inc.: Consultant, Research support

811. Antimicrobial activity of ceftaroline tested against respiratory tract infection (RTI) pathogens isolated from USA medical centers in 2013

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Background. Ceftaroline fosamil (CPT) is a broad-spectrum cephalosporin prodrug with potent activity against pathogens causing community-acquired (CA) RTI, including ceftriaxone (CRO)-resistant (R) *Streptococcus pneumoniae* (SPN) and methicillin-R *Staphylococcus aureus* (MRSA). We evaluated the potency and spectrum CPT and several comparators tested against CA-RTI pathogens.

Methods. 4,533 unique patient isolates were collected from 149 USA medical centers during 2013. The collection includes 3,099 *S. pneumoniae* (SPN; 6.5% CRO-non-S), 931 *Haemphilus influenzae* (HI; 23.8% β-lactamase-positive [BL +]), 99 *H. parainfluenzae* (HPAR) and 404 *Moraxella catarrhalis*(MCAT). Susceptibility (S) was tested by CLSI broth microdilution methods against CPT and other antimicrobials used to treat CA-RTI.

Results. CPT ($MIC_{50/90}$, ≤0.015/0.12 μg/mL was eight-fold more potent than CRO ($MIC_{50/90}$, ≤0.06/1 μg/mL) against SPN, and highly active against CRO-non-S SPN strains (n = 201; MIC_{90}, 0.25 μg/mL). S rates for SPN were 92.8% for penicillin (MIC, ≤2 μg/mL), 88.5% for amoxicillin/clavulanate, 56.0% for erythromycin, 77.0% for tetracycline and 98.8% for levofloxacin (LEV). CPT was very active against HI ($MIC_{50/90}$, 0.008/0.015 μg/mL), including BL+ strains (CPT $MIC_{50/90}$, 0.015/0.03 μg/mL). S rates for clarithromycin, azithromycin and LEV among HI were 90.3, 99.1 and 99.8%, respectively. CPT was also active against HPAR ($MIC_{50/90}$, 0.008/0.03 μg/mL) and MCAT ($MIC_{50/90}$, 0.06/0.12 μg/mL; table).

Organism (no. tested)	Cumulative % at ceftaroline MIC (μg/mL) of: ≤0.015	0.03	0.06	0.12	0.25	0.5
S. pneumoniae (3,099)	62.5	72.3	82.1	96.4	99.6	100.0
Ceftriaxone-non-S (201)	–	0.5	1	51.2	94.0	100.0
H. influenzae (931)	90.2	98.3	99.7	99.9	100.0	–
β-lactamase-positive (222)	77.5	94.6	98.6	99.5	100.0	–
H. parainfluenzae (99)	87.9	94.9	97.0	99.0	99.0	100.0
M. catarrhalis (404)	10.1	33.7	66.3	91.3	99.3	100.0

Conclusion. CPT exhibited high activity against bacterial pathogens from CARTI recently (2013) collected from 149 USA medical centers; all organisms (100.0%) were CPT-S. CPT was particularly active against CRO-non-S SPN. Based on these results, CPT represents a valuable agent for treatment of CA-RTI, including multidrug-R isolates.

Disclosures. **H. S. Sader**, Forest: Grant Investigator, Research grant **D. J. Farrell**, Forest: Grant Investigator, Research grant **R. K. Flamm**, Forest: Grant Investigator, Research grant **R. N. Jones**, Forest: Grant Investigator, Research grant

812. Macrolide Use and Innate Immunity Components in Hospitalized Patients with Community-Acquired Pneumonia

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Background. Macrolides have been shown to modulate inflammatory responses. Because macrolides have potentially adverse effects, discovering the mechanism of immunomodulation is important. The objective of this study was to measure plasma cytokine levels and blood neutrophil functions in hospitalized patients with community-acquired pneumonia (CAP) treated with and without macrolide use. The secondary objective was to evaluate clinical outcomes in each group.

Methods. Subjects had peripheral blood analyzed for neutrophil function (secretory vesicle CD35 and specific granule CD66b release), and ten cytokine levels. Neutrophil function in healthy volunteers was also measured for reference. Values were measured on the day of enrollment and one or two more times over the next seven days depending on a patient's length of stay. Early and late clinical outcomes were also evaluated. All values were compared between those treated with and without a macrolide.

Results. A total of 40 subjects were in the study; 14 received macrolide treatment, and 26 did not. Neutrophil function in the macrolide group was not significantly different compared to the non-macrolide group. None of the median cytokine levels or IQRs were statistically significant between the groups. However, decreased IL-6, IL-8 and IFN-g levels, and favorable clinical outcomes trended towards significance in the macrolide group.

Conclusion. This pilot study found that the components of innate immunity that were measured were similar between patients with CAP treated with and without a macrolide, which suggests that immunomodulatory properties of macrolides do not include altered neutrophil function or systemic cytokine levels.

Disclosures. **All authors:** No reported disclosures.

813. Secondary Analyses of the Effect of Exercise or Mindfulness Meditation on the Incidence of Acute Respiratory Infections

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Background. Non-influenza acute respiratory infections (ARIs) are extremely costly. The Meditation or Exercise for Preventing Acute Respiratory Infection (MEPARI) trial tested exercise or mindfulness meditation to reduce ARIs, but initial analysis was limited. This secondary analysis further examines the effect of these interventions on ARI incidence.

Methods: Results. from the first cohort of the MEPARI trial have been published (1). Participants were randomized to 8 weeks of training in mindfulness meditation (n = 51), 8 weeks of training in moderate exercise (n = 51), or to serve as observational controls (n = 52). Participants self-reported ARI incidence, duration and daily severity and supplied a nasal wash for biomarker assay and viral identification.

Conditional logistic regression was used to calculate ARI incidence for each group. In addition, eight 30-day study periods were analyzed individually to determine the period of greatest effect on ARI incidence for each intervention.

Results. There were 93 total ARIs (26 in exercise, 27 in meditation, 40 in control). Crude risk of ARI was 0.624 (p = 0.0654) among exercisers as compared to controls. The risk of ARI was 0.636 (p = 0.0842) for meditators as compared to controls. After adjusting for age, smoking status, education, and area temperature, the risk of ARI was 0.627 (p = 0.0886) among exercisers and 0.580 (p = 0.0489) among meditators, as compared to controls.

Individual analysis of 30-day study periods found the month immediately following intervention to have the greatest effect on ARI incidence for both exercise (p = 0.0057) and mediation (p = 0.0718). During this month, adjusted ARI risk was 0.102 (p = 0.0101) among exercisers as compared to controls, and 0.150 (p = 0.0248) among meditators as compared to controls.

1. Barrett B, *et al.* Meditation or exercise for preventing acute respiratory infection: a randomized controlled trial. Ann Fam Med. 2012 July–August;10(4):337-46.

Conclusion. This analysis found 8-week periods of exercise or mindfulness meditation training may significantly reduce ARI risk. Data also suggest that the month following exercise or meditation training may have the greatest impact on ARI incidence. These results will inform collection and analysis of biomarker data to determine biological mechanisms of exercise or mindfulness meditation to prevent ARIs.

Disclosures. **All authors:** No reported disclosures.

814. A Prospective Analysis of the Clinical Spectrum of Different Subtypes Human Enterovirus and Human Parechovirus

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Background. Enterovirus (EV) and Human Parechoviruses (HPeV) are a major cause of aseptic meningitis in children. There a 4 species (A-D) human EV and 2 species parechoviruses (HPeV and Ljungan virus). The aim of this study is to prospectively describe the clinical spectrum of different EV and HPeV subtypes in children.

Methods. This study is part of a multicenter prospective study, involving children 0-16 years visiting three major general hospitals in the Netherlands. Children with clinical suspicion of an EV or HPeV infection were included and those with other cause of illness are excluded.

Results. From 285 included patients, 140 (39%) and 44 (12%) had an EV and HPeV infection, respectively. There were no significant differences in baseline characteristics. 54% of the EV infected children had a meningitis and 15% a gastro-enteritis. EV subtype A (EV-A) was found in 9 children and EV-B in 109, in 22 the subtype was unknown. Children with EV-B infection had significant more often a meningitis than children with an EV-A infection (60% vs 33%, p = 0.007). HPeV subtype 3 (HPeV-3) was most detected in 24 (55%) children, HPeV-1 in 6 (14%), HPeV-4 in 2 and HPeV-6 in 1, in 11 the subtype was unknown. Children with a HPeV-1 infection had more often a gastro-enteritis than children with a HPeV-3 infection (83% vs 4%, p < 0.01).

Conclusion. EV infection is more associated with meningitis than HPeV infection, especially EV-B. HPeV infection is more associated with a gastro-enteritis than EV infection, especially HPeV-1.

Disclosures. **All authors:** No reported disclosures.

815. Diagnosis of Pulmonary Nocardiosis

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Background. Pulmonary nocardiosis (PN) is an uncommon infection often seen in immunocompromised patients. Definitive diagnosis depends on identification of the organism by culture in a patient with a clinical presentation suggestive of PN. As Nocardia can grow slowly and other infections can present similarly in the immunocompromised patient, we sought to find the performance of respiratory sampling in making diagnosis.

Methods. Microbiologic data from1993-2013 was reviewed in any expectorated sputum (ES), bronchoalveolar lavage (BAL), and tissue biopsy in PN cases.

Results. 71 patients were analyzed. 45 had obtained ES. 34 underwent BAL +/- transbronchial biopsy (TBBx), 14 had percutaneous biopsy (PBx) and 5 had both BAL and PBx. 82% (37/45) had a diagnosis with positive culture in ES and 32% (12/37) suspected on the basis of organism morphology on smear (Gram stain, fungal or acid fast bacilli (AFB) stain). Of 37 positive cultures, 5/37 were positive on bacterial, 12/37 on fungal, 30/37 on AFB and 4/37 in multiple culture methods. Of 34 with BAL, 20% (7/34) had a suspected diagnosis by direct staining morphology, with a definitive diagnosis by culture in 82% (28/34); 10/28 positive on bacterial, 25/28 on fungal, 4/28 on AFB and 5/28 legionella cultures. TBBx had an overall sensitivity of 43% (6/14) by culture but secured a definitive diagnosis in an additional 2 patients. PBx made a diagnosis in 92% (12/13) of patients by positive tissue culture; 46% (6/13) had an organism with consistent morphology on direct staining and 9/13, 12/13 and 3/13 in positive bacterial, fungal and AFB cultures respectively. Acute inflammation was seen in 12/34, 3/14 and 13/13 patients in pathology of BAL, TBBx and PBx.

Conclusion. Although an uncommon infection, PN should be suspected in the immunocompromised patient with pneumonia. If the suspicion is high, aggressive diagnostic assessment with bronchoscopy and/or percutaneous biopsy is warranted for adequate exclusion of the disease. Fungal and AFB culture of respiratory samples significantly increases the sensitivity of diagnosing this bacterial infection. Given the frequent delay in definitive diagnosis, development of sensitive and rapid molecular diagnostic tests is needed.

Disclosures. **All authors:** No reported disclosures.

816. Legionellosis in Massachusetts: Commoner Than We Think! A Community Hospital Experience

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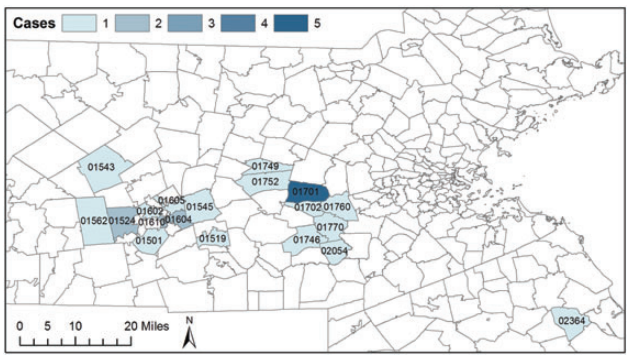
Background. The incidence of Legionnaires' disease in the USA has more than doubled from 2000 to 2009. There are currently an estimated 8,000-18,000 cases annually. These are frequently associated with underlying risk factors and exposure to an environmental source.

Methods. Patients of all ages and both genders who were admitted to MetroWest Medical Center, Framingham, MA and Saint Vincent Hospital, Worcester, MA with a confirmed diagnosed of Legionellosis between January 1, 2012 and December 31, 2013 were enrolled.



Map of number of Legionella pneumonia cases by zip code.

Results. Of 25 patients with legionellosis, all presented with respiratory symptoms, 14 (56%) also had gastrointestinal complaints and 4 (12%) a change in mental status. There was no geographic clustering of cases (figure) and no common exposure history. Two thirds were male. Nineteen (76%) had at least one risk factor. Fourteen (56%) had a significant smoking history and 4 (16%) chronic lung disease. Other risks factors included cirrhosis, corticosteroid use, tumor necrosis factor inhibitor use and malignancy. The majority of the patients presented during the summer and fall. A urinary legionella antigen test was positive in all patients. Initial laboratory abnormalities included 18 (72%) patients with hyponatremia and 10 (40%) with abnormal liver function tests. All had radiologically confirmed pneumonia; 7 (28%) multilobar and 5 (20%) with pleural effusion. No patient had *Legionella pneumophilaisolated* bacteriologically. Eight (32%) were admitted to ICU and 6 (24%) required intubation. All patients received levofloxacin or azithromycin for treatment. Infection was fatal in 4 (12%).

Conclusion. Current guidelines recommend screening for *L. pneumophila* infection in cases of severe pneumonia, given testing is relatively inexpensive, more widespread screening may help early de-escalation and provision of targeted antimicrobial therapy.

Disclosures. **All authors:** No reported disclosures.

817. The Association between Asthma and Invasive Pneumococcal Disease: A Nationwide Study in Korea

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Background. While there are a number of studies that have described effect of clinical risk factors in patients with invasive pneumococcal disease (IPD), there is limited data on the association of asthma with IPD. This study was conducted to investigate an association between asthma and IPD in Korea using a nationwide health insurance claim records.

Methods. A retrospective population-based cohort study was conducted using the Korean Health Insurance Review and Assessment (HIRA) database 2010-2011. Patients with asthma and IPD were identified using codes from the International Classification of diseases, Tenth Revision (ICD-10). Patients with diabetes mellitus (DM) were also identified to compare to patients with asthma as a risk factor for IPD.

Results. A total of 935,106 (2010) and 952,295 (2011) patients were included in this study, of whom 398 (2010) and 428 (2011) patients with IPD were identified. There was significant difference in the prevalence of IPD in patients with and without asthma: 0.07% vs 0.02% in 2010 and 0.08% vs 0.01% in 2011 ($P < 0.01$). After adjusting age and gender, patients with asthma showed over a three-fold increased risk of IPD compared with patients without asthma [adjusted odds ratio (aOR) 3.90, 95% confidence interval (CI) 3.02-5.03; $P < 0.01$ in 2010 / aOR 5.44, 95% CI 4.10-7.22; $P < 0.01$ in 2011]. These findings were also significant in children and adolescents (aOR 2.08; 95% CI 1.25-3.45; $P < 0.01$ in 2010 / aOR 3.26; 95% CI 1.74-6.11; $P < 0.01$ in 2011). Although DM was also significantly associated with IPD, relatively low ORs compared with those of asthma were noted (aOR 1.85; 95% CI 1.35-2.54; $P < 0.01$ in 2010 / aOR 2.40; 95% CI 1.78-3.24; $P < 0.01$ in 2011).

Conclusion. Asthma is a risk factor for IPD in both children and adults while diabetes mellitus has no association with IPD in children.

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818. Safety of ABT-450/r/Ombitasvir + Dasabuvir With or Without Ribavirin in HCV Genotype 1-infected Patients, by Baseline Demographics

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Background. ABT-450 is an HCV NS3/4A protease inhibitor dosed with ritonavir (r) 100mg, identified by AbbVie and Enanta. Ombitasvir (formerly ABT-267) is an NS5A inhibitor, and dasabuvir (formerly ABT-333) is an NS5B RNA polymerase inhibitor. The randomized phase 3 PEARL trials evaluated the safety and efficacy of the "3D" regimen of ABT-450/ritonavir/ombitasvir and dasabuvir with or without ribavirin (RBV) in HCV genotype 1-infected patients. SVR12 rates >90% were achieved in all treatment arms. Safety outcomes in these trials according to baseline demographics are reported.

Methods. Non-cirrhotic HCV GT1b treatment-experienced (PEARL II) and treatment-naive (PEARL III) patients, and non-cirrhotic HCV GT1a treatment-naive patients (PEARL IV) were randomized to co-formulated ABT-450/r/ombitasvir (150mg/100mg/25mg QD) + dasabuvir (250mg BID) with RBV or placebo/no RBV. The percentage of patients experiencing any treatment-emergent adverse event (AE), severe AE, serious AE, and AE leading to treatment discontinuation was determined according to sex, age, race, ethnicity, and history of diabetes. Homogeneity of treatment effect across subgroups for each event type was assessed using the Breslow-Day test.

Results. A total of 910 patients received at least one dose of study treatment in the PEARL-II (n = 186), PEARL-III (n = 419), and PEARL-IV (n = 305) trials. Most

patients experienced at least 1 AE, but the majority of events were mild. There were no statistically significant differences in event rates according to the categories analyzed (table). AEs occurring in >20% of patients in both the 3D + RBV and 3D groups were fatigue (29.9% and 26.5%) and headache (24.4% and 25.3%). Overall, 4 patients (0.4%, 2 in each treatment group) discontinued due to AEs (3D + RBV arm: 1 patient with anxiety, dyspnea, pyrexia and tachycardia, and 1 with pancreatitis that started prior to dosing; 3D arm: 1 patient with diverticulitis and 1 patient with drug abuse).

	Any AE		Severe AE		Serious AE		AE leading to discontinuation	
	3D+RBV	3D	3D+RBV	3D	3D+RBV	3D	3D+RBV	3D
	n/N (%)		n/N (%)		n/N (%)		n/N (%)	
Overall	332/401 (82.8)	383/509 (75.2)	4/401 (1.0)	6/509 (1.2)	9/401 (2.2)	7/509 (1.4)	2/401 (0.5)	2/509 (0.4)
Sex								
Male	180/221 (81.4)	193/272 (71.0)	2/221 (0.9)	4/272 (1.5)	6/221 (2.7)	3/272 (1.1)	1/221 (0.5)	2/272 (0.7)
Female	152/180 (84.4)	190/237 (80.2)	2/180 (1.1)	2/237 (0.8)	3/180 (1.7)	4/237 (1.7)	1/180 (0.6)	0
Age								
<65	296/362 (81.8)	345/461 (74.8)	3/362 (0.8)	5/461 (1.1)	8/362 (2.2)	6/461 (1.3)	2/362 (0.6)	2/461 (0.4)
≥65	36/39 (92.3)	38/48 (79.2)	1/39 (2.6)	1/48 (2.1)	1/39 (2.6)	1/48 (2.1)	0	0
Race								
Black	20/25 (80.0)	31/44 (70.5)	0	2/44 (4.5)	0	2/44 (4.5)	0	0
Non-black	312/376 (83.0)	351/464 (75.6)	4/376 (1.1)	4/464 (0.9)	9/376 (2.4)	5/464 (1.1)	2/376 (0.5)	2/464 (0.4)
Ethnicity								
Hispanic or Latino	13/16 (81.3)	21/25 (84.0)	0	0	1/16 (6.3)	0	1/16 (6.3)	0
Non-Hispanic or Latino	319/385 (82.9)	362/484 (74.8)	4/385 (1.0)	6/484 (1.2)	8/385 (2.1)	7/484 (1.4)	1/385 (0.3)	2/484 (0.4)
History of Diabetes								
Yes	17/22 (77.3)	24/29 (82.8)	0	2/29 (6.9)	0	3/29 (10.3)	0	0
No	315/379 (83.1)	359/480 (74.8)	4/379 (1.1)	4/480 (0.8)	9/379 (2.4)	4/480 (0.8)	2/379 (0.5)	2/480 (0.4)

Conclusion. The 3D regimen of ABT-450/r/ombitasvir + dasabuvir with or without RBV was well tolerated in non-cirrhotic HCV GT1-infected patients, with low rates of discontinuation. The AE profile of the regimen was similar with and without RBV regardless of age, gender, race, ethnicity, or history of diabetes.

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819. Daclatasvir in Combination with Peginterferon Alfa-2a and Ribavirin for Treatment-Naive Patients with HCV Genotype 4 Infection: Phase 3 COMMAND-4 Results

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Background. Options are limited concerning treatment of HCV genotype (GT) 4 infection, therefore, new regimens containing direct-acting antiviral agents are being evaluated. In phase 2b studies, daclatasvir (DCV), a pan-genotypic HCV NS5A inhibitor, combined with peginterferon-alfa/ribavirin (P/R) demonstrated greater efficacy in GTs 1-4 than P/R alone, including a 100% sustained virologic response (SVR) rate in GT 4. This phase 3 study (COMMAND-4; AI444042) evaluated the efficacy and safety of DCV plus P/R in treatment-naive patients with GT 4 infection.

Methods. Patients were randomized (2:1; blinded) and treated with DCV 60 mg (n = 82) or placebo (n = 42) once daily with peginterferon alfa 180 µg once weekly and ribavirin 1,000-1,200 mg/day (weight-based) twice daily. DCV-treated patients with undetectable HCV RNA at weeks 4 and 12 (eRVR) received 24 weeks of DCV + P/R; those without an eRVR received an additional 24 weeks of P/R. All patients in the placebo arm received 48 weeks of P/R. The primary endpoint was SVR at posttreatment Week 12 (SVR_{12}).

Results. Patients were 73% male, 77% white and 19% black; 75% were *IL28B* non-CC and 11% had cirrhosis. There was a diverse representation of GT 4 subtypes, with GT 4A, 4C, or 4D being the most common (57%). SVR_{12} rates (HCV RNA <LLOQ at posttreatment Week 12 or later) were 82% (67/82) with DCV + P/R vs 43% (18/42) with P/R alone (P < 0.0001). In DCV recipients, there were no notable effects on SVR_{12} rates according to baseline factors (*IL28B* genotype, age, race, gender, cirrhosis status, baseline viral load) known to impact response to P/R. 9.8% of DCV + P/R recipients experienced serious AEs and 3.7% discontinued due to an AE (neutropenia, uveitis, cerebrovascular accident); in patients receiving P/R alone, 4.8% had serious AEs and 7.1% discontinued due to an AE (Grave's disease, abdominal pain, hypersensitivity). There were no deaths.

HCV RNA Response, % (n/N)*,†	DCV 60 mg QD (N = 82)	Placebo (N = 42)
SVR12 (primary endpoint)	73.2 (60/82)	38.1 (16/42)
SVR12 on or after PT Week 12‡	81.7 (67/82)	42.9 (18/42)
SVR12 by IL28B genotype		
CC	81.8 (18/22)	77.8 (7/9)
CT	67.5 (27/40)	33.3 (9/27)
TT	75.0 (15/20)	0 (0/6)
SVR12 by cirrhosis		
Absent	71.0 (49/69¶)	39.5 (15/38)
Present	77.8 (7/9¶)	25.0 (1/4)
eRVR (Weeks 4 and 12)	79.3 (65/82)	11.9 (5/42)
EOTR	90.2 (74/82)	64.3 (27/42)
Relapse‡	2.7 (2/74)	29.6 (8/27)
Breakthrough¶	7.3 (6/82)	N/A**

*All data shown as mITT unless stated otherwise. †HCV RNA < LLOQ, TD or TND for SVR_{12}; HCV RNA <LLOQ, TND for RVR, eRVR, and EOTR. ‡Patients with missing data at follow-up week 12 were considered responders if the next available HCV RNA value was <LLOQ. ¶In 4 patients cirrhosis status was not reported at baseline. ‡Defined as HCV RNA < LLOQ TND at EOT followed by HCV RNA ≥LLOQ at any post treatment visit. ¶Defined as >1 log_{10} IU/ml HCV RNA on treatment increase from nadir, or confirmed increase in HCV RNA ≥LLOQ if HCV RNA previously declined to <LOQ TD or TND. **Breakthrough was only assessed in DCV-randomized patients. EOT, end of treatment; EOTR, EOT response; LLOQ, lower limit of quantitation; N/A, not assessed. PT, posttreatment; TD, target detected; TND, target not detected.

Conclusion. In treatment-naive patients with GT 4 infection, DCV + P/R achieved higher SVR_{12} rates than P/R alone, with the majority of DCV recipients requiring only 24 weeks of therapy. The safety and tolerability profile of DCV + P/R was comparable to that of P/R alone. These data support DCV-based regimens for GT 4 infection, including all-oral combinations with other direct-acting antivirals.

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820. Triple Combination Treatment With Peginterferon Lambda-1a, Daclatasvir and Ribavirin for 12 Weeks in Patients Infected With HCV Genotype 1b

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Background. Peginterferon lambda-1a (Lambda, Type III IFN) is currently under Phase 3 evaluation as part of combination treatment for HCV infection. The triple regimen of Lambda, daclatasvir (DCV; NS5A inhibitor) and ribavirin (RBV) achieved sustained virologic response (SVR) rates of >90% in a pilot study of patients chronically infected with genotype 1b HCV when treated for 24 weeks. This triple combination regimen was evaluated for 12 weeks of treatment in a cohort of patients with genotype 1b infection (Study AI452-008c).

Methods. 24 treatment-naive, non-cirrhotic HCV genotype 1b infected patients were treated with open-label Lambda 180 mcg/week + DCV 60mg daily + RBV 1,000-1,200 mg daily for 12 weeks. The primary endpoint is HCV RNA <LLOQ (25 IU/mL) at 12 weeks post-treatment (SVR12). SVR4 results are reported here with SVR12 available at presentation.

Results. Baseline characteristics were male 46%, Caucasian 96%, and IL28B non-CC genotype 67%. Mean baseline HCV RNA was 6.3 (range 5.1–7.4) log10 IU/mL. SVR4 was achieved in 21/23 (91%) patients with available data. Both patients who did not achieve SVR4 experienced relapse posttreatment. No patients discontinued treatment due to AEs or treatment futility; there were no deaths and no serious AEs. The most frequent AEs were asthenia, pruritus, dry skin and diarrhea. One patient each (n = 3/24) had a Grade 3/4 lab abnormality of elevated ALT/AST, reduced hemoglobin, or increased bilirubin.

	Observed	mITT
HCV RNA <LLOQ at end of treatment, n/N (%)	24/24 (100)	24/24 (100)
SVR4, n/N (%)	21/23 (91)*	21/24 (88)
Post-treatment relapse (n)	2	

*1 patient was lost to follow-up (Week 8 undetectable), counted as failure for mITT analysis

Conclusion. 12 weeks of treatment with Lambda + DCV + RBV achieved a high SVR4 rate in treatment-naïve, non-cirrhotic HCV genotype 1b-infected patients. The regimen was generally well tolerated.

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821. Daclatasvir and Asunaprevir Plus Peginterferon Alfa-2a and Ribavirin in Patients With HCV Genotype 1 or 4 Infection: Phase 3 HALLMARK-QUAD Results

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Background. Daclatasvir (DCV) is a potent, pangenotypic NS5A inhibitor. Asunaprevir (ASV) is an NS3 protease inhibitor with activity in HCV genotypes (GT) 1 and 4. DCV plus ASV in combination with peginterferon alfa-2a and ribavirin (DCV + ASV + P/R) has previously demonstrated potent antiviral activity in HCV GT 1-infected null responders. This phase 3 study (HALLMARK-QUAD; AI447029) evaluated DCV + ASV + P/R in patients with chronic HCV GT 1 or 4 infection who were prior null or partial responders to peginterferon/ribavirin.

Methods. In this open-label study, 354 GT 1 and 44 GT 4-infected patients received 24 weeks of treatment with DCV 60 mg once daily plus ASV 100 mg twice daily in combination with weekly peginterferon alfa-2a 180 µg and weight-based ribavirin twice daily. The primary endpoint was sustained virologic response at posttreatment Week 12 (SVR12).

Results. The median age of patients was 53 years, 69% were male, 76% were white, and 23% had cirrhosis; 67% of patients were prior null responders and 33% were partial responders. SVR12 was achieved by 93% of GT 1-infected patients and 98% of GT 4-infected patients; one GT 4 patient was not tested for SVR12 but achieved SVR24, yielding an SVR rate of 100% in GT 4-infected patients (Table). Prior P/R response, cirrhosis status, gender, age, race, or *IL28B* genotype did not influence SVR12. SVR12 rates for GT 1a were 87% (153/176) vs 99% (176/178) for GT 1b. Serious adverse events occurred in 6% of patients; 5% discontinued treatment due to an adverse event. One death occurred at posttreatment week 12 (pneumonia; not considered related to study therapy). Adverse events occurring in ≥20% of patients were fatigue, headache, pruritus, asthenia, influenza-like illness, insomnia and rash. Grade 3/4 laboratory abnormalities included neutropenia (22%), lymphopenia (16%), anemia (6%), thrombocytopenia (4%) and ALT/AST elevations (3%/3%).

HCV RNA Response, n (%)[a]	Genotype 1 N = 354	Genotype 4 N = 44
SVR12	329 (93)	43 (98)
SVR12 on or after PT Week 12[b]	330 (93)	44 (100)
SVR12 by subgroup		
Cirrhotic	66/73 (90)	19/20 (95)
Non-cirrhotic	263/281 (94)	24/24 (100)
Null responder	219/234 (94)	33/34 (97)
Partial responder	110/120 (92)	10/10 (100)
Week 4 (RVR)	292 (82)	36 (82)
End of treatment	337 (95)	43 (98)
Virologic failures		
Virologic breakthrough	11 (3)	0
Posttreatment relapse[c]	8/337 (2)	0

[a]All data are mITT unless stated otherwise. HCV RNA < assay lower limit of quantitation (LLOQ), TD or TND for SVR12; < LLOQ, TND for RVR and end of treatment response.

[b]For patients with missing posttreatment (PT) Week 12 HCV RNA, the first available measurement after posttreatment Week 12 was used.

[c]Relapse rates based on patients with end of treatment response.

mITT, modified intent-to-treat; SVR12, sustained virologic response at posttreatment Week 12; RVR, rapid virologic response; TD, target detected; TND, target not detected.

Conclusion. The QUAD regimen of DCV + ASV + P/R demonstrated high SVR12 rates of 93% and 100% in GT 1 or GT 4 prior non-responders. DCV + ASV + P/R was generally well tolerated; no additional safety and tolerability concerns were observed compared to P/R regimens. These results support the investigation of DCV in all-oral combinations in multiple patient populations across genotypes.

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822. Effect of Steady State Daclatasvir Plus Asunaprevir on the Single Dose Pharmacokinetics of the P-glycoprotein Substrate Digoxin in Healthy Adult Subjects

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Background. Daclatasvir (DCV) is a potent hepatitis C virus (HCV) NS5A replication complex inhibitor with pangenotypic (GT 1-6) activity *in vitro*. Asunaprevir (ASV) is a selective NS3 protease inhibitor with *in vitro* activity against GT 1, 4, 5 and 6. These two direct-acting antivirals (DAA) are in phase 3 development and regulatory review as a dual-DAA regimen (DCV + ASV) for the treatment of HCV GT 1b. DCV and ASV both inhibit P-glycoprotein (P-gp) and individually increase plasma concentrations of the P-gp substrate digoxin (DIG), increasing DIG C_{max} by 65 and 9% and AUC_{TAU} by 27 and 30%, respectively. The combined effect of DCV + ASV on the pharmacokinetics (PK) of DIG was therefore assessed in healthy subjects.

Methods. A single sequence, open-label, one-way interaction study assessed the effect of steady-state DCV (60 mg QD) plus ASV (100 mg BID [softgel capsule]) on the PK of single-dose 0.25 mg DIG in healthy subjects. Subjects (N = 16) received DIG on Day 1 and 16, and DCV + ASV on Days 6–20. Serial samples for DIG plasma concentrations were collected up to 120 h postdose on Day 1 and Day 16. Non-compartmental DIG PK parameters were derived. Geometric mean ratios (GMR) and 90% confidence intervals (90%CI) for DIG C_{max} and AUC_{inf} were derived from linear mixed effects models.

Results. All subjects (69% male, aged 23-45 years) completed the study. DCV + ASV dosed with DIG resulted in a 77% increase in DIG C_{max} and a 29% increase in AUC_{inf} (Table). Study drugs were well tolerated; all AEs were mild in intensity except 2 AEs of increased blood creatinine phosphokinase (1 moderate, 1 severe). No AEs were considered study drug-related and all resolved by study end.

	With DCV+ASV *Adj. Geo. Mean (90%CI)*	W/O DCV+ASV *Adj. Geo. Mean (90%CI)*	GMR *(90%CI)*
DIG C_{max}, *pg/mL*	1593 (1407, 1803)	902 (797,1021)	1.766 (1.504, 2.073)
DIG AUC_{inf}, *pg×h/mL*	23293 (21522, 25209)	18090 (15818, 20689)	1.288 (1.197, 1.385)

Conclusion. DCV and ASV effects on DIG PK are not additive and are similar to DCV alone. Caution is warranted when dosing DCV + ASV with DIG and other P-gp substrates with a narrow therapeutic window; a priori dose modification does not appear to be required. Therapeutic drug monitoring, if available, may be considered.

Disclosures. **T. Garimella**, Bristol-Myers Squibb: Employee, Salary **R. Adamczyk**, Bristol-Myers Squibb: Employee and Shareholder, Salary **M. Stonier**, Bristol-Myers Squibb: Employee, Salary **H. Kandoussi**, Bristol-Myers Squibb: Employee, Salary **M. Hesney**, Bristol-Myers Squibb: Employee, Salary **E. Colston**, Bristol-Myers Squibb: Employee, Salary **T. Eley**, Bristol-Myers Squibb: Employee and Shareholder, Salary **M. Bifano**, Bristol-Myers Squibb: Employee, Salary

823. Evaluation of Drug-Drug Interaction between Asunaprevir and Methadone or Buprenorphine/Naloxone

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Background. Asunaprevir (ASV) is a selective NS3 protease inhibitor with *in vitro* activity vs hepatitis C virus (HCV) GT 1, 4, 5 and 6. Methadone (MET) and buprenorphine (BUP) are opioid analgesics; patients on HCV therapy may also require MET or BUP to treat opioid dependence. The effect of ASV on MET or BUP/naloxone (NLX) pharmacokinetics (PK) was assessed in subjects on stable opioid therapy.

Methods. An open-label, 2-part study assessed the effect of steady-state ASV on the PK of MET (Part 1, P1) or BUP/NLX (Part 2, P2). Safety/tolerability and pharmacodynamics (PD; opiate withdrawal scales/overdose assessment) were also assessed. Subjects (P1, N = 15; P2, N = 16) received once daily oral MET (40–120mg) or BUP/NLX (8/2–24/6mg) based on prescribed stable dose throughout, in addition to ASV (100 mg BID) on Days 2–12. Serial PK sampling occurred on Days 1 and 12 up to 24 hours postdose. Non-compartmental PK were derived. Ratios of geometric means (GMR) and 90% confidence intervals (90%CI) for R-MET/S-MET/BUP/norBUP C_{max} and AUC_{TAU} with and without ASV were derived from linear mixed effects model on log-transformed data.

Results. Subjects were aged 20–53 years, mostly white (P1, 87%; P2, 100%) and male (P1, 67%; P2, 75%). All completed the study. No clinically meaningful effect was shown as GMR 90% CIs fell within pre-specified interval (P1, 0.7–1.4; P2, 0.5–2.0). ASV coadministration with MET or BUP/NLX was generally well tolerated (P1, 6 [40%] subjects had 9 generally mild AEs; P2, 7 [44%] subjects had AEs, all mild). ASV had no clinically meaningful effect on the PD of MET or BUP/NLX; 1 patient experienced moderate drug withdrawal syndrome but had mild withdrawal symptoms before the study, therefore the association is unclear.

	With ASV *Adj. Geo. Mean*	W/O ASV *Adj. Geo. Mean*	GMR *(90%CI)*
R-MET[a] C_{max}, *ng/mL*	116.2	120.2	0.97 (0.86,1.08)
AUC_{TAU}, *ng•h/mL*	1757.7	1924.2	0.91 (0.82,1.01)
BUP C_{max}	4.5	5.3	0.85 (0.71,1.01)
AUC_{TAU}	36.1	37.1	0.97 (0.73,1.30)
NORBUP C_{max}	2.1	1.8	1.17 (0.96,1.42)
AUC_{TAU}	33.0	30.1	1.10 (0.72,1.68)

[a]S-MET and total MET results similar

Exposures were normalized to lowest dose of MET or BUP.

Conclusion. Steady-state administration of ASV 100 mg BID had no clinically meaningful effect on the PK of MET or BUP/NLX and was generally well tolerated, suggesting that no dose adjustments are required.

Disclosures. **T. Garimella**, Bristol-Myers Squibb: Employee, Salary **T. Eley**, Bristol-Myers Squibb: Employee and Shareholder, Salary **B. He**, Bristol-Myers Squibb: Employee, Salary **W. L. Luo**, Bristol-Myers Squibb: Employee, Salary **J. Crowell**, Bristol-Myers Squibb: Employee, Salary **H. Kandoussi**, Bristol-Myers Squibb: Employee, Salary **E. Colston**, Bristol-Myers Squibb: Employee, Salary **R. Bertz**, Bristol-Myers Squibb: Employee, Salary **M. Bifano**, Bristol-Myers Squibb: Employee, Salary

824. An Open-Label Phase 3 Study of Isavuconazole (VITAL): Focus on Mucormycosis

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Background. Isavuconazole (ISA) is a novel, broad-spectrum triazole antifungal, available as a water-soluble prodrug in IV and oral formulations, for the treatment of invasive fungal disease (IFD). The objective of this analysis is to report the overall response, survival, and safety in a subset of patients with invasive mucormycosis (IM) who were treated with ISA.

Baseline demographics, study outcomes, and survival

Parameter	All patients (N=37)
Baseline characteristics	
Age (years), median (range)	50 (22–79)
Male, n (%)	30 (81)
Primary underlying condition, n (%)	
Hematological malignancy	22 (60)
Allogeneic bone marrow transplant	13 (35)
Diabetes mellitus	3 (8)
Immune status n, (%)	
Neutropenic	10 (27)
Corticosteroid use	10 (27)
T-cell immunosuppressant use	18 (49)
Organ involvement	
Pulmonary	22 (59)
Sinus	16 (43)
Central nervous system	6 (16)
Skin	2 (5)
Bone	5 (14)
Disseminated	11 (30)
Efficacy	
Overall Response at EOT, n (%)	
Complete	5 (14)
Partial	6 (16)
Stable	10 (27)
Progression	14 (38)
Missing[a]	2 (5)
Survival rate[b], % (95% CI)	
Day 42	65 (47, 78)
Day 84	59 (42, 73)
Day 120	56 (39, 71)
Day 180	53 (35, 68)

[a]Two people continued treatment at EOT cutoff

[b]Kaplan–Meier method.

Methods. VITAL was a Phase III, multicenter, open-label trial conducted to evaluate safety and efficacy of ISA treatment in patients with rare IFD. Eligibility criteria and evaluated outcomes are outlined in clinicaltrials.gov, NCT00634049. Patients received IV or PO ISA 200 mg TID for 2 days followed by 200 mg/day until day 180, end of treatment (EOT). An independent data review committee (DRC) categorized patients as having proven or probable IFD by EORTC/MSG criteria. DRC-assessed overall response at EOT, survival, and adverse events (AEs) using standard definitions are reported for patients with proven/probable IM.

Results. Overall 37 patients with IM received ISA for a median of 84 days (range 2–882). Baseline demographics, study outcomes, and survival are shown in the table. Survival at 180 days was 53%. Overall 95% of patients experienced an AE, 76% experienced a serious AE (SAE). Only 3 (8%) SAEs were attributed to ISA.

Conclusion. ISA appears to be a safe and promising agent for the treatment of mucormycosis in a particularly high-risk immunocompromised population.

Disclosures. **F. M. Marty**, Astellas: Grant Investigator, Research support; Chimerix: Grant Investigator, Research support; Merck: Consultant, Consulting fee; Vertex: Consultant, Consulting fee; Whiscon: Grant Investigator, Research support; Alexion: Consultant, Consulting fee; Gilead: Consultant, Consulting fee; ViroPharma: Grant Investigator, Research support; GlaxoSmithKline: Grant Investigator, Research support **J. R. Perfect**, Astellas: Grant Investigator and Scientific Advisor, Consulting fee; Merck: Investigator, Grant recipient; F2G: Scientific Advisor, Consulting fee; Scynerxis: Scientific Advisor, Consulting fee; Viamet: Scientific Advisor, Consulting fee **O. A. Cornely**, German Federal Ministry of Research and Education (BMBF grant 01KN1106): Grant Investigator, Grant recipient; European Commission: Grant Investigator, Grant recipient; Astellas: Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Gilead: Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee and Research grant; Merck/MSD: Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; Pfizer: Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant and Speaker honorarium; 3M: Consultant and Investigator, Consulting fee and Research grant; Cubist: Consultant and Investigator, Consulting fee and Research grant; Basilea: Consultant and Investigator, Consulting fee and Research grant; F2G: Consultant and Investigator, Consulting fee and Research grant; GSK: Consultant and Investigator, Consulting fee and Research grant; Optimer: Consultant and Investigator, Consulting fee and Research grant; Actelion: Investigator, Research grant; Sanofi Pasteur: Consultant, Consulting fee; Quintiles: Investigator, Research grant; Summit/Vifor: Consultant, Consulting fee; Viropharma: Investigator, Research grant; Celgene: Investigator, Research grant; Genzyme: Investigator, Research grant; Miltenyi: Investigator, Research grant **K. M. Mullane**, Astellas: Research Contractor and Speaker's Bureau, Research support; Anson Pharmaceuticals: Research Contractor, Research support; Chimerix: Research Contractor and Scientific Advisor, Research support; Cubist/Optimer: Research Contractor, Scientific Advisor and Speaker's Bureau, Consulting fee, Research support and Speaker honorarium; Merck Sharp and Dolme Corp: Research Contractor and Scientific Advisor, Consulting fee and Research support; Rebiotix: Research Contractor, Research support; Viropharma: Research Contractor, Research support; Pfizer: Research Contractor, Research support **G. Rahav**, Astellas: Grant Investigator and Scientific Advisor, Consulting fee and Research grant; MSD: Consultant, Grant Investigator and Scientific Advisor, Consulting fee, Research grant and Speaker honorarium **M. Lee**, Astellas: Employee, Salary **M. Ito**, Astellas: Employee, Salary **R. Maher**, Astellas Pharma Global Development: Employee, Salary **B. Zeiher**, Astellas: Employee, Salary **L. Ostrosky-Zeichner**, Merck: Consultant, Grant Investigator and Non-branded educational speaking, Consulting fee, Research grant and Speaker honorarium; Pfizer: Grant Investigator and Non-branded educational speaking, Research grant and Speaker honorarium; Astellas: Consultant, Grant Investigator, Non-branded educational speaking and Scientific Advisor, Consulting fee, Research grant and Speaker honorarium; T2 Biosystems: Grant Investigator, Research grant

825. A Phase 3, Randomized, Double-Blind, Non-Inferiority Trial to Evaluate Efficacy and Safety of Isavuconazole vs Voriconazole in Patients with Invasive Mold Disease (IMD): Outcomes in Patients with Pulmonary Infections

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Background. Isavuconazole (ISA) is a novel broad-spectrum triazole antifungal available as a water-soluble prodrug in IV and oral formulations for treatment of invasive fungal disease. A Phase 3 trial assessed the efficacy and safety of ISA vs voriconazole (VRC) in patients with IMD. Here we report outcomes in a pre-specified subset of patients from this non-inferiority trial, who had proven, probable, or possible pulmonary mold disease (PMD) without other site involvement (lower respiratory tract disease only).

Methods. Patients were randomized 1:1 to receive ISA or VRC for up to 84 days. Dosing regimens were: ISA 200mg IV TID for 2 days, followed by 200mg QD (IV or PO); VRC 6mg/kg IV BID on Day 1, 4mg/kg IV BID on Day 2, then either 4mg/kg IV BID or 200mg PO BID. Eligibility criteria and pre-specified outcomes are available at clinicaltrials.gov, NCT00412893. The primary efficacy endpoint was all-cause mortality by Day 42. All-cause mortality on Day 84, overall success (complete + partial response) at end of treatment (EOT) determined by an independent blinded data review committee were recorded. Safety and tolerability were also assessed, as reported by the Investigator.

Results. Overall 412 patients with proven/probable/possible PMD, primarily caused by *Aspergillus* spp. (n = 224), were enrolled. Patient characteristics, outcomes, and adverse events (AEs) are presented in the table. Outcomes in patients with proven/probable cases were similar to those with proven/probable/possible infections.

Efficacy and safety in patients with PMD

Parameter	ISA (n=200)	VRC (n=212)	Adjusted difference* % (95% CI)
All-cause mortality on Day 42	34 (17)	44 (21)	−2.9 (−10.4, 4.6)
All-cause mortality on Day 84	55 (28)	68 (32)	−3.8 (−12.4, 4.8)
Overall success at EOT	82 (41)	89 (42)	−1.8 (−11.1, 7.4)
Complete response	28 (14)	35 (17)	
Partial response	54 (27)	54 (25)	
Stable	53 (27)	60 (28)	
Progression	65 (33)	63 (30)	
Safety			P value
AEs	194 (97)	210 (99)	0.2
Study drug-related AEs	85 (43)	130 (61)	<0.001
Serious AEs	108 (54)	128 (60)	0.2
Study drug-related serious AEs	24 (12)	27 (13)	0.9
AE leading to permanent discontinuation	33 (17)	53 (25)	0.04

*(ISA–VRC)

Conclusion. ISA had comparable efficacy to VRC for the primary treatment of PMD patients, but had a lower rate of drug-related AEs vs VRC

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826. Health Economic Outcome Analysis of patients randomized in the SECURE Phase III Trial comparing Isavuconazole to Voriconazole for primary treatment of Invasive fungal disease caused by Aspergillus Species or other filamentous Fungi

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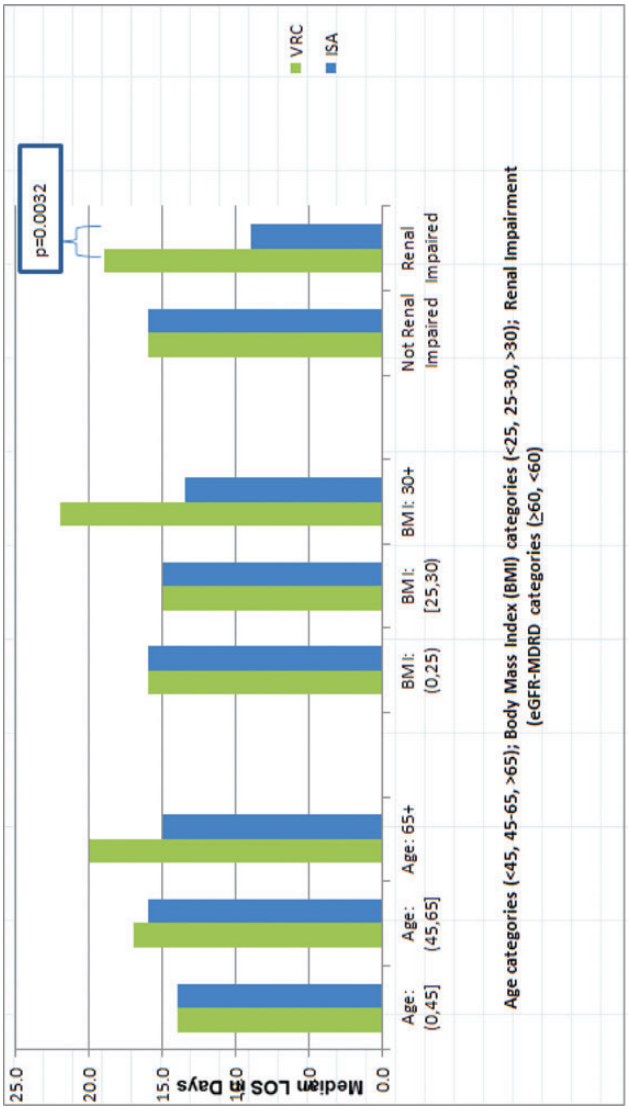
Background. Invasive aspergillosis (IA) is an emerging clinical problem and remains an important complication especially among immunocompromised patients. IA is associated with significant increases in morbidity, mortality, length of hospitalization stay (LOS) and costs. Case fatality is estimated to be at 60% in immunocompromised populations. Despite improved treatment options and advances in diagnostic testing, patient outcomes remain suboptimal. The SECURE trial was a Phase III,

double blind, randomized, multi-center, non-inferiority, study of Isavuconazole (ISA) vs Voriconazole (VRC). Patients >18 years of age, who had proven, probable or possible invasive fungal disease caused by *Aspergillus* species or other filamentous fungi were randomized 1:1 to receive ISA or VRC.

Methods. Primary objective of this analysis was to compare initial LOS during hospitalization and 30-day all-cause hospital readmission rates in patients who received ISA or VRC. Outcomes in subgroups of interest by age, Body Mass Index (BMI) and renally impaired patients (eGFR-MDRD category <60) were conducted. Ratio of total days on IV over total number of days of (IV + oral) therapy for study drugs and total number of additional days on potentially mould-active systemic antifungal therapy after end of study treatment were also analyzed.

Results. A total of 516 patients were included in the Intent-to-Treat (ITT) group. Median LOS days was found to be lower for ISA compared to VRC patients (13.0 vs 15.0). The 30-day readmission rate was lower for ISA compared to VRC patients (18.3% vs 24.4%, p = 0.114). Ratio of days on IV formulation to total days of (IV + oral) therapy were similar (ISA 0.38 (SD 0.39); VRC 0.38 SD (0.38)). Median additional days on potentially mould-active systemic antifungal therapy were comparable ISA vs VRC (32.0 vs 33.0). Median LOS days were similar across various subgroups (Figure 1), except in renal impaired subgroup where the difference was statistically significant in favor of ISA (ISA 9.0; VRC 19.0, p = 0.0032)



Conclusion. Health economic analyses in the SECURE trial favored ISA compared to VRC in median LOS days and 30-day readmission rates which were found to be lower with statistically significant difference in LOS in patients with renal impairment.

Disclosures. **N. Khandelwal**, Astellas: Employee, Salary **B. Franks**, Astellas: Employee, Salary **F. Shi**, Astellas: Employee, Salary **J. Spalding**, Astellas: Employee, Salary **N. Azie**, Astellas: Employee, Salary

827. The efficacy of single dose peramivir in acute uncomplicated influenza: an integrated subject-level meta-analysis

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Background. Peramivir is a parenteral neuraminidase inhibitor (NAI) with potent in vitro activity against all influenza sub-types. Although oseltamivir is widely used for the treatment of influenza, a need still exists for an effective and safe parenteral treatment. Peramivir has been studied as a single dose treatment in acute uncomplicated influenza

Methods. Subjects presenting within 48 hours of symptom onset of acute uncomplicated influenza were enrolled in four randomized, double-blind placebo-controlled trials of single dose peramivir (IV or IM doses ranging from 150-600 mg). Bioequivalence studies demonstrated equivalent systemic exposure for IM and IV administration. Subjects recorded severity of influenza signs and symptoms in a diary. Serial viral titers were measured from nasopharyngeal swabs. An integrated analysis of efficacy was performed.

Results. Of the 1131 subjects enrolled, 1028 subjects with influenza confirmed by laboratory test were included in the integrated efficacy analysis. Key clinical and virologic outcomes are shown:

Subgroup analyses by region, age, gender, race, smoking status, influenza virus subtype, symptom duration at baseline, and severity of illness showed consistency in demonstrating that peramivir was generally superior to placebo across the subgroups studied.

		Peramivir			
	Placebo N=408	150 mg N = 104	300 mg N = 262	600 mg N = 258	Overall N = 624
Time to alleviation of symptoms, median, hrs (95% CI)	107.4 (95.8, 115.9)	114.1 (95.2, 145.5)	84.1 (68.6, 102.0)	79.4 (69.3, 92.0)	87.6 (79.3, 95.0)
Time to resolution of fever, Median, hrs (95% CI)	47.2 (43.3, 55.6)	51.7 (43.5, 61.7)	39.1 (32.3, 41.0)	38.4 (31.5, 43.3)	40.8 (39.0, 42.7)
Time to resumption of usual activities, median, days (95%CI)	10.0 (8.0, 10.0)	10.0 (9.0, 12.0)	8.0 (7.0, 9.0)	6.0 (6.0, 7.0)	8.0 (7.0, 9.0)
Viral titer: change from baseline at 48 hrs, mean log_{10} $TCID_{50}$/mL (SD)	-1.43 (1.31)	-1.84 (1.43)	-1.94 (1.32)	-1.97 (1.52)	-1.91 (1.38)

Conclusion. Consistent, significant, dose ordered improvements were seen in each endpoint. The treatment effect size is similar to that reported for other NAIs.

Disclosures. **R. Whitley**, Gilead Sciences: Board Member, Consulting fee **P. Collis**, BioCryst: Employee and Shareholder, Salary **S. Dobo**, BioCryst: Employee and Shareholder, Salary **J. Elder**, BioCryst: Consultant, Consulting fee **W. Sheridan**, BioCryst: Employee and Shareholder, Salary

828. Incidence of Antimicrobial-resistant Nontyphoidal *Salmonella* Infections in the United States, 2004–2011

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Background. Nontyphoidal *Salmonella* (NTS) is a leading cause of bacterial foodborne illness in the United States. Antimicrobial agents are essential to treat serious illness. CDC's National Antimicrobial Resistance Monitoring System (NARMS) reports annual percentages of antimicrobial resistance among NTS. Incidence estimates of resistant infections have not been reported, in part because data on certain NTS serotypes and resistance are sparse or missing for some states. Using a Bayesian hierarchical model (BHM), a commonly used method to address sparse and missing data, we estimate the incidence of ceftriaxone-resistant NTS infections.

Methods. From 2004 through 2011, 50 states reported NTS isolates received from clinical laboratories to the Laboratory-based Enteric Disease Surveillance (LEDS) and forwarded every 20thisolate to NARMS for antimicrobial susceptibility testing. We defined ceftriaxone resistance as minimum inhibitory concentration ≥4 µg/mL. We used NARMS (number and percent of resistant isolates, total tested), LEDS (number of culture-confirmed infections), and U.S. Census (population) data, aggregated by state and year and grouped into two periods, 2004–2007 and 2008–2011. The BHM incorporated spatially correlated random effects of neighboring states and temporal correlations between periods.

Results. Of 17,498 isolates tested in NARMS, 3.3 % were ceftriaxone-resistant during 2004–2007 and 2.9 % during 2008–2011. Serotypes Typhimurium, Newport, and

Heidelberg accounted for 76% of ceftriaxone-resistant isolates. Estimated incidences of resistant infection per 100,000 person-years for 2004–2007 and 2008–2011, with 95% credible intervals (CIs), are: overall NTS 0.41 (0.36–0.46), 0.43 (0.38–0.48); Typhimurium 0.10 (0.08–0.13), 0.11 (0.09–0.14); Newport 0.13 (0.11–0.15), 0.13 (0.11–0.16); Heidelberg 0.05 (0.03–0.06), 0.06 (0.05–0.08).

Conclusion. Using one BHM, we estimated the annual incidence of culture-confirmed NTS infection with resistance to ceftriaxone at 0.41 to 0.43 per 100,000. Estimates for each of the three major serotypes ranged from 0.05 to 0.13 per 100,000 across the study period. This approach has promise for improving incidence estimation in the presence of sparse and missing data, providing information needed to target control measures.

Disclosures. **All authors:** No reported disclosures.

829. Highly Drug-Resistant Non-Typhoidal *Salmonella* in the United States, 1996–2012

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Background. Non-typhoidal *Salmonella*(NTS) causes an estimated 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths in the United States each year. While not indicated for most infections, antimicrobial treatment is critical for severe salmonellosis. We describe the epidemiology of the most highly drug-resistant NTS detected by the National Antimicrobial Resistance Monitoring System (NARMS).

Methods. Participating health departments submitted every 10th (1996–2002) or 20th(2003–2012) NTS isolate from humans to the NARMS program at CDC, as well as patient demographic and laboratory information. We tested for susceptibility to 14 antimicrobial agents in 8 classes. We defined isolates as 'highly drug-resistant' (HDR) if they were non-susceptible to ≥7 antimicrobial classes or ≥3 of 4 clinically important agents: ceftriaxone, ciprofloxacin, ampicillin, trimethoprim-sulfamethoxazole. We calculated odds ratios (OR) and 95% exact confidence intervals (CI) for categorical variables comparing HDR infections to those susceptible to all agents.

Results. During 1996–2012, 2.2% (689/31,931) of NTS isolates were HDR (627 were non-susceptible to ≥7 antimicrobial classes, and 202 were non-susceptible to ≥3 clinically important agents; 140 met both HDR criteria). The HDR proportion increased from 0% in 1996 to 2.2% in 2012, peaking at 3.6% in 2003. HDR isolates included 43 serotypes, most commonly Newport (54.4%), Typhimurium (23.8%), Agona (3.6%) and Dublin (3.3%). Among pansusceptible isolates (n = 25,083), the most common serotypes were Enteritidis (20.5%), Typhimurium (14.0%), Newport (10.6%), and Javiana (5.7%). HDR infections were associated with patient age ≥18 years (OR = 1.4, 95% CI = 1.2–1.7) and residence in a US region other than the South (OR = 4.1, 95% CI = 3.2–5.3).

Conclusion. Infections with HDR *Salmonella* emerged and persisted during 1996–2012. These infections were most common in adult patients and least common in the South. Four serotypes, all of which commonly display resistance in food animals, accounted for 85% of the infections. As treatment options for these infections are limited, prudent use of clinically important antimicrobial agents in both humans and animals is crucial to preserve their effectiveness.

Disclosures. **All authors:** No reported disclosures.

830. Reduction in Acute Gastrointestinal Infection among Military Trainees: Secondary Effects of a Hygiene-based Cluster-Randomized Trial for SSTI Prevention

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Background. Acute gastrointestinal infections (AGI) commonly occur in military populations and negatively impact both training and field operations. Handwashing has been shown to reduce AGI rates; however, the impact of chlorhexidine has not been assessed. We evaluated the effect of hygiene-based intervention strategies, which included weekly use of chlorhexidine body wash, on the incidence of AGI in military trainees.

Methods. This was a secondary objective of a field-based, cluster-randomized trial to evaluate the effect of hygiene-based intervention strategies on skin and soft-tissue infections (SSTI). Participants were Infantry trainees at Fort Benning, GA from May 2010-January 2012. There were three study groups with incrementally increased education and hygiene-based interventions: Standard (S), Enhanced Standard (ES), and Chlorhexidine (CHG). We compared the incidence of first-episode AGI between study groups.

Results. The study population consisted of 30,196 trainees (9,321 S, 10,858 ES, 10,026 CHG). During the study period, 780 cases of AGI were identified. The S group had an incidence density of 2.30 cases per 1,000 person-weeks (PW), while the ES group and CHG group had incidence densities of 1.62 and 1.91 cases per 1,000 PW, respectively. When compared to the S group, both the ES and CHG groups had significantly decreased relative risk (RR) of AGI (RR = 0.70, 95% CI = 0.59-0.84; and RR = 0.83, 95% CI = 0.70-0.98, respectively). There was no difference in rates between ES and CHG groups.

Conclusion. Additional hygiene education was associated with a decrease in the incidence of AGI. Hygiene-based strategies that include additional education are useful in preventing AGI in military trainees and may benefit other settings at risk for AGI.

Disclosures. **All authors:** No reported disclosures.

831. Clinical Characteristics and Outcomes in Patients with Hospital-Acquired, Healthcare-Associated and Community-Acquired Spontaneous Bacterial Peritonitis

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Background. Spontaneous bacterial peritonitis (SBP) is associated with poor clinical outcomes. Empiric treatment of SBP with a third-generation cephalosporin (3rd-ceph) is standard of care. Studies show increasing rates of 3rd-ceph resistance, but limited data is available from the United States.

Methods. Cirrhotic patients diagnosed with SBP at The Mount Sinai Hospital were retrospectively identified by ICD-9 code. Clinical and demographic data were collected. Health care-associated SBP (HCA-SBP) was defined as hospitalization in the prior 90 days; hospital-acquired SBP (HA-SBP) was defined as diagnosis after 72 hours of hospitalization. Among those who underwent repeat paracentesis, initial treatment failure was defined as <25% decrease in ascitic fluid neutrophil count on treatment day 2 or 3. Risk factors for 30-day mortality were analyzed.

Results. Between January 1, 2010 and July 31, 2013, 186 patients with SBP were identified. Mean age was 59; 70% of patients were male. Average MELD score at time of SBP diagnosis was 26. Cirrhosis was due to hepatitis C in 53% of patients and alcohol in 33%. HCA-SBP was observed in 40%; HA-SBP in 30%; and community-acquired SBP (CA-SBP) in 30% of the patients.

	HA-SBP	HCA-SBP	CA-SBP
Any culture +	17/55 (31%)	20/74 (27%)	20/57(35%)
Ascitic fluid culture + only	8/55 (15%)	12/20 (60%)	6/20 (30%)
Blood culture + only	6/55 (11%)	7/20 (35%)	9/20 (45%)
Both cultures +	3/55(5%)	1/20 (5%)	5/20 (25%)
Gram-positive bacteria	10/17 (59%)	13/20 (65%)	10/20 (50%)
Most frequent bacteria	*E. coli*(4, 2 ESBL) *Klebsiella*(3, 1 ESBL) VRE (3)	*E. coli*(3, 2 ESBL) *Enterococcus*(2,1 VRE) MRSA (2)	*E. coli*(7, 2 ESBL) *Klebsiella*(3) *S. pneumoniae* (2)
Initial tx with 3rd-ceph	29/55 (53%)	56/74 (76%)	40/57 (70%)
3rd-ceph resistance	7/20 (35%)	6/21 (29%)	3/24 (13%)
Initial treatment failure	4/41 (15%)	22/43 (51%)	15/38 (39%)
30-day mortality	32/55 (58%)	16/74 (22%)	6/57 (11%)

Increased 30-day mortality was significantly associated with HA-SBP (OR 4.99, 95% CI 2.46-10.13) and recent (<30 days prior to SBP diagnosis) antibiotic exposure (OR 2.35, CI 1.21-4.57). Decreased 30-day mortality was significantly associated with repeat paracentesis at day 2-3 (OR 0.33, CI 0.16-0.70).

Conclusion. HA-SBP and recent antibiotic exposure were significantly associated with early mortality. 3rd-ceph resistance was more common in HA-SBP and HCA-SBP.

Disclosures. **All authors:** No reported disclosures.

832. Predictive Factors of Spontaneous Bacterial Peritonitis Caused by Gram-positive Bacteria in Cirrhotic Patients

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Background. Spontaneous bacterial peritonitis (SBP) in cirrhotic patients is known to be mostly caused by Gram-negative bacteria. Although SBP due to Gram-positive bacteria is increasing, less is known about the predictive factors of the infection.

Methods. We performed a retrospective, observational cohort study consisting of patients, aged 18 years or older, with SBP due to Gram-positive and Gram-negative bacteria from January 2006 to December 2013 at Severance hospital, Seoul, Korea. Only the first episode for each patient was included in the analysis.

Results. We identified 77 patients with SBP. 27 (35%) patients had Gram-positive infection and 50 (65%) patients had Gram-negative infection. Univariate analysis revealed that low SOFA score (P = 0.001), having catheters or prosthetic devices (OR, 12; 95% CI, 2.36 ~ 60.95; P = 0.001) and previous use of antibiotics within 30 days (OR, 3.07; 95% CI, 1.15 ~ 8.2; P = 0.023) were associated with Gram-positive infection. Multivariate analysis showed that having catheters or prosthetic devices was a remarkable predictor of Gram-positive bacterial infection (OR, 5.72; 95% CI, 1.01 ~ 32.33; P = 0.048). And, previous use of antibiotics within 30 days was also a remained independent predictive factor of Gram-positive infection (OR, 4.04; 95% CI, 1.16 ~ 14.13; P = 0.029). Gram-negative infection had higher SOFA score than Gram-positive (6.68 vs 4.93; P = 0.001), but there was no statistically significant difference in 28-day mortality between two groups (48% vs 37%; P = 0.407).

Conclusion. In the current study, indwelling catheters or prosthetic devices, prior antimicrobial therapy within 30 days and a lower SOFA score were significantly associated with SBP caused by Gram-positive bacteria in patients with cirrhosis.

Disclosures. **All authors:** No reported disclosures.

833. Lactobacillus GG (LGG) Does Not Eliminate Colonization by Vancomycin Resistant Enterococcus (VRE) in Adults with Comorbidities

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Background. VRE is an endemic hospital-acquired organism in the US. There are no proven methods or means of decreasing or eliminating carriage of VRE which is a risk factor for invasive disease. Two small clinical studies showed reduction or elimination of VRE colonization using the probiotic LGG but neither study cultured stool for the presence of LGG, raising questions about whether effects on VRE colonization were due to LGG or other factors.

Methods. To determine whether LGG can eliminate colonization by VRE, we undertook a randomized, double blind, placebo controlled trial in which subjects with VRE received 2 weeks of LGG or placebo. Stool samples were collected and cultured for the presence of VRE and LGG at baseline and days 7, 14, 21, 28 and 56. Presence of LGG was also assessed by PCR on day 14 samples from a subset of 7 subjects. Subjects were monitored closely for adverse events.

Results. Of 694 patients screened, 11 were randomized. Five subjects received LGG and 6 received placebo. VRE was not eliminated during or after treatment in any subject. No significant decreases in VRE colony counts occurred in the subjects receiving LGG (table). LGG was recovered from stool in 2/5 subjects who received LGG. These 2 subjects were among 3/5 who received LGG and were also treated with antibiotics. LGG was detected by PCR in 4/4 samples from subjects who received LGG and 0/3 subjects in the placebo group. Adverse events were similar in the 2 groups.

Median Stool VRE Counts by Study Day

	Placebo group n=6 Median Log(CFU/g)	Placebo group range			LGG group n=5 Median Log(CFU/g)	LGG group range	
Day	VRE	low	High	Day	VRE	low	high
Day 0	6.97	4.48	7.72	Day 0	7.18	4.36	9.53
Day 7[a]	7.49	5.72	8.46	Day 7[b]	8.11	1.04	8.65
Day 14	6.26	4.51	9.54	Day 14	7.86	2.79	8.56
Day 21	6.90	4.60	7.43	Day 21[b]	7.28	2.54	8.45
Day 28	6.59	4.18	7.38	Day 28	8.28	6.08	8.83
Day 56[b]	5.26	3.81	7.52	Day 56[b]	6.74	<1[c]	7.20

[a] one positive swab included, no CFU available

[b] one sample not received

[c] lowest level of detection based on 1ml plated

Conclusion. Although the probiotic LGG is safe in patients with comorbid conditions, we were unable to demonstrate that it resulted in elimination of VRE in an RCT, likely because of continued administration of antibiotics in this patient population.

Disclosures. **All authors:** No reported disclosures.

834. Spontaneous Spinal Epidural Abscess: Clinical Comparison of *Staphylococcus aureus* and non-*Staphylococcus aureus* Infections

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Background. The incidence of spinal epidural abscess (SEA) has recently increased. *Staphylococcus aureus* is the most common cause of SEA though literature is lacking comparing the clinical characteristics of SEA caused by different pathogens. Our objective was to analyze the predisposing factors, clinical features, diagnosis and management of patients with spontaneous SEA and to compare the characteristics of *Staphylococcus aureus* with non-*Staphylococcus aureus* associated infections.

Methods. A retrospective review of 88 adult patients diagnosed with spontaneous SEA based on radiographs and/or intraoperative findings from a single tertiary medical center, during January 2009 through December 2012. Exclusion criteria included those with post spinal surgery infections, Pott's disease and isolated discitis/osteomyelitis.

Results. See the table.

	Staphylococcus aureus (N=54)	Non-*Staphylococcus aureus* (N=34)	p value*
Age at infection-years (mean±SD)	56±14	55±18	0.70
Preexisting degenerative disease of spine	57%	53%	0.68
Diabetes mellitus	33%	36%	0.85
Intravenous drug use	24%	30%	0.58
Fever	39%	21%	0.07
SIRS (Systemic inflammatory response syndrome)	54%	35%	0.09
Vertebral osteomyelitis on diagnostic imaging	57%	85%	**0.006**
Discitis on diagnostic imaging	52%	82%	**0.004**
Positive blood culture	84%	45%	**< 0.001**
Positive needle aspiration culture	75%	38%	0.07
Positive intraoperative culture	80%	58%	0.05
Medical and surgical management	91%	71%	**0.014**
Time to surgery from established diagnosis-days (mean±SD)	12±31	11±20	0.87

*independent samples t-test for continuous variables; chi square test or Fisher's Exact Test for categorical variables

Conclusion. SEA caused by *S.aureus* is more likely to present with SIRS and associated bacteremia. The intraoperative and needle aspiration cultures were of higher yield in *S.aureus* infections. Vertebral discitis and osteomyelitis on imaging appears to be relatively delayed in *S.aureus* infection. This may be explained by the virulent nature of *S. aureus* that may lead to a rapid epidural involvement prior to the onset of imaging abnormalities consistent with discitis or osteomyelitis. Furthermore, a subgroup analysis revealed no differences between the infections caused by methicillin-resistant *S.aureus* and methicillin-sensitive *S. aureus*.

Disclosures. **All authors:** No reported disclosures.

835. Comparison of the Clinical Characteristics and Outcomes of *Klebsiella pneumoniae* Meningitis and *Streptococcus pneumoniae* Meningitis

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Background. *Klebsiella pneumoniae* is an uncommon cause of community-acquired bacterial meningitis. The clinical and laboratory characteristics of community-acquired *K. pneumoniae* meningitis (CA-KPM) remain to be elucidated. In this study, we compared the clinical and laboratory features, and outcomes, of CA-KPM with those of community-acquired *Streptococcus pneumoniae* meningitis (CA-SPM).

Methods. This multi-center, retrospective cohort study was performed at 8 general hospitals in the Republic of Korea. Using a clinical microbiology computerized database, all patients whose cerebrospinal fluid (CSF) cultures yielded *K. pneumoniae* or *S. pneumoniae* between January 1997 and March 2013 were identified. Adult patients with clinical meningitis were identified by detailed review of medical records.

Results. A total of 83 patients, 27 with CA-KPM and 56 with CA-SPM, were included. The proportion of males (KPM, 55.6% vs SPM, 55.4%, $P = 0.99$) and median age (KPM, 59 year vs 59 year, $P = 0.23$) were not significantly different between the groups. Diabetes mellitus (KPM, 48.1% vs SPM, 21.4%; $P = 0.01$) and liver cirrhosis (KPM, 22.2% vs SPM, 5.4%; $P = 0.05$) were more common in the CA-KPM group. Although the profiles of CSF analyses did not differ significantly between the groups, comatose mentality was more frequent in the CA-KPM group (KPM, 40.7% vs SPM, 12.5%; $P = 0.01$). Septic shock (KPM, 44.4% vs SPM, 89%; $P < 0.001$) and concomitant extrameningeal infection were also more common in the CA-KPM group (KPM, 37% vs SPM, 7.1%; $P = 0.001$). Vancomycin plus cefotaxime/ceftriaxone was the most frequently used initial empirical therapy (KPM, 74.1% vs SPM, 85.7%; $P = 0.23$) in both groups. However, 28-day mortality (KPM, 44.4% vs SPM, 10.7%; $P < 0.001$) and in-hospital mortality (KPM, 51.9% vs SPM, 14.3%; $P < 0.001$) were higher in the CA-KPM group.

Conclusion. Diabetes mellitus and liver cirrhosis are more common in *K. pneumoniae* meningitis than *S. pneumoniae* meningitis, and the former is more likely to present severe manifestations and poor outcomes.

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836. Central Nervous System Infections Caused by *Acinetobacter baumannii.*

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Background. Central Nervous System(CNS) infections caused by *Acinetoacter baumannii,* particulary carbapenem resistant strains, are emerging as a complication of neurosurgical procedures. Clinical outcomes of these infections have not been largely explored. In our study, we aimed to compare patients with *A. baumannii* CNS infections to patients with other Gram-negative CNS infections. We used clinical cure and crude mortality as outcomes.

Methods. We conducted a retrospective cohort study at Jackson Memorial Hospital, Miami, from January 2004 to December 2011. The cohort group consisted of cases with *A. baumannii* CNS infections; whereas the comparison group consisted of patients with CNS infections due to other Gram-negative bacilli. SAS software was used to perform statistical analysis.

Results. The *A. baumannii* group consisted of 26 patients, and the Gram-negative group included 39 patients. The *A. baumannii* patients were more likely to be in the Intensive Care Unit (ICU)($p = 0.005$), intubated ($p = 0.005$) and have carbapenem resistance($p = 0.001$) than the comparison group. Groups were otherwise similar in terms of age, renal function, nosocomial acquisition of infection, prior neurosurgical procedures, appropriate antibiotic initiation within 24 hours of cerebrospinal fluid collection, and mean number of days to appropriate therapy. Crude mortality for the *A. baumannii* group and the comparison group was 38% and 25 % respectively, with relative risk(RR) of 1.5(95% CI, 0.73 –3.09). Clinical resolution was 77 % in the *A. baumannii* group, and 84% in the comparison group, with RR 1.5 (95% CI: 0.1-22.9). In univariate analysis, carbapenem resistance was associated with increased crude mortality ($p = 0.037$). However, when controlling for the group, carbapenem resistance was associated with increased mortality in the Gram-negative group only but not in the A. *baumannii* group ($p = 0.013$ vs $p = 1.000$ respectively).

Conclusion. The *A.baumannii* patients were more likely to be intubated, in the ICU, and have carbapenem resistance. However, this did not result in difference in outcomes between the two groups. Carbapenem resistance was associated with increased mortality only in the Gram-negative bacilli group. This could possibly be related to difference in the organisms' degree of virulence, with A. *baumannii* being generally a low grade pathogen.

Disclosures. **All authors:** No reported disclosures.

837. Early Goal Directed Therapy for Acute Bacterial Meningitis in Malawian Adults

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Background. Acute bacterial meningitis (ABM) in sub-Saharan African adults occurs in young, HIV co-infected people, is predominately caused by *S. pneumoniae,* and mortality exceeds 50%. We tested if nurse-led Early Goal Directed Therapy (EGDT) was feasible for ABM in a resource-limited hospital in Malawi.

Methods. We prospectively recruited patients with suspected ABM in the emergency department of a Malawian referral hospital in a before/after design. EGDT was adapted from surviving sepsis guidelines, targets were set using outcome predictors from historical meningitis data. Routine care for suspected ABM was monitored in year one (Phase 1), study nurses delivered EGDT in year two (Phase 2). Protocolised care included rapid antibiotics, airway support, oxygenation, seizure control and fluid resuscitation for shock. Primary endpoints were proportions of clinical targets achieved, the secondary endpoint was outcome measured as death or disability (modified Rankin Score of => 2) at 40 days. ISRCTN96218197.

Results. 273 adults with suspected ABM were monitored in Phase 1 (P1), 71 with ABM were followed to day 40. 290 patients received EGDT in Phase 2 (P2), 61 had confirmed ABM. 61% were male, median age was 33 years, 75% were HIV co-infected.

In the feasibility comparison of EGDT, significantly more clinical targets were met in cases of proven ABM in P2 compared to P1. Of patients requiring one target, 81% achieved that target in P1, compared to 112% in P2. 36% achieved two targets in P1 compared to 110% in P2, 0% achieved three targets in P1 compared to 91% in P2, and 0% achieved four targets in P1 compared to 12.5% in P2. The overall composite mean target difference between P1 and P2 was highly significant $p < 0.001$

EGDT substantially reduced time to antibiotics (1hr 55 mins in P1 vs 1hr 13 mins in P2 $p < 0.001$), IV fluids and blood were more frequently given to shocked patients; airway placement in coma was more likely. No significant difference was seen in outcome at 40 days; death or disability occurred in 29/57 (51%) in P1 and 38/60 (63%) in P2 $p = 0.19$.

Conclusion. Nurse led EGDT was feasible for adults with ABM in Malawi and led to important improvements in clinical care delivery. Mortality remains high and testing EGDT for ABM in a large randomised trial is now required.

Disclosures. **All authors:** No reported disclosures.

838. Patient Outcomes and Surgical Complications in Coccidioidal Meningitis: An Institutional Review

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Background. *Coccidioides immitis* infection is endemic to the southwestern U.S. Chronic coccidioidal meningitis (CM) is frequently associated with multiple complications including hydrocephalus (HCP). We describe the treatment and outcomes of surgical complications of CM.

Methods. Data from CM patients surgically treated in a single institution between 2005 and 2013 was retrospectively collected. Charts were reviewed to obtain clinical presentation, treatment, and outcomes.

Results. We identified 146 patients with CM. Eighty-seven patients underwent a total of 177 neurosurgical procedures. The mean age was 44.3 years, male gender 72.4%. Patients of Asian and African descent were overrepresented in the cohort when compared to regional demographics. Comorbidities were present in 47.1%, and prior history of pulmonary coccidioides infection in 43.7%. Presenting symptoms included: headaches, encephalopathy, fever, ataxia, visual disturbances, nausea, and vomiting. All patients received anti-fungal therapy, most frequently with an azole. Twelve percent received concomitant intrathecal Amphotericin B. HCP was present in 57.8%. The most common surgical procedure was insertion of a ventriculoperitoneal (VP) shunt in 84% (n = 73). Other procedures included placement of Ommaya reservoirs and external ventricular devices. The overall shunt failure rate was 50%; the average number of shunt revisions was 2.5 (range 1-8); eighty one percent were due to mechanical obstruction in the draining system. Other complications included CNS device infection, stroke, and seizures. CM was associated with high morbidity, requiring prolonged inpatient care in 25% of patients.

Conclusion. The majority of patients with CM developed complications requiring surgical intervention, most of which involved at least two surgeries. Furthermore, a significant proportion required complex care. We recommend a multidisciplinary approach, with early neurosurgical evaluation for the optimal management of CM.

Disclosures. **All authors:** No reported disclosures.

839. Cerebrospinal fluid analysis of meningitis due to scrub typhus

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Background. Scrub typhus (ST) is a re-emerging zoonotic infectious disease in India and central nervous system (CNS) involvement is seen in up to 41% of patients. CNS manifestations of ST include aseptic meningitis, encephalitis, seizures,

opsomyoclonus etc. However literature on cerebrospinal fluid analysis (CSF) in meningitis due to ST is scant.

Methods. All patients admitted to a tertiary hospital in South India with ST and had clinical features of meningitis were included in this retrospective observational study from 2007-2012. ST was confirmed by the presence of a pathognomonic eschar and/or ST IgM Enzyme Linked Immunosorbent Assay (InBios International, Seattle, WA) positivity. Other common CNS infections were ruled out by appropriate tests. This study documents the details of CSF analysis among patients with meningitis due to ST.

Results. The study cohort contained 190 patients with meningitis due to ST. The mean age of the patients was 41 ± 4 years, and there was a slight male predominance (56.8%). The mean duration of fever prior to presentation was 9.4 ± 3 days. Common presenting complaints were headache (64.2%), nausea/vomiting (60%), altered sensorium (53.7%), and seizures (22.1%). An eschar was seen in 27.3% (52/190) of patients. The mean CSF WBC count was 80 cells/cu mm (range: 5-740 cells/cu mm). There was clear lymphocyte predominance (mean-87.6%). The mean CSF protein level was 105 mg% (range: 13-640 mg %). The mean CSF sugar level was 63.9 mg% (range: 25-350 mg %) and the CSF sugar level was less than 45 mg% in 18.2% of cases. Hepatic involvement was seen in 59.6% of patients, pulmonary involvement in 19.7%, renal dysfunction in 18.6% and cardiovascular involvement in 15% of the patients. The mortality rate was 6.3% (12/190). Univariate analysis showed the presence of an eschar (15.4% vs 2.2%; p = 0.002; OR: 8.1) and altered sensorium (9.8% vs 1.1%; p = 0.012; OR: 9.2) to be significant predictors of mortality.

Conclusion. In endemic areas Scrub typhus should be considered one of the differentials of aseptic meningitis. CSF analysis in ST may show very high WBC count with lymphocyte predominance, elevated protein level or low sugar level and should be differentiated from other CNS infections.

Disclosures. **All authors:** No reported disclosures.

840. Neurologic Manifestations of Rocky Mountain Spotted Fever in Children and Adults

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Background. Rocky Mountain Spotted Fever (RMSF) is the most common rickettsial disease in the U.S., and central nervous system (CNS) involvement has been reported. Despite this association, there are limited data on the spectrum of neurologic disease attributable to RMSF.

Methods. All patients with a positive IgG or IgM *Rickettsia rickettsii* serology from 2007 to 2013 at a single center were identified, and chart review performed. Inclusion criteria included fever and two of the following: headache, rash, thrombocytopenia, or elevated transaminases; patients with an alternate diagnosis were excluded. Patients meeting the case criteria for acute RMSF infection who had neurologic involvement during their illness were included in this analysis.

Results. Eighty cases of acute RMSF were identified, with 20 (25%) having CNS involvement. Clinical and neurologic findings are described in the table. Meningoencephalitis characterized by altered mental status and CSF pleocytosis was common in both adults and children, with seizures and need for ICU care showing a nonsignificant trend in the pediatric group.

	Children < age 18 (n = 10)	Adults (n = 10)	p-value
Age, years, median (range)	7.3 (0.6-16.1)	56.1 (27.8-72.1)	
Tick exposure in the month prior to illness	3 (30%)	6/9 (66.7%)	0.18
Max. temp (F), median	104.3 (102.9-105.7)	103.3 (102.1-105.2)	NS
Rash	10 (100%)	6 (60%)	0.09
Palms/soles	5 (50%)	0 (0%)	0.03*
Petechial	8 (80%)	1 (10%)	0.005*
Headache	7 (70%)	8 (80%)	NS
Confusion	8 (80%)	9 (90%)	NS
Seizure	4 (40%)	0 (0%)	0.09
Meningismus	3 (30%)	1 (10%)	NS
Hospitalized	10 (100%)	9 (90%)	NS
Required ICU care	7 (70%)	3/9 (33.3%)	0.18
Head CT - Abnormal	0/9 (0%)	1/4 (25%)	NS
Brain MRI - Abnormal	8/8 (100%)	2/3 (66.7%)	NS
CSF WBC, median	163 (2-964)	3.5 (1-399)	NS
CSF protein, median	112 (3-850)	136 (72-273)	NS

Conclusion. We identified 20 patients (10 adult and 10 pediatric) with RMSF involving the CNS. The majority of our population met criteria for meningoencephalitis and had abnormal neuroimaging, with MRI being much more sensitive than CT in identifying inflammation. Neurologic involvement in RMSF is a serious condition, with 95% of the population requiring hospitalization, 53% in the ICU setting. Adult patients were less likely to manifest petechial skin lesions, potentially delaying empiric therapy for this important and treatable cause of meningoencephalitis.

Disclosures. **All authors:** No reported disclosures.

841. Estimation of Undiagnosed Neuroinfectious Deaths with the Epidemiologic Pattern of Primary Amebic Meningoencephalitis Caused by *Naegleria fowleri*

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Background. *Naegleria fowleri*causes primary amebic meningoencephalitis (PAM), an acute, nearly always fatal disease. Cases are rarely reported (0–8 per year in the United States [US]), accounting for <0.5% of diagnosed encephalitis. The presentation can be confused with other infectious meningoencephalitides and clinical and diagnostic expertise is limited, all of which complicate the diagnosis. These complexities, combined with the fact that the true incidence is unknown, raise the concern that there are potentially missed cases.

Methods. A list of International Classification of Diseases, Tenth Revision (ICD-10) codes for undiagnosed possibly neuroinfectious deaths was developed using previously published data; ICD-10 codes from death certificates of known PAM cases; and expert opinion. US multiple cause-of-death mortality data for 1999–2010 were used to select deaths listing any of these codes anywhere on the death record. We then narrowed this group of deaths by applying known risk factors for PAM (age 2–22 years, high incident states, July–September month of death, and male sex) to estimate the number of deaths that fit the typical epidemiologic pattern for PAM.

Results. Undiagnosed neuroinfectious deaths accounted for 0.4% (1,688/410,389) of all US deaths among 2–22 year olds during 1999–2010. Males comprised the majority of deaths (910 [54%]). Applying the common epidemiologic risk factors, 101 (6%) undiagnosed neuroinfectious deaths, an average of 9 per year, fit the typical pattern of PAM. Using ICD-10 codes for PAM, we applied the same epidemiologic risk factors to assess how many diagnosed cases would be captured. This grouping of factors captured 9 of 16 (56%) cases of PAM.

Conclusion. While undiagnosed PAM cases likely occur, we estimate that this is a rare disease, with other epidemiologically similar pathogens accounting for some of the cases. Because not all PAM cases fit the typical profile, our estimate of 9 deaths per year likely does not capture all possible undiagnosed PAM deaths, evidenced by the fact that the epidemiologic criteria only applied to 56% of known cases. Using established risk criteria might be less effective because of the changing epidemiology of PAM, highlighted by recent cases in northern states and those with exposure to non-recreational water sources.

Disclosures. **All authors:** No reported disclosures.

842. First Primary Amebic Meningoencephalitis Death Associated with Exposure to Tap Water from a Treated Public Drinking Water System

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Background. *Naegleria fowleri* is a climate sensitive thermophilic ameba found in freshwater which causes primary amebic meningoencephalitis (PAM) (0–8 infections per year in the U.S.) when it enters the nose and migrates to the brain. While historically associated with recreational water use, other types of water exposures have recently been associated with PAM including using tap water to perform nasal rinsing for medical or religious purposes. In July 2013, a 4-year-old child died of PAM from a Louisiana parish where a previous PAM case associated with neti pot use had also lived.

Methods. To determine exposure, we reviewed medical records and conducted family interviews. To further investigate drinking water as a possible exposure source, we collected samples from in and around the family home and from various locations around the parish's water distribution system. We performed field water quality testing and the samples were tested for the presence of *N. fowleri* using culture at 42°C and real-time PCR.

Results. During the two weeks prior to becoming ill, the child had no contact with surface water (lake, pond, river, ditch, or puddle) but had played on a slip-n-slide supplied with public drinking water from two garden hoses connected to the home's outdoor faucet. The household tap water chlorine levels were below the limit of detection of the test (<0.02 mg/L) and the water temperature ranged from 29–46°C. Of the 12

household samples, five (42%) from hot and cold water systems were positive for *N. fowleri* by real-time PCR, culture, or both. Four (25%) of 16 water distribution system samples had detectable *N. fowleri*. There was no detectable chlorine residual and the water temperature was > 30°C at the four sampling locations where *N. fowleri* was found to be present.

Conclusion. This investigation marks the first detection of *N. fowleri* in a U.S. treated drinking water distribution system linked to a fatal infection. Favorable environmental conditions (i.e., no detectable chlorine and water temperatures > 30°C) allowed *N. fowleri* to thrive in the drinking water distribution system and in the home plumbing. Clinicians in all regions of the United States should be aware of PAM and recognize that not all patients have the traditional exposure to recreational freshwater.

Disclosures. **All authors:** No reported disclosures.

843. Enhancing Pathogen Identification Using a Comprehensive PCR System in Adult and Pediatric Patients with Meningitis and a Negative Gram Stain

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Background. Meningitis with a negative CSF Gram stain represents a diagnostic and therapeutic challenge, as the majority of the causative organisms are unknown. Novel and fast molecular techniques may increase the detection of the etiological agents.

Methods. Patients admitted to 4 hospitals in Houston, TX between November 2008 - March 2014 with community-acquired meningitis (fever, headache, vomiting, photophobia, stiff neck, focal neurological symptoms), CSF cell count > 5 cells/mm^3 and a negative CSF Gram stain were eligible. Residual patient CSF underwent additional testing by a research use only version of the FilmArray™ Meningitis/Encephalitis panel (FA ME, BioFire Diagnostics, LLC). The panel requires 200 µL CSF and simultaneously tests for 6 bacteria (*S. pneumoniae, N. meningitidis, S. agalactiae, H. influenzae, L. monocytogenes, E. coli* K1*),* 8 viruses (Herpes simplex types 1, 2, 6, Cytomegalovirus, Epstein-Barr virus [EBV], Enterovirus, Parechovirus, Varicella zoster virus [VZV]) and 2 fungi (*Cryptococcus neoformans* and *gattii*).

Results. Of the 149 patients enrolled, 48 (32.2%) had residual CSF (38 adults, 10 children < age 18) available for FA ME testing. Pathogens were identified in 14 (29.2%) of 48 samples by standard evaluation and 15 (31.2%) by FA ME. Among FA ME results, viral pathogens were most common [EBV (8), HSV2 (3), VZV (3), HSV1 (1), enterovirus (1)], followed by bacterial [*S. pneumoniae* (2)] and fungal [*C. neoformans* (1)]. Co-detections were present in 6 patients (12.5%); EBV was present in all (6) along with VZV (2), HSV1 (1), HSV2 (1), *C. neoformans* (1), and *S. pneumoniae* (1). In 8 (16.6%) patients, FA ME identified pathogens not previously identified. Standard evaluations identified pathogens in 5 (15.2%) of 33 FA ME negative samples [West Nile Virus (WNV) (4), *Histoplasma capsulatum*(1)].

Conclusion. Testing with the FA ME panel resulted in pathogen detections not previously recognized and for which treatment is recommended. The FA ME panel did not, however, detect some pathogens identified by standard techniques; assays for WNV and *Histoplasma* are not contained on the panel. Rapid, comprehensive testing for the most common pathogens causing meningitis will aid in the diagnosis and treatment of patients with meningitis.

Disclosures. **A. Hemmert**, BioFire Diagnostics: Employee, Salary

844. The Clinical Significance of Cerebrospinal Fluid Neutrophilic Pleocytosis in Viral Central Nervous System Infections

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Background. Viral meningitis and encephalitis is typically characterized by a cerebrospinal fluid (CSF) lymphocytic pleocytosis. A CSF neutrophilic pleocytosis presentation has been described but its prognostic and clinical significance is unknown. The objectives of our study were to compare the clinical and laboratory characteristics of viral central nervous system (CNS) infections with CSF neutrophilic to lymphocytic predominance and to evaluate factors associated with adverse clinical outcomes (ACO).

Methods. We conducted a retrospective study of 182 patients with confirmed viral CNS infections from Houston, TX and New Orleans, LA from 1999 to 2013. The patients were divided into CSF neutrophilic pleocytosis (neutrophils >50%) (n = 45) and CSF lymphocytic pleocytosis (lymphocytes + monocytes >50%) (n = 137). We compared the clinical characteristics, laboratory findings, imaging results and clinical outcomes between two groups. An adverse clinical outcome was defined as a Glasgow outcome scale 1-4.

Results. Of the 182 patients, 45 (25%) patients had CSF neutrophilic pleocytosis. CSF neutrophilic predominance was more frequently seen in patients with enteroviral infection (64% vrs 33%; $p < 0.001$) and less commonly in herpetic infections (20% vrs 46%; $p = 0.003$). The CSF neutrophilic pleocytosis group also presented more commonly in younger patients ($p = 0.001$) with more respiratory symptoms ($P = 0.04$) and had higher CSF WBC ($p = 0.004$). An adverse clinical outcome was presented in 29 patients (16%). Factors associated with ACO included arboviral infection, Caucasian race, Charlson comorbidity index ≥ 1, Age ≥ 60, fever, focal neurological deficit, altered mental status, encephalitis, and abnormal MRI ($p < 0.05$).

Conclusion. CSF neutrophilic pleocytosis occurs in 25% of patients with confirmed viral CNS infections and is most likely seen in younger patients with enteroviral infections and is associated with higher CSF pleocytosis but is not associated with higher adverse clinical outcome.

Disclosures. **All authors:** No reported disclosures.

845. Prediction of Outcome from Adult Bacterial Meningitis in a High HIV Seroprevelence, Resource-Poor Setting Using a New Severity Scoring Tool, the Malawi Adult Meningitis Score (MAMS)

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Background. Bacterial meningitis in sub-Saharan African adults is associated with mortality rates in excess of 50%, is predominately caused by *S. pneumoniae*, is strongly HIV-associated and occurs primarily in young adults. To improve this poor outcome, a severity prediction tool is required to inform both interventional trials and clinical management, aiming to optimise inter-hospital referrals, duration of antibiotics and hospital stay. However, a previously derived European severity score for bacterial meningitis was poorly predictive when applied to Malawian data.

Methods. We utilised individual predictors of death derived from a Malawian clinical trial dataset (n 400) to develop a severity prediction tool that can be applied in a high HIV seroprevelence, resource-poor setting (Malawi Adult Meningitis Score, MAMS). Five of fifteen variables tested (Cerebrospinal Fluid (CSF) culture, CSF white cell count, Haemoglobin, Glasgow Coma Score (GCS) and pulse rate) were shown to be strongly associated with poor outcome on multivariate analysis, and were converted into a predictive tool using a nomogram. The nomogram was tested against a separate clinical trial data-set for validation (n 193).

Results. Concordance (*c* statistic) of the nomogram in the validation dataset between predicted and actual outcome was 0.74 (95% CI 0.65 : 0.82), agreement 62.5%, Kappa 0.6, with an estimated sensitivity of 75% and specificity of 55%.

Conclusion. MAMS has equivalent power to predict outcome when applied in Malawi as the European meningitis score (EMS) when applied in Europe (EMS *c* statistic 0.81 (95% CI 0.74 - 0.87). Comparison of the two scores may help us understand both the pathophysiological differences and the difference in efficacy of adjunctive therapies such as corticosteroids between these two populations. MAMS has the potential to be a useful clinical and research tool.

Disclosures. **All authors:** No reported disclosures.

846. Outcome predictors of alpha herpes virus central nervous system infection

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Background. Alpha herpes virus infection, herpes simplex virus (HSV) and varicella zoster virus (VZV), is one of the well-known causes for aseptic meningitis and viral encephalitis. The polymerase chain reaction (PCR) test in cerebrospinal fluid (CSF) is the diagnostic method and widely available. Diseases spectrum ranges from self-limited to permanent disability. The prognostic factors, besides encephalitis, were not yet identified. The objectives of this study were to describe the spectrum of alpha herpes virus central nervous system (CNS) infection and define the predictors associated with the adverse clinical outcome (ACO).

Methods. We reviewed 1180 episodes of CNS infection in our retrospective database from Houston, TX and New Orleans, LA from 1999-2013. The cases with positive HSV PCR or VZV PCR were enrolled into our study. Basic demographic data, presenting symptoms, signs, laboratory results and imaging results were reviewed. Glasgow outcome scale 1-4 was used to identify adverse clinical outcome (ACO) group.

Results. Total of 66 cases (5.6% from total) were identified with positive HSV PCR or VZV PCR in CSF. Of those, 45/66 (68.2%) were HSV meningitis, 13/66 (19.7%) were HSV encephalitis, 7/66 (10.6%) were VZV meningitis, and 1/66 (1.5%) was VZV meningitis. Only 4/66 (6.1%) had recurrent episode with the mean follow up

of 1913 days and all were HSV meningitis. The outcome data was available in 57 cases; 22 (38.6%) had ACO. Charlson's score > 1, the diagnosis of encephalitis and findings associated with encephalitis (seizure, focal neurological deficit, abnormal imaging or EEG) was a strong predictor for ACO ($p < 0.001$). Type of infection (VZV vs HSV), gender, race, age (< 65 or > 65), HIV status (positive or negative), presenting symptoms (fever, headache, nausea, stiff neck, photo phobia, skin rash) and signs (Brudzinski's sign, Kernig's sign), laboratory result (total white blood cells, CSF leukocyte, CSF protein, CSF glucose) and treatment (received antiviral or not received antiviral) were not statistically significant associated with outcome.

Conclusion. The diagnosis of encephalitis and a Charlson's score > 1 are associated with ACO in the alpha herpes virus CNS infection.

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847. Clinical Prognostic factors to evaluate outcomes in Adult Patients with acute encephalitis

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Background. Encephalitis continues to be a significant cause of morbidity and mortality, there are few studies assessing prognostic factors in patients with acute encephalitis. An objective was to evaluate predictors of outcomes at hospital discharge for adult patients with acute encephalitis after inpatient evaluation.

Methods. This was a retrospective study done at Memorial Hermann Hospital in Houston, Texas and Tulane Medical Center/Charity Hospital in New Orleans, Louisiana from 1999-2013. We used bivariate and logistic regression analysis to evaluate baseline variables in patients with encephalitis to identify predictors of an adverse clinical outcomes (ACO) as defined as a Glasgow Outcome Scale of 1-4.

Results. Our evaluation included 143 patients. 65 patients (43%) required intensive care unit admission. The median age was 49 years. 77 were male (53%). 37 (25%) had confirmed viral encephalitis. 43 (30%) had an altered immune status. An adverse clinical outcome was found in 42% of the patients. ICU admission ($p = 0.041$), Glasgow coma scale (GCS) <8 ($p = 0.017$) and age > 60 years ($p = 0.04$) were associated with an ACO on bivariate analyses. On logistic regression analysis, Age > than 60 (Odds ratio [OR] 4.114, 95% Confidence Interval [CI] 1.554-10,888), and a GCS< 8 (Odds ratio [OR] 5.501 95% Confidence Interval [CI] 1.702-17.785) were independently associated with an ACO.

Conclusion. Prognostic factors predicting a poor outcomes in patients with acute encephalitis include age >60 years and a Glasgow coma scale <8.

Disclosures. **All authors:** No reported disclosures.

848. Risk Factors for Death and Major Morbidity among Children with Acute Bacterial Meningitis in Guatemala City

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Background. Acute bacterial meningitis (ABM) remains a significant contributor to pediatric morbidity and mortality in low and middle income countries (LMIC). Identifying risk factors and validating predictive scoring systems may guide interventions to reduce poor outcomes.

Methods. A prospective surveillance study was conducted for all children (aged 0-59 months) admitted to 3 referral hospitals in Guatemala City (2,000-2,007) and diagnosed with ABM by positive cerebrospinal fluid (CSF) culture or positive latex agglutination for *H. influenzae* type B (Hib), *S. pneumoniae* (Spn), or *N. meningitidis*; CSF WBC > 100; or positive CSF gram stain. Among children with non-missing data, we conducted univariate and multivariate analyses of risk factors documented at hospital admission that predicted death or major morbidity (hydrocephalus, convulsions, cerebral stroke, or cranial nerve paralysis) during hospitalization. We also performed a validation of the Herson-Todd Score (HTS).

Results. Of 827 children with ABM, 404 (49%) survived without major morbidity, 228 (28%) survived with major morbidity, and 195 (24%) died. Among 382 children with non-missing data, the most significant univariate predictors for death or major morbidity were seizure (OR 22.5, $p < 0.001$), coma (OR 11.8, $p < 0.001$), shock (OR 5.5, $p < 0.001$), CSF glucose < 20 (OR 4.2, $p < 0.001$), growth of Hib or Spn on CSF culture (OR 3.5, $p < 0.001$), hemoglobin < 11 (OR 2.4, $p = 0.001$), symptoms > 4 days (OR 2.3, $p = 0.001$), and positive CSF gram stain (OR 2.1, $p = 0.003$); age < 12 months was protective (OR 0.4, $p = 0.008$). In the multivariate analysis, significant predictors of death or major morbidity were CSF glucose < 20 (OR 27.3, $p < 0.001$), seizure (OR 4.8, $p < 0.001$), symptom duration > 4 days (OR 2.7, $p = 0.003$), shock (OR 2.7, $p = 0.036$), and coma (OR 1.4, $p = 0.049$). Of 229 children with a HTS score > 5, 213 (93%) died or suffered major morbidity (OR 12.8, $p < 0.001$). Among vaccine-eligible children, 101 (98%) of 103 with Hib ABM and 87 (93%) of 94 with Spn ABM were unvaccinated.

Conclusion. ABM is a cause of considerable morbidity and mortality in Guatemala. Several individual factors and the composite Herson-Todd Score predicted death or major morbidity. These predictors could help clinicians in LMIC guide medical care for ABM, and could provide a severity measure for the public health impact of vaccination programs against Hib and Spn.

Disclosures. **All authors:** No reported disclosures.

850. Preventing Device-Associated Infections in U.S. Hospitals: National Surveys from 2005 to 2013

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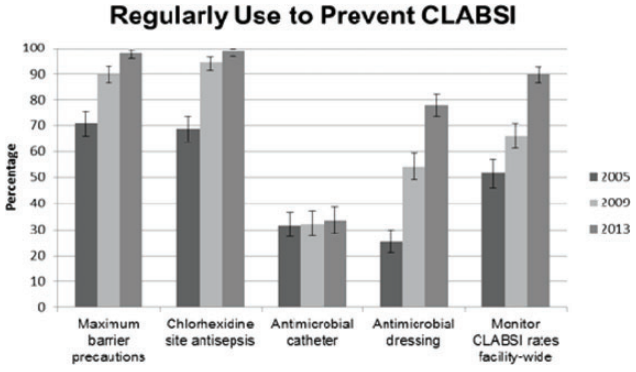
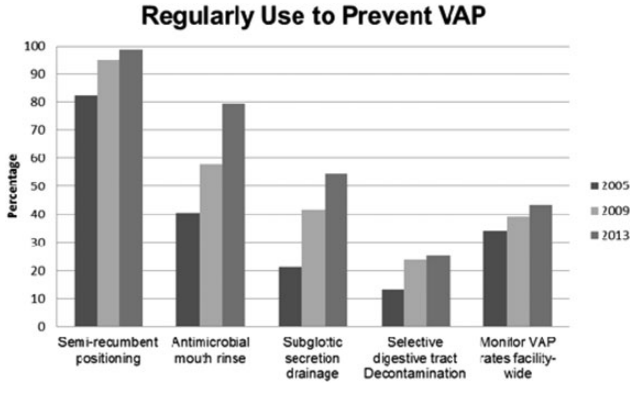
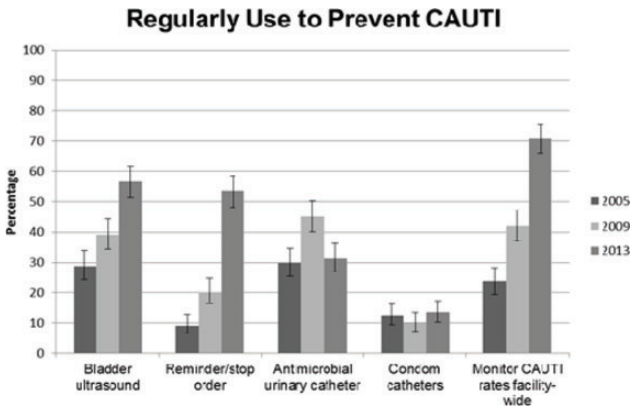
Background. Numerous initiatives have focused on reducing device-associated infections, including payment policies, mandated reporting of infection rates, and learning collaboratives. Accordingly, recent data from the CDC indicate that device-associated infection rates appear to have declined. However, the specific actions taken by hospitals that may contribute to this decline have not been well-described. We assess use of key practices to prevent device-association infections by U.S. acute care hospitals from 2005 to 2013.

Methods. We mailed surveys to infection preventionists at a national random sample of ~600 U.S. acute care hospitals in 2005, 2009 and 2013. Our survey asked about the use of practices to prevent the 3 most common device-associated infections: central line-associated bloodstream infection (CLABSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infection (CAUTI). Using sample weights, we estimated the percent of hospitals reporting regular use (a score of 4 or 5 on a scale from 1, never use to 5, always use) of prevention practices from 2005 to 2013.

Results. The response rate was ~70% all 3 years. Use of most recommended practices for preventing CLABSI, VAP and CAUTI increased significantly over time (figures). Among those showing the greatest increase from 2005 to 2013 were use of an antimicrobial dressing for preventing CLABSI (25% to 78%, $p < .001$), use of an antimicrobial mouth rinse for preventing VAP (41% to 79%, $p < .001$) and use of catheter removal prompts for preventing CAUTI (9% to 53%, $p < .001$). Likewise, a significant increase in facility-wide surveillance was found for all 3 infections, most notably for CLABSI and CAUTI. Practices for which little change was observed included use of antimicrobial catheters to prevent either CLABSI or CAUTI.







Conclusion. U.S. hospitals have responded to the call to reduce infection by increasing their use of key recommended practices with nearly universal adoption of maximum barrier precautions, chlorhexidine site disinfectant and semi-recumbent positioning. However, persistent vigilance is needed to ensure sustained improvement and additional strategies may still be required, given an apparent continuing lag in CAUTI prevention efforts.

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851. Reducing Bio-burden and Healthcare Associated Infection Risk Among Hospitalized Patients: Adoptability of Chlorhexidine Gluconate Bathing Among Non-ICU Patients

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Background. Daily CHG application has been shown to reduce all-cause and central line associated bloodstream infections in intensive care units (ICUs) where most patients are sedated and bathing is done by nursing staff. Recent literature suggests similar gains may be possible in non-ICU settings. No data are available on successful adoptability of daily CHG bathing in awake, non-ICU patients, some of whom self-bathe. We describe patient-reported CHG bathing practices and compliance in an academic hospital where daily 2% CHG bathing was implemented hospital-wide.

Methods. We conducted a two-part, verbally administered survey of a convenience sample of adult patients in non-ICU medical and surgical wards from November 2013 - March 2014. Surveys included 53 questions for self-bathers and 51 questions for those bathed by nursing staff. We excluded psychiatric, rehabilitation, and peripartum wards.

Results. 153 adults completed the surveys. 37% (n = 56) self-bathed with CHG cloths while the remainder were bathed by nursing staff. Among self-bathers, the following proportions received proper instructions: to massage CHG onto their skin (48%), to allow CHG to air dry (66%), and to use all six cloths (65%). Among self-bathers who had a temporary indwelling device (central venous catheter (CVC), drain, urinary catheter) or wound, only 43% and 14%, respectively, were informed that CHG should be used to clean those areas. Among patients receiving assisted baths, 67% had CHG massaged onto their skin, 83% allowed CHG to air dry, and 70% had all six cloths used on their body. Among assisted patients with a device or a wound, 66% and 39%, respectively, reported that CHG was used to clean those areas.

Conclusion. Expected gains in reducing healthcare associated infections with CHG in non-ICU inpatients necessitates proper application, particularly in body areas at highest risk for infection. Instructions to patient self-bathers on proper CHG application was poor or poorly retained, especially for high risk areas such as devices and wounds. Even with nursing assistance, over 30% and 60% patients did not report proper application of CHG to devices and wounds, respectively. Successful hospital-wide adoption of daily CHG bathing requires significant patient and nursing education.

Disclosures. **S. S. Huang**, Sage Products: Conducting a clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting a clinical trial for which contributed product is being provided to participating hospitals, Contributed product

852. Housewide use of Chlorehexidine Bathing to reduce Healthcare Associated Infections

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Background. Healthcare associated infections negatively impact patient outcomes and increase healthcare costs. Interventions have focused on specific risk factors, the presence or absence of indwelling urinary catheter for example, and interventions that could be applied across broadly have been limited. Following the publication of the experience with Chlorhexidine bathing on central line infections and MDRO acquisition in critically ill and bone marrow populations, we sought to examine the impact of this intervention on CLA-BSI, CA-UTI, and MDRO acquisition when applied to patients in both critical and acute care.

Methods. This qausi-experimental study examined the impact of CHG-bathing to all patients (1) in an adult critical care unit or (2) on an acute care floor if the patient had a central line, indwelling urinary catheter, or colonized with CRE. At the request of the stem cell attending, allogeneic bone marrow transplant patients were excluded. The rate of device related infections where compared pre and post intervention.

Results. For CAUTI, The average monthly rate per 1,000 IUC days fell from 4.3 prior to HG bathing to 2.8 post implementation (p-value <0.001). For CLA-BSI, the average rate for the whole hospital declined from 3.2/1,000 central line days to 0.88/1,000 central line days (p-value <0.001). MDRO transmission is still being analyzed.

Conclusion. CHG bathing throughout the hospital setting targeting at patient with specific risk factors was associated with a marked decline in both our CA-UTI and CLA-BSI rate. Analysis of this trend over time and a dose response are pending.

Disclosures. **All authors:** No reported disclosures.

853. Pathogen Distribution and Selected Resistance Profiles of Central Line-Associated Bloodstream Infection Isolates Reported to the National Healthcare Safety Network from Pediatric and Neonatal Intensive Care Units, 2011-2013

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Background. Previous antimicrobial resistance (AR) reports from the National Healthcare Safety Network (NHSN) have aggregated data across intensive care unit (ICU) types. Pediatric specific data are needed to guide prevention. We describe central line-associated bloodstream infection (CLABSI) pathogens and AR in pediatric and neonatal ICUs (PICUs and NICUs).

Methods. Among pathogens implicated in CLABSIs and reported with antimicrobial susceptibility test results to NHSN for the years 2011-2013, proportions testing resistant (R) or nonsusceptible (NS) to ampicillin (AMP-R), methicillin (MR), carbapenems (imipenem, meropenem or doripenem, CARB-NS), extended-spectrum cephalosporins (ESC-NS), and fluconazole (FLC-R) were determined. Log binomial regression was used to detect differences in %R/NS between ICU types.

Results. 2472 CLABSI due to 2797 organisms were reported from 320 PICUs, and 5720 CLABSI due to 6121 organisms were reported from 734 NICUs. Pathogen distribution differed in the 2 unit types (Table); staphylococci caused 54% of NICU CLABSI as compared to 29% of PICU CLABSI. Although proportions of resistant *S. aureus*, *Enterococcus* and *Candida* spp. were similar in the 2 ICU types, ESC-NS among Enterobacteriaceae causing CLABSI was significantly more common in the PICU than the NICU.

Pathogen	PICU CLABSI Pathogens Rank	N (%) N=2797	NICU CLABSI Pathogens Rank	N (%) N=6121	P-value
Coagulase-negative staphylococci	1	457 (16.3)	1	1835 (30.0)	<.0001
Enterococcus faecalis	2	361 (12.9)	3	501 (8.2)	<.0001
%AMP-R		1.6		2.2	0.53
Staphylococcus aureus,	3	360 (12.9)	2	1460 (23.9)	<.0001
%MR		31.8		32.1	0.92
Klebsiella pneumoniae/ oxytoca	4	288 (10.3)	5	415 (6.8)	<.0001
%ESC-NS		14.6		4.5	<.0001
%CARB-NS		1.4		0.3	0.22
Enterobacter spp.	5	213 (7.6)	7	244 (4.0)	<.0001
%ESC-NS		44.8		27.0	.002
%CARB-NS		4.0		3.2	0.67
Candida spp., non-*albicans*	6	199 (7.1)	6	249 (4.1)	<.0001
%FLC-R		4.3		6.3	0.57
Candida albicans	7	125 (4.5)	8	208 (3.4)	0.01
%FLC-R		1.5		3.9	0.42
Pseudomonas aeruginosa	8	104 (3.7)	9	161 (2.6)	0.01
%CARB-NS		17.2		7.6	0.03
Escherichia coli	9	91 (3.3)	4	471 (7.7)	<.0001
%ESC-NS		17.9		10.3	0.05
%CARB-NS		1.4		2.1	0.72

Conclusion. Pathogen profiles and AR patterns in PICUs and NICUs are distinct. To better inform interventions to reduce AR spread in hospitals, data from neonatal, pediatric and adult locations should be reported separately.

Disclosures. **All authors:** No reported disclosures.

854. Potential for Risk Adjustment for Central Line-Associated Bloodstream Infections Using Comorbidity Measures Derived from Medical Records from a Tertiary Care Hospital

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Background. Current risk adjustment for central line-associated bloodstream infections (CLABSI) follows National Healthcare Safety Network (NHSN) Centers for Disease Control and Prevention (CDC) guidelines, which only adjust for ICU type. With increasing public reporting policies at the state and national level, improved risk adjustment methods are needed. Our aim was to investigate whether comorbid conditions from ICD9 components of the Charlson Comorbidity Index (CCI) and the medication-components of the Chronic Disease Score (CDS) provide information useful for further adjustment.

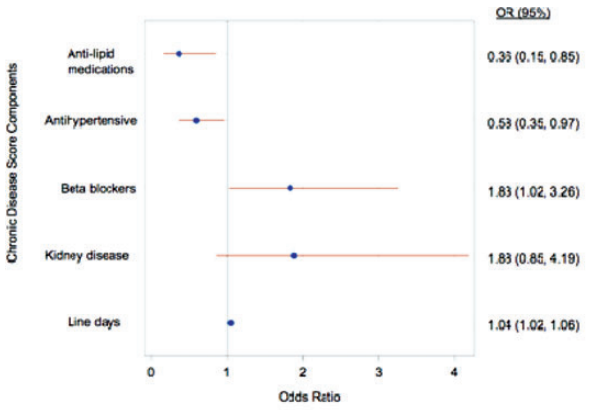

Figure 1. Chronic Disease Score component multivariable logistic regression model. The blue dots are adjusted OR estimates with confidence intervals shown in red.

CLABSI= Anti-lipid medications + Antihypertensive + Beta blockers + Kidney disease + Line days

Methods. We studied a University of Maryland Medical Center cohort of adult ICU patients admitted from July 2010 to December 2012. Data, including comorbid conditions, were from electronic medical records. CLABSIs were defined by infection preventionists. Eligible patients had a central line for at least 48 hours and no prior CLABSI during the study period. Two separate logistic regression models were constructed, one using CDS and the other using CCI components. Both models also included the number of line days.

Results. 4011 subjects with 4950 central lines were included, with a total of 32577 line days at risk and 76 CLABSIs (CLABSI rate: 2.33 per 1,000 line day). The mean ICU length of stay for those with a CLABSI was 30.1 days and 14.7 days for those without a CLABSI ($p < 0.0001$). The mean days with a central line for those with a CLABSI was 10 days and 5.8 days for those without a CLABSI ($p < 0.01$); line days was predictive of CLABSI in both models. In the CDS model, medication use associated with hypercholesterolemia and hypertenstion (calcium channel blockers) was protective, while hypertension (beta blockers) and kidney disease were associated with CLABSI (Figure 1). In the CCI model, myocardial infarction and kidney disease were associated with CLABSI (Figure 2).

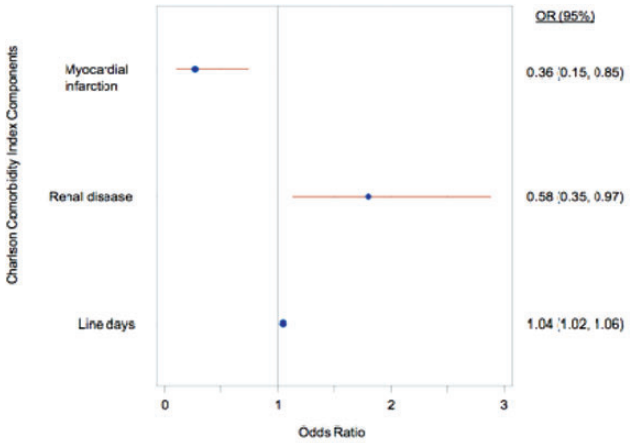

Figure 2. Charlson Comorbidity Index component multivariable logistic regression model. The blue dots are adjusted OR estimates with confidence intervals shown in red.

CLABSI= Myocardial infarction + Renal disease + Line days

Conclusion. We demonstrate several risk factors for the development of CLABSI, including duration of central line and several components of the CDS and CCI such the use of lipid-lowering agents. These factors are commonly measured and often available in electronic medical records. Further study is warranted to determine if these and other risk factors will improve risk adjustment methods used by the NHSN/CDC.

Disclosures. **All authors:** No reported disclosures.

855. Risk Factors for Peripherally Inserted Central Catheter (PICC) Bloodstream Infection (BSI)

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Background. PICC use may have lower risk of BSI compared to other central catheters but little data exist regarding risks for PICC associated BSI. This study evaluates risks for PICC BSI among patients (pts) at an academic hospital.

Methods. PICC BSI rate was calculated among all pts with PICCs inserted between July 2009-July 2012. A nested case control study (1:3 ratio of PICC BSI cases to no BSI controls) matched for operator (interventional radiology [IR], Infectious Diseases [ID], or nurse venous access team [VAT]) was conducted to assess risks for PICC BSI. Pt characteristics, PICC type (antimicrobial impregnated [ABXI] or not) and indication for PICC were recorded from chart review. Logistic regression was used.

Results. 89 PICC BSI occurred among 5372 PICC placements over the study (rate 1.66%). Mean days to infection were 32 and this was not different dependent on use of an ABXI PICC. Having an IR operator was associated with a 1.75 fold higher risk for PICC BSI compared to ID ($p = 0.02$) and a 4.22 fold higher risk compared to VAT ($p = 0.0008$). There was no difference in risk comparing ID to VAT operators. After multivariate analysis, non-ABXI PICC, PICC inserted for chemotherapy (CXT), tunneled PICC, leukemia, and AIDS were significant independent risks for PICC BSI (Table).

Logistic Regression Analysis of Risk Factors for PICC BSI

	Odds Ratio	95% CI	p-value
Univariate Analysis			
Sex (M)	1.67	1.03-2.71	0.04
Non-ABXI PICC	3.46	1.65-7.25	0.001
Indication CXT	5.66	2.68-11.96	<0.001
Tunneled PICC	4.47	1.81-11.0	0.001
Charlson score	1.15	1.03-1.28	0.01
Leukemia	8.25	3.27-20.83	<0.001
AIDS	11.23	2.29-55.06	0.003
Multivariate Analysis			
Sex (M)	1.47	0.84-2.57	0.2
Non-ABXI PICC	5.45	2.10-14.18	0.0005
Indication CXT	2.64	1.02-6.84	0.05
Tunneled PICC	9.35	2.94-29.79	0.0002
Charlson score	1.02	0.88-1.17	0.8
Leukemia	4.57	1.48-14.13	0.008
AIDS	11.76	1.81-76.37	0.01

Conclusion. PICC BSI rate was lowest if the PICC operator was ID or VAT. Use of a non ABXI PICC significantly increased risk for PICC BSI. Highest risk was among pts with AIDS and leukemia and if the indication for PICC was CXT. Tunneled PICCs were placed for pts at high risk for PICC infection or complications. Given our findings, catheter tunneling should be studied further to determine if PICC BSI risk is mitigated.

Disclosures. **All authors:** No reported disclosures.

856. Hospital Acquired *Staphylococcus aureus* Primary Blood Stream Infection: A Comparison of Events That Do and Do Not Meet Central Line Associated Bloodstream Infection (CLABSI) Definition

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Background. Hospital acquired bloodstream infection (HABSI) due to *Staphylococcus aureus* (SA) causes infectious complications in hospitalized patients. We assessed the outcomes of primary SA HABSIs that meet and do not meet the NHSN CLABSI definition.

Methods. Cases of primary SA HABSI were identified using an infection prevention surveillance database from January 1, 2010 to December 31, 2013 and categorized as being CLABSI or non-CLABSI (nCLABSI) according to NHSN definitions. The electronic medical record was reviewed to obtain clinical variables. Complicated bacteremia was defined as the presence of: septic thrombophlebitis, cardiac device infections, vertebral osteomyelitis, or infective endocarditis. Primary outcomes were mortality at 30 days and 1 year, septic thrombophlebitis, cardiac device infection, vertebral osteomyelitis, infective endocarditis, and complicated bacteremia.

Results. CLABSI and nCLABSI infections numbered 78 and 44, respectively, and are described in the table. 26 nCLABSI infections were associated with a peripheral IV (16) or a midline catheter (10). Mean time from admission to first positive culture was shorter for nCLABSI infections (6 vs 16.3 days; p = <0.001). The Charlson Comorbidity Indices, rate of ID consultation, 30 day and 1 year mortality were not different between the groups.

Comparison of CLABSI vs nCLABSI using Univariate Cox Proportional Hazards

	CLABSI		Non-CLABSI		
Variable	Number	Percent of CLABSI Cohort	Number	Percent of Non-CLABSI Cohort	P-value
Male	44	56.4%	25	56.8%	0.97
Evidence of PIV Infection	0	0%	16	20.4%	<0.001
Midline Placement Prior to Infection	3	3.8%	10	22.7%	0.002
MRSA	38	48.7%	19	43.2%	0.56
Septic Thrombophlebitis	17	21.8%	18	40.9%	0.025
Vertebral Osteomyelitis	0	0%	2	4.6%	0.13
Infective Endocarditis	0	0%	3	6.8%	0.046
Operation for Bacteremia	0	0%	4	9.1%	0.016
Cardiac Device Infections	0	0%	3	2.3%	0.045
Complicated Bacteremia	17	20.8%	22	50%	0.001

Conclusion. Primary SA nCLABSIs are a substantial clinical problem with more complications and similar mortality when compared to SA CLABSIs. Explanations may include decreased vigilance regarding source of infection, lack of a removable focus, and midline catheter usage. Focused practice improvement is necessary to prevent morbidity related to primary SA BSI even in the absence of a central-venous catheter.

Disclosures. **All authors:** No reported disclosures.

857. A Case Control Study of the Risk Factors for Central Venous Catheter Related Mixed Candidemia Infection

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Background. Central venous catheters (CVC) are a major risk factor for candidemia. Mixed candidemia with bacteremia due to CVCs has been increasingly reported in recent times. However, the risk factors for this dual infection have not been clearly identified. The aim of this study was to identify the risk factors for CVC associated mixed candidemia.

Methods. This was a prospective case control study conducted at a tertiary care hospital in South India which included all the patients with CVC related candidemia from May 2011 to July 2013. Inpatients with CVC insitu for >48 hours with candida isolated from blood were considered as CVC related candidemia. Mixed infection was defined as the isolation of both Candida and bacteria from a single set or different sets of blood cultures obtained within a 48 hours period. Cases (mixed infection) were compared with controls (only candidemia) with respect to risk factors and outcome. The chi-square test test were used to compare categorical variables, and Student's t-test was used to compare continuous variables. Statistical analysis was performed using SPSS version 16.0.

Results. During the study period, there were a total of 103 episodes of candidemia of which 33 (32%) episodes were due to mixed candidemia. Most of the mixed infections were due to gram negative bacteria (67%). In multivariate analysis, risk factors associated with CVC related mixed candidemia were prior ICU stay > 4 weeks (odds ratio; 95% Confidence Interval (CI): 3.39; 1.4, 7.2), prior antibiotic use > 14 days (2.73; 1.3, 5.9), > 3 antibiotics (6.55; 3, 14.3) and blood transfusions (4.02; 2.2, 7.4). There was no difference in the duration or site of CVC or the distribution of Candida species in the two groups. The 30-day survival of cases was significantly lower than controls (12.1% vs 42.9%; p = 0.002).

Conclusion. Mixed candidemia is relatively frequent with CVC related candidemia and negatively impacts the outcome. Duration of ICU stay, number and duration of antibiotic usage are risk factors associated with not only CVC associated candidemia but also for mixed infection. However, our study found blood transfusion as an additional risk factor for mixed candidemia. Further studies on the clinical relevance of Candida - bacterial interactions are needed.

Disclosures. **All authors:** No reported disclosures.

858. Evaluation of Current Methods for the Diagnosis of Catheter-Related Blood Stream Infections (CRBSI) at the Hospital for Sick Children

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Background. Central-line associated blood stream infections (CLABSI) are a significant cause of morbidity and mortality for critically ill and immunocompromised patients. The diagnosis can be challenging in children, as prophylactic antibiotics are often started prior to cultures. The purpose of this study was to review the value of catheter tip cultures in diagnosing CLABSI in children and to determine whether alternative laboratory methods of diagnosis might be indicated.

Methods. We performed a retrospective review of all semi-quantitative catheter tip cultures from 2010–11. All blood culture data in the preceding two weeks were reviewed to determine their predictive value for CLABSI. Central lines that had a second culture (peripheral or other central line culture) taken within 24h of each other were analyzed separately as a pair. A survey of HCP (physicians and nurse practitioners) on the diagnosis of CLABSI in children with central lines was conducted.

Results. A total of 274 catheter tips were cultured from 237 patients. The majority of patients had cultures performed in the preceding two weeks (87%). Positive tips cultures were obtained in 13% (n = 35); 28 (80%) had a preceding blood culture with the same organism. Of those patients, 86% (n = 24) had a set of paired cultures sent.

Analysis of tip cultures is outlined in the figure, and paired cultures are described further in the table.

The survey was distributed to 300 people, with a 25% response rate. Respondents felt line removal had significant clinical impact. Respondents were generally in agreement with IDSA guidelines on indications for line removal.

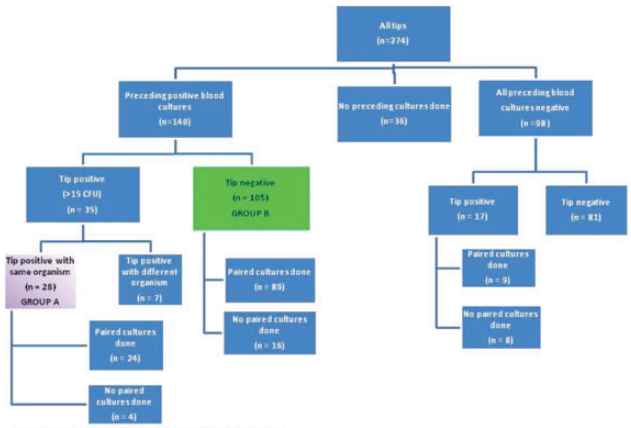

Figure 1: Analysis of tip cultures, and paired cultures

Analysis of tip cultures, and paired cultures.

Analysis of positive line tips and negative line tips

	Tip positive and same organism in preceding blood cultures (Group A)	Tips negative with preceding positive cultures (Group B)
Total # of tips	28	105
Total # that had paired cultures	24 (86%)	89 (85%)
Total # of paired cultures done	38	164 pairs
Mean # of pairs done per tip (range, SD)	1.4 (0 to 5, Std Dev 1.06)	1.6 (0 to 8 , Std Dev 1.46)

Conclusion. Our current methods of diagnosis are not adequate for the diagnosis of CLABSI, further research is needed to assess other techniques (i.e., differential time to positivity).

Disclosures. **All authors:** No reported disclosures.

859. The Epidemiology of Bloodstream Infections in a Tertiary Care Burn ICU Over a 5 Year Period

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Background. Infections continue to be the leading cause of death among burn patients, and many types of nosocomial infections (NIs) can be present in the burned patient. The presence of bloodstream infections (BSI) has been shown to result in a four-fold increase in mortality in this population.

The purpose of this study is to review the rates and epidemiology of hospital acquired bloodstream infections in a tertiary care center burn unit over a five year period from 2009-2013. We also assessed risk factors that have been associated with a documented increase in the number of BSI in 2013 at our institution.

Methods. This study is a retrospective cohort study conducted at a 650 bed tertiary care hospital in Edmonton, Canada. All patients admitted to the burn ICU and had a nosocomial bloodstream infection (defined according to CDC criteria) from January 2009 to December 2013 were included. Charts were then reviewed for additional epidemiologic data.

Results. Twenty one patients developed 30 episodes of BSI. The majority of BSIs were associated with skin/burn infection (13/30). Eight episodes were classified as central-line associated BSI, making this the second most common cause of BSI.

In 2013 the BSI rate increased dramatically to 58.18 per 1,000 admissions, compared with an average rate of 9.56 (8.9-10.07) per 1,000 admissions from 2009-2012. This was associated with increased median length of hospital stay (25.57 days vs 96.75 days) and burn severity (TSB: 58% vs 85%).

The most common pathogen isolated was *Pseudomonus aeruginosa* (7/30). There were seven episodes of multidrug resistant BSIs. All multidrug resistant (MDR) BSIs were seen > 4 weeks after admission. The mortality rate in the bacteremic group was 13%.

Conclusion. Burn patients are at high risk for BSI and this is closely related to % TBSA and length of hospitalization. The mortality is associated with severity of burn injury, older age and resistant pathogen bacteremia.

Disclosures. **All authors:** No reported disclosures.

860. A Multidisciplinary Approach to Reduction of Central Line Associated Bacteremia in Non-ICU Patients

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Background. In March 2014, CDC reported a national decrease in central line-associated bloodstream infections (CLABSIs) in ICU patients. Similar reductions have not yet been reported in non-ICU settings. At Boston Medical Center (BMC), sickle cell (SS) and hemodialysis (HD) patients with unique medical, socio-economic, and behavioral challenges are at high risk of developing CLABSIs in non-ICU settings.

Methods. A multidisciplinary team was formed to identify gaps in existing data and practice using an A3 Process Mapping tool. The following 6 improvement opportunities were identified: utilize electronic information systems to facilitate measurement of central line (CL) days and CLABSI rates on all non-ICU wards; identify best practices for care of SS and HD patients; revise staff communication policies; promote the use of a CL order set; monitor staff compliance with CL care protocols; and develop a patient education brochure describing risks and care of CL. Changes were implemented in March 2012. Non-ICU CLABSI rates and CL utilization ratios were measured before and after the interventions. Rates of CLABSI among HD and sickle cell patients were compared. A two-sample z-test was used to measure statistical significance.

Results. The CLABSI rate for all non-ICU patients decreased from 0.60/1,000 CL days in 2012 to 0.42/1,000 CL days in 2013 ($p = 0.43$). The CL utilization ratio in non-ICU patients decreased from 0.30 in 2012 to 0.21 in 2013 ($p < 0.001$). Non-ICU CLABSIs accounted for 83% (15/18) of all CLABSIs at BMC during 2012, and 43.7% (7/16) in 2013 ($p = 0.016$). One third of the non-ICU CLABSIs in 2012 occurred in HD and sickle cell patients but no CLABSIs occurred in these groups in 2013 ($p = 0.08$).

Conclusion. Involving key stakeholders to define, document, analyze, prioritize, recommend, and implement solutions resulted in a reduction in the rate of CLABSI, improvement in patient care, and reduction in cost. Hospital-wide dissemination of compliance rates and increased education has also contributed to a decline in rates. Efforts continue to improve compliance with use of the central line order set.

Disclosures. **All authors:** No reported disclosures.

861. Evaluation of Infection Control (IC) Knowledge for Central Venous Catheter (CVC) Insertion and Maintenance among the Medicine (MED) Housestaff

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Background. Prevention of CVC-associated bloodstream infections is essential to ensure patient safety. Physicians play an important role in preventing infections during the insertion and maintenance of CVC. It is crucial to assure proper knowledge of evidence-based practices among the Housestaff. The objectives are to assess MED Housestaff knowledge of IC practices for CVC insertion and maintenance and to determine if the methods used to educate the Housestaff are sufficient.

Infection Control Elements for Central Venous Catheter Insertion and Maintenance
Results from Survey of Medicine Housestaff

Questions from survey	Answers	Overall	PGY3	PGY1	PGY3 vs. PGY1, p-value
Elements of Hand Hygiene					
How long do you perform hand hygiene with soap and water?	15-20 seconds	26% (30/114)	19% (5/26)	28% (25/88)	0.35
How long do you perform hand hygiene with hand sanitizer?	15-20 seconds and/or until hands are dry	61% (70/114)	62% (16/26)	61% (54/88)	0.99
What is the best method for hand hygiene (most of the time)?	hand sanitizer	60 % (64/107)	48% (11/23)	63% (53/84)	0.19
Elements of Central Venous Catheter (CVC) Insertion					
What type of personal protective equiment do you need?	cap, mask, gown, gloves	95% (101/106)	100% (24/24)	94% (77/82)	0.22
What technique is used to insert a CVC (clean vs. sterile)?	sterile	97% (104/107)	100% (24/24)	96% (80/83)	1.00
How long to you apply 2% chlorhexidine gluconate with 70% isopropyl alcohol on the skin?	30 seconds	39% (43/111)	65% (17/26)	31% (26/85)	0.002
What method do you use to apply 2% chlorhexidine gluconate with 70% isopropyl alcohol (circular vs. back-and-forth motion)?	back-and-forth motion	36% (39/107)	46% (12/26)	33% (27/81)	0.24
Elements of Central Venous Catheter Maintenance					
What needs to be done before accessing a CVC line?	scrub the hub	91% (70/77)	100% (18/18)	88% (52/59)	0.13
How long do you need to do it?	15 seconds	56% (55/99)	54% (13/24)	56% (42/75)	0.88
What do you do if a CVC lumen is clogged? Can you continue using the CVC?	use of thrombolityc agent and/or change of central venous catheter	85% (56/66)	93% (13/14)	83% (43/52)	0.35
Elements of Public Infection Control Reporting					
What are the hospital-acquired infections publicly reported?	Central venous catheter-associated bloodstream infection	49 % (55/113)	64% (16/25)	44% (39/88)	0.08
All Questions		61% (687/1121)	66% (169/256)	60% (518/865)	0.08

Methods. The Housestaff learn CVC insertion practices from their peers and IC elements are reviewed annually via a required on-line self-learning module. Additional videos on CVC insertion are available and optional. There is no standardized class for this practice. The IC nurse surveyed the MED Housestaff on entry to the Intensive Care Unit rotation via 11 questions covering hand hygiene, CVC insertion and maintenance and public infection control reporting (table.) An overall score was calculated for each question and individually for PGY1s and PGY3s. The results were compared using the Chi-Square test.

Results. 114 surveys were completed from June 2012 to January 2014 (PGY3 = 26, PGY1 = 88). The overall score for 1121 questions was 61%. 4 of 11 questions scored higher than 85% (personal protective equipment, sterile technique, scrub the hub for accessing a line, clogged lumen management). Scores for the other 7 questions ranged from 26% to 61%. PGY3s performed slightly better than PGY1s (66% vs 60%, p = 0.08). PGY3s scored significantly higher only for the use of chlorhexidine/alcohol for 30 seconds prior to CVC insertion (65% vs 31%, p = 0.002).

Conclusion. MED Housestaff knowledge of CVC insertion and maintenance and general IC practice is weak despite education provided by their peers and an on-line module. PGY3s, who are in their last year of residency, performed only slightly better than PGY1s and both scored less than 70%. This survey revealed the weakness of our current process. Standardized education with systematic evaluation rather than relying on independent learning and peer review may be a solution. Further research is needed to identify optimal teaching and learning methods, and ongoing evaluation is crucial to assure that the information has been assimilated.

Disclosures. **All authors:** No reported disclosures.

862. Alcohol-Impregnated Disinfectant Caps Reduce The Rate Of Central-Line Associated Bloodstream Infections And Nosocomial Bacteremia

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Background. Improvements in central line placement practices have decreased the rates of central line associated bloodstream infections (CLABSI). Further progress in reducing infection may rest on processes related to line maintenance and care.

Methods. We evaluated the effect of an alcohol disinfection cap on rates of nosocomial bacteremia. The plastic caps fit on the exposed ends of IV needless access devices and contain a pad saturated with 70% isopropyl alcohol for disinfection: we alternated between similar products by two different manufacturers. The caps were placed on all ports of peripheral and central lines when not in use. Four hospital units with higher central line use were chosen for this yearlong intervention (an intensive care unit, a step down unit, and two medical surgical units). Nosocomial bloodstream infections and CLABSI were monitored for these units, along with four units not part of this intervention (to control for changes over time). The year prior to implementation served as comparison. Chi-square was used to test for change in the incidence of infection.

Results. The rate of CLABSI fell from 1.5 per thousand line days (kld) (16 CLABSI / 10 441 line days) to 0.4 per kld (4 / 9 536, P = 0.013). There was no significant change for units not using the caps, 0.6 (4 / 6 871) to 0.4 per kld (3 / 7 790, P = 0.59). The rate of nosocomial BSI also fell significantly, 0.73 per thousand patient days (kpd) (40 BSI / 33 037 patient days) to 0.47 (21 / 36 362), P = 0.005). Rates did not differ significantly between the two different products.

Conclusion. Using alcohol disinfectant caps on all IV access ports significantly reduced the rate of CLABSI and nosocomial bacteremia for a variety of inpatient hospital units.

Disclosures. **All authors:** No reported disclosures.

863. Reduction in CLABSIs with Alcohol Port Protectors

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Background. Central line (CL)-associated (CLABSI) cause significant patient morbidity and mortality; prevention is an important priority. In the setting of an increased CLABSI rate, our medical center, a large VA with multiple levels of care (acute care, ICU care and a Community Living Center) introduced a passive alcohol disinfection cap (PADC, Curos caps manufactured by Ivera) for use on all central and peripheral lines in 2012. Chlorhexidine bathing was also introduced in our ICUs in November 2012, near the middle of our intervention period. The rationale for PADC is that central line hubs are not adequately disinfected on a routine basis.

Methods. Number of infections were compared for 12 months prior to the intervention (period April 1, 2011-March 2012) and 12 months after the intervention (period August 2, 2012-July 2013, after a wash-out period of 4 months with intensified education on PADC usage) using a poisson regression model in Stata. Incidence rates were also compared over these 2 time periods.

Results. With the alcohol caps, there were 5 infections/12,263 line days (rate .41/1,000 line days) in period 2 compared to 22 infections/14,308 line days (rate 1.54/1,000 line days) in period 1; p = 0.0033. Rates were reduced in all levels of care. Using a poisson regression model, the level of care and introduction of chlorhexidine bathing in the ICU were not significant. Our final model showed that there was significant reduction in our outcome, # of infections, with PADC, incidence rate ratio .25, 95% CI 0.09; 0.66, p = 0.005.

Conclusion. CLABSI infections were significantly decreased, in all levels of care in the period, with the introduction of PADC. Although this is a before-after study, we accounted for the other major change in practice that occurred during this time period.

Disclosures. **All authors:** No reported disclosures.

864. A Prospective Study of Ethanol Lock Therapy in Children with Central Line-associated Bloodstream Infections

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Background. Central venous catheters (CVCs) are commonly used in pediatric patients who need continuous venous access. Central Line-associated Bloodstream Infection (CLABSI) is a serious complication in these children and a cause of catheter replacement. Some recent literature reported the efficacy of ethanol lock therapy (ELT) for children with CLABSI. But most of them were retrospective studies and protocols for ELT including factors such as dwell time and duration were varied. To investigate the most optimal method, we undertook a prospective study of ELT.

Methods. Between April 2012 and March 2014, pediatric patients diagnosed with CLABSI at the St. Marianna University Hospital in Kanagawa, Japan were enrolled. All of them were under 20 years of age and used Broviac-type tunneled CVCs. They were treated with instillation of 70% ethanol lock with a dwell time of 4 hours per day. Duration of ELT was 5 days from blood cultures were confirmed completely negative. Ongoing utilization of CVCs for venous access was permitted. The definition of successful ELT required negative blood cultures taken from all lumens of CVCs within 3 days of ELT being started and no subsequent isolation of the original organism from blood cultures with retention of the CVCs for 30 days.

Results. During the observation period, 11 patients were treated for CLABSI with ELT. Their median age was 14.2 years (range: 2-17 years). The organisms that caused CLABSI included *Staphylococcus epidermidis* (n = 5), other coagulase-negative *staphylococci* (n = 4), *Serratia marcescens* (n = 1), and *Candida parapsilosis* (n = 1). Nine of 11 (82%) patients completed ELT and retained their CVC. Two other patients (18%) failed to complete ELT; one patient was 9-year-old boy who had *C. parapsilosis*. The other patient was a 14-year-old girl who continued culture positive for over 3 days with *S. epidermidis* and her catheter was cracked. There was no significant adverse event with ELT.

Conclusion. Our study suggests that ELT is safe and effective in treating CLABSI, avoiding removal of CVC in pediatric patients even with a short dwell time of 4 hours per day, and allowing ongoing utilization for venous access. A limitation of this study is a small sample size, and a larger study is necessary in the future to validate these findings.

Disclosures. **All authors:** No reported disclosures.

865. Utility of Electronic Medical Records to Assess the Relationship between Total Parenteral Nutrition and Central Line-associated Blood Stream Infections

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Background. Parenteral nutrition has been associated with an increase in central line-associated blood stream infections (CLABSIs), which are significantly associated with increased morbidity, mortality, and costs. To develop more effective methods for CLABSI prevention, large electronic databases will be an important tool to identify independent risk factors. Study aims were to evaluate the utility of using electronic data sources to identify risk factors, including total parenteral nutrition (TPN) for CLABSI, to assess the association between CLABSI and administration of TPN, and to identify potential factors associated with a higher risk of CLABSI.

Methods. Data were obtained for all discharges of adult patients in whom a central line was inserted between September 1, 2007 and December 31, 2008 in a large, academically affiliated hospital network in New York, NY. CLABSI was defined electronically using a modified CDC definition. A manual chart review was also undertaken to assess validity/reliability of the electronic database and gather additional information. Risk factors for CLABSI incidence were examined using logistic regression.

Results. Among 4,840 patients, there were 220 CLABSIs, an incidence density of 5.4 CLABSIs per 1,000 central line days. Significant risk factors included TPN (odds ratio [OR] = 4.33; 95%CI, 2.50 – 7.48), ICU stay (OR = 2.26; 95%CI, 1.58 – 3.23), renal disease (OR = 2.79; 95%CI, 2.00 – 3.88), immunodeficiency (OR = 2.26; 95%CI, 1.70 – 3.00). Diabetes mellitus was associated with reduced CLABSI rates (OR, 0.63; 95% CI, 0.45–0.88).

Conclusion. Utility of electronic medical records for determining risk factors is limited by such things as free-text data entry. However, using a hybrid between fully electronic and manual chart review, reliable data were obtained. Parenteral nutrition is associated with a high risk for CLABSI. Rates for CLABSI in a population highly selected for indications for TPN is significantly higher than prior comparable reports.

Disclosures. **All authors:** No reported disclosures.

866. Observational Study of Central Venous Catheter (CVC) Occlusions and Central Line-Associated Blood Stream Infections (CLABSI) Using the Clave™ Negative Displacement Connector

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Background. We performed a year-long observational study in a large cohort of patients to evaluate the incidence of CLABSI and CVC lumen occlusion using a negative displacement connector in a setting where disinfection caps containing 70% isopropyl alcohol cover all unused connectors.

Methods. CVCs placed between October 2012 and October 2013 at NorthShore (4 hospitals, 832 beds) were prospectively monitored for the development of CLABSI and/or CVC lumen occlusion. Patients were followed from the time of CVC insertion through 2 days following removal or through final hospital discharge if there was no documentation of removal. CLABSI was defined using NHSN criteria. Relevant data including evidence of lumen clots (e.g., ultrasound or use of plasminogen activators) were abstracted from the electronic medical record (EMR) and medical staff interview. Direct observations were performed on a subset of patients to assess adherence to hospital policy regarding the insertion and maintenance of CVCs.

Results. Throughout the 12 month study, 2,264 patients underwent CVC placement. 85 direct observations demonstrated insertion protocol adherence in 881 of 925 (95%) measured criteria. There were 21 CLABSI for a rate of 0.84% of lines and 0.62 per 1,000 line days. 378 clots occurred for a rate of 15.05% of lines and 11.23 per 1,000 line days. Infection and clot rate by hospital are in the table.

Infection and clot rate by hospital

	Total patients	Total lines	Total line-days	Lines with Infection	Lines with Clot	Event per 100 lines Infection	Event per 100 lines Clot	Event per 1,000 line days Infection	Event per 1,000 line days Clot
Hospital 1	921	1,056	14,925	8	231	0.76*	21.88†	0.54*	15.48†
Hospital 2	552	596	8,286	4	69	0.67	11.58	0.48	8.33
Hospital 3	397	428	5,030	3	38	0.70	8.88	0.60	7.56
Hospital 4	394	432	5,427	6	40	1.39	9.26	1.11	7.37

*, $p>0.05$ for all; †, $p<.0001$ for 1 vs 2, or 3, or 4

Conclusion. In this very large study of CVC-related complications we demonstrated that lines placed with standardized methods using a negative displacement connector and a disinfection cap can achieve very low rates of complications. The risk of infection was 5 to 10-fold lower than previously reported. Assessment of new devices should approach clinical trials with the concept that very low rates of complications are achievable using contemporary devices and practices.

Disclosures. **L. Peterson**, Cepheid: Investigator, Research grant

867. Metaanalysis on the Relative Risk of Central Line-associated Bloodstream Infections Associated with a Needless Intravenous Connector with New Engineering Design

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Background. Needleless-intravenous-connectors (NC) with desired patient safety design may facilitate effective intravenous line care and reduce the risk for central line-associated bloodstream infections (CLA-BSIs). We conducted a meta-analysis to determine the risk for CLA-BSI associated with the use of MaxPlus™ Tru-Swab™ Positive Displacement Connector (MP), a newer generation NC with improved engineering design.

Methods. We reviewed MEDLINE, Cochrane Review, EMBASE, ClinicalTrials, and studies presented in 2010-2012. Studies reporting the CLA-BSIs in patients using MP compared to negative- or neutral-displacement NCs were analyzed. We estimated the relative risk (RR) of CLA-BSI with the MP for each study and then the pooled effect using the random effects method.

Results. Seven studies met the inclusion criteria: four were conducted in intensive care units, one in a home-health setting, and two in long-term-acute-care settings. In the comparator period, total central venous line (CVL) days were 111,255; the CLA-BSI rate was 1.5 events/1,000 CVL days. In the MP period, total CVL days were 95,383; the CLA-BSI rate was 0.5 events/1,000 CVL days. The pooled random effects model revealed 63% CLA-BSI risk reduction associated with the MP (RR: 0.37; 95% Confidence Interval [CI]: 0.16, 0.90). The Poisson model showed 69% CLA-BSI risk reduction associated with MP (RR: 0.31, 95% CI: 0.19, 0.47).

Conclusion. A needless connector with improved engineering design is associated with lower CLA-BSI risk.

Disclosures. **Y. P. Tabak**, CareFusion: Employee and Shareholder, Salary **W. Jarvis**, Baxter: Consultant, Consulting fee; CareFusion: Consultant, Consulting fee; Johnson and Johnson: Consultant, Consulting fee; Gojo: Consultant, Consulting fee **X. Sun**, CareFusion: Employee, Salary **C. Crosby**, CareFusion: Employee and Shareholder, Salary **R. Johannes**, CareFusion: Employee and Shareholder, Salary

868. Improving Appropriateness of Peripherally Inserted Central Catheter Utilization and Decreasing the Incidence of Central Line-Associated Blood Stream Infection

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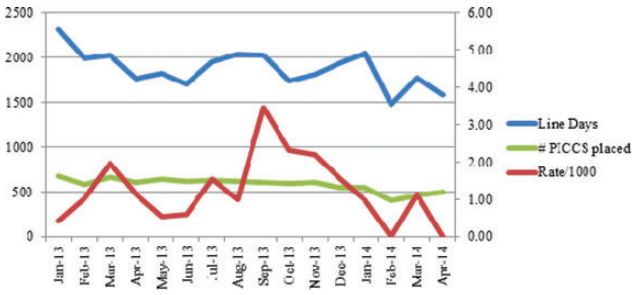
Background. Central line associated blood stream infection (CLABSI) is a preventable health care associated infection associated with increased mortality and cost. In September 2013 there was an increase in intensive care unit (ICU) CLABSI rates. Upon investigation, it was noted that peripherally inserted central catheter (PICC) utilization at DMC had increased substantially over the past several months and that approximately one-half of CLABSI cases at DMC were associated with PICCs.



PICCs Placed, Central Line Days and ICU CLABSI Rate

Methods. Four acute-care hospitals, including 15 adult ICUs were included in this project. A multi-disciplinary group including infection preventionists, hospital epidemiologists, intensivists, nurses, vascular access team nurses, interventional radiologists and pharmacists was organized to implement the CLABSI Prevention Plan. A major focus of the plan was to decrease the frequency with which PICCs were inappropriately utilized. Guidelines were drafted pertaining to best practices for temporary central venous catheter and PICC utilization, insertion and removal. A comprehensive educational intervention regarding vascular catheter utilization and care was implemented throughout DMC.

Results. The CLABSI Prevention Plan was put into place in September 2013. Seven months following implementation of the plan, the frequency of PICC utilization decreased by 35% (figure). CLABSI rates decreased from a peak of 3.5/1,000 catheter days in September 2013 to 1.13/1,000 in March 2014 with statistically significant trend ($p = <0.001$) (figure).

Conclusion. Overuse of PICCs, including inappropriate utilization, contributed to increases in CLABSI rates. Interprofessional educational strategies to improve line maintenance were implemented. The work of a multi-disciplinary team resulting in an almost 1/3 reduction in the frequency of PICC utilization and ICU CLABSI rates. Formal guidelines for the appropriateness of PICC utilization as well as improved efforts to appropriately utilize and place peripheral lines and centrally placed lines are needed.

Disclosures. **All authors:** No reported disclosures.

869. Impact of Changes in the NHSN Catheter-Associated Urinary Tract Infection (CAUTI) Definition on the Frequency and Epidemiology of CAUTIs in Intensive Care Units (ICUs)

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Background. In January 2013, the wording of the NHSN definition for CAUTI was changed to include fever as a diagnostic criteria regardless of the presence of an alternative fever source. The objective of this study was to determine the impact of changes in the CAUTI definition on the frequency and clinical relevance of CAUTI cases meeting NHSN criteria.

Methods. We conducted a retrospective cohort analysis at the Detroit Medical Center (DMC). We included 4 DMC sites and 15 adult ICUs from July 1, 2012 to June 30, 2013. Patients were identified who met CAUTI criteria, based in part, on the presence of fever. Detailed data collection was conducted to identify other potential fever sources.

Results. A total of 107 patients who met current NHSN criteria for CAUTI were studied, with a mean age of 57.1 ± 17.3 and 60.8% were female. Prior to urine culture, the median ICU length of stay was 20 days (IQR 7,33) and median foley days was 6 days (IQR 3,12). The most common pathogens responsible for CAUTI was *Candida glabrata* (23.1%) and enterococcus species (14.1%). 48 (44.8%) patients had another NHSN-defined infection other than CAUTI, including pneumonia (27.1%) and bloodstream infection (21.5%). Twelve patients (11.2%) had a non-infectious etiology of fever. Patients with alternative fever sources (n = 60) were categorized as having CAUTI according to NHSN 2013 definitions only and would not have been diagnosed with CAUTI according to previous NHSN definitions. These patients were compared to those patients for whom CAUTI was the only source of fever (and thus would have been diagnosed with CAUTI by both older and new NHSN definitions) (n = 47). There were no significant differences between the two groups although there were trends for a higher frequency of physician-diagnosed "other infections" (OR 5.8, p < 0.001) among patients in the "new CAUTI only" group. Presence of *Candida spp.* was also more frequent among patients this group (OR 1.8, p = 0.17).

Conclusion. The change in NHSN CAUTI definition led to a more than 2-fold increase in CAUTIs. Using current, 2013 definitions, CAUTIs are frequently diagnosed in the presence of other infections. Positive urine cultures, (e.g., *Candida spp.*) often represent colonization rather than clinically meaningful urinary tract infection.

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870. The Epidemiology of CAUTI due to *Candida spp*. in the Intensive Care Unit (ICU) - Infection or Colonization?

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Background. In January 2013, the National Healthcare Safety Network of (NHSN) reworded the CAUTI definition criteria to include fever regardless of the presence of an alternative fever source. At Detroit Medical Center (DMC) the change resulted in a sharp increase in CAUTI, particularly due to *Candida* spp. This study was conducted to better understand the epidemiology and clinical relevance of CAUTI due to *Candida spp*.

Methods. This study was conducted at 15 adult ICUs at 4 DMC hospitals from July 1, 2012 to June 31, 2013. It was a nested study from a cohort of ICU patients with CAUTI diagnosed according to current NHSN criteria, in which fever was the only symptom criteria present. Patients with CAUTI due to *Candida spp*. were compared to patients with CAUTI due to bacteria.

Results. Of 99 patients with CAUTI and fever, 44 (44.4%) had *Candida spp.* as a pathogen and 55 (55.6%) had bacteria. The mean age of patients was 57.3 ± 17.2 and 58.59% were female. The median duration of the foley catheterization prior to positive urine culture was significantly longer in the Candida group (7.06 vs 4.57 days in bacteria group, p = 0.01) as was median length of stay (LOS) (31 vs 16 days, p = 0.007) and ICU LOS prior to urine culture (11.59 days vs 5.98) (p= 0.003). 43.2% of Candida CAUTI patients had diabetes compared to 25.5% of bacterial CAUTI (p= 0.09). SIRS criteria was present in 90.9% of patients in the Candida group and 76.2% in the bacteria group (p= 0.07).

Fever sources other than CAUTI (mainly pneumonia and bloodstream infections) were more often present in the Candida group than the bacteria group (50% and 38.1%, p = .35) as was the proportion of patients with physician-diagnosed infections (68.2% vs 47.2%, p = 0.04). In-hospital mortality was 29.6% in the Candida group and 18.2% in the bacteria group (p = 0.15).

Conclusion. Compared to bacterial CAUTI patients, Candida CAUTI patients had more intensive healthcare exposure, longer durations of indwelling urinary catheters, and more frequently had co-infections at the time of CAUTI diagnosis. These factors suggest that in many cases, Candida CAUTI is a marker or increased severity of illness, represents colonization rather than true infection and is not clinically relevant. NHSN criteria should be modified to account for these factors.

Disclosures. **All authors:** No reported disclosures.

871. NHSN CAUTI Rates in the ICU: The Impact of Fever Prevalence, Length of Stay (LOS) and Frequency of Obtaining Urine Cultures

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Background. Catheter-associated urinary tract infection (CAUTI) represents a common hospital-acquired infection. Urine cultures are often obtained without appropriate indications, and positive urine cultures in the setting of fever can meet the National Healthcare Safety Network (NHSN) definition of CAUTI without clinically significant findings. We hypothesized that increased prevalence of fever, longer length of stay (LOS) and higher frequency of urine cultures are associated with higher rates of CAUTI in the intensive care unit (ICU) using NHSN criteria.

Methods. We collected data on fever prevalence, LOS, urine culture results and numbers of CAUTI per the NHSN definition, from January 1, 2013 to December 31, 2013, from the medical (MICU), surgical (SICU) and cardiovascular (CVICU) intensive care units at an 804-bed tertiary care, teaching hospital. Data were analyzed using ANOVA, chi square, the Kruskal Wallis (KW) test and z-test for proportions.

Results. The CAUTI rate was significantly higher in the SICU compared to MICU and CVICU. In addition, patients in the SICU had significantly longer LOS, and higher fever prevalence (table-KW test was used due to skewed distributions). The average number of patient-days with fever was 1.18 ±2.83 for SICU, 0.75 ±1.75 for MICU, and 0.48 ±1.29 for CVICU. More urine cultures were sent in the SICU vs the MICU, but percent positive urine cultures were significantly fewer in the SICU. The CVICU sent the most urine cultures, however positive urine cultures were fewer and fever prevalence was lower.

Urine culture data, fever prevalence, LOS and CAUTI rates by ICU.

	Urine culture sent/1,000 patient days	% Positive urine cultures	Mean Patient days with fever (±SD)	Mean LOS in days (±SD)	NHSN CAUTIs/1,000 catheter days
	SICU	48.50	28.2%	1.18 (±2.83)	5 (±6.0)
7.0					
	MICU	44.73	37.6%	0.75 (±1.75)	4 (±3.51)
2.4					
	CVICU	52.68	22.2%	0.48 (±1.29)	4 (±3.6)
2.2					
		p=0.002*	p<0.0001^	p<0.0001^	CVICU vs SICU p=0.022** MICU vs SICU p=0.002**

*chi square ^KW test **z-test

Conclusion. ICUs have different patient characteristics and practices which may influence NHSN CAUTI rates. Fever prevalence, urine culture practices, and LOS can impact NHSN CAUTI rates, and this measure may not represent the true clinical burden of CAUTI in the ICU.

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872. The Yield of Urine Cultures in Intensive Care Unit Patients with Indwelling Urinary Catheters

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Background. Catheter associated urinary tract infections (CAUTIs) are the most frequent healthcare-associated infection (HAI). Intensive care unit (ICU) CAUTIs identified using the National Healthcare Safety Network (NHSN) definition are publicly reported and are considered as a quality measure. However, clinicians are often challenged with differentiating CAUTI from asymptomatic bacteriuria. We sought to delineate the epidemiology of ICU CAUTIs in order to identify the role of urine cultures in the ICU setting.

Methods. All ICU CAUTIs identified in 2012 and 2013 by Infection Control using the NHSN definition were reviewed. Patient demographics, urinary catheter data, and culture results were obtained from the Infection Control database. Additional chart

review was done to abstract information on indications for urine culture, symptoms, antimicrobial therapy, adverse drug reactions and patient outcome.

Results. A total of 105 ICU CAUTIs were identified for a CAUTI rate of 2.5 per 1,000 catheter days. 3,767 ICU catheter urine cultures were submitted during this time period, for a CAUTI rate of 2.8%. The most common organisms were yeast (53%), *E. coli* (18%), *Enterococcus* spp (12%), and *Pseudomonas*spp (7%). The primary indication of urine culture for patients who had CAUTIs was fever (97%). In the majority of patients an alternative explanation of fever was found: fever due to infection other than CAUTI (51%), and non-infectious cause of fever (17%). Pneumonia (53%) was the most common infection identified. Of the 34 (32%) patients with positive urine cultures and no other identifiable cause of fever, only 17/34 (50%) received antimicrobials directed at the urinary pathogen.

Conclusion. Urine cultures are frequently obtained in ICUs for an evaluation of fever, but they have a low yield. Fever was attributed to an alternative cause in most patients. When an alternative cause was not found, urine culture results were not used to guide antimicrobial therapy in the majority of patients. Urine cultures in all catheterized ICU patients with fever is likely not a cost-effective strategy. There are no clinical findings that distinguish bacteriuria from CAUTI in the febrile ICU patient in most cases.

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873. Using natural language processing on electronic medical notes to detect the presence of an indwelling urinary catheter

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Background. We set out to develop a natural language processing (NLP) algorithm to extract concepts related to indwelling urinary catheters from electronic medical notes.

Methods. A concept lexicon was developed based on domain knowledge, prior expertise and review of medical notes. Concepts were classified as evidence of either catheter presence or catheter absence. A reference standard set of 1595 randomly selected documents from inpatient admissions were annotated by human reviewers to identify all positively and negatively asserted concepts. An NLP algorithm was tuned using 100 documents from the set. Novel lexicon semantics including evidence of catheter absence and inherently negated terms were used. Electronic medical record note titles with the highest hit rate for concepts were identified. The NLP algorithm was then tested on a set of 1495 documents to determine agreement between NLP and human reference standard, sensitivity and positive predictive value (PPV).

Results. The overall cohort included 5,589 unique patients with 77,938 hospital days from two VA hospitals over a one-year period. The lexicon contained 590 concepts for catheter presence (e.g., Foley catheter was placed) and 18 for evidence of absence (e.g., Patient has bathroom privileges). Iterative review of NLP outputs on the training set included false positive analyses and fine-tuning of the algorithm. Overall, nurse's notes were the most frequent inpatient note titles; these also yielded the highest number of concepts with respect to urinary catheters. The overall agreement between the NLP and reference standard was 71%. With 348 instances of 'evidence of catheter presence' the system found 246 for a sensitivity of 87%. With 84 false positive concepts associated with catheter presence, the PPV was 59%. For 'evidence of catheter absence', the agreement was 72% (450 instances), sensitivity was 77% and PPV was 68%.

Conclusion. We have shown that it is possible to identify the presence of an indwelling urinary catheter from the free text of electronic medical notes. Further refinement and scaling-up of NLP algorithms to large document sets is ongoing. This is the first key step in developing protocols to assist humans in large-scale review of patient charts for CAUTI.

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874. Risk Factors for Complicated Urinary Tract Infection (cUTI) due to Pseudomonas

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Background. Treatment of cUTI due to Pseudomonas is challenging because of the organism's propensity to form biofilms and its intrinsic and acquired resistance to many antibiotics. Our objective was to identify risk factors for Pseudomonas as the causative pathogen among hospitalized patients with cUTI.

Methods. We conducted a retrospective cohort study of cUTI among adult inpatients at an academic medical center from May 1, 2009 – December 31, 2013. Pregnant patients or those without microbiology data were excluded. cUTI was defined as catheter-associated UTI (CAUTI); acute pyelonephritis; UTI in patients with uropathy or other urinary tract functional abnormality (UT abnormality), urogenital/anorectal surgery, urinary calculi, quadriplegia/paraplegia, spinal cord injury/disorder, kidney transplant, or end-stage renal disease; or UTI in males. Chi-square and Fisher's exact tests were used for bivariable analysis; forward stepwise multivariable logistic regression with $p < 0.25$ entry and $p < 0.05$ stay criteria was used to identify independent predictors of pseudomonal cUTI.

Results. Among 2,598 patients included in the cohort, 202 (7.8%) had Pseudomonal cUTI. Bivariable analysis showed that patients with history of $1^{st}/2^{nd}$ generation cephalosporin use, multiple sclerosis (MS), quadriplegia/paraplegia, UT abnormality, or male sex (all $p < 0.01$) were more likely to have Pseudomonal cUTI. In the multivariable regression model, male sex (OR: 2.2, 95%CI: 1.6-3.0), CAUTI (OR: 1.5, 95% CI: 1.1-2.1), $1^{st}/2^{nd}$generation cephalosporin use (OR: 1.8, 95% CI: 1.3-2.5), MS (OR: 2.6, 95% CI: 1.4-4.9), quadriplegia/paraplegia (OR: 3.0, 95% CI: 1.9-4.7), spina bifida (OR: 0.2, 95% CI: 0.1-0.7), and UT abnormality (OR: 1.9, 95% CI: 1.3-2.7) were identified as independent predictors of Pseudomonal cUTI.

Conclusion. Patients with CAUTI or certain comorbidities associated with voiding problems or increased catheterization may be more likely to develop pseudomonal cUTI, however, those with spina bifida may be at reduced risk. While further work is needed to verify these risk factors and their mechanism for conferring risk, valid predictors may be useful to identify which cUTI patients should receive empiric anti-Pseudomonal agents.

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875. Prospective Monitoring of Indwelling Urinary Catheters in Hospitalized Patients

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Background. Indwelling urinary catheters (IUCs) in hospitalized patients can lead to catheter-associated urinary tract infections (CA-UTIs) or be placed in those with UTIs. Not infrequently, broad spectrum gram negative (BS-GN) coverage is used as empiric treatment when providers lack data available to make treatment choices.

Methods. We prospectively followed IUCs in medical inpatients: those inserted at admission (ADM), during the hospital stay (HS) and those with chronic IUCs. EMR allowed retrospective review of outcomes, UTI-related provider documentation, urine studies including cultures (ucx) and treatment decisions.

Results. In 2yrs, 549 IUCs were followed; 55% placed during HS, 41% at ADM and 4% were chronic. Our cohort was predominantly male (98%) with mean age 73.2 ± 12.5yrs; IUC indications were genito-urinary obstruction (41%), tracking ins/outs (26%), decubiti (5%) with 18% inserted while critically-ill. The 28d mortality was 21% and 12% died during hospitalization. Median IUC duration 5d (1-60d)and mean insertion time from admission of 5.5 ± 13.3d (1-117d). Compared to ADM IUCs, chronic and HS IUCs were in longer (+12.1d and +4.7d, <0.001). Providers treated over a third of patients with IUCs for UTI (184/549,34%). Provider documentation allowed CDC CAUTI definition in 16% and a quarter of ucxs were unevaluable. Empiric BS-GN coverage was initiated in a third of UTIs; 10% of cxs demonstrating ESBL/MDR GNs. Our EMR adjudication disagreed with providers in over 40% of treated UTIs.

Conclusion. Patients admitted with IUCs are a potentially vulnerable group. Age, debilitation and overlapping illness understandably contribute to a providers willingness to treat empirically. Frequently opting for BS coverage, a provider's decisions may be hampered by inability to remove IUC, unclear symptomology and/or contaminated cultures. IUCs are an important target for antimicrobial stewardship.

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876. Strategies for Success in Emergency Department Catheter-Associated Urinary Tract Infection Prevention Programs

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Background. The emergency department (ED) is a primary source of urinary catheterization in hospitals; yet, CAUTI prevention bundles have been developed in the inpatient setting. We aimed to identify successful strategies used among EDs who were early, successful adopters of CAUTI prevention programs.

Methods. Qualitative study of early adopting EDs. Using data from a prior nationwide survey and national publicity, we screened over 400 EDs and identified 6 ED CAUTI programs with early, successful adoption of CAUTI prevention programs, defined as utilizing criteria for urinary catheter (UC) placement and tracking ED-placed UCs. We conducted 6 ED site visits, 58 semi-structured interviews and 9 focus groups with key personnel. In total we enrolled 102 participants (e.g., ED nurses, doctors, infection control staff). We assessed motivations, barriers and successful strategies, focusing on UC use, insertion practices, and maintenance. We transcribed interviews verbatim and 3 coders used content analysis to code material in NVivo9. The primary coder subsequently reviewed all codes and transcripts to identify themes of CAUTI programs, which were reviewed by all authors and discussed to ensure consensus.

Results. ED staff reported that they were motivated to prevent CAUTI by feeling accountable for UC use, and believing that program compliance results in better patient care. Successful approaches to minimize UCs in the ED included: requiring doctors to use decision support tools, nurse use of UC criteria checklists, and removal of default UC orders from trauma protocols. Programs cited the following strategies to ensure proper insertion technique: modifying workflow of insertions (e.g., use of specified staff), changing UC products, training staff on placement, and conducting insertion audits. Barriers to process change included difficulty proving that CAUTI originated in the ED and goal conflict in urine culture practice patterns with some EDs routinely culturing UCs, whereas others limited testing.

Conclusion. Among EDs that successfully adopted CAUTI prevention programs, common motivations, barriers and strategies emerged. Workflow redesign around UC utilization and insertion technique was cited as most critical to success by participants.

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877. Prevention of Catheter Associated Urinary Tract Infections (CAUTIs): results and challenges

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Background. CAUTIs are one of the most common hospital acquired infections. Basic and specific practices to prevent CAUTIs have been applied in different institutions but reducing rates of CAUTIs and Foley catheter days remains challenging.

Methods. Implementation of specific practices to reduce CAUTIs including Nurse Driven Foley Catheter removal protocol, monthly Infection control team unit rounds for education and assessment of catheter indications and a Foley Catheter Bundle that have guidelines for Foley insertion best practice competency and urinary catheter best practice algorithm.

Results. This study was conducted in a 941 bed tertiary center which includes 100 ICU beds. In addition to basic CAUTI prevention practices, the above mentioned specific practices were implemented in October 2012. Prior to specific practices interventions, we had per month mean patient days of 19,313, Foley days of 3662 (3426-4031) and 10.08 CAUTIs (7-13) in compare to post interventions where we had mean patient days of 19,916, Foley days of 3211 (2866-3556) and CAUTI number of 6.69 (2-10). CAUTI rate per 1,000 catheter days was reduced by 30% from 2.94 to 2.08. CAUTI rate per 10,000 patient days decreased from 5.59 to 3.35 with 41% reduction despite the fact that Foley days was reduced by 14% only. We faced many challenges including healthcare professional commitment to engage in the application of these specific measures, definitions of CAUTIs by CDC/NHSN lack complete validation and CAUTI rates can vary depending on the reporting method used. In addition, we noticed more than 50% of urine cultures grew yeast which can be a colonizer or a contaminant rather than an infectious agent. Also, patients transferred from long term facility or other centers are more likely to develop CAUTIs.

Conclusion. CAUTIs can be reduced by implementing specific measures which included nurses driven protocol, infection control team Foley catheter rounds, and Foley catheter bundles. Further studies are needed to evaluate these measures. In addition, further work is needed to validate and modify CDC/NHSN definitions and criteria for CAUTI to help better understand the effectiveness of these prevention methods. Education programs for healthcare professionals concerning CAUTIs and its complication will be helpful to implement prevention methods.

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878. Sustained Reduction in Catheter-associated Urinary Tract Infection (CAUTI) Rates Using a Collaborative Program Approach

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Background. Approximately 15-25% of hospitalized patients receive a urinary catheter during their hospital stay. Among UTIs acquired in the hospital, approximately 75% are associated with a urinary catheter.

Methods. Our hospital, a large tertiary-care facility with a substantial spinal cord injury population and on-site nursing care center, were experiencing significant symptomatic CAUTI rates. We implemented a collaborative CAUTI prevention program in late 2011 using our MICU and one ward as trial areas employing a closed system silver urinary catheter (SUC) trial for two weeks with concurrent targeted intense nursing and support staff education of proper insertion and maintenance of SUC with no CAUTI during the trial; weekly CAUTI tracers were used to monitor practices. A second trial was conducted early 2012 for 7 months within all acute care units, emergency department, and nursing care center involved; weekly tracer monitoring continued.

Results. Our CAUTI rates declined from 5.1/1,000 urinary catheter days (UCD) late 2011 (pre-intervention) to 3.5/1,000 UCD in early 2012 with the first trial implementation; this further decreased to 1.4/1,000 UCD overall rate with the full hospital implementation in 2012. Our overall CAUTI rate for 2013 was 1.1/1,000 UCD.

Conclusion. Our overall collaborative approach which involved: engagement of frontline staff in targeted education on maintenance of indwelling urinary catheters and CAUTI prevention efforts; a strong interdisciplinary clinical focus; greater spread of evidence-based practice standards through the use of SUC technology; and excellent communication, contributed to the significant and sustained aggregate reduction of symptomatic CAUTI incidence rates throughout our inpatient care areas.

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879. Systematic Review of Interventions to Reduce Catheter-Associated Urinary Tract Infection in the Long-Term Care Setting

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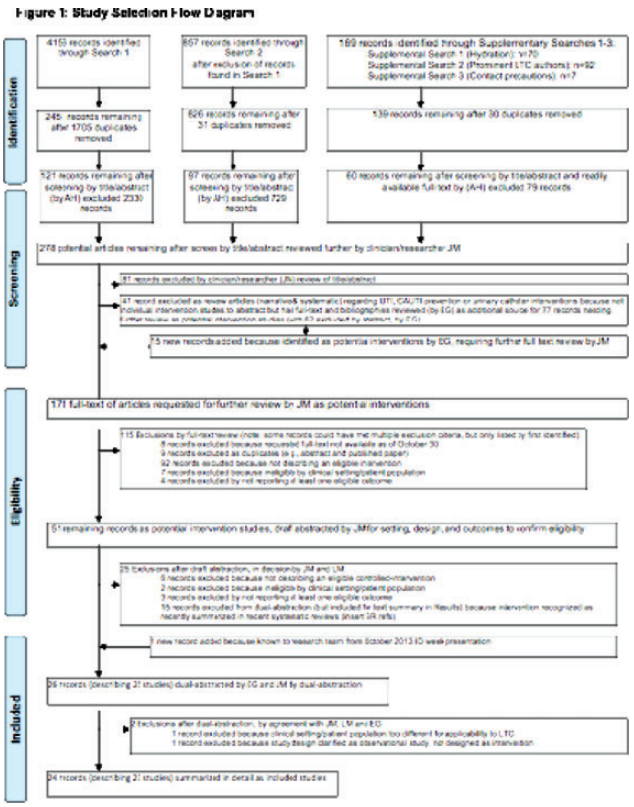
Background. Catheter-associated urinary tract infection (CAUTI) is a common, costly and morbid nosocomial infection for residents of long-term care (LTC).

Methods. We systematically searched for controlled interventions (randomized or non-randomized) aiming to reduce UTIs (categorized as nosocomial UTI, CAUTI or bacteriuria) and/or urinary catheter use (all types) in the LTC setting (nursing homes, skilled nursing facilities) or rehabilitation and spinal cord programs in English through November 13, 2013 using the electronic databases of Ovid MEDLINE, Cochrane Library via Wiley, CINAHL, Web of Science and Embase.com. Two authors abstracted data and assessed study quality using a modified Downs and Black Quality Index, with abstract discrepancies addressed by third author.



Results. 24 records (Figure) describing 23 controlled-interventions were included; several reported decreased UTIs, CAUTIs or urinary catheter use though often underpowered to assess significance. No analyses were pooled given heterogeneity of interventions, study designs, and outcomes. Study quality was variable (score range 4-27, median: 11.8). CAUTI prevention bundles have been implemented with some evidence of success in LTC, with similarities to acute-care bundles (e.g., hand hygiene, strategies to avoid placement and prompt removal of catheters, proper catheter insertion/maintenance) plus interventions focused on chronic catheter needs, incontinence and preemptive barrier precautions.

1. **C**atheters in newly admitted patients should be removed to assess if still needed;
2. **A**septic insertion of indwelling catheters, hand hygiene before and after every resident contact, and barrier precautions during intimate care (i.e., toileting, bathing);
3. **U**se catheters only if indicated; routine assessments of catheter need (daily in short-term residents, otherwise monthly) should be conducted with alternatives considered;
4. **T**raining and mentorship of staff and family regarding catheter care;
5. **I**ncontinence plans to address individual resident challenges and solutions.

Conclusion. Reviewing the available evidence**,** we propose 5 "C.A.U.T.I" bundle components to prioritize for preventing CAUTI in the LTC setting:

Disclosures. **J. Meddings**, AHRQ: Grant Investigator, Salary; SHEA: Member, Speaker honorarium; QuantiaMD: invited speaker/developer for educational webinar, Speaker honorarium **S. Krein**, Blue Cross and Blue Shield of Michigan Foundation: Grant Investigator, Research grant and Research support; Department of Veterans Affairs: Employee and Investigator, Research support and Salary **A. Hickner**, AHRQ: Collaborator, Salary and staff member on grants and contracts; VA HSR&D: Collaborator and Employee, Salary and was employee during project; University of Michigan: Employee, employee (now part-time) during project, Salary; Yale Medical Library: Employee, Salary after work on this project completed **H. Reichert**, AHRQ: Collaborator, Salary and statistician, analyst on grant of Jennifer Meddings **E. Gaies**, AHRQ: Collaborator, Research associate as staff on grants and contracts, Salary; VA HSR&D: Employee, Salary **S. Mcnamara**, University of Michigan: Employee, Salary; AHRQ: Collaborator, Salary and staff member on grants and contracts; NIH: Collaborator, Salary and staff member on grants and contracts of Lona Mody

880. Incidence rates of ventilator-associated events and ventilator-associated pneumonia in the National Healthcare Safety Network, 2012-2013

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Background. Surveillance for ventilator-associated events (VAEs) is based on detecting conditions associated with increased oxygen or positive end-expiratory pressure (PEEP) settings. In 2013 the National Healthcare Safety Network (NHSN) replaced traditional ventilator-associated pneumonia (tVAP) with VAE surveillance in adult inpatient units. In August 2013 a minor PEEP criterion change was made. We compared VAE rates before and after the change and tVAP to VAE rates in 9 intensive care unit (ICU) types.

Methods. We analyzed data from ICUs with >50 ventilator days that followed NHSN tVAP (2012) and VAE (2013) protocols. We calculated pooled mean (PM) incidence rates/1,000 ventilator days before (January-July, 2013) and after (August-December, 2013) the change, and annual PM (APM) VAE (2013) and tVAP (2012) rates, and compared them using rate ratios (RRs) and 95% confidence intervals (CIs) (OpenEpi 3.01).

Results. Of 2,269 ICUs submitting VAE data in 2013, 1766 (78%) reported before and after the change. VAE rates increased after the change in trauma ICUs only (table). Of 1487 ICUs that participated in tVAP and VAE surveillance, VAE rates were highest in trauma and neurology ICUs. VAE rates were significantly higher than tVAP rates in all except burn ICUs (table).

	VAEs/1,000 vent days, Before and after definition change				Events/1,000 vent days, VAE and tVAP			
ICU	# ICUs	Before, PM	After, PM	RR (95% CI)	# ICUs	VAE APM	tVAP APM	RR (95% CI)
Trauma	64	10.18	11.60	0.88 (0.78-0.99)	50	10.99	3.46	3.18 (2.80-3.60)
Neurology	16	9.65	9.13	1.06 (0.78-1.43)	13	10.28	2.11	4.87 (3.22-7.36)
Neurosurg	75	9.30	8.52	1.09 (0.95-1.26)	54	8.59	2.27	3.78 (3.13-4.50)
Surgical	142	7.81	7.92	0.99 (0.89-1.09)	106	8.04	2.37	3.40 (3.02-3.82)
Medical	242	7.04	7.35	0.96 (0.89-1.03)	197	7.03	0.95	7.38 (6.51-8.27)
Cardiac	148	6.95	6.80	1.02 (0.89-1.17)	112	7.74	0.85	9.13 (7.30-11.43)
Burn	26	6.44	8.62	0.75 (0.51-1.08)	24	6.27	4.71	1.33 (0.95-1.87)
Cardiothoracic	169	5.72	6.80	0.96 (0.85-1.09)	132	6.26	1.82	3.45 (2.99-3.98)
Med/surg	884	5.36	5.52	0.97 (0.92-1.02)	799	5.40	1.15	4.68 (4.39-5.00)

Conclusion. The impact of the PEEP criterion change on VAE rates was limited. In most ICU types VAE rates were higher than tVAP rates, reflecting VAE's capture of a wide range of conditions. Work is needed to understand VAE rate differences among ICU types.

Disclosures. **All authors:** No reported disclosures.

881. New Ventilator Associated Event (VAE) Definition: Persistence of Subjective Variability

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Background. The National Healthcare Safety Network (NHSN) has recently supported efforts to shift surveillance away from ventilator associated pneumonia (VAP) to ventilator associated events (VAE) to decrease subjectivity in surveillance and increase clinical correlation. This study compares the results of an automated surveillance strategy using the new VAE definition to a prospectively performed clinical application of the definition.

Methods. All patients ventilated for 2 or more days in the medical and surgical intensive care units (ICUs) were evaluated by two methods: 1) retrospective surveillance using an automated algorithm combined with manual chart review following the NHSN VAE methodology and 2) prospective surveillance with some modifications of the NHSN methodology by pulmonary physicians in collaboration with the clinical team administering care to the patient at the bedside.

Results. Of the 1209 patients evaluated, 69 were found to have VAE by the retrospective surveillance while the prospective surveillance identified 67 events. 56 patients were determined to have VAE by both methods (kappa = 0.81, p = 0.04). There were 24 patients considered to be VAE by only one of the methods. Most discrepancies were the result of clinical disagreement with the NHSN VAE methodology.

Conclusion. There was good agreement between the study teams. Overall, a similar number of events were called by each method (69 vs 67). Awareness of the limitations of the surveillance definition for VAE can help infection prevention personnel in discussions with critical care partners about optimal use of these data.

Disclosures. **S. Micek**, Tetraphase: Grant Investigator, Research support **M. Kollef**, Cubist: Speaker's Bureau, Speaker honorarium; Basilea: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium

882. Risk Factors for Ventilator Associated Events

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Background. Surveillance definitions for four hierarchically related ventilator associated events (VAEs) were introduced in 2013: ventilator associated condition (VAC), infection related ventilator associated condition (IVAC), possible and probable ventilator associated pneumonia (VAP). VAEs are associated with increased duration of mechanical ventilation, prolonged hospital stay and increased risk of death in hospital. Risk factors for VAEs remain to be determined.

Methods. The medical records of all patients undergoing their first episode of mechanical ventilation of over 48 hours duration from April 1 to September 30, 2013, in the medical or surgical intensive care unit (ICU) of a 214 bed hospital were reviewed. VAEs were identified using January 2013 definitions from the National Healthcare Safety Network. Information was collected on 35 patient demographic or health characteristics at ICU admission and on 15 processes of care or complications of health appearing after ICU admission. Risk factors for VAE were evaluated using single variable Cox proportional hazards regression models, where relative risks (RR) and 95% confidence intervals (CI) were estimated.

Results. 191 patients met criteria for study. Median age was 65 years and 110 patients (58%) were male. The most common admission diagnoses were central nervous system disease (24%), sepsis (18%), and cardiovascular disease (17%). VAC, IVAC, possible VAP and probable VAP were identified in 36, 18, 12 and 1 patients. Median days from intubation to VAE, IVAC and possible VAP were 4, 5 and 5 respectively. Acute respiratory distress syndrome was associated with the subsequent appearance of VAC (RR: 2.69, CI 1.28-5.66, P = 0.009) and IVAC (RR 3.43, CI 1.26-9.32, P = 0.016). Renal replacement therapy (RR 2.43, CI 1.02-5.76, P = 0.044), insertion of a nasogastric tube (RR 0.38, CI 0.15-0.94, P = 0.036) and mechanical ventilation at ICU admission (RR 0.49, CI 0.25-0.95, P = 0.035) were associated with VAC.

Conclusion. Identification of risk factors were limited by the small size of the cohort and number of VAEs. However relevant processes of care and complications of

health, particularly those occurring shortly after intubation and related to the development of ARDS, may not have been included. Studies of larger cohorts derived from careful review of patients who sustain a VAE are warranted.

Disclosures. **All authors:** No reported disclosures.

883. Is the Patient the Problem? A look at baseline characteristics of patients with Infectious Ventilator Associated Events

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Background. Ventilator associated events (VAEs) are associated with increased hospital length of stay, duration of ventilation, costs and mortality. VAEs exist along a continuum ranging from ventilator associated complications (VAC) to infectious ventilator associated complications (IVAC) to ventilator associated pneumonia (VAP). Because these events occur on ventilators, most research looks to environment or pathogen factors for prevention and intervention. We sought to examine host characteristics and compare patients with VAC, IVAC and VAP in terms of demographics and severity of illness.

Methods. This study was performed as a retrospective chart review. Eligible patients were age >18 with a ventilator associated event as defined by Centers for Disease Control/National Health Surveillance Network definition, and research authorization on file with our institution. Case finding was done via an infection control database maintained at our institution which identifies all VAEs. VAEs were then categorized as VAC, IVAC or VAP by one of the investigators via chart review. Demographic data, including Acute Physiology and Chronic Health Evaluation (APACHE) score calculated 1 and 24 hours after intensive care unit admission abstracted using an electronic data mart maintained on all intensive care patients.

Results. In the study period, 122 VAC, 31 IVAC and 14 VAP were identified. Demographic data characteristics were not significantly different between groups including age (means in years, VAP = 51.8, IVAC = 57.6, VAC = 56.3, p = 0.41), gender (% male, VAP = 64.3%, IVAC = 71.9%, VAC = 69.7%, p = 0.87), or BMI (vac = 30.4, IVAC = 31.0, VAP = 29.5). APACHE scores were similarly no different at 1 hour (VAC = 58.0, IVAC = 62.3, VAP = 56.6, p = 0.69) or 24 hours (VAC = 78.0, IVAC = 73.6, VAP = 86.0, p = 0.43). Sensitivity analyses treating variables as dichotomous (VAC vs all others) similarly showed no difference.

Conclusion. Although limited by the low baseline rate of VAE at our institution and thus small sample size, these data indicate that host factors in terms of acute physiology or demographics are not major determinants of which patient will progress to VAP. Pathogen and environment factors should be focus of further efforts for VAC detection and prevention.

Disclosures. **All authors:** No reported disclosures.

884. Optimization of PEEP as a Strategy to Reduce Ventilator-Associated Events

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Session: 111. Device-Associated HAIs
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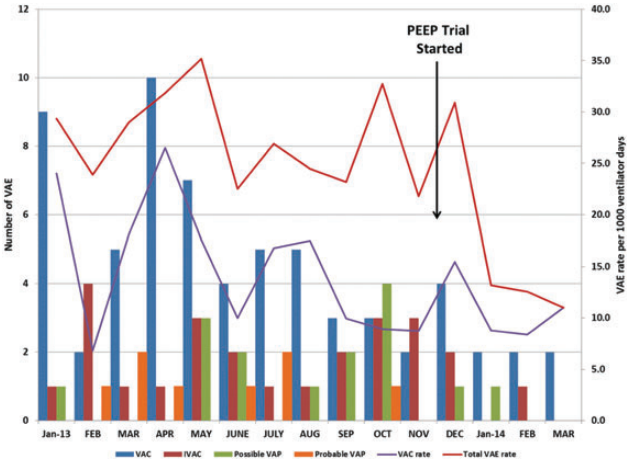
Background. Current ventilator bundles primarily aim to prevent pneumonia. New ventilator-associated event (VAE) definitions launched by the National Healthcare Safety Network (NHSN) in January 2013 detect other physiologic processes than pneumonia. Use of higher positive end-expiratory pressure (PEEP) may reduce other causes of VAE, such as atelectasis and acute lung injury.

Methods. We initiated a pilot project in a 22-bed surgical/trauma ICU, part of a large community-based academic health care system, in December 2013. The project involved initiating PEEP of 8 cm H_20, rather than 5, as the standard option for all newly ventilated patients in the study ICU. Respiratory therapists were educated as to the protocol and conducted spontaneous breathing trials and ventilator weaning per their usual practice. We tracked number and rate of VAEs (per 1,000 ventilator-days), mean ventilator-days per month, and mean ICU days per month.

Results. During the 4-month pilot, 263 patients underwent mechanical ventilation in the study ICU. The total VAE, IVAC, and possible/probable VAP rates decreased during the pilot, while the VAC rate remained stable (Table; Figure). Compared to the preceding 4 months (with 291 ventilated patients), average ventilator days decreased slightly during the PEEP trial (4.6 ± 4.8 days vs 5.1 ± 5.9 days, p = 0.3) and average ICU length of stay remained stable (6.7 ± 8.3 days vs 6.8 ± 7.9 days). No barotrauma or other complications were detected.

VAE type	Preceding 4 months n (rate per 1,000 vent-days)	Pilot n (rate per 1,000 vent-days)	Rate ratio (95% CI)
VAC	13 (11.3)	10 (11.0)	1.0 (0.4-2.2)
IVAC	9 (7.8)	3 (3.3)	0.4 (0.1-1.5)
Possible/probable VAP	8 (6.9)	2 (2.2)	0.3 (0.04-1.4)
Total VAE	30 (26.0)	15 (16.5)	0.6 (0.3-1.2)

VAC, ventilator-associated condition; IVAC, infection-related VAC; VAP, ventilator-associated pneumonia



Conclusion. Pilot data suggest that higher standard PEEP levels at time of initiation of mechanical ventilation may help to reduce VAE, without increasing harm. Other ventilator bundle components were utilized simultaneously and likely also contributed to decreased events. Further study is warranted in additional ICUs, for longer duration, and of additional outcomes such as antimicrobial utilization.

Disclosures. **All authors:** No reported disclosures.

885. Challenges Associated with Using Biomedical Big Data for Research on Healthcare-Associated and Community-Acquired Infections

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Session: 112. HAI Surveillance and Public Reporting
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Background. Health information technology yields digital data on large patient populations which may be useful for surveillance and outbreak investigations, evaluating impacts of treatments and infection control policies, and identifying infection risk factors. However, these data have limitations. Our aim is to describe issues encountered during development of a large electronic clinical database for research on infections.

Methods. We retrospectively built a database encompassing the electronic medical, billing, and demographic information of all patients discharged from four hospitals within a New York City network from 2006-2012 (>760,000 discharges). Data were collected from the electronic medical record, admission-discharge-transfer system, clinical data warehouse, and departmental records. Computerized algorithms were developed to identify infections.

Results. Issues included incomplete documentation in electronic health records and billing codes, which resulted in over/underestimation of urinary and central venous catheter days, inaccurate records of onset/discontinuation of isolation precautions, limited sensitivity of billing codes for identifying infections, and limited availability of present-on-admission billing codes for determining whether risk factors were present prior to infection. Changes to data collection and storage over time created artificial increases/decreases in risk factors (e.g., central line days, admission source) and infection rates. Approaches for improving data quality included validating electronic data against departmental records, discussing charting practices with clinical staff and coding practices with billers to understand whether and how various data fields are used, examining data longitudinally to identify unexplained changes, and working with clinical staff to determine whether differences reflect real practice changes or artifact.

Conclusion. Electronic data holds promise for research and quality improvement, but data must be carefully validated. Interdisciplinary collaboration between clinicians, programmers, and data analysts is essential for ensuring that electronic data accurately represents patients' clinical experiences.

Disclosures. **All authors:** No reported disclosures.

886. Correlation Between Methods to Calculate Denominators for Dialysis Event Surveillance Using Electronic Health Record Data, Tennessee, 2012

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Background. To reduce the burden of manual denominator data collection, the National Healthcare Safety Network (NHSN) uses number of patients dialyzed at a clinic during the first two working days of a reporting month as a proxy measure for the total number of patient-days at-risk during that month. Some stakeholders have expressed concerns that these methods may not reflect patient volume as well as proxies based on other time intervals during a reporting month. We compared various denominator measures using electronically obtained denominator data from 13 outpatient dialysis clinics belonging to the same organization.

Methods. All 13 clinics used a uniform electronic health record (EHR) system. From the EHR, we captured all patient dialysis sessions at each clinic between January and October 2012 to calculate: the monthly total denominator (i.e., total number of patients dialyzed at the clinic during all days of the month), and three denominator proxies (i.e., using the first two, last two, and two randomly selected consecutive working days of the month). Linear correlation between the NHSN proxy method and the other denominator measures was evaluated.

Results. During the study period, the EHR included 94,953 patient-months of denominator data from 13 clinics (range: 2,272 – 10,108 per facility). A strong correlation was observed between monthly total denominator and NHSN denominator proxy (Pearson Correlation Coefficient [PCC]: 0.988, $p < 0.0001$), and between the NHSN denominator proxy and the other proxy methods (PCC: 0.988–0.991). Correlation between NHSN and total denominator with PCC> 0.3 was found in 11 of the 13 clinics. Denominators stratified by vascular access types (i.e., central line, arteriovenous fistula and arteriovenous graft) also showed strong correlation between the denominator measures.

Conclusion. Analysis of EHR-generated denominator data suggests use of the NHSN denominator based on 2 consecutive working days at the start of the month was a satisfactory proxy for the total monthly denominator in most of these dialysis clinics.

Disclosures. **All authors:** No reported disclosures.

887. Opportunities to Improve Completeness of MRSA Bloodstream Infection Reporting From Outpatient Hemodialysis Facilities to the National Healthcare Safety Network

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Background. In 2012 the Centers for Medicare and Medicaid Services provided incentives for outpatient dialysis facilities to report bloodstream infections (BSIs) among hemodialysis (HD) patients to the National Healthcare Safety Network (NHSN). Use of a BSI metric for performance measurement requires accurate and complete data from the > 5,000 dialysis facilities now participating in NHSN. We compared data reported to NHSN with data from the CDC's Emerging Infections Program (EIP) to evaluate the completeness of NHSN BSI reporting.

Methods. EIP conducts active, population-based surveillance in 9 states for invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections, including BSIs, and collects data regarding chronic dialysis status and the setting where blood cultures were drawn. Positive blood cultures drawn as an outpatient or on day 1 or 2 of hospitalization in a chronic HD patient are reportable to NHSN. Cases of MRSA BSI from EIP during January–June 2013 among chronic HD patients were matched to NHSN BSIs reported from dialysis facilities within EIP geographic areas by patient sex and date of birth. Two events were classified as a match if the reported BSI event dates were within 5 days of each other.

Results. Among HD facilities within the EIP geographic area, 275 *S. aureus* BSIs were reported to NHSN: 72 (26%) MRSA, 134 (49%) methicillin-sensitive, and 69 (25%) without susceptibility data. EIP surveillance identified 332 MRSA BSIs among chronic HD patients. Of these, only 33 (10%) matched to a NHSN MRSA BSI, 16 (5%) matched to a NHSN *S. aureus* BSI without susceptibility data, and 283 (85%) did not match. An additional 39 MRSA BSI were reported to NHSN but not EIP. Among EIP MRSA BSIs initially identified at dialysis facilities, 36/57 (63%) matched to a NHSN *S. aureus* BSI, whereas only 17/275 EIP MRSA BSIs (6%) with initial blood culture drawn on day 1 or 2 of hospitalization matched to a NHSN *S. aureus* BSI ($P < 0.001$).

Conclusion. MRSA BSI data identified substantial gaps in reporting of MRSA BSI from outpatient HD facilities to NHSN, particularly those identified in hospitals. Opportunities also exist to improve antimicrobial susceptibility reporting. Improving completeness of dialysis facilities' reporting will require coordinated efforts to strengthen inter-facility communication.

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888. Performance Characteristics and Associated Outcomes for an Automated Surveillance Tool for Blood Stream Infection

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Background. In the era of widespread electronic health records, a semi-automated surveillance tool could reduce the time and manual effort required to screen patients for central line-associated blood stream infection (CLABSI).

Methods. Carefusion's MedMined is an automated surveillance tool that flags potential healthcare associated infections via the Nosocomial Infection Marker (NIM). We sought to determine the positive predictive value (PPV) of the blood NIM and to determine its association with outcomes of mortality, length of stay (LOS), and cost. We reviewed records of 237 patients with blood NIMs using a gold standard of the National Healthcare Safety Network (NHSN) definition for primary BSI. We developed a propensity model to predict the probability of blood NIM during hospitalization. We matched cases with up to 5 non-cases by propensity score and exposure time. We estimated the attributable mortality, LOS, and cost impacts of NHSN-reportable CLABSI and non-NHSN-reportable BSI (i.e., not reportable because no central line or secondary to another infection) compared to non-cases.

Results. Among patients with central lines present, the PPV of the blood NIM for CLABSI was 74.2%. For all patients (with or without central lines), the PPV for BSI was 53.6%. 77% of the 'false positive' NIMs met criteria for NHSN-defined infection other than BSI. The table shows outcomes associated with blood NIMs vs matched non-cases.

Conclusion. Although many of the cases detected by the tool were not NSHN-reportable, they were associated with adverse outcomes and higher costs, suggesting that detecting them may be an important component of a quality and cost containment program.

Outcomes for NHSN Reportable and Non-Reportable Cases Compared to Matched Non-Cases

	BSI	Propensity and Exposure Matched Non-Cases	P-value
NHSN-Reportable CLABSI			
n	57	276	
Mortality, % (n)	17.5% (10)	9.4% (26)	0.0976
LOS, Median (Q1, Q3), days	21 (11, 30)	16 (11, 24)	0.0298
Total Charge, Median (Q1, Q3), $	143,935 (89,794, 257,447)	115,267 (74,937, 173,053)	0.0098
Days to NIM, Mean (SD), days	11.5 (8.4)		
Non- Reportable BSI			
n	89	445	
Mortality, % (n)	23.6% (21)	6.7% (30)	<0.0001
LOS, Median (Q1, Q3), days	14 (9, 20)	10 (6, 17)	0.0001
Total Charge, Median (Q1, Q3), $	86,927 (54,728, 156,669)	62,929 (36,743, 115,693)	<0.0001

Disclosures. **J. P. Ridgway**, CareFusion: Research Contractor, Research support **X. Sun**, CareFusion: Employee, Salary **Y. P. Tabak**, CareFusion: Employee and Shareholder, Salary **R. Johannes**, CareFusion: Employee and Shareholder, Salary **A. Robicsek**, CareFusion: Research Contractor, Research support

889. Assessment of an Automated Surveillance System for Detection of Ventilator Associated Events

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Background. New surveillance definitions for four hierarchically related ventilator associated events (VAEs) were introduced in 2013: ventilator associated condition (VAC), infection related ventilator associated condition (IVAC), and possible and probable ventilator associated pneumonia (VAP). The criteria for the definitions are objective and readily identifiable in the medical record. An automated method for review of an electronic medical record (EMR) to expedite identification of VAEs was developed. The goals of this study are to assess the validity and value of the automated surveillance system.

Methods. Nightly automated review of the preceding 24 hours of data entered to the EMR of a 214 bed hospital was introduced in January 2013 to identify VAC and possible IVAC (pIVAC). Retrieval of information on antibiotic administration that was necessary to determine whether a pIVAC was an IVAC was not automated. The 2013 VAE surveillance definitions did not allow for automated detection of possible or probable VAP. The results of automated surveillance from April 1 to September 30, 2013 were compared to the non-automated review of the EMR of all patients undergoing mechanical ventilation for over 48 hours.

Results. 193 patients underwent mechanical ventilation for over 48 hours during the study period. 44 VAC, 21 IVAC, 12 possible VAP and 1 probable VAP were identified by review of the EMR of all patients. The sensitivity, specificity, positive predictive value, negative predictive value and kappa statistic of the automated surveillance for VAC and pIVAC were: 93%, 100%, 95%, 100%, 0.94 and 95%, 100%, 95%, 100%, 0.95 respectively. The sensitivity and specificity of the detection of IVAC, possible VAP and probable VAP by automated surveillance for pIVAC were 96% and 15%; 92% and 10%; and 100% and 7.5% respectively. The time required for identification of possible or probable VAP by non-automated review of the EMR vs non-automated review of the EMR supplemented by the automated surveillance system was 100 vs 6 hours.

Conclusion. The accuracy and precision of the detection of VAC and pIVAC by the automated surveillance system were good. Use of the automated surveillance system allowed detection of VAE during a 6 month period within 6 hours, reducing the time spent on surveillance for VAE by 94 hours.

Disclosures. **All authors:** No reported disclosures.

890. VAP to VAE: Exploring the Epidemiology of a New Surveillance Definition

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Background. Due to concerns about the subjectivity and inter-rater reliability of the surveillance definition for VAP (ventilator-associated pneumonia), a more objective outcome measure, VAE (ventilator-associated event), was released in 2013. We examined the epidemiology of the traditional VAP and new VAE measures in 6 adult intensive care units (ICUs) and hypothesized that VAE rates would be considerably higher than the traditional VAP rates and that correlation between VAEs and traditional VAPs would be low.

Methods. Traditional VAP events (TradVAP) and VAEs in six adult ICUs (medical, surgical, burn, trauma, cardiovascular, and neurosciences) at an academic medical center were determined by trained personnel for the study period from July to December 2012. VAEs were classified as a ventilator-associated condition (VAC), infection-related VAC (IVAC), and possible/probable VAP (PossVAP) based on NHSN definitions. Descriptive analyses were conducted to assess the proportion of TradVAPs that were also identified as VAEs; TradVAP and VAE rates were also compared.

Results. During the study period, 15 TradVAPs and 91 VAEs were identified in all ICUs combined. Only 8/15 (53%) TradVAPs met the VAE definition, but of these, 75% (6/8) were identified as a PossVAP; the other two TradVAPs met criteria for an IVAC only. The VAE rate was higher than the TradVAP rate across all units, but units differed in the degree of rate increase (Table).

Traditional VAP and VAE events by unit

ICU	TradVAP	VAE	VAC alone	IVAC alone	Possible/ Probable VAP	TradVAP rate per 1,000 vent days	VAE rate per 1,000 vent days	Fold increase, TradVAP to VAE rate
Burn	1	6	3	2	1	3.1	18.6	6x
Cardiovascular	1	19	6	11	2	0.8	15.6	19.5x
Medical	0	8	3	4	1	0	7.0	N/A
Neurosciences	1	14	6	6	2	1.3	17.4	13.4x
Surgical	6	20	10	8	2	5.3	17.6	3.3x
Trauma	6	24	9	3	12	4.2	16.6	4x
Total	15	91	37	34	20	2.5	15.0	6x

Conclusion. The overall VAE rate was 6-times higher than the TradVAP rate with wide variation in the degree of increase across ICU types. Only half of the identified TradVAPs were captured as a VAE event, but the majority of these VAEs were classified as a possible VAP. Further research is needed to determine causes of the VAEs in these units and the preventability of these events.

Disclosures. **All authors:** No reported disclosures.

891. Developing a user-friendly format for automated reports on urinary catheters and catheter-associated urinary tract infections

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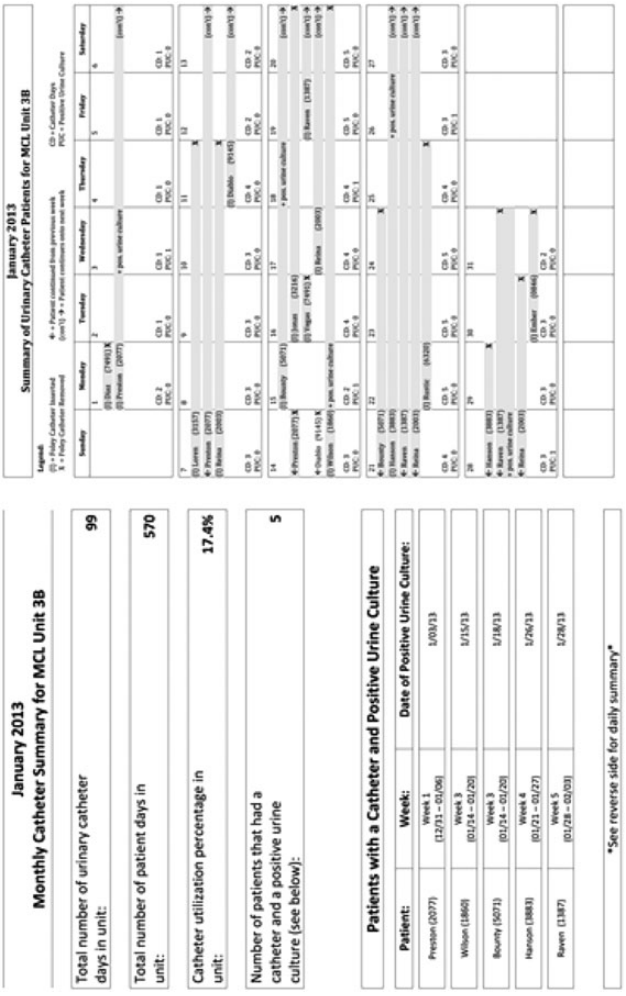
Background. Manual surveillance and reporting for both urinary catheter use and catheter-associated urinary tract infection (CAUTI) are time-consuming processes. Our goal was to develop a format for automated (computer-generated) CAUTI reports that would be comprehensible, useful, and trustworthy to providers engaged in CAUTI prevention.



Front and back sides of report version 2.

Methods. This study employed iterative design, in which we showed a sample data report to potential end-users, surveyed them about usability, and then revised the report accordingly. We went through 4 such cycles, but we grouped the first 2 iterations

into Version 1 and the second two into Version 2 because most design changes were made between iterations 2 and 3. Our prototype report format contained a month of actual data from an acute care medical ward in our hospital. The survey consisted of 10 questions exploring the following domains: layout, understandability, completeness of data, and ability to replace current reporting methods. We recorded the time participants spent looking at the report and asked one quiz question to assess whether the participant could correctly interpret data provided.

Results. The 40 participants surveyed included the following groups: physicians (12), ward nurses (15), nurse CAUTI champions (6), quality managers (4), and infection control specialists (3). The average time spent looking at the report was 47.2 seconds (*SD* = 31.5s). Report Version 1: Only 45% answered the quiz question correctly. Of the 4 domains, the lowest score was in layout, receiving an average of 3.3/5 points. Users' comments suggested that a more graphical display of catheter days was needed. Report Version 2 (figure): 76% answered the quiz question correctly. The lowest scoring domain was ability to replace current reporting methods, with an average score of 3.2/5 points. User comments suggested that the report will need to meet the disparate needs of different provider types.

Conclusion. The iterative design process improved users' abilities to correctly interpret urinary catheter data from our report. We identified different needs of different provider types in terms of catheter and CAUTI data, as a prelude to switching to automated surveillance.

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892. Cost-Benefit Analysis of Universal Screening and Contact Precautions for Methicillin-resistant *Staphylococcus aureus* Carriers from the Hospital Perspective

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Background. There are data suggesting potential benefit to screening hospitalized patients for MRSA colonization followed by institution of contact precautions for carriers. However, MRSA screening, like most prevention interventions, has associated costs that must be put into context of potential benefits. Given recent legislative mandates for MRSA surveillance, we sought to explore the economic impact to a hospital of universal MRSA screening for all inpatient admissions.

Methods. We modeled the direct economic impact to an individual hospital of starting universal MRSA screening and contact precautions for MRSA carriers. Projected costs and benefits were based on literature derived data. Our model examined outcomes of several screening strategies including the addition of non-nares MRSA screening and comparison of chromatogenic agar vs PCR based screening.

Results. In our base model, the cost of universal MRSA screening and contact precautions outweighed the projected benefits generated by preventing MRSA related infections, resulting in a cost of $103,000 per 10,000 admissions ([95% credibility range, $83,000 to $126,000]). Non-nares screening and PCR-based testing, both of which identified more MRSA colonized persons, resulted in more MRSA infections averted, but increased costs of the screening program. Our results were robust for most of the model's assumptions. Cost-savings associated with MRSA screening only occurred when the model was forced to simultaneously use estimates at the extremes of our sensitivity analyses for multiple key model assumptions.

Conclusion. We found that universal MRSA screening, while providing potential benefit in preventing MRSA infection, is relatively costly and may be economically burdensome from an individual hospital perspective. Policy makers should consider the economic burdens of MRSA screening and contact precautions in relation to other interventions when choosing to invest in programs to improve patient safety and outcomes.

Disclosures. **S. S. Huang**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product

893. Vancomycin Resistant Enterococcus (VRE) Rates in Ontario, Canada After the Discontinuation of VRE Screening and Control Practices by Some Hospitals: Interim Results

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Background. Since 2009, there has been mandatory public reporting of vancomycin-resistant Enterococcus (VRE) bacteremia by hospitals in the province of Ontario, Canada. Provincial best practice guidelines recommend VRE screening and control practices. In July 2012, 4 of 148 hospital corporations discontinued their VRE screening and control practices; all 4 were acute teaching hospital corporations. Public Health Ontario (PHO) sought to examine trends of VRE-bacteremia incidence in Ontario after July 2012. These are planned interim results; the study ends in December 2015.

Methods. All VRE-bacteremias reported by Ontario hospitals to the provincial Patient Safety Public Reporting database between July 2012 and March 2014 were validated by PHO. Poisson regression was used to assess changes in incidence of VRE-bacteremia rates per 100,000 patient-days after July 2012. Hospitals were stratified by presence of VRE screening and control practices (screening) or its absence (non-screening); this analysis was repeated for screening and non-screening acute teaching hospitals.

Results. In the study period, 39 hospital corporations reported 134 VRE-bacteremias. Screening and non-screening hospitals reported an increase in the VRE-bacteremia rate (0.4 to 0.7 per 100,000 patient-days and 1.0 to 2.5 per 100,000 patient-days, respectively). The change in rate between screening and non-screening hospitals was statistically significant ($p < 0.0001$). When the analysis was restricted to only acute teaching hospitals, there was a slight decrease in VRE bacteremias in screening acute teaching hospitals (1.3 to 1.2 per 100,000 patient days) although the change in rate between non-screening and screening acute teaching hospitals was not statistically significant ($p = 0.2$).

Conclusion. The interim results show that the change in rate of VRE bacteremias is significantly different for hospitals with and without VRE screening and control practices. PHO will continue to recommend that Ontario hospitals continue their VRE screening and control measures, and to await the final results of this study before making changes to their infection control programs.

Disclosures. **All authors:** No reported disclosures.

894. Evaluating Clinical Credibility of Surveillance Definitions for Healthcare-Associated Pneumonia and Lower Respiratory Infections

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Background. Recent data show that only a minority of healthcare-associated pneumonias are mechanical ventilator-associated (VA-PNEU). Though the limitations of VA-PNEU surveillance definitions in adult patients are well known, less is known about the performance of either National Healthcare Safety Network (NHSN) definitions for PNEU in non-ventilated adults or in children (whether mechanically ventilated or not), or lower respiratory infection (LRI) in any patient population. We evaluated the utility of PNEU for identifying clinical events in non-ventilated adults and in children (both ventilated and non-ventilated), and of LRI for identifying clinical events in any patient population.

Methods. We reviewed medical records of a random sample of patients with PNEU or LRI reported to NHSN from 8 Pennsylvania hospitals in 2011–2012, excluding adult VA-PNEU. We confirmed PNEU/LRI case classification with CDC staff and recorded documented clinical diagnoses corresponding temporally to the PNEU/LRI case.

Results. We reviewed 250 (30%) of 838 eligible NHSN-reported PNEU/LRI events; 29 (12%) did not fulfill PNEU or LRI criteria. Differences interpreting radiology reports accounted for most reclassification. Of 81 PNEU in non-ventilated adults, 68 (84%) had clinician-diagnosed PNEU; 17 (25%) were explicitly attributed to aspiration. Of 36 pediatric PNEU, 26 (72%) were VA, and 70% corresponded to a clinical PNEU diagnosis. Of 43 adult LRI, 38 (88%) were in mechanically ventilated patients, 14 (33%) with no corresponding clinical diagnosis (infectious or non-infectious) documented at the time of LRI. Of 61 pediatric LRI, 51 (84%) were in mechanically-ventilated patients, and 21% had no corresponding clinical diagnosis documented.

Conclusion. NHSN-defined PNEU in non-ventilated adults and in children regardless of ventilation status corresponded in most cases to a compatible clinical event. LRI occurred mostly in ventilated patients, and the definitions performed poorly in both adults and children, with no discernable clinical event documented during the same time frame in a large proportion of patients. Definitions that are objective and clinically credible are needed to improve surveillance and prevention of healthcare-associated PNEU.

Disclosures. **All authors:** No reported disclosures.

895. Rates and Pathogens Causing Hospital-Associated Respiratory Infections in a Regional Burn Center, 2008-2012

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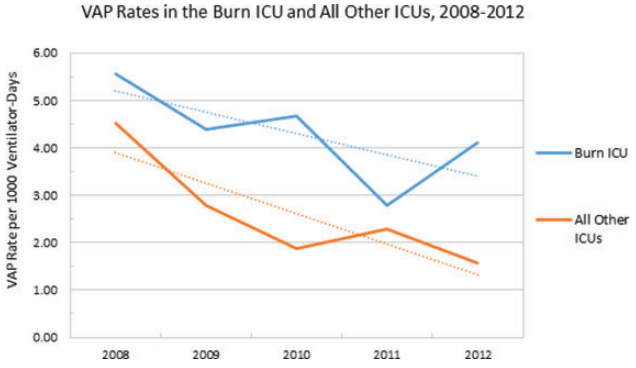
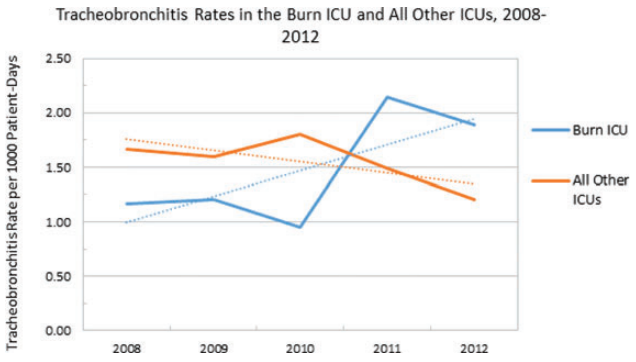
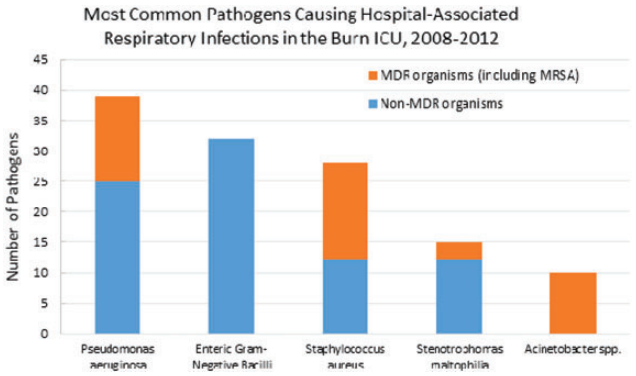
Background. Burn injuries are a common source of morbidity and mortality in the United States, but limited data exist on burn infections. Although the National Burn Repository reports pneumonia as the most frequent clinically related complication among acute burn admissions, no standard definition for pneumonia has been used. Inhalation injury and prolonged mechanical ventilation place burn patients at extremely high risk for hospital-associated respiratory infections (HARI). This study measured rates and pathogens causing HARI in a large regional burn center.







Methods. The University of North Carolina Hospitals is an 806-bed tertiary care facility that includes a 21-bed ICU for severely ill patients with burns and extensive exfoliating skin conditions. Comprehensive hospital-wide surveillance for HARI was collected over a 5 year period (2008-2012) in accordance with CDC/NHSN criteria. Incidence of ventilator-associated pneumonia (VAP) was calculated as infections per 1,000 ventilator-days. Incidence of tracheobronchitis was calculated as infections per 1,000 patient-days. Methicillin-resistant *S. aureus* and Gram-negative bacilli susceptible to ≤1 class of clinically relevant antibiotics were considered multidrug-resistant (MDR).

Results. The burn ICU VAP rates ranged from 2.78 to 5.55 per 1,000 ventilator-days compared to 1.57 to 4.53 in all other ICUs. While a trend towards decreased VAP rates was noted in both populations over time, the burn ICU had higher VAP rates than all other ICUs (Figure 1). Burn ICU tracheobronchitis rates ranged from 0.95 to 2.14 infections per 1,000 patient-days with little difference in rates over time or between the burn ICU and all other ICUs (Figure 2). In the burn ICU, 146 organisms were isolated from 119 HARI (1.23 pathogens/infection), with 30% classified as MDR. The most common pathogens were *P. aeruginosa*, enteric Gram-negative bacilli, *S. aureus*, *S. maltophilia*, and *Acinetobacter* spp. (Figure 3). A MDR *Acinetobacter* outbreak occurred in 2008 in the burn ICU.

Conclusion. HARI remains a major problem in the burn ICU with a high prevalence of MDR organisms. Continued surveillance and research is necessary to optimize prevention and treatment of these infections in burn patients.

Disclosures. **All authors:** No reported disclosures.

896. Longitudinal Trends in Infection Rates in US Nursing Homes, 2006 - 2011

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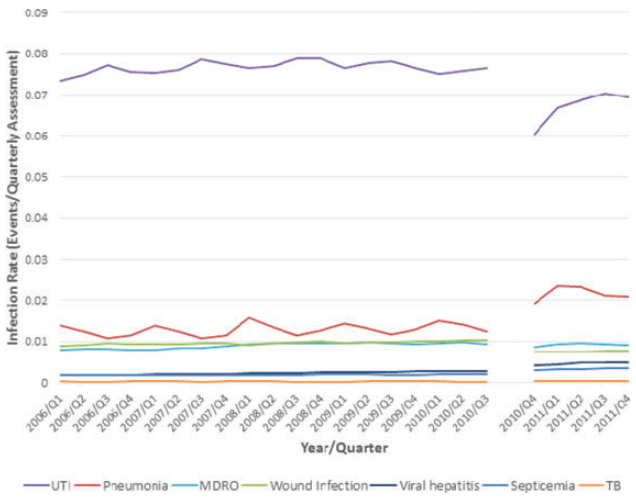
Background. Infections are a leading cause of morbidity and mortality in US nursing home (NH) residents with an estimated 1.6 – 3.8 million occurring annually. Minimum Data Set (MDS) assessments are performed on NH residents every quarter and provide data that can be used to track infections. A revised MDS (version 3.0) was implemented in 2010. This study aimed to estimate longitudinal trends in infection rates in US NH using MDS 2.0 data, describe infection item differences in the MDS 2.0 and 3.0, and evaluate impacts of MDS revisions on infection measurement.

Methods. MDS 2.0 (2006 – 2010) and 3.0 (2010 - 2011) annual and quarterly assessment data were used to estimate infection rates by quarter; MDS 2.0 data were used to estimate percent changes in infection rates between 2006 and 2010. Infection items on both MDS versions included multidrug-resistant organisms (MDRO), pneumonia, septicemia, tuberculosis (TB), urinary tract infection (UTI), viral hepatitis, and wound infection. Items were compared to assess differences.

Results. MDS data from 24 quarters and over 14,000 NH (n = 25,903,977 assessments) were used. With the exception of TB, infection rates in the MDS 2.0 changed with increases in viral hepatitis (69.7%), septicemia (25.2%), pneumonia (24.1%), MDRO (15.7%), and wound infections (4.6%); UTI rates decreased by 4.2% (all p-values <0.001). Changes in all infection items were noted between versions 2.0 and 3.0 and impacted all rates except for MDRO and TB (Figure). Items had two look-back periods in the MDS 3.0 (a 60-day disease identification period and a shorter diagnosis status period) but only one in the MDS 2.0 (the diagnosis status period). Also, compared with criteria used to identify UTI in the MDS 2.0, MDS 3.0 criteria included more specific signs or symptoms as well as evidence that the resident was receiving treatment.



Longitudinal trends in quarterly infection rates among residents in US NH from 2006 through 2011. The gap represents implementation of the MDS 3.0.

Conclusion. Substantively important growth in infection rates in NH were identified for most items evaluated. Further research is needed to understand these increases as well as best practices for infection prevention. Additionally, MDS revisions should be accounted for when evaluating longitudinal trends in NH infections over this time period.

Disclosures. **All authors:** No reported disclosures.

897. Feasibility of Using Existing Public and Private Data Sources for Nationwide Medical Device Post-marketing Safety Surveillance

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Background. The Food and Drug Administration (FDA) initiated a national strategy for monitoring post-market medical product safety using existing public and private electronic data. The Centers for Medicare and Medicaid Services (CMS) publicly report hospital central line-associated bloodstream infection (CLA-BSI) data. We explored the feasibility of expanding the current FDA Sentinel Initiatives on patient-level data to hospital-level data for surveillance of CLA-BSI associated with intravenous needleless connectors (NC).

Methods. We merged the 2013 CMS Hospital Compare CLA-BSI data with the MaxPlus™ Tru-Swab™ Positive Displacement Connector (MP) client database from CareFusion to identify hospitals using the MPs (MP hospitals) vs those not using the MPs (Comparator hospitals). MP is a newer generation of NC with enhanced patient safety engineering design features. We evaluated CLA-BSI rates associated with MPs vs Comparators.

Results. In the CMS Hospital Compare CLA-BSI database, 3,074 hospitals reported central line (CL) days >1, with 25% (n = 758) hospitals using MP NCs. The MP hospitals accounted for 30% (2,923,859/ 9,887,264) of CL days, and 28% (3,017/ 10,864) of CLA-BSI episodes. The MP hospitals had a lower observed CLA-BSI rate (1.03 per 1,000 CL days [3,017 CLA-BSIs / 2,923,859 CL-days]) compared to Comparator hospitals (1.13 per 1,000 CL days [7,847 CLA-BSIs / 6,963,405 CL-days], $P < 0.0001$). The univariate relative risk for CLA-BSI of MP hospitals was 0.91 (95% CI: 0.83, 0.98; $P = 0.02$). After adjusting for hospital bed size, teaching, urban status, and geographic regions, the multivariable relative risk for CLA-BSI of MP hospitals was 0.94 (95% CI: 0.86, 1.02; $P = 0.11$).

Conclusion. We demonstrated that it is feasible to link hospital-level data from public-private sources to support the FDA's electronic post-market medical device safety surveillance efforts. Manufacturers should be encouraged to participate in FDA's efforts.

Disclosures. **Y. P. Tabak**, CareFusion: Employee and Shareholder, Salary **R. Johannes**, CareFusion: Employee and Shareholder, Salary **X. Sun**, CareFusion: Employee, Salary **C. Crosby**, CareFusion: Employee and Shareholder, Salary **W. Jarvis**, Baxter: Consultant, Consulting fee; CareFusion: Consultant, Consulting fee; Johnson and Johnson: Consultant, Consulting fee; Gojo: Consultant, Consulting fee

898. The Impact of State Mandated Healthcare-Associated Infection Reporting on Infection Prevention and Control Departments in Acute Care Hospitals: Results from a National Survey

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Background. In addition to federally mandated reporting, most US states have adopted legislation requiring hospitals to submit healthcare-associated infection (HAI) data. Evidence that state HAI laws have increased patient safety and reduced HAI rates is inconsistent, however, and resources needed to comply are considerable. We evaluated the impact of state HAI laws on infection prevention and control departments (IPCD).

Methods. Web-based survey of a national sample of hospital IPCD was conducted in Fall 2011; all non-VA hospitals enrolled in the National Healthcare Safety Network were eligible to participate. States with HAI laws effective prior to Fall 2011 were identified using systematic legal review. Variations in IPCD resources and characteristics in states with and without laws were compared using χ^2or Wilcoxon-Mann-Whitney tests. Multinomial logistic regression was used to identify increases or decreases, vs no change, in resources and characteristics.

Results. 1,038 IPCD provided complete data (30% response rate); 756 (73%) were located in states with laws. When asked how mandatory reporting affected their IPCD, more respondents in states with laws reported differences in resources (42% vs 33%, $p < 0.01$), time for routine activities other than for mandatory reporting (79% vs 71%, $p < 0.01$), influence in hospital decision making (55% vs 48%, $p < 0.05$), and visibility of their department (75% vs 65%, $p < 0.001$); they also spent more hours per week fulfilling mandatory reporting requirements (17 vs 13, $p < 0.0001$). Based on regression analysis, respondents in states with laws were more likely to report increased resources ($p = 0.02$) and influence ($p = 0.04$) and decreased time for routine activities ($p < 0.01$). Perception of visibility in the hospital was mixed with reports of both increased ($p < 0.001$) and decreased ($p = 0.01$) visibility vs the same.

Conclusion. Respondents in states with laws reported a significantly higher burden to their IPCD, beyond what was required by federally mandated HAI reporting alone. However, they also reported receiving increased resources to offset demands on time for routine activities and fulfilling reporting requirements. Further research is needed to investigate resources necessary to comply with state HAI laws, and to evaluate their unintended consequences.

Disclosures. **All authors:** No reported disclosures.

899. Exclusion from SIR Analysis: Are low volume hospitals getting a pass?

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Background. In 2012, the Centers for Medicare and Medicaid Services (CMS) made it mandatory for all hospitals participating in the Inpatient Prospective Payment System (IPPS) to report surgical site infections (SSI) associated with qualifying abdominal hysterectomy (HYST) and colon procedures (COLO) to the National Healthcare Safety Network (NHSN). These data are then made available to the public on Medicare's Hospital Compare website. However, if a hospital does not perform enough procedures for the reporting period to calculate a valid standardized infection ratio (SIR), it is excluded from reporting. The objective of this study was to propose an alternate way to report a SIR for these low volume hospitals.

Figure 1: COLO SSI SIR 2012, 2013, and Combined

	2012		2013		2012 & 2013		
	Observed SSI	Expected SSI	Observed SSI	Expected SSI	Observed SSI	Expected SSI	SIR
Hospital 1	1	1.052	2	0.930	3	2.002	1.50
Hospital 2	0	0.523	2	1.754	2	2.677	0.75
Hospital 3	1	0.423	1	0.646	2	1.069	1.82

Figure 2: Hysterectomy SSI SIR 2012, 2013, and Combined

	2012		2013		2012 & 2013		
	Observed SSI	Expected SSI	Observed SSI	Expected SSI	Observed SSI	Expected SSI	SIR
Hospital 1	1	0.943	0	0.423	1	1.366	0.73
Hospital 2	0	0.352	0	0.366	0	0.718	Exp 55 <1
Hospital 3	0	0.302	0	0.212	0	0.514	Exp 55 <1
Hospital 4	0	0.761	0	0.739	0	1.500	0.00
Hospital 5	0	0.211	0	0.060	0	0.271	Exp 55 <1
Hospital 6	1	0.566	0	0.466	1	1.030	0.97

Methods. 2012 and 2013 COLO and HYST SIR were calculated using the "SIR - In-plan Complex AR SSI data by procedure" report in NHSN. Only low volume facilities (3 for COLO; 6 for HYST) in our system were included in this analysis. Low volume was defined as having at least one calendar year where the expected number of SSI for at least one of the surgery categories was less than 1, not allowing for a valid SIR to be calculated.

Results. See Figures 1 and 2. By analyzing 2 years COLO data together for each of our 3 low volume hospitals, we are able to calculate a valid SIR. By doing the same for our 6 low volume HYST hospitals, we were able to calculate valid SIR for 3 of them. The remaining 3 still do not have enough procedures to have an expected number of SSI greater than 1.

Conclusion. Combining data across years may allow SIR calculation for low volume hospitals, allowing for inclusion of these facilities in public reporting. For very low volume facilities, other alternative methods to evaluate performance may be needed.

Disclosures. **All authors:** No reported disclosures.

900. Present or Absent on Admission: Impact of Change in National Healthcare Safety Network Surveillance Definitions

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Background. In January 2013, the National Healthcare Safety Network (NHSN) definition of "present on admission" (POA) was modified to include only those infections that meet all components of a surveillance definition within 2 calendar days of admission. Previously, POA infections were those that were "present or incubating on admission."

Methods. Due to state requirements, infection preventionists at the Children's Hospital of Philadelphia perform house-wide healthcare associated infection (HAI) surveillance using all NHSN definitions. Utilizing existing surveillance data from 2013, we identified HAI that met the prior POA definition but did not meet the new definition (POA-HAI). Chart review was performed to identify specific surveillance criteria met.

Results. In 2013, we identified 632 HAI of which 43 were POA-HAI. The most common POA-HAI were skin and soft tissue infections (POA-SSTI) (n = 23,

53.5%). Nearly all POA-SSTI (n = 22, 96%) had at least 2 signs or symptoms documented within 2 days of admission. Delayed specimen collection for culture was noted for most POA-SSTI (18 of 23, 78%). Diagnostic procedures yielding a positive culture were performed on hospital day 3 in 10 cases (45.5%) and by day 7 in all but one case. Most POA-SSTI had additional evidence of infection documented within the first 2 days of hospitalization: radiographic evidence (n = 18, 78.2%) or physician diagnosis (n = 19, 83.6%). Review of past surveillance data showed a 58.9% increase in the total number of SSTI reported in 2013 (56) compared to 2012 (33). Other frequent types of POA-HAI included gastrointestinal (n = 8, 18.6%) and upper respiratory (n = 3, 7.0%) infections. The majority of these infections (n = 7, 63.6%) were classified as HAI due to a delay in obtaining a diagnostic test.

Conclusion. The recent change in POA definition led to a number of additional infections being classified as HAI despite evidence that many were clinically recognized within 2 days of hospitalization. These findings have important implications for states with mandatory HAI reporting using NHSN definitions. Possible strategies to address this issue include return to prior definition of POA or inclusion of additional elements (such as radiographic evidence of infection) in individual HAI definitions.

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901. Presumptive Isolation or Screen and Isolate for Patients at High Risk for Methicillin-resistant *Staphylococcus aureus*: A Monte Carlo Simulation of the Economic Impact to the Individual Hospital

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Background. A common strategy for preventing nosocomial MRSA transmission is reactive isolation after positive nares surveillance. However, nares screening has low sensitivity for MRSA carriage. In high-risk patients, some have considered non-nares screening or presumptive isolation without surveillance. We sought to model the economic implementation cost, from a hospital perspective, of strategies for high-risk admissions.

Methods. We modeled the economic impact of three body-site MRSA screening (nares, pharynx, and inguinal folds) and presumptive isolation for high-risk admissions from a hospital perspective. Projected costs and benefits were derived from the literature. We examined threshold values for 1) probability of MRSA carriage in an admitted patient and 2) impact of MRSA infection (in terms of increased length of stay) that would be cost-neutral (costs = benefits).

Results. In our baseline model, the costs of both screening and isolation and presumptive isolation exceeded savings generated by preventing MRSA infections. Nares screening and contact precautions prevented 0.6 infections (95% CR, 0.5-0.7) per 1,000 high-risk admissions, and yielded a net financial loss of $36,899 (95% CR, $31,525 to $42,690). Three body-site surveillance prevented 0.8 infections (95% CR, 0.7-0.9) per 1,000 high-risk admissions, but resulted in even greater higher financial loss $51,478 (95% CR, $45,566 to $57,821). Presumptive isolation prevented the most infections (1.0 infections; 95% CR, 0.9-1.1), but resulted in large financial losses $300,765 (95% CR, $296,155 to $304,835) of any model tested. Using optimistic estimates for the efficacy of isolation in terms of preventing new MRSA infections, three body-site surveillance could be cost-neutral in targeted populations at risk for high-complexity infections, e.g., prosthetic joint infections or post-operative mediastinitis. Presumptive isolation was never cost-neutral.

Conclusion. Although multiple body site surveillance or presumptive isolation for high-risk patients could reduce nosocomial MRSA infections, the program's overall cost exceeds any savings generated from infections prevented. For an individual hospital, the cost of screening and isolation needs to weighed against other infection control interventions and patient safety efforts.

Disclosures. **S. S. Huang**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product

902. Hospital Characteristics and Infection Prevention and Control Strategies Associated with Methicillin-Resistant *Staphylococcus aureus* (MRSA) and *Clostridium difficile* Infection (CDI) in Canadian Hospitals

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Background. Measurement of the prevalence of antibiotic resistance assesses the associated burden of disease while also identifying vulnerable patient populations and monitoring the effectiveness of interventions. The objective of this study was to determine institutional characteristics, and infection prevention and control (IP&C) policies associated with MRSA colonization/infection, and *C. difficile* infection.

Methods. In November 2012 a point-prevalence survey of MRSA and CDI was done in adult inpatients at Canadian acute-care hospitals with ≥50 beds. Information was also obtained regarding institutional characteristics and IP&C policies of each participating facility. Logistic regression models were designed using variables selected *a priori* and two-tailed *p* values less than 0.05 were considered significant.

Results. 132 (56% of eligible) hospitals representing all 10 Canadian provinces participated in the survey and were included in the analysis. 60% of facilities were located within the central region of Canada (Ontario and Quebec), the majority (54%) had fewer than 200 beds, and were non-teaching hospitals (68%). The median prevalence of MRSA colonization/infection was 3.9% (range: 0-26.8%) and median MRSA infection prevalence was 0.3% (range: 0-4.9%). The presence of pediatrics in the hospital ($p = 0.001$), performing targeted vs universal admission screening ($p < 0.001$), routine placement of MRSA carriers in a private room ($p < >0.001$), routine use of surgical masks by staff caring for patients with MRSA ($p = 0.005$), decolonization with mupirocin ($p < 0.001$), and enhanced environmental cleaning of MRSA rooms ($p = 0.006$) were independently associated with a lower prevalence of MRSA colonization/infection. The median prevalence of CDI for participating facilities was 0.9% (0-5.5%). Teaching hospitals ($p = 0.011$) and facilities with a shorter turn-around-time (< 24 hrs) for *C. difficile* toxin assay results ($p = 0.012$) were associated with a higher prevalence of CDI.

Conclusion. Although hospital characteristics are inalterable, this study identified IP&C policies that may be used to limit the spread of antibiotic resistance in acute-care hospitals.

Disclosures. **A. E. Simor**, Pfizer Canada Inc.: Grant Investigator and Scientific Advisor, Grant recipient and honoraria; Cubist Pharmaceuticals: Scientific Advisor, honoraria

903. Prediction of carbapenem-resistant *Klebsiella*-positive inpatient cultures using data from an electronic health record

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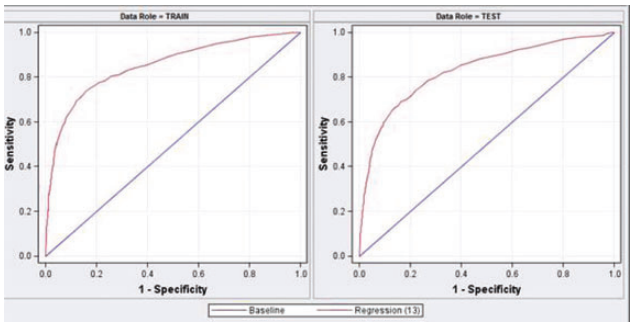
Background. Electronic algorithms to identify carbapenem-resistant *Klebsiella* (CRK) could improve infection control (IC) and guide empiric antibiotic therapy. We investigated the use of the large Veterans Affairs (VA) Electronic Health Record (EHR) database to predict CRK-positive (CRK+) clinical cultures.

Methods. In- and outpatient candidate predictor variables were extracted from VA EHR records between 2008 and 2012. Cases were defined as CRK+ admissions on acute care wards. Matched CRK-negative controls were randomly selected among admissions with clinical cultures on the hospital and calendar month of the case. Approximately 150,000 factors from the database (VA EHR) were screened for an association with CRK+ culture. 200 of the most highly associated variables were then used for logistic regression analysis. A conditional logistic regression was trained on half of the data set using stepwise selection (SAS Enterprise Miner 7.1). The model was validated on the remaining half.



Results. In 667,637 admissions with cultures, the overall prevalence of CRK+ cultures was 0.39%. The area under the receiver operating characteristic curve was 0.85 on the training set and 0.83 on the validation set (Figure 1). A total of 19 factors were retained in the model, including prior healthcare and antibiotic exposures, diagnoses,

clinical cultures, and physiologic parameters. Multi-collinearity precluded reporting individual predictors. Using a cutoff CRK+ culture risk of 0.63 yielded a sensitivity, specificity, and positive predictive value of 39.8%, 97.1%, and 5.0%, respectively.

Conclusion. A model with good predictive characteristics was derived from the large VA EHR database–a "first step" towards improving CRK infection control and empiric therapy. Because of the rarity of events, a substantial trade-off exists between false positives and sensitivity. Therefore, this model may be most useful in the context of higher-prevalence wards or hospitals. Our findings are limited to CRK+ clinical cultures and further work will be necessary to address CRK-carriage. To improve the accuracy of CRK prediction and control cost, a combination of initial evaluation with predictive analytics followed by targeted laboratory testing for carbapenem resistance may be of value.

Disclosures. **R. A. Bonomo**, AstraZeneca: Grant Investigator, Grant recipient; Merck: Grant Investigator, Grant recipient; Rib-X: Grant Investigator, Grant recipient; Steris: Grant Investigator, Grant recipient; TetraPhase: Scientific Advisor; NIH: Grant Investigator, Grant recipient; VA Merit Review: Grant Investigator, Grant recipient

904. Multidrug-Resistant Gram-Negative Bacteria (MRGN) in Intensive Care Units - Results from the German National Surveillance System for Nosocomial Infections (KISS)

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Background. The increasing incidence of infections and colonization with MRGN will put new challenges to health-care systems. It is important to adjust national health-care guidelines in response to the resistance situation. To obtain quantitative data on the current MRGN infection situation, a new national surveillance system for MRGN in German hospitals was initiated in early 2013.

Methods. The KISS module on Surveillance of MDROs (Multi drug resistant organism) allows for the documentation of colonization and infection with MDRO on intensive care units (ICUs). For each ICU colonization or infection, these bacteria (genus and species) is entered into the surveillance system. Furthermore, the user reports whether the MDRO was imported to or acquired on ICU. The present data consist of the surveillance data from 2013. In this analysis we focused on 4MRGN bacteria. The term 4MRGN was defined by the German federal institute for disease control and prevention in 2012 and pools organisms with a combined resistance to 4 antibiotic groups: acyl-ureidopenicillins, 3./4. generation-cephalosporins, carbapenems and fluoroquinolones.

Results. In 2013, 339 ICUs conducted a surveillance on 4MRGN. They reported 892 cases, of which 546 (61,2%) cases were imported and 356 (38.8%) were acquired. 505 (56.6%) cases were colonizations, and 387 (43.4%) cases were identified as infections. 354 (70.2%) cases of the colonizations (192 [49.6%] of the infections) were imported, and 151 (29.9%) cases were acquired on the unit (195 [50.4%] of the infections). Overall prevalence of 4MRGN was 0.30 cases per 100 patients, and prevalence at admission was 0.19 per 100 patients. Incidence density of infections with 4MRGN was 0.15 infections per 1,000 patient days. 498 cases (55.8%) of 4MRGN were *Pseudomonas aeruginosa*, 245 (27.4%) cases were *Enterobacteriacae* and in 116 cases (13.0%) the species was *Acinetobacter baumanii*. The remaining 33 cases were *Stenotrophomonas maltophilia*.

Conclusion. This surveillance system allows an analysis of the current resistance situation of 4MRGN in Germany. Changes in the occurrence of 4MRGN can be detected in detail. This offers a chance to respond early to newly emerging pathogens on a national level and to establish effective prevention measures.

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905. Screening and Isolation/Contact Precautions for Multi-Drug Resistant Organisms (MDRO) in Acute Care Hospitals: Results from a National Survey

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Background. Infections caused by MDRO lead to significant morbidity and mortality. Consequently, several states have mandated reporting of MDRO and *C. difficile*. Objectives of this study were: 1) to describe policies to screen and isolate for MDRO in U.S. hospitals; and 2) examine the relationship between state mandates for reporting of MDRO and implementation of screening and isolation/contact precaution policies.

Methods. A cross-sectional survey of hospitals enrolled in the National Healthcare Safety Network was conducted in the Fall of 2011. Descriptive statistics were computed. Differences in policies between hospitals located in states with and without MDRO reporting mandates at the time of the survey were examined using chi-square tests.

Results. 1,015 hospitals provided data (30% response rate). The majority (68%) reported targeted screening upon admission for methicillin-resistant *Staphylococcus aureus* (MRSA); screening for vancomycin-resistant Enterococci (VRE) and *C. difficile* were infrequently reported, 13% and 5%, respectively. Of hospitals with targeted MRSA screening, populations screened were ICU patients (73%) and transfers from skilled nursing facilities (57%) or other hospitals (43%). Contact precautions (CP) for patients with the following organisms were commonly reported: MRSA (95%), VRE (93%), and *C. difficile* (86%). While presumptive isolation/CP were common for *C. difficile* (78%), they were less common for MRSA (39%) and VRE (24%). Few hospitals routinely screened for other organisms, including methicillin-susceptible *Staphylococcus aureus* (12%), Acinetobacter spp (9%), *Klebsiella pneumoniae* (8%) and Pseudomonas spp (7%). Hospitals located in states with mandatory reporting of MRSA were more likely to have a policy for targeted MRSA screening ($p < 0.001$), and less likely to have a policy for presumptive isolation/CP pending a screen ($p = 0.024$).

Conclusion. This study found variation in the adoption of MDRO screening and isolation/contact precautions. Further research is needed to provide additional insight on effective strategies and to examine the impact of mandatory reporting of infections on implementation of policies and infection rates.

Disclosures. **All authors:** No reported disclosures.

906. How Mandatory Public Reporting Undermines Infection Prevention: An Ethnographic Study

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Background. In the United States, central line-associated bloodstream infection (CLABSI) rates are used as a measure of healthcare quality. Many states mandate public reporting of CLABSI rates. Although it is assumed that publicizing CLABSI rates will improve patient safety, we do not know how healthcare workers perceive and respond to this policy. The objective of this study was to examine healthcare worker perceptions of public reporting of CLABSIs and to understand the consequences of this perception for their motivation to implement infection prevention practices.

Methods. We conducted an innovative qualitative study combining 2250 hours of ethnographic observation of one hospital's infection prevention (IP) department coupled with 103 in-depth interviews with staff, purposively sampled to introduce variation by occupational role (doctors and nurses) and place in the organizational hierarchy (frontline clinicians, managers and hospital executives). Data were systematically analyzed in NVivo 10 using a modified grounded theory approach.

Results. Frontline clinicians perceived that the National Healthcare Safety Network (NHSN) surveillance definitions for healthcare-associated CLABSI are poorly aligned with what they believe to be "truly" hospital acquired infections. That the data generated by the NHSN definitions had to be publicly reported provoked frontline clinician resistance. Three social consequences emerged as a result of mandatory public reporting of CLABSIs. First, the credibility of the hospital's IP staff was eroded by their strict adherence to NHSN definitions. Second, frontline clinicians perseverated on the inconsistencies between surveillance definitions and clinical diagnoses at the expense of confronting known gaps in practice. Third, staff perceived that other hospitals "gamed" their rates of CLABSI because of the subjectivities inherent in the NHSN definition. This decreased staff motivation to learn from other hospitals and to commit to improvement work locally.

Conclusion. Public reporting of CLABSI rates may have the unintended social consequence of generating resistance amongst frontline staff that both distracts from and undermines the organizational goal of preventing infection.

Disclosures. **All authors:** No reported disclosures.

907. Validation of Surgical Site Infection Data in California Hospitals Demonstrates Variable Case Identification Following Abdominal Hysterectomy

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Background. Since 2011, California has required hospitals to report surgical site infection (SSI) data. SSI rates following abdominal hysterectomy are now used to determine Medicare reimbursement through CMS' Hospital Value-Based Purchasing Program. To assess variation in hospital SSI capture and reporting, the California Department of Public Health (CDPH) performed an external validation.

Methods. Infection preventionists (IPs) from CDPH performed on-site SSI data validation for abdominal hysterectomy procedures performed in volunteer hospitals

in 2012. Validation involved 1) provision by each hospital of patients with specified post-operative SSI claims codes, and 2) chart review of both SSI cases reported by hospital surveillance and cases flagged for review by SSI claims codes. We assessed the sensitivity of traditional surveillance and the added benefit of reviewing cases flagged by claims codes. We also evaluated the positive predictive value of claims-based surveillance and characteristics of infections missed by traditional surveillance.

Results. We reviewed 133 abdominal hysterectomy procedures at 34 hospitals, confirming 76 SSIs (30 superficial, 12 deep, and 34 organ/space). Traditional surveillance had a sensitivity of 68%, missing 7 superficial, 6 deep, and 11 organ/space SSIs. Claims-based surveillance had a sensitivity of 74%, missing 10 superficial, 1 deep, and 9 organ/space SSIs, with one SSI identified for every 2 records flagged for review. The combination of traditional plus claims-based surveillance changed the SSI rate for 35% of hospitals. Overall, 86% of SSIs were identified post-discharge, with 68% of patients requiring readmission. Traditional surveillance identified more cases in the outpatient setting (81% vs 57%, p-value = NS), but fewer cases on readmission (67% vs 79%, p-value = NS). Cases identified by traditional surveillance vs record review triggered by claims met similar CDC criteria.

Conclusion. Traditional surveillance missed one-third of SSIs following abdominal hysterectomy, with variable case identification across hospitals. Claims-based surveillance is a standardized approach that hospitals can use to improve SSI detection and health departments can use for external validation.

Disclosures. **All authors:** No reported disclosures.

908. Use of Claims Data to Identify Cases of Surgical Site Infection Following Colon Surgery Identified Many Unreported Infections in a State-Wide Validation

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Background. Since 2011, California has required hospitals to report surgical site infection (SSI) data using CDC's national surveillance system. SSI rates following colon surgery are now used to determine Medicare reimbursement through CMS' Hospital Value-Based Purchasing Program. To assess variation in hospital SSI capture and reporting, the California Department of Public Health (CDPH) performed an external validation.

Methods. Infection preventionists (IPs) from CDPH performed on-site SSI data validation for colon surgeries performed in volunteer hospitals in 2012. Validation involved 1) provision by each hospital of patients with specified post-operative SSI claims codes, and 2) chart review of both SSI cases reported by hospital surveillance and cases flagged for review by SSI claims codes. We assessed the sensitivity of traditional surveillance and the added benefit of reviewing cases flagged by claims codes. We also evaluated the positive predictive value of claims-based surveillance and characteristics of infections missed by traditional surveillance.

Results. We reviewed 561 colon procedures at 42 hospitals, confirming 239 SSIs (82 superficial, 55 deep, and 102 organ/space). This included 34% identified by both traditional surveillance and claims codes, 16% identified by traditional surveillance only, and 50% identified by claims codes only. Traditional surveillance had a sensitivity of 50% (46% for deep and organ/space SSIs), while claims-based surveillance had a sensitivity of 84% (88% for deep and organ/space SSIs). Claims-based surveillance identified one SSI for every 2.6 patients flagged for review. The 119 cases missed by traditional surveillance were more likely to have occurred during the surgical admission ($p < 0.01$) and less likely to have been re-opened by a surgeon ($p = 0.02$). Documentation of an SSI by the surgeon or attending physician was the same in the two groups ($p = 0.57$). Claims-based surveillance identified additional SSIs in 31 of 42 hospitals, 7 which had previously reported no SSIs.

Conclusion. Claims-based surveillance performed favorably compared to traditional surveillance. This method provides a comprehensive and efficient method for external validation by health departments.

Disclosures. **All authors:** No reported disclosures.

909. Comparison of three different data sources for Surgical Site Infection (SSI) Surveillance after Colon Surgery

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Background. There is considerable inter-facility variability in SSI rates based on method used for surveillance. NHSN and CMS are expected to propose strategies to standardize SSI surveillance. At our institution, SSI data is currently collected and reported by three methods: 1) NHSN; 2) administrative billing database; and 3) the National Surgical Quality Improvement Program (NSQIP).We compared these three data sources to understand the overlap and discrepancies in SSI reporting.

Methods. Annual colon surgery procedure volumes for all three data sources were compared. All episodes of SSI indentified in any data source were reviewed and reconciled using NHSN SSI criteria. The effect on SSI rates was evaluated.

Results. From January 1, 2011 to December 31, 2013, a total of 1723 eligible procedures were identified using the NHSN COLO operative procedure group. A total of 311 SSI were identified. NHSN surveillance captured 1686 of the procedures, administrative billing data identified 1723, and NSQIP reported a sample of 211 colon procedures for the same period. Of the 311 SSI, NHSN identified 295, administrative data identified 194, and NSQIP sampled 20. As a result SSI rates ranged from 9.5% to 17.5%.

	NHSN	Administrative	NSQIP	Gold Standard
Procedures	1686	1723	211	1723
SSI	295	194	20	311
	17.5%	11.5%	9.5%	18.0%

Conclusion. NHSN surveillance and administrative data identify the majority of at-risk procedures. Administrative data sources are less labor intensive but tend to miss a proportion of infections. Development of a standardized surveillance approach for SSI that is practical and accurate will require integration of administrative and NHSN surveillance strategies.

Disclosures. **All authors:** No reported disclosures.

910. Seasonal Variation of Surgical Site Infections Following Common Procedures

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Background. The relationship between time of year and surgical site infection (SSI) has not been well studied. We examined seasonal variation of SSI in a large cohort of patients in non-teaching community hospitals.

Methods. We performed a cohort study of patients undergoing the 10 procedures in 20 community hospitals affiliated with the Duke Infection Control Outreach Network from January 1, 2007-December 31, 2012. SSIs were defined using National Healthcare Safety Network criteria and identified using standardized surveillance methods. Summer was defined as July through September. The prevalence rate (PR) of SSI during the summer was compared to the remainder of the year by calculating PR ratios (PRR) and 95% confidence intervals. Procedure and organism type were examined by stratified analysis.

Results. We identified 3,182 SSIs following 361,857 surgical procedures (overall PR = 0.88/100 procedures). The most common pathogens were *S. aureus* (1450; 46%), coagulase negative *Staphylococci* (342; 11%), and *E.coli*(213; 6.7%). The overall rate of SSI during the summer months was significantly higher than the rate during the remainder of the year (0.97/100 vs 0.85/100 procedures; PRR 1.16, $p < 0.001$). The rates of SSIs were higher in summer months for infections caused by Gram positive cocci (PRR: 1.15, $p = 0.005$) and Gram negative bacilli (PRR: 1.29, $p = 0.001$). Seven out of the ten procedures demonstrated higher SSI rates during the summer (table).

SSI rate by season using Chi square analysis with stratification by organism group.

Organism	SSI Cases for "Summer"	Prevalence Rate for Summer / 100 surgeries	SSI Cases for "Rest of Year"	Prevalence Rate for "Rest of Year" / 100 surgeries	Prevalence Rate Ratio	P value
All	875/90,190	0.97 (0.91,1.03)	2,307/ 271,667	0.85 (0.81,0.88)	1.16 (1.06,1.26)	0.0007
Gram positive cocci	576/90,190	0.64 (0.59,0.69)	1,512/ 271,667	0.56 (0.53,0.59)	1.15 (1.04,1.26)	0.005
Gram negative rods	220/90,190	0.24 (0.21,0.28)	513/ 271,667	0.19 (0.17,0.21)	1.29 (1.10,1.51)	0.001
Other	159/90,190	0.18 (0.15,0.20)	478/ 271,667	0.18 (0.16,0.19)	1.00 (0.84,1.20)	0.98

Conclusion. To our knowledge, this is the first study to demonstrate seasonal variation of SSI in non-spinal surgery procedures. Higher SSI rates were observed during the summer regardless of organism and in several different procedure types. Further studies are needed to understand reasons for these findings.

Disclosures. **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

911. Development of an Automated Surveillance System for Identifying Surgical Site Infections and Triaging Clinical Review

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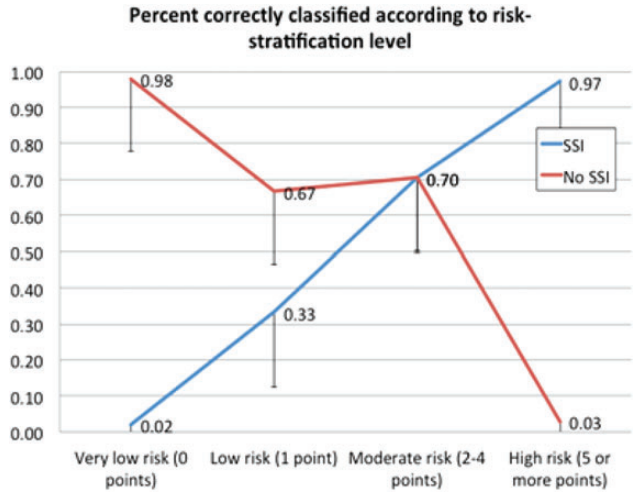
Background. Surgical site infections (SSIs) are a common and expensive healthcare-associated infection, costing an estimated $10 billion annually. SSI is also used as a benchmark for healthcare quality. As such, SSI detection and prevention are major targets of infection prevention programs. We sought to improve upon conventional manual detection methods by developing a simple, automated algorithm for SSI detection using administrative data.



Methods. We conducted a case control study among all surgeries performed at the Boston VA HCS during the two-year period from January 2008-December 2009. Cases of surgical site infection were matched to controls without surgical site infection. Clinical variables (administrative, microbiologic, pharmacy, radiology) were extracted and compared between the two groups to determine which variables (univariately) or combination of variables best detected SSI. Variables significantly associated with correct detection of SSI were then evaluated in a logistic regression model as independent predictors of accurate SSI detection. Points were assigned to variables based on the magnitude of the odds ratios from logistic regression.

Results. 70 cases of SSI were matched to 70 non-infected controls. Variables found on multivariable analysis to be significantly associated with SSI identification were ordering of a clinical culture, antibiotics prescriptions within the 30 day post-operative window, ordering of CT or MRI, and use of relevant ICD-9 code for post-operative infection. Among patients who fell into the "very low probability" category (Figure), 98% were correctly identified as having no SSI. Among patients in the "high probability" category, 97.1% were correctly identified as having SSI. The area under the curve for this model using entirely administrative data was 0.87.

Conclusion. We derived an automated surveillance algorithm for SSI detection with excellent operating characteristics. This algorithm could be used to streamline infection control efforts and reduce time required for manual review.

Disclosures. **K. Itani**, Sanofi: Investigator, Research grant; Merck: Investigator, Research grant

912. Assessment of Automated Surveillance Strategies to Identify Infectious Complications Following Implanted Cardiac Device Procedures

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Background. Infectious complication rates for implanted cardiac devices (ICD) have varied from <1% to >5%. The optimum approach for surveillance of these infections is unclear. The objective of this study was to create an automated surveillance tool for infectious complications after ICD procedures using ICD-9 and microbiology data.

Methods. All patients undergoing ICD procedures at Duke University Hospital from January 1, 2005-December 31, 2011 were identified using ICD-9 procedure codes. Potential infection-related complications among the cohort were noted using specific ICD-9 diagnosis codes and microbiology data for the 365 days following the index procedure. All potential cases identified from microbiology data and a subset identified using ICD-9 codes were reviewed for infection by expert reviewers. A subset of procedures without associated microbiology data or ICD-9 codes was also reviewed. Sensitivity, specificity, positive predictive values, and negative predictive values for specific queries were calculated.

Results. A total of 6,097 patients had 7,137 procedures during the 7-year timeframe. A total of 1,686 patients with potential infectious complications were identified: 174 met criteria from both ICD-9 and microbiology data; 14 met only microbiology criteria; and 1,498 met only ICD-9 criteria. We reviewed 558 cases, including all 188 microbiology cases, 250 randomly selected cases with ICD-9 criteria only, and 120 with neither microbiology nor ICD-9 codes. Of the 558 procedures reviewed, 71 unique infections were identified. Query test characteristics are shown in the table. Only 10 in 250 reviewed cases with ICD-9 codes but without microbiology were true infectious complications.

Test performance of surveillance strategies

Query Result	Number	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Micro + / ICD-9 +	174	100%	79%	41%	100%
Micro - / ICD-9 +	250	100%	36%	4%	100%
Micro + / ICD-9 -	14	0%	96%	0%	97%

Conclusion. Our surveillance tool using both microbiology and ICD-9 data was sensitive and specific for infectious complications following EP procedures. Further modifications of our query (e.g., type of ICD-9 code, time to infection) may further improve the performance of our automated surveillance.

Disclosures. **All authors:** No reported disclosures.

913. Impact of change in SSI surveillance definition on HPRO among patients with cancer

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Background. In January of 2013, the CDC altered the NHSN surveillance definitions for surgical site infections (SSI). Duration of surveillance for hip (HPRO) procedures was shortened from 365 days to 90 days. A recent report reviewed data from 43 community hospitals in 5 states and found that the new definition excluded infections and decreased SSI rates.

Methods. Memorial Sloan-Kettering is a 470 bed comprehensive cancer facility in Manhattan. In January of 2008, we began active prospective surveillance to detect SSI following a HPRO procedure. A retrospective analysis was performed on all SSIs following HPRO procedures that were reported to NHSN from 2009 – 2012. An SSI was determined to be excluded under the new definition if the event date was greater than 90 days from the procedure date.

Results. Out of 14 reported SSIs, 1 infection (7%) would have been excluded using the new NHSN SSI surveillance definition. However, the procedure that infection was related to had a duration that was >IQR5. Therefore both the procedure and the infection were excluded by NHSN and not calculated in the SSI rate.

	HPRO Procedures	SSI </= 90 days	SSI > 90 days	All SSIs
Total Reported	361	13 (3.6%)	1 (.3%)	14 (3.9%)
NHSN Adjusted*	328	**6 (1.8%)**	**0 (0%)**	**6 (1.8%)**

*Excludes procedures with duration >IQR5.

Conclusion. The shortened duration of surveillance for HPRO procedures had no impact on SSI rate for HPRO procedures among patients with cancer. The new definition did reduce manual chart reviews for both the outpatient orthopedic nurses and infection control personnel and would have had a time savings impact of 144 person-hours.

Disclosures. **All authors:** No reported disclosures.

914. A Single-Center 10-Year Analysis of Neurosurgical Patients with Nosocomial Bloodstream Infections: Incidence, Resistance Rates and Risk Factors for Mortality

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Background. In neurosurgery, there is limited data on the antibiotic resistance and prognosis following nosocomial bloodstream infection (NBSI). The aim of this study was to record incidence, antimicrobial resistance rates and risk factors for death in neurosurgical patients with NBSI.

Methods. Patients with a confirmed NBSI within the period 2003-2012 that were hospitalized in a neurosurgery department with a 4-bed intermediate care unit (IMCU) were included. NBSI was diagnosed when a blood sample obtained after the first 48 hours of hospitalization isolated a healthcare-associated pathogen. Blood cultures were performed with the BacTAlert automated system. Vitek 2 system was used for identification and antibiotic susceptibility. Risk factors for mortality were also assessed.

Results. A total of 236 patients with NBSI were identified. Blood samples recovered 378 isolates. Gram-negative bacteria (GNB) were the commonest isolates (54.5%). The predominant GNB pathogens were: *Klebsiella pneumoniae* (KP, 28.2%), *Pseudomonas aeruginosa* (PA, 27.1%) and *Acinetobacter baumannii* (AB, 24.3%). The commonest Gram positive bacteria (GPB) were *Staphylococcus epidermidis* (SE, 36.6%) and *Enterococcus* spp. (ES, 29.2%). Antibiotic resistance was high with 60% of KP and 70% of PA isolates resistant to gentamicin. Imipenem resistance was found in 90% of AB, 66% of PA and in KP isolates and it increased from 22% during 2003-2007 to 77% during 2008-2012 ($p < 0.001$). All GNB were sensitive to colistin. Of the coagulase negative staphylococci isolates, 94% were resistant to oxacillin. All GPB isolates were sensitive to vancomycin. Incidence of NBSI had a median of 4.2 infections/1,000 bed-days. Overall mortality was high (50.4%). Age, head injury, intracranial hemorrhage, surgery, GPB and GNB NBSI, central venous catheter use, stay in ICU, and stay in IMCU were associated with in-hospital death ($p < 0.05$). In multivariable analysis, age and stay in IMCU were independent risk factors for in-hospital mortality ($p < 0.05$).

Conclusion. High incidence of NBSI and increased mortality was noted in neurosurgical patients. A predominance of multidrug resistant GNB was found limiting the antibacterial drugs available for treatment.

Disclosures. **All authors:** No reported disclosures.

915. Is a hospital's surgical site infection rate among Medicare-insured patients a good indicator of outcome for commercially-insured patients?

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Background. The Centers for Medicare and Medicaid Services tracks quality measures, including surgical site infection (SSI) rates. The degree of correlation between hospitals' Medicare and Private Payer SSI outcomes is unknown.

Methods. Using 2009 inpatient claims data from California and New York, we evaluated SSI following coronary artery bypass graft (CABG) surgery for Medicare patients ≥65 years old vs Private Payer patients 18-64 years old. We screened claims within 90 days of surgery for codes suggestive of SSI. We separately analyzed the Medicare and Private Payer groups using generalized linear mixed models to predict the odds of infection at each hospital. Within group, models were adjusted for age, gender, and comorbidities. We assessed the relationship between the odds of infection for Medicare and Private Payer patients within the same hospital using a Pearson correlation. We repeated this process for hospitals performing ≥50 CABG procedures in each of the two groups (≥100 overall).

Results. 117 California and 40 New York hospitals performed CABG on both patient groups. 6-7% of Medicare patients had an SSI code, compared with 4-5% of Private Payer patients. Medicare patients were older (per study design), more likely to be female, and had higher rates of congestive heart failure, peripheral vascular disease, and renal insufficiency. Private Payer patients had higher rates of obesity. In California hospitals, the correlation between Medicare and Private Payer odds was 0.42 (95% CI 0.25-0.55) compared with 0.66 (95% CI 0.43-0.80) in New York hospitals. There was a larger proportion of relatively low volume hospitals (<100 CABG procedures) in California (47%) compared with New York (14%). Limiting the analysis to California hospitals performing ≥50 CABG procedures on both Medicare and Private Payer patients, the Pearson correlation improved to 0.60 (95% CI 0.15-0.83).

Conclusion. We found moderate-to-strong correlation in the adjusted odds of SSI in Medicare vs Private Payer patients undergoing CABG at individual hospitals. The poorer correlation in California compared with New York hospitals may reflect the large proportion of relatively low volume hospitals in California where small sample sizes limit precision in estimating SSI odds.

Disclosures. **K. Kleinman**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product

916. Electronic Syndromic Surveillance for Influenza-like Illness in Different Treatment Settings

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Background. Syndromic surveillance in an epidemiologic tool that utilizes near "real-time" clinical data to track disease. Currently, most syndromic surveillance for influenza-like illness (ILI) is performed using outpatient data. As hospitals adopt electronic health records, more electronic data will be available from different treatment settings for syndromic surveillance. It is not known how to best utilize this data to monitor ILI in different treatment settings (e.g., Emergency Department (ED), outpatient, and inpatient).

Figure 1: Details of Query for ILI Algorithm

Chief Complaint of FLU LIKE SYMPTOMS OR
Chief Complaint of FEVER AND Chief Complaint of COUGH, FLU LIKE SYMPTOMS, NASAL CONGESTION, PHARYNGITIS, SORE THROAT, or URI OR
Chief Complaint of FEVER AND Diagnosis of * OR
Diagnosis of FEVER AND Diagnosis of * OR
Temperature >100°F during encounter (or first 24 hours for inpatients) AND Diagnosis of * OR
Diagnosis of (any containing "influenza"*)

* Intelligent Medical Objects (Intelligent Medical Objects, Northbrook, Illinois) terms: acute asthmatic bronchitis, acute bronchitis, acute bronchitis with COPD, acute nasopharyngitis, acute nasopharyngitis (common cold), acute pharyngitis, acute respiratory failure, acute URI, acute URI of multiple sites, bronchitis, bronchitis with bronchospasm, bronchitis with obstruction, bronchitis with tracheitis, cough, dyspnea, fever 41.1°C (106.0°F) or higher, fever and chills, fever with chills, fever, unknown origin fever, unspecified head cold, influenza, influenza A, influenza and pneumonia, influenza B, influenza due to influenza virus type A, porcine influenza pneumonia, influenza with gastrointestinal tract involvement, influenza with other manifestations, influenza with other respiratory manifestations, influenza with pharyngitis, influenza with pneumonia, influenza with sinusitis, bronchopneumonia, influenza pneumonia, influenza-like symptoms, labored breathing, multiple URI, nasal discharge, nasopharyngitis, nasopharyngitis acute, nasopharyngitis infective, pneumonia, pneumonia and influenza, rapid breathing, respiratory distress, shortness of breath, sore throat (viral), unspecified viral pneumonia, viral bronchitis, viral pharyngitis, and viral pneumonia.
COPD = chronic obstructive pulmonary disease; URI = upper respiratory infection

Figure 2: Percentage of Encounters for ILI by Treatment Setting

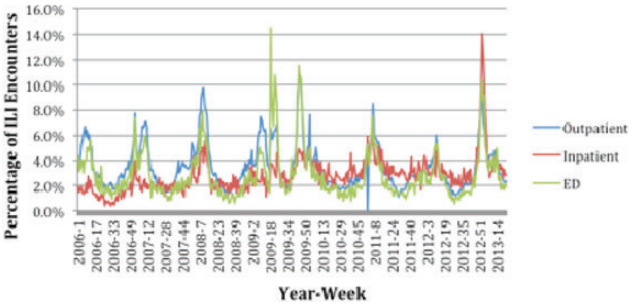
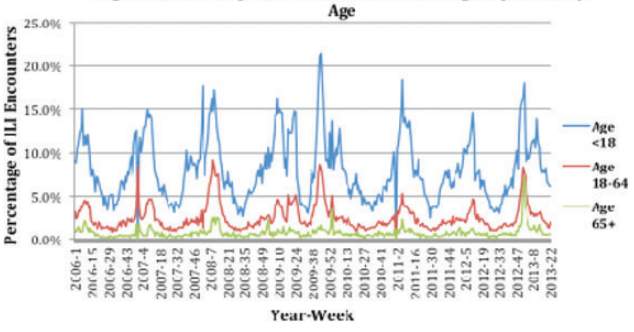


Figure 3: Percentage of Encounters for ILI Among Outpatients By Age



Methods. We conducted a retrospective cohort study in a 4-hospital health system. All inpatient encounters, ED encounters, and outpatient primary care encounters from January 1, 2006 through May 31, 2013 were included. We applied an ILI syndromic

surveillance algorithm that was previously validated in the outpatient setting to the ED and inpatient settings (Figure 1). Using the algorithm to query the Enterprise Data Warehouse (EDW), we calculated the percentage of encounters for ILI per week in each treatment setting. We compared results from different treatment settings using Pearson correlation coefficient.

Results. Over the study period, there were 3,443,913 outpatient visits, 393,835 inpatient encounters, and 610,002 ED encounters. ED algorithm results correlated closely with outpatient results (rho = 0.875), but inpatient algorithm results were less similar (rho = 0.375) (Figure 2). During the time period when H1N1 was circulating (April 2009-March 2010), outpatient-ED correlation was 0.8617 and outpatient-inpatient correlation was 0.6676. Correlation between outpatient and ED algorithm results was stronger among patients less than18 years old than among those over age 65 (rho = 0.79 vs 0.44). The seasonal uptick in ILI encounters for patients < 18 years old preceded the rise for older patients in the outpatient setting (Figure 3) and for children in other settings.

Conclusion. Data streams from the outpatient and ED settings provide similar syndromic surveillance information regarding ILI activity, whereas inpatient ILI data is less similar. Children in the outpatient setting see a seasonal rise in ILI activity before adults and children in other settings.

Disclosures. **All authors:** No reported disclosures.

917. Nosocomial Respiratory Viral Infections in Two Children's Hospitals

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Background. There are limited data on nosocomial viral respiratory infections (NVRIs). This study aims to report the rates of NVRIs in 2 children's hospitals, to compare the rates of different respiratory viruses, and to determine the hospital unit-specific rates of NVRIs.

Methods. NVRIs caused by adenovirus, human metapneumovirus (hMPV), influenza A and B viruses, parainfluenza viruses (PIVs) types 1, 2 and 3, respiratory syncytial virus (RSV) and rhinovirus were prospectively monitored over a 3-year period from April 2010 - March 2013 at Cohen Children's Medical Center of New York (CCMC) and Montreal Children's Hospital (MCH). A NVRI was defined as a positive viral test on a nasopharyngeal swab, the presence of symptoms, and a minimum time from hospital admission to onset of symptoms of 1-4 days that varied with the viral pathogen.

Results. CCMC and MCH have 163 and 130 beds, respectively, with mean annual patient-days of 46,519 at CCMC and 36,815 at MCH. The most common etiologies of NVRIs at both institutions were rhinovirus, followed by PIVs and RSV. The rates of NVRIs for the 3-year study period at MCH were higher than at CCMC (1.91 vs 0.79 per 1,000 patient-days, respectively; P < 0.0001). The combined total and unit-specific number of episodes and rate (per 1,000 patient-days) for each virus were as follows:

Respiratory Virus	All Hospital Units		PICU		NICU		Med/Surg		Heme/ Onc/ BMT	
	#	Rate	#	Rate	#	Rate	#	Rate	#	Rate
Adenovirus	27	0.11	9	0.29	0	0	17	0.14	1	0.04
hMPV	16	0.06	3	0.10	2	0.03	9	0.07	2	0.07
Influenza A and B	19	0.08	1	0.03	1	0.01	15	0.12	2	0.07
PIVs	61	0.24	6	0.19	4	0.06	42	0.34	9	0.33
RSV	45	0.18	4	0.13	2	0.03	32	0.26	7	0.26
Rhinovirus	154	0.62	25	0.80	33	0.47	74	0.61	22	0.81
All Viruses	322	1.29	48	1.54	42	0.60	189	1.55	43	1.58

Conclusion. NVRIs occurred frequently at 2 children's hospitals. Rhinoviruses were the most frequently detected viruses causing NVRIs followed by PIVs and RSV. NVRI burden was the lowest in the NICU. Given the importance of NVRIs, prospective active surveillance may be considered in pediatric facilities for quality improvement purposes.

Disclosures. **All authors:** No reported disclosures.

918. Trends of device-associated infections in intensive care units after the establishment of national nosocomial infection surveillance system: results from the Korean Nosocomial Infections Surveillance System

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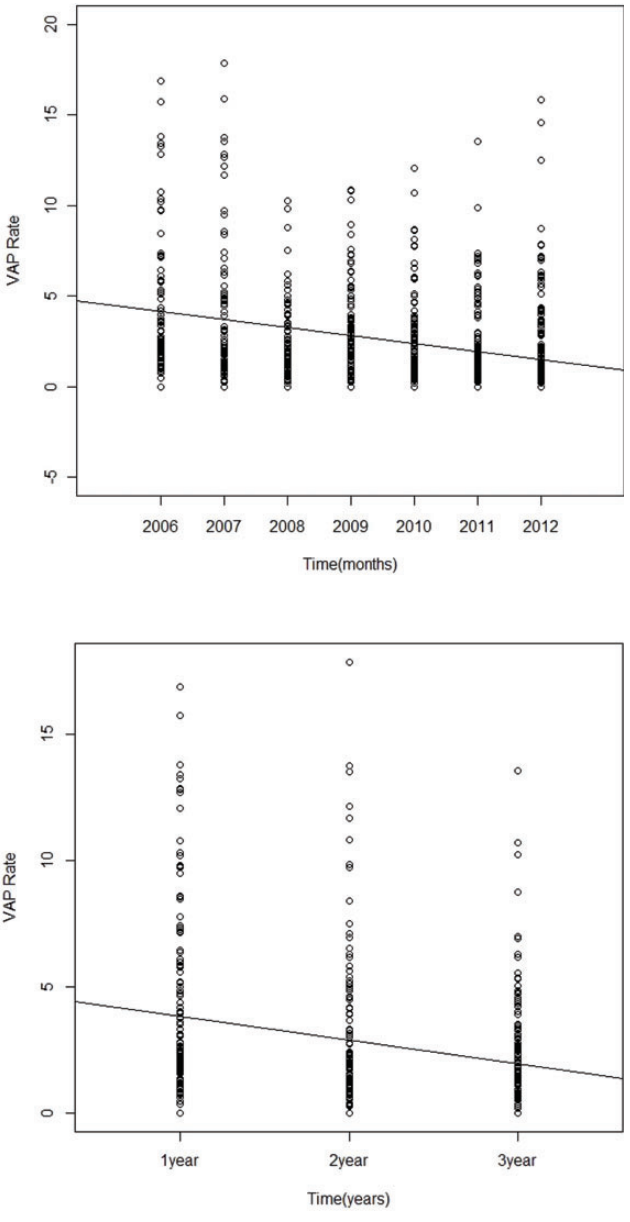
Background. We hypothesized that the rate of device-associated infections (DAIs) in ICU would have decreased since the establishment of Korean Nosocomial Infections Surveillance System (KONIS) by the voluntary efforts for each participating institutes to improve infection control practices.



Time trend of rate of ventilator associated pneumonia (VAP) in ICUs participating KONIS A. VAP rate from 2006 to 2012 (F=11, P<0.01) B. VAP rate of institutes that had participated in KONIS for at least 3 years (F=20.57, P<0.01)

Methods. Three major DAIs were studied: ventilator-associated pneumonia (VAP), central line-associated bloodstream infection (CLABSI), and catheter-associated urinary tract infection (CAUTI) in ICU. We evaluated the time trend of the incidence of DAIs from 2006 through 2013 in KONIS participating ICUs. The pooled incidences of DAIs were calculated for each year of participation. In addition, data from only institutions that had participated in KONIS for at least 3 consecutive years were analyzed to further evaluate the effects of KONIS participation on the incidence of DAIs.

Results. The number of ICUs participating KONIS gradually increased from 76 in 2006 to 162 in 2012. Rate of VAP significantly decreased from 2006 (3.48 per 1,000 mechanical ventilator days) to 2012 (1.64 per 1,000 mechanical ventilator days) ($F = 11$, $P < 0.01$). Rate of CAUTI decreased from 1.85 per 1,000 urinary catheter days to 1.26, but the reduction was not significant ($F = 2.02$, $P = 0.07$). The change of CLABSI rate was not significant, as well (from 3.40 per 1,000 central line days to 2.57, $F = 1.73$, $P = 0.12$). In 132 ICUs that had participated in KONIS for at least 3 consecutive years, the VAP rate significantly decreased from the first year to third year ($F = 20.57$, $P < 0.01$), but the rate of CAUTI ($F = 1.06$, $P = 0.35$) and CLABSI ($F = 1.39$, $P = 0.25$) did not decrease.

Conclusion. VAP rate in ICUs participating KONIS has decreased since the establishment of KONIS. Further efforts to reduce CLABSI rate should be performed in ICUs participating KONIS.

Disclosures. **All authors:** No reported disclosures.

919. Routine Hospital Acquired Infection surveys are feasible in low income health care settings and can inform quality improvement interventions

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Session: 112. HAI Surveillance and Public Reporting
Friday, October 10, 2014: 12:30 PM

Background. Prevention of acquisition of infection in the health care setting is imperative for reduction in morbidity and mortality for patients and health workers and improvement health care quality. However, data is scarce on prevalence and trends of hospital acquired infections (HAI) in low income settings, unlike in developed countries. We instituted annual surveys to determine HAI prevalence and determinants in a hospital in Gulu, Northern Uganda, an area recovering from over 20 years of war.

Methods. An external expert mentored local hospital staff at the request of the Board, to do HAI surveys for 2 years after which a local team continues the exercise. Using standard WHO checklists. A one-day survey is done, recruiting all patients admitted in the hospital for 48hours or more. Data is collected by doctors and nurses on demographics, new diarrhea, Urinary Tract Infections (UTI), respiratory conditions, wound infection and intravenous catheter infections that were absent during admission. Urinalysis was done to confirm UTI. Results were analysed using SPSS, reporting basic statistics and p values of chi square tests comparisons.

Results. A total 1174 clients were surveyed in four years, average 293 per survey. There was a 56% decline in HAI prevalence from 28% in 2010 to 14.2% in 2011 ($p < 0.0001$). Prevalence of HAI was 15.1% in 2013 and 14% in 2014. In different years, the key hospital acquired infections included UTI accounting for 39% (21.5-55%) of the total HAI, intravenous line infection 27% (18.2-30.4%), respiratory tract infections, 17.5% (5.5-25.5%), and surgical wound infections, 16.0% (8.7-20%). In 2013 which had UTI at 58%, UTI was present in 53.3% of catheterized clients, compared to 14.8% in 2011.

Conclusion. The HAI surveys are practical, and feasible to perform, even in poor settings. The surveys prompted the institution of the hospital infection control committee. HAI surveys can generate glaring gaps, which when intervened on, like urinary catheter overstay, poor wound care, duration of iv lines, and hand washing practices, can improve care quality. The surveys can suggest corrective actions for good care practices. Nevertheless, prevention of HAI needs continuous efforts of all health workers.

Disclosures. **All authors:** No reported disclosures.

920. Retrospective Analysis of Infective Endocarditis at an Urban Hospital

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Session: 113. Infective Endocarditits: Epidemiology, Diagnosis, and Management
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Background. Infective endocarditis (IE) is a disease that causes significant morbidity and mortality. A multinational study of the presentation, etiology, and outcome of patients infected with endocarditis has been described, but it is unknown whether these parameters are similar in an urban, socioeconomically disadvantaged patient population.

Methods. We conducted a retrospective analysis of patients of at least 18 years of age admitted to an urban, academic hospital with a diagnosis of endocarditis. Echocardiograms performed between September 2006 and September 2011 for the indication of endocarditis were evaluated for the presence of vegetations on one or more valves or intracardiac devices. Patient-specific risk factors (intravenous drug use, dialysis catheters, pacemakers), co-morbidities (diabetes), and sequelae (mortality, septic emboli, etc) were compared to a multinational cohort of patients diagnosed with endocarditis using chi-squared analysis.

Results. The results from more than 1880 echocardiograms were reviewed, revealing 180 cases of IE (165 cases were native valve IE and 15 were prosthetic valve IE). Men slightly outnumbered women (109 to 71). Fifty-five patients had implantable devices or catheters; 12 had an AV graft or fistula, 27 had permacaths, and 16 had pacers or AICDs (10 of which were infected). The organisms isolated were as follows: 104 *S. aureus*(65 MRSA), 16 viridans Streptococci, 14 beta-hemolytic Streptococci, 11 Enterococcus spp., 10 coagulase-negative Staphylococci, 2 HACEK organisms, and 5 Fungi. The mitral valve was most commonly involved (65 cases), followed by aortic (62), tricuspid (60), and pulmonic (4).

Our urban cohort had significantly higher percentages of patients with diabetes and intravenous drug use, more tricuspid valve disease, more frequent septic embolization, and fewer heart failure symptoms. Valvular surgery was less frequently performed, and there was a trend toward higher overall mortality (23% vs 18%; $p = 0.08$).

Conclusion. Patients in our cohort had more co-morbidities, were less likely to undergo valve replacement surgery, and had higher mortality than the multinational cohort. Further investigation is needed to in order to understand the difference in valve-replacement frequency between the two groups and whether this has any impact on mortality.

Disclosures. **All authors:** No reported disclosures.

921. Prevalence of Hepatitis C Infection and Epidemiology of Infective Endocarditis in Intravenous Drug Users in Central Kentucky

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Session: 113. Infective Endocarditits: Epidemiology, Diagnosis, and Management
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Background. During recent years, we have observed an increase in admissions for infective endocarditis (IE) at our academic center. We proposed a retrospective study to determine the prevalence of hepatitis C virus (HCV) infection and describe the epidemiology of IE in intravenous drug users (IDU) in Kentucky.

Methods. This retrospective, IRB approved study evaluated all adult intravenous drug users admitted to a teaching facility serving central Kentucky diagnosed with infective endocarditis based on the modified Duke's criteria from January 2010 to December 2012. Data collected included demographics, blood culture results, valve involvement, surgery, and outcomes. In addition, patients were screened for HIV and hepatitis C virus (HCV).

Results. Overall, 105 subjects (65 males and 40 females) between 18 and 63 years of age (mean 35) were evaluated. The majority (73%) of these patients were from rural Kentucky. The most common organism isolated from blood cultures was *Staphylococcus aureus* (50%), followed by *Streptococcus viridans* (16%) and *Enterococcus species* (13%). Of the *S. aureus* isolates, 59% were methicillin sensitive. The majority of patients had left sided endocarditis (56%) with an overall in-hospital mortality of 25%. There was no significant difference in mortality based on gender or affected valve type. However, mortality was significantly higher for patients that did not undergo surgery compared to those that did have surgery (39% vs 10%, $p = 0.0022$) Furthermore, 76% (68/90) of patients evaluated for HCV were positive. Whereas, none of the patients tested for HIV were positive (N-99). Mortality was significantly higher for HCV patients than non-HCV patients (32% vs 5%, $p = 0.0178$).

Conclusion. The prevalence and mortality associated with HCV compared to HIV in IDU diagnosed with infective endocarditis from rural Appalachia Kentucky was alarming. More studies evaluating the relationship between HCV and infective endocarditis should be performed.

Disclosures. **All authors:** No reported disclosures.

922. *Bartonella quintana* Blood Culture-Negative Endocarditis in Washington, D.C

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Session: 113. Infective Endocarditits: Epidemiology, Diagnosis, and Management
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Background. Prior studies have demonstrated *Bartonella* as one of the etiologies of blood culture negative endocarditis. The objective of this abstract is to describe three cases of *Bartonella quintana* endocarditis identified within one year in a large hospital in Washington, D.C.

Methods. Descriptive, retrospective study based on a review of medical records at an 800-bed urban hospital. All patients were identified between April 2013 and December 2013.

Results. All patients were men (median age 55, range 52-57), homeless, and reported a history of alcoholism. Blood cultures were negative for all patients.

Echocardiography demonstrated aortic and mitral valve perforation and regurgitation in one patient, aortic valve vegetation with regurgitation in the second, mitral and aortic valve vegetation with regurgitation in the third patient. All patients had a positive *Bartonella quintana* serum IgG with negative IgM. PCR on DNA extracted from cardiac valves was positive for *Bartonella*, and DNA sequencing of PCR amplicons identified *Bartonella quintana* in all patients. Patients received treatment with doxycycline/rifampin or doxycycline/gentamicin.

Conclusion. Although much of the existing literature regarding *Bartonella* endocarditis stems from Europe, our findings suggest that *Bartonella* endocarditis may be an under-recognized cause of culture-negative endocarditis in the U.S., and should be considered in patients with risk factors such as homelessness and alcoholism. Amplification of DNA extracted from affected cardiac valves may provide enhanced diagnostic accuracy.

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923. *Lactococcus garvieae* infective endocarditis requiring valve replacement: First case in the United States

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Session: 113. Infective Endocarditis: Epidemiology, Diagnosis, and Management
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Background. *Lactococcus*, a gram-positive organism of low virulence, is an uncommon cause of human infection. Infective endocarditis due to *Lactococcus* is extremely rare.

Methods. We present a case of native aortic valve endocarditis due to *Lactococcus garvieae* with severe aortic insufficiency requiring valve replacement.

Results. The patient is a sixty year old male with history of Waldenstrom's macroglobulinemia for which he had been receiving intravenous immunoglobulin infusions for the previous two years. He was admitted to the hospital with a two week history of fatigue, decreased appetite and worsening shortness of breath. Chest radiograph showed findings consistent with interstitial pulmonary edema. Blood cultures grew *Lactococcus garvieae.* A transesophageal echocardiogram showed a mobile echodensity on the aortic valve extending into the left ventricular outflow tract; there was associated leaflet perforation and severe aortic regurgitation. Two thirds of the aortic valve leaflets were essentially destroyed. The patient underwent aortic valve replacement with a pericardial valve. Surveillance blood cultures and cultures of the resected valve were negative. He was treated with vancomycin and gentamicin for two weeks, followed by ceftriaxone for a total of six weeks. The patient has done well since discharge from the hospital, with a follow up transthoracic echocardiogram showing a normally functioning bioprosthetic aortic valve.

Lactococcus. was placed in a separate genus from *Streptococcus* in 1985 based on genetic analysis. *L. garvieae* is a catalase-negative, facultatively anaerobic, serogroup N, gram-positive coccus. A review of the English literature revealed fifteen cases of infective endocarditis due to *L. garvieae*. More than half of the patients had a prosthetic or repaired valve. Most patients were treated medically with the majority receiving a six week course of β-lactams. All but one patients survived.

Conclusion. *Lactococcus garvieae* is an extremely uncommon cause of infective endocarditis. β-lactams appear to be the antibiotics of choice, and the prognosis is favorable. We believe our patient represents the first case in the US that required valve replacement.

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924. Clinical Decision Rule to Guide Use of Echocardiography in the Management of *Staphylococcus aureus* Bacteremia

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Session: 113. Infective Endocarditis: Epidemiology, Diagnosis, and Management
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Background. Infective endocarditis (IE) is a serious complication of *Staphylococcus aureus* bacteremia (SAB) that is associated with high morbidity and mortality. There is limited evidence-based guidance on defining which patients with SAB should be screened with echocardiography.

Methods. Risk factors associated with IE in SAB patients were analyzed to identify independent predictors of endocarditis. Clinical data were retrospectively reviewed with follow-up (at least 3-month) data of all adults hospitalized at our institution with SAB from 2006 to 2011. IE was defined using modified Duke's Criteria.

Results. Of the 757 patients who were screened, 678 individuals with SAB (24% community-onset, 56% healthcare-associated and 20% nosocomial) met study criteria and were included in the analysis. A total of 85 patients (13%) were diagnosed with definite IE within the 12 weeks of initial presentation. Community onset of SAB, presence of implantable cardiac device, and sustained bacteremia (≥ 72 hours) were identified as independent predictors of SAB from multivariable logistic regression. Two decision rules (Day 1 [admission day] and Day 5 [when results of day 3 blood cultures are known]) were derived based on the presence of these risk factors, weighted in magnitude by the corresponding regression coefficients, and summed together to define an individual's risk score (table). A score of <2 for Day 1 Rule had a sensitivity of 95.3% and negative predictive value (NPV) of 96.5% whereas a score of <2 for Day 5 Rule had a sensitivity of 98.8% and negative predictive value (NPV) of 98.5%.

Test Performance Characteristics of IE Clinical Risk Scores

Risk Score	Sensitivity	Specificity	PPV	NPV
Day 1 Score ≥				
High Risk 5	9.4%	99.5%	72.7%	88.5%
↑ 4^	21.2%	95.6%	40.9%	89.4%
3	35.3%	92.4%	40.0%	90.9%
2*	64.7%	70.2%	23.7%	93.3%
↓ 1	95.3%	18.4%	14.3%	96.5%
Low Risk 0	100%	0.0%	12.5%	-
Day 5 Score ≥				
High Risk 7	7.2%	99.7%	75.0%	88.2%
↑ 6	19.3%	97.9%	57.1%	89.4%
5	30.1%	96.7%	56.8%	90.6%
4	54.2%	83.1%	31.5%	92.7%
3*	86.7%	59.2%	23.4%	96.9%
2~	94.0%	41.1%	18.6%	97.9%
↓ 1	98.8%	11.4%	13.8%	98.5%
Low Risk 0	100%	0.0%	12.5%	-

Conclusion. We propose clinical decision rules that can accurately classify patients presenting with SAB into a low-risk group that can be managed without cardiac imaging. Larger prospective studies are needed to validate the classification performance of these decision rules.

Disclosures. **All authors:** No reported disclosures.

925. A Normal Transthoracic Echocardiogram can be Used to Rule Out Infective Endocarditis in Patients with *Staphylococcus aureus* Bacteremia

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Session: 113. Infective Endocarditis: Epidemiology, Diagnosis, and Management
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Background. *Staphylococcus aureus* is a major cause of bacteremia and often leads to infective endocarditis (IE). Current guidelines recommend performing transesophageal echocardiography (TEE) in all patients or treating empirically with prolonged intravenous antibiotics. Many physicians do not adhere to guidelines, and recent studies suggest that low-risk patients do not require TEE.

Methods. We retrospectively evaluated hospitalized patients with *S. aureus* bacteremia (SAB) from seven hospitals in Toronto, Ontario over a 3-year period. In 536 patients who received a TTE within 28 days of bacteremia, we randomly divided the sample into development (n = 268) and validation (n = 268) cohorts. We derived criteria to rule out infective endocarditis based on multivariable logistic regression analysis in the development cohort, and applied these criteria to the validation cohort to determine criteria diagnostic properties.

Results. In multivariable analysis, four criteria were useful to rule out infective endocarditis: a normal TTE ($p < 0.001$), non-community-acquired bacteremia ($p = 0.002$), no intravenous drug use ($p < 0.001$), and absence of high-risk cardiac conditions ($p < 0.001$). In the validation sample, failing any criteria had a 97% sensitivity, 52% specificity, 25% positive predictive value, and 99% negative predictive value for infective endocarditis. The negative likelihood ratio was 0.05.

Conclusion. A prediction model including normal TTE, non-community acquired bacteremia, no intravenous drug use, and absence of high-risk cardiac conditions is a useful tool to identify patients at low risk of infective endocarditis. Risk stratification combined with TTE may be adequate to rule out IE in most patients with SAB.

Disclosures. **All authors:** No reported disclosures.

926. What Impacts the Decision to Obtain Transesophageal Echocardiogram for *Staphylococcus aureus* Bacteremia?

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Session: 113. Infective Endocarditits: Epidemiology, Diagnosis, and Management
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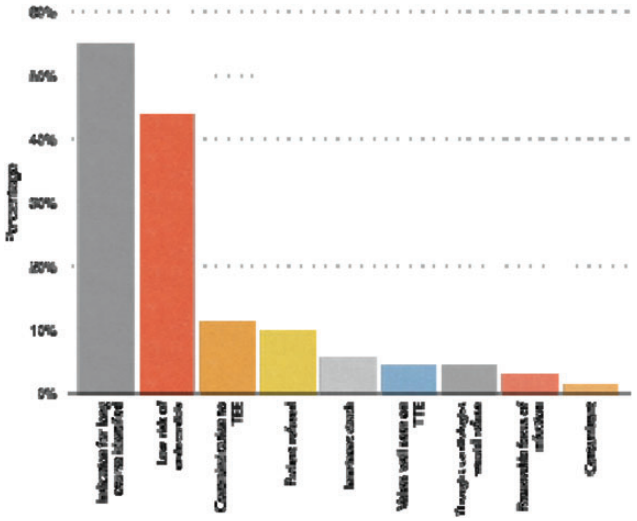
Background. IDSA guidelines recommend transesophageal echocardiogram (TEE) to rule out infective endocarditis (IE) in all patients with *Staphylococcus aureus* bacteremia (SAB). Despite this recommendation, TEE is uncommonly used for SAB. The low utilization of TEE is hypothesized to be due to poor access to TEE and the potential complications of anesthesia and endoscopy. The purpose of this study is to evaluate which factors are associated with obtaining TEE for SAB.



Reasons infectious diseases physicians do not obtain TEE in the setting of SAB.

Methods. This is a prospective observational cohort of hospitalized patients with SAB at an urban public safety net hospital in Denver CO between July 1, 2013 and April 29, 2014. Patient level information was obtained from the medical record. The attending ID physician was contacted via a standardized email to determine why TEE was/was not performed. Statistics were calculated using the chi-square, Kruskal-Wallis, and student's t-test of means.

Results. SAB was present in 93 patients, and 24% underwent TEE. Patient age, comorbid medical conditions, and source of SAB were not associated with TEE. 59 patients completed therapy during the study period. Patients who underwent TEE tended to have a longer duration of bacteremia (median 4.5 vs 3.0, P = 0.19). 11% of patients who received <28 days of treatment had a TEE while 24% of those who received ≥28 days of treatment had a TEE (P = 0.24). The most common reasons that ID physicians cited for not performing TEE were (1) low clinical suspicion of IE (55%); or (2) another indication for an extended duration of treatment (44%). More than 1 reason was cited in 41% of cases (Figure 1).

Conclusion. TEE is uncommonly used for the evaluation of SAB at this facility, particularly in patients who receive a short course of antibiotics. ID physicians reported not performing TEE because they clinically considered IE to be unlikely or had already identified an indication for an extended treatment duration. Further work must be done to determine if TEE results drove physicians to prescribe longer treatment duration or if TEE is a marker for patients with more complicated disease. Clinical outcomes should also be evaluated to ensure that not performing TEE is not associated with recurrent disease.

Disclosures. **All authors:** No reported disclosures.

927. Rifampin for Surgically Treated Staphylococcal Infective Endocarditis

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Background. Rifampin is recommended in the treatment regimen for staphylococcal prosthetic valve endocarditis (PVE), and for staphylococcal native valve endocarditis (NVE) treated with placement of prosthetic material at surgery. The evidence base for this is scant, and some clinicians opt to forgo rifampin. The purpose of this study was to examine if treatment with rifampin in patients with surgically-treated staphylococcal infective endocarditis (IE) results in better outcomes.

Methods. Patients operated for staphylococcal IE from April 1, 2008 to July 1, 2012 were identified from our institution's IE registry. Treatment was defined as at least 3 days of rifampin post-op. The propensity to receive rifampin was calculated in a model that included NVE vs PVE, *Staphylococcus* species, left side involvement, invasive disease (extending beyond annulus), positive valve culture, past history of IE, presence of a pacemaker/defibrillator, end-stage renal disease, hepatitis C, and concomitant medications that could interact with rifampin. Cox proportional hazards regression was used to compare a composite outcome of death or reoperation for IE, between patients treated and not treated with rifampin, adjusted for age, sex and propensity to receive rifampin.

Results. 189 patients were identified. Mean age was 56 years, 66% were male, 50% had PVE, 60% had *S. aureus* or *lugdunensis* infection, 89% had left side involvement, and 57% had invasive disease. 51 (27%) received at least 3 days of rifampin post-op. The median time to event was 979 days (IQR 191 - 1918). Rifampin treatment was associated with PVE (OR 2.93, p 0.001), left side involvement (OR 3.91, p 0.04), invasive disease (OR 2.26, p 0.02), and concomitant potentially interacting medications (OR 2.13, p 0.04). Patients treated with rifampin had a similar hazard of death or reoperation for IE as those not treated (HR 1.09, 95% CI 0.63 – 1.83), after adjusting for age, sex and propensity to receive rifampin. Results were similar when treatment was defined as at least one dose of rifampin, any pre-op rifampin, or rifampin at hospital discharge.

Conclusion. Among patients with surgically treated staphylococcal IE there was insufficient evidence to claim a reoperation-free survival benefit from treatment with rifampin.

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929. Comparison of Echinocandin vs Amphotericin B Based Therapy for *Candida* Infective Endocarditis: An Observational Cohort Study

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Session: 113. Infective Endocarditits: Epidemiology, Diagnosis, and Management
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Background. The optimal therapy for *Candida* infective endocarditis (IE) is unknown, and treatment guidelines are based largely on single site case series and case reports. The current guidelines have added echinocandins as a treatment option. We sought to compare amphotericin B based therapy to echinocandin based therapy, using two large, prospective, international, multi-center cohorts of patients with definite IE.

Methods. We identified cases of definite *Candida* IE presenting between June 1, 2000 and September 30, 2011 from the International Collaboration on Endocarditis – Prospective Cohort Study (ICE-PCS) and the International Collaboration on Endocarditis Plus (ICE-Plus). A supplemental case report form was sent to enrolling sites to gather detailed information on antifungal therapy. We compared clinical characteristics and outcomes based on antifungal regimen received.

	Amphotericin B (N=11)	Echinocandin (N=14)	p-value
Combination therapy	6 (54%)	6 (43%)	0.56
Surgery	6 (54%)	5 (36%)	0.35
Duration antifungal, days (median)	78	50	0.89
Suppressive therapy	5 (45%)	6 (43%)	0.90
Mortality			
42 d	4 (36%)	5 (36%)	1
1 y	7 (64%)	9 (69%)	1

Results. 72 cases of definite *Candida* IE were identified of which 33 had additional data on antifungal therapy available. The most common infecting species were *C. albicans* (n = 13) and *C. parapsilosis* (n = 12). Most patients received either an amphotericin B based regimen (33%) or an echinocandin based regimen (42%). Nearly half received combination antifungal therapy (45%) and surgical therapy was used in 13 patients (39%). There was no difference in either 42 day or 1 year mortality between those receiving an amphotericin B based regimen vs those receiving an echinocandin based regimen (36% vs 36% and 64% vs 69%, respectively, p = 1).

Conclusion. This is one of the largest prospective series of *Candida* endocarditis patients to date. In this cohort, there was no difference in mortality with echinocandin based therapy as compared to amphotericin B based therapy. This study is limited by small sample size and observational data, however it lends support to the current recommendation of echinocandin based therapy as a viable treatment option for *Candida* endocarditis.

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930. Endocarditis due to *Coccidioides* spp. – the Seventh Case

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Session: 113. Infective Endocarditis: Epidemiology, Diagnosis, and Management
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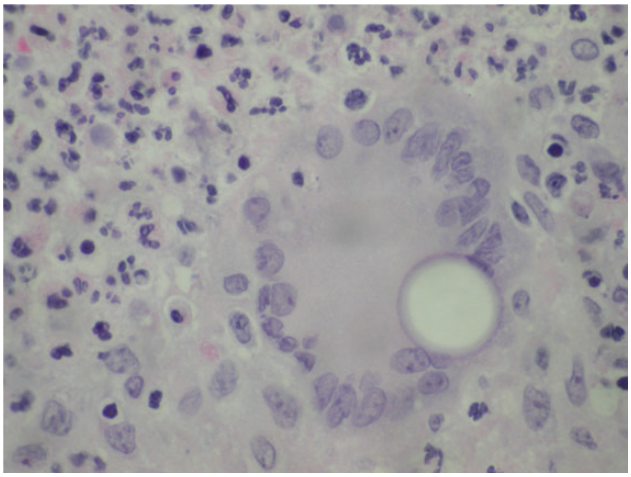
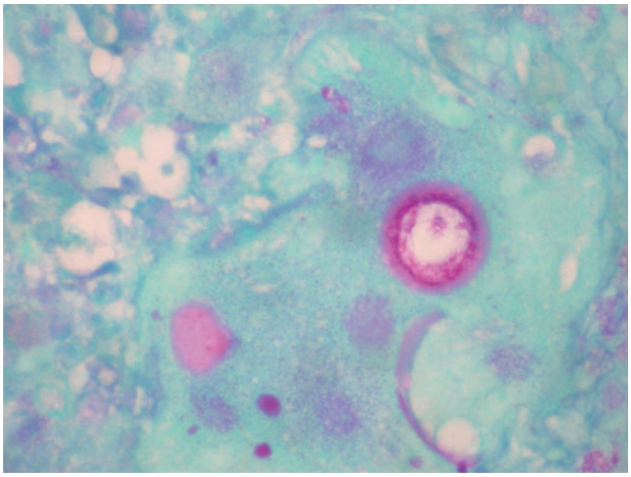
Background. *Coccidioides*, a dimorphic endemic fungus, primarily causes pulmonary disease but can disseminate to extrapulmonary sites. We describe a case of *Coccidioides* endocarditis, only the seventh ever reported.





A 34-year-old Hispanic woman presented to Kern Medical Center with Miliary Coccidioidomycosis in 2004. She had a complicated relapsing course including an anaphylactoid reaction to amphotericin. In early 2013 she presented with dyspnea and was found to be in heart failure secondary to aortic insufficiency. Echocardiography did not demonstrate a vegetation. Medical management failed at least in part due to poor adherence. She then presented to another institution where valve replacement was attempted but aborted secondary to mediastinal fibrosis. She was then transferred to Sequoia Hospital. On transfer, she was hypoxic and again found to be in heart failure. Aortic regurgitation was confirmed on echocardiogram but no vegetation was detected. 4 sets of blood cultures were negative. Chest CT showed a 3.5 cm by 2.0 cm soft tissue mass in the anterior mediastinum with possible paratracheal and periaortic adenopathy. In the operating room, she was again found to have a fibrotic mass adherent to the aorta and base of the heart, but no gross purulence. A successful aortic valve replacement was accomplished. Pathology of the aortic valve revealed granulomatous inflammation and a PAS stain with endosporulating spherules diagnostic of *Coccidioides* spp.

Culture of the native valve grew 1 colony identified by DNA probe as *Coccidioides* spp. Complement fixation titers were 1:8 with subsequent decrease to 1:2. The patient is doing well one year after surgery on Posaconazole liquid 400 mg every 12 hours.

Conclusion. *Coccidioides* very rarely causes endocarditis, vegetations may not be detected by echocardiography, but a successful outcome may be achieved with combined surgical and medical management.

Disclosures. **R. H. Johnson**, Astellas Pharma US: Speaker's Bureau, Speaker honorarium; Forest Phamaceuticals: Speaker's Bureau, Speaker honorarium; Pfizer Inc.: Investigator, Research support; Chevron: Grant Investigator, Grant recipient

931. A Prospective, Controlled Study of Multidrug-Resistant Organism Colonization among Healthcare Personnel

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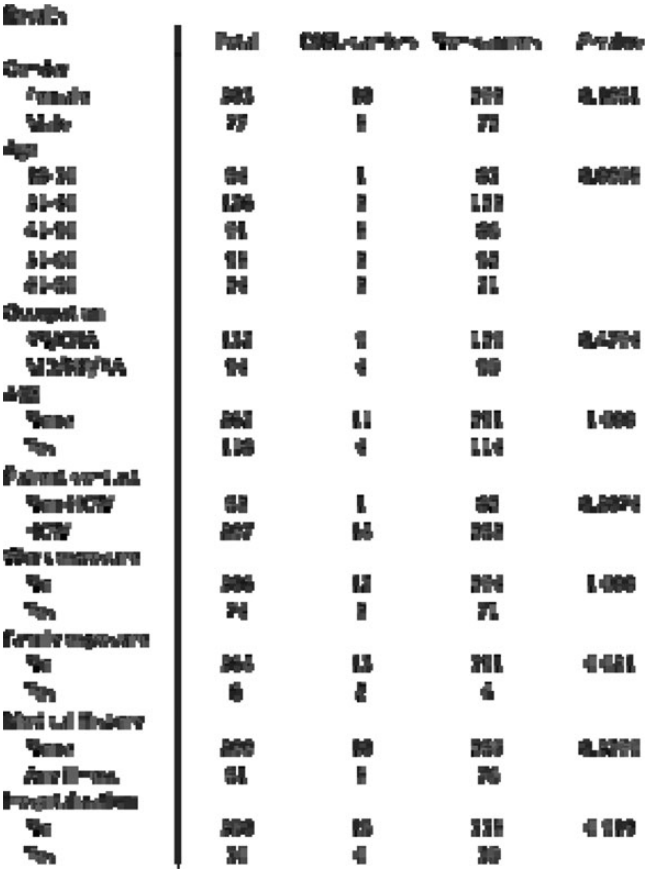
Background. Patients' healthcare-associated acquisition of multidrug-resistant organisms (MDRO) has been associated with prolonged hospitalization and antibiotic exposure. The role of healthcare provider intestinal colonization in disseminating MDROs is a source of concern, but remains unknown. Prior studies have evaluated healthcare personnel MDRO colonization in outbreak settings, but little is known about healthcare provider colonization in an endemic setting.



Methods. A convenience sample of healthcare and non-healthcare personnel employed at the National Institutes of Health voluntarily submitted two self-obtained perirectal swabs and a demographic survey assessing age, personal health, occupation, and occupational and family MDRO exposures. Swabs were processed using selective media by the Microbiology Service to detect vancomycin-resistant

enterococci (VRE ChromID), extended-spectrum b-lactamase organisms (ESBL CHROMagar), and carbapenem-resistant Enterobacteriaceae (KPC CHROMagar). Statistical analyses were performed using Fisher's exact test or chi-square test, as appropriate.

Results. 380 participants, including 297 healthcare personnel and 83 control subjects, submitted a survey and at least one swab. No participants reported a history of colonization or infection with VRE, ESBL, or CRE. Phenotypic ESBL organisms were detected in 15 individuals (3.9%; 14 healthcare professionals). No other MDROs were identified. ESBL colonization was not significantly associated with gender, underlying medical conditions, increasing age, occupation, use of antibiotics in the last 6 months, frequency of patient contact, or occupational exposure (Figure 1). ESBL colonization was significantly associated with self-reported ESBL colonization in a family member ($p = 0.02$).

Conclusion. At the midpoint of this study, we have found a small fraction of healthcare personnel and one control subject colonized with phenotypically ESBL-producing organisms. Despite frequent clinical detection among our patients, no VRE or CRE colonization has been detected. Healthcare provider colonization with an ESBL organism may be more closely associated with exposure to a colonized family member rather than with caring for colonized patients.

Disclosures. **A. F. Lau**, Bruker Corp: Collaborator, Research support **S. J. Blosser**, Bruker Corp: Collaborator, Research support **J. P. Dekker**, Bruker Corp: Collaborator, Research support **K. M. Frank**, Bruker Corp: Collaborator, Research support

932. Behaviors and attitudes towards Facial Protective Equipment (FPE) use among Healthcare Personnel (HCP) in the ResPECT study: Impact of study participation and a compliance education effort

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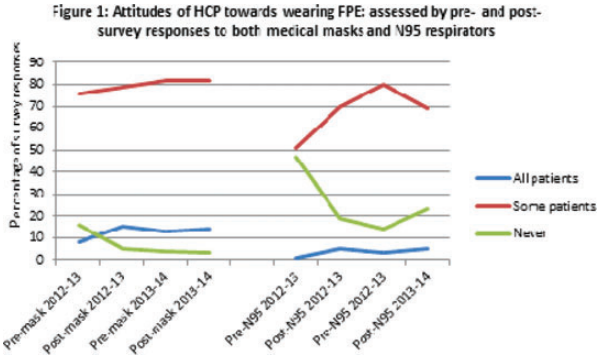
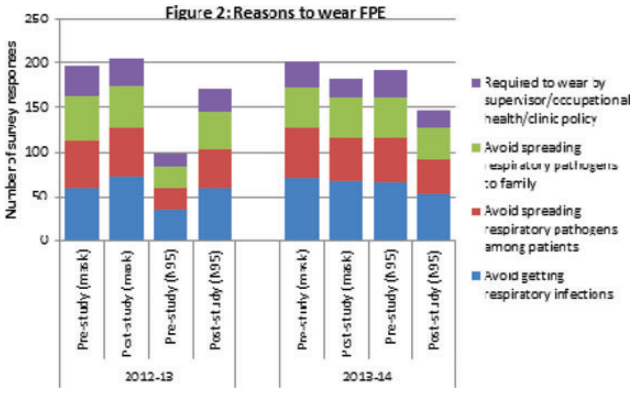
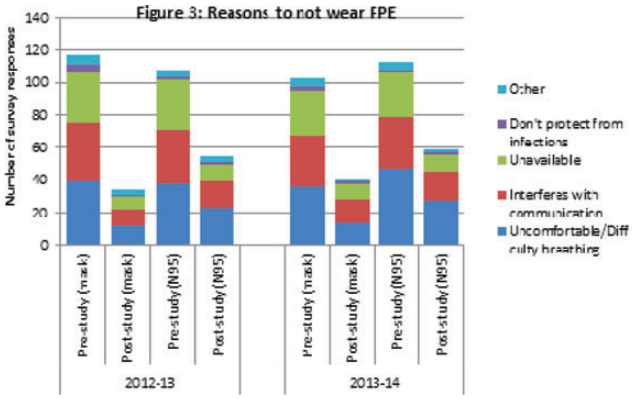
Background. Reasons for HCP non-compliance with FPE are complicated and may be related to their attitudes and beliefs. During the 2012-13 influenza season, we found that acceptance of FPE use improved among a cohort of study participants. Our aim is to evaluate if changes in attitudes and behavior were sustained and/or impacted further by participating the subsequent season; and the impact of an educational campaign at one of the seven study sites across the United States.

Methods. ResPECT is a cluster randomized clinical trial designed to compare the effectiveness of medical masks and N95 respirators for preventing acute respiratory illnesses (ARI) in outpatient HCP. During a 12-week peak period of influenza activity, participants wear FPE when within 6 feet of patients with ARI. Each season, all participants complete pre- and post-study surveys that include questions regarding attitudes and behaviors towards each FPE (regardless of study assignment). For the 2013-14 influenza season, at the Denver VA site, posters reminding staff to wear FPE were placed at vital sign stations, triage areas, nurse stations, staff offices and on electronic announcement boards.







Results. Of the 1388 participants in 2013-14, 606 (44%) also participated in 2012-13; the results are based on this subgroup. Based on pre- to post- survey analysis, during the 2012-13 season, the acceptance for FPE use significantly increased ($p < 0.0001$), was sustained during the off-study period (between the two seasons), but did not improve further during the 2013-14 season (Figure 1). During both study seasons, the most and least cited reasons "to wear FPE" were "to avoid getting respiratory infection" and "required to wear by supervisor/policy," respectively (Figure 2). The most cited reason "not to wear FPE" was "uncomfortable/difficulty breathing" (Figure 3). The educational campaign at the Denver VA did not affect the reported behaviors and attitudes of HCP towards wearing FPE.

Conclusion. The 2-year study participation did not significantly change HCP attitudes and behaviors, beyond what was observed after the first year. Not all changes were sustained during the off-season period. A poster based educational campaign had no impact on attitudes and behaviors towards FPE use.

Disclosures. **All authors:** No reported disclosures.

933. Between a Rock and a Hard Place: Why Physicians and Advanced Practice Providers Work While Sick

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Background. Hospital-acquired viral infections can lead to adverse patient outcomes including increased length of stay, delay of procedures, escalation of care and death. Healthcare personnel who provide care while ill can transmit viral infections to vulnerable patients. Little is known about why attending physicians and advanced practice providers (APPs) come to work sick.

Methods. We conducted an electronic, voluntary and anonymous survey of attending physicians and APPs, including nurse practitioners and physician assistants, working at a large children's hospital. The survey included closed- and open-ended questions. No incentives for participation were given. Quantitative data analyses were performed with Stata 13 and qualitative data analyses were performed via inductive coding of open-ended responses using NVivo 10.

Results. Of 459 attending physicians and 470 APPs surveyed, 280 (61%) attendings and 256 (54.4%) APPs responded. Working while ill was common: 444 (82.8%) respondents reported working sick ≥ 1 time in the past year, with 51 (9.5%) reporting working sick ≥ 5 times. Respondents reported working with significant symptoms including acute onset of substantial respiratory symptoms (n = 311; 58%), diarrhea (n = 161; 30%) and fever (n = 91; 16.9%). The majority of respondents (n = 512, 95.5%) believed that working while sick put patients at risk. Systematic qualitative analysis of open-ended responses from 316 respondents revealed reasons why attending physicians and APPs work while sick, including: the absence of a sick relief system and extreme difficulty finding coverage (n = 205; 64.8%); a strong cultural norm to come to work "unless you are dying" (n = 193; 61%); not wanting to let down patients (n = 181; 57.2%) and colleagues (n = 201; 63.6%); and the lack of clear guidelines about what constitutes "too sick to work" (n = 180, 56.9%).

Conclusion. The attending physicians and APPs we surveyed frequently work while sick, despite recognizing that this could put patients at risk. The decision to work while sick is shaped by both systems-level and sociocultural factors. Reducing presenteeism amongst attending physicians and APPs will require the development of robust coverage systems, a redefinition of "professional" behavior and high quality evidence that specifies when not to work while sick.

Disclosures. **All authors:** No reported disclosures.

934. Accidental Needle Sticks Due to Lidocaine Injections

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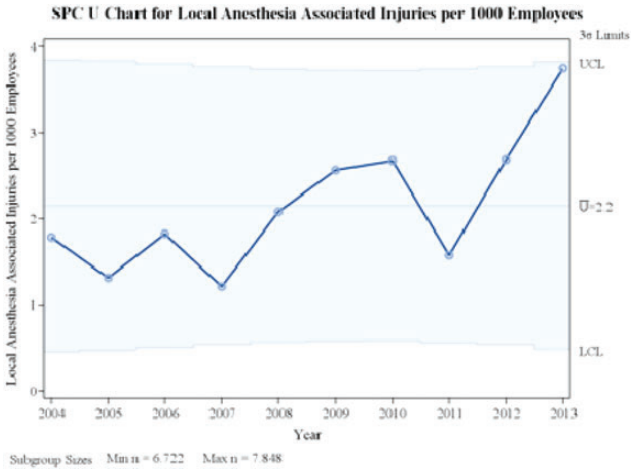
Background. Sharp exposures are a major risk for healthcare workers. Acute care hospitals are mandated to review all reported injuries and institute preventative measures. Routine surveillance suggested an increasing frequency of needlestick injuries in healthcare workers injecting local anesthesia; therefore, a comprehensive review was performed.



Incidence Rates/1,000 Employees

Year	Total Injuries	Local anesthesia associated injuries	Insulin needle injuries	Other hollow bore needle injuries	Suture needle injuries	Scalpel injuries	Other non hollow bore injuries	Unknown sharp injuries
2004	36.60	1.79	0.89	14.43	11.16	2.68	4.02	1.34
2005	34.89	1.31	0.58	15.18	9.93	2.04	4.67	1.17
2006	28.90	1.82	0.98	10.66	7.99	2.24	4.63	0.56
2007	28.97	1.21	1.35	11.05	7.55	2.29	4.85	0.67
2008	31.62	2.08	1.43	10.54	7.81	2.34	6.25	1.17
2009	30.78	2.57	1.41	9.36	9.36	2.69	3.98	1.41
2010	28.54	2.68	0.51	9.43	9.43	2.80	2.55	1.15
2011	27.97	1.57	0.79	7.62	9.59	3.81	4.46	0.13
2012	27.27	2.69	0.54	8.33	7.78	2.28	4.84	0.81
2013	27.09	3.75	0.58	7.64	8.64	2.31	3.17	1.01

Methods. All needlestick injuries at UMass Memorial Medical Center, an academic medical center, for the years 2004 through 2013 were collected, and rates of injuries per 1,000 employees were calculated. Descriptive statistics, test of trend, and U statistical process control charts were used to describe the sharps injury incidence rate over time.

Results. The rate and number of both total sharps injuries and non-insulin and non-local anesthesia associated hollow bore needlestick injuries per year showed statistically significant decreasing trends for the period 2004 to 2013 ($p < 0.0033$; $p < 0.0002$). In contrast, the incidence of local anesthesia associated injuries demonstrated a statistically significant increasing trend over time ($p < 0.0167$)(figure). There were no significant changes in the rates of other sharps injuries.

Conclusion. Over a 10 year period the rate of local anesthesia associated needle stick injuries increased at our institution as the overall rate of sharps injuries decreased. This trend may be related to persistent unsafe practices, as practitioners frequently perform repeat injections with the same needle when administering local anesthesia. Further investigation of this issue is warranted.

Disclosures. **All authors:** No reported disclosures.

935. Barriers to Acceptance of latent *Mycobacterium tuberculosis* Infection (LTBI) Treatment among Physicians at an Urban Tertiary Care Medical Center in Philadelphia

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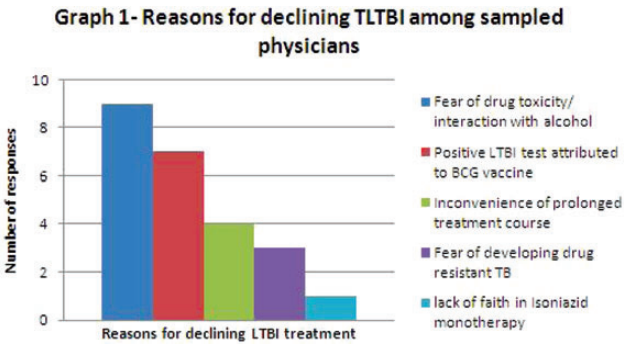
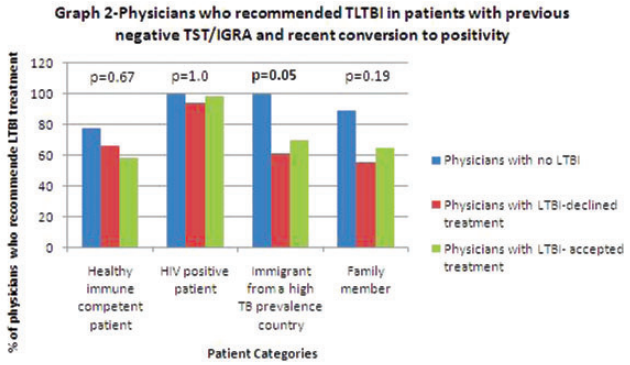
Background. Identification and treatment of latent tuberculosis infection (TLTBI) is the cornerstone of the U.S TB control strategy. LTBI treatment rates between 8 and 80% have been reported in physicians. We aimed to determine TLTBI rates, barriers to accepting TLTBI, and prescribing TLTBI among internal medicine physicians at a tertiary care hospital in Philadelphia.

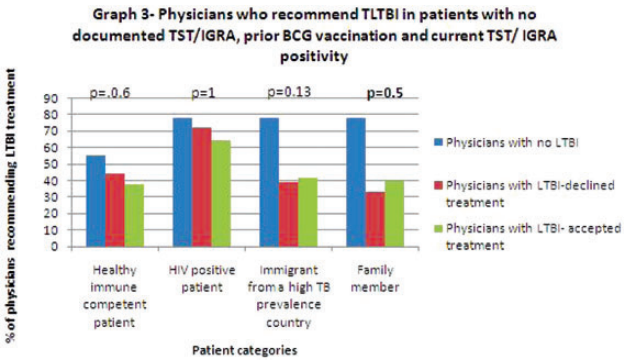
Methods. An online questionnaire including demographic information, tuberculin skin test (TST)/Interferon gamma release assay (IGRA) status, and LTBI treatment status was distributed to internal medicine residents, subspecialty fellows and faculty. Responses to hypothetical scenarios involving decisions to treat LTBI were collected. Data was analyzed using Stata 13. Fisher's exact test and Spearman's correlation were used for comparative statistics.





Results. Of 75 participants, 64%, 26% and 9% were residents, faculty and fellows respectively. 56 % had trained in regions with high rates of TB; 60% had received BCG vaccination. None of the respondents had been diagnosed with active TB. 36% of respondents had been diagnosed with LTBI 33% of whom started TLTBI. 2 failed to complete treatment owing to drug toxicity. 50% of respondents declined TLTBI owing to fear of drug toxicity and interaction with alcohol. Other reasons

for declining treatment are shown in Graph 1. Acceptance of TLTBI was associated with increased likelihood of recommending TLTBI in 2 of 8 hypothetical clinical scenarios (Graph 2, 3).



Conclusion. It is concerning that 36% of physicians sampled were diagnosed with LTBI and only a third of them accepted treatment. The main reasons for declining TLTBI were fear of drug toxicity, interaction with alcohol and the false perception that remote BCG vaccination influenced TST/IGRA results. Awareness of newer therapy such as the 12 dose Isoniazid/ Rifapentine regimen could result in higher acceptance rates of TLTBI. Although there was no clear correlation between physicians' willingness to accept, and recommend TLTBI, a larger study could prove this association. These results raise serious questions about physicians' attitudes towards TLTBI. It is important for physicians to be aware of current guidelines and strong indications for TLTBI to ensure national TB control.

Disclosures. **All authors:** No reported disclosures.

936. Tolerability, Adherence and Completion of New Occupational HIV Post-Exposure Prophylaxis Regimens (Tenofovir + Emtricitabine and Raltegravir)

Izona Bock, MD[1,2]; Uriel Felsen, MD[1,2]; Michela Catalano, MD[3,4]; Susan Hacker, MD[4]; Barry Zingman, MD[1,2]; [1]Infectious Diseases, Montefiore Medical Center, Bronx, NY; [2]Infectious Diseases, Albert Einstein College of Medicine, Bronx, NY; [3]Occupational Health, Albert Einstein College of Medicine, Bronx, NY; [4]Occupational Health, Montefiore Medical Center, Bronx, NY

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Background. Several studies suggest that HIV acquisition can be reduced significantly with antiretroviral post-exposure prophylaxis (PEP). Recently the recommended occupational HIV PEP regimen was changed by CDC and New York State Department of Health to tenofovir + emtricitabine and raltegravir (TNF/FTC/RAL), principally to lessen side effects and simplify regimen choices. Studies of TNF/FTC/RAL in non-occupational PEP have shown the regimen to be well tolerated and better completed, but there are no studies to date in an occupational setting. The goal of this study is to compare the newly recommended occupational HIV PEP regimen to prior regimens in terms of tolerability, adherence, and completion rates in exposed healthcare workers.

Methods. In this retrospective case control study, we reviewed the charts of 160 employees at risk for HIV infection due to occupational exposure at Montefiore Medical Center in the Bronx NY from 2007-2013. We assessed risk of the exposure, initial PEP regimen, changes in regimen, rates of completion, costs, and side effects due to medications.

Results. Of the 160 employees, 153 had initial and follow-up information. Of these, 93 initially started on zidovudine + lamivudine and lopinavir/ritonavir (ZDV/3TC/LPV) were compared to 48 initially started on TNF/FTC/RAL. 40 of 93 (43%) of those in the ZDV/3TC/LPV group completed 4 weeks of therapy vs 31 of 48 (65%) of those in the TNF/FTC/RAL group ($p = 0.015$). 68 of 93 (73%) of employees receiving ZDV/3TC/LPV reported side effects, compared to 27 of 48 (56%) of those receiving TNF/FTC/RAL ($p = 0.043$). Further analyses will be presented at the meeting.

Conclusion. Employees receiving tenofovir + emtricitabine and raltegravir for occupational HIV post-exposure prophylaxis were more likely to complete the recommended 4 week course of therapy, and reported fewer side effects than those who received the prior recommended regimen of zidovudine + lamivudine and lopinavir/ritonavir. Tenofovir + emtricitabine and raltegravir appears to be superior to older regimens in key parameters critical to the success of occupational PEP programs.

Disclosures. **All authors:** No reported disclosures.

937. Tuberculosis and HIV infection in health workers in the Maputo Central Hospital, the national reference hospital of Mozambique

Susannah K. Graves, MD[1]; Catarina David, MD[2]; Sofia Viegas[3]; Orvalho Augusto MD[4]; Anila Hassane, MD[5]; Philip Lederer, MD[1]; Kristen Lee, MD[1]; Salma Amade, MD[2]; Susete Peleve, MD[2]; Elizabete A. Nunes, MD, PhD[5]; Francesca Torriani, MD[6]; [1]Internal Medicine, University of California San Diego, San Diego, CA; [2]Internal Medicine, Maputo Central Hospital, Maputo, Mozambique; [3]Mozambique Tuberculosis Reference Laboratories, Maputo, Mozambique; [4]Biostatistics, National Institute of Health, Maputo, Mozambique; [5]Maputo Central Hospital, Maputo, Mozambique; [6]Division of Infectious Diseases, University of California San Diego, La Jolla, CA

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Background. In Mozambican hospitals, HIV drives transmission of tuberculosis (TB). This study employs active case finding along with latent TB infection (LTBI) and HIV screening to identify health workers (HW) at high risk for active TB.

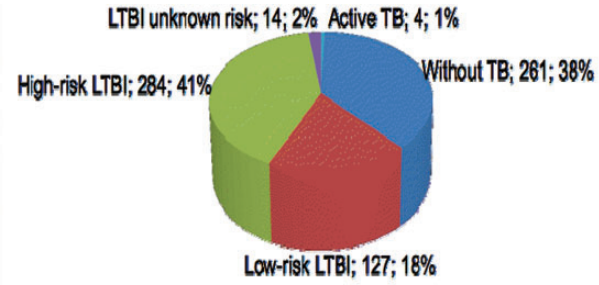


Figure 1. TB infection status and classification of screened participants (total n=690, data shown as n; %). High-risk LTBI defined as: HIV+ with TST ≥ 5mm, OR HIV- with TST ≥ 15mm AND QFT ≥ 1.0; Low-risk LTBI defined as HIV+ with TST < 5mm, OR HIV- with TST between 10-14mm OR QTF between 0.35-1.0.

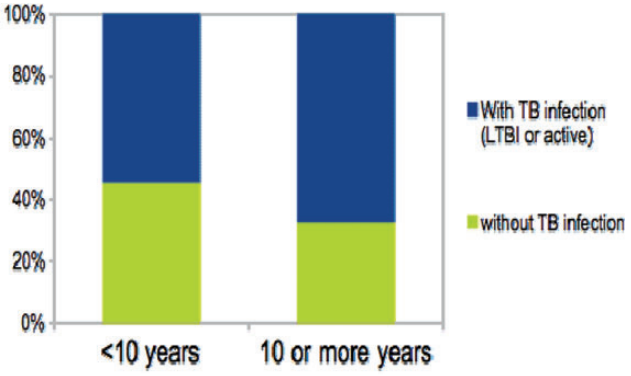
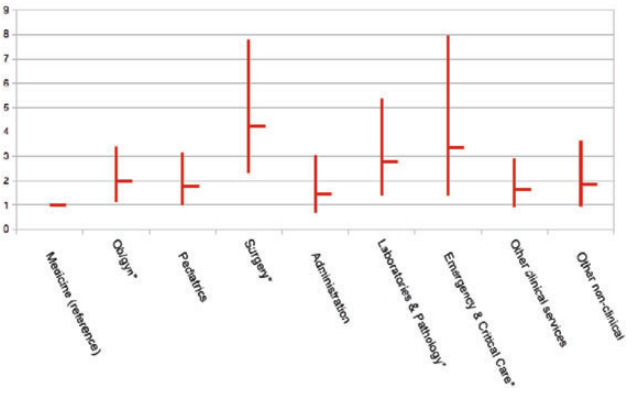


Figure 2. Percentage of those without and with TB infection categorized by years of hospital service at MCH (OR 1.67; 95% CI 1.21 – 2.30).



Methods. HW at Maputo Central Hospital (MCH) completed a symptom screen, chest X-ray, tuberculin skin- (TST), HIV- and Quantiferon TB-gold (QFT) testing. Sputum samples for acid-fast smear, mycobacterial culture and GeneXpert were solicited from symptomatic patients and those with suspicious X-ray findings. A logistic multivariate analysis with adjusted odds ratios is reported.

Results. In 690 enrolled HW, 4 cases of active TB were diagnosed. 425 (62%) LTBI cases were identified, 284 (67%) were classified as high-risk LTBI (Figure 1), 186 are on INH preventive therapy. 12% of HW were HIV+ with no significant difference between those with and without TB infection including LTBI (p = 0.3). The TST had a positive predictive value for QFT positivity of 82% in HIV+ individuals (95% CI 63 – 94) which did not differ significantly in HIV- individuals (79%, 95%CI 74 – 84). In the multivariate analysis, duration of service at MCH had a significant impact on LTBI (Figure 2) as did department of service (Figure 3).

Conclusion. Active and latent TB prevalence was high among HW at MCH. Furthermore, workers in several departments are at significantly higher risk of LTBI suggesting specific occupational risk, and indicating good targets for intervention including implementation of "FAST" (Finding TB cases Actively, Separating safely, Treating effectively). Follow-up is planned to evaluate the incidence of LTBI, active TB, and adherence to isoniazid preventive therapy.

Disclosures. **All authors:** No reported disclosures.

938. Identification of High Risk Healthcare Workers with Latent Tuberculosis Infection (LTBI) in an Inner City Healthcare System

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Background. Currently the CDC recommends the use of Interferon-Gamma Release Assays (IGRAs) as an alternative to tuberculin skin tests (TSTs) in the diagnosis of *M. tuberculosis* infection. IGRAs are typically preferred in persons who have received BCG or with poor rates of follow up evaluation. Additional situations where IGRAs may be useful include those in which increased sensitivity is indicated (such as a negative TST in someone at high risk, healthcare workers (HCWs) who have been told they have a history of latent tuberculosis (LTBI)), or to increase acceptance and adherence to treatment guidelines (in cases of foreign-born HCWs who believe their positive test is a result of BCG).

Methods. A retrospective review of IGRA results done at Detroit Medical Center (DMC) HCWs was conducted from March 2013 to March 2014. During the period, 6,138 T-Spot TB test results were obtained (4,631 employees, 343 staff and 1164 commercial clients, contractors, volunteers, students). Epidemiologic data on these HCWs was abstracted and their IGRA results compared with prior diagnosis of LTBI (defined as a prior TST result or on the basis of LTBI by history).

Results. T-Spot testing revealed 5,815 negative (94.7%), 249 positive (4.1%), and 74 invalid or borderline (1.2%) values. Prior latent TB infection (LTBI) status was known for 3,478. Of these persons, 732 (21.0%) had previously been determined to have LTBI (110 positive TST and 622 by history of LTBI), whereas only 214 (6.2%) tested positive on the T-Spot. When prior TSTs were negative (n = 2746), the T-Spot was negative 98.9% of the time. However, when prior LTBI history was positive (n = 732), the T-Spot was positive only 25% of the time.

Conclusion. T-Spot testing is very specific in identification of HCW with LTBI. Chemoprophylaxis, when based on TST results or a history of LTBI would be recommended three times more frequently than when based on T-Spot results. The use of IGRA testing may help identify HCW with a history of LTBI who are most likely to benefit from treatment for LTBI.

Disclosures. **All authors:** No reported disclosures.

939. Electronic Mail (email) Reminders as an Alternative to Directly Observed Therapy (DOT) for the Treatment of Latent Tuberculosis Infection (LTBI) using 12 weeks of Rifapentine and INH (R plus I) for Healthcare Workers (HCWs)

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Background. HCWs with LTBI are encouraged to be treated. Obstacles to the initiation and completion of treatment include concerns about the duration (especially 9 months of INH) and about side effects. With the aim of reducing the impact of these issues, MSK introduced the newly endorsed 12-week regimen of once weekly R plus I in January 2013 for HCWs. Additionally, email reminders, urine color checks, and feedback about compliance from MSK's pharmacy were utilized in lieu of DOT.

Methods. Since January 2013, MSK HCWs with LTBI were counseled on 3 available treatment options (INH alone, rifampin alone, or R plus I). Those HCWs who opted for R plus I, were instructed to take the medications every Wednesday for 12 weeks. Email reminders were sent every Tuesday during the treatment period. Complete blood count (CBC), liver function tests (LFTs), and urine color was checked during monthly follow-up visits on Thursdays. Dates of all prescription dispensing were confirmed at MSK's pharmacy. Upon completing treatment, HCWs were asked to complete a post-treatment survey. The study was registered with the MSK IRB.

Results. 26 HCWs with LTBI opted for R plus I and all completed the course. The treatment was well tolerated with no significantly abnormal LFTs and few CBC abnormalities (one patient with mild leukopenia and mild thrombocytopenia and another with mild eosinophilia). Urine was collected starting July 2013 from 16 individuals (48 specimens). 46 urine specimens were orange and 2 specimens were normal (straw) colored. One HCW had run out of medications before the follow-up visit and the other completed treatment a week prior to the scheduled appointment.

26 HCWs responded to the survey, and 100% of responders reported that the email reminders helped them to remember to take the medications. 20 of 26 respondents indicated that the reminders prompted them to take their medications at some point. The MSK pharmacy confirmed that all prescriptions were filled in a timely manner.

Conclusion. Overall the 12-week regimen of R plus I was well tolerated. These findings suggest that in a controlled setting with highly motivated HCWs, email reminders may be an effective alternative to DOT. This may lead to higher acceptance and completion rates of LTBI treatment among HCWs

Disclosures. **All authors:** No reported disclosures.

940. Universal Antibody Screening and Vaccination for Controlling Varicella among Health Care Workers: A 5-year Experience in A tertiary Hospital

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Background. Varicella-zoster virus (VZV) is highly infectious with potential to cause nosocomial outbreaks and healthcare workers (HCWs) are at risk. Universal serological investigation was seldom performed and effectiveness of varicella vaccination was unknown among HCWs.

Methods. All employees of Changhua Christian Hospital (CCH), Changhua, Taiwan, were tested for anti-VZV antibodies and seronegative staffs were advised to be vaccinated against varicella since May 2008 to December 2013.

Results. A total of 6,625 HCWs were investigated the varicella serostatus; the overall seroprevalence rate was 89.0%. A total of 731 HCWs were tested seronegative, including 303(4.5%) with equivocal and 428(6.5%) with negative results. The compliance rate to varicella vaccination was 62.9% and seroconversion rates were 98.6% and 68.1% in HCWs with equivocal or negative results respectively. Factors including younger age, female sex, higher level of pre-vaccination antibodies were associated with seroconversion for HCWs with negative result. In multivariate analysis, the pre-vaccination antibodies level (odds ratio (OR), 2431.0 [95% confidence interval (CI), 254.0 ~ 116112.6], p = 0.000) and new employees (OR, 4.39, [95% CI, 1.47 ~ 13.11], p = 0.008) predicted higher seroconversion rates. After the implementation of vaccination program, the annual incidence of varicella of HCWs improved from 2.0 to 0.4 per 1,000 person-years.

Conclusion. This study revealed great effectiveness of varicella vaccination in preventing and controlling varicella among HCWs. The result also helped to guide the development of a policy of varicella screening and immunization among HCWs especially for the consideration of cost-effectiveness.

Disclosures. **All authors:** No reported disclosures.

941. Concurrent exposure to drug-resistant *Staphylococcus aureus,* influenza A virus, and hepatitis E virus among industrial hog operation workers

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Background. In the US, there is growing evidence that industrial-scale livestock production is a reservoir of exposure to antimicrobial resistant bacteria, including *S. aureus,* and emerging viruses, including influenza and hepatitis E virus (HEV). The public health implications of multi-pathogen exposures at the human-animal interface have not been fully evaluated. We aimed to actively surveil industrial hog operation (IHO) workers to fill critical knowledge gaps about concurrence of exposure to drug-resistant *S. aureus*, influenza A virus, and HEV.

Methods. 22 IHO workers collected 316 nasal swabs before and after an IHO work shift over 7 days and again 14 days after enrollment. Swabs were cultured for *S. aureus* presence and assessed for multidrug-resistance (MDR = resistance to >2 antimicrobial drug classes), tetracycline-resistance (antimicrobial additive to livestock feed), clonal complex (CC), and absence of the *scn* gene (marker of livestock association). Influenza A virus matrix gene and hepatitis E virus (HEV) RNA per nasal swab were estimated by qPCR.

Results. Influenza A virus matrix gene RNA was detected in 10/208 nasal swabs from 8/22 workers. Of the eight workers carrying influenza A virus, six were persistent and two were intermittent *S. aureus* carriers. Four of the eight carried MDRSA and one persistently carried methicillin-resistant *S. aureus* (MRSA) that was also MDR. All eight workers carrying influenza virus also carried HEV in ≥ 1 other nasal swab. Two workers concurrently carried influenza A virus and HEV (1 swab each) – one was a persistent MDR-MRSA carrier and both were carriers of tetracycline-resistant, MDR, CC398, *scn* negative *S. aureus* (livestock-associated clones).

Conclusion. Concurrent exposure to influenza A virus and HEV among individuals who persistently carry drug-resistant, livestock-associated *S. aureus*, MRSA and MDR *S. aureus*, has important public health implications. Future active surveillance is warranted at the human-animal interface and should assess risks of broader transmission (from work into the home and community) as well as the infectivity and pandemic potential of zoonotic pathogen strains.

Disclosures. **All authors:** No reported disclosures.

942. How Do Hospitals Detect Outbreaks?

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Background. Prevention and containment of hospital-associated outbreaks require timely identification, investigation, and response to infectious clusters that could represent transmission within healthcare facilities.

Methods. We designed a 20-question survey to explore current hospital outbreak detection practices. Surveys were distributed to a convenience sample of infection prevention programs at 30 hospitals.

Results. Surveys were returned from 26 geographically diverse facilities representing teaching (12), community (13) or long term acute care (1) hospitals with a mean bed size of 471, 198, and 230 respectively. Most (73%) were completed by a respondent with 5+ years of experience in infection control and prevention. Although 22 (85%) hospitals kept a log of possible clusters or outbreaks, only 4 (15%) had a specified definition of a cluster or outbreak. For all hospitals, outbreak detection methods were limited to a narrow set of mostly antibiotic-resistant pathogens. Despite this narrow focus, 54% of the programs reported that they were confident or very confident that all clusters were being identified by their current methods. Overall, 62% of the programs reported satisfaction with their current outbreak detection practices, although nearly all of the programs (96%) reported that they felt that an automated outbreak detection system for hospital-associated pathogens would improve the comprehensiveness of their infection prevention program.

Conclusion. Of a convenience sample of 26 hospitals, 85% did not have a formal definition of what constituted a cluster or outbreak. Current detection methods heavily rely upon temporal or spatial clustering of a limited number of pre-specified pathogens. Despite the fact that half of the hospitals were confident that all clusters were being identified, 96% of them reported that an automated outbreak detection system could improve their current practice.

Disclosures. **All authors:** No reported disclosures.

943. Prospective evaluation of a cluster of *Pseudomonas aeruginosa* isolates identified by automated statistical software

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Background. Traditionally, nosocomial outbreaks are identified by reports from healthcare workers or review of microbiologic data. While these methods uncover the most egregious instances of nosocomial transmission, they are ultimately crude and insensitive. To improve upon the current state of outbreak detection we implemented a system which combines automated surveillance, epidemiological investigation and strain typing. In the present work, we report our initial experience with prospective assessment of a cluster of an important nosocomial pathogen identified by automated surveillance.

Methods. The WHONET-SaTScan cluster detection tool was used to identify clusters of *Pseudomonas aeruginosa* in clinical cultures between January 2013-February 2014. Simulated, prospective surveillance using the space-time permutation model was used to detect temporal clusters of unique isolates by patient on the same hospital unit with a maximum cluster length of 60 days. A cut-off value of $p = 0.05$ was used to identify clusters compared to a 1-year baseline incidence. Two evaluators independently assessed each cluster by analyzing records of patient movements and the antibiogram of the isolates. Isolates from a plausible cluster were analyzed by multilocus sequence typing (MLST).

Results. Epidemiological investigation indicated that nosocomial transmission was unlikely in 20 of 21 clusters identified by automated statistical surveillance. One epidemiologically plausible cluster of three isolates was not identified by routine surveillance. Genotyping of this cluster and control isolates from the same unit and a second unit showed a different sequence type for each isolate tested.

Conclusion. Prospective use of automated statistical surveillance identified clusters of potential transmission missed by standard approaches, and the application of investigative tools including strain typing ruled out recent transmission in an otherwise plausible cluster. This methodology is practical and may allow focused use of infection control measures targeted at interrupting transmission.

Disclosures. **All authors:** No reported disclosures.

944. Outbreak of Colistin-Resistant *Acinetobacter baumannii* in Intensive Care Units in Detroit, Michigan

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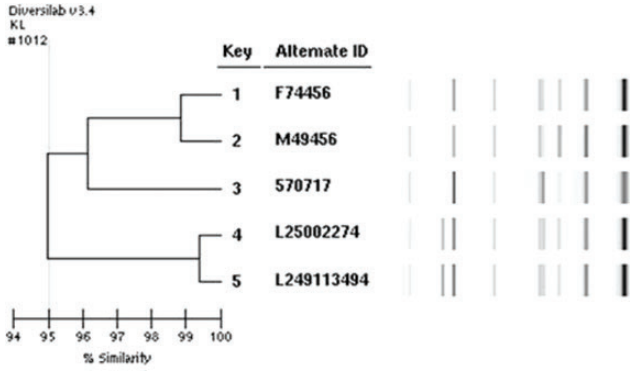
Background. *A. baumannii* is commonly recognized as an emerging multi-drug resistant (MDR) organism frequently impervious to majority of the commonly prescribed antibiotics. Colistin is one of the few therapeutic agents which possess activity against this pathogen, and its use has dramatically increased. As a result, colistin resistance is increasingly reported among *A. baumannii* and presents a unique challenge.

Methods. A cluster of colistin-resistant *A. baumannii* cases at Detroit Receiving Hospital were identified from May 1, 2013 to October 31, 2013. Colistin resistance was defined as an MIC of >2 μg/ml (E-test). Epidemiologic data for these cases were collected and isolates assayed for clonality with Diversilab rep-PCR and multi-locus sequence typing (ST).

Results. 11 cases were identified. The mean age of the patients was 48.8 years (range 17-76) and 10 (91%) resided in one of two intensive care units. All patients were treated with broad spectrum antimicrobials (but not colistin) prior to isolation of the colistin-resistant isolate. 9 (82%) patients were mechanically ventilated and the pathogen was detected from sputum specimen in 8 (73%) of patients. Other features frequently identified in these cases were the use of glucometer (73%) and tube feeds (82%). Colistin MIC ranged from 3-32. Environmental surveillance cultures were performed, but only one specimen was positive for the same organism. Genotyping was performed on 5 patient isolates which revealed 95% similarity between strains (figure) and all isolates were ST281. In order to contain the outbreak, optimal infection prevention practices were reinforced, active surveillance screening of high risk patients implemented, with presumptive contact isolation.



Genotype results

Conclusion. To our knowledge this is the first reported outbreak of colistin-resistant *A. baumannii* in United States. The hands of healthcare workers and environmental reservoirs are hypothesized to be the source of the outbreak. We observed a wide range of colistin MICs among outbreak strains, possibly due to 1) the emergence of heteroresistance or 2) differences in the population structure. A case-control study will help to further help delineate the cause of the outbreak.

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NIH: Grant Investigator, Grant recipient; VA Merit Review: Grant Investigator, Grant recipient

945. Outbreak of *Salmonella* Enteritidis Bloodstream Infections in a Nursing Home, New York, 2013

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Background. *Salmonella* Enteritidis (SE) is a common cause of gastrointestinal (GI) illnesses; bloodstream infections (BSI) infrequently develop. From February–December 2013, the New York State Department of Health (NYSDOH) and New York City Department of Health and Mental Hygiene (NYCDOHMH) investigated an outbreak of five SE BSI in a single nursing home (Facility A) in New York City. Epidemiologic assistance from the Centers for Disease Control and Prevention (Epi-Aid) was requested to characterize the outbreak, define the scope, and prevent additional illnesses.

Methods. A case was defined as infection with SE in Facility A residents or staff, with illness onset between August 1, 2012 and January 27, 2014. A study was conducted to assess risk factors for SE infection amongst case-patients and matched control-residents with overlapping residence dates at Facility A. Case-finding included review of infection control logs for GI illness and comparing the Facility A census to NYSDOH/NYCDOHMH reported SE infections. Environmental samples and stool specimens from residents and staff were cultured for *Salmonella*.

Results. No additional SE cases or unexplained increase in GI illnesses were identified during the field investigation. Of the five SE BSI case-patients, 4 (80%) died. Of two case-patients with stool cultures, none yielded *Salmonella*. Any GI symptom (OR: 16; 95% confidence interval: 1.6–788) and residence in a 4-bed room (OR: 6.7; CI: 1.1–75.5) were more common in case-patients than control-residents. Stool cultures from 36 residents, 84 food-handlers, and 4 staff did not yield *Salmonella* spp. No environmental samples yielded *Salmonella*, although 9/27 patient-areas (33%) revealed fecal bacterial contamination.

Conclusion. Invasive infection in 100% of case-patients with the absence of focal GI outbreak suggests that an unidentified healthcare-associated exposure is likely responsible. Enhanced environmental cleaning and improved access to hand hygiene products may prevent future infections.

Disclosures. **All authors:** No reported disclosures.

946. An Outbreak with Multidrug-Resistant *Klebsiella pneumoniae* Associated with Endoscopic Retrograde Cholangiopancreatography

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Background. Between December 6, 2012 and January 10, 2013, Carbapenem-resistant K. pneumonia (CRKP) was cultured from 5 patients staying on the nephrological ICU (ward A) in a 3.095 bed tertiary hospital. A multiplex PCR testing for Carbapenemase genes yielded a positive result for Oxa-48. Four weeks after the last CRKP was detected on ward A, additional 5 cases of Oxa-48-CRKP emerged on different locations of the hospital - three patients in a haemato-oncological unit (ward B), one patient in a surgical ICU (ward C) and one further patient in anaesthesiological ICU (ward D).

Methods. An outbreak investigation starts with record reviews, environmental testing and typing of pathogens.

Results. As 4 patients (1 from ward A, 1 from ward B and the 2 single patients from wards C and D) underwent duodenoscopy for ERCP, the endoscopy records were reviewed. Reviewing the endoscopy records revealed that the same duodenoscope had been used for these 4 CRKP patients. The review of the endoscope records identified 22 additional patients who underwent ERCP with the respective duodenoscope, of which 19 were still available for rectal screening. From 2 of these patients, CRKP were recovered from the rectal swabs. The environment of the endoscopy unit was sampled, as were all duodenoscopes of the unit. The flushing solutions and the swabs from the respective duodenoscope grew no CRKP, nor did the samples from the other duodenoscopes or the environment of the endoscopy unit. Only enterococci were cultured from the flushing solution of one of the other duodenoscopes as an indicator of an insufficient reprocessing process. Typing of the 12 CRKP strains (5 from ward A, 3 from ward B and the 4 patients with ERCP) revealed that all of them were closely related (in AFLP and PFGE). Apart from the ERCP procedure using the same duodenoscope, the review of the medical records did not develop any further linkage between the patients from wards A and B and the four single CRKP cases.

Conclusion. In this outbreak of CRKP, 6 of 12 CRKP cases occurred after the patients underwent an ERCP procedure using the same duodenoscope. Accurate and stringent reprocessing of endoscopic instruments is extremely important, which is especially true for more complex instruments like the duodenoscope involved in the outbreak described here.

Disclosures. **All authors:** No reported disclosures.

947. Pseudo-outbreak of Carbapenemase producing *Enterobacteraciae* (CRE) in a low prevalence acute-care hospital

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Background. Carbapenemase producing *enterobacteraciae* (CREs) are an emerging problem. The CDC recommends CRE control plans based on prevalence of CRE in a facility. Our facility is low prevalence for CRE in a state with recently introduced mandatory reporting.

Methods. A patient was admitted from another facility with CRE urinary tract infection. A second patient on the same unit grew CRE from urine with an identical resistance antibiogram. The second patient had no risk factors for CRE. An outbreak investigation was initiated. A prevalence survey for CRE was performed on all patients on the unit using rectal swabs. Staff were educated in order to answer any patient questions or concerns. Swabs were sent to Quest Laboratories for plating on a new CHROMagar CRE plate.

Results. All 22 patients on the inpatient unit underwent screening including the two patients with CRE initially identified from urine clinical cultures. No patients refused screening. Presumptive positive results were identified by growth on the CRE CHROMagar for 3 patients, as well as one of two patients with initially positive urine cultures. The three additional patients identified by screening were notified of these results and placed on Contact Precautions. However, the final identification of these 3 isolates by Vitek found them to be Stenotrophomonas and Pseudomonas species, and not CRE despite growth on the CRE plate. CRE designations were removed and patients re-educated with the updated results. The second patient had a repeat urine culture that did not grow CRE, despite no intervening treatment. In summary, of 5 patients who were thought to have CRE in this pseudo-outbreak, only one patient with CRE on admission was finally identified as positive.

Conclusion. Having a high index of suspicion for CRE in low prevalence settings carries a risk of false positive results. New CHROMagar methods of CRE detection must be interpreted carefully. As healthcare centers across the country develop strategies for identification and control of CRE, potential outbreaks will need to be approached with caution to minimize the impact on misidentified patients and to allay alarm among staff.

Disclosures. **All authors:** No reported disclosures.

948. Impact of active surveillance program to control VRE in a university hospital with low endemic rates

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Background. Several different strategies have been implemented to control VRE in hospitals outbreaks. From 2007 to 2009, a VRE outbreak in our hospital was controlled with: active surveillance of rectal swabs, isolation of colonized/infected patients, barrier precautions, and antibiotic policies. Since 2009 the same protocols have being continuously implemented. This study evaluated the impact of maintaining the protocols for reducing VRE colonization/infection from January 2010 to February 2014 compared to the data from 2007 to 2009.

Methods. In 2007, 2.3 VRE cases (colonized + infected) per 1,000 pts-days were identified. With the implementations of control measures, in 2008-09, the incidence of density (ID) decreased to 0.83 cases per 1,000 pts-days ($p<0.001$). This prospective study was conducted in a tertiary care university hospital performing active surveillance of rectal swabs, isolation and barrier precautions for VRE colonized/infected patients. Rectal swabs were screened for VRE in patients with > 7 days of hospitalization or when patients were transferred in

from other hospitals. The ID, incidence of new cases (colonized + infection) and infections for each biennium were evaluated and compared to the data from 2007-09. Statistical analyses were performed using Chi Square and exact Mid-P tests.

Results. 4,993 rectal swabs were collect and from 2010-11 and 3,128 from 2012-14. During 2010-11 and 2012-14, 122 and 157 new cases were diagnosed respectively; ID were 0.48 and 0.55 new cases per 1,000 patient-days and the incidence of new cases per 1,000 admission were 4.13 and 4.84. A significant decrease in the incidence of new cases from 2007-09 to 2010-11 (6.98 vs0.48; $p < 0.001$) and in the ID (0.83 vs 0.48; $p < 0.001$) was observed. No differences were noted in the incidence of infections (0.43 vs 0.34; $p = 0.17$) in the two periods. No differences were observed in 2012-14 compared to the other periods.

Conclusion. The significant reduction in the incidence of new cases of VRE after the control of the first epidemic period (2007-09) suggested that the strategies implemented to control the VRE outbreak, in our hospital, should be maintained to keep endemic rates low.

Disclosures. **All authors:** No reported disclosures.

949. A Cluster of Catheter-Related Bloodstream Infection due to Rapidly Growing Non-Tuberculous Mycobacteria in Patients with Hematologic Disorders at a Japanese Tertiary Care Center; an outbreak investigation and review of the literature

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Background. Increasing use of the central venous catheter has become associated with catheter-related bloodstream infection due to rapidly growing non-tuberculous mycobacteria, especially in immunocompromised patients. We identified an outbreak of central venous catheter-related bloodstream infection due to *Mycobacterium mucobgenicum and Mycobatereium canariasense* among patients with hematologic disorders during a 5-month period.

Methods. An outbreak investigation and infection control protocol were performed at a hematology ward at a Japanese tertiary care center. We conducted a retrospective chart review and environmental investigation to identify the source of rapidly growing non-tuberculous mycobacteria and patients' outcome.

Results. A total of five patients with bloodstream infection due to rapidly growing non-tuberculous mycobacteria were identified: three patients with acute myeloid leukemia, and one patient with acute lymphocytic leukemia developed a blood culture positive for *M. mucogenicum*. In addition one patient with aplastic anemia developed a blood culture positive for *M. canariasense*. The majority of patients received cord blood transplantation prior to developing bloodstream infection. All central venous catheters in patients with bloodstream infection due to *mycobacterium* spp. were removed. These patients promptly defervesced after catheter removal and were successfully managed without antimicrobial therapy. With extensive environmental examination, *M. mucogenicum* and *M. canariasense*were subsequently identified from water supplies in the hematology ward. We confirmed identification of the isolates from the bloodstream infection and environmental sources based on 16SrRNA gene sequencing.

Conclusion. The source of rapidly growing non-tubeculous mycobacteria in outbreak of bloodstream infection likely stemmed from the hematology ward tap water supply. Awareness of emerging catheter-related bloodstream infection due to *mycobacterium* spp. should be emphasized, especially in immunocompromised patients and treatment strategies should continue to be discussed.

Disclosures. **All authors:** No reported disclosures.

950. An Outbreak of Invasive Fusariosis in a Children's Cancer Hospital

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Background. *Fusarium* is considered an emerging pathogen and there are few reports of fusariosis in children. The objective of this study was to describe an outbreak of invasive fusariosis in a children's cancer hospital.

Methods. The outbreak occurred in a Children's Cancer Hospital with 15 beds. A neutropenic 17-year-old male hospitalized for 10 days for a relapse of acute myeloid leukemia, under chemotherapy, presented fever without any other symptoms; a thoracic computerized tomography showed bilateral pulmonary nodules. During voriconazole treatment, 1-cm, reddened and painful subcutaneous nodules appeared on arms and legs and the culture of a skin biopsy revealed *F.solani*. Another case occurred 11 days later and started an outbreak investigation. Water samples for cultures were collected from taps, showers and water reservoirs. Air from all patient rooms was sampled. Faucets and the drains of sinks and showers were swabbed and cultured. Environmental and clinical isolates were typed.

Results. There were 10 confirmed cases of infection caused by *Fusarium* spp. and 12 suspected cases. *F. oxysporum* and *F. solani* were isolated from water, swabs and air in patient rooms. Many control measures were instituted but the outbreak was only controlled one year after the first case, when water filters filtering 0.2 µm were installed at the exit of all faucets and showers in all patient rooms (points-of-use). Typing demonstrated that clinical isolates of *F. oxysporum* were similar to those of the environment.

Conclusion. To our knowledge this is the first reported outbreak of invasive fusariosis in children with onco-hematologic disease. It was controlled using 0.2 µm filters in all tap faucets and showers.

Disclosures. **All authors:** No reported disclosures.

951. Outbreak of Mixed fungemia in a Children's Hospital in the United States

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Background. *Candida pelliculosa* is a rare cause of infection in hospitalized patients. Outbreaks caused by *Candida parapsilosis* have been described in the literature. We report the first outbreak of *C. pelliculosa* fungemia in 5 children in the United States. The first three of these children had a mixed fungemia with *C. pelliculosa* and *C. parapsilosis*.

Methods. From June 2013 to January 2014, 5 patients with *C. pelliculosa* fungemia were identified in our hospital, the first 3 of whom had a mixed fungemia with *C. parapsilosis*. To confirm the outbreak, the *C. parapsilosis* isolates underwent molecular typing using a panel of 5 multilocus microsatellite markers. The *C. parapsilosis* isolates were genotyped using a published microsatellite type protocol. The *C. pelliculosa* isolates were genotyped using newly developed multilocus sequence typing of 5 different genes. Chart reviews were done on all patients admitted to the relevant unit within 6 days of each case's infection date. The proportions of select medications during the same time period were compared between the 5 cases and the remaining patient pool.

Results. Four cases occurred within 56 day period. The fifth case occurred 203 days after the fourth case. Two cases died. All 5 cases were admitted in the intensive care unit (ICU) (1 in the neonatal ICU and 4 in the pediatric ICU). Three cases were male and the median age was 293 days (range 10-369 days). Total Parenteral Nutrition (TPN) use was significantly higher in cases (5/5; 100%) when compared with controls (52/164; 31.7%); this difference was statistically significant ($p = .004$). The results of the genotyping data for the 3 *C. parapsilosis* isolates and the 5 *C. pelliculosa* isolates showed that the isolates from the patients were identical to one another and different from unrelated control isolates, suggesting a clonal origin.

Conclusion. The genotyping analysis of the *C. parapsilosis* and *C. pelliculosa* isolates confirmed identity of the strains and suggested an outbreak. TPN use was a risk factor and a possible source of infection. Environmental cultures may aid in identification of the point source. To our knowledge, this is the first reported outbreak of *C. pelliculosa* fungemia in children from the United States.

Disclosures. **All authors:** No reported disclosures.

952. An Outbreak of Hepatitis C Virus Associated with Alleged Narcotic Diversion

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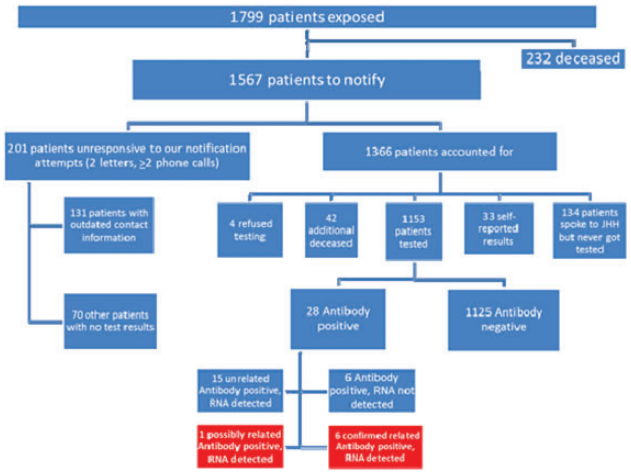
Background. In July 2012, investigators linked a series of hepatitis C virus (HCV) infections in New Hampshire to a healthcare worker (HCW) with HCV. Personnel records revealed that the HCW worked in the Cardiovascular Interventional Laboratory (CVIL) at Johns Hopkins Hospital (JHH), prompting an outbreak investigation.

Methods. Patients were considered exposed if they had a CVIL procedure during the period in which the HCW worked in CVIL. Patients were divided into risk groups based on degree of exposure the HCW had to the patient: direct care of patient, assigned to same room, assigned to adjacent room, and all other patients with procedures during period (indirect).

Patients were notified via certified letters and phone calls. Serologic testing was utilized to determine the presence of HCV infection, and direct sequencing and phylogenetic analysis with local controls was used to confirm the relatedness of infections.

Results. 1799 patients were potentially exposed, of whom 1525 patients were alive and 1324 patients were successfully contacted (86.8%) (figure). 1153 patients were tested for HCV. Twenty eight patients had the presence of HCV antibody (2.4%), 22 of whom had HCV RNA detected, indicating current HCV infection. Six patients with HCV genotype 1b infections were confirmed to be related to the exposure (0.52%) (table). One additional case was possibly related, but the sample could not be amplified sufficiently for confirmation. Five related cases had direct exposure, one related case had adjacent room exposure, and one possibly related case had indirect exposure.



Summary of Response and Testing Activities

Exposure Risks of Patients

	All Tested Patients (n=1153)	Related Cases (n=6)
Exposure Category		
Direct	12.4% (n=143)	83.3% (n=5)
Same Room	11.2% (n=129)	0.00% (n=0)
Adjacent Room	20.3% (n=234)	16.7% (n=1)
Indirect	56.1% (n=647)	0.00% (n=0)

Conclusion. The results of this large outbreak investigation and notification support the importance of using broad exposure criteria rather than only investigating patients with direct exposure, and demonstrate the importance of maintaining accurate records in order to minimize loss to follow up. Despite the tendency of HCV to evolve, molecular typing techniques confirmed relatedness among strains of HCV years after initial infection.

Disclosures. **All authors:** No reported disclosures.

953. Using Statistical-Derived Incubation Period Estimation in an Outbreak Investigation of Influenza A (H1N1) pdm09 in Operating Room Staff

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Background. Influenza A (H1N1) pdm09 was one of strains circulating in Thailand in early 2014. We reported using statistical-derived incubation period (IP) estimation to investigate an outbreak of influenza in our operating room (OR) staff from February 1 to April 1, 2014.

Methods. After 4 cases of influenza A infection were detected, cases of influenza-like illness (ILI) were actively identified in operating areas among staff. We confirmed the infection by using EIA or RT-PCT technique. All cases were interviewed and data were used to develop a timeline, geographic distribution and other potential risks for influenza acquisition. We applied the median IP of 1.4 days with dispersion of 1.51 days for each case and estimated probability of places where these staff acquired the infection.

Results. Among 82 OR staff, 18 cases (22%) of ILI were detected. Of these, 11 cases were confirmed as influenza A (H1N1). The 3 index cases were identified and based on modeling, the time period that they shared was linked to the highest probability of acquiring disease. They attended a 2-day class that was held before the OR outbreak started. We interviewed all 22 attendees and found the source case who had ILI during that class.

Conclusion. Using statistical-derived IP estimation model was very helpful to investigate influenza infection that had a short IP in areas where molecular epidemiology was not routinely used and sometimes unavailable. The model was useful in making transmission map of the outbreak, to detect the source case, and to identify patients who could acquire the illness from HCP. Such models have potential to guide interventions in settings with limited resources.

Disclosures. **All authors:** No reported disclosures.

954. Can Instituting Enhanced Measures (EM) during Influenza Season Reduce Healthcare Associated Influenza Infections (HAIIs)

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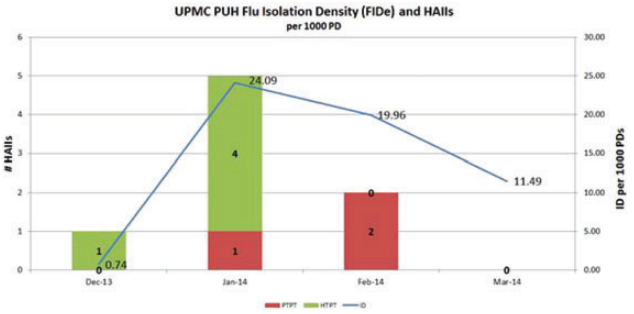
Background. Influenza is a respiratory illness caused by influenza virus and is spread from person to person. Influenza can be a life threatening infection and often leads to prolonged illness and hospitalization. UPMC Presbyterian (PUH) is a tertiary care hospital comprised of 158 ICU, 584 Med/Surg and 20 Rehab beds for a total of 762 licensed beds with a notably large immune compromised patient population (transplant). During flu season, ~20 influenza patients are cared for daily which includes care for those who require extracorporeal membrane oxygenation (ECMO). Since 2008 ≤3 HAII were identified annually except in 2010/2011. That year there were 13 HAIIs, all H1N1. By January 2014, 7 HAIIs (H1N1) were identified. All but 2 had no evidence of patient to patient transmission (PTPT). Because of a concern for healthcare personnel (HCP) to patient transmission (HTPT) enhanced measures (EM) were implemented. The objective of this study was to evaluate the effect of the EM on HAII secondary to HTPT.



Methods. On January 31, 2014, prescribed interventions were developed based on local and national epidemiologic indicators. Influenza Critical Time Period was defined as national Flu positivity ≥ 25% and Pneumonia and Influenza Mortality ≥15% above predicted. EMs included:

- Empiric HCP masking for high-risk (transplant) patients and/or high risk units until discharge
- Encourage HCP flu immunization

HAIIs defined by CDC criteria and categorized as PTPT or presumed HTPT. Flu isolation density (FIDe) was measured monthly and defined as flu isolation days (FIDs)/patient days (PDs). FIDs were determined using Theradoc software and PDs were extracted from our electronic medical record. % HCP flu immunized was calculated.

Results. Despite continued high FIDe in February 2014 they were no HTPT and only 1 PTPT HAII. Overall vaccination rates did not change over the time period (78% → 78.4%) and so was not likely a contributor to decreased HAIIs. HCP empiric masking for high-risk populations was associated with eliminated HTPT HAIIs.

Conclusion. Both HCP and patients can be exposed/infected with flu and may transmit disease to others. EM such as HCP empiric masking can prevent HAIIs

regardless of the influenza isolation density. FIDe can be high during Influenza critical time period.

Disclosures. **All authors:** No reported disclosures.

955. An Outbreak Investigation of Influenza among Healthcare Personnel (HCP) in a Tertiary Care Hospital, Bangkok, 2014

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Background. Thailand's 2014 influenza season occurred between January and April. The circulating influenza strains were A (H1N1) pdm09, A (H3N2) and B; all were included in the country's available vaccine. We report an outbreak investigation and describe factors determining disease acquisition, vaccine efficacy and patient impact.

Methods. After 4 cases of influenza among HCP were simultaneously identified, we actively looked for influenza-like illness (ILI) among HCP in 4 departments and triage areas. ILI was defined as fever (≥38°C), and cough and/or sore throat (in the absence of a known cause other than influenza). Influenza infections were confirmed by EIA or RT-PCR technique. A case-control study was undertaken to identify risk factors for acquiring influenza in all staff of these areas. HCP who did not have ILI were used as controls in the study. Medical records of the patients cared for by staff were reviewed. Patients, not admitted were called by infection preventionists to determine if they had developed an ILI.

Results. Forty-five cases were identified among 167 HCP (27%) between February 1 and April 1, 2014. Among these 45, 16 cases (36%) were confirmed with influenza, 13 cases for influenza A and 3 cases for influenza B. There was no difference in attack rate between cases and controls based on gender (male 40% vs 39.3%, OR 1.03, $p = 0.94$), predisposing medical conditions (22.2% vs 18.8%, OR 1.23, $p = 0.63$), or vaccination rate (73.3% vs 66.4%, OR 1.39, $p = 0.39$). Staff who worked in clinical areas had higher risk of acquiring influenza (86.7% vs 66.39%, OR 3.29, $p = 0.01$). We identified a subgroup of patients exposed to HCP with influenza who had operations during the outbreak. Sixty-one cases were contacted and we were able to contact 55 cases (90.2%). We visited 21 cases, reviewed 12 medical records and made 22 phone calls. No ILIs were identified among these patients. After infection control strategies were implemented, 2 more cases were detected within 2 days. No more additional cases were identified after these cases.

Conclusion. Early detection of influenza in HCP is an important component of infection prevention strategies. Strictly adherence to these practices can effectively control outbreaks. While, our numbers were small and we could not measure the impact of vaccine compliance, we still encourage all HCP to be vaccinated.

Disclosures. **All authors:** No reported disclosures.

956. Management of a respiratory outbreak due to concomitantly circulating influenza A and parainfluenza 1 in a residential care facility

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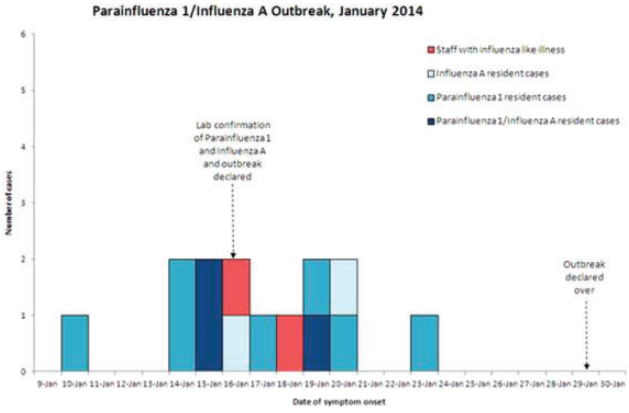
Background. Respiratory viruses are common causes of outbreaks in residential care. Multiplex PCR assays for respiratory viruses enable the detection of multiple viruses, though the clinical significance of dual infections is unclear. We describe an outbreak of 2 respiratory viruses co-circulating in a residential care facility in Vancouver, Canada.

Methods. Outbreak investigation was conducted in a facility with 216 residents distributed among 3 separate units in January 2014. Cases were defined as any resident or staff with acute onset respiratory illness [fever (>38.0°C) and cough], and with at least one of the following: sore throat, nasal congestion, malaise, chills, muscle aches, headache or change in mental status. Affected patients were placed on contact and droplet precautions. Nasopharyngeal swabs were collected on symptomatic residents and tested using an in-house multiplex PCR assay (influenza A/B, respiratory syncytial virus, parainfluenza 1/2/3, adenovirus and human metapneumovirus). An epidemic curve of the outbreak was created.

Results. The outbreak persisted for 13 days. Twelve patients were infected, including 7 with parainfluenza 1, 2 with influenza A and 3 with parainfluenza 1/influenza A co-infection (figure). All patients manifesting respiratory symptoms were tested (12/28, 43%), rather than empirically treating subsequent patients meeting case definition. Treatment with oseltamivir was provided for 5 patients positive for influenza A, with all others receiving prophylaxis. Two staff developed upper respiratory tract symptoms and were considered cases. Outbreak management also included cessation of group activities, closure to admissions and enhanced unit cleaning. Influenza vaccination rates were 94% for residents and 83% for healthcare workers.



Conclusion. Routine testing using a multiplex PCR assay detected a respiratory outbreak involving single and co-infections. Two circulating viruses can affect outbreak management. In this outbreak, all symptomatic residents were tested and confirmed rather than empirically treated. In addition to accurate classification and management of cases, overall consumption of oseltamivir prophylaxis can be reduced by monitoring for the persistence of both viruses.

Disclosures. **All authors:** No reported disclosures.

957. Household Products with Triclosan and Triclocarban Reduce Infectious Disease Symptoms in Newborns - Preliminary Data from an Ongoing Randomized Trial.

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Background. Triclosan and triclocarban (TCs) are broad spectrum microbicides found in commercial household and personal cleaning products (HPCP). Effective against gingivitis, TCs have not been proven to protect against other infectious diseases. The FDA, which is reviewing TCs, has requested further information on their efficacy.

Methods. Stanford's Outcomes Research in Kids (STORK) is a rolling cohort of pregnant women and their babies followed to age 36 months. STORK includes a nested, randomized intervention of HPCP with and without TCs to assess the effect of TCs on reported infection. Mothers report daily infectious diseases symptoms in babies using a weekly survey. We compared cumulative infection rates (reported days sick/total days followed) in each intervention arm. Urinary triclosan levels were measured in a subset of 20 babies. Analyses were blinded to intervention arm; Chi-square test or quasi-Poisson regression were used as appropriate.

Results. A total of 119 babies have been born with 52 (43.7%) and 63 (52.9%) randomized to the TC and non-TC arms, respectively (4 were not randomized). As of April 2014, babies had been followed for a median of 48 weeks (range: 3-135 weeks). Breast feeding rates were similar in both arms ($p = 0.56$). The cumulative infection rate was different between arms (8.3% and 12.3% in the TC and non-TC arms, respectively; $p < 0.001$) as was the median infection rate (i.e., per baby) (4.4% vs 7.7%, $p = 0.07$). Among sick babies, the proportions of days of cold, cough, ear pulling/tugging, diarrhea and fever did not differ significantly between arms; the proportion of vomiting days was less in the TC arm (7.2 vs 11.1%, $p < 0.001$).

Urinary triclosan was detected in 7 (88%) of 8 breastfed babies in the TC arm (mean: 125 pg/ml). While these levels are lower than those seen in TC-using adults (data not shown), they are significantly higher ($p = 0.02$) than levels in non-breast fed babies in the TC arm ($N = 2$), babies in the non-TC arm ($N = 7$) and babies who were not randomized ($N = 3$) (19.4, 11.7 and 8.8 pg/ml).

Conclusion. In this preliminary analysis, residence in a household randomized to TC-containing HPCP is associated with a lower incidence of infectious disease symptoms in infants. Low levels of TC exposure in infants appear to derive from breastfeeding.

Disclosures. **All authors:** No reported disclosures.

958. *Streptococcus pneumoniae* Serotype 3 Invasive Infections in Children

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Background. Invasive pneumococcal infections (IPI) due to *Streptococcus pneumoniae* serotype (ST) 3 have not declined as dramatically in children as other vaccine STs since the introduction in 2010 of the 13-valent pneumococcal conjugate vaccine, PCV13. While persistence of ST 3 isolates is likely due to capsule characteristics, genotypes with greater fitness may also emerge. We analyzed molecular characteristics of *S. pneumoniae* ST 3 isolates that were obtained from children with IPI.

Methods. IPI cases at 8 children's hospitals in the United States were prospectively identified from 2008-2013. ST 3 isolates were selected from the associated database. Isolates were typed by multilocus sequence typing (MLST). Select patient information was analyzed and antibiotic susceptibility patterns were compared. Statistical analysis included Wilcoxon rank-sum and Fisher's exact tests.

Results. Sixty-three patients with 62 isolates were identified from the database (Table); 36 were male. Median age was 3.7y (0.1-17.6y). Disease presentations were pneumonia (n = 33), meningitis (n = 9), bacteremia (n = 7), mastoiditis (n = 6), cellulitis/abscess (n = 7), and peritonitis (n = 1). Twelve (19%) patients had an underlying condition. The MLSTs were 180 (n = 58), 260, 338, 433 and 1116. The MLST distribution did not change over time. All isolates were penicillin and ceftriaxone susceptible. Only 3 were resistant to erythromycin and 2 were resistant to clindamycin.

Characteristics of pediatric serotype 3 infections, 2008-2013

Year	Total invasive SPN	Serotype 3 (% of total)	MLST 180	Pneumonia (% of total serotype 3)	Mean Age (years)
2008	197	11 (6%)	11	8 (73%)	3.1
2009	219	22 (10%)	20	7 (32%)	5.6
2010	165	8 (5%)	7	5 (63%)	3.4
2011	128	5 (4%)	4	1 (20%)	6.2
2012	112	6 (5%)	5	4 (67%)	5.7
2013	104	11 (11%)	11	8 (73%)	6.2
Total	925	63	58	33	5.0

Conclusion. ST 3 isolates chiefly caused pneumonia in this patient population and were mainly MLST180. MLST distribution did not change following introduction of PCV13. No statistical differences in distribution, age, disease presentation, age or, antibiotic susceptibility were observed. A modified vaccine, potentially including noncapsular antigens, is likely required to optimally reduce IPI due to ST 3 in children.

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959. Epidemiology and Treatment of *Enterobacteriaceae* Bacteremia: Combination vs Monotherapy

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Background. Bacteremia due to *Entrobacteriaceae* gram-negative rods (GNR) can be life threatening. Appropriate antimicrobial therapy is critical to reduce morbidity and mortality.

Methods. A retrospective cohort study (2008-2011) was conducted in children and young adults (<21 years of age) hospitalized with *Entrobacteriaceae* bacteremia with clinical signs and symptoms. We assessed if combination antimicrobial therapy is superior to monotherapy in treatment of Klebsiella, Ecoli or Enterobacter bacteremia. Monotherapy was defined as empirical therapy with β lactam alone, and combination therapy as β lactam with aminoglycoside for at least 48 hrs. Multi drug resistant (MDR) GNR were defined as those organisms resistant to at least one agent in three or more antimicrobial categories. Clinical outcome was measured as response to therapy and 7- and 30-day mortality. Response to therapy, defined as time to negative blood culture, was compared among patients given monotherapy vs combination therapy.

Results. Of 289 episodes of *Entrobacteriaceae* GNR bacteremia, 79 (27%) were due to Klebsiella species, of which 11 (14%) were MDR; 73 (25%) due to Escherichia coli, of which 11 (15%) were MDR; and 53 (18%) due to Enterobacter, of which 13 (25%) were MDR, 48 (16%) were Salmonella, Citrobacter and others. Of the 203 episodes of bacteremia caused by the three organisms of interest, 101 (50%) were treated with combination therapy. Patients with cancer were more likely to receive combination therapy ($p < 0.001$), while patients with gastrointestinal disease and those receiving total parenteral nutrition were more likely to receive monotherapy ($p = 0.006$ and $p = 0.013$, respectively). There were no differences in time to negative blood culture based on treatment group, organism or resistance pattern. The mean time to negative blood culture was 3 days (SD = 1.1 days). There was no significant difference in 7- and 30-day mortality between monotherapy and combination therapy group.

Conclusion. Combination therapy consisting of β lactam and aminoglycoside was not superior to mono-therapy with β lactam alone for managing *Entrobacteriaceae* GNR bacteremia in children and young adults.

Disclosures. **All authors:** No reported disclosures.

960. The Molecular Characterization of Extended-Spectrum Beta-Lactamase (ESBL) and Carbapenem- Resistant *Enterobacteriaceae* (CRE) in Chicago Children, a two center study

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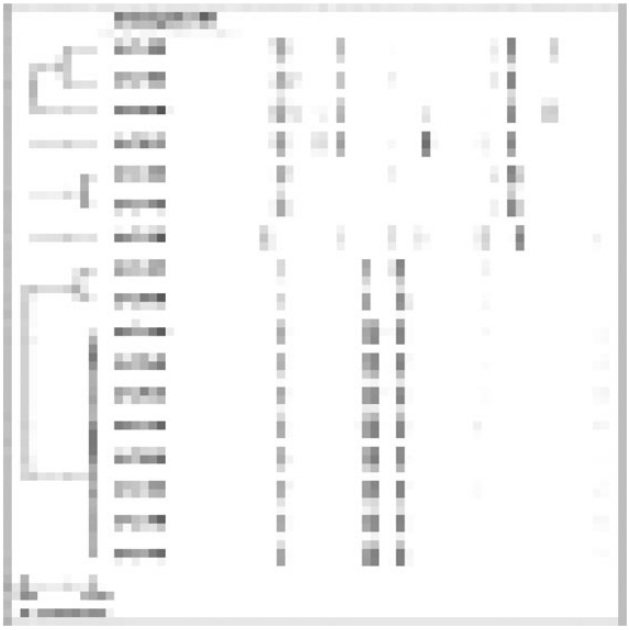
Background. The study objectives were to 1) determine the genetic basis of ESBL and CRE phenotypes in *Enterobacteriaceae* isolates from children in two medical centers; 2) determine genetic relatedness of dominant ESBL and CRE strains.

Methods. We conducted a retrospective cohort study of clinical gram-negative isolates obtained from children ages 0-17 years hospitalized between 2011-12 at Rush and Lurie Children's Hospitals. PCR amplification of b-lactamase (bla_{TEM}, bla_{SHV}, bla_{CTX-M}, bla_{KPC}) genes was performed using established primers and amplified under thermocycling conditions. Repetitive-sequence-based PCR (rep-PCR) was used to assess the similarity of strains. Multilocus sequence typing (MLST) and DNA sequencing was performed on representative isolates from rep-PCR strain types for bacterial nomenclature and characterization. Plasmid DNA was extracted from select isolates and transformed into electrocompetent *E. coli.*



Relatedness of E. coli

Results. Ninety-two isolates exhibited ESBL and/or CRE phenotypes. The predominant organism was *E. coli* 55/92 (59.8%) and predominant genotype was bla_{CTX-M} 37/92 (40.2%). Some isolates contained >1 *bla* gene. Rep-PCR performed on the 55 *E. coli* revealed a diverse group with the most predominant strain accounting for 8/55 (14.5%) isolates (Figure 1). MLST was performed on select *E. coli* (LC5, LC34, LC54) and *K. pneumoniae* (LC8 and LC77). LC34 represents the predominant *E. coli* strain by rep-PCR and LC54 was selected as an unrelated strain type. LC34 was ST43 (ST131 in Achtman's MLST scheme). DNA sequencing confirmed the *bla* as CTX-M-15. LC54 carrying bla_{TEM} was identified as ST3. LC5 and LC77 carried bla_{KPC}. ST types for LC5 and LC77 were ST29 and ST105 respectively and DNA sequencing confirmed presence of KPC-2 carbapenemase. DNA containing antibiotic resistance genes from LC5 (KPC-2) and LC34 (CTX-M-15) *E. coli* strains were successfully transferred suggesting plasmid-based origin.

Conclusion. ESBL and CRE in children are diverse in origin. *E. coli* carrying the bla_{CTX-M} gene are thought to be primarily community-acquired, whereas

dissemination of bla_{KPC} is traditionally in the healthcare setting. Like in adults, CTX-M is spread in *E.coli* ST131. In contrast, *K.pneumoniae* KPC bearing strains were non ST258, suggesting a different dissemination pattern than in adults.

Disclosures. **All authors:** No reported disclosures.

961. Reductions of Listeria Infections in Infants: Collateral benefit of Prophylaxis against Group B Streptococcus?

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Background. Ampicillin is included in antibiotic regimens for febrile infants due to concerns about Listeria. Several recent studies of febrile infants have not reported significant rates of Listeriosis and thus have raised questions about the continued need for ampicillin. It has been hypothesized that widespread prophylaxis against early onset Group B Streptococcus (GBS) has been a major contributor to this decrease, but as of yet, no direct evidence exists to support this. Our objective was to assess the changes in rates of Listeria in newborns over the past 20 years and to examine correlations with changes in GBS prophylaxis.

Methods. The Pediatric Health Information Systems (PHIS) database from 45 freestanding children's hospitals across the United States was used. We queried the database for all cases of Listeriosis (ICD9 code 027.0)in patients less than 30 days for the entire timespan of the database (1992-June 2013). We then assessed case rates per 10,000 patients using the total number of patients in that age cohort with data per year. We present incidence rate differences (RD), exact 95% confidence intervals and trend statistic p values.

Results. From 1992-2013, there were 182 cases of Listeria in infants less than 30 days of age. The median age of patients was 13 days (IQR 9, 15) and 53.9% were male. From 1992-1995, the average rate of Listeriosis in this age was 4.79 cases/10,000 patients. For 1996-2002, the rate dropped to 2.24 cases/10,000 (RD: -2.55 (-4.3, -.787), coinciding with implementation of the first published recommendations GBS prophylaxis. From 2003-2013, the rate dropped further to 1.41 cases/10,000 (RD -.83 (-1.5, -.179), coinciding with revision of those recommendations to universal culture-based screening. From 1992-mid 2013 cases of infant Listeria, overall trend statistic p-value was <.0001.

Conclusion. We observed decreases in rates of Listeriosis in infants less than 30 days over the last 20 years. These decreases clearly coincide with expansion of prophylaxis for early onset GBS disease. These results are the first to directly examine this correlation and further suggest that the need for ampicillin in febrile infants should no longer be driven by concerns for Listeria.

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

962. Recurrent Episodes of Stevens Johnson Syndrome (SJS): Clinical and Epidemiologic Characteristics

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Background. In the fall of 2013-2014, an outbreak of Stevens Johnson Syndrome (SJS) occurred among pediatric patients at a referral hospital in Colorado. During the outbreak investigation, 7 children were identified as having recurrent SJS, a rare condition.

Methods. Children with an ICD-9 diagnosis of SJS and meeting clinical criteria for SJS between March 2013 and March 2014 were included in the study. SJS clinical criteria were defined as an episode of acute illness with inflammation of 2 or more mucous membranes and consistent skin lesions. Incomplete SJS was defined as an episode with consistent rash and involvement of one mucus membrane, or involvement of 2 mucus membranes and no rash. Recurrent SJS was defined as an episode of SJS or incomplete SJS separated from any previous episodes by at least 1 month of symptom resolution.

Results. Seven children had 21 SJS or incomplete SJS episodes, with a median of 3 per child (range 2 to 4). All 7 children were male, 6 (86%) were Caucasian, and 4 (57%) had history of asthma. Nine oral mucositis only episodes were excluded from our analysis. Fourteen episodes (67%) met the clinical definition for SJS and 7 (33%) met the definition of incomplete SJS. Age during episodes ranged from 4 to 15 years. The median time between episodes was 15 months (range 48 days to 5.6 years). Two episodes were preceded by antibiotics and none by anticonvulsants. Eleven (52%) episodes had documented preceding upper respiratory symptoms and 4 (19%) had radiographic pneumonia. *Mycoplasma pneumoniae* was identified by throat PCR in 3 (50%) of 6 individuals tested and 4 (25%) of 16 episodes tested. Ten episodes were tested for HSV by throat/oral PCR and all were negative. No family history of SJS was reported. Steroids were given for 4 episodes and IVIG was given for 3 episodes. Three children (5 episodes) had ocular disease requiring temporary amniotic membrane grafts.

Conclusion. We report the largest case series of recurrent SJS. Recurrent SJS does not appear to be related to repeat use of offending medications. The clinical presentation of children with recurrent SJS varies between episodes and individuals. Possible hypotheses for recurrent SJS include a genetic or immunologic predisposition and recurrent *Mycoplasma pneumoniae* infections.

Disclosures. **All authors:** No reported disclosures.

963. Changes in Nasopharyngeal *Haemophilus influenzae* Colonization in Children 6 through 23 Months of Age at the Time of Diagnosis of an Episode of Acute Otitis Media (1999-2014)

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Background. Since the introduction of pneumococcal conjugate vaccines (PCV), a decrease in nasopharyngeal (NP) colonization with vaccine serotypes of *Streptococcus pneumoniae* (Spn) has been noted in children with acute otitis media (AOM). However, neither the overall prevalence of *S. pneumoniae*, nor the proportion of resistant strains has changed. Less is known about *Haemophilus influenzae* (Hflu) during this time frame. NP flora interact and compete; accordingly, we sought to describe changes in Hflu from our studies of young children with AOM spanning 15 years.

Methods. In 4 separate clinical trials carried out between 1999 and 2014, NP cultures were obtained from children aged 6-23 months presenting with a new episode of AOM. The first cohort was studied prior to the routine use of PCV7 (1999-2000). All children in cohorts 2 (2003-2005) and 3 (2006-2009) received ≥2 doses of PCV7. Children in cohort 4 (2012-2014) had at least 2 doses of PCV13. NP swabs were cultured for Spn and Hflu. Isolates of Hflu were tested for ß-lactamase production. ß-lactamase negative isolates of Hflu from cohorts 3 and 4 underwent MIC testing for ampicillin.

Results. A total of 887 children were evaluated in the 4 cohorts. NP colonization with Hflu was found in 26% of children in cohort 1 (pre-vaccine era; n = 175), 41% in cohort 2 (shortly after introduction of PCV7; n = 87), 33% in cohort 3 (n = 282) and 29% in cohort 4 (n = 343). Hflu colonization differed significantly between cohorts 1 and 2 (p = 0.01), then was followed by a decrease (p = 0.02 test for trend). Rates of ampicillin-resistance on the basis of ß-lactamase production were 27%, 36%, 33%, and 30% in each of the 4 cohorts, respectively. ß-lactamase negative Hflu with an MIC >1.0 were present in 1/62 isolates in cohort 3 and 4/65 isolates in cohort 4 (p = NS). Rates of Spn NP colonization for cohorts 1 through 4 were 49%, 38%, 50% and 50%, respectively. Rates of dual colonization with both Hflu and Spn were stable between 11% and 14%.

Conclusion. Rates of NP colonization with Hflu and ampicillin-resistance due to ß-lactamase production remained stable in the 4 cohorts. An initial increase in Hflu in cohort 2 suggested replacement of Spn after introduction of PCV7; however, this was followed by a decrease in Hflu colonization. Ongoing surveillance is needed.

Disclosures. **All authors:** No reported disclosures.

964. Seroepidemiology of Pediatric Pneumococcal Colonization and Infection Before and After 13-valent Pneumococcal Conjugate Vaccine (PCV13)

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Background. Routine heptavalent pneumococcal conjugate vaccine (PCV7) use since 2,000 changed serotype prevalence and antibiotic susceptibilities. In 2010, PCV13 added serotypes that emerged post-PCV7. We examined aspects of colonization, noninvasive disease, and invasive pneumococcal disease (IPD) in children during 3 years before and after PCV13 licensure.

Methods. To assess PCV13's impact, we analyzed clinical data and pneumococcal isolates from 2007 through 2013, excluding 2010 (transition year). This included demographic data, infection site, serotype by Quelling reaction and antimicrobial susceptibility.

Results. Overall, 709 pneumococcal isolates were serotyped. There was a marked decrease in pneumococcal cases following the introduction of PCV13. Of 453 isolates in 2007 through 2009 (pre-PCV13), 95 were colonizing, 216 noninvasive disease-related, and 142 IPD-related. Of 256 isolates in 2011 through 2013 (PCV13 era), 45 were colonizing (P = 0.05), 134 noninvasive disease-related (P = 0.03), and 77 IPD-related (P = 0.007). Predominant serotypes/serogroups were:

	Pre-PCV13			Post-PCV13			
Colonizing	23 (16%)	19A (15%)	6A (12%)	19A (16%)	23 (9%)	11 (9%)	3 (9%)
Noninvasive	19A (30%)	23 (8%)	6A (8%)	19A (13%)	23 (10%)	35 (10%)	15 (9%)
Invasive	19A (27%)	7 (18%)	33 (11%)	19A (14%)	3 (14%)	23 (12%)	15 (9%)

Pre-PCV13, 61% of IPD isolates were PCV13-related, whereas during the PCV13 era, 40% of IPD isolates were PCV13-related (P = 0.023). The average age of children with IPD pre-PCV13 was 43.5 months (range 1 week to 15.3

years) and it was 52.7 months (range 1 week to 16 years) for children with IPD in the post-PCV13 era. Central nervous system infections averaged 9.0 cases/year pre-PCV13, and 3.3 cases/year post-PCV13 (P = 0.05). An underlying medical condition was present in 32% of children with invasive disease in the pre-PCV13 era, and 43% of children in the post-PCV13 era (P = 0.14). Pre-PCV13, the distribution for highly susceptible, intermediate, and resistant organisms was 50.5%, 19.4%, and 30.1% respectively, whereas post-PCV13 the distribution was 69.4%, 20.5%, and 10.1% (P < 0.01).

Conclusion. There were significantly fewer pneumococci isolated in the post-PCV13 era, especially for cases of IPD. However, a sizable proportion of isolates, particularly IPD isolates, remain PCV13-related. There has been a considerable reduction in the proportion of penicillin-resistant isolated following the introduction of PCV13.

Disclosures. **D. Swanson**, Pfizer: Grant Investigator, Grant recipient **C. Harrison**, Pfizer: Investigator, Grant recipient; Forest Laboratories: Investigator, Grant recipient; GSK: Investigator, Grant recipient **C. Paap**, Pfizer Inc.: Employee and Shareholder, Salary **L. Puzniak**, Pfizer: Employee, Salary

965. Nosocomial MRSA Bacteremia in Children: Evidence for "Reverse Vancomycin Creep" and Limited Benefit of Elevated Vancomycin Serum Troughs

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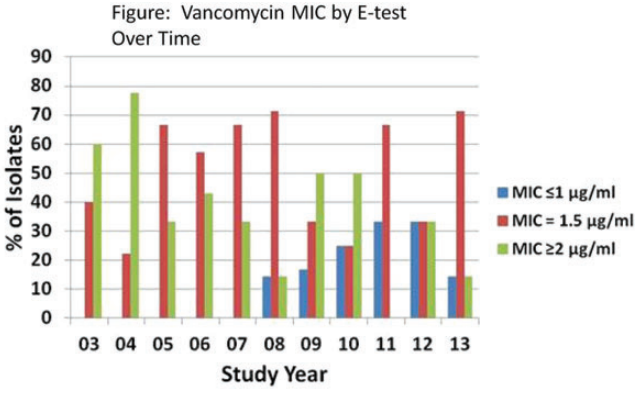
Background. Vancomycin is the most commonly used drug for the treatment of severe MRSA infections. Previous studies in adults with nosocomial infection have shown that vancomycin MICs have increased over time and that MIC > 1 μg/ml are associated with adverse outcomes. The IDSA recommends vancomycin goal trough levels 15-20 μg/ml in adults with severe MRSA infections. There are little data on these issues in children.

Methods. Isolates and patients with nosocomial MRSA bacteremia during the years 2003-2013 were identified from a prospective surveillance study. Vancomycin MICs were determined by E-test. Medical records were reviewed; acute kidney injury (AKI) was defined as a doubling of the baseline creatinine.



Results. During the study period there were 60 MRSA nosocomial bacteremias. 50% of MRSA isolates had a vancomycin MIC = 1.5 μg/ml and 38.3% with MIC= 2 μg/ml; no upward vancomycin creep was observed. The proportion of isolates with an MIC≥ 2 μg/ml decreased by 50% after 2008 (p = 0.03, Figure). The median age of patients was 4 months; the most common diagnosis was central-line associated bloodstream infection (CLA-BSI, 51.7%). The overall median duration of bacteremia was 2 days (IQR: 1-5). For patients without CLA-BSI, an MIC ≥2 μg/ml was associated with a longer duration of bacteremia (5 vs 2 days, p = 0.02). Increasing vancomycin troughs were not associated with a shorter duration of bacteremia; troughs ≥ 10 μg/ml were associated with a greater risk of AKI (44.4% vs 0%, p = 0.02). For patients with CLA-BSI, neither vancomycin MIC or serum trough influenced the duration of bacteremia; however, line removal after day 2 of bacteremia was associated with a longer duration of bacteremia (4 vs 1 day, p = 0.002).

Conclusion. Vancomycin MIC by E-test ≥2 μg/ml is associated with a delay in microbiologic cure in children with non-CLA-MRSA bacteremia. A decrease in vancomycin MICs in nosocomial MRSA bacteremia isolates was observed. For MRSA CLA-BSI, early line removal may have a greater therapeutic impact than either vancomycin MIC or serum trough. High vancomycin troughs were not associated with improved microbiologic outcomes in this population but with more AKI. Large studies are needed to further understand the impact of elevated vancomycin troughs on MRSA bacteremia in pediatrics.

Disclosures. **S. L. Kaplan**, Pfizer: Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient

966. Risk factors for colonization or infection with multi-drug resistant *Escherichia coli* in children

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Background. The recent increase in community-associated (CA) multidrug-resistant (MDR) *E. coli* has been well described in adults, but not in children. Accordingly, we sought to identify risk factors for infection or colonization with MDR *E. coli* in children.

Methods. We conducted a retrospective cohort study of children from birth through 18 years with *E. coli* cultured from extraintestinal specimens at our institution between January 1, 2012 to December 31, 2012. Clinical data were abstracted from medical records. Pansusceptible (PS) isolates were susceptible to all antibiotic classes, while MDR isolates were resistant to at least 3 different antibiotic classes, excluding ampicillin. Risk factors for MDR *E. coli* were determined using univariable and multivariable logistic regression.

Results. 368 children (mean age 8.3 years) each contributed 1 isolate. Most isolates were CA (82%), and from females (86%), outpatients (86%), and urine (90%). The distribution of resistance phenotypes was 53% PS, 35% resistant to various agents but not MDR, 13% MDR, and 3% resistant to extended spectrum cephalosporins.

In univariable analysis, features significantly associated with having an MDR strain were healthcare acquisition, cerebrospinal or genitourinary (GU) tract anomaly, invasive procedure within the prior 90 days, presence of an invasive device, history of international travel, hospitalization in the preceding year, and antibiotic use within the preceding 3 months. In multivariable analysis, GU tract anomaly (OR 3.87 [95% CI 1.49-10.07]), presence of an invasive device (OR 2.90 [95% CI 1.01 – 8.35]) and prior hospitalization (OR 2.57 [95% CI 1.17 – 5.66]) were significantly associated with MDR. Among the subset of patients with community-associated *E. coli* (n= 297), multivariable risk factors for MDR were GU tract anomaly (OR 5.53 [95%CI 1.57-19.51]), and hospitalization in the prior year (OR 2.83 [95%CI 1.12-7.18]).

Conclusion. In this cohort of children in the US Midwest, community-associated MDR *E. coli* was not common among healthy children, but was significantly associated with GU anomalies and prior hospitalization. Pediatric providers should be aware of these risk factors when prescribing empiric antimicrobial therapy for *E. coli*.

Disclosures. **All authors:** No reported disclosures.

968. Changes in Serotypes of Group B Streptococcus in Infants with Invasive Bacterial Infection in Korea; from 1994 to 2013

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Background. We examined the serotype distribution of Group B streptococcus (GBS) in infants with invasive bacterial infection over a 20-year period according to diagnoses, age of onset and time period.

Methods. GBS isolates previously obtained from infants with invasive GBS disease at Seoul National University Children's Hospital (1994-2013), Seoul National University Bundang Hospital (2003-2013) and Chonbuk National University Hospital (2001-2013) were serotyped by PCR. Clinical records were reviewed retrospectively.

Results. Among a total of 58 cases, 13 (22.8%) were early-onset disease (EOD, 0-6 days), 42 (73.7%) were late onset disease (LOD, 7-89 days) and 2 (3.5%) were late-late onset disease (LLOD, 90-180 days). Among EOD, bacteremia was the most common by 38.5%, followed by meningitis (23.1%), pneumonia (23.1%) and osteomyelitis or septic arthritis (15.4%). In LOD, meningitis was the most common by 52.4%, followed by bacteremia (42.9%) and osteomyelitis or septic arthritis (4.8%). Among 58 isolates, the predominant serotypes were III (43.1%), V (31%), Ia (13.8%) and Ib (10.3%). This distribution was the same for both EOD and LOD. According to disease, serotype III was the most common by 50% for meningitis and serotype V accounted for 44% in bacteremia. In the first 10 years (1994-2003) serotype III and V predominated (29.4%), followed with Ib (23.5%), Ia (11.8%) and VI (5.9%), and in the recent 10 years (2004-2013), serotype III predominated (48.8%) followed by V (31.7%), Ia (14.6%) and Ib (4.9%).

Conclusion. Among infants with invasive GBS disease in Korea, serotype III was the most common followed by serotype V. There was a change in serotype distribution over the years, however a majority of the isolates were serotypes Ia, Ib, III and V. A vaccine including serotypes Ia, Ib and III would show coverage for 67.2% and coverage would increase by 98.3% when including serotype V in Korea.

Disclosures. **H. J. Lee**, National Research Foundation of Korea: Investigator, Research grant

969. Macrolide resistant mycoplasma did not have worse clinical course in children's hospital in Japan

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Background. In 2,000, macrolide resistant *M pneumoniae*was reported among Japanese children. It was gradually increased up to 50% by 2012. Little is known regarding to its clinical entity in pediatric patients at children's hospital. The objective was to evaluate clinical characteristics of macrolide-resistant mycoplasma pneumonia in children.

Methods. Children with mycoplasma pneumonia were recruited from March 2011 to March 2014 at Tokyo Metropolitan Children's Medical Center. Mycoplasma pneumonia was diagnosed with presence of chest X ray infiltration and detection of *M pneumoniae*gene by a loop-mediated isothermal amplification assay in throat swab or sputum. Macrolide resistance gene for 23S ribosome mutation was tested by PCR. Charts were reviewed and compared for clinical characteristics between macrolide susceptible and resistant group.

Results. Forty two children with mycoplasma pneumonia were identified. Girls and boys were 26 and 16, respectively. Macrolide resistant group (MR group) tend to be older than macrolide susceptible group (MS group), but the difference lacked statistical significance (100.5 months vs 85.7 months; $p = 0.390$). Macrolide resistant was detected in 35 cases (83.3%). Only one of MS group required intensive care. Average febrile days of MR group were significantly longer than those of macrolide susceptible group (8.9 days vs 4.5 days, $p = 0.004$). Hospital stay periods in MR group were not longer than MS group (7.0 days vs 7.1 days, $p = 0.943$). Duration of oxygen demand in MR group did not differ from susceptible group (6.8 days vs 7. 0 days, $p = 0.806$).

Conclusion. Although macrolide resistant mycoplasma pneumonia was found in 83.3%, it might be selection bias of referral hospital. Macrolide resistant *M pneumoniae* was associated with prolonged fever. However, interestingly, clinical severity did not differ. It may be due to its nature of self-resolving disease.

Disclosures. **All authors:** No reported disclosures.

970. Safety of *Bifidobacterium longum infantis* and *Lactobacillus reuteri* in Bangladeshi Infants

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Background. Although probiotics are being intensively studied in the US for many different pediatric endpoints, few studies have been performed in low-income countries. We sought to investigate safety of two commonly used probiotics in Bangladeshi infants.

Methods. Infants age 4 to 12 weeks were randomized to one month of a combination of *Lactobacillus reuteri* DSM 17938 and *Bifidobacterium longum infantis* on three different schedules: daily, weekly, or biweekly (every two weeks) or to non-probiotic control. Infants were followed for three months with mothers reporting daily health status. We compared gastrointestinal (GI) and lower respiratory (LR) symptom rates (days with symptoms/total follow-up days) across arms and assessed hospitalizations; tests for trend were also performed.

Results. As of April 2014, 123 infants have been randomized and had health data reported with a mean of 8.1 weeks of follow-up. Overall GI symptoms were rare; cough and congestion were the most common LR symptoms (table). Although some differences between arms were statistically different, no clear patterns in relation to dosing frequency were seen. 7 infants (3 from biweekly arm, 2 from weekly arm, and 2 from daily arm) were hospitalized for a total of 9 occasions–5 for pneumonia and 4 for diarrhea–and recovered fully; these hospitalizations were neither temporally related to probiotic use nor considered probiotic-related by the DSMB. No allergic responses or other reactions were observed after probiotic administration.

Percent of follow-up days with symptoms per arm

	Diarrhea	Watery or soft stool	Vomiting	Poor feeding	Colic	Cough	Congestion	Difficulty breathing
Daily	0.36	2.65	1.9	3.11	2.25	20.01*	18.89*	0.61
Weekly	0.18	4.11*	2.40	5.69*	2.52	25.51*	22.58*	3.87*
Biweekly	1.18	4.37*	3.19*	6.91*	5.20*	22.70*	25.71*	3.84*
Control	0.68	2.03	1.29	3.01	1.78	13.21	14.00	1.29
p for trend	0.0157	ns	ns	ns	ns	<0.0001	0.0068	ns

*Significantly different than control arm; ns: >0.05

Conclusion. Interim analysis identified no clear association between probiotic dosing frequency and GI or LR symptoms in young Bangladeshi infants. In this group, the two probiotics tested appeared to be safe but, in this early stage of the study, did not demonstrate a symptomatic clinical benefit.

Disclosures. **S. Luby**, Procter and Gamble: Consultant, Consulting fee

971. Clinical Spectrum of Group B Streptococcol Cellulitis-Adenitis Syndrome

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Background. Cellulitis-adenitis syndrome is an uncommon manifestation of late-onset group B streptococcal (GBS) infection. We aimed to characterize GBS cellulitis-adenitis in the 21st century.

Methods. Retrospective review of GBS cultures in infants aged < 1 year, from January 2000 through December 2013 hospitalized at Texas Children's Hospital, Houston. Infants with invasive infection, defined as positive blood or cerebrospinal fluid (CSF) cultures, had medical records reviewed to determine if cellulitis-adenitis was present.

Results. Among 237 infants with blood and/or CSF cultures that grew GBS, 15 (6.3%) presented with GBS cellulitis-adenitis (5 cellulitis, 3 adenitis, 7 cellulitis-adenitis). Eight infants (53%) were male; 7 (47%) were Hispanic, 5 (33.3%) were white and 3 (20%) were black. The median infant birth weight was 1415 grams (range 940-4252) and gestation was 32 weeks (27-41). Five infants were born at term (>37-weeks), 6 were preterm (28-36 weeks) and 4 were extremely preterm (<28-weeks). Only 2 mothers (13%) were known to be GBS colonized. Median infant age at presentation was 58 days (16-109). Most infants had symptoms for < 24 hours (93%). Common features noted at admission were irritability (80%), poor feeding (60%), fever (47%), swelling (47%), erythema (40%) and respiratory distress (33%). Seven (47%) infants had shock at admission and 5 (33%) were admitted to intensive care units. Sites of cellulitis/adenitis included submandibular or preauricular regions (11), inguinal, (2), chest (1), and periorbital (1). One infant with submandibular adenitis had a prevertebral phlegmon by imaging. All infants had bacteremia; 2 of 13 (15.4%) who had lumbar puncture performed also had meningitis. GBS types III, Ib, and Ia accounted for 69%, 23%, and 8%, respectively, of 13 typed isolates. All infants recovered. Two infants with submandibular cellulitis developed overlying eschars that improved with medical therapy and wound care.

Conclusion. Cellulitis-adenitis was a presenting feature of 1 in 16 cases of GBS bacteremia, and most often occurred in submandibular and preauricular areas, although other sites were also involved. GBS type III accounted for approximately 70% of cases. Except for the rate of preterm infants, cellulitis-adenitis syndrome is similar to cases in the 20th century.

Disclosures. **C. M. Healy**, Sanofi Pasteur: Grant Investigator, Research grant; Novartis: Grant Investigator and Scientific Advisor, Consulting fee and Research grant

972. Impact of Genetic Polymorphisms on the Risk of Sepsis in Premature Neonates

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Background. Despite significant advances in supportive care, neonatal sepsis continues to be a major cause of morbidity and mortality, particularly among premature infants. Susceptibility to, and the severity and outcome of sepsis depend on various factors, including environmental exposure, host immune status and inflammatory responses. Identifying single nucleotide polymorphisms (SNPs) in the genes involved in sepsis may help to clarify the pathophysiology of neonatal sepsis. The aim of this study was to evaluate the relationships between sepsis in preterm neonates and genes potentially involved in the response to invasion by infectious agents.

Methods. The study involved all 101 pre-term neonates born between June 2008 and May 2012 with a diagnosis of microbiologically confirmed sepsis, 98 pre-term neonates with clinical sepsis and 100 randomly selected, otherwise healthy pre-term neonates born during the study period. During the study, 47 SNPs in 18 candidate genes were genotyped on Guthrie cards using an ABI PRISM 7900 HT Fast real-time and MAssARRAY for nucleic acids instruments.

Results. Genotypes CT and TT of rs1143643 (the *IL1β* gene) and genotype GG of rs2664349GG (the *MMP-16* gene) were associated with a significantly increased

overall risk of developing sepsis ($p = 0.03$, $p = 0.05$ and $p = 0.03$), whereas genotypes AG of rs4358188 (the *BPI* gene) and CT of rs1799946 (the *DEFβ1* gene) were associated with a significantly reduced risk of developing sepsis ($p = 0.05$ for both). Among the patients with bacteriologically confirmed sepsis, only genotype GG of rs2664349 (the *MMP-16* gene) showed a significant association with an increased risk ($p = 0.02$). Genotypes GG of rs2569190 (the *CD14* gene) and AT of rs4073 (the *IL8* gene) were associated with a significantly increased risk of developing severe sepsis ($p = 0.05$ and $p = 0.01$). Genotype AG of rs1800629 (the *LTA* gene) and genotypes CC and CT of rs1341023 (the *BPI* gene) were associated with a significantly increased risk of developing Gram-negative sepsis ($p = 0.04$, $p = 0.04$ and $p = 0.03$).

Conclusion. These results show that genetic variability seems to play a role in sepsis in pre-term neonates by influencing susceptibility to and the severity of the disease, as well as the risk of having disease due to specific pathogens.

Disclosures. **All authors:** No reported disclosures.

973. Use of Concomitant Antibiotics During Treatment for *Clostridium difficile* Infection (CDI) in Pediatric Inpatients

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Background. The incidence of *Clostridium difficile* among children has increased. The use of concomitant antibiotics during *C. difficile* infection (CDI) treatment results in an increased risk of recurrent infection. Reducing unnecessary exposure, especially among immunocompromised patients at greatest risk of recurrence, is a potential antibiotic stewardship target. The objective of this study was to characterize concomitant antibiotic use among hospitalized children with CDI

Methods. This retrospective multi-center cohort included children with CDI admitted between 2008 and 2013 to one of 43 US children's hospitals contributing data to the Pediatric Health Information System. Patients were included if they were <18 years old on admission, had an ICD-9 code for CDI, and received either oral or intravenous metronidazole or oral vancomycin. Concomitant antibiotic use was defined as ≥3 consecutive days during which both CDI treatment and non-CDI antibiotics were given on the same day. ICD-9 and APR-DRG codes were used to identify immunocompromised patients, defined as those with malignancy, solid organ transplant, or bone marrow transplant. Descriptive statistics were used to summarize concomitant antibiotic use and patient characteristics

Results. During the study period, 16,777 patients met the definition of CDI, for an observed rate of 5.29 per 1,000 discharges. After removing antibiotics commonly used for prophylaxis, the prevalence of concomitant antibiotic use was 46%. The median duration of concomitant use was 7 days (IQR: 4, 11). The most frequent concomitant agents used were intravenous vancomycin (20%), cefepime (12%), and carbapenems (12%). Approximately 31% of CDI patients were immunocompromised. Among these, 64% of patients with malignancy and 79% with transplant received concomitant antibiotics, respectively

Conclusion. Hospitalized children are commonly prescribed concomitant antibiotics during CDI treatment. Concomitant antibiotic exposure is frequent for immunocompromised patients, populations at high risk for recurrence. Antimicrobial stewardship programs should consider interventions to identify potentially modifiable or unnecessary concomitant therapy, especially for immunocompromised patients

Disclosures. **J. Newland**, Pfizer: Grant Investigator, Grant recipient

974. The Clinical and Molecular Epidemiology of Pediatric *Clostridium difficile* Infection: Predominance of Restriction Endonuclease Analysis (REA) Group DH

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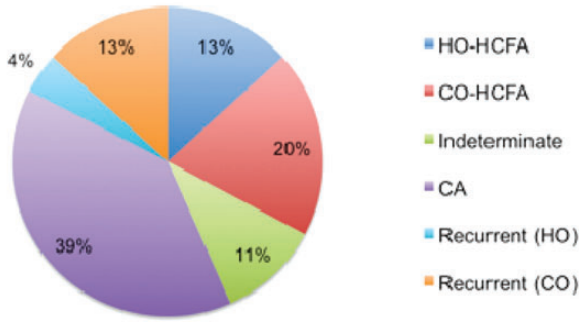
Background. The clinical epidemiology of pediatric *Clostridium difficile* infection (CDI) has been frequently described, but the molecular epidemiology of pediatric CDI is understudied.

Methods. A retrospective cohort study was performed using all laboratory-identified cases of CDI in patients > 1 year old at an academic children's hospital over a 1-year period (December 2012-December 2013). Saved *C. difficile* toxin B gene PCR-positive stool specimens underwent culture and REA typing.

Clinical Characteristics of Pediatric CDI (n = 189)

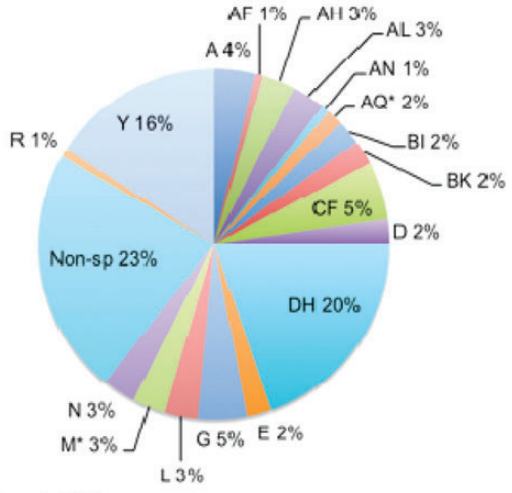
Characteristic	Percent
Male	59%
Age	
12-36 months	18%
3-10 years	46%
11-17 years	29%
18-20 years	7%
Comorbidities	
Inflammatory Bowel Disease	20%
Malignancy	28%
Solid organ transplant	7%
Any immunocompromised condition	48%
Gastrostomy tube	16%
Any antibiotic exposure (past 30 days)	51%
Clindamycin	8%
Fluoroquinolones	4%
Cephalosporins	29%

Figure 1: Classification of Pediatric CDI (n=189)



HO: hospital onset; CA: community-associated

Figure 2: REA Grouping of Pediatric CDI Isolates (n=132)



*non-toxigenic REA group
Non-sp: unrelated non-specific REA groups

Results. 189 CDI episodes among 143 patients were included. Of these, 156 (83%) stool specimens were saved by the laboratory, and 132 (85%) were culture positive. The table and Figure 1 describe the clinical characteristics and disease classification of cases, respectively. Severe CDI and recurrent CDI within 8 weeks occurred in 27 (14%) and 32 (17%) cases, respectively. Recurrent CDI was associated with malignancy (risk ratio [RR] 2.6, 95% confidence interval [CI] 1.4-4.8) and was less likely to occur in patients with community-onset (CO) CDI (RR 0.47, 95% CI 0.24-0.89). Strain BI was

identified in 3 CDI cases from the same patient. Strain DH, the predominant strain identified (Figure 2), was not associated with severity or recurrence, but was associated with malignancy (RR 2.2, 95% CI 1.1-4.4), healthcare facility-associated (HCFA) CDI (RR 3.2, 95% CI 1.5-7), and cephalosporin use (RR 4.2, 95% CI 2.1-8.4).

Conclusion. Molecular epidemiologic assessment of pediatric CDI revealed a paucity of BI/NAP1/027 and predominance of DH/NAP11/106, a common epidemic strain in the UK but infrequent in the US. Although DH was not associated with severe or recurrent CDI, DH was associated with cephalosporin use, HCFA-CDI, and malignancy, the latter of which was associated with recurrent CDI.

Disclosures. **L. Kociolek**, Merck: Grant Investigator, Grant recipient **D. Gerding**, Sanofi Pasteur: Board Member, Consulting fee; Actellion: Board Member, Consulting fee; Merck: Board Member, Consulting fee; Rebiotix: Board Member, Consulting fee; Viropharma: Consultant, Consulting fee; Summit: Consultant, Consulting fee; Viropharma: patent holder, patent

975. Exposure to Gastric Acid-Suppression Therapy is Associated with Healthcare-Associated and Community-Associated *C. difficile* Infection in Children

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Background. Acid-suppression therapy, particularly with proton pump inhibitors (PPIs), has been associated with an increased risk of *C. difficile* infection (CDI) and associated diarrhea in adults. Limited data exist regarding such an association in children.

Methods. To determine whether gastric acid-suppression therapy is associated with CDI in both inpatient and outpatient pediatric populations, we conducted a retrospective case-control study at a 200-bed academic pediatric hospital and associated outpatient clinics in the time frame 2005-2010. We defined cases as children 1-18 years of age with a first positive test for *C. difficile* toxin A/B (Meridian Bioscience) on liquid stool, and matched each case to 2 controls without C. *difficile.* We conducted chart review to elicit selected comorbidities and exposure to gastric acid-suppression therapy (including H2 blockers and PPIs) and antibiotics in the 3 months preceding the infection or encounter date. We used bivariate and multivariable logistic regression to evaluate the association between antacid use and CDI, controlling for potential confounders.

Results. We identified 138 children with CDI (61% community-associated, the remainder healthcare-related or indeterminate) and 276 controls. Use of any acid suppression therapy was more common in cases compared to controls (34% vs20%, p <0.01). When adjusted for demographic variables and comorbidities, gastric acid-suppression therapy remained significantly associated with CDI (adjusted odds ratio [aOR], 1.8; 95% confidence interval [CI], 1.01-3.10). Antibiotic use (aOR, 1.7; 95% CI, 1.1-2.7) and immunosuppressed state (aOR, 2.5; 95% CI, 1.2-5.2) were also associated with CDI in our adjusted model.

Conclusion. Gastric acid-suppression therapy was associated with both healthcare-associated and community-associated CDI in children. Larger pediatric studies are necessary to determine the role of PPIs specifically in causing CDI in children.

Disclosures. **All authors:** No reported disclosures.

976. Antiseptic tolerance and antimicrobial susceptibility of nosocomial *Staphylococcus aureus* at Texas Children's Hospital: 2007-2013

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Background. Antiseptics such as chlorhexidine have been utilized to decrease the incidence of healthcare associated infections. A number of genes in *S. aureus*, notably *qacA/B* and *smr*, have been associated with tolerance to antiseptics. Work at our institution has revealed the emergence of *S. aureus* possessing these genes among pediatric cancer and cardiac surgery patients. We examined the prevalence of antiseptic tolerant *S. aureus* among all nosocomial isolates at our institution as well as provided molecular and clinical characterization of these organisms.

Methods. Isolates were obtained from an ongoing prospective *S. aureus* surveillance study; isolates obtained after more than 72 hours of hospitalization during the years 2007-2013 were identified. Antimicrobial susceptibility was determined by the clinical microbiology lab in the routine course of clinical care. All isolates underwent PCR for the antiseptic tolerance genes *qacA/B* and *smr*; isolates positive by PCR were further characterized by PFGE.

Results. 280 isolates were included in the study of which 114 (40.7%) were methicillin-resistant (MRSA). The median age of patients was 3.3 months (IQR: 0.9-73.2). Ninety isolates (32.1%) were positive for *smr* while 61 (21.4%) were positive for *qacA/B*; 28 isolates (10%) carried both genes. The proportion of isolates positive for these genes varied from year-to-year but was lowest in 2007 (<5%) and was highest for *smr* in 2009 (92%) and for *qacA/B* (87.2%) in 2013. *smr* positive isolates were more often MRSA (53.3% vs 34.7%, p 0.004), clindamycin resistant (33.3% vs 24.7%, p 0.08) and associated with invasive infections (78.9% vs 64.7%, p 0.01). *qacA/B* positive isolates were more often associated with the diagnosis of bacteremia specifically (50.8% vs 35.6% p 0.03). The most common PFGE type among antiseptic tolerant isolates was USA300 (20%); numerous other pulsotypes accounted for the remainder of isolates.

Conclusion. *S. aureus* possessing antiseptic tolerant genes are common among nosocomial isolates at our institution. These isolates are more often associated with a multidrug resistant phenotype and more severe infections. These trends should be monitored in light of the continued use of antiseptics both in the hospital and community settings.

Disclosures. **S. L. Kaplan**, Pfizer: Grant Investigator, Research grant; Cerexa: Grant Investigator, Research grant

977. Impact of Decolonization on Methicillin-resistant *Staphylococcus aureus* Transmission in Hospitalized Neonates

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Background. MRSA is a leading cause of healthcare associated infections. Decolonizing hospitalized patients may eliminate a bacterial reservoir to reduce MRSA transmission and prevent infections. Our objective was to measure the association of colonization pressure with transmission in the neonatal intensive care unit (NICU) and to determine whether decolonization decreases MRSA transmission.

Methods. Neonates admitted to our tertiary care NICU have weekly nares cultures to detect MRSA colonization. We identified neonates with a positive culture for MRSA between January 2007 and December 2013. Some neonates with a positive culture growing MRSA were decolonized with mupirocin. Hand hygiene compliance was monitored. Weekly colonization pressure was defined as the percentage of total patient-days in the preceding 7 days that were MRSA-colonized patient–days. The association of colonization pressure and decolonization with MRSA acquisition was estimated using negative binomial regression models to calculate incidence rate ratios (IRRs).

Results: There were 4,746 neonates admitted in the NICU, accounting for 101,082 patient days. One hundred and one neonates who had positive cultures for MRSA accounted for 3,356 MRSA colonized patient-days; neonates who were decolonized accounted for 2,227 patient-days, while neonates who were not decolonized accounted for 1,129 patient-days. In unadjusted analysis, for every 1% increase in colonization pressure there was a 7% increase in the risk of MRSA acquisition (IRR 1.07, 95% CI 1.00, 1.14). After adjusting for decolonization and hand hygiene compliance, there was an increase in the incidence of MRSA associated with colonization pressure due to untreated colonized neonates (IRR 1.14, 95% CI 1.01, 1.28), but there was no increase in the incidence of MRSA associated with colonization pressure due to treated colonized neonates (IRR 1.01, 95% CI 0.92, 1.12). Compliance with hand hygiene was not associated with MRSA incidence (IRR 1.00, 95% CI 0.99, 1.02).

Conclusion. Our results suggest that colonization pressure is associated with MRSA transmission, and decolonization may decrease colonization pressure and reduce MRSA transmission in the NICU.

Disclosures. **All authors:** No reported disclosures.

978. Infectious Complications of Extended Peripheral Intravenous Catheters (EPIVs) in a NICU

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Background. Central line-associated bloodstream infections (CLABSIs) are important causes of morbidity and mortality in neonatal intensive care unit (NICU) patients. Extended peripheral intravenous catheters (EPIVs) are increasingly used as an alternative to central venous catheterization in some NICUs, but data about infectious complications are lacking. The frequency of infectious complications of EPIVs in 101-bed Level IV NICU utilizing these catheters since November 2011 is described.

Methods. All BSIs were prospectively identified in neonates cared for in a NICU between January and December 2013. CLABSIs were designated according to NHSN definitions. Infections that would have met the NHSN CLABSI definition but had an EPIV in place rather than a CL were classified as EPIV-associated blood stream infections (EPIV-aBSIs).

Results. Between January, 1 and December 31, 2013, there were 227 EPIV insertions. Bacteremia developed in 3 infants with EPIVs (*E. coli* = 2, methicillin-resistant *S. aureus* (MRSA) =1). The EPIV-aBSI rate was 1.8/1,000 catheter days, compared to the

CLABSI rate of 1.04/1,000 device days (total infections = 7). Two infants developed local infectious complications (abscess or necrosis at line site).

Conclusion. EPIVs were associated with appreciable infectious morbidity in this NICU. The EPIV-aBSI rate was higher than the CLABSI rate. Standardized, evidence-based protocols for the insertion and maintenance of EPIVs are needed. Reporting only CLABSI rates in the NICU underestimates the burden of bacteremia associated with intravenous catheterization.

Disclosures. **All authors:** No reported disclosures.

979. Preventing Central Line Associated Bloodstream Infections (CLABSIs) in an Outpatient Pediatric Hemodialysis (HD) Unit

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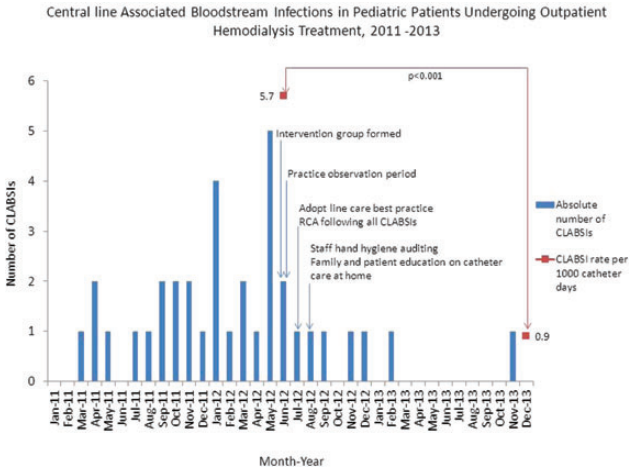
Background. In 2008, 37,000 CLABSIs occurred in American HD patients. Pediatric patients are particularly vulnerable; but few evidence-based prevention strategies exist. This study describes a stepwise approach to prevent CLABSIs in a pediatric HD patient cohort.

Methods. This study includes CLABSIs identified between January 2011 and December 2013 in HD patients treated at Children's National Health System. CLABSIs were defined using the Centers for Disease Control National Healthcare Safety Network definition. Interventions, including blind audits of staff hand hygiene, were developed by systematically reviewing evidence-based practices and derived from root cause analyses (RCA). Effectiveness of interventions was examined by plotting the CLABSI cases against the calendar month, and Poisson Regression to test changes of IR before (January 2011–June 2012, Phase 1) and after (July 2012–December 2013, Phase 2) the interventions.

Results. 12 patients developed 35 CLABSIs including 28 (5.7 per 1,000 catheter days) in Phase 1 and 7 (0.9 per 1,000 catheter days) in Phase 2 (IR Ratio [IRR]: 6.3, $p < 0.001$). In Phase 1, 10 CLABSIs occurred in 3 patients < 4 years (yr); 10 in 7 patients aged 4 – 13.9 years, and 8 in 4 patients aged 14 – 19 years. The 7 CLABSIs in phase 2 occurred in 4 patients aged 4 – 13.9 years. Leading pathogens in Phase 1 were *Staphylococcus epidermidis* (n = 13, 33%) followed by *Enterococcus faecalis* (n = 11, 28%); compared to *Staphylococcus epidermidis* (n = 3, 23%) and *Staphylococcus aureus* (n = 2, 17%) in Phase 2. Staff hand hygiene compliance rate increased from 38% in August 2012 to 100% in December 2013. The Figure depicts interventions instituted since July 2012.



Conclusion. Multifactorial interventions that include improving staff hand hygiene, adopting best practice for catheter care, collecting timely information through RCAs, and improving patient and caregiver knowledge about catheter care at home are effective in preventing CLABSIs in pediatric HD patients.

Disclosures. **All authors:** No reported disclosures.

980. Pediatric Patients with Gastrointestinal Conditions and Central Line-Associated Bloodstream Infections

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Background. While standardization of central line insertion and maintenance practices has led to significant reductions in central line-associated blood stream infections (CLABSI), there is concern that not all infections are preventable by current CLABSI prevention bundles. Gastrointestinal (GI) conditions may increase the risk of bloodstream infection by translocation of enteric bacteria due to mucosal barrier injury (MBI). This study aimed to describe patient and infection characteristics of hospitalized pediatric patients with GI conditions who develop CLABSI.

Methods. A multi-center retrospective cohort study of non-critically ill pediatric patients (excluding oncology patients) with GI conditions and hospital-onset CLABSI (January 2009-June 2012). A pediatric gastroenterologist focus group derived an a priori list of GI conditions that could be associated with MBI. CLABSI surveillance data were supplemented by chart review to identify parenteral nutrition (PN) exposure and GI conditions.

Results. Four sites submitted data on 71 patients with GI conditions and CLABSI. At the time of CLABSI, patients were hospitalized on surgery (n = 60, 85%), GI (n = 6, 8%) and rehabilitation (n = 5, 7%) units. Most patients had >1 MBI conditions (n = 64, 90%). The most common MBI conditions were gastroschisis/omphalocele (n = 26, 37%), necrotizing enterocolitis (n = 18, 24%), and motility disorder (n = 9, 13%). Nearly all patients (n = 67, 94%) had PN exposure within 7 days of infection. Enteric organisms, including *Enterobacteriaceae* (25%), yeast (14%), *Enterococcus spp.* (13%), and polymicrobial with an enteric organism (11%), accounted for 62% of CLABSI.

Conclusion. Many pediatric patients with GI conditions who develop CLABSI have a history of intra-abdominal surgery for neonatal-onset GI conditions. While most CLABSI in these hospitalized GI patients were due to enteric organisms, approximately one-third were non-enteric and thus might be prevented through enhanced adherence to existing CLABSI prevention bundles. Novel prevention practices might be needed to prevent CLABSI due to enteric organisms in patients with MBI.

Disclosures. **D. Zerr**, Sage Products: Investigator, Research support; Chimerix, Inc.: Investigator, Research support

981. Catheter Complications in Children Discharged with Peripherally Inserted Central Catheters (PICCs)

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Background. Increasingly, patients are discharged from the hospital with a PICC to complete treatment. PICC complications include thrombus formation, non-thrombotic occlusion, infection, and others. Our objective was to identify the frequency of risk factors for complications necessitating PICC removal after hospital discharge.

Methods. We included children discharged with a PICC from Johns Hopkins Children's Center between January 1, 2003 and December 31, 2013. We determined risk factors for complications necessitating PICC removal using logistic regression. We performed a subcohort analysis of patients with catheters placed for antibiotic therapy before 2010.

Results. During this study period, 1,901 catheters remained in place after discharge in 1,254 children. One hundred eighty six PICCs (10.02%) were removed due to a complication during 44,798 catheter-days (IR 4.1/1,000 catheter-days). Forty five (24.19%) were removed due to infection. In adjusted analysis, the odds of complication decreased by 4% per year of age (OR 0.96; 95% CI 0.93, 0.98). Patients had a 1% increased risk of complications per day of hospital stay (OR 1.01; 95% CI 1.00, 1.02), and had a 1% increased risk of complications for each day the catheter was in place after discharge (OR 1.01; 95% CI 1.00, 1.01). PICCs inserted with a midline tip location had a 5-fold increase in the odds of complication (OR 5.16; 95% CI 2.96, 9.01) compared to those with a central tip location. There were 976 PICCs placed for antibiotic therapy in 670 children. One hundred one (10.35%) of these PICCs developed a complication after discharge requiring removal during 16,736 catheter days (IR 6.0/1,000 catheter-days). Of these, 15 (14.85%) were infectious. In addition to age, tip location, and catheter dwell time after discharge, having public insurance was an independent risk factor for complications in this sub-population (OR 1.87; 95% CI 1.06, 3.31).

Conclusion. Younger age, catheter tip location, longer hospital stay and longer catheter dwell time after discharge are associated with PICC complications that occur after hospital discharge. Improved strategies are needed to decrease the risk of catheter complications in high risk children who are discharged with PICCs.

Disclosures. **All authors:** No reported disclosures.

982. Pediatric Central Line Maintenance Bundle – Standardizing the Approach

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Session: 117. Pediatric Healthcare Associated Infection Epidemiology and Prevention
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Background. Hospital acquired infections (HAI) lead to increased morbidity and mortality with hospitalized patients. Implementing practices to decrease harm to the patient and reducing additional costs associated with HAI's is a healthcare focus. Hospital acquired central line associated blood stream infections (CLABSI) pose a challenge for hospitals. Proper insertion and appropriate maintenance of central lines are crucial in prevention of CLABSI's. Inconsistent practices towards central line maintenance place patients at risk for increased morbidity and mortality from CLABSI's.

Methods. Using the Centers for Disease Control and Prevention recommendations,a central line maintenance bundle was developed for use in the pediatric setting. Five elements were chosen to become part of the updated maintenance bundle:

1. Documentation of central line dressing, tubing, and cap change
2. Daily CHG bath and linen change
3. Appropriate central line medication administration
4. Dressing is dated, current, clean, dry, and intact
5. All tubing is dated and current

Maintenance bundle education was disseminated to nursing staff. Clinical nursing specialists, unit managers, clinical educators, and infection preventionists were trained as super users. Principles of implementation science were used for the roll out. Bundle rounds were conducted and aggregated monthly to assess for bundle compliance. All elements were observed individually to assess for deficiencies in addition to total compliance for each patient. Total compliance was determined to be appropriate only when every element had been completed. Partial credit was not given.

Results. This study shows that high total bundle compliance reduces the rate of CLABSI. When the total bundle achieved a rate of 80% compliance, the CLABSI rate declined. During the first 4 months of this implementation, 4 CLABSI's were identified, with a rate of 2.34 and 66% bundle compliance. The last 4 months of this implementation, 0 CLABSI's were identified, a rate of 0.0 and 85% bundle compliance.

Conclusion. In conclusion, standard and consistent practices relating to appropriate central line maintenance contributes to reduction of CLABSI in pediatric patients.

Disclosures. **All authors:** No reported disclosures.

983. Outbreak of multi-drug resistant *Klebsiella pneumoniae*: A 4 month epidemiologic follow-up in a tertiary teaching hospital in Rwanda

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Background. Multi-drug resistant (MDR) nosocomial *Klebsiella pneumoniae* (KP) is an emerging problem in the developing world. MDR gram-negative infections are increasingly reported in neonatal units in resource-limited settings, with high mortality.

We describe an outbreak in a tertiary Neonatal Intensive Care Unit (NICU) at Butare University Teaching Hospital (BUTH) in Rwanda, and the infection control measures taken to interrupt transmission.

Methods. Microbiologic data from cultures taken during clinical care from infants hospitalized at BUTH NICU from January-May 2013 were reviewed. Environmental cultures were collected from equipment in contact with infected infants.

Results. KP was isolated in 21 neonates evaluated for sepsis. Eighteen (86%) infants grew KP in blood, and 3 (14%) grew KP from infected surgical sites. Seven infants (33%) developed KP early-onset sepsis in the first 3 days of life, and 14 (67%) cases were late-onset. Mortality was high, and 5 babies died (24%). Antibiotic susceptibility testing showed high levels of resistance; 14/17 (82.5%) Gentamicin, 12/15 (80%) Cefotaxime, 4/12 (33%) Ciprofloxacin, 4/17 (24%) TMP/SMX. No isolates were resistant to Meropenem. Although most isolates had the same susceptibility pattern, clonality could not be assessed. Environmental cultures revealed KP from the water reservoir of 1 incubator. Pseudomonas aeruginosa was obtained from 1 incubator, 1 jug for transporting distilled water, 1 CPAP reservoir and 1 portable oxygen concentrator. The outbreak was controlled after temporary ward closure with terminal cleaning, infant cohorting, contact isolation, and reinforcing hand hygeine. No cases occurred after May, 2013.

Conclusion. An outbreak of MDR KP in a resource-limited setting was controlled by early recognition, thorough investigation, isolation and deep cleaning measures.

Disclosures. **All authors:** No reported disclosures.

984. Siblings Sharing Everything, Including Viruses: Age-based Visitor Restriction as a Successful Infection Prevention Measure in a Children's Hospital

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Background. As seasonal respiratory virus activity increases in the Pacific Northwest region, enhanced infection prevention measures are annually implemented in our tertiary-care university children's hospital. To minimize our most vulnerable patients' risk of healthcare-associated infection (HAI), these measures focus on the pediatric hematology/oncology inpatient unit and outpatient clinic.

Methods. During the 2013-2014 season, in addition to placing all patients with suspected or confirmed respiratory viral illness in contact and droplet isolation precautions, the following enhanced infection prevention measures were enacted at different time-points: Beginning December 16, 2013, all employees and visitors to the pediatric hematology/oncology inpatient unit and outpatient clinic were required to check-in at the front desk, sign an attestation form confirming no respiratory viral symptoms, and wear a day-of-the-week sticker as proof that active screening was complete. Beginning January 6, 2014, (1) all bone marrow transplant (BMT) patients were placed in contact and droplet isolation precautions (regardless of respiratory symptoms) if <100 days post-BMT or >100 days if severely immunosuppressed with active graft-vs-host-disease (GVHD), and (2) no visitor <12 years of age was allowed entry to the pediatric hematology/oncology inpatient unit, including siblings.

Active laboratory surveillance was performed by the Department of Infection Prevention and Control. HAI case definitions were defined for respiratory syncytial virus (RSV), parainfluenza, influenza, adenovirus, rhinovirus and metapneumovirus.

Results. Despite rigorous employee and visitor symptom screening, 2 respiratory viral HAI cases occurred. However, after implementation of age-based visitor restrictions and expanded isolation precautions for BMT patients, no additional HAI cases have been identified to date.

Conclusion. Regardless of a season in which sustained, moderate respiratory viral activity was noted in the community, an enhanced infection prevention policy focusing on restricting young visitors effectively assisted in preventing respiratory viral HAI in our pediatric hematology/oncology unit.

Disclosures. **All authors:** No reported disclosures.

985. Uncommon Outcomes due to Common Colds: Epidemiology and Outcomes Associated with Nosocomial Viral Infections in Children

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Background. Hospitalized children are at risk for healthcare-associated infections (HAI), including nosocomial viral infections (NVI). Previous studies have described the complications associated with RSV and influenza in hospitalized children, but less is known about the epidemiology and outcomes associated with other respiratory and gastrointestinal (GI) viruses.

Methods. Cases of NVI were identified from existing surveillance data at the Children's Hospital of Philadelphia during a 13 month period between January 2013-2014. Infections meeting CDC surveillance criteria as an upper respiratory infection (URI), bronchitis/bronchiolitis, gastroenteritis or pneumonia caused by a viral pathogen were included. Demographic and clinical data were obtained through systematic chart review of cases to identify outcomes. Additional outcome data were abstracted from data collected during apparent cause analysis (ACA) performed on all NVI. Data analyses were performed with Stata 12.1.

Results. During the study period, 174 NVIs were identified in 133 patients. Median age of affected patients was 1.5 years (interquartile range (IQR) 0.6 – 5.8 years). The majority of infections were respiratory (68%). Rhinovirus was the most common respiratory pathogen (75, 43%) and norovirus was the most common GI pathogen (29, 17%). Most patients with NVI were in the intensive care units (ICU) (34%), medical/surgical (21%) and oncology (13%) units. The most common chronic comorbid conditions include respiratory (37%), cardiovascular (35%) and gastrointestinal (34%). NVI cases occurred year-round, but most were identified during the winter (37%) and spring (29%) months. Median length of stay was 27 days (IQR 9-108 days) at time of infection onset. Adverse outcomes within 48 hours of NVI onset included transfer to the ICU (13%), initiation of non-invasive ventilation (11%), and intubation (5%). 22 patients (17%) experienced a delay in discharge and 7 (4%) died within 30 days of infection.

Conclusion. NVIs can lead to serious complications in hospitalized children, including escalation of care and prolonged length of stay. Efforts to reduce transmission should target both respiratory and GI infections. Additional data on risk factors for acquisition are needed to guide improvement.

Disclosures. **All authors:** No reported disclosures.

986. Human Metapneumovirus in a Children's Hospital – Should We Pay More Attention?

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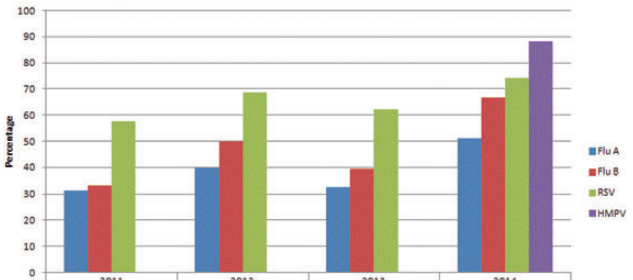
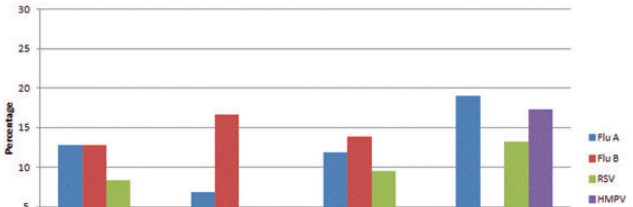
Background. Viral respiratory infections are a major cause of hospitalization and Intensive Care Unit (ICU) admission. At childrens' hospitals, Infection Prevention closely tracks Respiratory Syncytial Virus (RSV) and Influenza, including rates of healthcare associated infections (HAI). There is conflicting data on the contribution of human Metapneumovirus (hMPV) infections to respiratory morbidity in hospitalized children.

Figure 1. Winter Viral Patients Requiring Admission



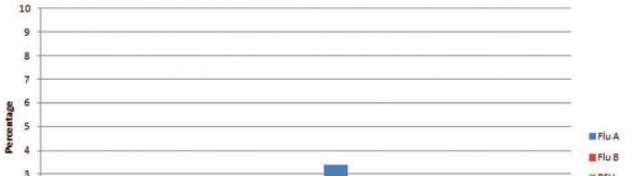
	2011	2012	2013	2014
Flu A	31	40	33	51
Flu B	33	50	39	67
RSV	58	69	62	74
HMPV				88

Figure 2. Winter Viral Patients Admitted to PICU/CVICU/NICU



	2011	2012	2013	2014
Flu A	13	7	12	19
Flu B	13	17	14	0
RSV	8	5	10	13
HMPV				17

Figure 3. Winter Viral Patients with a Healthcare Acquired Infection



	2011	2012	2013	2014
Flu A	2	2	3	0
Flu B	2	0	2	0
RSV	0	1	1	1
HMPV				3

Methods. hMPV testing was added in the 2013-14 winter viral season (D3 Ultra DFA Respiratory Virus Screening and ID Kit; Diagnostic Hybrids). Hospitalization rates, ICU admission and HAI rates were prospectively monitored and compared to current and past seasons of RSV and Influenza. Clinical information was extracted retrospectively on those patients with hMPV and RSV requiring ICU admission.

Results. For children who underwent viral respiratory testing at our facility, rates of hospitalization, ICU admission and HAIs for hMPV were comparable to or exceeded those of RSV and Influenza for the current and past 4 winter seasons (Figures 1, 2 and 3). Of 19 patients with hMPV requiring ICU admission, the average age was 6 years (y) 5 months (m) (range 8 m – 21 y 7 m), compared with an average age of 1 y 8 m (range 0 m – 15 y 4 m) for 35 ICU admitted RSV patients ($p < 0.05$). Of hMPV infected patients, 16/19 (84%) had underlying medical diagnoses, including chronic lung disease in 10 (53%), and tracheostomy in 8 (42%). Six (32%) required mechanical ventilation. Only 12/35 (34%) RSV ICU admitted patients had underlying medical diagnoses; none had tracheostomies, 5 (14%) had chronic lung disease, 13 (37%) required mechanical ventilation. Length of hospitalization averaged 9.9 days (range 2-34 days) for hMPV and 7.7 days (range 1 – 25 days) for RSV ICU admits. Total contact isolation days were not significantly higher this season, likely due to a milder RSV season.

Conclusion. Among children tested for winter viral pathogens in 2013-14, hMPV rates of hospital admission, ICU admission and HAIs met or exceeded those for RSV and Influenza. ICU admitted patients with hMPV were older than those with RSV. There were more ICU admissions in hMPV patients with tracheostomy and chronic lung disease. Future efforts at surveillance and vaccine development should target this population.

Disclosures. **All authors:** No reported disclosures.

987. Carbapenem-resistant *Klebsiella pneumoniae* (CRKp) in Children. Clinical and Epidemiological Characteristics from Infected and Colonized Inpatients in a Tertiary care Hospital in Medellín, Colombia

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Background. Multidrug resistant Gram-negative infections represent a growing problem and a serious global threat. Data in children is scarce. *K. pneumoniae* carbapenemases (KPC) are the most common mechanism of resistance this bacteria have developed. We report the clinical characteristics and outcomes from a cohort of children infected or colonized with carbapenem-resistant *K.pneumoniae* at Hospital Pablo Tobón Uribe in Medellín, Colombia. A KPC-2 producing *K. pneumoniae* outbreak started in our institution in 2008. Despite the implementation of several control measures including strict contact isolation, patient cohorting and routine surveillance cultures, the outbreak spread from adult to pediatric wards.

Table 1. Demographic and clinical characteristics

Characteristic	Infected (N = 34) No. (%)	Colonized (N = 55) No. (%)
Age in months	22,8 (0 - 38)	33,7 (0 - 168)
Male	26 (76,5)	36 (65,5)
Department		
General pediatrics ward	25 (58,2)	22 (40)
PICU	18 (41,8)	33 (60)
Days between admission and infection/colonization	65 (0 - 771)	27,5 (1 - 118)
Length of stay	110 (9 - 812)	61 (1 - 323)
Previous hospital admissions	32 (94,1)	50 (91)
Previous PICU admissions	24 (70,5)	50 (91)
Indwelling devices	34 (100)	50 (90,9)
Previous comorbidities	34 (100)	49 (89)
Prior antibiotic exposure	32 (94,1)	51 (92,7)
Surgical history	27 (79,4)	31 (56,3)
Immunosupression	12 (35,3)	18 (32,7)
Mortality	13 (38,2)	12 (21,9)

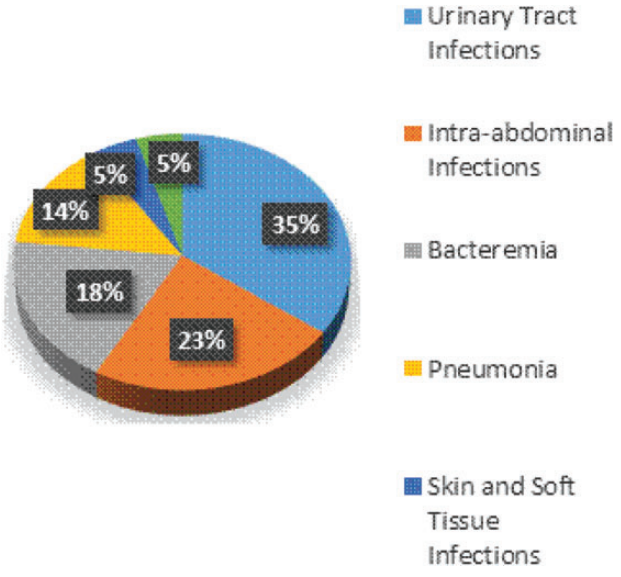
Methods. We performed a retrospective chart review of all pediatric cases in whom CRKp were identified from 2008 to 2013. Clinical and demographic characteristics and outcomes were recorded.

Results. A total of 34 infected children (median age 22,8 months) with 43 episodes (1 had two episodes, 2 patients had three and one with 5) and 55 colonized patients (median age 33 months) were identified. Demographic and clinical characteristics from infected and colonized patients are shown in Table 1. Urinary tract and intra-abdominal infections were the most common type of infections (Figure 1). Antimicrobial therapy and outcomes from infected patients are presented on Table 2. Severely ill children received combined antimicrobial therapy. Mortality was lower with

meropenem containing regimens (p = 0,03).

Table 2. Outcome of patients according to antimicrobial regimen

Antimicrobial regimen	No. Episodes (43) Total	Survived	Died	Mortality
Combination therapy	22	13	9	36%
Meropenem containing regimen	5	5	0	0%
Meropenem + colistin	4	4	0	0%
Meropenem + ciprofoxacin	1	1	0	0%
Meropenem sparing regimen	17	8	9	48%
Colistin + aminoglycoside	3	0	3	100%
Colistin + aminoglycoside + tigecydine	4	2	2	50%
Colistin + tigecycline	1	0	1	100%
Colistin + ciprofloxacin	2	1	1	50%
Colistin + ciprofloxacin + aminoglycoside	1	1	0	0%
Cefepime + aztreonam	1	0	1	100%
Cefepime + aminoglycoside	1	1	0	0%
Ciprofloxacin + aminoglycoside	1	1	0	0%
tigecycline + aminoglycoside	3	2	1	33%
Monotherapy	19	17	2	8%
Colistin	12	10	2	17%
Aminoglycoside	5	5	0	0%
Ciprofloxacin	2	2	0	0%
No active agent	2	0	2	100%



Conclusion. CRKp infections occur more frequently in children with comorbidities, prolonged hospital stays and prior antibiotic exposure. Mortality is high. A meropenem containing regimen seems to be the best choice in severely ill children.

Disclosures. **All authors:** No reported disclosures.

988. Infectious Disease Symptoms and Growth in Infants

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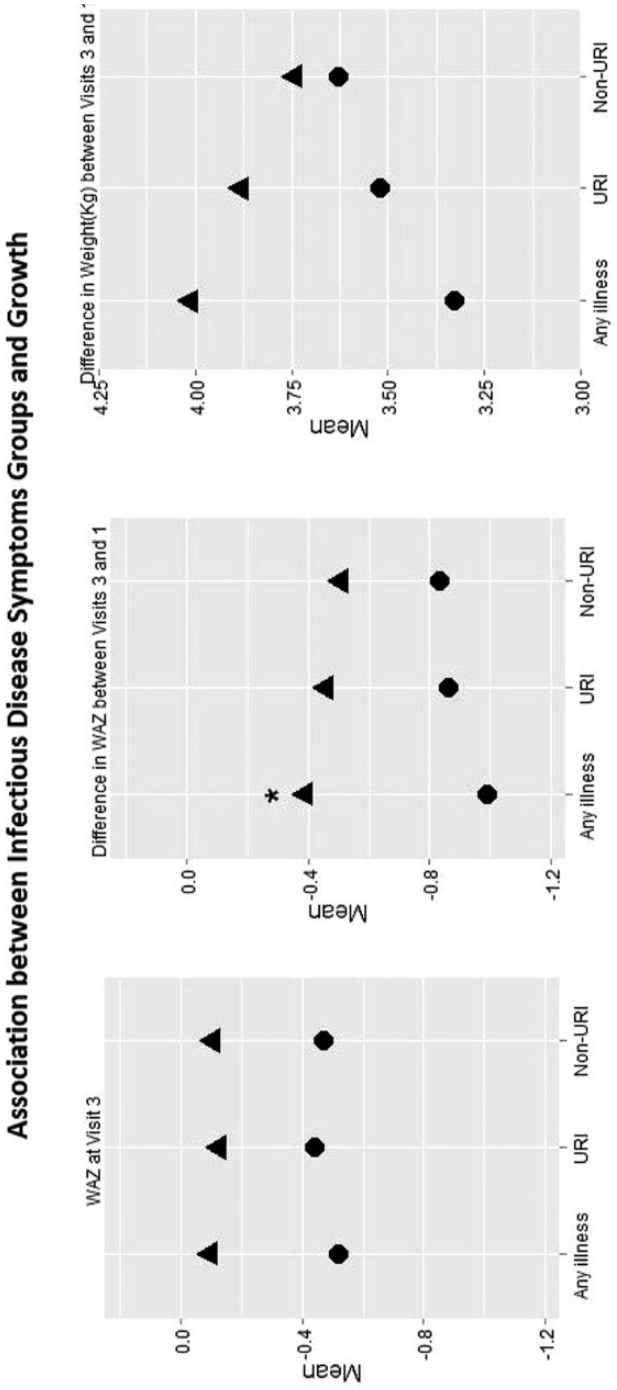
Background. In developing countries, recurrent infection in infants results in stunting and underweight. We sought to determine whether routine infectious disease symptoms in healthy children in the US also correlated negatively with growth.

Methods. Stanford's Outcomes Research in Kids (STORK) is an ongoing rolling cohort of healthy pregnant women and their babies. Using a weekly, automated survey, we assessed days of infectious diseases symptoms (IDS) (sneezing/cold; cough; ear-pulling; diarrhea; vomiting; fever) and breast feeding status of infants over time. At household visits performed every 4 months, the child's weight was measured. We calculated the percent of days with IDS (PIDS) from birth to the 3rd household visit, both overall and as either upper respiratory infection (PURI) [sneezing/cold; cough; and/or ear-pulling] or non-URI conditions (PNURI) [diarrhea, vomiting and/or fever]. Babies were categorized into high or low illness groups based on the median percent days of illness. Between these groups, we compared the mean weight-for-age Z-score (WAZ) at the 3rd household visit, and change in both WAZ and weight between visits 1 and 3.

Results. As of April 1, 2014, 57 babies with complete illness information had been followed to their 3rd household visit (mean age: 10.6 months). Median PIDS, PURI and PNURI from birth to this visit were 7% (Q1-Q3:4-11; mean: 10), 5% (Q1-Q3:3-8; mean: 9) and 2% (Q1-Q3:1-3; mean: 3), respectively. Overall mean WAZ at the third visit was -0.29 (Q1-Q3:-1.19-0.72; median:-0.63), with mean differences between visits in WAZ of -0.67 (Q1-Q3:-1.38 - -0.20; median:-0.94) and in weight of 3.69 kg (Q1-Q3: 2.77-4.49, median: 3.45). Greater PIDS, PURI or PNURI correlated with lower WAZ, greater change in WAZ and less weight gain at visit 3 although this finding was statistically significant only for change in WAZ (see * in figure). These growth patterns were particularly striking among never-breast fed babies although the sample size is as yet too small to make statistical comparisons (n = 11).



Conclusion. Among children in the US, routine childhood infectious diseases appear to result in decreased growth in babies up to ten months of age.

Disclosures. **All authors:** No reported disclosures.

989. Pediatric Patients Hospitalized for Community Acquired Respiratory Viral Infections – Comparison of Virus-Specific Mortality, Length of Stay, and Hospital Charges

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Background. Respiratory viral (RV) infection is one of the most common illnesses, causing more yearly doctor visits and absences from school and work than any other illness. The viruses involved may be respiratory adenoviruses (Adeno), parainfluenza (paraflu) viruses, human metapneumovirus (HMPV), influenza (Flu) viruses, respiratory syncytial virus (RSV), and rhinoviruses (Rhino). This study described and compared the clinical and financial impact of these infections in a pediatric hospital serving the District of Columbia metropolitan area.

	Adenovirus	Flu, Type A (H3N2 Seasonal)	Flu, Type A (H1N1 pandemic (2009))	Flu, Type B	HMPV	Rhino/Entero	Para Flu	RSV
Overall								
Number of cases	188	74	114	108	267	1776	198	941
Average age (years)	3.72	6.08	7.73	6.7	3.98	4.26	4.22	1.62
LOS (days): average	6.65	4.31	7.65	8.6	7.29	7.41	7.35	5.55
Expired upon discharge	4	0	1	1	4	17	3	3
Case-fatality	2.1%	0.0%	0.9%	0.9%	1.5%	1.0%	1.5%	0.3%
Charges ($): average	$90,664	$38,987	$90,097	$98,412	$96,668	$86,511	$80,376	$53,175
Patient Admitted to Intensive Care Unit (ICU)								
ICU admissions	52	12	41	26	101	572	59	217
ICU admissions %	27.7%	16.2%	36.0%	24.1%	37.8%	32.2%	29.8%	23.1%
ICU LOS (days): average	6.75	3.42	7.8	11.3	12.2	5.7	5.36	6.62
Charges ($): average	$192,729	$80,758	$175,492	$280,527	$192,583	$138,524	$118,936	$131,948

Methods. This cohort study included children and adolescents admitted to the institution between September 2011 and December 2013 for a community-acquired RV infection, defined as the isolation of one or more respiratory viral pathogens detected in Nasopharyngeal aspirates using multiplex PCR, in patients with clinical symptoms within four days of admission. Information on patient demographic, discharge diagnoses, length of stay (LOS), intensive care unit (ICU) admission and LOS, and discharge disposition was extracted from the hospital's administrative database. A patient that had greater than 1 RV detected in one specimen was excluded from the analysis.

Results. The study identified 2905 patients who encountered 3666 hospitalizations resulting in a total of 25,151 days LOS and $2.86 million hospital charges. Nearly 30% (29.5%) of patients were admitted to the ICU for a total LOS in the ICU of 6,852 days. Thirty-three (0.9%) patients died during the hospitalization. The majority of hospitalizations was due to Rhino/enterovirus (48.7%), followed by RSV (25.7%). The average hospital charges per hospitalization were the highest in Flu (Type B) followed by HMPV. The proportion of ICU admissions was the greatest in HMPV (37.8%) followed by Flu (Type A, H1N1 pandemic 2009) (36.0%). The case-fatality rate was the highest in Adeno (2.1%) followed by HMPV and paraflu infections (1.5%).

Conclusion. This study demonstrated that RV infections in pediatric patients are associated with substantial healthcare expenses. It remains prudent to improve measures such as public vaccination and education to reduce severe infections that would require medical attentions and hospitalizations.

Disclosures. **All authors:** No reported disclosures.

990. Implementation of Routine Testing for Human Rhinovirus (HRV) detection and quantitation: Impact of Coinfections, Age and Disease Severity

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Background. HRV are a frequent cause of upper but also lower respiratory tract infections (LRTI) in children. In the clinical setting it is not uncommon to identify HRV with other respiratory viruses. Whether HRV loads are different between single HRV vs HRV coinfections and associated disease severity has not been well characterized.

Methods. From July 28, 2011 to December 31, 2013 all respiratory samples sent to the Virology Lab at Nationwide Children's Hospital for respiratory viruses testing by real time PCR were reviewed. The standard panel included: HRV, respiratory syncytial virus, parainfluenza virus, influenza A&B, adenovirus and human metapneumovirus. Semiquantitative viral loads were reported as Ct values and compared between patients with single HRV vs HRV coinfections according to age and disease severity assessed by the need for hospitalization and type of admission unit.

Results. During the study period 3215 respiratory samples tested positive for HRV: 2578 (80.2%) were positive for HRV alone and 637 (19.8%) for HRV in combination with other respiratory virus. Children infected with HRV alone were significantly older than those with HRV coinfections (median IQR in months: 17[4-60] vs 11[4-23] p <0.0001). Viral loads were significantly higher (lower Ct values) in HRV only vs HRV coinfections (24.9 [21.5-28.6] vs 26.8 [23.3-31.2]; p < 0.0001). Lastly, single HRV infections were significantly more common in inpatients and specifically in neonates requiring ICU care (NICU) and in the hematology/oncology ward, while HRV coinfections were significantly more common in the outpatient setting.

	HRV Only (N=2578)	Coinfection (N=637)	P
Demographic Characteristics			
Age, median, IQR (months)	17 [4-60]	11 [4-23]	<0.0001
Gender, n(%)			
Male	1526 (59.2)	391 (38.6)	0.313
Female	1052 (40.8)	246 (61.4)	
Admission Unit, n (%)			<0.0001
ICU	387 (15.0)	82 (12.9)	
NICU	51 (2.0)	5 (0.8)	
Non-ICU	1540 (59.7)	364 (57.1)	
Heme/Onc	108 (4.2)	13 (2.0)	
Outpatient	423 (16.4)	162 (25.4)	
OP Controls	69 (2.7)	11 (1.7)	
Ct values HRV, median, IQR	24.9 [21.5-28.6]	26.8 [23.3-31.2]	<0.0001

Conclusion. HRV loads were influenced by the presence of other respiratory viruses and were significantly higher in children with single HRV infections. In addition,

HRVs were more commonly identified as single pathogens in older children and in children requiring ICU or treatment for cancer.

Disclosures. **All authors:** No reported disclosures.

991. Characteristics of Human Rhinovirus Infection in Pediatric Age

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Background. Evaluation of the etiologic role of human rhinovirus (HRV) found in the nasopharynx of children with acute respiratory problems is difficult because it was reported that HRV can be carried by asymptomatic subjects or found in healthy children with previous disease. However, phylogenetic analysis of HRV has shown that a great number of different HRV strains can simultaneously circulate and infect people, suggesting possible continuous re-infection. Differentiation of HRV persistence from re-infection is critical and genotyping of sequentially identified strains could help at this regard. This study was planned to evaluate genetic characteristics of HRV sequentially identified in young children.

Methods. From November 1, 2013 to March 31, 2014, a group of otherwise healthy children aged 1 to 18 months was studied. Parents were asked to collect every week a nasopharyngeal swab, to return to the Center for a monthly control visit and, when a febrile episode occurred, to complete a diary recording child's clinical problems and medical prescriptions. RT-PCR was performed to identify HRV and positive samples were used for sequencing analysis and for reconstructing the phylogenetic tree.

Results. A total of 91 children was enrolled. HRV was identified in 516 swabs. All but 3 subjects had at least one swab positive in most of the cases without significant clinical problems. HRV types were identified in 392 samples (76.0%; HRV-A 151, 38.5%; -B 62, 15.8%; -C 179, 45.7%). Positivity for ≥4 consecutive samples was found in 38 (43.2%) children. Of these, only 12 had the same strain (A12 in 3 cases and one case each for A10, A76, A89, B14, B86, B103, C1, C25, C43).

Conclusion. This study indicates that in healthy children HRV tends to persist in the nasopharynx for a limited period of time and re-infection is the most common cause of repeated HRV identification in the same subject. Prolonged HRV persistence is found in a minority of children. Further studies are needed to evaluate whether this depends on host or virus characteristics.

Disclosures. **All authors:** No reported disclosures.

992. Respiratory syncytial virus infections in children in rural Nepal: a prospective community-based study

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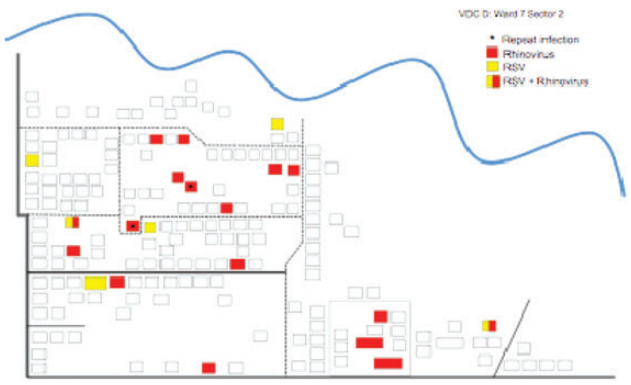
Background. Acute lower respiratory tract infections are responsible for the greatest burden of deaths in children worldwide. Respiratory syncytial virus (RSV) is the most important cause of viral pneumonia. No prior studies have evaluated the disease burden and transmission patterns of RSV in a community-based rural setting in south Asia.



Methods. A prospective randomized controlled trial of clean cookstove installation was conducted in rural Nepal. Households with children age 1-36 months were enrolled and followed through weekly home visits. In a subsample of households, mid-nasal swabs were collected from children with symptoms of a respiratory illness and tested for RSV and 11 other respiratory viruses by PCR. RSV sequencing was performed using a semi-nested PCR assay.

Results. From July 2011 to September 2013, 258 children in 247 households experienced 298 illness episodes. Among these households, the median number of household members was 9 (IQR: 7, 13), of whom 3 (IQR: 2, 4) were under age five. Eighty-eight (36%) households had members who smoked. RSV was detected in 76 (26%) illness episodes; 31 (41%) episodes had other respiratory viruses detected, including 20 (65%) with rhinovirus. Clinical data are available for 36 children with 46 RSV illness episodes; median age at illness was 11 months (SD: 6) and 12 (33%) were male. RSV illness episode symptoms included refusal to feed (n = 22; 48%), chest indrawing (n = 8; 17%), cyanosis (n = 1; 2%), and lethargy or unconsciousness (n = 13; 28%). Mean respiratory rate was 24 (SD: 5), and mean oxygen saturation was 97% (SD: 3%). RSV peaked in September to January in all 3 years. Subtype A was detected in 61 and subtype B in 14 samples. Only RSV A was detected in 2011-2012, while both subtypes circulated in 2012-2013. Three geographic clusters of RSV were detected in Season 1. One cluster of six illness episodes occurred in one village between October and December 2011 (Figure 1). Identical genotypes were observed to cluster in 2011-2012 as well.

Conclusion. In a rural setting in south Asia with home-based surveillance, RSV caused a significant burden of illness in young children. There was a clear seasonality to RSV over 3 years, with temporal and geographic clustering of RSV by subtype and genotype.

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993. Role of Maternal Antibodies in Human Parechovirus Type 3 Infection in Young Infants

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Background. Human parechovirus type 3 (HPeV3) is an emerging pathogen that causes sepsis and meningoencephalitis in neonates and young infants. Although HPeV3 infection presents with serious clinical manifestations, other genotypes do not cause similar infections in young infants; thus, it is necessary to determine why HPeV3 results in severe infection in this age group. We tested the hypothesis that maternal antibodies are important in the pathogenesis of HPeV3 infection.

Methods. Cord blood samples were collected from healthy neonates born at full term in a city hospital in Niigata, Japan from September 2013 through January 2014. Neutralizing antibody titers (NATs) to HPeV1, 3, and 6 were measured using LLC-MK2 cells. NATs were also prospectively measured in young infants (n = 4) with clinically suspected HPeV3 infection that was later confirmed by real-time PCR and direct sequencing of the VP1 region of the virus.

Results. We evaluated 175 cord blood samples. Median gestational age (range) was 39.7 (37.1-41.9) weeks, and median maternal age (range) was 32 (16-44) years. The geometric mean (95% CI) titer of antibodies to HPeV3 was 33.9 (25.4-45.3), as compared with 52.0 (40.5-66.8) for HPeV1 and 48.9 (35.7-66.9) for HPeV6. At a cutoff of 1:8, the seropositivity rate for HPeV3 was 81%, which was similar to the rates of 89% for HPeV1 and 83% for HPeV6. The four patients infected with HPeV3 had low NATs (≤1:16) at disease onset and subsequently were confirmed to have high NATs (≥1:512) after the infection. The geometric mean (95% CI) titer of antibodies to HPeV3 in mothers aged 16-24 years (336.5 (176.1-642.9), n = 11) were higher than those in mothers aged 25-34 years (31.9 (22.0-46.4), n = 107) or aged 35-44 years (24.4 (15.4-38.6), n = 57) ($P < 0.001$), suggesting dominant exposure to the specific age group in this population.

Conclusion. The present findings suggest that maternal antibodies to HPeV3 are important in the pathogenesis of HPeV3 infection in neonates and young infants. Antibody supplementation may thus help improve the clinical course of affected patients.

Disclosures. **All authors:** No reported disclosures.

994. Human Parechovirus Type 3 Infection as a Cause of Apnea in Premature Infants

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Background. Human parechoviruses (HPeVs) are newly recognized viruses, which have been reported to be associated with gastroenteritis or respiratory symptoms in young children. Among them, HPeV type 3 (HPeV3) has been known as a pathogen causing sepsis-like syndrome, central nervous system infections, and sudden infant death syndrome in young infants. Although respiratory-syncytial virus (RSV) and pertussis are known to cause apnea in young infants, little information is available regarding a role of HPeV3 on apnea in young infants.

Methods. We experienced four infants with apneic episodes caused by HPeV3 infection diagnosed by PCR and later confirmed by the direct sequencing of the VP1 region of the virus. The clinical courses of the cases were retrospectively reviewed. The nucleotide sequences of VP1 region were analyzed phylogenetically.

Results. All four cases were preterm infants (median gestational age (GA) 30.5 weeks) and required oxygen supplementation for apnea and oxygen desaturation. Case 1 and 2 were monozygotic twins, delivered at GA of 27 weeks and hospitalized in NICU due to prematuity. On day 81 and 83, respectively, they presented with fever, lethargy, tachycardia and apnea. HPeV3 was detected in their serum and stool samples. Their mother had rhinorrhea and diarrhea a few days prior to their onset of disease and her stool samples were positive for HPeV3. Case 3 and 4 were dizygotic twins, delivered at GA of 34 weeks. They presented with fever, poor sucking, rash on trunks, and apnea on day 60 and 63, respectively, and required hosipitalization for sepsis work-up. Case 3 required mechanical ventilation for 3 days due to acute respiratory failure. All four cases survived without any sequelae.

The viral sequencing analysis of VP1 region demonstrated that each isolate was identical by 95% with the original strain A308/99 found in Japan in 1999, suggesting that these infections were caused by the same circulating strain.

Conclusion. This is the first case series of premature infants presented with apneic episodes caused by HPeV3. Although RSV and pertussis are known to be the common causes for apnea in young infants, HPeV3 infection should be included in the differential diagnosis of apneic infants, especially in those with prematurity.

Disclosures. **All authors:** No reported disclosures.

995. Comparing the Clinical Presentation of Viral Causes of Pediatric Acute Gastroenteritis

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Background. Children with acute gastroenteritis (AGE) present with vomiting, diarrhea, or both. The objective of our study was to compare the clinical presentation of viral causes of AGE when seeking medical care.

Methods. AGE surveillance for children ≥15 days and <18 years was performed at Vanderbilt Children's Hospital outpatient (OP) clinics and emergency department (ED). Stool specimens were tested by RT-PCR at the TN Department of Health central laboratory for norovirus (NoV) genogroups 1 and 2, sapovirus (SaV), and astrovirus (AsV). ELISA for rotavirus (RoV) VP6 antigen (Rotaclone®) was performed at Vanderbilt. AGE presentation was characterized as fever, vomiting only, diarrhea only, or both.

Results. From December 1, 2012-November 30, 2013, 1217 AGE cases (763 [63%] ED, 454 [37%] OP) were enrolled, and 965 stool specimens (590 [61%] ED, 374 [39%] OP) were collected, with 52% males; 59% white, 36% black, and 38% Hispanic and a median age of 43 months. 422 (44%) patients had at least one virus detected, with 55 (13%) with more than one virus detected. Frequencies of viruses were: NoV G1, 15 (2%); NoV G2, 142(15%); NoV G1 and G2, 5 (<1%); RoV, 155 (16%); SaV, 117 (12%); and AsV, 49 (5%). One patient was excluded from the analysis because diarrhea status was unknown. Table 1 summarizes AGE presentation overall. Table 2 summarizes presentation by each virus, without co-detection.

Table 1: AGE presentation

	Vomiting	Diarrhea	Both	Fever	Total
All AGE	342 (28%)	230 (19%)	644 (53%)	782/1211 (65%)	1216
AGE with stool	246 (26%)	191 (20%)	527 (55%)	625/960 (65%)	964

Table 2: AGE presentation by Virus, no co-detection

	NoV	RoV	SaV	AsV	No Virus
Vomiting	38 (28%)	**22 (18%)***	22 (26%)	7 (26%)	149 (28%)
Diarrhea	**8 (6%)***	**11 (9%)***	13 (16%)	7 (26%)	144 (27%)
Both	**88 (66%)***	**89 (73%)***	49 (58%)	13 (48%)	**249 (46%)***
Fever	**69 (51%)***	77 (64%)	51 (61%)	21 (78%)	**377 (70%)***
TOTAL	134	122	84	27	542

*p<0.05, fisher exact comparing study cohort

Conclusion. Cases of RoV and NoV were more likely to have both vomiting and diarrhea, but less frequently had symptoms of diarrhea alone. In contrast, isolated vomiting was less common among subjects who tested positive for RoV. Children with NoV were less likely to present with fever, while children with no detected virus were more likely to present with fever.

Disclosures. **All authors:** No reported disclosures.

996. Predictors of Sensorineural Hearing Loss (SNHL) in Infants with Symptomatic Congenital CMV Infection

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Background. Congenital CMV (cCMV) is the leading non-genetic cause of sensorineural hearing loss (SNHL) in the U.S. Approximately 40-60% of infants with symptomatic cCMV infection develop long term sequelae such as hearing loss. Currently, there are no identified predictors of hearing loss. The objectiveis to determine clinical predictors of SNHL in infants with symptomatic cCMV infection.

Methods. Findings from a longitudinal follow-up study of children with symptomatic cCMV at the University of Alabama (UAB) were analyzed. Infants were considered to have symptomatic cCMV infection if they were positive for CMV by saliva or urine rapid culture and had findings suggestive of congenital infection at birth. Infants with jaundice, petechiae, purpura, hepatosplenomegaly, elevated aspartate aminotransferase, thrombocytopenia and lacked CNS involvement were considered to have transient symptoms. Infants with microcephaly, seizures, abnormal neurological examination, and abnormal neuroimaging findings with/without any of the transient symptoms were categorized as the group with CNS involvement. Incidence of SNHL was compared between the groups with transient symptoms, CNS involvement and only petechial rash.

Results. 176 infants with symptomatic cCMV infection were followed at UAB. CNS involvement and transient findings were found in 56% and 31% of infants, respectively while 13% of infants only had a petechial rash. Hearing outcome was available in 96% of study children. The overall incidence of hearing loss was found to be highest in the group with CNS involvement followed by those with transient findings and infants with only a petechial rash [59% (54/92) vs 39% (21/54) vs 22% (5/23) respectively; p = 0.0004). SNHL at birth was significantly more frequent in infants with CNS involvement compared to infants with transient findings or only petechial rash [42% (39/92) vs 24% (13/54) vs 13% (3/23) respectively; p = 0.0019]. The incidence of late onset hearing loss was not significantly different between these groups (p = 0.08).

Conclusion. Among infants with symptomatic cCMV infection, those with evidence of CNS involvement in the newborn period are at the greatest risk for SNHL overall and congenital hearing loss. However, findings in the newborn period are not predictive of late onset hearing loss.

Disclosures. **All authors:** No reported disclosures.

997. Saliva vs Urine PCR: The Ideal Sample for congenital CMV Screening and Diagnosis

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Background. Congenital CMV infection (cCMV) is a common congenital infection and a significant contributor to non-genetic sensorineural hearing loss (SNHL). Real-time PCR of newborn saliva specimens has been shown to be highly sensitive and specific compared to culture based methods for CMV screening. Although both saliva and urine samples are known to be acceptable for identifying infants with cCMV, it is thought that urine samples may contain more virus and thus, are optimal for cCMV screening. The objective is to compare viral load (VL) levels between saliva and urine samples from a large cohort of infants with cCMV infection identified through a newborn screening program.

Methods. As part of the NIDCD CHIMES study, newborns at 7 U.S. medical centers were screened for CMV by saliva and dried blood spot PCR. Infants who screened positive were enrolled in a follow-up study to confirm congenital infection by testing saliva and urine samples using a previously described real-time PCR assay. CMV viral load in saliva samples obtained at screening and enrollment was compared to urine collected at enrollment in follow-up.

Results. Of the 100,332 newborns screened for CMV from 2007 to 2011, viral load levels in both saliva and urine samples were available in 73% (336/462) of infants with

confirmed cCMV. Of these, 36% (121/336) were enrolled within the first 3 weeks of life. The median viral load level in saliva at screening and enrollment ($2.x10^6$ IU/ml and $1.1x10^7$ IU/ml, respectively) was significantly higher than in urine ($8.3x10^5$ IU/ml; $p < 0.0001$). There was no significant difference between VL in saliva and urine in infants with and without symptomatic disease and with and without congenital SNHL. In the smaller cohort of infants enrolled within 3 weeks of birth, median saliva VL at screening and enrollment ($1.1x10^6$ IU/ml vs $9.3x10^6$ IU/ml, respectively) was higher than urine VL ($7.9x10^5$IU/ml; $p < 0.0001$).

Conclusion. Infants with congenital CMV infection shed large amounts of virus in both saliva and urine. However, saliva samples contained higher viral load than urine, are easier to collect and do not require DNA extraction. Therefore, we propose that saliva should be considered the ideal specimen and real-time PCR of saliva is appropriate for both newborn screening and diagnosis of cCMV.

Disclosures. **D. Bernstein**, Genocea: Research Contractor, Research support

998. Detection of Cytomegalovirus (CMV) in Cerebrospinal Fluid of Infants with Congenital CMV Infection: Is It Worth Doing the Lumbar Puncture?

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Background. Congenital CMV infection is a leading cause of sensorineural hearing loss (SNHL) and neurodevelopmental impairment in childhood. Information on CMV detection in cerebrospinal fluid (CSF) and its association with outcomes is limited. The objective of this study was to determine the significance of CMV detection in CSF of infants with congenital CMV infection.

Methods. Retrospective review of cases of congenital CMV infection diagnosed at Nationwide Children's Hospital, Parkland Memorial Hospital/Children's Medical Center Dallas, and the University of Oklahoma Health Sciences Center from 1996-2014. Diagnosis of congenital CMV was made by culture or PCR from urine or saliva within the first 3 weeks of age. Detection of CMV in CSF was performed by culture or PCR. Clinical, laboratory, radiographic, and audiologic data was reviewed. Infants in whom CMV was detected in CSF were compared to those whose CSF was negative for CMV.

Results. Twenty-two infants with congenital CMV infection who had a lumbar puncture performed and CSF tested for CMV were enrolled. All 22 infants had clinically apparent ("symptomatic") disease. 10 (45%) infants had CMV detected in CSF (CSF+) and were compared to the 12 infants whose CSF was CMV-negative (CSF-). The CSF+ infants did not differ from those whose CSF was CMV negative (CMV-) in age at diagnosis (median/range; 1.5 [1-8] vs1 [1-17]; $p > 0.05$), platelet count ($p = 0.47$), alanine aminotransferase ($p = 0.11$), direct bilirubin concentration ($p = 0.08$), or CSF analyses including white blood cell count ($p = 0.98$), protein content($p = 0.39$), or glucose concentration ($p = 0.31$). Of the CSF+ infants, 6 (60%) had SNHL, while 10 (83%) CSF- infants had SNHL. Abnormalities on CNS imaging studies, either ultrasound/CT/MRI, were comparable between groups.

Conclusion. CMV was frequently detected in CSF of infants with clinically apparent congenital CMV infection. However, its detection was not associated with increased rate of SNHL or neuroimaging abnormalities. Larger studies that incorporate neurodevelopmental assessments are needed to determine the potential role of CSF evaluation in the management of infants with congenital CMV infection.

Disclosures. **All authors:** No reported disclosures.

999. The Role of Quantitative Blood PCR in the Management of Congenital *Cytomegalovirus* Infection

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Background. The role of quantitative blood PCR (qPCR) in the management of congenital CMV infection has not yet been determined. The objective of this study was to determine the time to undetectable viral load (uVL) among infants treated with oral valganciclovir (VGCV) for congenital CMV infection.

Methods. All cases of congenital CMV diagnosed and treated between 2003 and 2013 at Centre Hospitalier Universitaire Sainte-Justine were identified retrospectively through the laboratory and clinical database. Cases were included for analysis if at least two blood qPCRs were done at any time after diagnosis while on treatment. CMV viral loads in QIAamp extracted DNA blood samples were estimated with an *in-house* qPCR method using TaqMan® MGB Hydrolysis probes/primers designed for UL83 gene and performed on a ABI 7500 platform. Treatment start time was at the discretion of the consultant physician, and treatment was stopped when qPCR became undetectable. Survival analysis was used to determine time to uVL and factors associated with a more rapid decline.

Results. 27 cases of congenital CMV were identified during the study period. Among them, only 9 of the treated infants had follow-up qPCRs; 2 received sequential IV and oral therapy, 7 received oral VGCV alone. Mean dose of VGCV was 15.2 mg/kg/dose (range 8.7-17.1 mg/kg/dose). Median initial qPCR was 79 460 copies/ml (IQR 12 1333- 203 525), and mean time to uVL was 199 days (range 30-450 days). After 6 months of treatment, only 44% (95% CI 20.0-79.6) had achieved uVL. This increased to 70.4% at 9 months (95% CI 39.0-94.8) and 85% (95% CI 53.0-99.0) 12 months after treatment was started. Infants were more likely to attain uVL if their initial viral load was <100,000 copies/ml (HR 1.99, $p = 0.51$), initiated treatment at <7 days of life (HR 4.46, $p = 0.18$), and initiated sequential IV then oral vs oral therapy alone (HR 2.31, $p = 0.36$), though none of these differences were statistically significant.

Conclusion. The use of serial qPCR may be a useful tool to monitor CMV disease activity and to guide treatment decisions in congenital CMV infection. Our results suggest that the recommended treatment duration of 6 weeks to 6 months may be too short to achieve an uVL in infants. Larger longitudinal studies are needed to confirm these findings, and to correlate viral load to clinical outcome.

Disclosures. **All authors:** No reported disclosures.

1000. Effect of *Cytomegalovirus* Infection on Breastfeeding Transmission of *HIV* and on the Health of Infants Born to HIV-infected Mothers

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Background. Cytomegalovirus (CMV) infection can be acquired in utero or postnatally through horizontal transmission and breastfeeding. The effect of postnatal CMV infection on postnatal HIV transmission is unknown.

Methods. The Breastfeeding, Antiretrovirals and Nutrition (BAN) study conducted in Lilongwe, Malawi, randomized 2369 mother-infant pairs to 3 antiretroviral (ARV) prophylaxis arms: mother (triple regimen), infant (nevirapine), or neither, for up to 28 weeks of breastfeeding, followed by weaning. We evaluated CMV infection by performing PCR on stored plasma and peripheral blood mononuclear cells at 24 weeks of age in 492 infants with available specimens. Infants testing CMV-positive at 24 weeks were also tested at birth to approximate the congenital CMV infection rate, while those CMV negative at 24 weeks were tested again at 48 weeks. Study arms were compared and a Cox proportional-hazards model was used to determine if CMV infection was associated with infant morbidity, mortality, or postnatal HIV acquisition.

Results. At 24 weeks of age, CMV infection was detected in 345/492 infants (70.1%); the median plasma CMV viral load was 176.4 copies/ml. Of those CMV-positive at 24 weeks, 8 were also positive at birth, for an estimated congenital CMV infection rate of 2.3%. Of those CMV-negative at 24 weeks, 28.1% were CMV-positive at 48 weeks of age, for an estimated rate of CMV infection of 78.5% at 48 weeks. Among infants HIV-infected perinatally, congenital CMV infection rate was 10%. Plasma CMV viral load was significantly higher in HIV-infected, compared with uninfected, infants (median 1,258.6 vs 174.2 copies/ml; $p = 0.045$). CMV infection at 24 weeks was associated with subsequent acquisition of HIV infection through breastfeeding (HR = 4.52; $p = 0.15$), infant mortality (HR = 4.05; $p = 0.18$), and with HIV infection or death between 24-48 weeks of age (HR = 4.27; $p = 0.05$). There was no difference in CMV infection rates by ARV study arm.

Conclusion. Most breastfed infants of HIV-infected mothers in this resource-limited setting are infected with CMV by 24 weeks of age. The estimated rate of congenital CMV infection is higher than that reported for infants in other settings, and even higher for infants HIV-infected at birth. Early CMV infection may be a risk factor for HIV infection through breastfeeding and for infant mortality.

Disclosures. **All authors:** No reported disclosures.

1001. Success of Perinatal Hepatitis C Testing: Philadelphia, 2011 - 2013

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Background. Vertical transmission of Hepatitis C Virus (HCV) from mother to infant is the most common route of infection among children. Five percent of infants born to mothers with chronic HCV are unable to clear the infection by 18 months and live with chronic disease. HCV positive infants and young children are often asymptomatic so screening in the early years of life is crucial for appropriate diagnosis. There are guidelines that require testing of both hepatitis B virus positive pregnant mothers and their infants, but no protocols exist for perinatal HCV. This study demonstrates provider success in appropriately testing infants born to HCV positive mothers in a major US city with a high burden of HCV.

Methods. HCV antibody and RNA tests reported to the Philadelphia Department of Public Health (PDPH) between 2008 and 2013 were used to identify maternal and infant testing. Additional tests were retrospectively collected from the three largest laboratories serving the pediatric population. Datasets were matched with 2011-2013 birth certificates to identify infants born to HCV infected mothers and to ascertain reporting of infant testing practices. HCV seropositivity among infants born to HCV positive mothers was compared to the expected rate of 5%.

Results. PDPH received reports on 8,152 females who were HCV positive and 12-45 years of age in 2011-2013. Of these, 730 (9%) were found to have delivered at least 1 child, accounting for 816 (1%) of the 74,718 infants born in Philadelphia in the study period. Forty-six of these infants matched to the HCV data (6% overall; 17% from RNA positive mothers), 3 (7%) of whom were RNA-positive. Assuming a rate of 5%, an additional 38 infants would be expected to develop chronic HCV infection.

Conclusion. Repetitive and conclusive testing of pregnant women and infants in their first 18 months is necessary to identify vertical transmission of HCV and initiate infected infants into care. This data shows that an insufficient number of infants are being tested for HCV after birth, likely resulting in a pool of chronically infected children whose disease remains unmonitored. Testing practices should be expanded to include HCV screening for pregnant women and confirmatory HCV testing for their infants.

Disclosures. **All authors:** No reported disclosures.

1002. Active Screening Strategies and Education for Hepatitis C Infected Pregnant Women are Needed to Improve the Identification of Hepatitis C Exposed Newborns

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Background. Hepatitis C virus (HCV) infection is a silent disease and major public health concern that affects ~3.2 million, making it the most common chronic blood borne infection in the US. While most children acquire HCV perinatally, without appropriate maternal screening, <5% of cases are identified. The American Academy of Pediatrics and Centers for Disease Control and Prevention (CDC) recommend testing of all infants born to mothers with HCV, yet CDC and American College of Obstetrics and Gynecology (ACOG) recommend testing only high risk pregnant women. The objective of this study was to improve identification of HCV exposed newborns.

Methods. The project was conducted in 2 phases. Intervention 1: An educational handout regarding testing of newborns exposed to HCV was developed and given to HCV positive mothers after delivery along with an appointment for testing the newborn. HCV testing and newborn follow-up data were analyzed pre-intervention (January-December 2012) and post-intervention (January-December 2013). Intervention 2: To further improve identification of HCV exposed newborns, collaborative measures between Obstetrics (OB) and Pediatric Infectious Disease programs, were implemented. A HCV risk screening questionnaire based on ACOG recommendations was administered to all pregnant women attending a university OB clinic. Women identifying risk factors were tested for HCV antibody. Results from pre-intervention (January-March 2013) and post-intervention (January-March 2014) periods were compared.

Results. Prior to intervention 1, 3 (23%) of 13 newborns were tested and all were negative. After intervention 1, 14 (50%) of 28 newborns were tested, 1 was HCV PCR positive. Prior to intervention 2, only 8 (0.7%) of 1112 pregnant women were tested for HCV and all were negative, compared to 116 (12%) of 977 women after intervention 2 ($p < .0001$, chi-square test). 7 (6%) were HCV antibody positive.

Conclusion. Our data suggest that educational handouts improve HCV testing of exposed newborns. In addition, many HCV infected pregnant women and their exposed newborns would not be identified unless active interventions for screening are in place. Universal testing of pregnant women may be a better strategy to identify HCV exposed newborns.

Disclosures. **All authors:** No reported disclosures.

1003. The Impact of Cidofovir on the Renal Function of Pediatric Solid Organ Transplant Recipients

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Background. The experience with cidofovir in pediatric SOT is limited. The study aimed to assess the impact of cidofovir use on the renal function.

Methods. Summary statistics were presented for demographics and outcomes, Wilcoxon signed-rank tests to compare changes in renal function and Wilcoxon rank-sum tests to test association with potential confounding factors.

Results. We included 25 patients (mean age 4.2years; SD 4.6): liver-small bowel (15), small bowel (4), liver (3) and kidney (3) transplant recipients. Viral infections: adenovirus (20), BKv (2), HHV6 (1), and EBV (1). 24% of patients while on cidofovir compared with 4% at baseline ($p = 0.03$) were on renal replacement therapy (RRT). For patients not on RRT, there was no difference: 1) in the median creatinine clearance between baseline and one month after ($p = 0.32$) or end of cidofovir treatment ($p = 0.23$); 2) in the creatinine from baseline to end of cidofovir therapy ($p = 0.2$); there was marginal decrease in the median creatinine from baseline to one month post-cidofovir treatment ($p = 0.06$). Less patients had proteinuria (72.2% vs 27.8%; $p = 0.02$) and hematuria (22.2% vs 0%) at the end than at the beginning of cidofovir treatment. No evidences of associations were found between changes in creatinine clearance (by univariate analysis) with: exposure to vancomycin ($p = 0.44$), amikacin ($p = 0.13$), dopamine ($p = 0.66$), epinephrine ($p = 0.99$), norepinephrine ($p = 0.48$), intravenous contrast ($p = 0.41$) and surgery ($p = 0.59$).

Conclusion. Cidofovir was mainly used to treat adenovirus infections. In our study, cidofovir did not have nephrotoxic effects during the treatment and 1 month after treatment in pediatric transplant recipients, although they required RRT while on cidofovir because of fluid overload.

Disclosures. **All authors:** No reported disclosures.

1004. Technical and Logistical Issues in Incorporating Statistical Process Control into Healthcare-Associated Infection Surveillance Programs

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Background. Statistical process control (SPC) can be an effective complement to healthcare-associated infection (HAI) surveillance. Since this use of SPC somewhat differs from its manufacturing origins, some issues warrant exploration to maximize SPC's value in detecting outbreaks and reducing HAIs. Little empirical investigation has been conducted to develop a framework for managing signals from such a system.

Methods. A team of HAI (DU) and SPC (NU) experts retrospectively applied conventional SPC methods to 10 years of de-identified surgical site infection (SSI) data from 40 community hospitals in the Duke Infection Control Outreach Network (DICON), focusing on 8 known SSI outbreaks. We met bi-weekly to review results and issues potentially important to implementing such an approach. Discussions were organized around 3 categories: detection performance and optimization, alternate methods, and logistics of managing resultant outbreak signals. Pilot investigations were conducted using empirical data and Monte Carlo analysis.

Results. Shewhart and EWMA control charts detected all 8 outbreaks 0-12 months earlier than originally identified via standard surveillance. The table illustrates the detection of one outbreak 0-3 months early. Issues affecting detection included what baseline data, aggregation level (hospital, surgeon, procedure), and EWMA smoothing factor to use. The value of dual, start-up, and sequential probability ratio SPC methods was identified as worthwhile to investigate.

Empirical performance of Shewhart and EWMA charts illustrating one known outbreak, using different design parameters and baselines (A: Hospital's year 1 data, B: DICON average benchmark).

	Shewhart		EWMA ($\lambda = 0.2$)		EWMA ($\lambda = 0.4$)	
Performance	A	B	A	B	A	B
# of months from first signal until known outbreak	-	3	-	2	-	3
# of signals in 12 months before known outbreak	0	3	0	3	0	3
# of total signals in non-outbreak years (before and after outbreak)	1	7	1	17	2	12

Conclusion. While SPC methods appear useful for HAI surveillance, several technical considerations need addressing to maximize their benefit, each with potential impact on detection performance. Other SPC methods also may improve detection speed and therefore warrant both theoretic and empirical investigation.

Disclosures. **All authors:** No reported disclosures.

1005. Empirical Performance of Statistical Process Control Methods for Regional Hospital-Acquired Infection Surveillance: A 10-Year Multi-State Study

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Background. Use of statistical process control (SPC) in healthcare is increasing but remains less common than in other industries. Healthcare-associated infections (HAIs) are important applications that can benefit from SPC methods, including use within existing surveillance programs to trigger investigation and intervention. The empirical value of SPC, however, typically is anecdotal and remains unclear to many practitioners.

Methods. We retrospectively applied Shewhart and EWMA SPC charts to 10 years (2003 to 2013) of de-identified surgical site infection (SSI) data, including 8 known SSI outbreaks, from the Duke Infection Control Outreach Network of 40 community hospitals. For both methods, we computed the number of outbreaks detected, months of earlier detection vs traditional surveillance, and total signals produced (TS) over the entire study period as a workload measure. To distinguish between minor unsustained vs major sustained HAI rate increases, we additionally calculated the number of months with signals during the year prior (PS) to each outbreak, monthly consecutive signals (CS) before each outbreak, and signals during each outbreak period (DS).

Results. All known outbreaks were detected by all charts 0 to 12 months earlier than known start dates, on average by 5.8 (Shewhart) and 6.8 (EWMA) months (table). 62.5% of these earlier detections included more than one signal. The total number of signals over the study period (outbreaks, uncertain, or false alarms) averaged 5.5 (Shewhart) and 16.5 (EWMA) per outbreak hospital.

Performance of Shewhart and EWMA control charts to detect known outbreaks (TS: total, PS: previous year, CS: consecutive, DS: during).

	Number of signals				Early detection (months prior to traditional detection)	
Method	Total (TS)	Previous year (PS)	Consecutive (CS)	During (DS)	First signal	First consecutive signal
Shewhart	5.5	1.6	1.1	0.9	5.8	0.6
EWMA	16.5	3.1	1.9	3.3	6.8	1.5

Conclusion. SPC methods appear useful and practical for augmenting current HAI surveillance programs with empirical ability to detect outbreaks earlier. EWMA charts exhibited fastest detection, agreeing with theoretic comparisons in the literature. Alarm rates appear manageable in terms of investigation burden on health systems.

Disclosures. **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

1006. Rates of Complex Surgical Site Infection in a Community Hospital Network Are Declining

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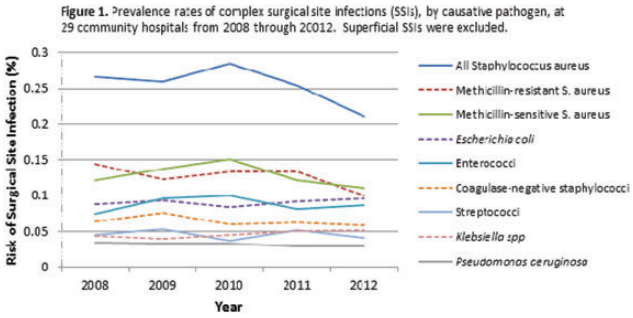
Background. Surgical site infection (SSI) is a common healthcare-associated infection that causes significant morbidity and mortality. Only limited published data are available regarding the epidemiology of SSI in community hospitals during the past 5 years.

Methods. We prospectively collected data from complex SSIs (deep-incisional and organ/space infections) in our network of community hospitals from 2008 through 2013. We determined the overall prevalence rate (PR) of SSI in 2013 and then stratified both by procedure and organism. Among the 29 hospitals participating in our network over the entire study period, we compared the rates of SSI caused by specific organisms, including *S. aureus*, each year from 2008 through 2012. We did not compare SSI rates from 2013 to prior years because of surveillance definition changes.

Results. In 2013, 753 complex SSIs occurred following 124,358 procedures (PR, 0.61 SSI/100 procedures) performed at 40 hospitals. Rate of SSI was highest after peripheral vascular bypass (PR, 3.1/100 procedures); abdominal surgery of the bile duct, liver, pancreas, spleen, or small bowel (PR, 2.7/100 procedures); and colon surgery (PR, 2.7/100 procedures). *S. aureus* was the most common pathogen, isolated from 221 SSIs (PR, 0.18/100 procedures) in 2013; methicillin-sensitive *S. aureus* (MSSA) (n = 114; PR, 0.09/100 procedures) was slightly more common than methicillin-resistant *S. aureus* (MRSA) (n = 107; PR, 0.09/100 procedures) (Figure 1).

Overall SSI rates from the 29-hospital cohort decreased from 2008 (PR, 0.76/100 procedures) to 2012 (PR, 0.69/100 procedures; prevalence rate ratio [PRR], 0.90; 95% confidence interval [CI], 0.82-1.00). The rate of SSI due to *S. aureus* (PR, 0.27 vs 0.21/100 procedures; PRR, 0.79; 95% CI, 0.67-0.95) also decreased over this four-year time period. Rates of SSI from other pathogens were relatively unchanged.



Conclusion. *S. aureus* remained the most common cause of SSI in our cohort of community hospitals. The rate of *S. aureus* SSI declined due to decreases in both MRSA and MSSA, which paralleled the decline in the overall prevalence of complex SSI. These data suggest that surgery is becoming safer in community hospitals in our network largely due to decreased rates of SSI due to *S. aureus*.

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1007. Forced Air Warming (FAW) products and Surgical Site Infections (SSIs)

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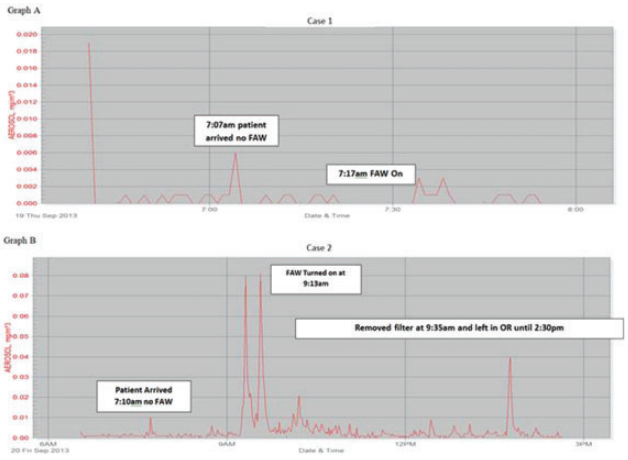
Background. In August 2013 concerns were raised about a recently published study (*Clinical Quality & Infection Control)* that suggested a correlation betweenFAW and SSI caused by aerosolized particulates in air currents. Several other studies had similar findings but none were done in clinical areas. (Camus Y, et al. *Anesthesia & Analgesia*. 1993; 77(5): pp. 995-9) The objective was to determine if FAW is associated with increase in particulates or bacterial/fungal contamination.



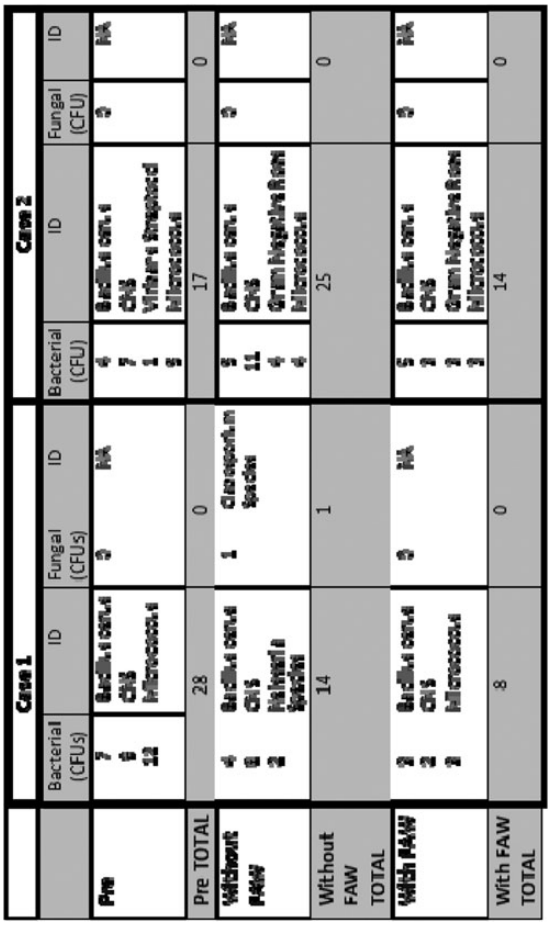
Methods. Testing was performed during 2 operative cases in 2 separate operating rooms.

Case 1 - orthopedic spine case

Case 2 - neurosurgical spine case

Continuous air monitoring was done during 3 time periods: Pre patient, patient without FAW, patient with FAW (graphs A/B) and 3 sets of bacterial and fungal cultures were collected and reported as colony forming units (CFUs).

Results. Continuous air monitoring – Particulate Counts



Bacterial/Fungal Cultures

Conclusion. There was no difference in Bacterial and fungal CFUs regardless of whether the FAW was in use. There were no significant pathogens identified. It is unlikely that FAW would have an association SSIs. There was no difference in particulate counts regardless of whether the FAW was in use.

Disclosures. **All authors:** No reported disclosures.

1008. An Outbreak of Surgical Site Infection Linked to Assisted Gloving Technique

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Background. The study examined the epidemiology of a sudden increase in number of surgical site infection (SSI) following cesarean section.

Methods. There was a retrospective, case-control study to determine risk factors in patients who developed SSI after cesarean section during June 7 and July 7, 2013, compared with patients' epidemiology, pre-, intra-, and post-operative methods and care. We also investigated surgical materials and methods. After the analysis was done, we visited the operating areas and interviewed their staff.

Results. Five patients having deep incisional SSIs were identified from a total of 31 cases who had the operations during the outbreak period (16 cases per 100 operations). No difference in age (30.2 vs 29 years, OR 0.97, $p = 0.68$), body mass index (28.0 vs 28.0 kg/m^2, OR 0.99, $p = 0.99$), estimated blood loss (380 vs 418 ml, OR 1.0, $p = 0.73$), and other potential risk factors (e.g., ASA score, emergency procedure, duration of surgery) between cases and controls. Higher attack rate were found among patients of surgeon B (75% vs 7%, OR 39, $p < 0.01$) and lower rate in scrub nurse A (0% vs 10%, $p < 0.01$). In multivariate analysis, a significant risk factor for SSIs was only in operations done by surgeon B. We interviewed and found that changing in sterile gloving techniques from open- to assisted-technique was the key of the outbreak.

Conclusion. Sterile gloving technique is one of the fundamental of infection prevention strategies to prevent SSIs. Although all kinds of technique are efficient, it is more important for surgeon to practice the new techniques they are not familiar with.

Disclosures. **All authors:** No reported disclosures.

1009. Invasiveness Index as a Risk Factor for Deep Surgical Site Infection after Fusion, Refusion and Laminectomy

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Background. Invasiveness index (II), which is determined by surgical approach, procedure, and number of spine levels treated, has been independently associated with surgical site infection (SSI) risk in patients undergoing elective spine surgery. The use of this measure has not been evaluated in previous risk assessment models for SSI using National Health Safety Network (NHSN) definitions including all fusion (FUSN), refusion (RFUSN) and laminectomy (LAM) procedures. We performed a retrospective cohort study to determine potential SSI risk factors in patients undergoing NHSN spine surgery procedures.

Methods. Patients undergoing FUSN, RFUSN, LAM procedures at our institution from 2007-13 were identified by Infection Control using NHSN definitions as part of routine surveillance. Variables were abstracted from electronic hospital databases (Admission- Discharge-Transfer, Microbiology, Pharmacy, Infection Control) and validated with manual chart review. To assess potential risk factors for deep or organ/space (O/S) SSI, univariate analyses were performed using Chi-square for binary variables and logistic regression for continuous or categorical variables.

Table 1: Variables associated with SSI on univariate analysis

	Variable	No SSI	SSI	%	p-value
Age	Age = 65	1173	25	2.1	$p = 0.01$
	Age < 65	3121	34	1.1	
ASA score	ASA = 4	229	7	3.1	$p = 0.03$
	ASA = 3	4065	52	1.3	
Prior spine surgery	Yes	2095	48	2.3	$p < 0.01$
	No	2199	11	0.5	
Trauma	Yes	64	4	6.3	$p < 0.01$
	No	4230	47	1.1	
Invasiveness Index	<10	3090	21	0.7	Reference
	10-15	711	15	2.1	$p < 0.01$
	15-20	292	6	2.0	$p = 0.02$
	20-25	121	4	3.3	$p < 0.01$
	>25	80	5	6.25	$p < 0.01$
Duration above median for FUSN					$p < 0.01$
Duration above median for LAM					$p = 0.01$

Results. Among 6600 patients, 46 deep infections (0.69/100 procedures) and 16 O/S infections (0.24/100 procedures) were identified. Of the 4353 patients with complete data for calculation of II, there were 2624 (60%) FUSN, 1490 (34%) LAM, and 239 (6%) RFUSN. On univariate analyses, higher II, age > 65, ASA score ≥ 4, prior spine surgery, duration of surgery and trauma were significantly associated with SSI (table).

Conclusion. II may be associated with SSI in patients undergoing FUSN, RFUSN, and LAM for elective and non-elective indications. Further study is needed to determine if II will enhance prediction of SSI risk when classified using NHSN definitions.

Disclosures. **All authors:** No reported disclosures.

1010. Cumulative incidence of surgical site infection in patients with prosthetic joint operations in Japan: a 12-month cohort study in a teaching hospital

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Background. Little is known about incidence for surgical site infection (SSI) after prosthetic joint operations in Japan. We aimed to determine cumulative incidence of SSI after operations of hip replacement (HPRO) or knee replacement (KPRO) during 12-month postoperative periods in a Japanese hospital.

Methods. We performed a 12-month retrospective cohort study on all consecutive patients who underwent HPRO or KPRO during 20 months from May 2010 in a 401-bed community-based university-affiliated teaching hospital. Our study design was based on the methodology of the National Healthcare Safety Network (NHSN) and SSI definition was based on the US-CDC criteria. A certified nurse specialist in infection control nursing collected follow-up data and identified SSI in patients with HPRO or KPRO by using electronic medical records. Definition of SSI required double-check and confirmation by a hospitalist physician investigator. Cumulative incidence of SSI was determined and compared to the benchmark data of US or European surveillances. Risk factors for SSI were analyzed using logistic regression model.

Results. During the 20-month period, 223 patients underwent prosthetic joint operations. In 12-month follow-up, 26 patients developed SSI with cumulative incidence of 11.7% (95% CI, 7.8-16.6%). In these 26 patients, 19 patients (73%) had superficial incisional SSI. Among 147 patients with HPRO, 6 patients developed SSI with cumulative incidence of 4.1% (95% CI, 1.5-8.7%) and, in these 6 patients, 5 patients (83%) had superficial incisional SSI. Among 76 patients with KPRO, 20 patients developed SSI with cumulative incidence of 26.3% (95% CI, 16.9-37.7%) and, in these 20 patients, 14 patients (70%) had superficial incisional SSI. Based on logistic regression analysis, significant risk factors for SSI included total joint replacement (*OR = 33; 95% CI, 14-125*) and ASA score ≧3 (OR = 8.26; 95% CI, 1.99-34.3). The cumulative incidence of SSI was significantly greater than those of US (NHSN) or European (ECDC) benchmark surveillance data (P < 0.01).

Conclusion. In a Japanese teaching hospital, SSI cumulative incidence was high, although majority of them were considered to be superficial incisional SSI.Implementation for its preventive strategy is needed in Japan.

Disclosures. **All authors:** No reported disclosures.

1011. Quick But Not Dirty: Short Operative Time and Surgical Site Infection Rates In Knee and Hip Arthroplasty Procedures

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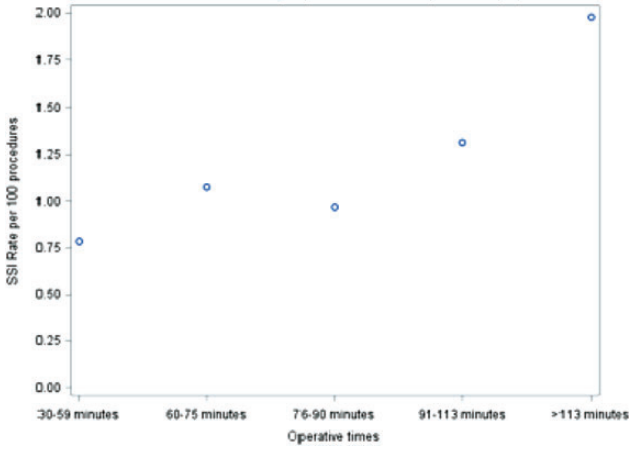
Background. Prolonged operative time is a well-established risk factor for surgical site infection (SSI); however, the risk of SSI in procedures with shorter than average operative times has not been well studied. The aim of this study was to examine the relationship between short operative times and SSI rates following hip and knee arthroplasties.

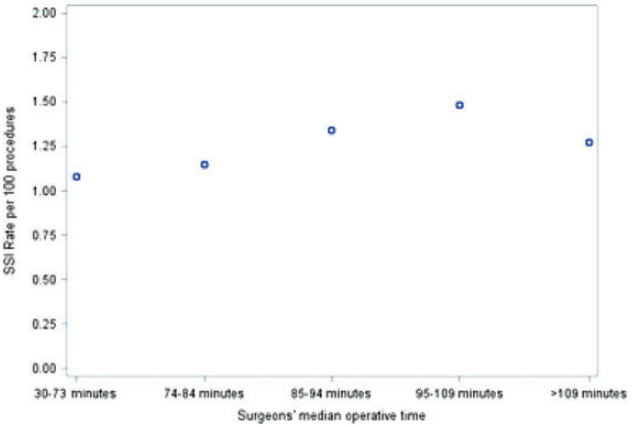
Figure 1. Rates of SSIs following hip and knee arthroplasties by operative time.



Methods. We analyzed prospectively collected SSI surveillance data from 36 community acute care hospitals and 1 ambulatory surgery center participating in the Duke Infection Control Outreach Network. Patients who developed SSI by National Healthcare Safety Network criteria within 365 days of knee or hip arthroplasties performed from January 1, 2008-December 31, 2012 were included in the analysis. Arthroplasties with a duration of <30 minutes or >300 minutes were excluded (522, 0.65%). We ranked procedures by operative time and created five equally distributed operative time groups. We then calculated the SSI rate (SSI/100 procedures) for each group. We followed the same approach to evaluate the relationship between surgeon-specific median operative times and rate of SSI.

Results. 79,572 hip and knee arthroplasties performed by 201 surgeons were included in the analysis. The median operative time for hips and knees was 80 minutes (IQR 62,106) and 83 minutes (IQR 64,106), respectively. The SSI rate was the lowest for arthroplasties in the shortest operative time group (0.78 SSI/100 procedures) compared to the middle group (RR 0.81, 95% CI 0.64-1.03, p-value 0.08); in contrast, SSI rate was highest for arthroplasties in the longest operative time group (1.98 SSI/100 procedures) compared to the middle group (RR 2.04, 95% CI 1.68-2.48, p-value <0.001)(Figure 1). SSI rates were similar across surgeons grouped by median operative time (Figure 2).

Figure 2. Rates of SSIs following hip and knee arthroplasties by surgeons' median operative time.



Conclusion. SSI risk increased with increasing operative time, but was not increased among surgeons whose median operative time was shorter or longer than their peers. The observed increased SSI risk in prolonged cases is more likely due to case-specific factors than surgeon-specific factors.

Disclosures. **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

1012. The Effect of Modification of Operative Procedure Category in the Surgical Site Infections Surveillance in Japan: Toward the Better Stratification

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Background. Surgical site infection (SSI) surveillance is one of the key activities for the prevention of SSI. Incidence of SSI is useful as a benchmark and quality indicator of healthcare facilities, provided that the indicator is risk stratified and standardized. Both of the classical National Nosocomial Infections Surveillance (NNIS) Risk Index and the new procedure-specific modeling method use operative procedure category as the primary and definite risk factor. However, some of the procedure category, such as gastric surgery and hepatobiliary surgery, include many different types of operations. In 2012, the Japanese Healthcare-Associated Infections Surveillance (JHAIS), Japanese nationwide SSI surveillance system, changed its operative procedure category by dividing gastric and hepatobiliary surgeries into three groups, respectively. The aim of this study is to evaluate the appropriateness of the division using our own surveillance data.

Methods. Surveillance data on gastric surgery (GAST) and hepatobiliary surgery (BILI) submitted to the JHAIS system in 2012 were analyzed. GAST was divided into three groups: distal gastrectomy (GAST-D), total gastrectomy (GAST-T) and others (GAST-O). BILI was divided into three groups: pancreatoduodenectomy (BILI-PD), hepatic resection without reconstruction of biliary tract (BILI-L) and others (BILI-O). Difference in the incidence and site of SSI was analyzed. Statistical analyses were performed using chi-square test.

Results. The incidence of SSI of GAST-T was 13.4% (146/1,087), and significantly higher than that of GAST-D (7.2%, 143/1,982) and GAST-O (9.1%, 71/782). The incidence of SSI of BILI-PD was 31.6% (173/548), and significantly higher than that of BILI-L (11.2%, 127/1,132) and BILI-O (13.5%, 101/749). The proportion of organ/space SSI in GAST-T (69.1%, 101/146) was significantly greater than that in GAST-D (48.9%, 70/143) and GAST-O (46.4%, 33/71). The proportion of organ/space SSI in BILI-PD (72.2%, 125/173) was significantly greater than that in BILI-L (38.6%, 49/127).

Conclusion. Total gastrectomy and pancreatoduodenectomy had greater risk of SSI and greater proportion of organ/space SSI. Our division of the two operative

procedures into three groups was appropriate for better comparison of SSI incidence between hospitals.

Disclosures. **All authors:** No reported disclosures.

1013. Delay in diagnosis of invasive surgical site infections following knee arthroplasties compared to hip arthroplasties

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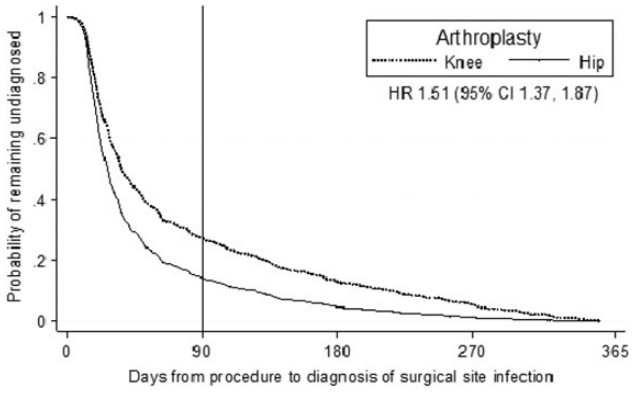
Background. The timing of diagnosis of invasive surgical site infections (SSI) following joint replacement surgery is an important criterion used to determine subsequent medical and surgical management. We aimed to characterize the relationship between site of arthroplasty (knee vs hip) and timing of diagnosis of invasive SSI.

Methods. We conducted a retrospective cohort study of surgical surveillance data from 36 acute care community hospitals and 1 ambulatory surgery center participating in the Duke Infection Control Outreach Network. Invasive (i.e., deep incisional or organ/space as defined by National Healthcare Safety Network) SSIs occurring within 365 days of knee or hip arthroplasties performed from January 1, 2007-December 31, 2011 were included in the analysis. A Cox regression model was fit to estimate the association between procedure type and time to diagnosis of SSI, adjusted for age, pathogen virulence, American Society of Anesthesiologists' (ASA) score, and hospital surgical volume.

Results. 661 invasive SSIs were included in the analysis; 401 (61%) occurred following knee arthroplasties. The median time to diagnosis of SSI following knee arthroplasty was 42 days (IQR 21-114) vs 25 days (IQR 17-48) following hip arthroplasty; unadjusted HR 1.60, 95% CI 1.37-1.87, $p < 0.001$. The time to diagnosis of invasive SSI was significantly longer for knee compared to hip arthroplasties after adjusting for age, pathogen virulence, and hospital surgical volume; HR 1.51, 95% CI 1.28-1.78, $p < 0.001$ (figure).



Predicted time to SSI diagnosis, adjusted for age, pathogen virulence, and surgical volume

Conclusion. In our large cohort of community hospitals, the diagnosis of invasive SSI was delayed following knee arthroplasties compared to hip arthroplasties. This relationship was not fully explained by confounding due to patient age or pathogen virulence. We hypothesize that differences in symptom manifestation between the two surgical sites and disparities in access to care may contribute to the observed differential timing of diagnosis of SSIs following knee vs hip arthroplasties. Our findings have important implications for the management of these infections, as prosthesis removal is often required to cure infections diagnosed more than 90 days post-operatively.

Disclosures. **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

1014. Risk Factors and Causative Organisms for Surgical Site Infection Following Head and Neck Cancer Surgery

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Background. Head and neck cancer (HNC) is the sixth most common type of cancer. Worldwide, an estimated 650,000 new cases of HNC are diagnosed each year. More recently, the incidence of oropharyngeal cancer in younger population has been increasing. Wide resection and reconstruction as standard therapies for HNC have improved cure rates. Despite higher cure rates, postoperative surgical site infection (SSI) has been reported in 10-45% of patients who undergo surgery for HNC. SSI is the leading cause of nosocomial infection and increased medical expenses. To date, however, the main factors contributing to SSI and causative pathogens are unclear. The aim of this study was to clarify the risk factors and causative agents for SSI after HNC surgery and to identify effective strategies for preventing SSI.

Methods. A retrospective cohort study was performed on adult patients diagnosed with HNC who underwent major oncological surgery for HNC from January 2006 to June 2010 at Kangdong Sacred Heart Hospital (Seoul, South Korea). Patients undergoing thyroid and salivary gland operations without lymph node dissection were excluded.

Results. We assessed the risk factors and causative pathogens associated with SSI in 370 patients who underwent surgery for HNC. A total of 73 patients (19.7%) had SSIs, and 120 pathogens were identified at infection sites. Significant risk factors for SSI identified with multivariate analysis were male sex (OR = 4.10, 95% CI= 1.338-12.532), cardiovascular disease (OR = 2.311, 95% CI = 1.130-4.726), Cerebrovascular disease (OR = 4.762, 95% CI = 1.342-16.896), and operation time > 6hours (OR = 5.089, 95% CI = 1.577-21.397). The most common pathogen was *staphylococcus aureus* (45/120, 37.5%). Methicillin-resistant *S.aureus* was found in 84.4% of all *S.aureus*. *Klebsiella pneumoniae* (17/120, 14.2%), *Pseudomonas aeruginosa* (12/120, 10.0%), *Enterococcus faecalis* (7/120, .8%), and *Acinetobacter baumannii*(5/120, 4.2%) were frequently cultured.

Conclusion. High-risk patients of SSIs after major HNC surgery are predicted. Preventive measures or closed monitoring in these patients may be required to reduce the likelihood of postoperative SSIs. Even though additional research is necessary, we would consider the change in regimen of propylactic antibiotics according to causative organisms.

Disclosures. **All authors:** No reported disclosures.

1015. Facilitators and Barriers to SSI Bundle Implementation in Select Surgical Procedures

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Background. The Study to Optimally Prevent SSIs in Select Cardiac and Orthopedic Procedures (STOP SSIs) tested an evidence-based bundle to reduce the incidence of surgical site infections caused by *S. aureus*in patients having cardiac operations or hip or knee arthroplasty. Twenty hospitals in a national health system implemented the bundle.

Methods. Investigators collected qualitative data about implementation from monthly coaching calls and an end-of-study video conference call with study champions from participating hospitals. Data were imported into MAXQDA and coded for thematic content regarding facilitators and barriers to bundle implementation.

Results. Numerous factors influenced bundle implementation at and across 3 nested levels: the healthcare network, the hospital, and the individual. Vital facilitators at the network level included a corporate physician champion, infrastructure and resources, and the ability to share practical solutions. These facilitators did not always help participants overcome barriers at the hospital level (e.g., culture, slow committee approval, implementation for urgent and emergent procedures, hardwiring practice across days and shifts), individual level (e.g., resistance or autonomy), or across levels (e.g., competing priorities, decentralized offices, complex communication channels between patients and providers and between levels of care and screening locations). Also, new staff could change existing relationships and processes, or staff who successfully managed bundle implementation might be unable to maintain adherence as other network- or hospital-level demands increased. Facilitators at one level also could create barriers at other levels (e.g., audits of bundle adherence facilitated overall implementation but increased work for study champions). Facilitators and barriers differed between hospitals and hospitals differed in their capacity to overcome barriers.

Conclusion. This qualitative study found that hospitals varied in their ability to implement the bundle and to overcome obstacles. Hospitals also shared some barriers and facilitators to implementation. This data identifies common facilitators and barriers during implementation and supports hardwiring to sustain evidence-based surgical care practices.

Disclosures. **All authors:** No reported disclosures.

1016. Surgical Site Infection Risk Stratification for Kidney Surgery: Use of Endoscopy as an Effect Modifier

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Background. Risk factors of surgical site infection (SSI) for kidney surgery have not been determined yet because the number of procedures is not enough. To estimate the risk and find the risk factors of SSI for kidney surgery, the Japan Nosocomial Infections Surveillance (JANIS) SSI division, which is a voluntary based, national-level surveillance in Japan, was analyzed.

Methods. Logistic regression analysis using data on kidney surgery in the JANIS SSI division database from January 1, 2008 to December 31, 2010, was conducted separately for procedures with and without the use of endoscopy.

Results. A total of 1819 procedures of kidney surgery were analyzed. Twelve cases of SSI occurred in 837 endoscopic surgeries (1.4%), and 17 cases of SSI occurred in 982 open surgeries (1.7%). Associations between SSI incidence and age, wound class, and American Society of Anesthesiology (ASA) score differed according to whether endoscopy was used. For endoscopic surgery, age (adjusted odds ratio (AOR), 1.07 [95 percent confidence interval (95% CI), 1.00–1.14]; $P = 0.04$) and duration of surgery (AOR, 1.01 [95% CI, 1.00–1.01]; $P = 0.02$) were associated with SSI. For open surgery, wound class other than clean (AOR, 4.82 [95% CI, 1.07–21.59]; $P = 0.01$) and ASA score ≥3 (AOR, 4.28 [95% CI, 1.51–12.15]; $P = 0.01$) were associated with SSI.

Logistic regression analysis of factors associated with surgical site infection with kidney surgery, JANIS, 2008–2010

	Endoscopic surgery ($n = 837$)			Open surgery ($n = 982$)		
Risk factor	AOR	95%CI	*P* value	AOR	95%CI	*P* value
Age	1.07	1.00–1.14	0.04	0.99	0.96–1.02	0.47
Sex						
Male	ref.			ref.		
Female	0.69	0.18–2.66	0.59	1.00	0.35–2.83	1.00
Wound class						
C	ref.			ref.		
CC, CO, or D	0.68	0.20–2.30	0.54	4.82	1.07–21.59	0.04
ASA score						
1, 2	ref.			ref.		
3, 4, 5	2.06	0.53–8.05	0.30	4.28	1.51–12.15	0.01
Duration of surgery	1.01	1.00–1.01	0.02	1.00	1.00–1.01	0.06
Combined surgery						
No	ref.			ref.		
Yes	1.38	0.26–7.28	0.71	2.12	0.53–8.53	0.29

NOTE. AOR, Adjusted odds ratio; ASA, American Society of Anesthesiology; JANIS, Japan Nosocomial Infections Surveillance; 95%CI: 95 percent confidence interval; C: clean, CC: clean-contaminated, CO: contaminated, D: dirty.

Conclusion. Since the risk factors for SSI differed between endoscopic and open kidney surgery, they should be analyzed separately when predicting the risk of SSI.

Disclosures. **All authors:** No reported disclosures.

1017. Risk Factors for Post-Operative Infections after Cesarean Section

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Background. The objective was to determine the prevalence of post-operative infections after cesarean section and identify modifiable risk factors associated with post-cesarean section infections.

Methods. Retrospective chart review of patients who underwent a cesarean section between January 1, 2013–June 30, 2014 was conducted at an academic institution. Post-operative infection was defined as any infection within 30 days from date of primary surgery using the CDC criteria as guideline. Chi square was used for comparison of all categorical data and we reported spearman correlation coefficient. The Student T test was used for continuous variables and p values reported. Univariate analysis was done with significance determined at $P < 0.05$. Variables with $P < 0.05$ were then subsequently run through a multivariate analysis. A total of 1,189 charts were included in our final analysis.

Results. We had 56% (n = 672) primary and 44% (n = 526) repeat cesarean sections. 47% were scheduled (n = 564), 48% unscheduled (n = 571) and 5% emergent (n = 62).

Post-operative infection after cesarean section was 7.6% (n = 91). On univariate analysis, risk factors associated with post-operative infections include primary cesarean section (OR,1.66 [95% CI,1.05-2.63]), Non-Elective cesarean section (OR, 1.92 [1.03-3.57]); sexually transmitted infection in pregnancy (OR, 3.83 [1.50-9.79]), cervical shortening <15cm (OR, 3.72 [1.34-10.33]), PPROM (OR, 5.3 [1.82-15.38]) gestational HTN (OR, 2.38 [1.08-5.23]), asthma (OR, 3.83 [1.50-9.79]), intraoperative estimated blood loss >1,000 mL (OR, 2.27 [1.08-4.77]), Chorioamnionitis, (OR, 2.8 [1.5-5.1], p = .0004), and blood transfusion during the hospital stay (OR, 3.5 [95% CI, 1.5-8.2]). On subgroup analysis, skin closure with staples was associated with increasing rates of wound infection (OR, 1.88 [1.08-3.33]). Continuous or Multi-categorical values associated with post-operative infection were decreasing post-operative hemoglobin (p = 0.0229), length of membrane rupture (<0.0001), increasing BMI (p = 0.0042), Classical Incision (p < 0.0003), any intraoperative complication (p = .0048), and Emergent Surgery (p < 0.001).

Conclusion. Study identifies modifiable risk factors for post-operative infection after cesarean section. Identification of these risk factors allows targeted measures to be instituted, resulting in reduced infection rate.

Disclosures. **All authors:** No reported disclosures.

1018. Risk Factors for Surgical Site Infection Following Cardiovascular Surgery

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Background. Prior studies evaluating the risk of cardiovascular (CV) sternal incisional surgical site infection (SSI) have been small and have not evaluated for SSI risk factors using standard epidemiologic definitions. We sought to identify patient- and procedure-related risk factors for sternal incisional SSI following CV surgeries.

Risk Factors for SSI Among Patients Undergoing Cardiovascular Surgery

	All Subjects		CABG		Valve		Deep/ Organ Space	
# In Analysis Group	3997		3005		1709		3997	
# of SSIs (%)	114 (2.9%)		94 (3.1%)		36 (2.1%)		61 (1.5%)	
	HR	p- value	HR	p-value	HR	p-value	HR	p-value
Female	3.19	<.0001	3.90	<.0001	2.15	0.0296	3.11	<.0001
BMI								
Normal/ Underweight (<25)	Ref		Ref		Ref		Ref	
Overweight (25-30)	1.86	0.0709	1.58	0.2097	3.96	0.0800	1.62	0.2653
Obese (>30)	4.85	<.0001	3.45	0.0002	13.70	0.0004	1.62	0.0005
History of MRSA	2.78	0.0046	-		3.20	0.0175	2.42	0.0455
Peripheral Vascular Disease	-		1.66	0.0425	-		2.20	0.0089
Hypertension	-		3.52	0.0324	-		-	
ADP Inhibitor	1.67	0.0263	-		-		-	
Fiscal Year								
2013	0.51	0.1338	-		-		-	
2012	0.34	0.0251	-		-		-	
2011	0.50	0.0692	-		-		-	
2010	0.55	0.1236	-		-		-	
2009	1.15	0.6749	-		-		-	
2008	1.13	0.7152	-		-		-	
2007	0.91	0.7852	-		-		-	
2006	Ref							
Case Type								
Elective					Ref			
Urgent	-		-		0.96	0.9407	-	
Emergent	-		-		5.90	0.0043	-	

Variables not included in final model denoted by (–).

Methods. All patients undergoing coronary artery bypass grafting (CABG) or valve replacement surgery October 2005-May 2013 were included. Data was aggregated from Society of Thoracic Surgeons and Hospital Epidemiology databases. SSIs were classified as superficial and deep or organ/space (D/OS) using National Healthcare Safety Network criteria. The primary outcome was SSI occurring within 90 days of surgery. Subgroup analyses were performed by procedure type and restricted to D/OS SSI outcomes. Modeling was performed using multivariate proportional hazards regression with stepwise selection.

Results. 114 (2.9%) of 3997 patients (717 undergoing both CABG and valve replacement) developed any SSI, including 53 (46.5 %) superficial SSIs and 61 (53.5 %) D/OS SSIs. Final multivariable models are presented in the table.

Conclusion. Female sex and obesity were robustly associated with increased hazard of SSI, including among surgery subgroups and when restricting to

D/OS SSI outcome. Future prevention efforts should consider issues related to obesity, particularly among women, which may be related to tension across sternal incision.

Disclosures. **All authors:** No reported disclosures.

1019. *Bipolaris* Surgical Site Infections among Cardiothoracic Surgery Patients —Texas, Arkansas, and Florida, 2008–2013

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Background. The environmental mold *Bipolaris* causes sinusitis or skin infection; surgical site infections (SSI) are extremely rare. In November 2013, state officials were alerted to seven *Bipolaris* cardiothoracic SSIs, with five deaths, occurring since May 2013 at three Texas and Arkansas hospitals. We conducted an investigation to describe this cluster and identify possible sources.

Methods. Cases were defined as *Bipolaris* spp. isolated from a sterile site during 2008–2013 in patients with prior cardiothoracic surgery. Nationwide case-finding was conducted through state infection control alerts and listservs, such as ClinMicroNet. We abstracted clinical and medication/product information from medical records and reviewed microbiology records. Environmental sampling was conducted at five hospitals. Multi-locus sequence typing (MLST) was performed on case-patient and environmental isolates.

Results. We identified 21 case-patients at 10 hospitals in Texas, Arkansas, and Florida; 11 (52%) occurred in 2013. Median case-patient age was 55 years (range: 3 days–82 years), and 19 (90%) were male. Nine (43%) had coronary artery bypass (CABG) or valve surgery, seven (33%) had heart transplant; 15 (71%) required more than one surgical procedure (median: 3, range: 1–11). Thirteen (62%) had delayed sternal closure with chest left open for a median of 8 days (range 2-22). Fifteen (71%) had mediastinitis, and 16 (76%) died. No common compounded or commercial products administered primarily to case-patients were identified. MLST showed substantial variation among clinical and environmental isolates. Microbiology records indicated an overall increase in *Bipolaris* isolates, particularly from non-sterile sites, during 2000–2013 at multiple hospitals in the region, including those without cases.

Conclusion. *Bipolaris* SSI occurred in children and adults undergoing different types of cardiac surgeries, especially those with multiple surgeries and delayed sternal closure. Epidemiological and microbiologic evidence does not support a common product exposure. *Bipolaris* may be an emerging cause of infection in the southern United States; surgeons and infection control staff should be aware of this infection and have a low threshold to culture for mold.

Disclosures. **All authors:** No reported disclosures.

1020. Unintentional Hypothermia as a Risk Factor for Abdominal Hysterectomy-Related Surgical Site Infection

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Background. Unintentional perioperative hypothermia is a risk factor for surgical site infection (SSI) for various surgical procedures, but few data are available regarding its role in SSI related to abdominal hysterectomy. We conducted a study to assess the potential role of hypothermia as a risk factor for abdominal hysterectomy-related SSIs.

Methods. A case-control study included all 37 SSIs related to abdominal hysterectomy procedures performed in 2013 at Yale-New Haven Hospital. 100 randomly selected patients who did not develop SSIs after abdominal hysterectomy in 2013 served as controls. An intraoperative temperature < 36.0 C was defined as hypothermia. Variables recorded included the number of each patient's temperature readings reported in EPIC EMR that were < 36.0 C, age, BMI, presence of diabetes mellitus or cancer, surgical approach (laparoscopic or robotic-assisted vs open) and operative procedure time. Statistical analysis included chi-square tests, Mann-Whitney tests and forward stepwise logistic regression.

Results:. Intraoperative temperature records were available for 35/37 cases and 99/100 controls. There were no significant differences between cases and controls with respect to age, BMI, presence of diabetes mellitus or cancer, or procedure time by univariate analysis. Nineteen (54%) of cases, but only 33(33.3%) of controls had > 50% of intraoperative temperatures < 36.0 C ($p = 0.029$) The mean number of intraoperative temperatures in the hypothermic range for cases (5.97) was significantly greater than that for controls (4.46) ($p = 0.015$) Overall, 50 (96%) of 52 patients with > 50% of temperatures < 36.0 C met SCIP-INF-10 criteria for normothermia. A logistic regression model using the single best predictor of SSI (the number of hypothermic temperatures) was significant ($p < 0.05$). When surgical approach was added to the model, it was still significant ($p < 0.05$). Therefore, the number of hypothermic temperatures and the surgical approach were the best predictors of SSI.

Conclusion. The results suggest that hypothermia is also a significant risk factor for abdominal hysterectomy-related SSIs, and that continued efforts are needed to minimize hypothermia during abdominal hysterectomy procedures.

Disclosures. **J. Boyce**, 3M Company: Collaborator, Consultant, Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant, Research support and Speaker honorarium; Gojo Industries: Consultant, Investigator and Scientific Advisor, Consulting fee, Research grant and Speaker honorarium; Clorox Company: Consultant, Investigator and Scientific Advisor, Consulting fee, Research grant, Research support and Speaker honorarium

1021. Surgical Site Infection Reduction among Patients Undergoing Cesarean Section in a Tertiary Care Academic Facility

Kerri Huber, RN, MSN, CIC[1]; Geeta Sood, MD[2]; Cynthia Argani, MD[3]; Jonathan M. Zenilman, MD, FIDSA[2]; Trish M. Perl, MD, MSc, FIDSA, FSHEA[4]; [1]Infection Control, Johns Hopkins Bayview Medical Center, Baltimore, MD; [2]Johns Hopkins University School of Medicine, Baltimore, MD; [3]Johns Hopkins University, Baltimore, MD; [4]Medicine, Johns Hopkins Medical Institutions, Baltimore, MD

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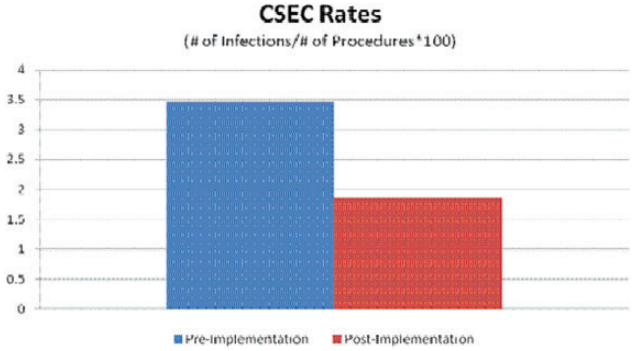
Background. The incidence of delivery via Cesarean section (CSEC) in the US has increased significantly over the past decade, now accounting for 33% of all births. Because of the often emergent nature of CSEC deliveries patients are at an increased risk of developing complications, including surgical site infections (SSI). Our facilities SSI rate for CSEC was almost double the National Healthcare Safety Network (NHSN) benchmark of 1.84 for calendar year (CY) 2012.

Methods. SSI surveillance was conducted according to NHSN definitions. Denominators are collected at the end of the month via a report from the Labor and Delivery operating room census. Events were declared after 100% case review by an Infection Control Practitioner and validation by the Hospital Epidemiologist. The Hospital Epidemiologist conducted a clinical review of all events and their microbiology, when available. During Quarter (Q) 1 of CY2012 pre-operative antibiotic prophylaxis was changed from Cefazolin to Cefotetan and Azithromycin. A providine-iodine vaginal prep was added to the surgical preparation process. CSEC SSI rates from CY2012 were compared to those for Q2 and Q3 of CY2013.

Results. The mean CSEC SSI rate for CY2012 was 3.47. This included a total of 16 SSI's. Of these infections, 8 (50%) were superficial SSI's and 8 (50%) were organ space consisting of Endomyometritis, Intra-abdominal, and other reproductive sites. Microbiologically significant organisms were identified for 9 of the infections. The mean CSEC SSI rate for the post-implementation phase of CY2013 Q2 and 3 was 1.87. These infections consisted of 4 events. Of these infections 1 (25%) was superficial and 3 (75%) were organ space. All 4 included identification of the organism associated with the infection.



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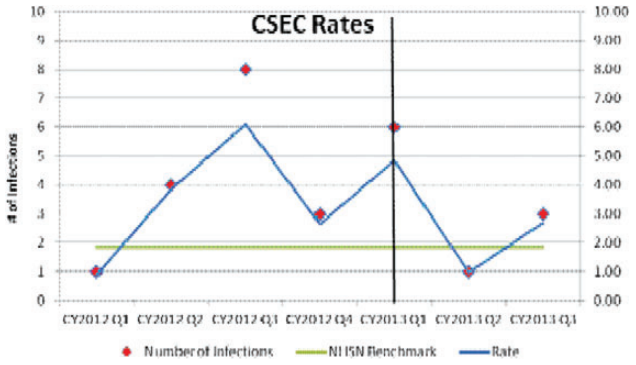

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Conclusion. After clinical and microbiological review of the events and organisms associated with each, we determined that the most significant epidemiology of infections were host contamination from vaginal flora. After implementing expanded antibiotic coverage and adding a pre-operative vaginal prep we have seen a significant reduction in CSEC infections. More time is needed to determine if this reduction will be sustained.

Disclosures. **All authors:** No reported disclosures.

1022. Infectious morbidity in laboring vs non-laboring patients undergoing Cesarean section

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Background. According to the CDC there are 4 million births in the US annually and 32% of these births are via Cesarean sections (C-sections). It is estimated that 5% of these procedures are complicated by infection. We reviewed the epidemiology of peri-partum morbidity including infections at our tertiary care academic hospital.

Methods. We reviewed the medical records of a cohort of all patients undergoing Cesarean section at our 400 bed hospital from January 1, 2012- November 30, 2013. The physician and nurse epidemiologist and the director of labor and delivery abstracted data. Fever was defined as 30.0 degrees C and infections were definied using both NHSN defined criteria and clinical assessment.

Results. Among the 869 deliveries by Cesarean section during this time period, 868 medical records were available for review. The average age of women undergoing C section was 28.8. 24.8% of women were African American, 29.3% were Caucasian, and 27.7% were Hispanic. Ethnicity was not documented in 10.2% of charts. 23.8% of women were positive for group B streptococcus, 59.3% were negative and 16.5% had unknown group B streptococcus status. The overall infectious morbidity was 22% (190/868). 13% (115/868) of women had a fever pre or post-delivery and 58.8% of women labored prior to cesarean delivery. In women who were laboring prior to cesarean, the infectious morbidity rate was 27.6% (141/511) with an NHSN defined infection rate of 4.5%. The overall infectious morbidity in patients who did not labor was significantly lower at 10.6% (38/357) with an NHSN defined infection rate of 1.1%.

Conclusion. Our results demonstrate that there is a higher than expected burden of infectious complications related to Cesarean section delivery, and that laboring patients have a higher rate of febrile illness compared to non-laboring patients. As more patients are allowed labor after previous Cesarean section, preventable risk factors for surgical site infections among these patients need to be identified to develop evidence based interventions.

Disclosures. **All authors:** No reported disclosures.

1023. Infectious Complications of Pediatric Ambulatory Surgery

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Background. In the U.S., more than 75% of all surgical procedures are performed at an ambulatory surgical center (ASC). Little is known about the risk of infection after pediatric ambulatory surgery.

Methods. We conducted structured parental interviews 30 to 45 days after ambulatory surgery at a children's hospital or 3 affiliated ASC over a 13-month period. Parenteral report of a surgical site infection (SSI), antibiotic prescription with abnormal wound or wound culture triggered chart review by an Infection Preventionist. Cases were categorized as National Healthcare Surveillance Network SSI (NHSN-SSI), a suspected SSI (for cases had 2 or more elements consistent with an SSI but failed to meet an NHSN definition), or NHSN infection at a secondary site related to surgery.

Results. We conducted 4513 parental interviews after 6280 targeted surgeries (71.9%), including 732 hernia repairs, 549 lesion excisions, and 757 orthopedic procedures. A total of 74 procedures (1.6%) underwent IP investigation. Nine NHSN-SSI were identified (overall SSI rate 0.2%), including 5 after orthopedic (orthopedic SSI rate 0.7%) and 2 after urologic procedures (urologic SSI rate 0.3%). Investigation also identified 46 suspected SSI and 1 infection at a secondary site for a possible post-operative infection rate of 1.2%.

Conclusion. The overall rate of infectious complications after pediatric ambulatory surgery may be higher than previously appreciated although relatively few cases meet the NHSN definition for SSI.

Disclosures. **All authors:** No reported disclosures.

1024. Surgical Site Infections Following Pediatric Spine Fusion Procedures, Based on Type of Perioperative Antibiotic Prophylaxis

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Background. A bactericidal antibiotic such as cefazolin is recommended to prevent surgical site infections (SSIs) following pediatric spine fusion. The objective was to retrospectively explore whether use of vancomycin or clindamycin rather than cefazolin was associated with a higher incidence of SSIs following pediatric spine fusion.

Methods. Risk factors for deep SSIs were explored in Cleveland Clinic patients < 18 years undergoing spine surgery between 2006 and 2013. Data was retrieved using a CPT code based algorithm. SSI definitions were as per the National Healthcare Safety Network. Fischer's exact test was used for statistical analyses.

Results. SSIs developed in 4.4% (27 of 608) of children. For cefazolin the rate was 3.9% (20 of 513) compared to 11.5% for vancomycin (3 of 26; P 0.09) and 23.5% for clindamycin (4 of 17; P 0.005). The rate for cefazolin plus vancomycin or clindamycin was 0% (0 of 43), which was significantly lower than for vancomycin or clindamycin (P 0.01), but not for cefazolin (P 0.39). Among patients treated with clindamycin vs cefazolin, the rate of both early (11.8% vs 1.9%; P 0.05) and late onset (11.8% vs 1.9%; P 0.05) infection was higher; vancomycin use was associated with a higher rate of early (11.5%; 0.05) infection. Clindamycin use was a risk factor for *P. acne* SSI (3 of 510 vs 3 of 17; P 0.0004). The penicillin allergy rate was 6.2% for cefazolin, 38.5% for vancomycin (P <0.0001) and 88.2% for clindamycin (<0.0001). The screening rate for *S. aureus* colonization was 21.1% for cefazolin, 38.5% for vancomycin (P 0.05), and 17.6% for clindamycin. None of the 4 *MRSA* colonized patients developed an SSI: 3 treated with cefazolin and one with vancomycin.

Conclusion. Monotherapy with vancomycin or clindamycin was used in only 7.1% of the pediatric spine fusion cases, but this small group accounted for 25.9% of our SSIs. Compared to cefazolin, this translates to a 319% increased SSI rate. Efforts need to be directed at identifying those patients who require pre-operative allergy evaluation and at promoting the use of cefazolin for those patients who do not have a true contraindication to cephalosporin use. When surgical prophylaxis with vancomycin or clindamycin is indicated, combination therapy with cefazolin should be strongly considered.

Disclosures. **All authors:** No reported disclosures.

1025. Impact of Nasal Decontamination with Nasal Iodine as part of a Preoperative Surgical Site Infection (SSI) Prevention Bundle in Orthopedic Implant Surgeries

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Background. Nasal carriage of *Staphylococcus aureus* (SA) has been shown to be an independent risk factor for SA surgical site infections (SSI), with a SSI rate 2-9 times higher in carriers. Decolonization with nasal mupirocin is often recommended for

carriers or high risk individuals, however this process requires preoperative screening and patient compliance with application days prior to surgery. Nasal decontamination with nasal iodine just prior to surgery offers a rapid method of decreasing the nasal burden of SA in high risk joint implant surgeries.

Methods. Nasal decontamination with nasal iodine (3M^{TM} Skin and Nasal Antiseptic) of all patients undergoing hip and knee prosthetic joint replacement was implemented pre-operatively since March 2013 at Detroit Receiving Hospital. This intervention was coupled with reinforcement with perioperative CHG bathing and the addition of vancomycin to routine B-lactam prophylaxis. Hip arthroplasty (HPRO) and knee arthroplasty (KPRO) infection rates were reviewed for 1 year before and after intervention.

Results. There was a 28.3% reduction in HPRO and KPRO infections during this time period. A decrease in the average rate from 2.59 to 1.86 infections per 100 procedures (OR-0.56, p = 0.23) was seen. SA infection were reduced from an average rate of 1.29 to 0.63 infections per 100 procedures (OR – 0.48, p = 0.30). This resulted in a reduction of 5 infections and an approximate net cost saving of $142,409.

Conclusion. Nasal decontamination with iodine offers an alternative to nasal decolonization with mupirocin in the prevention of orthopedic implant infections and was effective as part of a perioperative SSI prevention bundle.

Disclosures. **K. Kaye**, Cubist Pharmaceuticals: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Grant recipient and Speaker honorarium

1026. Swabbing Surgical Sites Does Not Improve the Detection of *Staphylococcus aureus* Carriage in High-Risk Surgical Patients

Jennifer Brown, MD[1]; Chin-Shang Li, PhD[2]; Mauro Giordani, MD[3]; Kiarash Shahlaie, MD, PhD[4]; Eric Klineberg, MD[3]; Joanna Tripet-Diel, MPH[1]; Marie Ihara, BS[1]; Stuart Cohen, MD, FIDSA, FSHEA[1]; [1]Division of Infectious Diseases, University of California, Davis Medical Center, Sacramento, CA; [2]Department of Public Health Sciences, Division of Biostatistics, University of California, Davis, Davis, CA; [3]Department of Orthopedic Surgery, University of California, Davis Medical Center, Sacramento, CA; [4]Department of Neurological Surgery, University of California, Davis Medical Center, Sacramento, CA

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Background. A major risk factor for surgical site infections (SSIs) is *Staphylococcus aureus* carriage. *S. aureus* carriers have a 9X greater risk for SSIs compared with non-carriers. Preoperative screening for *S. aureus* carriage is controversial. Yet, targeted screening in high-risk patients or from clinically relevant sites may be beneficial. We aimed to determine whether *S. aureus* detection in high-risk surgical patients would be increased by culturing surgical sites, in addition to the nares, vs nares-only culturing.

Methods. Adults undergoing preoperative evaluations in orthopedic and neurosurgical clinics were eligible for participation. Patients with active infections or use of anti-staphylococcal antibiotics within 90 days of evaluation were excluded. For each subject, specimens were collected from the nares and from the proposed surgical site with Transporter Liquid Stuart Culture Swabs (HealthLink, Jacksonville, FL). Samples were inoculated onto methicillin-resistant *S. aureus* (MRSA)-selective chromogenic agar plates and blood agar plates.

Results. Of the 150 subjects, 80 (53.3%) were women and 70 (46.7%) men. The mean age was 61 years and 77/150 (51.3%) had a BMI > 30. Proposed operations included knee or hip arthroplasty, spine surgery, and brain stimulator placement. Culture results were available for 147/150 subjects. Of the 147 surgical site cultures, 54 (36.7%), 51 (34.7%), and 28 (19.0%) were collected from knee, hip, and lumbar sites, respectively; the remaining 14 (9.5%) were from cervical, thoracic, or infraclavicular sites. Overall, 35/147 (23.8%) nasal cultures grew *S. aureus*; 29/147 (19.7%) grew methicillin-susceptible *S. aureus* (MSSA), and 6/147 (4.1%) grew MRSA. Only 2/147 (1.4%) surgical site cultures grew *S. aureus;* both grew MSSA and MSSA was cultured also from the nasal swabs of these subjects. Using nasal culture -+ surgical site culture as "true positive," the percentage of additional *S. aureus* carriers detected by the addition of surgical site screening was zero as compared to nasal screening alone.

Conclusion. The detection of *S. aureus* carriage in high-risk surgical patients is not improved by swabbing surgical sites in addition to the nares.

Disclosures. **All authors:** No reported disclosures.

1028. The Prevalence of *Clostridium difficile* Infection (CDI) is Highly Correlated with the Prevalence of Surgical Site Infection (SSI)

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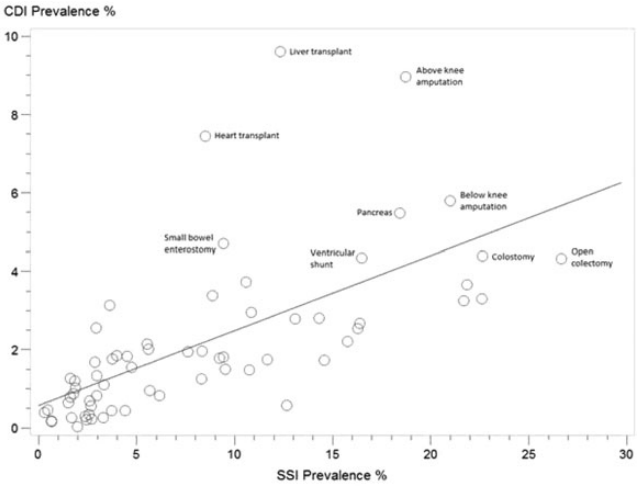
Background. CDI incidence has been rising in the US. SSIs result in increased exposure to antibiotics and longer length of stay in hospitals; both are risk factors for CDI. We studied the association between post-operative SSI and CDI using an inpatient billing dataset.

Methods. We performed a retrospective cohort study using the longitudinal 2009 California State Inpatient Database (SID), part of the Healthcare Cost and Utilization Project. We identified surgical procedures in persons aged ≥18 years as defined by a modification of the NHSN (National Healthcare Safety Network) classification for SSI surveillance. Some of the 40 NHSN surgery categories were split to more specific groups resulting in 73 total surgery groups. Multiple same-admission surgeries were assigned to the highest SSI risk surgery. 90-day hospital readmissions were identified starting from discharge date of the index hospitalization. The Observation period for SSI and CDI was censored at time of a subsequent surgery within 90 days. SSI and CDI were determined using ICD-9-CM diagnosis codes.

Results. A total of 624,984 index surgical hospitalizations in 593,794 patients were identified in 2009. There were 26,654 (4.3%) SSIs and 5,727 (0.9%) CDIs in total. Surgeries were categorized into 3 groups based on SSI prevalence. Surgeries with SSI prevalence of <4%, 4-10% and >10% had median (minimum-maximum) CDI prevalence of 0.65% (0.04-3.14), 1.81% (0.00-7.45) and 3.11% (0.58-9.61), respectively (Kruskal-Wallis test, p <0.0001). SSI and CDI prevalence for each surgery were plotted in a scatterplot (figure). The correlation coefficient between SSI and CDI prevalence was 0.65. The top 5 surgeries with highest prevalence of CDI were (SSI prevalence, CDI prevalence): liver transplant (12.32%, 9.61%), above knee amputation (18.73%, 8.96%), heart transplant (8.51%, 7.45%), below knee amputation (21.00%, 5.80%) and pancreas surgery (18.41%, 5.49%).



90-day Prevalence of SSI and CDI after Various Surgery Groups

Conclusion. Our results show a strong correlation between SSI and CDI prevalence within 90 days after a wide variety of surgeries. SSI prevention may also lead to a reduction in CDI.

Disclosures. **M. Olsen**, Sanofi Pasteur: Consultant and Investigator, Consulting fee and Research support; Pfizer: Consultant, Consulting fee **E. R. Dubberke**, Sanofi Pasteur: Consultant and Investigator, Consulting fee and Research support; Merck: Consultant and Investigator, Consulting fee and Research support; Viropharma: Investigator, Research support; Optimer: Consultant and Investigator, Consulting fee and Research support; Rebiotix: Consultant, Consulting fee; Pfizer: Consultant, Consulting fee

1029. Infection-Related Hospital Readmissions Following Prostate Biopsy in United States Men

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Background. Common antibiotic prophylactic strategies for prostate biopsy may be insufficient to prevent procedure-associated sepsis, particularly with the rise of Gram-negative pathogens that are resistant to fluoroquinolones. We aim to describe all-cause and infection-related readmission rates and costs in a national sample of men undergoing prostate biopsy.

Methods. We compared mean rates of readmission within 30 days of prostate biopsy from January 2005 to December 2011. Insurance claims data was obtained from the Marketscan Commercial Claims and Encounters database. Yearly rates of prostate

biopsy and readmissions were calculated from the number of inpatient admissions and outpatient services (including emergency room visits) in men of at least 40 years of age with a documented CPT-4 code of 55700 for prostate biopsy. Patients were required to be continuously enrolled in at least one insurance program for at least 30 days after prostate biopsy for inclusion in the analysis.

Results. 447,486 men with a prostate biopsy were eligible for inclusion. Mean age of the population was 62.8 years of age (SD 8.9). 13,154 of these patients (2.9%) were readmitted within 30 days of biopsy. Median length of stay during readmission was 3 days (IQR: 2) and mean total payment for the hospitalization was $14,749.09 (SD $22,767.11). The most common major diagnostic category upon readmission was reproductive diseases (4786 readmissions) followed by infectious diseases (2539 readmissions; 0.6% of all prostate biopsies).

Conclusion. Despite widespread use of antibiotic prophylaxis for prevention of infection following prostate biopsy, infection remains the second most common reason for 30-day hospital readmission, possibly due in part, to the emergence of multidrug resistant pathogens. Continued efforts are needed to optimize prophylaxis strategies.

Disclosures. **All authors:** No reported disclosures.

1030. Temporal trends of infectious complications following transrectal ultrasound-guided prostate biopsy at a Canadian tertiary cancer center

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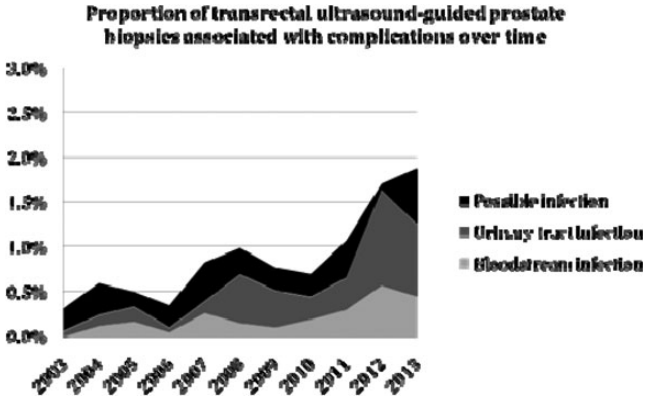
Background. Antimicrobial prophylaxis prior to transrectal ultrasound (TRUS)-guided prostate biopsy reduces the risk of infectious complications. Despite increasing *E. coli* resistance to fluoroquinolones, oral ciprofloxacin remains the most widely used agent for this indication. We reviewed the temporal trends of infection-related complications following TRUS-guided prostate biopsy at Princess Margaret Cancer Center, a Canadian tertiary care hospital where ciprofloxacin prophylaxis is used.

Methods. Surveillance for complications following TRUS-guided prostate biopsy at our center has been conducted since 2003. Complications that occurred within 30-days of the procedure were included. Definite infections were defined as either a positive blood or urine culture in a patient meeting National Healthcare Safety Network (NHSN) criteria for bloodstream or urinary tract infection, respectively. Possible infections were defined as empiric treatment for cystitis, pyelonephritis, prostatitis, epididymo-orchitis, or sepsis without culture confirmation.

Results. Of 19279 men who underwent TRUS-guided prostate biopsy between 2003 and 2013, 159 (0.8%) developed infectious complications. Between 2006 and 2013, definite urinary tract infection increased from 0.05% to 0.8% ($p < .0001$); bloodstream infections increased from 0.1% to 0.6% ($p < 0.0001$); and overall infections, including definite and possible infections, increased from 0.3% to 1.9% ($p < .0001$) (Figure). *E. coli* represented (85/89) 95% of isolates from urine and blood cultures of which 93% were resistant to ciprofloxacin. Resistance of *E. coli to* trimethoprim/sulfamethoxazole, gentamicin, cefazolin, ceftriaxone, and nitrofurantoin was 58%, 42%, 33%, 32%, and 8%, respectively.



Conclusion. The proportion of TRUS-guided prostate biopsies associated with infectious complications has increased significantly over the past decade, likely driven by the emergence of *E. coli* resistance to ciprofloxacin. Emerging antibiotic resistance may make current prophylaxis strategies with ciprofloxacin less effective, emphasizing the need for prospective evaluation of other prophylactic regimens and other non-antibiotic prevention strategies.

Disclosures. **All authors:** No reported disclosures.

1031. Comparative Epidemiology of Complicated Urinary Tract Infections (cUTI) by Age among US Hospitals

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Background. Data from national nosocomial infection surveillance (NNIS) system indicates that cUTI is a frequent cause of hospitalization across all age groups. However, few data are available on the comparative epidemiology and outcomes associated with cUTIs due to key Gram-negative pathogens by age among hospitalized patients. The objectives of this study were to compare the epidemiology and outcomes (hospital LOS and cost) by age among patients with cUTIs due to Gram-negative bacteria across US Hospitals.

Methods. Retrospective observational study using Premier hospital database was conducted. Inclusion criteria: (1) age ≥ 18 years, (2) patients with an admission to hospital for > 2 days between July 2012-June 2013, (3) primary diagnosis of cUTI by ICD-9 codes (590.1, 590.80, 590.8, 599.0), (4) ICD-9 codes for *E.coli* (041.4), *K. pneumoniae* (041.3) or *Pseudomonas* (041.7), and (5) received intravenous antibiotic within 3 days of hospital admission. Demographics, comorbid conditions, Gram-negative pathogens, and outcomes were compared between age categories (18-49 years, 50-64 years, and >= 65 years).

Results. During the study period, 20688 hospitalized patients across 487 hospitals had a primary diagnosis of a cUTI and met the above criteria. Patient characteristics, causative pathogens and outcomes are presented in table.

Patient Characteristics	18-50 years	51-64 years	>=65 years
Female, N (%)	2839(86.7)	2229(72.1)	10774(75.2)
Caucasian, N (%)	1979(60.5)	2105(68.1)	10955(76.5)
Charlson Comorbidity Score, N (%)			
0	2091 (63.9)	953 (30.8)	3922 (27.4)
1	629 (19.2)	818(26.4)	3706(25.9)
2	314 (9.6)	518(16.7)	2608(18.2)
>=3	239(7.3)	804(26.0)	4086(28.5)
G^- pathogen, N (%)			
E.coli	2834(86.6)	2320(75.0)	10250(71.6)
K. pneumoniae	284(8.7)	500(16.2)	2559 (17.9)
Pseudomonas	111 (3.4)	203(6.6)	1196(8.4)
Polymicrobial	44 (1.3)	70(2.3)	317(2.2)
Patient Outcomes			
LOS, mean(Sd)	3.7 (2.8)	4.7 (6.7)	4.8 (3.6)
Total hospital cost, mean(Sd)	$ 5852.7 (7682.3)	$ 7343.1 (8753.7)	$ 7429.5 (6962.3)

Conclusion. Compared to younger patients, older patients (≥50 years) were more likely to have a cUTI due *to K. pneumoniae* or *Pseudomonas*. In addition, patients ≥ 51 years, on average, had longer LOS and higher hospitalization cost relative to patients < 50 years.

Disclosures. **M. Mocarski**, Forest Research Institute: Employee, Salary **Q. Zhao**, Forest Research Institute: Employee, Salary **M. Ding**, Forest Research Institute: Employee, Salary **S. Dixit**, Forest Research Institute: Employee, Salary **T. Lodise**, Forest Research Institute: Consultant, Consulting fee

1032. Microbiologically-evaluable Complicated Urinary Tract Infection: Characterization in an Observational Data Source

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Background. Informative data on microbiologically-evaluable (ME) complicated urinary tract infection (cUTI) typically arise from clinical trials. Characterization of ME cUTI in electronic medical record (EMR)-linked administrative databases will provide standards of care diagnostics, treatments, and outcomes in broader populations.

Methods. Retrospective cohort study was conducted to characterize ME cUTI cases in Health Facts®, Cerner Corp, Kansas City, MO. Inclusion criteria were >18 years old with cUTI hospital episode in years 2008-2010 defined by International Classification of Diseases, 9th Revision, Clinical Modification codes, a urine culture report, and >1 antimicrobial prescription. Descriptive analyses were conducted in SAS version 9.1.3 (The SAS Institute, Cary, NC).

Results. Final cohort of 7754 adults was selected from 1.2 million hospital episodes. There were 4634 (60%) women, 53% were >65 years old, 3789 (49%) had acute pyelonephritis (AP), and 5566 (72%) had ME urine cultures. Comorbidities, categorized by Clinical Classifications Software, revealed age-stratified distinctions. Among ME cUTI subjects, a single, definitive pathogen was reported for 78% with AP and 63% in non-AP. In AP, the top-ranked pathogens were *Escherichia coli* (55%), *Klebsiella pneumoniae* (7%), and *Proteus mirabilis* (5%); in non-AP these were *E. coli* (26%), *Pseudomonas aeruginosa* (8%), and *Enterococcus faecalis* (8%). Among isolates with susceptibility data, multidrug-resistance (MDR) to >3 drug classes was detected in 7% Enterobacteriaceae and 14% non-Enterobacteriaceae. Initial treatment, by drug class, was highest for fluoroquinolones (26%), extended-spectrum cephalosporins (21%), and glycopeptides/oxazolidinones (13%). In ME cUTI subjects, 1193 (21%) had bacteremia with the same uropathogen. Overall mean length of stay was 7.7 (SD 9.3) days and 147 (2%) had in-hospital mortality.

Conclusion. This study provides recent epidemiology of ME cUTI and MDR pathogens in hospitalized adults. The algorithms created to identify the urine specimen, pathogens, and susceptibility data in the microbiology files provide a framework for detection of MDR pathogens in future population-based studies using EMR-linked observational data sources.

Disclosures. **L. Mundy**, GlaxoSmithKline: Employee, Salary **F. Mitrani-Gold**, GlaxoSmithKline: Independent Contractor, Consulting fee **N. Suppapanya**, GlaxoSmithKline: Employee, Salary **S. St. Laurent**, GlaxoSmithKline: Employee, Salary

1033. Rapid detection of bacteriuria with a simple immunoassay test

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Background. Urinary tract infections (UTIs) are frequently encountered in clinical practice and most commonly caused by *E. coli* and other Gram negative uropathogens. Given current concerns about cost of treatment and antimicrobial resistance, rapid confirmation of bacteriuria in patients under consideration for empiric treatment of UTI would potentially reduce expenditures and unnecessary antimicrobial treatment. Current diagnostic methods are suboptimal: nitrite dipsticks have low sensitivity and specificity and cultures take days. We tested a rapid immunoassay for bacteriuria developed by Silver Lake Research Corporation (SLRC) in comparison with standard bacterial culture using urine specimens submitted to a clinical microbiological laboratory in an urban academic medical center.

Methods. Study urines (N = 966) were obtained as de-identified discarded specimens from the University of Washington Medical Center microbiology laboratory. SLRC's immunoassay test was performed in accordance with instructions, providing a +/- result in about 15 minutes. Standard urine cultures were performed in parallel and all organisms were identified to the species level.

Results. 79% of urine specimens were from an outpatient setting and 21% were from inpatients. With urine culture used as the gold standard, the SLRC test kit identified as positive 244/270 (sensitivity 90%) of samples with *E. coli* or species of the genera *Klebsiella*, *Proteus*, *Citrobacter*, *Pseudomonas*, *Serratia*, *Acinetobacter* or *Enterobacter* at a level of $\geq 10^3$ CFU/ml. The specificity of the test on samples with $<10^3$ CFU/ml of Gram negative uropathogens was 94% (523/555).

Conclusion. A new rapid immunoassay test kit for direct detection of Gram negative bacteriuria in patient urine samples performed at high sensitivity (90%) and specificity (94%) as compared with standard culture of urine samples from both outpatient and inpatient settings. Using this assay in point-of-care diagnosis of UTI has the potential to reduce cost of treatment and overuse of antimicrobials for this common infection.

Disclosures. **All authors:** No reported disclosures.

1034. Clinical Laboratory Practices in Speciating Organisms and Reporting Results of Voided Urine Cultures

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Background. Studies comparing midstream voided and catheter urine specimens in symptomatic women have shown that colony counts of *E. coli* as low as 10^2CFU/mL in midstream voided urine (MSU), even when in mixed growth, are predictive of bladder infection. Given that clinical laboratories generally do not quantify organisms in MSU cultures to this level, the use of MSU cultures in the diagnosis of cystitis may lead to inappropriate interpretation of culture results. We queried laboratories to ask about their MSU culture and reporting practices.

Methods. A convenience sample of clinical microbiology laboratories in Miami, Florida, and nationally were queried. We called the laboratories to ask the microbiology laboratory manager and/or the clinical microbiologist about their practices in speciating and reporting results of MSU cultures and to send us any written algorithms relevant to such practices.

Results. We queried 11 local and 3 national clinical microbiology laboratories for our study. We were able to talk by telephone with laboratory personnel in all 14 laboratories to obtain study information, but only 8 laboratories sent us their MSU culture algorithms. No laboratory refused to provide us with information. Results are shown in the table.

Species identification and reporting of organisms growing in MSU.

No. organisms grown and colony counts	No. (%) of labs speciating and reporting
≥ 3 organisms at any colony count	0 (0)*
≤ 2 organisms, CFU/mL for either or both	• 14 (100)
• $\geq 10^4$CFU/mL	• 1 (7.1)†
• 10^3 - $<10^4$ CFU/mL	• 0 (0)‡
• $<10^3$ CFU/mL	

*9 laboratories report such cultures as "mixed flora," 3 "contaminated urine" and 2 "multiple organisms present"; 5 of 14 also suggest to repeat the specimen

†4 other laboratories report growth at 10^3- $<10^4$ CFU/mL but don't speciate; 9 report as "no growth"

‡9 report "no growth"; 5 report "$<10^3$ CFU/mL of unidentified organism"

Conclusion. Only one of 14 clinical microbiology laboratories speciate and report organisms in MSU if ≤2 organisms grow at 10^3- $< 10^4$ CFU/mL, and none do if ≥ 3 organisms grow at any colony count. Lack of awareness by clinicians as to how their clinical microbiology laboratory reports MSU results may result in misinterpretation of such results, including underdiagnosis of low colony count or mixed growth *E. coli* UTIs.

Disclosures. **All authors:** No reported disclosures.

1035. New Urine Reporting Criteria to Accurately Report Nosocomial Clinical Urinary Tract Infection

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Background. Reducing unnecessary antimicrobial therapy is critical to patient safety. We previously conducted an analysis to establish a colony count threshold predicting clinically significant UTI developing in hospitalized patients (AJCP 2012;137:778-84). Patients with urine culture colony counts $>10^5$ CFU/ml were 74 times more likely to have a clinically significant UTI than patients with colony counts $<10^5$ CFU/ml. With the approval of the Departments of Urology, Infectious Disease, Quality, and Infection Control we modified our urine culture laboratory reporting criteria for voided and Foley catheter samples from hospitalized patients with a length of stay of >2 days. For these patients, a positive test consists of 1-2 organisms at $>10^5$CFU/ml. Any other colony count or mixture of bacteria is reported as "Negative for Nosocomial UTI" (NNUTI). We hypothesize that this new reporting scheme would accurately report the absence of a UTI in >95% of samples. The first 5 months of the new reporting approach was validated with chart review.

Methods. Inpatient urine cultures were assessed to determine if 1) a patient had been in the hospital >2 days when the culture was taken and 2) the urine was a voided or Foley sample. The culture report was assessed with chart review by a single Infectious Disease Physician to determine if the patient had signs and symptoms of a UTI when NNUTI was the result. Parameters to determine UTI included fever >100.4°F, frequency, dysuria, or flank pain, and change in clinical status with no other reason other than UTI. A negative urinalysis and no therapy supported the NNUTI diagnosis.

Results. In 5 months, 29226 urine samples were evaluated. 401 patients were reported as NNUTI. Of these, only 5 (1.2%) patients met criteria for potential symptomatic UTI. Two patients treated for asymptomatic UTI were subsequently diagnosed with *Clostridium difficile* infection and renal failure, respectively. The second patient died of an adverse reaction to antibiotic therapy. No patient was adversely impacted by a NNUTI culture report.

Conclusion. The new reporting criteria accurately reported the absence of a UTI in >98% of samples that had bacterial counts of $<10^5$ CFU/ml. Overtreatment of UTI has serious clinical consequences.

Disclosures. **All authors:** No reported disclosures.

1036. Estrogen Hormone Replacement Therapy May Lower Risk of Recurrent Urinary Tract Infections in Postmenopausal Women

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Background. Urinary tract infections (UTIs) are a frequent problem among postmenopausal women necessitating antimicrobial use, and resistance is increasing. Every year, 8-10% of postmenopausal women have 1 episode of a UTI; of these, 5% will have a recurrence in the next year.[1] Most women have been taken off estrogen hormone replacement therapy (HRT). While studies have demonstrated systemic HRT does not reduce the incidence of UTIs,[1-4] topical HRT reduced the number of UTIs in 2 small studies.[5,6]To our knowledge no study has compared both treatment groups with a control.

Methods. Retrospective charts (2011-2013) were randomly reviewed of women age 60-75 with a documented history of UTI (N = 448). Excluded were patients taking antibiotics for UTI prophylaxis; patients treated with antibiotics for other reasons than UTI for >2 weeks, patients on both topical and systemic HRT, and patients on chronic methenamine hippurate. Pts were separated into 3 groups (N = 75/group): those using systemic HRT, topical HRT, and control. The primary outcome was number of UTIs/patient over 1 year.

Results. UTIs/patient/year differed significantly between conditions ($F(2,222) = 8.75$, $p < 0.001$), with post-hoc Tukey tests showing a significant difference between topical and systemic ($p < .001$), and topical and control ($p < .05$), but not systemic and control. The control group had an average of 1.24 UTIs/patient/year, compared to 1.01 in the systemic group and 0.65 in the topical group. There were no significant differences in age or other baseline characteristics of incidence of diabetes mellitus, chronic kidney disease or urinary incontinence; however in the control group, 8% had a history/baseline diagnosis of atrophic vaginitis compared to 11% in the systemic HRT group and 72% in the topical HRT group ($\chi^2_{(2)} = 93.24$, $p < 0.001$).

Conclusion. UTIs are one of the most common reasons that antibiotics are prescribed[7]. Increasing antimicrobial resistance among pathogens associated with UTIs has been a real concern to the infectious disease community, and options for prevention are becoming increasingly more important. In our study, topical HRT was associated with a lower incidence of UTIs compared to the control group and may be beneficial when other preferred agents cannot be utilized. Future studies should evaluate dosing/duration of HRT for most effective outcomes.

Disclosures. **All authors:** No reported disclosures.

1037. The risk factors for resistant *Esherichia coli* infections after prostate biopsy under fluoroquinolone prophylaxis

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Background. To evaluate the risk factors of fluoroquinolone resistant or ESBL-producing *E coli* infections after prostate biopsy under flouroquinolone prophylaxis

Methods. From January 2003 to December 2012, we evaluated the records of 2215 patients who underwent TRUS guided 12-core prostate biopsy under flouroquinolone prophylaxis. The risk factors including age, diabetes mellitus, hypertension, history of hospital admission within 30 days, prior use of quinolons within 6 months of the biopsy, first or repeat biopsy were evaluated for the development of flouroquinolon resistance and ESBL producing E coli

Results. Of the 2215 patients, 153 had positive urine cultures such as 129 (84.3%) *E coli*, 8 (5.2%) *Enterococcus spp*, 6 (3.9%) *Enterobacter spp*, 5 (3.2%) *Pseudomonas spp*, 3 (1.9%) MRCNS, 2 (1.3%) *Klebsiella spp*. Of the positive urine cultures yielded *E coli*, 99 (76.7%) were evaluated for fluoroquinolone (ciprofloxacin) resistance. In these group 83 (83.8%) were fluoroquinolone resistant. In addition to 129 *E coli* strains were examined for ESBL producing and ESBL positivity was found in 67 (51,9%) of these strains. When the risk factors regarding the infection caused by ESBL producing or quinolon resistant *E coli* strains were examined, the use of quinolones in the last 6 months and a history of hospitalization in the last 30 days were found to be significant (p = 0,00, p = 0,021 and p = 0,034, p = 0,041 respectively)

Conclusion. We found that while fluoroquinolone prophylaxis started before TRUS-guided prostate biopsy is still effective in preventing infectious complications that might develop after biopsy, fluoroquinolone-resistant or ESBL-producing *E coli* strains might be a common microorganism in patients with this kind of complication. This study examined various risk factors for the development of infection in both ESBL-producing strains and strains that developed resistance to fluoroquinolones. Among these factors, a history of the use of fluoroquinolones in the last 6 months and hospitalization in the last one month were found to be significant.

Disclosures. **All authors:** No reported disclosures.

1038. Assesing the Management of Urinary Tract Infections at a Large, Urban Teaching Hospital

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Background. Recently, Grady Heath System (GHS) updated its urinary tract infection (UTI) management guidelines. Despite these guidelines, variability in the diagnosis and treatment of UTIs at GHS has been noted. Such deviation of clinical practice can have a tremendous impact on patient outcomes; therefore, we aimed to evaluate the preliminary efficacy of a pharmacist-driven educational pilot intervention in improving the management of UTIs.

Methods. From October 1, 2013 to March 31, 2014 a three-phase pilot study was conducted to identify patients 18 years or older with a urinalysis (UA) ordered for evaluation of a potential UTI. The initial phase involved retrospective chart review; UTIs were categorized as adherent or non-adherent based on whether their management was in line with GHS guidelines. The intervention phase involved the delivery of pharmacist-led education sessions focusing on recommendations for appropriate management of UTIs and the provision of informational pocket cards with diagnostic and treatment algorithms based on GHS guidelines. The final phase of the study consisted of a prospective chart review assessing UTI management similar to the initial phase. Lastly, a pharmacist provided real-time feedback to a physician member of the treatment team if non-guideline-based UTI management was identified.

Results. Data for 100 patients was analyzed for the retrospective phase of the study. Of these, 86% were managed in compliance with guidelines. Data for 100 patients was analyzed for the prospective phase of the study. Of these, 90% were managed in compliance with guidelines, leaving 10% that were non-compliant requiring intervention. All UTIs evaluated were treated with guideline-compliant duration of therapy. Empiric antibiotic selection was in compliance with guidelines 66% of the time during the pre-intervention phase, compared to 76% during the post-intervention phase. Annualized cost savings based on antibiotic use avoidance resulting from pharmacist intervention were calculated as $5,000 for a 7-day course of antibiotics.

Conclusion. Pilot findings suggest that a simple, pharmacist-driven educational intervention can impact adherence to hospital UTI management guidelines, and thus result in improved antibiotic stewardship and substantial cost savings.

Disclosures. **All authors:** No reported disclosures.

1039. Urinary Tract Infections in an African Teaching Hospital, a Comparison of Antimicrobial Susceptibility of Inpatient and Outpatient and Catheter Associated Risks.

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Background. Nosocomial infections associated with resistant micro-organisms leads to increased morbidity. Urinary tract infections (UTI) especially catheter associated UTI (CAUTI) is one of the common nosocomial infections. We compared isolation rates and antibiotic susceptibility patterns between isolates from In-patients and Outpatients and from CAUTI and non-CAUTI patients.

Methods. A four month prospective study involved 2232 urine samples from patients at the Komfo Anokye Teaching Hospital in Kumasi, Ghana. Of these, 759 patients were randomly selected and interviewed to determine whether they had been catheterized or not. Bacteria were identified by standard microbiological and biochemical methods. Antimicrobial susceptibility testing was performed on all bacterial isolates.

Results. The median age of patients was 28 years and in-patients made up 46.3% of participants. The rate of positive cultures was 26% and the most frequent isolates were *E. coli*- 42.5%, *Klebsiella spp*-25.9%, Coliforms-7.4% and *Candida spp*-3.4%.

Inpatients had more positive cultures (31.3% vs 22.8%, p value <0.0001) but the micro-organisms isolated were similar. The odds of a catheterized patients having UTI was 1.99 (95%CI 1.40-2.85). Positive cultures was significantly higher in catheterized than non-catheterized patients (43.4% vs 27.7%, p value < .0001) and Isolates were similar except for *Pseudomonas aeruginosa*being the 4th leading isolate from the CAUTI group.

The most effective antimicrobials against gram negative bacteria were meropenem and amikacin with sensitivities of 97.4 and 96.7% respectively. Resistance of *E. coli* to antimicrobials was significantly lower in Outpatient than Inpatient, including gentamicin 48.7% vs 66.1%, ciprofloxacin 57.7% vs 65.6%, ceftriaxone 65.7% vs 87.5% and ceftaxidime 36.8% vs 48.9%. *Klebsiella spp* had a similar trend as *E. coli*. There was no significant difference of antimicrobial resistance between isolates from catheterized and non-catheterized patients.

Conclusion. *E.coli* was the commonest pathogen. Resistance rates of urine pathogens amongst In-patients were higher than in Out-patients. These findings suggest that different empirical prescriptions may be necessary for Inpatients and Outpatients.

Disclosures. **All authors:** No reported disclosures.

1040. Describing Antibiotic Utilization Patterns and Healthcare Costs for Ambulatory and Inpatient/ED Treatment of Complicated Urinary Tract Infection (cUTI)

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Background. The study objective was to describe ambulatory antibiotic (ABX) utilization patterns and total healthcare costs among patients with cUTI managed in an ambulatory care (AMB) setting or AMB plus inpatient/ED (IPED) care setting

Methods. This was a retrospective analysis of the HealthCore Integrated Research Environment (HIRE) database for the period 2006 through 2013. Patients with cUTI (defined as treatment failure to first AMB ABX administration) were selected and categorized into IPED and ABM groups. The IPED cohort required an initial AMB visit and an ABX prescription for UTI followed by an inpatient/ED admission within 30 days. The AMB cohort was required to have a second office visit and two distinct ABX, on different service dates, within 30 days of initial AMB visit. The index date for the IPED cohort was the cUTI-related admission date and for AMB it was the first cUTI-related physician office visit. AMB patients were followed for 30 days post index date and IPED patients were followed for 30 days pre-index date through the index hospital/ED discharge.

Results. The IPED cohort consisted of 29,533 (41.5%) patients and the AMB cohort consisted of 41,605 (58.5%) patients. Patients were primarily female (IPED: 81%, AMB: 86%) and the average age was similar (IPED =54 and AMB =52) for the two groups. AMB patients had fewer co-morbidities and their Deyo-Charlson Co-morbidity score (mean: 0.8) was lower compared with the IPED cohort (mean: 1.3). During outpatient treatment most patients in both cohorts were treated with an oral antibiotic (AMB = 99.7%; IPED = 96.2%). AMB patients filled an average of 2.6 prescriptions and had 2.1 distinct oral ABX compared to IPED patients who filled 1.4 prescriptions and had 1.3 distinct oral ABX. The AMB cohort also had a greater percentage of IV-ABX use (16.3% vs 12.3%). All cause mean costs for AMB cohort were $2,871 and $13,612 and $3,720 for the IPED cohort with and without the index hospital/ED admission.

Conclusion. cUTI is a refractory and expensive to treat illness. Long-term antibiotic resistance is a treatment risk. These results provide a basis for future research on improved AMB management strategies that may help prevent or shorten IPED treatment.

Disclosures. **S. Karve**, AstraZeneca: Employee, Salary **J. Hackett**, Astra Zeneca: Employee, Salary

1041. Economic Burden Associated with Key Gram-negative Pathogens among Patients with Complicated Urinary Tract Infections across US Hospitals

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Background. cUTI is a frequent cause of hospitalization and results in considerable morbidity and mortality. While this is well appreciated, scant data are available on the economic burden posed by the various Gram-negative pathogens that cause cUTIs. The objectives of this study were to compare hospital length of stay (LOS) and total hospital costs for patients with cUTI due to different Gram-negative bacteria.

Methods. Retrospective observational study using Premier research database was conducted. Inclusion criteria: (1) age ≥ 18 years, (2) patients with an admission to hospital for > 2 days between July 2012-June 2013, (3) primary diagnosis of cUTI by ICD-9 codes (590.1, 590.80, 590.8, and 599.0), (4) ICD-9 code for *E. coli* (041.4), *K. pneumoniae* (041.3), or *Pseudomonas* (041.7), and (5) received intravenous antibiotic within 3 days of hospital admission. Demographics, comorbid conditions, and outcomes were compared between pathogens of interests.

Results. During the study period, 20688 hospitalized patients had a primary diagnosis of a cUTI across 487 hospitals and met the above criteria. Patient characteristics and outcomes are presented in the table.

Conclusion. Economic burden associated with complicated urinary tract infection is substantial, especially for patients infected with gram negative infections. In our study, cUTI due to *Pseudomonas* and > 1 Gram-negative pathogen pose greater economic challenges underscoring the need for new agents to treat these increasingly difficult infections.

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Patient Characteristics	*E. coli* N=3343	*K.pneumoniae* N=15404	*Pseudomonas* N=1510	*Polymicrobial* N=431
Age, mean(Sd)	73.5(15.1)	68.4(19.8)	74.1(15.2)	72.0(15.6)
Female, N (%)	2455(73.4)	12339 (80.1)	741(49.1)	307(71.2)
Caucasian	2500(74.8)	11091(72.0)	1143(75.7)	305(70.8)
Charlson Comorbidity Score, N (%)				
0	837(25.0)	5638(36.6)	390(25.8)	101(23.4)
1	817(24.4)	3899(25.3)	322(21.3)	115(26.7)
2	640(19.1)	2412(15.7)	306(20.3)	82(19.0)
>=3	1049(31.4)	3455(22.4)	492(32.6)	133(30.9)
Patient Outcomes	*E. coli* N=3343	*K. pneumoniae* N=15404	*Pseudomonas* N=1510	*Polymicrobial* N=431
LOS, median (IQR)	4.0(3.0)	3.0(2.0)	5.0(4.0)	5.0(4.0)
Total Hospital Cost, median (IQR)	$ 5751.7 (4657.4)	$ 5320.4 (4087.3)	$ 7002.4(5673.3)	$ 6974.4 (6106.0)

1042. Prevalence of Fluoroquinolone- and Ceftriaxone-resistant *E. coli* among U.S. Emergency Department Patients with Acute Pyelonephritis

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Background. To determine the prevalence of and potential risk factors for fluoroquinolone-resistant and ESBL-producing *E. coli*, we report preliminary results of patients with acute pyelonephritis presenting to a network of U.S. emergency departments (EDs, *EMERGE*ncy ID NET).

Methods. This is a prospective observational study of patients ≥18 years old with flank pain and/or costovertebral angle tenderness, ED temperature ≥38°C, and clinically suspected acute pyelonephritis. Historical and examination data were collected during the index visit. Enrolled patients provided a urine specimen and cultures growing *E. coli* $>10^3$ cfu/ml were tested for antimicrobial susceptibility. Some isolates with a ceftriaxone MIC >1 μg/ml were tested for ESBL at site labs, and all will have confirmatory testing at a reference lab. Prevalence of resistance was compared to a similar study conducted in 2000-2004.

Results. We have enrolled 371 subjects since July 2013 from 9 EDs; 62 were excluded because a urine culture was not done or the specimen was contaminated. Of 309 subjects, median age was 37 years and 86.4% were female. Of the 230 (74.4%) that grew a pathogen, 210 (91.3%) grew *E. coli*. Among those with *E. coli* infection, the isolate was fluoroquinolone-resistant in 13.9% and ceftriaxone-resistant in 8.1%. Among those with any or none of antibiotic exposure in the previous 2 months, hospitalization or residence in a long term care facility (LTC) in the previous 90 days, the prevalence of fluoroquinolone resistance was 22.9% and 11.3%, and ceftriaxone resistance was 18.8% and 5.0%, respectively. Among those with ceftriaxone-resistant *E. coli* infection, 47.1% used antimicrobials in the previous 2 months, and 17.6% had been hospitalized or resided in a LTC in the previous 90 days. At site labs, 11/17 ceftriaxone-resistant *E. coli* isolates were tested for ESBL and all were positive. In 2000-2004, among a similar ED population, the prevalence of *E. coli* fluoroquinolone resistance was 4.0% and no ESBL infections were found.

Conclusion. Based on our preliminary data, the prevalence of *E. coli* fluoroquinolone resistance has increased, and ceftriaxone resistance, often due to ESBL production, is now being seen in U.S. ED patients, including among those without recent health care setting exposure.

Disclosures. **D. Talan**, Centers for Disease Control and Prevention: Grant Investigator, Research grant

1043. Fluoroquinolone Resistance in Community-acquired Acute Pyelonephritis: Clinical Characteristics, Risk Factors and Clinical Response according to Fluoroquinolone MIC of Uropathogens

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Background. The objective of this study was to investigate clinical characteristics, risk factors of community-acquired acute pyelonephritis (CA-APN) caused by fluoroquinolone-resistant (FQ-R) uropathogen, and clinical response according to FQ MICs of uropathogen.

Methods. We performed prospective observational study, which collected clinical data of CA-APN women with identified urinary pathogen from urine or blood cultures visiting 11 university hospital from March 2010 to February 2012.

Results. Among 775 CA-APN patients, 587 with FQ susceptibility results were analyzed. Numbers of FQ-R and fluoroquinolone-susceptible (FQ-S) group were 127 (21.6%) and 460 (78.4%). In clinical characteristics, more patients in FQ-R group had an age >65 years (56.7% vs 44.6%, $p = 0.015$), history of antibiotics usage within 1 year (48.1% vs 24.3%, $p < 0.001$), history of admission within 1 year (43.7% vs 22.8%, $p<0.001$), Charlson co-morbidity index >1 (26.8% vs 21.3%, $p = 0.191$), and extended-spectrum β-lactamase positivity (27.2% vs 4.2%, $p < 0.001$). Clinical response within 72 hours (early clinical response, ECR), final clinical response and mortality were not different between the two groups, although duration of hospitalization was longer in FQ-R group (median 9.0 vs 7.0 days, $p = >0.001$). In subgroup of 142 subjects using FQ during initial 72 hours, final clinical response or mortality was not different between the two groups. However, ECR was more frequent (50.0% vs 75.0%, $p = 0.012$) and duration of hospitalization was shorter (median 10.5 vs 7.0 days, $p<0.001$) in FQ-S than FQ-R group. Multivariate logistic regression proved that age >65 years (OR 1.572, CI 1.004-2.460, $p = 0.048$) and history of antibiotics usage within 1year (OR 2.902, CI 1.842-4.573, $p < 0.001$) were significant risk factors for FQ-R. Among the 142 subjects, FQ MICs of *Escherichia coli*from urine or blood were available in 64 patients, and ECR according to FQ MIC was analyzed: 72.5% (29/40) in patients with MIC <0.004 ~ 0.125 μg/ml, 76.9% (10/12) with 0.19 ~ 3 μg/ml, 80% (4/5) with 4 ~ 16 μg/ml and 57.1% (4/7) with >32 μg/ml.

Conclusion. Risk factors of FQ-R were age >65 years and history of antibiotics usage within 1 year, and duration of hospitalization was longer in FQ-R than FQ-S group. Patients with FQ MIC ≤16 μg/ml showed a similar ECR to those with susceptible isolates.

Disclosures. **All authors:** No reported disclosures.

1044. Efficacy of Ceftolozane/Tazobactam vs Levofloxacin in the Treatment of Complicated Urinary Tract Infections (cUTI) caused by Levofloxacin-resistant Pathogens: Results from the ASPECT-cUTI Trial

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Background. Ceftolozane/tazobactam demonstrates excellent activity in vitro against Gram-negative pathogens, including extended spectrum β-lactamase–producing Enterobacteriaceae and multidrug-resistant *Pseudomonas aeruginosa*. The efficacy of ceftolozane/tazobactam in the subset of patients with cUTI, including pyelonephritis, caused by levofloxacin (LVX)-resistant pathogens was examined from pooled efficacy data of 2 Phase 3, randomized, controlled, double-blind trials (NCT01345929 and NCT01345955).

Methods. Hospitalized patients ≥18 years old with pyuria and clinical symptoms of cUTI were randomized to either intravenous ceftolozane/tazobactam 1.5 g every 8 hours or intravenous LVX 750 mg/day for 7 days, prior to availability of susceptibility data. Primary outcome was the composite microbiological eradication and clinical cure (composite cure) rate at the test-of-cure (TOC) visit 5-9 days after the end of therapy in the microbiological modified intent-to-treat (mMITT) and microbiologically evaluable (ME) populations.

Results. A total of 1083 patients were enrolled, 800 were included in the mMITT population, and 212 had LVX-resistant baseline uropathogens; 176/212 were susceptible to ceftolozane/tazobactam. Ceftolozane/tazobactam demonstrated significantly higher composite cure rates and per-pathogen microbiological eradication rates vs LVX in the mMITT and ME populations (Table).

Conclusion. Ceftolozane/tazobactam demonstrated superior composite cure rates vs LVX in cUTI caused by LVX-resistant pathogens. Ceftolozane/tazobactam may offer an alternative treatment for cUTI in settings of increasing fluoroquinolone resistance among common uropathogens.

Disclosures. **G. Sakoulas**, Cubist Pharmaceuticals: Consultant and Speaker's Bureau, Consulting fee and Speaker honorarium **O. Umeh**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **J. Huntington**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **D. Cloutier**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **J. Steenbergen**, Cubist Pharmaceuticals: Employee and Shareholder, Salary **G. Yuan**, Cubist Pharmaceuticals: Employee, Salary **M. Yoon**, Cubist Pharmaceuticals: Employee, Salary **E. Goldstein**, Cubist Pharmaceuticals: Grant Investigator, Scientific Advisor and Speaker's Bureau, Grant recipient

Outcomes in the LVX-resistant Population at TOC	Population	Ceftolozane /Tazobactam % (n/N)	LVX % (n/N)	Difference % (95% Confidence Interval)
Composite Cure Rate	mMITT	60.0 (60/100)	39.3 (44/112)	20.7 (7.23 to 33.17)
	ME	64.0 (57/89)	43.4 (43/99)	20.6 (6.33 to 33.72)
Per-pathogen Microbiological Eradication Rate	ME			
Enterobacteriaceae		71.4 (55/77)	45.2 (38/84)	26.2 (10.96 to 39.72)
Escherichia coli		72.9 (43/59)	44.1 (30/68)	28.8 (11.59 to 43.55)
Klebsiella pneumoniae		81.8 (9/11)	30.0 (3/10)	51.8 (9.50 to 75.05)
P. aeruginosa		100.0 (3/3)	37.5 (3/8)	62.5 (-2.09 to 86.32)

1045. Linezolid Compared to Daptomycin for the Treatment of Vancomycin-resistant Enterococcal Urinary Tract Infections

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Background. *Enterococcus* remains the second most frequently isolated organism from the urine of hospitalized patients. With as many as 30% of all enterococcal isolates resistant to vancomycin, treatment options are limited.

Methods. A retrospective cohort study was conducted of all patients at a VA medical center with a urine culture positive for vancomycin-resistant enterococci (VRE) and treated with ≥ 7 days of either linezolid or daptomycin between January 1 2007 and December 31 2012. Patients who received >24 hours of any agent active against VRE before initiation of either antibiotic, those with a urinary tract infection (UTI) in the previous year, those with more than 1 organism found on urine culture, patients on hemodialysis, and those with absolute neutrophil counts <500 cells/mm^3 were excluded.

The primary outcome was therapeutic failure, defined as a new urine culture positive for VRE within 1 month of completing initial antibiotic therapy. Secondary outcomes were a composite of treatment failure, which included a new urine culture positive for VRE, or the prescribing of any antibiotics for a UTI, or a urine analysis with >10 WBC/hpf within 1 month of initial therapy completion.

Results. Twenty-nine patients met inclusion criteria; 21 were treated with linezolid and 8 with daptomycin. One patient treated with linezolid experienced therapeutic failure (4.76%) compared to no patients treated with daptomycin ($p > 0.05$). Five patient (23.8%) treated with linezolid and 1 patient (12.5%) treated with daptomycin experienced the composite outcome treatment failure ($p = 0.50$). A regression analysis for the variables of agent selected, presence of an indwelling catheter, or spinal cord injury or nursing home resident was completed; only spinal cord injury or nursing home resident was significant with an odds ratio of 11.0 (95% CI 1.27-95.18; $p = 0.025$). No patients in either group experienced significant adverse effects while receiving therapy.

Conclusion. In this small, retrospective cohort of patients with VRE UTIs there was no significant difference in outcomes between patients treated with linezolid or daptomycin. Patients with spinal cord injuries or who were nursing home residents had a higher risk of treatment failure.

Disclosures. **All authors:** No reported disclosures.

1046. Economic Burden of Herpes Zoster by Age Group in Immunocompetent Patients in the United States

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Background. While the Advisory Committee on Immunization Practices (ACIP) recommends vaccination against herpes zoster (HZ) for those 60 and older, FDA approval extends vaccination to those aged 50-59. This study sought to examine direct and indirect medical costs of HZ among immunocompetent persons in the U.S. by age groups informed by vaccination recommendations.

Methods. This was a retrospective case-control analysis using the Truven Health MarketScan® Research databases (2008-2011) to determine the incremental direct and indirect cost associated with HZ. Cases were identified by a diagnosis code for HZ (ICD-9-CM: 053.xx), continuous enrollment 12 months pre/post diagnosis, and lacking a prior diagnosis for or vaccination against HZ. Cases were matched to immunocompetent controls without HZ using demographic and clinical variables and baseline medical expenditures. Healthcare costs, resource utilization, and indirect costs were descriptively compared between those with and without HZ from 21 days prior through one year following diagnosis.

Results. A total of 98,916 cases were identified and matched 1:1 to controls. We found a significant difference in average total healthcare cost between patients with HZ and patients without HZ ($6,241 vs $4,933, $p < 0.001$), leading to an average incremental healthcare cost of $1,308. Total cost to treat HZ and related utilization increased with age, peaking at over $13,000 for those 80 years and older. Incremental costs to treat HZ in patients aged 50-59 was higher than in patients aged 60-69, ($1,614 vs $1,249, $p < 0.001$). Significant incremental indirect costs due to work absence (ABS) and short-term disability (STD) were also observed in HZ patients aged 50-59 (ABS = $885, STD = $206) and those aged 60-64 years (ABS = $715, STD = $304).

Conclusion. HZ burden in adults can lead to considerable incremental healthcare and work loss-related costs. Significant resources are currently being expended on patients aged 50-59, for which the vaccine is approved, but not yet ACIP recommended.

Disclosures. **J. Gatwood**, Truven Health Analytics: Employee, Salary **B. Johnson**, Truven Health Analytics: Employee, Salary **L. Palmer**, Truven Health Analytics: Employee, Salary **G. Lenhart**, Truven Health Analytics: Employee, Salary **K. Kawai**, Merck and Co., Inc.: Employee, Salary **C. Acosta**, Merck and Co., Inc.: Employee and Shareholder, Salary

1047. Use of electronic data to identify new zoster cases for a vaccine effectiveness study

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Background. In the pilot phase of a study of the long-term effectiveness of Zostavax™(live zoster vaccine indicated for the prevention of herpes zoster (HZ)), we examined the performance of combinations of diagnostic codes, medications, and laboratory tests in identifying new HZ cases.

Methods. In the Kaiser Permanente Northern California Region, we used computerized data to identify first HZ diagnoses (no HZ diagnoses in the previous 12 months) among study participants 50 years of age or older from 2007 through 2012. We then used ICD9 codes, "internal" diagnostic terms (more specific than ICD9 codes), health care setting (outpatient, emergency department, hospital), coding position (primary diagnosis or other), antiviral medications, and VZV and HSV laboratory tests to create mutually exclusive categories of potential cases which were expected to have a low, medium, or high predictive value for incident HZ. Representative samples of medical charts from each category were reviewed and diagnoses were adjudicated by two physicians independently, with discordant cases adjudicated by a third clinician

Results. We identified 39,570 cases of HZ over the pilot study period, after restricting the diagnosis to cases that did not also have a post-herpetic neuralgia (PHN) internal diagnostic term at the time of their first HZ code. 36,417 (92%) cases were classified in the high category, which consisted of any HZ diagnoses with an antiviral medication or positive VZV lab result, or a primary HZ diagnosis so long as there was no indication of HSV. Of 200 adjudicated cases from the high category, 185 (92.5%) were confirmed as having received a diagnosis for incident HZ (95% CI, 87.9%-95.7%).

Conclusion. It is feasible to use electronic data to identify a large subset of new HZ diagnoses that are highly predictive of the diagnosis of new-onset HZ.

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1048. Pregnancy Registry for Varicella-Zoster Virus-Containing Vaccines: 18-Year Summary of Pregnancy Outcomes

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Background. VARIVAX®, ProQuad® and ZOSTAVAX® contain live attenuated varicella zoster virus (VZV) and are contraindicated during pregnancy. Merck and Co., Inc. and the Centers for Disease Control and Prevention collaboratively established a pregnancy registry for VZV-containing vaccines to monitor congenital varicella syndrome (CVS) and other birth defects in offspring of women inadvertently exposed to these vaccines during pregnancy. A summary of 18 years of registry data is presented.

Methods. Health-care providers from the United States, Puerto Rico, and Canada voluntarily report administration of VZV-containing vaccines to women within 3 months before or during pregnancy. Follow-up is conducted to obtain pregnancy outcomes. Reports are classified by timing of registry notification (before vs after pregnancy outcome is known), VZV serostatus at vaccination, and timing of exposure in relation to gestational age. The theoretical risk for CVS is defined as "high" if vaccination occurred during the 1st or 2nd trimester. Prospective reports (received before the outcome of pregnancy was known) are used for rate calculations. Metropolitan Atlanta Congenital Defects Program methodology is used to define birth defects and calculate rates.

Results. From March 17, 1995 through March 16, 2013, 893 prospective reports with outcomes available for analysis were received. Most exposures (n = 886) were to VARIVAX. No features consistent with CVS were identified among all 810 live births in the registry or among those of varicella-susceptible women exposed during the high risk period (n= 95, rate = 0%, 95% confidence interval [CI] 0.0, 3.8). Major birth defects were reported in 18 offspring of women with pregnancy outcomes ≥20 weeks gestation resulting in a birth prevalence of 2.1 per 100 liveborn infants (95% CI 1.2, 3.4), similar to the prevalence in the general population. No specific pattern or clustering by type of defect was identified.

Conclusion. We observed no cases of CVS and no increased prevalence for other birth defects after exposure to VZV-containing vaccines during pregnancy. However, the number of exposures is insufficient to exclude a very low risk of CVS in varicella-susceptible women exposed during the high risk period. VZV-containing vaccines remain contraindicated for pregnant women.

Disclosures. **All authors:** No reported disclosures.

1049. Evaluating the Population Impact of HPV Vaccine on High Grade Cervical Intraepithelial Neoplasia Rates in an Era of Decreasing Screening

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Background. Vaccination for two oncogenic human papillomavirus (HPV) types has been available since 2006. Current efforts focus on the effectiveness of this vaccination in reducing the risk of high grade cervical intraepithelial neoplasia (CIN). Monitoring of the impact of vaccine on CIN grade 2 or higher (CIN2+) has been ongoing in Monroe County, NY since 2008 as one of five sites participating in the HPV-IMPACT study which is part of the Centers for Disease Control and Prevention (CDC) Emerging Infections Program. Because CIN2+ cases are detected through routine cervical cancer screening and can be impacted by changes in screening, screening rates in the HPV-IMPACT catchments are also estimated as part of the project. To elucidate the potential independent impact of HPV vaccination, we examined the reduction in CIN2+ case rates while adjusting for the change in screening rates.

Methods. Screening rates and CIN2+ incidence rates from 2008-2012 were calculated for females aged 18-29, in Monroe County, New York. Screening data were obtained from three local laboratories that collectively process all Monroe County PAP smear test specimens. Cases of CIN2+ were ascertained according to the HPV-IMPACT protocol from all pathology laboratories serving Monroe County residents. The 2010 Census population was used as the denominator for both rates. Poisson regression was used to determine Rate Ratios (RRs) and 95% CIs of CIN2+ cases over 5 years using 2008 as reference year, with and without adjusting for change in screening rates.

Results. From 2008-2012, rates of screening and CIN2+ cases declined by 34.9% and 49%, respectively. The crude RR for screening [0.64 (0.63, 0.65)] and CIN2+ incidence [0.51 (0.44, 0.60,)] indicate declines in 2012 compared to 2008. While adjusting for screening rates somewhat attenuated the RR for CIN2+ incidence, it remained lower in 2012 than in 2008 [0.71 (0.60, 0.84)].

Conclusion. CIN2+ cases and cancer screening rates have both declined since 2008. CIN2+ incidence rates declined independently of screening rates, suggesting that HPV vaccination may have contributed to the reduction of CIN2+ disease incidence.

Disclosures. **All authors:** No reported disclosures.

1050. Evaluation of syncope and related events following vaccination with quadrivalent human papillomavirus vaccine (2006-2013)

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Background. Since licensure of quadrivalent human papillomavirus vaccine (qHPV) in 2006, several large studies have confirmed the favorable benefit- risk of qHPV. Syncope has been seen following qHPV. In some instances the paroxysmal loss of consciousness caused by cerebral hypoperfusion occurring with vasovagal syncope may be associated with seizure-like movements; health care providers (HCPs) may misinterpret these syncopal events as convulsions. The objective of this analysis is to characterize spontaneous, postmarketing reports of convulsion and syncope after qHPV.

Methods. Case characteristics, including time to onset, patient age, and clinical course were analyzed. All case reports of convulsion were medically evaluated and classified as follows: probable syncope; convulsion in an individual with a history of seizures; new onset of convulsion; a diagnosis inconsistent with syncope or convulsion; or insufficient data. Reporting rates were calculated for syncope and convulsion (total number of case reports divided by the number of vaccine doses distributed).

Results. The reporting rate for syncope was 3.9/100,000 doses distributed worldwide. The majority (72%) of syncope cases was reported in vaccinees 10-18 years of age and 88% occurred on the day of vaccination. The reporting rate for convulsion was 0.95/100,000 doses. Medical review revealed 44% are likely cases of convulsive syncope (fainting with myoclonic jerks); 6% are post vaccination seizure in patients with pre-existing seizure disorders; 6% involve diagnoses other than syncope or seizure; and ~22% could represent cases of new onset seizure. The remaining 21% are not evaluable due to lack of data. New onset cases and cases in individuals with a history of convulsion occurred at a rate of 0.27/100,000 doses.

Conclusion. Syncope has been reported following qHPV vaccination at a low rate. HCPs should be aware of the potential and take precautions. Reported cases of convulsion post vaccination have been clinically reviewed. Many are more consistent with convulsive syncope rather than convulsion. Misinterpreting a vasovagal episode may result in unnecessary treatment; careful clinical assessment is recommended.

Disclosures. **F. Lievano**, Merck and Co.: Employee, Salary **M. A. Goss**, Merck and Co: Employee, Salary

1051. Well-child Visits and HPV Vaccination Rates in Privately Insured Females Aged 9-21 Years in the United States, 2007-2012

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Background. Well-child visits provide the best opportunities for vaccinations in the US. The Advisory Committee on Immunization Practices (ACIP) recommends vaccination of 11-12 year old preteens with Tdap (Tetanus, Diphtheria and Pertussis), Meningococcal Conjugate Vaccine (MCV4) and HPV (Human Papillomavirus) Vaccines. The objectives of this study was to understand utilization of well-child visits, estimate HPV vaccination rates during well-child visits, and compare HPV vaccination rates during well-child visits in 11-12 year girls with Tdap and MCV4 and with different vaccination rates in other age categories.

Methods. This was a retrospective database (MarketScan®) cohort study. Eligible subjects were 9-21 year old females who had continuous enrollment since June 1, 2006 or January 1 of the year when a child turned 9 years old, had well-child visits, and didn't initiate HPV vaccine series previously. Vaccination rates for HPV during well-child visits were estimated and compared with Tdap and MCV4 for 11-12 year old females. Females who got the first dose of HPV vaccine during well-child visits were followed for two years to estimate HPV vaccine series completion rates. Descriptive and multivariate analyses were used in assessing the study's objectives.

Results. Well-child visits among 11-12 year old females were the highest (55.7% in 2012) and among ages 18-21 were the lowest (24.5%) ($p < 0.0001$). As compared to 11-12 year olds, ages 13-15 were 24% less likely to come in for a well-child visit ($p < 0.0001$). HPV vaccination rates during a well-child visit were similar in the 11-12 and 13-15 year age groups (19.0% and 21.1% in 2012). In 2012, HPV vaccination rates (19.0%) in 11-12 year old females during well-child visits were significantly lower than Tdap (33.7%) and MCV4 (32.0%) ($p < 0.0001$). HPV vaccine three-dose series completion rates during a 2-year follow-up were 59.0% in 11-12 year old females and 49.1% in ages 13-15 for those who initiated the first dose during a well-child visit in 2010.

Conclusion. As determined from this claims analysis, 11-12 year old females are more likely to come in for a well-child visit and more likely to complete the HPV vaccine series compared to other age groups. Our analyses suggest that well-child visits at 11-12 years of age provide the best opportunity to maximize the potential of the HPV vaccination program in the US.

Disclosures. **D. Zhang**, Merck: Employee, Salary **N. N. Borse**, Merck: Consultant, Consulting fee **A. S. Kulkarni**, Merck: Employee, Salary **L. Niccolai**, Merck: Collaborator, Research Contractor and Scientific Advisor, Consulting fee

1052. Antibody and Cellular Immune Responses to 2011-2012 Seasonal Inactivated Influenza Vaccine in HIV-Infected and Uninfected Children and Young Adults

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Background. HIV infection is associated with lower antibody responses to influenza vaccines. We compared antibody and cellular responses between HIV-infected and uninfected children and young adults to the 2011-2012 seasonal inactivated influenza vaccine (IIV3).

Methods. 11 HIV-infected subjects and 7 controls received one dose of 2011-2012 IIV3. Plasma and cells were frozen pre-vaccination (T1) and 2-4 weeks post-vaccination (T2). At each timepoint, hemagglutination inhibition (HAI) was done for all 3 vaccine strains; antibody avidity (AI), B-cell memory (IgG ELISPOT), T cell response (IFNγ and IL-2 ELISPOT) for pH1N1; and B- and T-cell phenotypes (flow cytometry). All subjects were surveyed on vaccination history during the 2010-2011 season and whether they were vaccinated prior to the 2010-2011 season.

Results. Average CD4 count of HIV-infected was 555 (median 590), and 9/11 (82%) were on cART. There was no significant difference between the cohorts in HAI at either timepoint, or in rates of seroprotection/seroconversion for any viruses. Individuals in both cohorts who had not been vaccinated in prior years had a higher fold-raise (FR) in HAI to pH1N1 but not to H3 or B viruses ($p = 0.008$). The median AI for pH1N1 was higher at baseline for HIV-infected vs controls, 0.32 and 0.19 ($p = 0.003$) respectively. The AI was not different at T2 nor was the change from T1 to T2. T cell ELISPOT results were similar between cohorts. IgG ELISPOT in HIV-infected vs controls showed no difference in numbers at T1 (4.5 vs 4, p = NS); a trend difference at T2 (6.8 vs 23.5, $p = 0.07$); and significant differences in the absolute change and FR from T1 to T2 (2 vs 18.5, $p = 0.04$; 0.9 vs 5.22, $p = 0.04$). History of prior influenza vaccine was associated with a significant difference in IgG ELISPOT FR (2.44 for vaccinated vs 0 for unvaccinated, $p = 0.05$) for HIV-infected, but not for controls (2.5 vaccinated vs 15.3 unvaccinated, p = NS). Flow cytometry revealed higher percent of tissue-like (7.8% vs 4.1%, $p = 0.03$) and immature (25.6% vs 8.9%, $p = 0.02$) B cells in HIV-infected vs controls at baseline.

Conclusion. Despite high cART uptake and high CD4 count, the HIV-infected cohort showed significantly lower memory B cell responses compared with controls. A history of influenza vaccine was advantageous to HIV-infected but not controls in developing a B cell IgG response.

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1053. Low Uptake of Influenza Vaccine Among University Students: Evaluating Predictors Beyond Cost and Safety Concerns

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Background. Annual influenza vaccine coverage for young adults (including college students) remains low, despite a 2010 recommendation for annual immunization of all people 6 months and older. College students are at high risk for influenza morbidity given close living and social spaces and extended travel during semester breaks when influenza circulation typically increases. We sought to evaluate influenza vaccine uptake following an on-campus vaccine campaign (using on-campus informational tables to direct students to the University Health Center for vaccination) at a large, public New York State university.

Methods. Consecutive students presenting at the University Health Center were recruited for a self-administered, anonymous, written survey. Students were asked about recent influenza vaccination, barriers to influenza vaccination, and willingness to get vaccinated to prevent the spread of influenza to vulnerable individuals around them. Frequencies and proportions were evaluated.

Results. Of 653 students approached, 600 completed surveys (92% response rate); respondents were primarily female (61%) and non-Hispanic white (59%). Influenza vaccine coverage was low (28%). Compared to coverage among non-Hispanic white students (30%), coverage was similar among Hispanic (30%) and other race/ethnicity students (28%) and lowest among non-Hispanic black students (17%). The most commonly selected vaccination barriers were "Too lazy to get the vaccine" (32% of unvaccinated) and "Don't need the vaccine because I'm healthy" (29%); cost was cited as a barrier by 6% of unvaccinated students. After being informed that vaccinating healthy people can protect other vulnerable individuals (e.g., infants, elderly), 77% of unvaccinated students indicate this would increase their willingness to get vaccinated.

Conclusion. Influenza vaccine coverage among college students is very low. While making vaccine easily obtained may increase vaccine uptake, college students need to be motivated to get vaccinated. Students may not perceive a need for influenza vaccine, as they are typically healthy; education about vaccinating healthy individuals to prevent the spread of influenza to other vulnerable individuals may provide this motivation to get vaccinated.

Disclosures. **All authors:** No reported disclosures.

1054. Immunogenicity And Safety of Quadrivalent Influenza Vaccine Administered Intradermally (ID) in Adults 18 through 64 Years of Age

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Background. The investigational ID Quadrivalent Inactivated Influenza vaccine (IIV4-ID) was developed from licensed split-virion trivalent influenza vaccine (IIV3-ID1, Fluzone® Intradermal) by adding a second B strain hemagglutinin (HA) antigen of the alternate B lineage (Victoria). A Phase III study was conducted during the 2012-13 influenza season to show that the addition of a second B strain does not interfere with the immune response to the other vaccine HA components or alter the safety profile.

Methods. The vaccines were administered ID at 9 µg HA per virus strain to adults 18-64 years old using the BD Soluvia™ microinjection system. IIV3-ID1 contained the 2012-13 year B Yamagata lineage strain and IIV3-ID2 contained the alternate B Victoria lineage. Hemagglutination inhibition (HAI) antibody titers were measured in 2/3 of pre- and 28 day post vaccination paired sera. Injection-site and systemic reactions, and adverse events (AEs) were recorded.

Results. 1,676 subjects received IIV4-ID, 837 the licensed IIV3-ID1 and 847 the investigational IIV3-ID2. IIV4-ID induced robust immune responses in terms of geometric mean HAI titers (GMTs), seroconversion rates (SCRs; 4-fold rise in HAI titer pre- to post vaccination) and seroprotection rates (HAI titer ≥ 1:40) for all 4 virus strains. The immune response to IIV4-ID was statistically non-inferior for the 4 virus strains assessed by GMT ratios (GMTRs) and SCRs vs the control IIV3-ID vaccines. GMTRs and SCRs to both B strains in IIV4-ID were statistically superior to the IIV3-ID without the corresponding B strain. IIV4-ID had a safety profile similar to the two IIV-3ID groups. The most commonly reported solicited reactions were pain, pruritus, myalgia, headache, and malaise, and most were mild or moderate, occurring within 3 days of vaccination. IIV4-ID was statistically non-inferior to the two IIV3-ID vaccines in terms of rates of at least one grade 2 or 3 systemic reaction.

Conclusion. IIV4-ID was well-tolerated without safety concerns. Antibody responses to B strains in the IIV4-ID were superior to IIV3-ID containing the alternate strain and non-inferior for the A and matched B strains. By avoiding vaccine B strain mismatch to the circulating strain, IIV4-ID could improve vaccine efficacy.

Disclosures. **G. J. Gorse**, Sanofi Pasteur: Investigator and Spouse is shareholder, Reimbursable travel expenses **A. Falsey**, Regeneron: Consultant, Consulting fee; Hologic: Consultant, Consulting fee; Sanofi Pasteur: Research Contractor, Research grant; AstraZeneca: Research Contractor, Research grant; ADMA Biologic Inc.: Research Contractor, Research grant **V. Landolfi**, Sanofi Pasteur: Employee, Salary **A. Ozol-Godfrey**, Sanofi Pasteur: Employee and Shareholder, Salary **P. Tsang**, Sanofi Pasteur: Employee, Salary

1055. Antibody Response to Intradermal and High Dose Influenza Vaccine in 2012-13 Among Adults Who Did and Did Not Respond to Standard Dose Vaccine in 2011-12

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Background. We compared antibody responses to influenza vaccine in adults ≥50 years old in two consecutive seasons. In 2011-12, all participants received trivalent inactivated influenza vaccine (IIV3). In 2012-13, those age 50-64 received intradermal (ID) and those age ≥65 received high-dose vaccine (HD). In 2012-13, the WHO-recommended vaccine strains were modified for H3N2 and B.

Methods. Participants were recruited in 2011 and vaccinated in the fall of 2011 and 2012. In both years, pre- and post (21-28 days)-vaccination sera were tested for antibody response to vaccine [measured by hemagglutination inhibition (HI) titer]. We compared geometric mean titers (GMT) and titer fold rise from pre- to post-vaccination in 2012, among 2011-12 responders (≥4-fold rise in HI titer from pre-to post-vaccination) and 2011-12 non-responders (<4-fold rise in HI titer) to the corresponding vaccine strain.

Results. 183 adults received IIV3 in 2011 and either HD (N = 82) or ID (N = 101) in 2012. For the 2011-12 vaccine, 56 (31%) responded to the H1N1 strain, 68 (37%) responded to H3N2, and 28 (15%) responded to B. Among HD recipients, post-vaccination GMT for H3N2 was higher among 2011-12 responders vs non-responders (p = 0.04). Fold rise did not differ significantly for any vaccine strains between responders vs non-responders.

		HD recipients		ID recipients	
		2011-12		2011-12	
Strain	2012-13 Response	Non-responders	2011-12 Responders	Non-responders	2011-12 Responders
H1N1	Post-vaccination GMT (IQR)	93 (57, 160)	128 (80, 320)	78 (40, 226)	105 (40, 160)
	Median fold rise (IQR)	4 (2, 8)	4 (1, 8)	2 (1, 4)	2 (2, 4)
H3N2	Post-vaccination GMT (IQR)	154 (80, 320)*	242 (160, 452)	120 (57, 320)	118 (40, 226)
	Median fold rise (IQR)	4 (2, 8)	4 (2, 11)	2 (1, 4)	2 (1, 8)
B	Post-vaccination GMT (IQR)	185 (80, 320)	180 (80, 320)	137 (80, 320)	163 (80, 320)
	Median fold rise (IQR)	3 (1, 8)	2 (2, 11)	2 (1, 6)	3 (1, 16)

* p < 0.05 for comparison of 2011-12 responders and non-responders.

Conclusion. Prior response to 2011-12 vaccine antigen was not associated with response to the new H3N2 or B antigens in 2012-13, nor was it associated with response to the H1N1 antigen used in both the 2011-12 and 2012-13 vaccines.

Disclosures. **M. Sundaram**, MedImmune, LLC: Project scientist on funded grant, Research grant; **H. Mclean**, MedImmune, LLC: Grant Investigator, Research grant **R. K. Zimmerman**, Sanofi: Grant Investigator, Research grant; Pfizer: Grant Investigator, Research grant **M. P. Nowalk**, Sanofi: Grant Investigator, Research support; Pfizer: Grant Investigator, Research support; Merck: Grant Investigator, Research support; MedImmune: Consultant, Consulting fee **C. J. Lin**, MedImmune, LLC: Consultant, Consulting fee Sanofi Pasteur: Grant Investigator, Research grant; Merck: Grant Investigator, Research grant **E. Belongia**, MedImmune, LLC: Grant Investigator, Research grant

1056. Factors Associated with Pre-season Seroprotection to B Lineage Influenza Viruses in Children

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Background. Few studies have examined the duration of immune response against B lineage influenza viruses in relation to prior vaccination and/or influenza infection. We examined factors associated with seroprotective antibody titers in fall 2013 among children 5-17 years old with known influenza vaccination and infection status from the previous season.

Methods. Serum was drawn from 163 children prior to 2013-14 influenza vaccination, including 53 (33%) with PCR-confirmed B lineage infection in 2012-13, 91 (56%) who received the 2012-13 vaccine (Yamagata lineage) and 21 (13%) who were both vaccinated and infected. Antibody titers were measured by hemagglutination-inhibition (HI) assays for both influenza B lineage strains licensed for use in the 2013-14 vaccines. The association between seroprotective titer (≥1:40) and prior vaccine exposure or infection was examined in a modified Poisson regression model. Potential predictors included age, prior vaccine receipt, number of lineage specific vaccines received in the past 5 seasons, and lineage specific B infection in the prior season. Titers were analyzed separately for B/Yamagata and B/Victoria.

Results. Of 163 children, 96 (59%) had seroprotective titers for B/Victoria, 106 (65%) had seroprotective titers for B/Yamagata, and 73 (45%) had seroprotective titers for both viruses; 22 (13%) had been infected with B/Yamagata and 31 (19%) with B/Victoria in 2012-13. Vaccination in the 2012-13 season and ≥1 dose of B/Yamagata containing vaccine in the past 5 seasons were significantly associated with seroprotective titers for B/Yamagata in univariate analyses; prior infection was not significant. In the multivariate model, only 2012-13 vaccine receipt was significantly associated with a seroprotective titer for B/Yamagata (RR 1.5, 95%CI 1.2-1.9). A seroprotective titer for B/Victoria was independently associated with receipt of 2012-13 vaccine (RR 1.4, 95%CI 1.1-1.8) and with B/Victoria infection the 2012-13 season (RR 1.4, 95%CI 1.1-1.8) in the multivariate analysis.

Conclusion. Prior vaccine receipt is an important determinant of seroprotective titers for both B lineages in children. Prior receipt of B/Yamagata vaccine was associated with heterologous titers to B/Victoria.

Disclosures. **H. Mclean**, MedImmune, LLC: Grant Investigator, Research grant **M. Sundaram**, MedImmune, LLC: Project scientist on funded grant, Research grant **E. Belongia**, MedImmune, LLC: Grant Investigator, Research grant

1057. Factors Associated with Influenza A (H1N1)pdm09 (pH1N1) Vaccine Failure among Children Aged 5-17 Years

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Background. Immunologic factors associated with influenza vaccine failure in children are not well understood. In 2013-14, we prospectively followed a cohort of vaccinated children 5-17 years old and examined factors associated with pH1N1 infection.

Methods. We recruited children who were enrolled in a study of influenza vaccine effectiveness during the prior 2012-13 season; all had medically attended acute respiratory illness, were tested for influenza, and had known vaccination history. Participants received one dose of 2013-14 vaccine, either inactivated influenza vaccine (IIV3) or quadrivalent live attenuated influenza vaccine (LAIV4), based on preference. Hemagglutination-inhibition (HI) titers against pH1N1 were measured pre- and 21 days post-vaccination. Seroprotection was defined as HI titer ≥1:40. Children <9 years were classified as partially vaccinated if they had received no prior dose of a vaccine containing pH1N1. Active surveillance was performed for acute respiratory illness; nasal and throat swabs from ill children were tested by RT-PCR. Cases were children with pH1N1 infection (vaccine failures); all other children served as controls. Logistic regression was used to assess factors associated with vaccine failure.

Results. During 2013-14, among 162 vaccinated children, 11 (7%) were pH1N1 cases. Eight (73%) cases and 54 (36%) controls had received 2013-14 LAIV4 ($p = 0.02$). Postvaccination HI titers against pH1N1 were <1:40 in 10 (91%) cases and 34 (23%) controls ($p < 0.001$). Compared to children 9-17 years, risk of vaccine failure was higher in children 5-8 years with no prior pH1N1 vaccination (OR 74; 95% CI 7.7, 720), and in children 5-8 years with ≥1 prior pH1N1 vaccinations (OR 5.9; 95% CI 1.2, 31). There were no differences between vaccine failures and controls by sex, high risk condition, history of influenza infection in 2012-13, or age at first influenza vaccination.

Conclusion. Vaccine failure in children was associated with receipt of LAIV4, low postvaccination HI titer, and younger age. The risk was highest among children 5-8 years old who had not been previously vaccinated. Larger studies in children are needed to better understand risk of vaccine failure.

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1058. Frequency and Predictors of Refusal of Seasonal Influenza Vaccination among Patients at a Large Tertiary Referral Hospital

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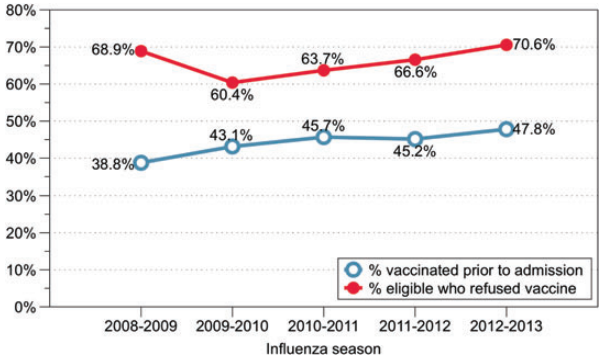
Background. Seasonal influenza vaccination rates in the US are far below desired levels. Vaccination of hospitalized patients is considered an underutilized opportunity to increase vaccination rates. Our objective was to evaluate rates of influenza vaccination at admission and vaccination refusal for eligible patients, and to identify factors associated with refusal, at a large tertiary referral hospital in Baltimore, MD.

Methods. We obtained electronic medical record data for all patients ≥ 18 years admitted during 5 influenza seasons (October 1 to March 31, 2008 to 2013). Only the first admission per season per patient was included. We described vaccination and refusal rates by season, and identified factors associated with refusing the vaccine using multivariable logistic regression.

Results. There were 52,141 first admissions assessed for vaccination status over 5 influenza seasons. Self-reported influenza vaccination prior to admission ranged from 39% in 2008–2009 to 48% in 2012–2013 (Figure 1).

Of the 29,113 unvaccinated patients, 3% (n = 742) had contraindications. Of 28,371 vaccine-eligible patients, refusal rates ranged from 60% in 2009–2010 to 71% in 2012–2013 (Figure 1). Reasons for refusal included "believes not at risk" (50%; n = 9,243), "wants further advice" (16%; n = 2,950), and "fear of adverse events" (13%; n = 2,416), and "other" (22%; n = 4,102). Distributions of refusal reasons were similar for individual influenza seasons.

After controlling for influenza season, female sex, being currently employed, and English as a primary language were associated with higher odds of refusing vaccine. Current smoking and admission to an ICU were associated with lower odds of refusing vaccine.



Self-reported seasonal influenza vaccination prior to first hospital admission and refusal rates of seasonal influenza vaccine among eligible patients in a given influenza season.

Conclusion. Influenza vaccination rates prior to admission were similar to those of the general adult US population. During the past 5 influenza seasons, nearly two-thirds of vaccine-eligible inpatients refused the vaccine. A number of factors were found to be associated with refusal and may help develop focused interventions to decrease influenza vaccine refusal among inpatients.

Disclosures. **All authors:** No reported disclosures.

1059. Expanded immunogenicity of high-dose inactivated influenza vaccine compared to standard-dose inactivated influenza vaccine in older adults

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Background. Previous studies have demonstrated the superior immunogenicity of high-dose inactivated influenza vaccine (IIV-HD) in older adults compared to standard-dose inactivated influenza vaccine (IIV-SD), as measured by hemagglutination inhibition (HAI) antibody titers against egg-propagated vaccine antigens. The 2012-2013 northern hemisphere influenza season was characterized by high H3N2 activity and by mismatch between predominant circulating strains and egg-propagated vaccines. There is growing interest in evaluating influenza vaccine immune responses beyond the traditional HAI assay.

Methods. Samples collected as part of a randomized controlled trial (NCT01427309, sponsored by Sanofi Pasteur) evaluating the efficacy of IIV-HD vs IIV-SD in adults ≥65 years were available for testing; one third of trial participants provided post-vaccination sera. This sub-study utilized a case-cohort design, in which 675 representative samples collected during the 2012-2013 season of the study (from individuals who either developed polymerase chain reaction/culture confirmed H3N2 influenza illness [N = 123] or belonged to a random subset of 10% of non-cases [N = 552]) were selected for expanded testing. Expanded immunogenicity was assessed with an HAI assay using an MDCK cell-propagated A/Victoria/361 (H3N2) antigen, a viral neutralization assay (NT) using both egg- and cell-propagated A/Victoria/361 (H3N2) antigens, and an enzyme-linked lectin assay (ELLA) for anti-neuraminidase (N2) antibodies. Geometric mean titers (GMT) were estimated for IIV-HD and IIV-SD recipients using weighted averages and were compared as GMT ratios (IIV-HD/IIV-SD).

Results. Samples from 318 IIV-HD and 357 IIV-SD recipients were assayed. The GMT ratios (and 95% Confidence Intervals) were 1.48 (1.26; 1.73), 1.53 (1.29; 1.82), 1.75 (1.43; 2.15), and 1.42 (1.23; 1.65) for cell-propagated HAI, egg-propagated NT, cell-propagated NT, and N2-ELLA, respectively. The GMT ratio for the full immunogenicity subset (2879 IIV-HD and 2872 IIV-SD recipients) assessed by HAI assay using egg-propagated A/Victoria/361 was 1.82 (1.71; 1.94).

Conclusion. IIV-HD is associated with significantly improved immunogenicity compared to IIV-SD in older adults as assessed using a range of different assays.

Disclosures. **C. Diazgranados**, Sanofi Pasteur: Employee, Salary **B. Hu**, Sanofi Pasteur: Employee, Salary **T. Voloshen**, Sanofi Pasteur: Employee, Salary **A. J. Dunning**, Sanofi Pasteur: Employee, Salary **H. K. Talbot**, Sanofi Pasteur: Research Contractor, Research support; MedImmune: Research Contractor, Research support; Teva: Scientific Advisor, Consulting fee **V. Landolfi**, Sanofi Pasteur: Employee, Salary

1060. The Effect of Live Attenuated Influenza Vaccine (LAIV) on Bacterial Colonization in Healthy 2-4 Year Old Children. A Randomised Controlled Study

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Background. Common childhood respiratory virus infection may cause increased rates or density of nasopharyngeal (NP) carriage of bacteria such as *S.pneumoniae* (Sp), *M.catarrhalis* (Mc), *H.influenzae* (Hi) or *S.aureus* (Sa), possibly leading to changes in colonization dynamics and transmission rates to new hosts. We used LAIV, an effective vaccine against influenza which causes mild symptoms of URTI to test this hypothesis.

Methods. 151 2-4 year old children were recruited and randomized to receive LAIV either at the start of the study (2 doses 4 weeks apart) or a month later allowing comparison between vaccinated and unvaccinated children. NP swabs were taken at baseline (0) and at 7, and 28 days. Bacterial carriage and density was determined by qPCR using *LytA* for Sp, *ompJ* for Mc, *hdp* for Hi and *sodC* for Sa using <35 cycles (CT) as a threshold of detection. Standard curves were generated against broth cultures to convert CT values to colony forming units (CFU/ml). Bacterial carriage rates and densities (summarised as area under the curve) were compared in the 2 groups using unpaired t-tests. A logistic regression model was used to analyze the relationship between age and bacterial load.

Results. Bacterial carriage rates (Sp 67%, Hi 58%, Mc 77%, and Sa 11%) were higher (except Sa which was lower) with increasing age. The same trends were observed for density (all $p < 0.025$). No significant differences were detected comparing carriage rates in vaccinated and unvaccinated children over 28 days. However, vaccinated children had highly significantly greater total bacterial densities observed over the 28 days for all 4 species when compared with controls, (all $p < 0.01$).

Conclusion. In this randomised controlled trial of young healthy children with high bacterial carriage rates, using qPCR to measure the presence and density of bacteria, we found that age is inversely related to bacterial density, which is a novel finding. High bacterial load may be important for transmission of bacteria between hosts and we found that LAIV seems temporarily to increase the density of the bacteria studied in the first month after vaccination in the absence of any known clinically significant safety signal. Further studies may reveal more marked or clinically important effects of wild-type respiratory viral infections.

Disclosures. **All authors:** No reported disclosures.

1061. The Role of CD4 T Cell Mediated Immunity in Pandemic Influenza Protection

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Background. Vaccination against pandemic influenza poses significant challenges as the viral strain that will be responsible for the next influenza pandemic is unpredictable. Given the time lag between initiation of a pandemic and significant vaccine production, a pandemic vaccine will rarely be available until after significant viral circulation has occurred. One possible strategy to circumvent this limitation is to prime individuals against potentially pandemic strains before a pandemic strikes.

Methods. To further investigate the role of influenza-specific CD4 T cells after immunization with a drifted H5 influenza vaccine, subjects previously enrolled in a trial of an inactivated A/Vietnam/1203/2004 H5 vaccine and previously naïve subjects were immunized with an inactivated subunit A/Indonesia/5/05 H5 vaccine. Neutralizing antibody responses were measured by microneutralization assay and CD4 T cell responses were measured using IFN gamma Elispot assays following ex-vivo stimulation with pools of peptides representing distinct influenza proteins.

Results. In previously primed individuals, neutralizing antibody responses were greatly accelerated. While vaccination induced detectable CD4 T cells specific for hemagglutinin (HA) and the internal viral proteins in both groups, previously primed individuals had greater HA-specific CD4 T cells at the pre-vaccination timepoint and mounted a more robust CD4 T cell response to HA-specific peptide epitopes at day 14 post vaccination. There were no differences between vaccination groups when CD4 T cell responses to the much more conserved NP protein were examined. Interestingly, neutralizing antibody responses were significantly higher in individuals able to mount a CD4 T cell response to the HA but not the NP protein.

Conclusion. These findings suggest that prepandemic vaccination promotes a broadly cross-reactive and rapid response on challenge with a closely related virus that may be in part attributable to recruitment of an enriched population of HA-specific CD4 T cells. Prepandemic vaccination strategies that include priming of HA-specific CD4 T cells may help to induce broad protection against diverse, potentially pandemic strains of influenza.

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1062. Compassionate Use of Intravenous (IV) Zanamivir During the 2013-2014 Influenza Season: Case Series of Three Patients

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Background. No IV antiviral agents for the treatment of severe influenza are currently approved in the U.S. Since 2009, IV zanamivir has been authorized for compassionate use through an Emergency Investigational New Drug (EIND) application to the Food and Drug Administration (FDA) as an investigational treatment for patients with serious influenza infection. We report the compassionate use of IV zanamivir in 3 patients at Cedars-Sinai Medical Center during the 2013-2014 influenza season.

Methods. Use of IV zanamivir was approved by the institution's investigational review board and an EIND was granted by the FDA for each patient. We performed a descriptive analysis of demographics, vaccination status, baseline co-morbidities, virologic test results, other antiviral treatments, supportive care modalities, treatment duration, adverse events and 30 day-outcome.

Results. The decision to start IV zanamivir and the duration of therapy depended on the clinical judgment of the treating physician. IV zanamivir was initiated after a lack of clinical improvement from oseltamivir use. At the time of EIND request, all three patients were in the intensive care unit with respiratory failure and acute respiratory distress syndrome. All patients received a 5 day course of IV zanamivir. No medication related adverse events were identified. Please see the table for further details.

	Patient 1	Patient 2	Patient 3
Age (years)	63	34	29
Gender	Female	Female	Male
Vaccination status	Unknown	Not vaccinated	Unknown
Co-morbidities	Hypertension, smoking	None	Morbidly obese
Influenza strain	A, not typed	2009 H1N1	A, not typed
Duration (days) of influenza symptoms prior to starting oseltamivir	5	7	2
Duration (days) of oseltamivir prior to starting zanamivir	9	5	13
Supportive care	ECMO	Mechanical ventilation	ECMO
Superimposed bacterial pneumonia	MSSA	None	MSSA, *Streptococcus pneumoniae*
30-day Outcome	Death	Survived	Survived

Key: MSSA (Methicillin susceptible *Staphylococcus aureus*), ECMO (extracorporeal membrane oxygenation)

Conclusion. In addition to efficacy and activity against oseltamivir resistant strains, IV zanamivir offers an important alternative route of administration in critically ill patients with severe influenza.

Disclosures. **All authors:** No reported disclosures.

1063. Estimating Health Outcomes of Antiviral Use in Influenza (flu) Outbreaks by Linking PK/PD and Epidemiology via Transmission Dynamic Model: A Novel Approach

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Background. Whilst the potential for pharmacokinetic/pharmacodynamic (PK/PD) optimisation of anti-influenza therapy to improve individual patient outcomes has been published, the indirect benefits of reducing disease transmission has not been described. We explored the latter using a novel approach to link oseltamivir (OS) PK/PD to epidemiological models of influenza (flu) transmission. With this linked PK/PD-Epi model, we examined the impact of high and low doses of OS on flu attack rates (AR) under different levels of infectiousness and percentages of patients receiving OS.

Methods. OS active metabolite (OC) AUC distributions were simulated for 75 and 150mg po BID via a published population PK model. In the model, flu viral shedding duration (T_{shed}) is impacted by OC exposure according to published PK/PD breakpoints. The effect of treatment with OS on T_{shed} was linked to an SEIR (Susceptible, Exposed, Infected, Recovered) compartmental model incorporating OS treatment. Using Monte Carlo simulation (including sampling relevant OC AUC and T_{shed} distributions), populations of 100,000 were simulated over one flu season. One thousand flu seasons were then simulated for scenarios including OS 75mg and 150mg bid assuming treatment of 25, 50, and 80% of the infected population, for viruses of low and high infectiousness.

Results. The AR/1,000 patients infected generated from the model by OS dose, percentage of patients receiving treatment, and infectiousness are shown in the table.

The proportion of simulated Flu seasons that had AR >5% tended to be lower as the percentage of patients receiving treatment and/or dose was increased.

Infectiousness	Percentage of patients receiving OS	75mg bid	150mg bid
High (Reference AR 675)	25%	593.29	530.32
	50%	413.31	317
	80%	209.41	128.81
Low (Reference AR 371)	25%	51.33	32.55
	50%	10.6	4.81
	80%	4.67	0.85

Conclusion. This is the first study utilising PK/PD modelling to inform a compartmental epidemiological model to estimate the potential impact of OS dose on influenza infection rates. The novel approach suggests that antiviral PK/PD optimised treatment may have direct and indirect benefits reducing societal burden of flu, including containment strategies. Linking PK/PD and epidemiological models may have utility for other antivirals and for other infections.

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1064. Influenza Infection in the Department of Veterans Affairs (VA): 2013-2014

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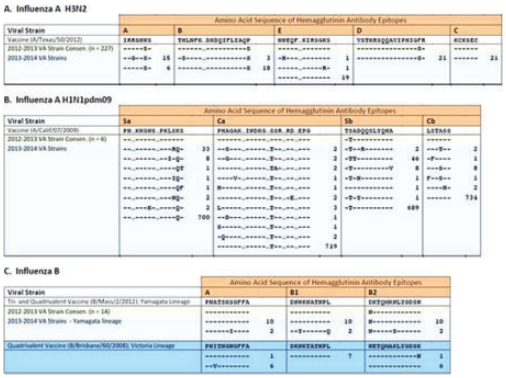
Background. Influenza is associated with significant annual morbidity and mortality and VA's large elderly population is at risk. We conduct ongoing surveillance and herein describe 2013-2014 national influenza activity in VA.

Methods. Percent influenza-like illness (ILI); influenza hospitalizations; telephone triage calls; and laboratory testing and positive results from September 29, 2013-May 3, 2014 were obtained using VA Healthcare Associated Infection and Influenza Surveillance System and Corporate Data Warehouse, and compared to 2 previous seasons. Influenza vaccinations were captured starting August 1, 2013. A convenience sample of positive nasopharyngeal specimens from 23 VA facilities underwent hemagglutinin (HA) and neuraminidase (NA) gene sequencing. HA sequences were compared to 2013-2014 vaccine strains.

Results. ILI ranged from 1.2-3.7% throughout the season. Surveillance measures are reported in the table. Over 1.9 million vaccinations were recorded, representing 30% of patients treated in Fiscal Year 2013 which was similar to the previous season. For 2013-2014 season, 1,037 were tested with 888 being typed/subtyped for H1N1 (835 [94%]), H3N2 (30[3%]), and B (25[3%]) strains. Of 823 strains tested for NA inhibitor (NAI) resistance, 7 H1N1 strains had oseltamivir resistance (3 H275Y, 3 S247N, and 1 I222K). Compared to vaccine strains, amino acid changes were found in HA gene epitopes among all 831 strains (Figure 1).

Selected VA Influenza Surveillance Metrics

	2011-2012	2012-2013	2013-2014
Influenza-coded hospitalizations Patients aged ≥65	373 192 (51%)	2,136 1,352 (63%)	2,091 924 (44%)
Influenza-coded telephone calls	4,907	7,022	5,931
Influenza tests performed	9,953	27,972	35,875
Influenza positive	701 (7%)	4,879 (17%)	5,700 (16%)
Influenza A	644 (92%)	3,677 (75%)	4,862 (85%)
Influenza B	52 (7%)	1,159 (24%)	790 (14%)
Both A & B or type not specified	5 (1%)	43 (1%)	48 (1%)



Variability in Influenza HA Epitopes

Conclusion. The 2013-2014 influenza season was similar in resource utilization compared to 2012-2013 season. A lower percentage of patients over 65 years old were hospitalized with influenza this season. Strain characterization demonstrated little NAI resistance and heterogeneity of HA epitopes compared to vaccine strains.

Disclosures. **All authors:** No reported disclosures.

1065. Surveillance and Vaccine Effectiveness Results from the Department of Defense (DoD) Global, Laboratory-Based, Influenza Surveillance Program

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Background. Influenza has the potential to cause high morbidity rates and undermine the readiness of the military population. Military members and their families are often stationed in areas where new strains are likely to appear and their high mobility across the world could result in the spread of a pandemic strain.

Methods. The DoD Influenza Surveillance Program is a year-round sentinel-based program where more than 80 pre-selected DoD sites worldwide are asked to submit 6-10 respiratory specimens per week from patients who meet an influenza-like illness case definition, along with a patient questionnaire, in order to document valuable epidemiologic data. A case-control method was used to calculate 2013-2014 mid-season influenza vaccine effectiveness (VE) estimating the effectiveness of the vaccine against currently circulating influenza strains.

Results. The program collected and tested 3,079 specimens from 1,283 service members, 1,573 dependents (spouses/children), and 223 retirees/other beneficiaries. 989 specimens were positive for influenza A and 58 specimens were positive for influenza B. The program also identified 1,124 other respiratory pathogens. Mid-season VE analyses found statistically significant VE among military dependents/retirees for overall vaccine type (66% [50.91, 76.19]) and inactivated influenza vaccine type (73% [59.59, 82.73]) analyses. A service members' only analysis did not demonstrate significant VE among overall or vaccine specific analyses.

Conclusion. With more than 80 sentinel sites across the world submitting specimens, the DoD Influenza Surveillance Program has the ability to identify strains that are currently circulating and track the genetic changes of strains through molecular sequence analysis. The program demonstrated moderate VE against medically-attended influenza among the dependent/retiree population. The same could not be demonstrated among the service member population; there is no single clear reason for this and this finding does deserve further scrutiny.

Disclosures. **All authors:** No reported disclosures.

1066. Delay in the Norwegian Immunisation Programme

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Background. In Norway vaccination coverage at age 2 years is ≥ 93 % on national and ≥ 85% on subnational level based on a universal immunisation registry (SYSVAK), however this does not reflect the true proportion of children that is optimal protected at al times. Delayed primary series increase risk of pertussis, pneumococci and measles in early childhood. The Norwegian vaccination schedule says diphteria, tetanus, pertussis, polio, Hib, pneumococcal at 3,5 (primary series) and 12 months except for measles, mumps and rubella (MMR vaccine) at 15 months. Bacille de Calmette Guérin (BCG) and hepatitis B vaccines are offered to risk groups.The aim was to assess monitoring of annual vaccination delay the first 24 months of life.

Methods. We analysed SYSVAK data, age < 2 years, born in 2010 from May 23rd 2013. 63382 children aged <2 were resident in the national population registry. Delay counting started from the day the child was due + 1 month.

Results. Delay was present in 28336 of 63382 (44.7%) children aged < 2 years. Number of days delayed was 139 (mean). 17 % were delayed for the primary pertussis series. Children delayed for pertussis, first dose, were more likely to be delayed for measles, first dose (2881 of 4070 (70.8%) vs 15611 of 59312 (26.3%) RR(95%CI) 2.69 (2.63,2.75). Vaccinated children who according to month of birth were scheduled for vaccines in July (summer) were more frequently delayed than vaccinated children who according to month of birth were scheduled to vaccines in other months (first dose pertussis vaccine 323 of 5117 (6.3%) vs 2068 of 56586 (3.7%) RR (95% CI) 1.73(1.54, 1.94); first dose measles vaccine 1867 of 4901 (38.1%) vs 12313 of 54169 (22.7%), RR (95% CI) 1.68 (1.61, 1.74)). BCG vaccinated (17%) were more delayed for the complete series than non BCG vaccinated children (5638 of 10773 (52.3%) vs 21205 of 51116 (41.5%) RR (95 % CI) 1.26 (1.24, 1.29).On county level, 62.6- 42.2% were not delayed (median delay, range 23-42 days). The two counties (Vestfold 44.2% delay for measles; Troms 33.4% delay for pertussis 2nd dose) with the lowest proportion of children immunised on time had vaccination coverage for the complete series on natiional level at age 2 years.

Conclusion. Delay was common and was dependent on geography, season and BCG vaccine status. Annual monitoring would increases programme surveillance and is a tool to enhance improvements.

Disclosures. **All authors:** No reported disclosures.

1067. Multi-Attribute Ranking Tool for Vaccines: Strategic Priority Setting to Support Vaccine Development

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Background. Various factors influence vaccine development efforts. Historically, single criterion valuation with life years saved or cost-effectiveness have been used to obtain static lists of vaccine development priorities. We discuss an ongoing effort at the Institute of Medicine focused on the development and refinement of a dynamic, user-informed software tool called SMART Vaccines that could potentially be applied in a range of decision scenarios.

Methods. Using axiomatic principles of multi-criteria decision making (specifically, multi-attribute utility theory), SMART Vaccines includes 28 attributes in eight broad categories (e.g., health, economic, demographic, policy, scientific and business) and allows additional user-defined attributes. The multi-attribute utility model was implemented and tested in MATLAB. A population process model simulates demographic changes, with necessary data and proxies obtained from a number of sources (including World Health Organization and the Global Burden of Diseases). Preferential weights applied by users on the attributes determine the final rank order of the vaccine candidates.

Results. Output results—SMART Scores—combine computed values and user weighted entries, making the scores meaningful only to the users of the software. We evaluated ten vaccine candidates for hypothetical development in the United States and South Africa, and are pursuing use case analyses in collaboration with public and private vaccine decision makers to determine the software efficacy, and its usability across different scenarios. Built-in sensitivity analysis tools enable users to carry out a number of "what if" scenarios comparing specific health, demographic, economic and vaccine impacts to arrive at a decision independently or cooperatively with other users.

Conclusion. Test results, sensitivity analyses, and initial applications of SMART Vaccines indicate the need for a broad community driven effort to advance the software and data development efforts. Enhanced applications of the software are possible to help compare public health and other interventions beyond vaccines, and notably as an educational tool in academic public health courses.

Disclosures. **All authors:** No reported disclosures.

1068. Vaccine Coverage at Milestone Ages among Infants in the United States, 2009-2012

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Background. The coverage rate for rotavirus vaccine (RV) in the U.S., as assessed at 19 to 35 months of age, is lower than that for other vaccines, such as pneumococcal conjugate vaccine (PCV) and diphtheria, tetanus, and acellular pertussis vaccine (DTaP). RV differs from these other vaccines, however, in that administration at or beyond 8 months of age is not recommended. It is important to determine if the discrepancy in coverage rates arises during the first 6 months of life, when RV is being given along with DTaP and PCV, or if it arises after 8 months, when there is opportunity for catch-up dosing of DTaP and PCV but not for RV.

Methods. The MarketScan Commercial database was used to examine vaccination coverage for infants born between January 1, 2009 and May 31, 2012 and had at least 13 months of continuous enrollment in their respective health plans. Current Procedural Terminology (CPT) codes were used to identify vaccines administered as of milestone ages (3, 5, 7, 8, 10, and 13 months). Coverage was computed as the proportion of all infants eligible for vaccination according to the recommended schedule who had received the given vaccines. Coverage rates were stratified by variables such as gender and year of birth, among others.

Results. Of 392,160 eligible infants, coverage for the first dose at 3 months of age was 76%, 84% and 80% for RV, DTaP, and PCV respectively. At 7 months, coverage for the last dose of RV (dose 2 or 3, depending on product) and for 3 doses of DTaP and PCV, respectively, was 65%, 71% and 67%. At 13 months, the respective coverage rates were 69%, 81% and 82%. We observed an increase in coverage for each vaccine over the 4 study years, with the highest rate in 2012; in that year, coverage for all 3 vaccines was similar at 7 months of age, but differences were pronounced at 13 months of age (Table).

Vaccine	Vaccine Coverage in 2012				
	3 months	5 months	7 months	8 months	13 months
RV	80%	75%	69%	73%	73%
PCV	82%	76%	69%	75%	84%
DTaP	86%	80%	73%	78%	83%

Note: Vaccine coverage is 1 dose at 3 months, 2 doses at 5 months and 3 doses (2 or 3 doses of RV) at 7, 8 and 13 months

Conclusion. Coverage for RV is similar to DTaP and PCV at milestone ages of 3, 5, and 7 months. The observation of higher coverage rates for DTaP and PCV at 13 months of age is probably due to catch-up opportunities for these vaccines but not for RV.

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1069. Long-term effect of a Birth Vaccination Promotion Strategy

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Background. Infants' immunization coverage rates remain low, and below defined health objectives in Quebec, Canada. Delays in the first vaccinations at 2, 4 and 6 months have been associated with a higher probability for delay in age-appropriate vaccination during childhood. The aim of this study was to assess the long-term effectiveness of an information session targeting immunization that was performed during postpartum hospitalization on vaccination coverage in children.

Methods. A quasi-randomized controlled trial was conducted in the Sherbrooke University hospital nursery. Between March 1, 2010 and February 28, 2011, an individual educational information session regarding immunization of infants at 2, 4 and 6 months was proposed or not to parents according to date and time of birth. Based on the Quebec Immunization protocol a five-point standardized information plan on vaccination was elaborated. Motivational Interviewing using Miller and Rollnick's trans-theoretical model of Prochaska were used during the session. Immunization data were obtained through the Eastern Townships Public Health registry at 3, 5, 7, 13 and 24 months of age.

Results. Respectively, 1140 and 1249 families were included in the experimental and control groups. A significant increase in vaccination coverage was observed at three (91.3 vs 88.1%; +3.2%; p = 0,01), five (83.2 vs 78.3%; +4.9%; p = 0.003) and 7 months of age (75.9 vs 68.6%; +7.3%; p < 0.001). There is a persistent effect on vaccination coverage at 13 months (66.2 vs 60%; +6.2%; p < 0.001) and 24 months of age (79.5% vs 74.7%; +4.8%; p = 0.006).

Conclusion. An educational information session at birth about immunization, based on motivational interviewing and given during postpartum hospitalization improves vaccination coverage in infants at 2, 4 and 6 months of age, but also at 13 and 24 months. This Birth Vaccination Promotion strategy not only improves the first vaccinations, but also could enhance the entire childhood vaccinations schedule.

Disclosures. **All authors:** No reported disclosures.

1070. Validation of Febrile Seizures Identified in the Mini-Sentinel Post-Licensure Rapid Immunization Safety Monitoring (PRISM) System

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Background. The Mini-Sentinel system was established in response to the FDA Amendments Act to monitor the safety of FDA-regulated medical products. We evaluated the positive predictive value (PPV) of ICD9-based algorithms to identify post-vaccination febrile seizures (FS). We also describe an adaptation of Brighton Collaboration (BC) definition for seizures for use in medical record review.

Methods. We identified ICD9 diagnosis (dx) codes for fever and seizures in the emergency or inpatient setting after influenza, diphtheria tetanus acellular pertussis-containing, and 13-valent conjugate pneumococcal vaccines from July 1, 2010 to June 30, 2011. We estimated the PPV for FS. BC criteria for seizures included documentation of loss of consciousness (LOC, defined as witnessing sudden LOC or history of unconsciousness)

and generalized motor manifestations. Because medical record documentation may be insufficient for LOC, we included other consistent symptoms, including altered states of consciousness (ASC, e.g., documentation of eyes rolled back or unresponsiveness).

Results. Of 216 potential FS identified with ICD9 codes for seizures, 152 were chart-confirmed to have documentation of fever and seizure within 24 h or a clinician dx of FS (PPV = 0.70, 95% CI 0.64, 0.76). Two ICD9 codes (780.31, 780.32) specific for FS produced the highest PPV (PPV = 0.91, 95% CI 0.85, 0.95) and accounted for 140 (92%) of confirmed FS. In the absence of these codes, other non-specific seizure codes yielded much lower PPVs, regardless of the presence of same day codes for medically attended fever (PPVs ranging from 0.19 to 0.20).

Only 9 of the 152 confirmed FS met BC criteria for LOC and generalized motor manifestations. By including criteria for ASC, we captured an additional 101 confirmed FS. An additional 42 confirmed FS cases did not meet LOC/ASC and/or generalized motor manifestations criteria, but did have documentation of fever and seizure within 24 h or a clinician dx of FS.

Conclusion. Although ICD9 code algorithms based on any seizure code yielded a moderate PPV, restriction to specific FS codes yielded a higher PPV and accounted for a large proportion of confirmed FS. The use of ASC in validation criteria captured a larger number of cases beyond those meeting BC criteria.

Disclosures. **C. McMahill-Walraven**, Aetna: Employee, Salary

1071. Attitudes, Preferences, And Behaviors Of Adults Who Received Vaccinations In Traditional and Non-Traditional Settings

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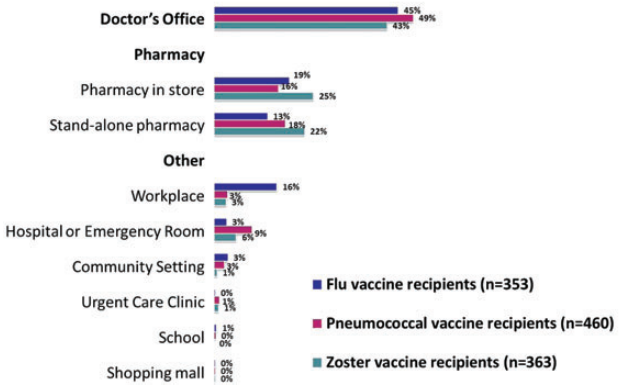
Background. Adult vaccinations are increasingly delivered outside of a doctor's office. However, vaccination behaviors in alternative settings remain unclear, particularly for non-influenza vaccinations. This study aims to examine, from the patient's perspective, vaccination patterns and drivers to adult vaccination across all settings.

Methods. In 2013, a cross-sectional online survey was conducted in U.S. nationally representative adults aged at least 19 years who received either influenza, pneumococcal, or zoster vaccine within the past 6 months. From choosing vaccines to deciding locations, the survey explored attitudes, preferences, and behaviors of adults vaccinated at various settings. Descriptive and bivariate analyses were applied to analyze patients' responses by each vaccine and setting.

Results. Among 1,178 qualified respondents, most were vaccinated at the doctor's office or pharmacy (Figure 1). Most common alternative settings to receive influenza vaccine was workplace, and hospital/emergency room for pneumococcal and zoster vaccine. Approximately half of recipients for each vaccine chose to get vaccinated as preventative health routine or following healthcare provider recommendation. Zoster vaccine recipients were more likely to get vaccinated after seeing a commercial or ad. Consistent across all three vaccines, adults are more likely to know about vaccines offered at doctor's office from the doctor, at pharmacy from signs in pharmacy; and at other settings from seeing or hearing about it at the location. While most adults vaccinated at the pharmacy went there specifically to get vaccinated, those vaccinated at the doctor's office were mostly there for a routine check-up. Main drivers for selecting vaccination settings were "vaccination without an appointment," followed by "shorter wait time," and "location accepts my insurance." Among all respondents, 17.7% received two or more vaccines concurrently. Convenience and healthcare provider recommendation were the main drivers to receive concurrent vaccinations.

Figure 1. Patterns of adult vaccination at traditional and non-traditional settings



Conclusion. Our study suggests opportunities to improve adult vaccination at non-traditional settings through highlighting convenience and healthcare provider recommendation to adults.

Disclosures. **H. K. Yang**, Merck: Employee, Salary **C. Shao**, Merck: Employee, Salary **J. Fitzgerald**, Merck: Research Contractor, Research support **M. Laferriere**, Merck: Research Contractor, Research support **R. Hahn**, Merck: Research Contractor, Research support **J. D. Grabenstein**, Merck and Co., Inc.: Employee and Shareholder, Salary **P. Singhal**, Merck: Employee, Salary

1072. Utilization of pre-travel clinic for administration of routine vaccinations in adults: a lost opportunity?

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Background. The pre-travel counseling visit represents an ideal opportunity for updating routine and destination specific immunizations. The American College of Immunization Practices (ACIP) recommends pneumococcal vaccination (PPSV) for adults ≥ 65 years and Zostavax in those ≥ 60 years. Recent updates also recommend Hepatitis B vaccination for diabetics. To examine coverage and factors associated with the failure to address routine adult vaccinations listed above, we analyzed data collected in the TravMil study at the pre-travel visit.

Methods. The TravMil cohort is comprised of DoD beneficiaries evaluated pre-travel at 3 military travel clinics (Walter Reed National Military Medical Center (WRNMMC), National Naval Medical Center San-Diego (NMCSD), and Naval Medical Center Portsmouth (NMCP)). Vaccination status and vaccine prescriptions were evaluated. Multivariate Poisson regression with robust error variance was used to examine factors associated with failure to immunize adults who met criteria for immunization with PPSV, Zostavax, and Hepatitis B.

Results. Non-white race [RR: 1.42 (1.04-1.92)] was associated with a failure to vaccinate with Zostavax and/or PPSV, as was evaluation at NMCP [Ref WRNMMC; RR 2.46 (1.43-4.24)]. Female diabetics were less likely to receive Hepatitis B vaccination [RR: 1.60 (1.08-2.39)].

Vaccine Status	Overall	WRNMMC	NMCP	NMCSD
Hepatitis B in Diabetics	n=86	n=8	n=29	n=49
Up to date	26(30.2)	5(62.5)	5(17.2)	16(32.7)
Administered at pre-travel visit	14(16.3)	1(7.1)	9(31.0)	4(8.2)
PPSV in adults ≥65	n=352	n=39	n=97	n=216
Up to date	241(68.5)	29(74.4)	59(60.8)	153(70.8)
Administered at pre-travel visit	72(20.5)	9(23.1)	22(22.7)	41(19.0)
Zostavax in adults ≥60	n=477	n=54	n=139	n=284
Up to date	301(63.1)	39(72.2)	72(51.8)	190(66.9)
Administered at pre-travel visit	41(8.6)	5(9.3)	3(2.2)	33(11.6)

Conclusion. Even in a setting with free access to care and vaccinations, significant variability in coverage of recommended vaccines was noted by race, gender and clinic site. Factors associated with these differences need to be studied further.

Disclosures. **All authors:** No reported disclosures.

1073. Missed Opportunities to Adhere to the ACIP Vaccine Initiation Schedule among Privately Insured Preteens in the United States, 2010-2012

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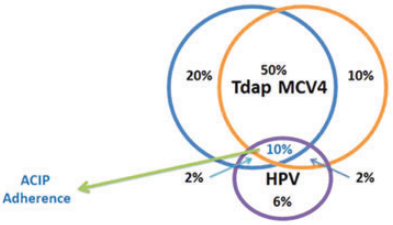
Background. The Advisory Committee on Immunization Practices (ACIP) recommended that preteens get three vaccines (Tetanus, Diphtheria and Pertussis (Tdap), Meningococcal Conjugate Vaccine (MCV4) and Human papillomavirus (HPV)) during a single clinic visit. However, the vaccine initiation rates for these three vaccines as per the CDC's NIS 2012 were 54% for HPV, 74% for MCV4 to 85% for Tdap. The objective of this study was to assess and compare adherence to the ACIP recommended vaccine initiation schedule for preteens.

Methods. This study used the MarketScan Commercial Claims database of 1,245,336 eligible preteens between age 11 and 12 years, who were continuously enrolled and had a vaccination visit for at least one of the three recommended vaccines between January 2010 and December 2012. Adherence to ACIP recommendation was assessed for the very first vaccination visit. Adherence to ACIP recommendations was defined as preteens who received all three vaccines during their first vaccination visit as recommended by the ACIP.

Descriptive statistics were used to assess adherence to ACIP recommendations. Multivariate analysis was also carried out to understand association of adherence to ACIP recommendations with variables such as sex, year, age and region.

Results. Only 10% of the preteens received all three vaccines during a single visit (first vaccination visit) per ACIP recommendations, 36% were given only one of the three vaccines and 54% had any two recommended vaccines. The most prevalent practice (50%) was to give Tdap and MCV4 (Figure 1). The HPV vaccine was missed in 63% of preteens who received 1 or 2 vaccines in a single visit (data not shown) and in 93% of preteens who received Tdap and MCV4 in a single visit (Figure 2). Though adherence to ACIP recommended vaccination schedule has doubled from 7% in 2010 to 14% in 2012, it is still very low. Adherence to ACIP recommendations was significantly lower in 12 year olds (OR: 0.83) and in West and South regions (OR: 0.43 and 0.56 respectively) compared to North-East region and was higher for females (OR: 2.99) and for each additional year (OR: 2.23).

Figure 1: Vaccines given during the first vaccination visit among privately insured preteens in the US, 2010-12 (N = 1,245,336)



1 = P(HPV only) + P(Tdap only) + P (MCV4 only) + P(HPV U Tdap) + P(HPV U MCV4) + P(Tdap U MCV4) + P(HPV U Tdap U MCV4)

Figure 2: Missed opportunities for vaccination among privately insured preteens who had only two of the three recommended vaccines among during the first vaccination visit by sex, 2010-12 (n= 1,245,336)

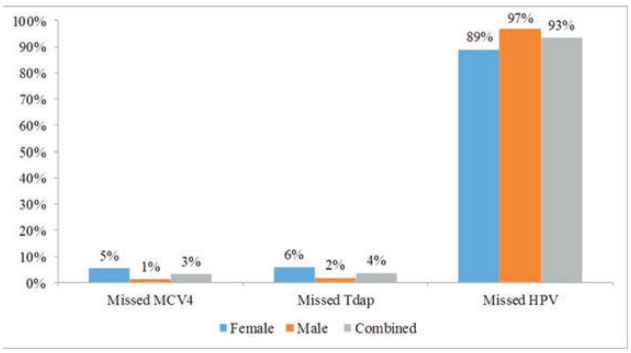
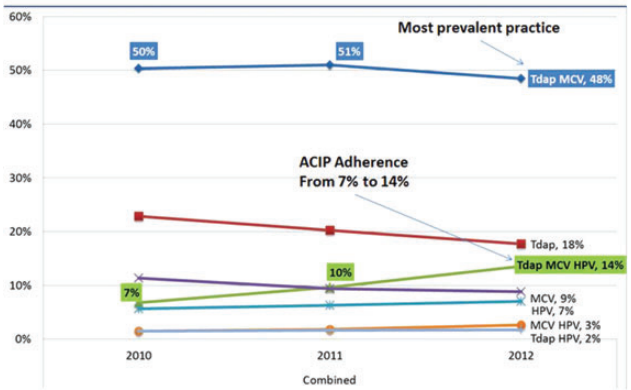


Figure 3: Trend analysis of vaccinations given during the first vaccination visit among privately insured preteens in the US, 2010-12



Conclusion. Adherence to ACIP guidelines is low as very few preteens receive all three vaccines in a single visit. Of the three vaccines mentioned in the ACIP recommendations, HPV vaccine poses as the biggest missed opportunity.

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1074. Immunization Practices of Pediatric Oncology Providers Towards Children with Acute Lymphoblastic Leukemia that have Completed Chemotherapy

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Background. As the population of pediatric acute lymphoblastic leukemia (ALL) survivors grows, there is an increased focus on long term supportive care measures including reimmunization . There are no ALL-specific guidelines for reimmunization in the post-chemotherapy period. We aimed to better understand the approach of pediatric oncology providers for reimmunizing children that have completed chemotherapy for ALL.

Methods. A cross-sectional study was performed using survey methodology. An anonymous 33-item questionnaire was electronically distributed on three separate occasions over a 4 week period via REDCap to members of the American Society of Pediatric Hematology and Oncology (ASPHO). The questionnaire was adapted with permission from a previously validated survey instrument.

Results. The questionnaire was completed by 350 of 1602 ASPHO members (21.9% response rate). Respondents were primarily clinicians (75%) at university-affiliated (75%) pediatric institutions (58%). A majority of respondents (95%) believe that immunizations are extremely effective in the general population; only 31% believe immunizations are extremely effective in children after ALL chemotherapy. Most respondents agree it is safe to give vaccines >12 months (99%) and 6 to 12 months (71%) after completion of chemotherapy. Only 13% agree that vaccines are safe in the first 6 months post chemotherapy. 42% of care providers always or often recommend re-immunization after chemotherapy for ALL while 40% rarely or never recommend re-immunization. When providers do re-immunize, the majority do so after 6 months (73%). Common reasons for not re-immunizing include a perceived lack of need, lack of published evidence, and lack of guidelines.

Conclusion. These results reveal significant variation in the approach to reimmunization for children that have completed ALL chemotherapy. Lack of evidence and guidelines to direct clinicians as to who and when to reimmunize were identified as barriers. Future efforts should focus on establishing universal guidelines to standardize care and identify research gaps for further investigation.

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1075. Effectiveness and Safety of Immunization with Live-attenuated and Inactivated Vaccines for Pediatric Liver Transplantation Recipients

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Background. Liver transplantation recipients are at high risk of severe complications of many viral infections because they are treated with immunosuppressive drugs affecting the immune system. Vaccination for liver transplantation candidates is generally recommended before surgery, but the opportunities for vaccination prior to transplantation in pediatric candidates are often limited by severe disease conditions. The effectiveness and safety of immunization with vaccines in standard vaccination programs for pediatric liver transplantation recipients thus need to be elucidated.

Methods. Participants in this study comprised 39 pediatric recipients of living donor liver transplantation. Criteria for administering live-attenuated (measles, rubella, mumps, and varicella) and inactivated vaccines (hepatitis B, pertussis, and Japanese encephalitis) were as follows: 1) >1 year after transplantation; 2) no use of systemic steroids to treat acute rejection within the last 6 months; 3) serum trough concentration of tacrolimus <5 ng/ml; 4) no severe immunosuppression according to blood examinations; and 5) provision of written informed consent. Median age at transplantation was 17 months old and median period from transplantation to the beginning of immunization was 18 months.

Results. Seroprotection rates for measles, rubella, mumps, varicella, hepatitis B, pertussis, and Japanese encephalitis after post-transplant immunization were 31% (8/26), 70% (19/27), 48% (12/25), 37% (7/19), 83% (19/23), 87% (13/15), and 88% (7/8), respectively. Seroprotection rates for measles, rubella, mumps, and varicella after 2nd vaccination for recipients with primary vaccine failure after the first vaccination were 67% (6/9), 50% (1/2), 71% (5/7), and 50% (5/10). While 4 recipients caught the mumps and eight contracted varicella before immunization, one recipient developed varicella after immunization. No serious systemic adverse events were observed in vaccinated recipients.

Conclusion. Seroprotection rates for measles, rubella, and varicella appeared low in children after the first posttransplantation vaccination. Immunizations with four live-attenuated and three inactivated vaccines were safe and effective for pediatric liver transplantation recipients who were not severely immunosuppressed.

Disclosures. **All authors:** No reported disclosures.

1076. Assessment of the Status of Measles Elimination in the United States, 2001-2013

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Background. Although measles was declared eliminated in the U.S. in 2,000, importations from remaining endemic areas in the world continue to occur, and lead to outbreaks in pockets of unvaccinated. Due to an apparent increase in the number of cases and outbreaks in recent years, and concerns of increasing vaccine hesitancy, we evaluated transmission from imported cases to assess measles elimination status in the U.S.

Methods. Measles elimination was assessed by evaluation of the effective reproduction number *R*, the average number of secondary cases that result from an importation; elimination is indicated by maintenance of $R < 1$. Four previously described methods for estimating *R* were applied to national surveillance data reported to the CDC from 2001-2013. Method 1 estimates *R* as 1-*P*, where *P* is the proportion of all cases that are imported. Methods 2 and 3 estimate *R* by fitting a model of the spread of infection, based on a branching process, to data on the observed sizes and generations of outbreaks, respectively. An outbreak was defined as 1 or more cases. Method 4 estimates *R* from the observed epidemic curves of the largest outbreaks, using a likelihood-based estimation approach. Inverse-variance-weighting was applied to year-specific *R* estimates to analyze trends overtime.

Results. During 2001-2013, a total of 1153 confirmed measles cases were reported, of which 447 were importations. These constituted 525 outbreaks, ranging in size from 1 to 58 cases; 145 had >1 case. Median outbreak duration was 15 days (range 1-89 days). Across all study years, *R* was <1 with all 4 methods: 0.62 (95% CI: 0.54-0.72) using method 1, 0.52 (95% CI: 0.39-0.64) using method 2, 0.66 (95% CI: 0.62-0.71) using method 3, and 0.63 (95% CI: 0.60-0.66) using method 4. A statistically significant trend in annual *R* estimates overtime was not identified (p-value > 0.2).

Conclusion. Our estimates of *R* demonstrate that elimination of endemic measles transmission is maintained in the U.S. The congruence in results using different methods augments the validity of the estimates and provides a framework for continued monitoring of elimination. Sustained high vaccination coverage and prompt outbreak response strategies have proven successful in halting prolonged transmission of measles in the U.S.

Disclosures. **All authors:** No reported disclosures.

1077. Adverse events following measles, mumps, and rubella (MMR) vaccine in adults reported to the Vaccine Adverse Event Reporting System, 2003-2013

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Background. The Centers for Disease Control and Prevention (CDC) recommends adults born in 1957 or later have documentation of at least one dose of MMR vaccine and high risk adults and healthcare workers have a second dose. Limited data exists on the safety of MMR vaccine in adults. We reviewed reports of adverse events (AEs) to the Vaccine Adverse Event Reporting System (VAERS) in order to assess safety in this previously under-studied group.

Methods. VAERS is the national spontaneous vaccine safety surveillance system co-administered by CDC and the FDA. We searched the VAERS database for US reports of adults 19 years of age and older who received MMR vaccine from January 1, 2003 to July 31, 2013. For serious reports, pregnancy reports, and reports with selected pre-specified outcomes (Guillian-Barré syndrome (GBS), anaphylaxis, arthritis or arthralgia, encephalitis, idiopathic thrombocytopenic purpura (ITP), myocarditis or pericarditis, myocardial infarction, and vaccine virus shedding), we reviewed available medical records.

Results. During this period, VAERS received 3,175 US AE reports after MMR vaccine in adults. Of these, 161 (5%) were serious, including 9 reports of deaths. Median onset to outcome was 2 days (range 0 to 954). Median age of vaccine recipients was 37 years. Most reports, 2,448 (77%), were in females. The most common signs and symptoms for all reports were pyrexia (19%), rash (17%), pain (13%) and arthralgia (13%). The most common terms for serious reports were pyrexia (24%), headache (21%), hypoesthesia (19%), and asthenia (19%). There were a total of 19 GBS, 12 anaphylaxis, 15 arthritis/ arthralgia, 9 encephalitis, 5 ITP, 4 myocarditis reports, and 1 myocardial infarction report. We did not observe any new safety findings in empirical Bayesian data mining. In 131 reports, MMR vaccine was inadvertently given to pregnant women; the majority of vaccinations were in the first trimester. In 82 (63%) pregnancy reports, no AE was reported.

Conclusion. In our review of VAERS data, we did not detect any new or unexpected safety concerns for MMR vaccine in adults. We identified reports of pregnant women exposed to MMR in whom the vaccine is contraindicated, which demonstrates the need for provider education on vaccine recommendations and screening.

Disclosures. **L. Sukumaran**, National Institute of Health: T32 grant recipient, Research grant

1078. Risk Factors Associated with Developing Fever Following First Dose Measles-Containing Vaccines

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Background. Seven to ten days after a first dose of a measles-containing vaccine (MCV) – i.e., MMRV or MMR –, children have elevated risk of fever which can be associated with febrile seizures. To identify whether there are particular children at higher risk, we examined host and familial factors associated with developing fever 7-10 days after a MCV.

Methods. We included all children who were enrolled in the Vaccine Safety Datalink from January 1, 2000 through December 31, 2012 and were < 36 months of age at the first MCV dose. We identified all medically-attended visits (outpatient or emergency department) coded for fever 7-10 days after a first dose of any MCV. We evaluated factors associated with a visit for fever 7-10 days after a MCV using $X^2$and multivariate logistic regression analyses.

Results. Among 946,806 MCV-immunized children, 98% of whom were ≤ 24 months of age, we identified 7480 (0.8%) fever visits 7-10 days after any first dose MCV. Compared with children without fever after MCV, logistic regression analysis found that children with fever were more likely to have received MMRV than MMR (OR 1.2 95% CI 1.1-1.3), be between 15-18 months of age (OR 1.24 95% CI 1.16-1.3), have had fever following prior vaccines (OR 1.4 95% CI 1.2-1.6), have had fever at any other previous time (OR 1.9 95% CI 1.8-2.0), have had at least 1 prior seizure (OR 2.0 95% CI 1.7-2.4), and have had > 3 medical visits within the 6 months before their MCV (OR 1.7 95% CI 1.6-1.8). They were less likely to have missed vaccine-associated medical visits by age 7 months (OR 0.82 95% CI 0.76- 0.89). In the subset of children who had siblings also exposed to a first dose of MCV, those whose siblings had fever 7-10 days after MCV were much more likely themselves to also have fever 7-10 days after a MCV (OR 4.5 95% CI 3.7-5.5).

Conclusion. While healthcare seeking behavior is likely a factor, fever after a first dose of a MCV was associated with MMRV vaccine, being 15-18 months old at time of vaccination, prior fever events, including after previous vaccines, and seizures during the first year of life. Children with fever tended to also have siblings with fever after MCV. These results suggest that some individuals or families may be more susceptible to the fever associated with MCV.

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1079. Single-Nucleotide Polymorphism Associations in Common with Humoral and Cellular Immune Responses to Measles and Rubella Vaccines

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Background. In our previous studies, we identified several associations between genotype and phenotypic immune response to both measles vaccine and rubella vaccine. Because immunization against measles and rubella is provided by one vaccine, finding genetic associations shared between measles-specific and rubella-specific immune responses is of great interest. Single-nucleotide polymorphisms (SNPs) in candidate immune response genes were examined for associations with measles- and rubella–specific neutralizing antibodies, IFN-γ, and IL-6 secretion in two separate association analyses in a cohort of healthy immunized subjects.

Methods. We recruited 1,052 schoolchildren from Rochester, MN, between the ages of 11 and 22 years, who received two doses of measles-mumps-rubella vaccine (MMR, Merck).

Results. We identified six SNP associations shared between the measles-specific and rubella-specific immune responses, specifically neutralizing antibody titers (*DDX58*), secreted IL-6 (*IL10RB, IL12B*) and secreted IFN-γ (*IFNAR2, TLR4*). An intronic SNP (rs669260) in the antiviral innate immune receptor gene, *DDX58*, was significantly associated with increased neutralizing antibody titers for both measles and rubella viral antigens post-MMR vaccination (p-values 0.02 and 0.0002, respectively). Significant associations were also found between *IL10RB* (rs2284552; measles study p-value 0.006, rubella study p-value 0.00008) and *IL12B* (rs2546893; measles study p-value 0.005,

rubella study p-value 0.03) gene polymorphisms and variations in both measles- and rubella virus-specific IL-6 responses. We also identified associations between individual SNP in the *IFNAR2* and *TLR4* genes that were associated with enhanced IFN-γ secretion for both measles- and rubella vaccine-specific immune responses.

Conclusion. These data indicate that there are SNP associations in common across measles and rubella vaccine immune responses, and that SNPs from multiple genes involved in innate and adaptive immune response regulation may contribute to the overall human antiviral response. Understanding the functional and mechanistic consequences of common genetic variations on immune response variations could assist in directing new vaccine design, and in better understanding the generation of immune responses.

Disclosures. **All authors:** No reported disclosures.

1080. Antibody Persistence 5 Years After Vaccination at 2 to 10 Years of Age With Quadrivalent MenACWY-CRM Conjugate Vaccine, And Responses To a Booster Vaccination

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Background. MenACWY-CRM vaccine was immunogenic in 2–10 year-old children in 1- and 2-dose schedules. As only limited data is available on antibody persistence we assessed bactericidal antibodies 5 years after primary vaccination and response to a booster dose, compared with age-matched vaccine-naïve controls (clinicaltrials.gov NCT01823536).

Methods. We enrolled two groups of 7–10 year-olds after 1 (n = 101) or 2 (n = 73) doses of MenACWY-CRM as 2–5 year-olds, and a group of 11–15 year-olds after 1 dose (n = 66) as 6–10 year-olds, with age-matched naïve-controls (n = 120 and 101). We measured serum bactericidal activity with human complement (hSBA) at baseline and 30 days after a booster or first MenACWY-CRM vaccination. Local and systemic reactions and any adverse events were recorded.

Results. Five years postvaccination levels of antibodies were still higher than controls in the three vaccinated groups, who displayed anamnestic responses to a booster dose, with 99–100% having hSBA titers ≥ 8 against all four serogroups.

			Percentages with hSBA ≥ 8 [95% CI]							
			7–10 years (2 doses)		Naïve Controls		11–15 years (1 dose)		Naïve Controls	
Group	(1 dose)									
Time	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**	**Pre**	**Post**
n/N	*13/99*	*99/99*	*5/71*	*68/69*	*0/119*	*88/118*	*15/65*	*64/64*	*5/101*	*80/99*
A	**13** [7, 21]	**100** [96, 100]	**7** [2, 16]	**99** [92, 100]	**0** [0, 3]	**75** [66, 82]	**23** [14, 35]	**100** [94, 100]	**5** [2, 11]	**81** [72, 88]
n/N	*32/99*	*98/98*	*34/72*	*71/71*	*26/119*	*96/118*	*37/65*	*64/64*	*21/100*	*85/99*
C	**32** [23, 42]	**100** [96, 100]	**47** [35, 59]	**100** [95, 100]	**22** [15, 30]	**81** [73, 88]	**57** [44, 69]	**100** [94, 100]	**21** [13, 30]	**86** [77, 92]
n/N	*73/99*	*99/99*	*60/72*	*69/69*	*62/119*	*110/118*	*52/65*	*64/64*	*55/101*	*91/99*
W	**74** [64, 82]	**100** [96, 100]	**83** [73, 91]	**100** [95, 100]	**52** [43, 61]	**93** [87, 97]	**80** [68, 89]	**100** [94, 100]	**54** [44, 64]	**92** [85, 96]
n/N	*48/99*	*98/98*	*37/73*	*71/71*	*28/119*	*101/119*	*35/65*	*63/63*	*37/101*	*80/99*
Y	**48** [38, 59]	**100** [96, 100]	**51** [39, 63]	**100** [95, 100]	**24** [16, 32]	**85** [77, 91]	**54** [41, 66]	**100** [94, 100]	**37** [27, 47]	**81** [72, 88]

Reactogenicity was similar across groups, 50–67% and 27–36% of children had mild to moderate solicited local and systemic reactions. No vaccine-related SAEs were reported.

Conclusion. 5 years after 1- and 2-dose MenACWY-CRM vaccination in 2–10 year-olds, half or more of the children still had persistent antibodies against serogroups C, W and Y with robust responses to a booster dose.

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1081. Immunogenicity of Human Papilloma Vaccine Coadministered with an Investigational Bivalent rLP2086 Vaccine Against Meningococcal Serogroup B in Healthy Adolescents

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Background. This Phase 2, randomized study evaluated coadministration of a licensed quadrivalent vaccine against human papillomavirus (HPV4) with bivalent rLP2086, an investigational vaccine against invasive disease caused by *Neisseria meningitidis* serogroup B (MnB), in healthy adolescents ≥11 to <18 years of age.

Table 1. Comparison of Geometric Mean Titers at 1 Month After Vaccination 3 (Evaluable Immunogenicity Population)

	Group 1 rLP2086 + HPV4		Group 2 rLP2086 + Saline			Group 3 Saline + HPV4		
Strain [Variant]	**n[a]**	**GMT[b] (95% CI)[c]**	**n[a]**	**GMT[b] (95% CI)[c]**		**n[a]**	**GMT[b] (95% CI)[c]**	**Ratio[d] (95% CI)[e]**
HPV antigens (Group 1 vs Group 3)								
HPV-6	813	451.8 (417.5, 489.0)				423	550.3 (490.4, 617.6)	0.82 (0.72, 0.94)
HPV-11	813	892.9 (839.5, 949.6)				423	1084.3 (997.3, 1179.0)	0.82 (0.74, 0.91)
HPV-16	813	3695.4 (3426.3, 3985.7)		NA		423	4763.4 (4285.9, 5294.2)	0.78 (0.68, 0.88)
HPV-18	813	744.0 (687.7, 805.0)				423	1047.4 (939.0, 1168.3)	0.71 (0.62, 0.81)
hSBA strains (Group 1 vs Group 2)								
PMB80 [A22]	803	53.3 (50.2, 56.7)	801	57.8 (54.4, 61.4)			NA	0.92 (0.85, 1.00)
PMB2948 [B24]	788	25.8 (24.1, 27.6)	793	28.0 (26.2, 29.9)				0.92 (0.84, 1.01)

CI=confidence interval; GMT=geometric mean titer; HPV=human papillomavirus; hSBA=serum bactericidal assay using human complement; LLOQ=lower limit of quantitation; NA=not applicable.
Note: LLOQ=11 mMU/ml for HPV-6, 8 mMU/ml for HPV-11, 11 mMU/ml for HPV-16, and 10 mMU/ml for HPV-18. LLOQ=1:16 for A22, 1:8 for A56, B24, and B44. Results below the LLOQ were set to 0.5*LLOQ for analysis.
a. n=number of subjects with valid and determinate assay results for the given antigen or strain.
b. Geometric mean titers (GMTs) were calculated using all subjects with valid and determinate assay results at 1 month after Vaccination 3.
c. Confidence intervals (CIs) are back transformations of confidence levels based on the Student t distribution for the mean logarithm of assay results.
d. Ratios of GMTs (Group 1/Group 3 for HPV antigen titers and Group 1/Group 2 for hSBA strain titers).
e. Confidence intervals (CIs) for the ratio are back transformations of a confidence interval based on the Student t distribution for the mean difference of the logarithms of the measures (Group 1 - Group 3 for HPV titers and Group 1 - Group 2 for hSBA strain titers).

Methods. Subjects received HPV4 + bivalent rLP2086 (Group 1), bivalent rLP2086 - + saline (Group 2), or saline + HPV4 (Group 3) at months 0, 2, and 6. Sera were collected at baseline and after doses 2 and 3. Immune responses to HPV4 antigens (HPV-6, 11, 16, and 18) were determined by competitive Luminex immunoassays. Bivalent rLP2086 immunogenicity was measured by serum bactericidal assay using human complement (hSBA) to 4 MnB test strains expressing vaccine-heterologous fHBP variants (A22, A56, B24, B44). Primary immunogenicity endpoints, all after dose 3, included geometric mean titers (GMTs) against HPV antigens in Groups 1 and 3 and hSBA GMTs for strains

expressing variants A22 and B24 in Groups 1 and 2. Secondary endpoints included seroconversion rates for HPV antigens in baseline seronegative subjects in Groups 1 and 3. Safety of bivalent rLP2086 was assessed after concomitant administration with HPV4 or saline.

Results. The prespecified noninferiority criteria set at 1.5-fold (0.67 lower limit of 95% CI for GMRs) were met for 3 of 4 HPV antigens (not HPV-18) and both MnB test strains (Table 1). Seroconversion rates in Groups 1 and 3 were ≥99% for all HPV antigens (Table 2). Greater local reactogenicity occurred after rLP2086 compared with saline but did not increase with later doses; injection site pain was the most common local reaction. Systemic events in all 3 groups were generally mild and moderate in severity.

Table 2. Comparison of Subjects Achieving HPV Seroconversion at 1 Month After Vaccination 3 – Baseline HPV Seronegative Evaluable Immunogenicity Population

		Group 1 rLP2086 + HPV4			Group 3 Saline + HPV4			Difference	
Antigen	Seropositive Criteria	N[a]	n[b] (%)	(95% CI)[c]	N[a]	n[b] (%)	(95% CI)[c]	(%)[d]	(95% CI)[e]
HPV-6	≥20 mMU/mL	802	797 (99.4)	(98.6, 99.8)	414	411 (99.3)	(97.9, 99.9)	0.1	(-0.9, 1.5)
HPV-11	≥16 mMU/mL	801	798 (99.6)	(98.9, 99.9)	417	415 (99.5)	(98.3, 99.9)	0.1	(-0.7, 1.3)
HPV-16	≥20 mMU/mL	800	797 (99.6)	(98.9, 99.9)	413	411 (99.5)	(98.3, 99.9)	0.1	(-0.7, 1.3)
HPV-18	≥24 mMU/mL	805	801 (99.5)	(98.7, 99.9)	418	414 (99.0)	(97.6, 99.7)	0.5	(-0.6, 1.9)

CI=confidence interval; HPV=human papillomavirus.
a. N=number of subjects with baseline HPV seronegative status for the given antigen.
b. n=Number of subjects achieving seroconversion (prespecified criteria) at 1 month after Vaccination 3 for the given antigen.
c. Exact 2-sided confidence interval (Clopper and Pearson) based upon the observed proportion of subjects.
d. Difference in proportions, expressed as a percentage.
e. Exact 2-sided confidence interval (based on Chan & Zhang) for the difference in proportions, expressed as a percentage.

Conclusion. Robust immune responses to both vaccines were generated after concomitant administration of rLP2086 + HPV4. Prespecified noninferiority criteria were met for 5 of 6 antigens. Although GMRs to HPV-18 narrowly missed noninferiority criteria, the high proportion of responders (≥99%) indicates clinical effectiveness is expected to be maintained after concomitant administration. Bivalent rLP2086 was well tolerated and elicited a robust immune response to test strains expressing fHPBs heterologous to those in the vaccine.

Disclosures. **P. Bhuyan**, Pfizer: Employee, Salary **J. Eiden**, Pfizer: Employee and Shareholder, Salary **T. R. Jones**, Pfizer: Employee, Salary **L. J. York**, Pfizer: Employee and Shareholder, Salary **J. Ginis**, Pfizer: Employee, Salary **K. U. Jansen**, Pfizer: Employee and Shareholder, Salary and Stockolder **J. L. Perez**, Pfizer: Employee, Salary

1082. Safety, Tolerability, and Immunogenicity of an Investigational Meningococcal Serogroup B Bivalent rLP2086 Vaccine in Healthy Adolescents Aged 11 to 18 Years in Three Phase 2, Randomized, Controlled Studies

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Background. *Neisseria meningitidis* serogroup B (MnB) is a major cause of invasive meningococcal disease in adolescents. A conserved, surface-exposed lipoprotein, LP2086 (factor H binding protein [fHBP]), is a promising vaccine target to protect against invasive disease caused by MnB. Safety, tolerability, and immunogenicity of an investigational bivalent, recombinant MnB vaccine (bivalent rLP2086) were examined in three phase 2, randomized, controlled studies in healthy adolescents 11–18 years of age.

Methods. Study 1012 examined 5 vaccine regimens of bivalent rLP2086, whereas studies 1010 and 1011 evaluated a 3-dose schedule of bivalent rLP2086 vaccine given concomitantly with the TdaP-IPV and HPV-vaccines, respectively. Each dose of bivalent rLP2086 contained 60 µg of the rLP2086 subfamily A variant A05 and 60 µg of the rLP2086 subfamily B variant B01. To assess immunogenicity, serum bactericidal assays using human complement (hSBA) were performed with 4 MnB test strains expressing the heterologous fHBP variants A22, A56, B24 and B44, which were selected to represent relevant diversity of fHBP, as well as to provide a perspective on the breadth of the vaccine-elicited immune response against strain expressing epidemiologically prevalent fHBP variants. Adverse events (AEs) and solicited local and systemic reactions were assessed.

Results. A large number of subjects in all 3 studies achieved hSBA titers above the lower limit of quantification (LLOQ) for each of the 4 MnB test strains 1 month after dose 3 (Table). Most systemic events and local reactions were mild to moderate in severity; AEs were generally not serious or vaccine-related. Co-administration of rLP2086 with TdaP-IPV or HPV-vaccines did not interfere with immune responses elicited by rLP2086.

Table. Proportion of Subjects Achieving an hSBA Titer ≥LLOQ for Each fHBP Variant Expressed by Each Test Strain 1 Month After the Last Dose of the Bivalent rLP2086 Vaccine

	% of Subjects			
fHBP variant expressed by hSBA test strain	A22	A56	B24	B44
Study 1012 (dosing regimen)				
Group 1 (0, 1, 6 mo); n=354–360	91.4	99.4	89.0	88.5
Group 2 (0, 2, 6 mo); n=352–359	95.0	98.9	88.4	86.1
Group 3 (0, 6 mo); n=356–370	93.2	98.4	81.1	77.5
Group 4 (0, 2 mo); n=234–240	90.8	100.0	73.0	70.1
Group 5 (0, 4 mo); n=110–113	91.0	99.1	69.1	73.0
Study 1010 (dosing regimen: 0, 2, 6 mo)				
rLP2086+TdaP-IPV Vaccine; n=146–158	95.6	100.0	96.8	81.5
Study 1011 (dosing regimen: 0, 2, 6 mo)				
rLP2086+HPV Vaccine; n=833–849	94.0	98.9	90.5	82.7
rLP2086+Saline; n=847–848	96.3	99.4	92.6	85.7

LLOQ=lower limit of quantification; fHBP=factor H binding protein; hSBA=serum bactericidal assays using human complement; TdaP-IPV Vaccine=Tetanus, Diphtheria, Pertussis, Polio Vaccine.
LLOQ=the lowest amount of an analyte in a sample that can be quantitatively determined. hSBA titer ≥ 1:4 are a correlate of protection for invasive meningococcal disease. hSBA titers ≥LLOQ are above the minimal correlate. LLOQ was 1:16 for A22; and 1:8 for A56, B24, and B44.

Conclusions. Serum bactericidal antibody titers above 1:4 protect against invasive meningococcal disease. The demonstration of hSBA titers ≥LLOQ to 4 MnB test strains, each heterologous to vaccine antigen, in each of these adolescent phase 2 studies, suggest that 3 doses of the bivalent rLP2086 vaccine provided a functional antibody response that may be broadly active against diverse MnB disease-associated strains. Vaccinations with the bivalent rLP2086 were generally well tolerated.

Disclosures. **J. Beeslaar**, Pfizer: Employee, Salary **J. Eiden**, Pfizer: Employee and Shareholder, Salary **Q. Jiang**, Pfizer: Employee, Salary and Stock option **S. Harris**, Pfizer: Employee, Salary **L. J. York**, Pfizer: Employee and Shareholder, Salary **D. Morgenstern**, Pfizer: Employee and Shareholder, Salary and stock **P. Bhuyan**, Pfizer: Employee, Salary **J. L. Perez**, Pfizer: Employee, Salary

1083. Comparative Evaluation of Two Different Investigational Meningococcal ABCWY Vaccine Formulations in Adolescents and Young Adults

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Background. Novartis has licensed meningococcal vaccines against serogroups A, C, W and Y (MenACWY-CRM) and serogroup B (4CMenB). We evaluated 2 investigational formulations of MenABCWY vaccines, with primary objectives to assess their noninferiority compared with the licensed vaccine for ACWY serogroups and formulation selection based on a desirability index (DI) (Clinicaltrials.gov NCT01272180).

Methods. 480 healthy subjects, aged 10–25 years, were randomized to four groups and received either: one of two MenABCWY formulations with full or quarter doses of outer membrane vesicles (OMV), 4CMenB, or Placebo/MenACWY-CRM. Each was given as a 2-dose series at 0 and 2 months. A serum bactericidal assay with human complement (hSBA) was used to measure antibodies against serogroups A, C, W, Y and serogroup B test strains at baseline and 30 days after dose 2; seroresponses and hSBA GMTs were assessed. For MenABCWY vaccines we also compared a DI based on immunogenicity (post-vaccine hSBA GMT ratios) and reactogenicity parameters (percentages of doses associated with severe local and severe systemic reactions).

Results. Percentages of subjects with seroresponses to A, C, W and Y were significantly higher after 2 doses of either MenABCWY formulation (with full and quarter OMV) than after a single dose of MenACWY; respectively 90/92% vs 73% for A; 95/93% vs 63% for C; 80/84% vs 65% for W; and 92/90% vs 75% for Y. Prespecified noninferiority criteria were met. Both MenABCWY vaccines induced robust immune responses against serogroup B test strains, comparable with 4CMenB. Among the three serogroup B-containing formulations, DI analyses were comparable, although the full dose OMV vaccine induced higher GMTs than the quarter dose vaccine against most of the serogroup B test strains. Reactogenicity profiles of the MenABCWY vaccines were similar to each other and to that of 4CMenB. No vaccine-related serious adverse events were reported.

Conclusion. The MenABCWY vaccines had comparable immunogenicity for serogroups ACWY and for serogroup B, although GMT responses against B test strains appeared to be higher for the full OMV formulation. Reactogenicity was comparable between the investigational and the 4CMenB vaccine.

Disclosures. **S. L. Block**, Novartis Vaccines: Investigator, Consulting fee **L. Szenborn**, Novartis Vaccines: Investigator, Consulting fee **W. Daly**, Novartis Vaccines: Investigator, Consulting fee **T. Jackowska**, Novartis Vaccines: Investigator, Consulting fee **V. Narasimhan**, Novartis Vaccines: Employee, Salary **D. D'Agostino**, Novartis Vaccines: Employee, Salary **L. Han**, Novartis Vaccines: Employee, Salary **P. M Dull**, Novartis Vaccines: Employee, Salary **I. Smolenov**, Novartis Vaccines: Employee, Salary

1084. Persistence of Meningococcal Antibodies and Response to a Booster Dose after a Two-dose Vaccination Series with Investigational MenABCWY Vaccine Formulations in Adolescents

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Background. Novartis has developed a glycoconjugate vaccine against *Neisseria meningitidis* serogroups A, C, W and Y (MenACWY-CRM), and a recombinant protein vaccine against serogroup B, and is now evaluating different formulations of a MenABCWY vaccine combining antigens against all 5 serogroups (clinicaltrials.gov NCT01367158).

Methods. Among adolescents aged 11–18 years who had previously received 2 doses (0 and 2 months) of four different MenABCWY vaccines (with varying B components) or control vaccines, 440 subjects were enrolled to examine immune response to a third dose (4 months after dose 2), and antibody persistence 10 months after a 2-dose series. Antibodies against A, C, W, Y and B antigens were measured by serum bactericidal assay with human complement (hSBA). Frequencies of local and systemic reactions and other adverse events were assessed.

Results. Prior to dose 3, 92–100% of subjects in all MenABCWY groups had hSBA titers ≥ 8 against serogroups C, W and Y, and 52–79% against A. One month after dose 3, 96–100% of subjects in all MenABCWY groups had hSBA titers ≥ 8 against A, C, W, and Y. After dose 3, percentages of subjects with hSBA titers ≥ 5 against serogroup B test strains increased across MenABCWY groups, with highest percentages (87%–100%) being in subjects who received a MenABCWY vaccine containing outer membrane vesicles (OMV).

Persistence of antibodies against A, C, W and Y, 10 months after dose 2 of MenABCWY was similar for all groups, and was at least equal to that after one dose of MenACWY-CRM. For all MenABCWY groups, antibody titers against B test strains declined most rapidly within 4 months after dose 2, and then declined gradually over the subsequent 6 months. Overall, the OMV-containing MenABCWY vaccines had the highest GMTs over time against most B test strains.

Most frequent solicited reactions were injection site pain (71%), myalgia (42%), and headache (33%). OMV-containing MenABCWY groups had higher frequencies of local reactions, myalgia, and arthralgia.

Conclusion. All MenABCWY vaccine formulations elicited robust immune responses to A, C, W, Y, and B after a third dose. Subjects given OMV-containing MenABCWY vaccines had the highest antibody titers against serogroup B test strains 10 months after dose 2.

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1085. Persistence of Meningococcal Bactericidal Antibodies and Booster Response at 60-Months of Age in Children Who Received Infant Or Toddler Doses of MenACWY-CRM Conjugate Vaccine

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Background. A quadrivalent meningococcal glycoconjugate vaccine (MenACWY-CRM) is immunogenic in 4-dose infant or 2-dose toddler schedules. We report on persistence of bactericidal antibodies in each group at 60 months of age, and responses 1 month after a booster.

Methods. In this phase IIIb, multi-center, open-label, controlled study (clinicaltrials.gov NCT01148017), subjects vaccinated as infants or toddlers were re-evaluated at 60 months of age, with age-matched vaccine-naïve controls. Bactericidal antibodies with human complement (hSBA) measured before and 1 month after booster are expressed as geometric mean titers (GMT) and proportions with seroprotective titers (≥ 8).

Results. We enrolled 131 infant- and 54 toddler-vaccinated subjects, and 50 controls. At 60 months titers had waned, but GMTs were higher in toddler-vaccinated than in infant-vaccinated, and both were higher than controls. Immune responses to another dose of MenACWY-CRM were higher in both prevaccinated groups, who displayed anamnestic responses. GMTs for serogroups A, C, W, and Y were 177, 206, 1706 and 1135 in infant-vaccinated, 356, 723, 1960 and 1187 in toddler-vaccinated, and 47, 44, 37 and 18 in controls, respectively; 96–100% developed titers ≥ 8 compared with 73–89% of controls (table).

	Percentages with hSBA ≥ 8 [95% CI]					
Group	Infant (4 doses)		Toddler (2 doses)		Controls	
Timing	Preboost	Postboost	Preboost	Postboost	Preboost	Postboost
	n/N	*7/122*	*111/115*	*12/48*	*45/45*	*1/45*	*39/45*
Serogroup A	**6** [2, 11]	**97** [91, 99]	**25** [14, 40]	**100** [92, 100]	**2** [0.1, 12]	**87** [73, 95]
	n/N	*32/122*	*109/114*	*26/48*	*44/44*	*10/45*	*38/45*
Serogroup C	**26** [19, 35]	**96** [90, 99]	**54** [39, 69]	**100** [92, 100]	**22** [11, 37]	**84** [71, 94]
	n/N	*82/120*	*103/103*	*38/47*	*42/42*	*18/45*	*39/44*
Serogroup W	**68** [59, 77]	**100** [96, 100]	**81** [67, 91]	**100** [92, 100]	**40** [26, 56]	**89** [75, 96]
	n/N	*68/121*	*110/110*	*35/48*	*44/44*	*11/44*	*32/44*
Serogroup Y	**56** [47, 65]	**100** [97, 100]	**73** [58, 85]	**100** [92, 100]	**25** [13, 40]	**73** [57, 85]

MenACWY-CRM vaccination at 60 months caused mainly mild or moderate solicited reactions in 62% of infant, 64% of toddler and 76% of control groups. No SAEs were reported.

Conclusion. Modest antibody persistence after infant or toddler vaccination with MenACWY-CRM was observed at 60 months of age with a robust booster effect and high seroprotection rates postvaccination.

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1086. 5-year Antibody Persistence and Booster Response to a Meningococcal ACWY Tetanus Toxoid Conjugate Vaccine in Healthy Adolescents and Young Adults

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Background. We evaluated antibody persistence 5 years after a single dose of *Neisseria meningitidis* serogroups A, C, W-135 and Y tetanus toxoid conjugate vaccine (MenACWY-TT) or MenACWY diphtheria toxoid conjugate vaccine (MenACWY-DT) in healthy adolescents and young adults, and subsequent MenACWY-TT booster vaccination in both groups compared to MenACWY-TT primary vaccination in newly enrolled, age-matched subjects.

Methods. In this phase II, open, controlled, multicenter study in the United States (NCT00715910), subjects aged 15– < 31 years received a MenACWY-TT booster dose 5 years after MenACWY-TT (N = 183) or MenACWY-DT (N = 38) vaccination in study NCT00454909; naïve subjects aged 15– < 31 years (N = 101) received 1 MenACWY-TT dose. Immunogenicity was assessed pre- and 1 month post-vaccination by serum bactericidal antibody assay using human complement (hSBA; primary endpoint: 1:8 cut-off). Solicited and unsolicited adverse events (AEs) were recorded for 4 and 31 days post-vaccination, respectively; subjects were followed up for serious AEs (SAEs) and the new onset of chronic diseases (NOCDs) for 6 months post-vaccination.

Results. Five years after 1 dose of MenACWY-TT or MenACWY-DT, ≥78.6% of subjects had hSBA titers ≥1:8 for MenC, MenW-135 and MenY, and ≥37.9% for MenA (Table). One month post-vaccination, ≥99.1% of previously primed and ≥92.5% (except MenA: 77.2%) of previously naïve subjects had hSBA titers ≥1:8 for each serogroup (Table). Geometric mean titers were higher in previously primed vs naïve subjects, and similar in MenACWY-TT-primed or MenACWY-DT-primed subjects (exploratory analyses). The most commonly reported solicited local and general AEs were pain (≤58.8% of subjects) and headache (≤35.9% of subjects) after booster vaccination compared to pain (60.4%) and fatigue (33.0%) after primary vaccination. No grade 3 vaccine-related unsolicited AEs, and no vaccine-related SAEs or NOCDs were reported.

Table: Percentage of subjects with hSBA antibody titers ≥1:8 and GMTs, before and 30 days after primary or booster vaccination with MenACWY-TT (ATP immunogenicity cohort at Month 61)

Antibody	Group	Timing*	N	% ≥1:8 (95%CI)	GMTs (95%CI)
MenA	MenACWY-TTbst[a]	PRE	104	48.1 (38.2; 58.1)	7.6 (5.7; 10.2)
		POST	106	99.1 (94.9; 100)	783.8 (601.7; 1020.9)
	MenACWY-DT[b]	PRE	29	37.9 (20.7; 57.7)	6.6 (3.5; 12.7)
		POST	28	100 (87.7; 100)	952.0 (600.9; 1508.2)
	MenACWY-TTpri[c]	PRE	79	24.1 (15.1; 35.0)	3.9 (2.9; 5.1)
		POST	79	77.2 (66.4; 85.9)	79.7 (46.3; 137.4)
MenC	MenACWY-TTbst	PRE	106	89.6 (82.2; 94.7)	72.1 (48.8; 106.3)
		POST	109	99.1 (95.0; 100)	5020.4 (3995.4; 6308.4)
	MenACWY-DT	PRE	28	78.6 (59.0; 91.7)	28.2 (13.7; 57.8)
		POST	29	100 (88.1; 100)	6722.1 (3950.9; 11437.2)
	MenACWY-TTpri	PRE	71	71.8 (59.9; 81.9)	26.9 (16.4; 44.1)
		POST	81	95.1 (87.8; 98.6)	534.7 (308.0; 928.1)
MenW-135	MenACWY-TTbst	PRE	105	87.6 (79.8; 93.2)	98.7 (70.4; 138.5)
		POST	109	100 (96.7; 100)	5517.6 (4573.6; 6656.4)
	MenACWY-DT	PRE	28	82.1 (63.1; 93.9)	75.4 (31.0; 183.0)
		POST	29	100 (88.1; 100)	3729.0 (2415.4; 5757.1)
	MenACWY-TTpri	PRE	79	46.8 (35.5; 58.4)	12.7 (7.9; 20.4)
		POST	80	92.5 (84.4; 97.2)	237.7 (150.4; 375.8)
MenY	MenACWY-TTbst	PRE	106	91.5 (84.5; 96.0)	178.1 (128.6; 246.5)
		POST	109	100 (96.7; 100)	5664.3 (4590.0; 6990.1)
	MenACWY-DT	PRE	29	93.1 (77.2; 99.2)	135.7 (78.1; 235.8)
		POST	29	100 (88.1; 100)	6546.4 (4312.3; 9938.0)
	MenACWY-TTpri	PRE	78	66.7 (55.1; 76.9)	35.6 (21.6; 58.8)
		POST	84	97.6 (91.7; 99.7)	755.1 (522.4; 1091.4)

[a]MenACWY-TTbst, subjects primed and boosted with MenACWY-TT; [b]MenACWY-DT, subjects primed with MenACWY-DT and boosted with MenACWY-TT; [c]MenACWY-TTpri, previously naïve subjects primed with MenACWY-TT; *Timing: PRE, pre-booster vaccination for MenACWY-TTbst and MenACWY-DT groups, and pre-primary vaccination for MenACWY-TTpri group; POST, 1 month post-booster vaccination for MenACWY-TTbst and MenACWY-DT groups, and 1 month post-primary vaccination for MenACWY-TTpri group; N, number of subjects with available results; %, percentage of subjects with titer ≥1:8; GMT, geometric mean antibody titer; ATP, according-to-protocol; CI, confidence interval.

Conclusion. Antibody persistence for serogroups C, W-135 and Y was observed in most subjects up to 5 years after 1 dose of MenACWY-TT or MenACWY-DT. A MenACWY-TT booster dose at year 5 elicited robust anamnestic responses, irrespective of the meningococcal vaccine used for priming, and was well-tolerated in 15– < 31 year-olds.

Disclosures. **R. Baxter**, GSK: Grant Investigator, Research grant; Novartis: Grant Investigator, Research grant; Sanofi Pasteur: Grant Investigator, Research grant; Merck: Grant Investigator, Research grant **Y. Baine**, GlaxoSmithKline: Employee, Own stock and Salary **D. Kolhe**, GlaxoSmithKline: Employee, Salary **C. Baccarini**, GSK: Employee, Salary and Stock ownership **J. M. Miller**, GSK: Employee, Restricted Stock Grants and Salary **M. Van Der Wielen**, GSK Vaccines: Employee, Salary and Shares

1087. Immunogenicity and Safety of 3-Dose Primary Vaccination with Combined DTPa-HBV-IPV/Hib Vaccine in Canadian Aboriginal and non-Aboriginal Infants

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Background. It has been observed that immune responses to vaccination can vary between populations, in particular that immune responses to *Haemophilus influenzae* type b (Hib) vaccines are lower in certain ethnic groups. This study was undertaken to assess the immune response of Canadian Aboriginals (First Nations, Inuit, Métis) to the Hib and hepatitis B virus (HBV) components of the combined hexavalent diphtheria, tetanus, acellular pertussis, HBV, inactivated poliovirus and Hib vaccine (DTPa-HBV-IPV/Hib; GlaxoSmithKline Vaccines).

Methods. Phase IV, open-label, parallel-group study conducted at 3 centers in Canada (NCT00753649). Healthy Aboriginal and non-Aboriginal infants received DTPa-HBV-IPV/Hib at 2, 4 and 6 months of age. Immune responses to Hib polyribosyl ribitol phosphate (PRP) and HBV surface antigen (HBs) were measured 1 month post-dose 3. Medically-attended and serious adverse events (MAAEs/SAEs) were recorded up to 1 month post-dose 3.

Results. Seroprotection against Hib and HBV, 1 month post-dose 3, was comparable in the 94 Aboriginal and 107 non-Aboriginal infants included in the per-protocol analysis (Table). Anti-PRP antibody geometric mean concentrations (GMCs) were 1.7 fold higher in Aboriginal infants (Table).

Seroprotection rates and GMCs for Hib and HBV, with 95% confidence intervals

		Aboriginal	Non-Aboriginal
Hib PRP	**% ≥0.15 µg/ml**	**97.9** (92.5–99.7)	**99.1** (94.9–100)
	% ≥1 µg/ml	**88.3** (80.0–94.0)	**85.0** (76.9–91.2)
	GMC (µg/ml)	**6.1** (4.5–8.3)	**3.5** (2.7–4.5)
HBs	**% ≥10 mIU/ml**	**100** (96.0–100)	**100** (96.5–100)
	GMC (mIU/ml)	**1797.9** (1375.1–2350.7)	**1544.4** (1210.4–1970.5)

23.2% Aboriginal and 17.0% non-Aboriginal infants recorded MAAEs. 7 SAEs (bronchiolitis, pyrexia, bacterial pneumonia, respiratory syncytial virus infection and 3 cases of convulsion) were recorded in 6 Aboriginal infants; only 1 case (pyrexia) was assessed as vaccine-related; all SAEs had resolved by study end.

Conclusion. 3-dose primary vaccination with DTPa-HBV-IPV/Hib elicited immune responses to the Hib and HBV antigens that were at least as high in Aboriginal as in non-Aboriginal Canadian infants. No safety concerns were identified.

Disclosures. **D. W. Scheifele**, GlaxoSmithKline Vaccines: Grant Investigator, Research grant **M. Ferguson**, GlaxoSmithKline: Employed as an investigator at Colchester Research Group, which conducts multiple clinical trials with companies including GSK. PI in this study. My wife, Dr. Linda Ferguson, is CEO/Owner of CRG which has conducted clinical trials with multiple sponsors over the last 10 years; she has also received renumeration to present papers at conferences and discussions. **D. Assudani**, GlaxoSmithKline: Employee, Salary **S. Kuriyakose**, GlaxoSmith Kline Pharmaceuticals: Employee, Salary **O. Van Der Meeren**, GlaxoSmithKline: Employee and Shareholder, Salary **H. H. Han**, GlaxoSmithKline: Employee and Shareholder, Salary

1088. Provider and patient attitudes regarding adult pertussis vaccination

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Session: 128. Vaccines: Pertussis
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Background. There has been a substantial increase in infant pertussis cases over the past decade. Immunization is the primary method of pertussis prevention. Recommendations for pertussis vaccine (Tdap) have expanded to include a dose of Tdap for all adults, with particular attention to pregnant women in the 3rd trimester of each pregnancy and contacts of infants less than 1 year of age.

Methods. We surveyed adults with children 3 years of age or younger accessing services provided by Upstate Medical University in Syracuse, New York to determine community awareness of pertussis infection and Tdap receipt. We then surveyed obstetric (OB) and pediatric providers across New York State to determine provider attitudes regarding Tdap.

Results. 502 adults (86% female) were surveyed. 344 (69%) and 118 (24%) correctly identified pertussis symptoms and the population at high-risk for developing complications from infection, respectively. 401 (80%) adults stated that they have heard of the pertussis vaccine. 211 (42%) and 299 (60%) adults stated their doctor or child's pediatrician have discussed Tdap with them, respectively. Only 181(36%) participants stated that they have received Tdap in the past 5 years. Tdap receipt was strongly associated with a provider recommendation ($p < 0.05$). A total of 123 OB and 438 pediatric providers responded to the surveys. OB providers (14/123, 11%) were more

likely than pediatric providers (5/438, 1%) to express concerns with Tdap safety ($p < 0.05$). 12% of both OB and pediatric providers expressed concerns regarding Tdap efficacy. While 113/123 (92%) of the OB providers knew that Tdap is recommended with each pregnancy, only 99 (80%) recommended Tdap to eligible pregnant patients, and only 80 (65%) administered Tdap in their practice. 174/438 (40%) pediatric providers state they never discuss parental vaccine status at patient visits and 64/123 (52%) of OB providers state they never discuss pediatric vaccines with their pregnant patients.

Conclusion. Patient and provider hesitancy regarding Tdap vaccine continues. Hesitancy among obstetrical providers is particularly common. Interventions that improve both provider and patient attitudes regarding pertussis infection and vaccine will likely improve Tdap vaccination rates.

Disclosures. **All authors:** No reported disclosures.

1089. Safety and Immunogenicity of DTaP-IPV (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed Combined with Inactivated Poliovirus Vaccine) Compared to DAPTACEL® (Diphtheria and Tetanus Toxoids and Acellular Pertussis Vaccine Adsorbed) + IPOL® (Poliovirus Vaccine Inactivated) as the 5th Dose in Children 4 to 6 Years of Age

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Background. A phase III multicenter controlled study assessed safety and immunogenicity of DTaP-IPV vaccine given as a 5th dose concomitantly with MMR and Varicella (V) vaccines compared to separately administered DAPTACEL and IPOL vaccines. DTaP-IPV is the liquid component of Pentacel used to reconstitute PRP-T. NCT01346293

Methods. Healthy 4-6 year-olds previously vaccinated with 4 doses of DAPTACEL and/or Pentacel were planned for randomization to 4 groups: 640 subjects to immunogenicity Groups 1 (DTaP – IPV + MMR +V) or Group 2 (DAPTACEL + IPOL - + MMR + V) (1:1 ratio) and 2700 subjects into safety Group 3 (DTaP – IPV + MMR + V) or Group 4 (DAPTACEL + IPOL + MMR + V) (8:1 ratio). Immunogenicity between Groups 1 and 2 was compared by: 1) Pertussis (PT, FHA, PRN, and FIM) booster responses and geometric mean concentrations (GMCs), 2) Diphtheria and tetanus booster responses and GMCs, 3) IPV booster responses and geometric mean titers (GMTs). Noninferiority margins were 10% for booster responses and 0.67 for GMC or GMT ratio. Local and systemic reactions were compared between DTaP-IPV (Groups 1 + 3) and DAPTACEL + IPOL (Groups 2 + 4) recipients.

Results. 3372 subjects were randomized. 2743 received DTaP-IPV and 629 received DAPTACEL + IPOL. 97.4% of subjects completed all study activities up to day 28. DTaP-IPV was noninferior to DAPTACEL + IPOL as a fifth dose booster for all immunogenicity parameters evaluated:

- In the context of similar baseline titers, DTaP-IPV was associated with higher anti-pertussis GMCs than DAPTACEL. Booster response rates were also significantly higher for all pertussis antigen among DTaP-IPV recipients
- The GMCs and booster responses to diphtheria and tetanus antigens were noninferior in those who received DTaP-IPV when compared to subjects who received DAPTACEL + IPOL
- The GMTs and booster responses to poliovirus antigens (types 1, 2, and 3) were noninferior in those receiving DTaP-IPV compared to those receiving DAPTACEL + IPOL
- Seroprotection rates for diphtheria, tetanus and polio were all at or close to 100%.

Local and systemic reactions to vaccine were comparable among all vaccine groups.

Conclusion. DTaP-IPV was shown to be safe and immunogenic as a 5th dose booster in children 4-6 years of age. Study funded by Sanofi Pasteur.

Disclosures. **M. Smith**, Sanofi Pasteur: Investigator, Research support **X. Sheng**, Sanofi Pasteur: Employee, Salary **E. Jordanov**, Sanofi Pasteur: Employee, Salary **P. Tsang,** Sanofi Pasteur: Employee, Salary

1091. Serotype Distribution of *S. pneumoniae* Community Acquired Pneumonia (CAP) in Adults in the Netherlands in the CAPiTA (Community-Acquired Pneumonia Immunization Trial In Adults) Study Period

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Background. The CAPiTA (Community-Acquired Pneumonia Immunization Trial in Adults) trial was conducted in the Netherlands from September 2008-October 2013 to evaluate the efficacy of 13-valent pneumococcal conjugate vaccine (PCV13) for the prevention of vaccine-type (VT) pneumococcal community-acquired pneumonia (CAP) in adults aged ≥65 years. This trial provides a unique opportunity to evaluate the serotype distribution of PCV13 serotypes in CAP in adults over time in a setting where pneumococcal conjugate vaccines have been part of the infant national immunization program (NIP) since 2006, and where 23-valent pneumococcal polysaccharide vaccine (PPSV23) is not routinely administered to adults aged 65+.

Methods. In this double-blind, placebo-controlled, study, 84,496 immunocompetent adults aged ≥65 years were vaccinated with a single dose of PCV13 or placebo. The study continued until a pre-specified number of VT-CAP cases had occurred; episodes were identified using a PCV13-serotype-specific urinary antigen detection assay or by isolation of VT pneumococcus from a sterile site. Seven-valent pneumococcal conjugate vaccine (PCV7) was introduced for Dutch infants in 2006 as a 3 + 1 schedule, replaced by ten-valent pneumococcal conjugate vaccine (PCV10) in 2011; vaccination uptake is ~95%. Serotype distribution of PCV13 serotypes overall, and among placebo recipients (as a surrogate for the 65+ Dutch population) is described for each study year.

Results. All 13 PCV13 serotypes were confirmed among first episodes of VT-CAP (per-protocol population) over the duration of the study; most frequently identified were serotypes 1, 3, 7F, 19A. There were 4 episodes of PCV7-type CAP in placebo recipients in 2009, 3 in 2010, 6 in 2011, 2 in 2012, and 3 in 2013. For the additional serotypes in PCV13, there were 12, 17, 18, 16, and 9 episodes in 2009, 2010, 2011, 2012, and 2013 (7 months only), respectively.

Conclusion. Despite an infant NIP recommending PCV10, the most frequently observed serotypes in CAP among CAPiTA subjects included 1 and 7F. PCV7 serotypes persisted and their prevalence remained stable over the study. Furthermore, there was no evidence of a change in the frequency of the additional PCV13 serotypes.

Disclosures. **R. Hollingsworth**, Pfizer Vaccine Clinical Research: Employee and Shareholder, Salary **C. Webber**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **S. Gault**, Pfizer Vaccine Clinical Research: Employee and Shareholder, Salary **S. D. Patterson**, Pfizer Vaccines Clinical Research: Employee, Salary **W. Gruber**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **D. E. Grobbee**, Pfizer Vaccines Clinical Research: Investigator, Research grant **M. Bonten**, Pfizer Vaccines Clinical Research: Investigator, Research grant

1092. Immunogenicity of a 23-valent pneumococcal polysaccharide vaccine in the elderly

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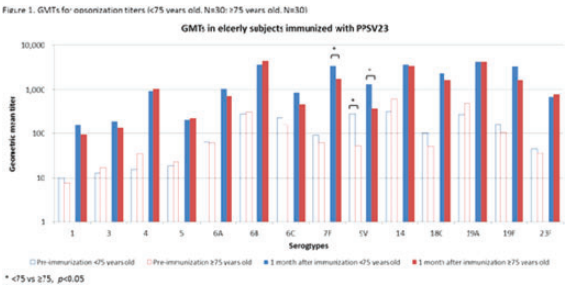
Background. The pneumococcal polysaccharide vaccine (PPSV) was introduced into national immunization program for elderly (≥ 65 years of age) in Korea on 2013. To evaluate the immune response in this population, anti-pneumococcal antibody titers were studied.

Methods. Sera from 60 pneumococcal vaccine-naïve adults were obtained. They were divided two groups according to their age (65 ~ 75 and ≥ 75). The qualitative antibody response were determined by multiplexed opsonophagocytic killing assay (MOPA) for 14 serotypes (1, 3, 4, 5, 6A, 6B, 6C, 7F, 9V, 14, 18C, 19A, 19F and 23F) before and one month after vaccination.

Results. The geometric mean titers (GMT) for pre- and postimmunization opsonic titers are shown in Figure 1 and the table. Reverse cumulative distribution curves are shown in Figure 2. The GMT increased significantly after immunization. The response to the pneumococcal polysaccharide vaccine showed similar responses in both age groups except for serotype 7F and 9V.



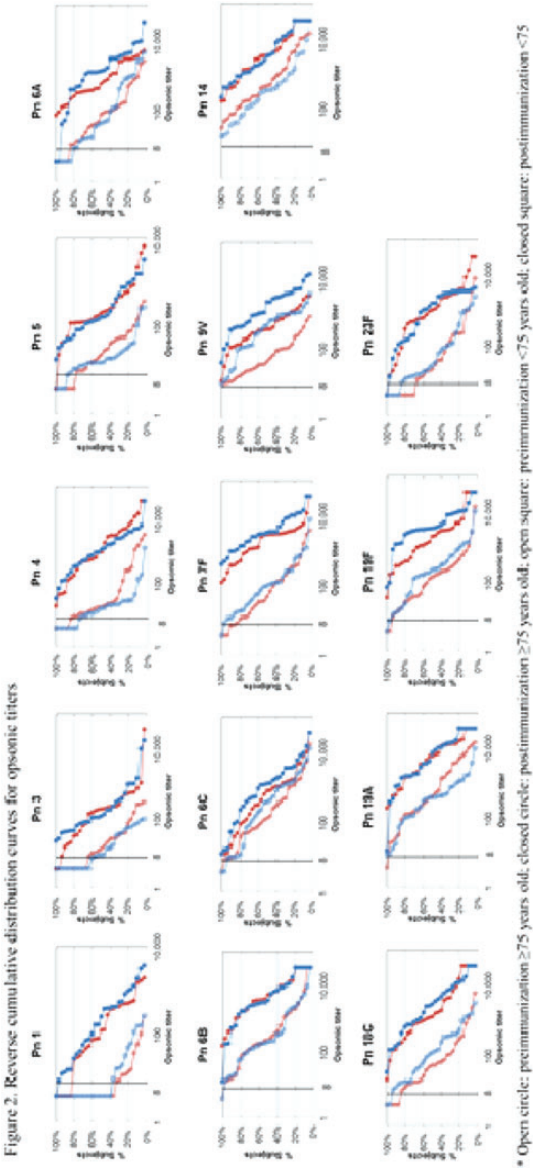
Geometric means for opsonization titers (<75 years old, N=30; ≥75 years old, N=30)

Serotypes	Age	Preimmunization GMT	Preimmunization 95%CI	Postimmunization GMT	Postimmunization 95%CI
1	<75	10	6.1-16.6	162	83.1-315.9
	≥75	8	5.0-11.2	94	46.1-191.9
3	<75	13	8.4-19.7	191	107.9-339.9
	≥75	17	10.2-28.7	132	68.2-255.6
4	<75	16	9.9-24.9	938	545.1-1,613.9
	≥75	34	16.6-69.5	1,032	502.5-2,121.2
5	<75	18	12.7-26.7	207	128.1-334.9
	≥75	23	14.2-37.0	225	131.9-384.7
6A	<75	64	28.4-145.9	1,036	485.8-2,207.7
	≥75	61	30.8-121.8	715	456.5-1,121.1

continued.

Serotypes	Age	Preimmunization GMT	Preimmunization 95%CI	Postimmunization GMT	Postimmunization 95%CI
6B	<75	280	130.3-600.1	3,732	1,934.0-7,202.3
	≥75	309	138-692	4,477	2,591.2-7,735.3
6C	<75	228	99.5-523.6	853	415.2-1,752.3
	≥75	161	75.9-341.1	450	215.3-940.6
7F	<75	93	50.4-173.1	3,443*	2,279.5-5,201.4
	≥75	63	31.5-127.5	1,719	1,094.9-2,700.1
9V	<75	282*	157.8-502.6	1,315*	792.0-2182.7
	≥75	53	33.7-83.9	369	231.3-589.0
14	<75	317	160.4-627.3	3,702	2091.6-6551.4
	≥75	593	307.6-1,144.1	3,461	1,928.1-6,211.4
18C	<75	103	53.6-199.5	2,268	1,187.5-4330.3
	≥75	52	26.1-104.9	1,611	787.2-3,297.7
19A	<75	273	149.3-497.4	4,333	2,266.4-8,285.2
	≥75	477	220.6-1,030.3	4,210	2,432.9-7,286.2
19F	<75	165	84.5-322.1	3,416	2,098.2-5,561.2
	≥75	104	54.0-202.1	1,598	867.0-2,944.3
23F	<75	46	22.7-92.3	696	353.3-1372.1
	≥75	36	16.2-78.9	790	359.4-1,735.1

* <75 vs ≥75, $p<0.05$



Conclusion. PPSV induces a functional immune response for 12 vaccine serotypes as well as 2 vaccine-related serotypes (6A, 6C). PPSV could offer protection against pneumococcal infection in the elderly.

Disclosures. **All authors:** No reported disclosures.

1093. Regional Differences in Adult Invasive Pneumococcal Disease (IPD) Rates in Tennessee (TN)

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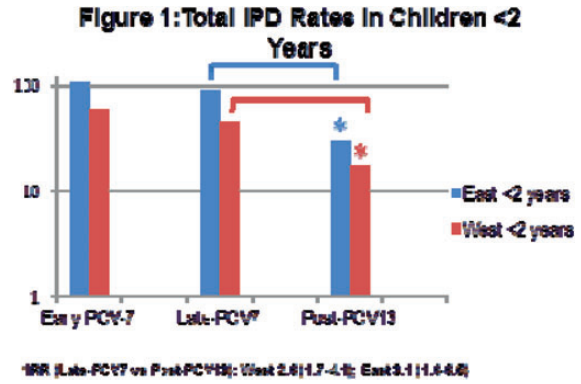
Background. Although pediatric IPD rates for TN have been reported, regional differences within TN have not been examined. We aimed to determine pediatric IPD rates in TN regions before and after PCV13 introduction (2010).

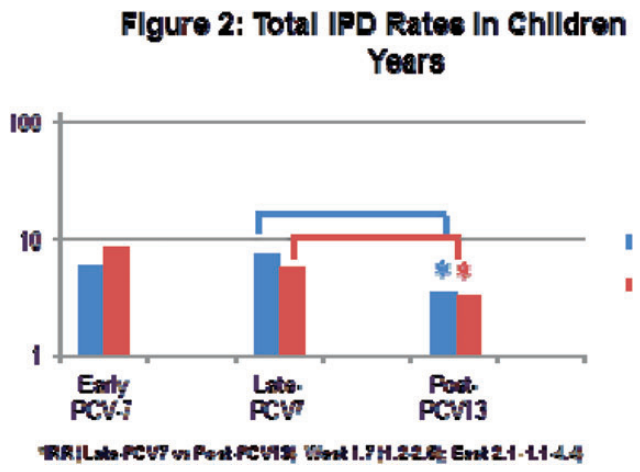
Methods. Active population and laboratory-based surveillance identified IPD cases from 11 TN counties from 2001-2012. Counties were separated into East (2) and West (9). For each case, trained nurses collected clinical data, and the isolates were sent to CDC for serotyping. IPD incidence was calculated using U.S. census data and was expressed per 100,000 person-years. Groups were stratified by age: <2 and 2-18 years (years). Incidence rates were calculated for 3 time periods: Early-PCV7 (2001-2004), Late-PCV7 (2005-2009), and Post-PCV13 (2011-2012). The transition year 2010 was excluded and incidence rate ratios (IRR) were calculated to compare East and West TN IPD rates.

Results. The table shows IPD rates by serotype, region, age group, and time period. Figures 1 and 2 illustrate the decline in IPD rates by time period and region.

Annual IPD RATE per 100,000 EARLY-PCV7 ERA	East <2 yrs	West <2 yrs	IRR (95% CI)	East 2-18 yrs	West 2-18 yrs	IRR (95% CI)
EARLY-PCV7 ERA						
PCV7	**33.8**	**18.9**	**1.8 (1.0-2.3)***	2.6	3.7	1.4 (0.8-2.4)
PCV13	**23.5**	**11.4**	**2.1 (1.0-3.9)***	1.3	1.4	1.1 (0.4-2.5)
Non-PCV	29.4	19.7	1.5 (0.8-2.5)	1.7	1.7	1.0 (0.5-2.1)
Not-typed	**19.1**	**7.5**	**2.6 (1.2-5.4)***	**1.9**	**0.5**	**3.5 (1.4-9.0)***
Total	**106**	**57.5**	**1.8 (1.4-2.5)***	**6.1**	**8.7**	**1.4 (1.0-2.0)***
LATE-PCV7 ERA						
PCV7	1.1	1.2	0.9 (0.02-9.4)	**0.9**	**0.3**	**3.6 (1.1-12)***
PCV13	**33.3**	**19.1**	**2.3 (1.5-3.5)***	2.3	2.7	0.9 (0.5-1.5)
Not-typed	**17.8**	**8.1**	**2.2 (1.1-4.2)***	**1.8**	**0.8**	**2.2 (1.0-4.7)***
Non-PCV	**27.7**	**16.4**	**1.7 (1.0-2.8)***	2.3	1.9	1.2 (0.6-2.1)
Total	**91.0**	**44.8**	**2.0 (1.5-2.7)***	7.4	5.7	1.3 (0.9-1.8)
POST-PCV13 ERA						
PCV7	0	0	NA	0.3	0	NA
PCV13	5.3	3.6	1.5 (0.1-9.0)	1.3	0.9	1.4 (0.3-5.0)
Not-typed	5.3	0.7	7.4 (0.4-434)	0.7	0.4	1.8 (0.2-1.0)
Non-PCV	18.7	13.1	1.4 (0.5-3.6)	1.3	2.1	0.6 (0.2-1.8)
Total	29.4	17.4	1.7 (0.8-3.6)	3.6	3.4	1.1 (0.5-2.1)

*CI excludes 1 indicating significant differences





Conclusion. Overall IPD rates Post-PCV13 decreased in all regions and age groups. IPD rates among children were significantly higher in East TN during the Early-PCV7 and Late-PCV7 period; however, those regional disparities were eliminated in the Post-PCV13 era.

Disclosures. **A. De St. Maurice**, Pfizer: Grant Investigator, Grant recipient **N. Halasa**, Pfizer: Grant Investigator, Salary **C. Fonnesbeck**, Pfizer: Grant Investigator, Research grant **W. Schaffner**, Pfizer, GlaxoSmithKline, Dynavax: Limited consulting fee, Consulting fee; Merck and Sanofi-Pasteur: Data safety monitoring board, Board membership benefits **C. G. Grijalva**, Pfizer: Consultant and Grant Investigator, Consulting fee and Research grant

1094. Pneumococcal Vaccination Coverage In The Elderly In The United States: Missed Opportunities Continue

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Session: 129. Vaccines: Pneumococcal
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Background. All elderly 65 years and older are recommended by the U.S. Advisory Committee on Immunization Practices to receive pneumococcal vaccination, with a coverage goal of 90% per the Healthy People 2020 objectives. This study aimed to provide real-world data on pneumococcal vaccination coverage and factors associated with receiving pneumococcal vaccination in a large U.S. managed care elderly population.

Methods. This retrospective observational cohort study included elderly who were 65 years and older from 2008 to 2011 with at least 2-year continuous enrollment in Humana administrative claims database. Descriptive and regression analyses were applied to examine their pneumococcal vaccination coverage.

Results. Among the 56,587 elderly cohort, 31.7% were healthy, 30.4% had one, 20.6% had two, and 17.3% had three or more medical conditions. On average, these elderly visited pharmacy 43.6 times, doctor office 21.6 times, outpatient hospital 6.4 times, inpatient hospital 0.6 times and emergency department 11.1 times during the follow up period. Nevertheless, the overall coverage of pneumococcal vaccination was 21.8% after 2 years. The majority of vaccination (77.2%) was received at doctor office and only 9.6% at pharmacy. There were no significant differences in health status and number of chronic medical conditions between the vaccinated and non-vaccinated. Elderly who had primary care physicians, who received influenza or zoster vaccination, or who had increased healthcare encounters were more likely to receive pneumococcal vaccination.

Conclusion. Pneumococcal vaccination coverage in US elderly was far below the Healthy People 2020 objective. Findings suggest missed opportunities continue and better interventions needed to improve pneumococcal vaccination during healthcare encounters for the elderly.

Disclosures. **H. K. Yang**, Merck: Employee, Salary **C. Shao**, Merck: Employee, Salary **J. D. Grabenstein**, Merck and Co., Inc.: Employee and Shareholder, Salary **D. Zhang**, Merck: Employee, Salary

1095. Invasive Pneumococcal Disease in Children with Underlying Conditions Has Higher Case Fatality and Unique Serotype Distribution

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Background. Despite the success of pneumococcal conjugate vaccine (PCV), children with underlying conditions remain at increased risk for IPD. We evaluated the serotype distributions and outcomes of IPD in children with selected underlying conditions.

Methods. Cases of IPD in Massachusetts (MA) children <18 years of age were identified via enhanced surveillance of *Streptococcus pneumoniae* (SP) isolates from sterile body sites. All SP isolates are submitted to the MA Department of Public Health and parents/physicians are interviewed for demographic and clinical data. Isolates are confirmed as SP, serotyped with Quelling reaction. Underlying conditions were classified as at-risk or high-risk for IPD per the 2012 Report of the Committee on Infectious Diseases. Logistic regression was used to compare IPD outcomes in children with and without comorbidities.

Results. Between April 2002 and April 2014, 1052 IPD cases were reported in MA children <18 years old; 22.1% had at least one comorbidity. Immunocompromising conditions (32.1%) and chronic respiratory diseases (22.5%) were most common. Children with comorbidities were older at the time of IPD diagnosis (median 54 months vs 23 months, $p < 0.001$), had higher hospitalization rates [OR 1.8 (95%CI 1.2-2.8)] and case fatality rates [OR 4.3 (95%CI 1.3-14.8] compared to children without known underlying conditions. Bacteremic pneumonia was observed more often in children with asthma (OR 3.2, 95% CI 1.5-6.9). Children with comorbidities were more likely to have IPD caused by serotypes with lower invasive capacity (i.e., 6C, 23A, 11A, 35B, 19F, 15A and 15BC) compared to children with no known underlying condition [45/142 (31.7%) vs 91/498 (18.3%), respectively] (p 0.001).

One fifth of IPD cases among Massachusetts children during the last decade had an underlying comorbidity; ~1/3 had an immunocompromising condition and ~1/5 had a chronic respiratory disease. Cases with underlying conditions were older, and had higher hospitalization and mortality rates compared to kids with no comorbidity. Children with comorbidities were more likely to have disease caused by serotypes with lesser invasive capacity. Further research is needed, specifically to evaluate additional strategies for prevention of IPD in children with comorbid conditions.

Disclosures. **S. I. Pelton**, GSK, Pfizer, Merck: Consultant and Investigator, Research grant

1096. Impact of Universal Pneumococcal Vaccination in Children in Argentina

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Background. Universal pneumococcal vaccination (UPV) in Argentina began in January 2012 using a 2 + 1 schedule using PCV13; vaccine coverage rate reached 50% in 2012, 75% in 2013. The objective was to evaluate the PCV13 impact 2 years after implementation.

Methods. Multicenter (5 hospitals), prospective study. Hospitalized children (CH) < 60 months with confirmed Invasive Pneumococcal Disease (IPD) and/or consolidated pneumonia (CP) (WHO criteria) during 5 years (prevaccine period: 2009-2011 and post-vaccine period: 2012-2013) were included. Patients (pts) with CP or empyema (E) confirmed by any other agent than *S.pneumoniae* were excluded. Demographic and clinical data were recorded.

Results. Pts included 1528; 1194(78%) CP, of 51/1120(4,5%) defined as Pneumococal-CP (P-CP); E:249(16.3%), 84/234(35.9%) of them confirmed as Pneumococal-E (PE) by culture; Meningitis 38(2,5%); other IPD:51(3,3%), including bacteremia, peritonitis, arthritis. The coverage rate in 2012 was 50% and 75% in 2013.

The decrease of IPD, CP and Pneumococcal Pulmonary Disease (PPD) (defined as P-CP + PE), after vaccination was:

		Global IPD		CP		PPD (P-CP + PE)	
Period	Average of Admissions	Average No cases	Rate* (95%CI)	Average No cases	Rate* (95%CI)	Average No. of cases	Rate* (95%CI)
2009-2011	34,038	56	16,5 (12,0 - 20,9)	300	88,1 (78,1 - 98,2)	37	10,9 (7,2-14,5)
2012-2013	32,952	28	8,5 (5,2 - 11,8)	147	44,6 (37,5 -52)	12,5	3,9 (1,6 - 6,2)
Decrease		-50%		-51,00%		-67,80%	
p		0,003		<0,0001		0,001	

* Rate/10,000 admissions

The number of admission decreased 738 (-65.1%) and admission to ICU also was reduced 45(-38.8%); in addition the decrease of number of invasive procedures avoided was: central line 30 (-37%), thoracoscopy: 20 (-83%), pleural drainage 82(-59.4%), pleural decortication 22(-48.9%); the average days of antibiotic use was reduced in 1154 (-55.08%) after vaccination program implementation

2. Hospitalizations by IPD and/or CP decreased 65.1% and requirement of ICU 38.8% after 2 years of UPV using PCV13 in our setting.

Conclusion. A rapid and statistically significant decrease of IPD, CP and PPD was observed after 2 years of UVP in Argentina with a non-high coverage rate.

Disclosures. **All authors:** No reported disclosures.

1097. Cost-Effectiveness of Pneumococcal Vaccines for Adults in the United States

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Background. Recently published efficacy data for 13-valent pneumococcal conjugate vaccine (PCV13) and 23-valent pneumococcal polysaccharide vaccine (PPV23) provides an opportunity to update cost-effectiveness analyses of the current ACIP recommendations as well as potential extensions of the ACIP recommendations.

Methods. We applied an economic model in a US cohort of 50-year old adults to evaluate the cost-effectiveness of three pneumococcal vaccination strategies. Consistent with ACIP recommendations, the cohort was divided into 3 target vaccination groups at baseline: healthy, immunocompetent-with-comorbidities, and immunocompromised. Vaccination strategies included the 2012 ACIP recommendations (S1) and two other vaccination strategies that either replace PPV23 with PCV13 for healthy and immunocompetent-with-comorbidities adults (S2), or extend the sequential PCV13-then-PPV23 strategy to the three target vaccination groups (S3). Vaccine effectiveness was based on recently published data (table). Sensitivity analyses were conducted to examine the impact of varying assumptions on vaccine effectiveness and the duration of vaccine protection.

Results. The most efficient strategy was the 2012 ACIP recommendations (S1), with an ICER of $22,793 per QALY gained compared to no vaccination. Replacing PPV23 with PCV13 for healthy and immunocompetent-with-comorbidities adults (S3) had an ICER of $195,843 per QALY gained. However, adopting a sequential PCV13 -PPV23 strategy for all three groups (S2) was both less effective and less efficient than the S3 strategy. Sensitivity analyses indicated that these results were highly influenced by changes in vaccine efficacy estimates and the duration of vaccine protection.

Pneumococcal vaccine serotype-specific effectiveness estimates for pneumococcal disease observed over follow up period

Data Source	Vaccine	Follow-up period (y)	Vaccine Effectiveness: Non-Bacteremic Pneumococcal Pneumonia (NBPP)	Vaccine Effectiveness: Invasive Pneumococcal Disease (IPD)
CAPITA (2014)	PCV13	4	45%	75%
Ochoa-Gondar (2014)	PPV23	3	-	74%
Cochrane Review (2013)	PPV23	3	48%	-

Conclusion. The 2012 ACIP recommendations appear to be a cost-effective vaccination policy given recently published vaccine efficacy data.

Disclosures. **H. K. Yang**, Merck: Employee, Salary **J. D. Grabenstein**, Merck and Co., Inc.: Employee and Shareholder, Salary **E. J. Dasbach**, Merck: Employee, Salary

1098. The Immunogenicity of PCV13 compared to PPSV23 in Immunocompetent Older Adults with Stable High Risk Conditions

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Background. Predisposing factors for serious pneumococcal community-acquired pneumonia and invasive pneumococcal disease include common chronic medical conditions such as cardiovascular and pulmonary disease as well as diabetes mellitus. Previous studies of the immunogenicity of PCV13 have shown that the vaccine elicits robust immune responses in populations of immunocompetent adults 50 years and over that included healthy adults as well as those with stable high risk conditions. In this evaluation, we compared the functional immune responses of study participants with cardiovascular, pulmonary disease or diabetes mellitus after PCV13 and PPSV23 administration.

Methods. We evaluated two studies that enrolled pneumococcal vaccine naïve adults aged 60-64 years. In these studies, serotype-specific functional antibody titers 1 month after vaccination with PCV13 or PPSV23 were determined by opsonophagocytic activity (OPA) assays. To increase sample size OPA data from study participants with stable cardiovascular disease, pulmonary disease, or diabetes mellitus were pooled from both studies and OPA geometric mean titers (GMTs) after PCV13 and PPSV23 were descriptively compared.

Results. The clinical studies were not stratified for risk conditions at enrolment, and numbers of subjects varied. In each high risk group OPA GMTs increased from before to after PCV13 vaccination for all serotypes. PCV13 elicited numerically higher OPA GMTs compared to PPSV23 for the majority of serotypes and statistically significantly higher OPA GMTs for 4 (cardiovascular disease), 7 (diabetes mellitus), and 9 (pulmonary disease) of 12 serotypes common to both vaccines and for serotype 6A unique to PCV13. High-risk subjects exhibited similar OPA responses to PCV13 compared to non-high risk subjects.

Conclusion. In adults 60-64 years of age with underlying stable cardiovascular disease, pulmonary disease or diabetes mellitus, PCV13 induces higher functional antibody responses than PPSV23 for the majority of serotypes, and similar responses compared to non-high risk subjects, indicating that vaccinating these immunocompetent high-risk adults with PCV13 likely results in improved benefits to those vaccinated with PPSV23, for serotypes in common and 6A.

Disclosures. **B. Schmoele-Thoma**, Pfizer: Employee, Salary and stock, stock options **L. A. Jackson**, Pfizer: Research Contractor, Research support and Travel **R. N. Greenberg**, Pfizer: Research Contractor, Research grant **R. Frenck**, Pfizer: Research Contractor, Received funds for clinical trials; GSK: Research Contractor, Received funds for clinical trials and am chairing DSMB for upcoming vaccine trial; Ligocyte: Research Contractor, Received funds for clinical trials **A. Gurtman**, Pfizer: Employee, Salary **V. Sundaraiyer**, Pfizer: Employee of a CRO contracted to work on Pfizer projects, Service fee **W. Gruber**, Pfizer, Inc.: Employee and Shareholder, Salary and Stock and Stock Options **D. A. Scott**, Pfizer: Employee, Salary and Stock, stock options

1099. 13-valent Pneumococcal Conjugate Vaccine Efficacy is Declining with Old Age: Results from an Exploratory Analysis of the CAPiTA Trial

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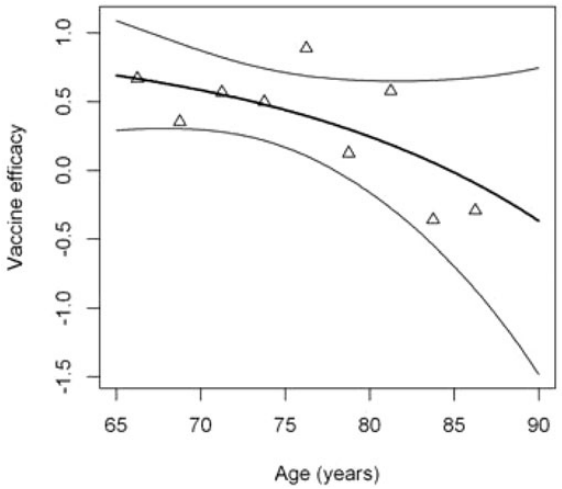
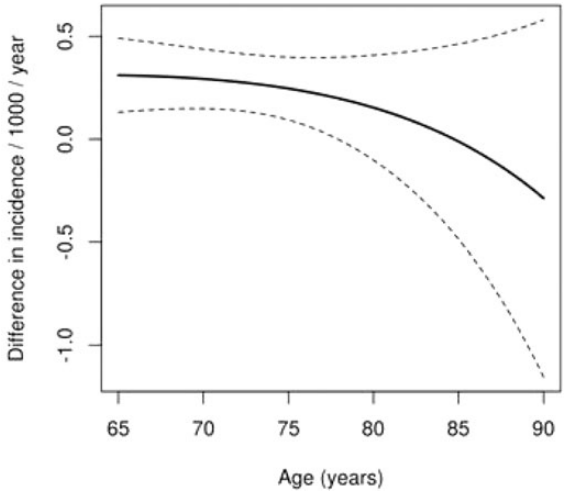
Background. Immunogenicity of vaccines may be impaired in adults of high age. We retrospectively analyzed the impact of age on the efficacy of 13-valent pneumococcal conjugate vaccine (PCV13) in the prevention of vaccine-type community-acquired pneumonia (VT-CAP) in healthy subjects aged 65 years and older using data from the CAPiTA trial.



Model derived vaccine efficacy



Absolute reduction of VT-CAP incidence

Methods. The CAPiTA trial was a randomized controlled study where 84,496 subjects aged 65 and over were randomized to PCV13 or placebo. The effects of vaccination, age and a vaccine-age interaction term were assessed using Cox proportional hazard models, with the first episode of X-ray confirmed VT-CAP as the outcome. Relative vaccine efficacy (VE) by age was calculated as 1 – hazard ratio (HR) and absolute reduction of VT-CAP was calculated from the model-predicted incidences.

Results. The median age was 71 years (IQR 68-76), and 47,252 (56%) were male. During a mean follow-up period of 4 years, 139 first episodes of VT-CAP were recorded. The vaccine-age interaction was statistically significant (p = 0.036), with the HR of vaccination increasing with 6% per year (table). The model-predicted VE declined from 69% (95%CI 29-100%) in 65 year olds to 44% (17-71%) in 75 year olds (Figure 1). Absolute reduction of VT-CAP incidence was declining less rapidly (Figure 2). There were too few cases in subjects above 80 years of age to determine VE in this age group. In sensitivity analysis with subjects aged < 85 years, which had 130 episodes of VT-CAP, the interaction effect was attenuated to 3.6% per year and not statistically significant, suggesting that the size of the interaction effect may have been overestimated caused by the few VT-CAP episodes in the highest age group in PCV13 vaccinated subjects.

Vaccine-age interaction

	HR (95%CI)
vaccine	0.309 (0.162;0.589)
age - 65	1.022 (0.987;1.059)
vaccine * (age - 65)	1.061 (1.004;1.122)

Conclusion. The model predicted a decrease in VE with increasing age. Since this trial was not designed to study vaccine-age interaction, and number of cases in the oldest age groups were too few to draw VE conclusions, observational studies should be considered to evaluate this question further. These findings may be relevant for policy makers, vaccination program managers, and health workers.

Disclosures. **C. Webber**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **B. Schmoele-Thoma**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **S. D. Patterson**, Pfizer Vaccines Clinical Research: Employee, Salary **W. Gruber**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **D. E. Grobbee**, Pfizer Vaccines Clinical Research: Investigator, Research grant **M. Bonten**, Pfizer Vaccines Clinical Research: Investigator, Research grant

1100. Notable Serotype Replacement of Invasive *Streptococcus pneumoniae* in Kagoshima, Japan, after the Sequential Introduction of 7-valent and 13-valent Pneumococcal Conjugate Vaccines

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Background. Heptavalent pneumococcal conjugate vaccine (PCV7) was introduced in Japan for voluntary and routine immunization in February 2010 and April 2013, respectively. It was completely replaced by PCV13 in November 2013. The vaccination rate of PCV7/13 in 2013 is estimated to be approximately 90% in our district. Although ACIP recommended a single supplemental dose for all children aged 14-59 months who have received 4 doses of PCV7 or another age-appropriate, it was not implemented as the routine immunization program in Japan. This study evaluates annual changes in the incidence of invasive pneumococcal disease (IPD) and the distribution of serotypes in Kagoshima, Japan.

Methods. Prospective, population-based, active surveillance of IPD in children was performed in Kagoshima, Japan, from 2008 through 2014. Pneumococci isolated from blood or cerebrospinal fluid of IPD patients were serotyped using the conventional Quellung reaction.

Results. Overall, 62 IPD cases were recorded. The annual total incidences of IPD in children < 5 years of age per 100,000 population were as follows: 2008, 10.7; 2009, 9.3; 2010, 14.7; 2011, 12.0; 2012, 6.7; and 2013, 16.0. The tentative incidence in 2014 is 40.0 (10 cases) as of end-April. Incidence of IPD caused by PCV7 serotypes during the period 2010-2011 vs 2013-2014 April decreased by 88%. On the other hand, incidence of IPD caused by PCV13 additional serotypes drastically increased: 2008-2009, 0; 2010-2012, 2.2; 2013-2014, 12.0. Serotype 19A accounted for 83.3% (15/18) of PCV13 serotypes. Furthermore, incidence of IPD caused by non-PCV13 serotypes also rapidly increased: 2008-2012, 1.3; 2013-2014, 8.0. Serotype 24F accounted for 50.0% (4/8) of non-PCV13 serotypes in 2013/2014.

Conclusion. The incidence of IPD in children < 5 years of age declined in 2012 after the introduction of PCV7; however, it increased prominently in 2013/2014, although PCV7 was replaced by PCV13. The increase is due to the notable serotype replacement of invasive *Streptococcus pneumoniae* and partly due to the low vaccination rate of PCV13 supplemental dose for children who have received 4 doses of PCV7. Implementation of the supplemental dose of PCV13 in Japan and a new global vaccine strategy targeting non-PCV13 serotypes are needed to prevent and control IPD.

Disclosures. **J. Nishi**, Pfizer Japan Inc.: lecturer, lecturer's fee

1101. The Gap Widens: Invasive Pneumococcal Serotype Distribution among Adults

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Background. Indirect effects of routine pediatric use of pneumococcal conjugate vaccines (PCVs) influence which serotypes cause adult invasive pneumococcal disease (IPD). We sought to describe how those changes correspond to the proportion of IPD cases targeted by the 23-valent pneumococcal polysaccharide vaccine (PPSV23) or PCV13, using the most recent data available.

Methods. We reviewed PubMed and national websites for reports from 2003 to 2014 describing the proportions and incidence of adult IPD matching PPSV23 or PCV13. Eligible studies came from settings with widespread uptake of PCV10 or PCV13 among children, involved >= 150 adult isolates, typed for >= 20 serotypes, and excluded cases <2 years of age.

Results. Eligible studies described Australia, Austria, Canada, Denmark, England, France, Germany, Ireland, New Zealand, Norway, Portugal, and the USA. The European CDC reported a composite measure for 23 countries. For adult IPD serotype distribution before pediatric PCV7 use, the proportion of IPD isolates matching the 23-serotype bundle was 88.4% and 74.8% for the 13-serotype bundle, with a median differential between the two bundles of 16.3%. In the most recent analyses, after widespread pediatric PCV uptake, IPD proportions were 77.1% for the 23-serotype bundle and 49.2% for the 13-serotype bundle, with a median differential of 28.8%. Germane articles describing serotype-specific adult IPD incidence rates from settings with widespread pediatric adoption of PCV10 or PCV13 were not yet available on May 1, 2014.

Conclusion. The differences between the proportions of IPD cases due to serotypes included in PPSV23 vs PCV13 have widened further, consistently across multiple countries, following extensive pediatric use of PCV10 or PCV13. Clinicians and policy-makers should consider the increasing proportion of adult IPD cases caused by serotypes targeted by PPSV23 when making vaccine decisions.

Disclosures. **J. D. Grabenstein**, Merck and Co., Inc.: Employee and Shareholder, Salary **M. A. Kohn**, Merck and Co., Inc.: Employee and Shareholder, Salary **D. J. Weber**, Merck and Co., Inc.: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium

1102. Immunogenicity and Safety of a Second Administration of 13-Valent Pneumococcal Conjugate Vaccine Five Years after Initial Vaccination in Adults 50 Years and Older

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Immunogenicity and Safety of a Second Administration of 13-Valent Pneumococcal Conjugate Vaccine Five Years after Initial Vaccination in Adults 50 Years and Older

Background. Adults ≥50 years are at increased risk for invasive disease and pneumonia caused by S pneumoniae. Previously, we reported a study assessing simultaneous administration of 13-valent pneumococcal conjugate vaccine (PCV13) and trivalent inactivated influenza vaccine (TIV). We now present data on revaccination with PCV13 five years after initial vaccination.

Methods. This was a phase 3, randomized trial. Pneumococcal vaccine-naive subjects, 50–59 years old, were vaccinated with PCV13 and TIV, given concomitantly or 1 month apart. All were revaccinated with PCV13 five years after initial vaccination. Blood samples were obtained before and approximately 1 month after each vaccination. Anti-pneumococcal polysaccharide immunoglobulin G (IgG) geometric mean concentrations (GMCs) and opsonophagocytic activity (OPA) titers (GMTs) were determined. Local reactions and systemic events were collected for 14 days after revaccination, and adverse events (AEs) for 6 months. Deaths were recorded throughout the study.

Results. 727 of the 1116 randomized subjects were revaccinated at year 5; 712 completed the 6-month follow-up. Mean age at revaccination was 59.8 ±2.8 years. For all serotypes, IgG GMCs (except serotype 3) and OPA GMTs before revaccination with PCV13 had declined in the 5 years since initial vaccination, but remained significantly higher than levels before initial vaccination. OPA GMTs and IgG

GMCs significantly increased from before to 1 month after revaccination with PCV13. OPA GMTs (Table 1) and IgG GMCs (Table 2) were generally comparable or higher 1 month after revaccination compared to levels 1 month after initial PCV13 vaccination. Local reactions were mostly mild. Fever was reported by <4% of subjects; all <39.0°C. AEs were reported by <5% of subjects in the month after revaccination and <1% up to 6 months after revaccination. No serious AEs were vaccine-related. Seven deaths occurred in years 1–5, all before revaccination, none were vaccine-related.

Table 1. OPA GMTs 1 Month After PCV13 Vaccinations (N=368-390)

Serotype	After Initial PCV13 Vaccination (Year 0)	After PCV13 Revaccination (Year 5)	GMFR	(95% CI)
1	217	183	0.8	(0.70, 1.02)
3	69	61	0.9	(0.79, 1.01)
4	1905	1589	0.8	(0.73, 0.95)
5	129	300	2.3	(1.92, 2.80)
6A	2779	4196	1.5	(1.31, 1.74)
6B	3089	3541	1.1	(1.00, 1.31)
7F	2196	1768	0.8	(0.67, 0.96)
9V	1343	1768	1.3	(1.08, 1.60)
14	1169	1135	1.0	(0.83, 1.13)
18C	1728	1772	1.0	(0.86, 1.22)
19A	879	858	1.0	(0.88, 1.08)
19F	472	1139	2.4	(2.01, 2.90)
23F	494	1955	4.0	(3.26, 4.80)

CI=Confidence Interval; GMFR=geometric mean fold rise; GMT=geometric mean titer; OPA=opsonophagocytic activity; PCV13=13-valent pneumococcal conjugate vaccine.

Table 2. IgG GMCs 1 Month After PCV13 Vaccinations (N=378-391)

Serotype	After Initial PCV13 Vaccination (Year 0)	After PCV13 Revaccination (Year 5)	GMFR	(95% CI)
1	4.77	5.88	1.23	(1.07, 1.42)
3	1.26	0.74	0.59	(0.54, 0.64)
4	2.9	5.13	1.77	(1.56, 2.01)
5	6.52	8.25	1.26	(1.14, 1.41)
6A	6.13	13.52	2.21	(1.97, 2.47)
6B	8.87	20.7	2.33	(2.08, 2.61)
7F	9.24	8.4	0.91	(0.81, 1.02)
9V	5.83	6.07	1.04	(0.95, 1.14)
14	11.98	15.04	1.25	(1.10, 1.43)
18C	11.64	8.25	0.71	(0.64, 0.79)
19A	17.43	18.48	1.06	(0.96, 1.17)
19F	6.56	18.26	2.78	(2.44, 3.17)
23F	8.03	20.17	2.51	(2.23, 2.83)

CI=Confidence Interval; GMC=geometric mean concentration; GMFR=geometric mean fold rise; IgG=immunoglobulin G; PCV13=13-valent pneumococcal conjugate vaccine.

Conclusion. PCV13 revaccination 5 years after initial PCV13 vaccination in pneumococcal-naive 50–59 year-olds elicited generally comparable or higher antibody responses for all serotypes compared to initial PCV13 vaccination, and demonstrated an acceptable safety profile

Disclosures. **R. W. Frenck Jr.**, Pfizer: Investigator, Funds for clinical trials; GSK: Chairing DSMB for upcoming trial and Investigator, Received funds for clinical trials; Ligocyte (now Takeda): Investigator, Received funds for clinical trials **A. Fiquet**, Pfizer: Employee, Salary and stock options **A. Gurtman**, Pfizer: Employee, Salary **J. Rubino**, Pfizer: Investigator and Shareholder, Research grant **W. Smith**, Volunteer Research Group: Investigator, payment to conduct Clinical Research Trials **V. Sundaraiyer**, Pfizer: Employee of a CRO contracted to work on Pfizer projects, Service fee **M. Sidhu**, Pfizer: Employee, Salary **E. A. Emini**, Pfizer: Employee and Shareholder, Salary **W. C. Gruber**, Pfizer: Employee and Shareholder, Salary **D. A. Scott**, Pfizer: Employee and Shareholder, Salary **B. Schmoele-Thoma**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary

1103. Immunogenicity of 13-valent conjugate pneumococcal vaccine in patients 50 years or older with end stage renal disease on dialysis

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Background. The burden of pneumococcal disease in patients (pts) with end stage renal disease (ESRD) is high, with *S. pneumoniae* accounting for more than half of the reported cases of pneumonia in dialysis pts. A diminished immune response to pneumococcal polysaccharide vaccine can be observed in pts with chronic renal failure requiring dialysis. The response to 13-valent conjugate pneumococcal polysaccharide vaccine (PCV13) has not been well studied in patients with ESRD on dialysis.

Methods. Pts were recruited at Lansing, MI area dialysis centers. Eligible pts ≥ 50years of age with ESRD on dialysis, who have not received pneumococcal vaccination in the last 5 years, were given a single dose of 0.5-mL of PCV13 vaccine. Blood samples for serum antibody titers against pneumococcal capsular polysaccharide 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F was measured at baseline and at 2 months post-vaccination. Response to vaccine was defined as a ≥ 2-fold increase in antibody concentration from baseline and an absolute post-vaccination value of at least 1 µg/ml.

Results. Twenty four pts consented to participate in the study. The mean age of pts was 64.5 years (range 50-84 years). Thirteen (54%) pts were female. Antibody response to PCV13 is shown in the table. Vaccine response to at least 1 serotype was seen in 23/24 (95.8%) pts. Response to serotype 6B was seen in 17/24(71%) pts, while 66.7% (16/24) responded to serotypes 14, 19F and 23F each. Nine (37.5%) pts responded to ≥ 10 vaccine serotypes. Local reaction was seen in 2/24 (8.3%)pts.

Geometric mean titers (GMT) (95% CI) (n=24)

Serotype	Pre-vaccination GMT (µg/ml)	2 months post-vaccination GMT(µg/ml)	p-value
1	0.87 (0.38-1.35)	3.07 (2.49- 3.64)	0.002
3	0.42 (0.15- 0.68)	1.34 (0.67- 2.0)	0.03
4	0.44 (0.15- 0.72)	0.79 (0.34- 1.23)	0.025
5	0.85 (0.33- 1.36)	5.34 (4.59- 6.08)	0.008
6A	0.5 (0.26- 0.73)	4.30 (3.44- 5.15)	0.008
14	1.6 (0.77- 2.42)	7.79 (7.01- 8.56)	0.049
19F	1.12 (0.61- 1.62)	5.83 (5.24- 6.41)	0.025
23F	0.53 (0.17- 0.88)	4.24 (3.47- 5.0)	0.009
6B	0. 49 (0.10- 0.87)	4.04 (3.18- 4.89)	0.01
7F	0.86 (0.36- 1.35)	3.41 (2.72- 4.09)	0.026
18C	0.96 (0.44- 1.47)	5.46 (4.83- 6.08)	0.01
19A	1.41 (0.70- 2.11)	6.16 (5.42- 6.89)	0.028
9V	0.89 (0.46- 1.31)	2.23 (1.67- 2.78)	0.029

Conclusion. Response to vaccination with PCV13 was noted in most pts with ESRD on dialysis. Several pts showed response to multiple vaccine serotypes. Vaccine was well tolerated.

Disclosures. **All authors:** No reported disclosures.

1104. 13-Valent Pneumococcal Conjugate Vaccine (PCV13) Immunogenicity in the Community Acquired Pneumonia Immunization Trial In Adults (CAPiTA)

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Background. The CAPiTA study, which was a randomized, double-blind clinical trial in 84,496 participants 65 years of age and older in the Netherlands demonstrated efficacy against first episodes of vaccine type (VT) community acquired pneumonia and first episodes of VT-IPD. Results of the primary and secondary endpoints have been previously reported.

Methods. A subset of the subjects (2,011) was enrolled utilizing home based visits in a single region in the Netherlands. Blood samples for immunogenicity analysis were taken at baseline before vaccination, one month, 12 months and 24 months after vaccination. Serotype specific opsonophagocytic activity (OPA) titers and anticapsular polysaccharide immunoglobulin G (IgG) concentrations (µg/mL) were measured at each of these time points for all PCV13 serotypes and compared to placebo.

Results. For both OPA and IgG, there were significant increases in antibody levels for all serotypes one month after vaccination compared to before vaccination with PCV13. One month after vaccination the ratios for OPA geometric mean titers (GMTs) of PCV13 to placebo ranged from 4.4 (serotype 9V) to 62.6 (serotype 4); after 12 months the ratios ranged from 2.2 (serotype 9V) to 13.9 (serotype 4) and after 24 months from 1.6 (serotype 9V) to 8.0 (serotype 4).

One month after vaccination the ratios for IgG geometric mean concentrations (GMCs) of PCV13 to placebo ranged from 2.97 (serotype 3) to 12.12 (serotype 18C); after 12 months the ratios ranged from 1.66 (serotype 3) to 5.72 (serotype 18C) and after 24 months from 1.56 (serotype 3) to 4.76 (serotype 18C).

The ratios for both OPA GMTs and IgG GMCs in the age subgroups ≥65 to <70 years; ≥70 to <80 years and ≥80 years followed a similar pattern indicating that measurable antibody responses extended out at least two years after vaccination for all age groups.

Conclusion. The observed immune response data support the demonstrated efficacy of PCV13 against VT-CAP and VT-IPD in adults 65 years and older. Both binding IgG antibodies and functional OPA antibodies persisted at least two years after vaccination at levels above baseline. (Funded by Pfizer, Inc.; ClinicalTrials.govnumber NCT00744263.)

Disclosures. **E. A. M. Sanders**, Pfizer: Grant Investigator and Scientific Advisor, Consulting fee, Educational grant, Research grant and Research support; GSK: Grant Investigator and Scientific Advisor, Consulting fee, Research grant and Research support **C. Webber**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **M. Patton**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **D. A. Scott**, Pfizer Vaccines Clinical Research: Employee and Shareholder, Salary **M. Sidhu**, Pfizer: Employee and Shareholder, Salary **W. Drews**, Pfizer: Independent Contractor, Consulting fee **M. Bonten**, Pfizer Vaccines Clinical Research: Investigator, Research grant

1105. Chronic Kidney Disease and Invasive Pneumococcal Disease in Adults

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Background. Despite widespread vaccination, *Streptococcus pneumoniae* (SPN) continues to cause invasive pneumococcal disease (IPD), particularly in the immunocompromised. Current recommendations in the United States target the immunocompromised for use of the 13-valent conjugate vaccine. We examined the impact of chronic kidney disease on the development of invasive pneumococcal disease (IPD).

Methods. Kaiser Permanente Northern California (KPNC) is an integrated health care plan serving approximately 3.3 million members. IPD cases (defined as cultured from a normally sterile body site) were identified from the KPNC Lab system from May 2005 - April 2013. We used diagnostic codes from the electronic medical record to identify chronic kidney disease (CKD) as CKD3 (Glomerular filtration rate [GFR] 30-59 ml/minute), CKD4 (GFR 15-29 ml/minute) and CKD5,6 (GFR <15 or on dialysis). We estimated rates of IPD in KPNC members with CKD and compared to rates of IPD in the general membership. We used KPNC registries to identify members with asthma, coronary artery disease (CAD), diabetes (DM), stroke, heart failure (HF), and HIV infection for the analysis. We ran a single multivariate poisson regression model to estimate the incidence of IPD, and included age, race and each condition as predictor variables.

Results. The unadjusted relative risk of IPD in members of all ages with CKD compared to the general membership was 4.1 for CKD3; 5.7 for CKD4; and 15.1 for CKD5,6. After controlling for multiple underlying factors in the multivariate analysis, CKD3 was associated with a 2.29 (95% CI 1.63-3.19) RR for IPD; and CKD 4,5 with a 7.10 RR (3.95-12.23) (preliminary analysis).

Conclusion. In adults, chronic kidney disease is strongly associated with an increased risk of IPD. This has important implications for recommendations on who should receive conjugated pneumococcal vaccines.

Disclosures. **R. Baxter**, GSK: Investigator, Research grant; Merck: Investigator, Research grant; Pfizer: Investigator, Research grant; Novartis: Investigator, Research grant; MedImmune: Investigator, Research grant; Sanofi Pasteur: Investigator, Research grant **N. P. Klein**, GSK: Investigator, Research grant; Merck: Investigator, Research grant; Pfizer: Investigator, Research grant; Novartis: Investigator, Research grant; MedImmune: Investigator, Research grant; Sanofi Pasteur: Investigator, Research grant **S. Pelton**, Pfizer, Inc.: Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient; GSK bio: Scientific Advisor, Consulting fee **B. Atkinson**, Pfizer: Employee and Shareholder, Salary and Stock options **C. Paap**, Pfizer: Employee and Shareholder, Salary **D. Hewlett Jr.**, Pfizer: Employee and Shareholder, Salary **V. Snow**, Pfizer Vaccines: Employee, Salary

1106. Modeling of nasopharyngeal acquisition as a function of anti-capsular serum antibody concentrations and of ethnicity after vaccination with pneumococcal conjugate vaccines (PCVs)

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Background. A large 13- and 7-valent PCV study in Israel provided sufficient nasopharyngeal (NP-) acquisition and immunogenicity data for the 7 common serotypes (4, 6B, 9V, 14, 18C, 19F, 23F) and PCV7 cross-reacting serotype 6A (which is in PCV13) to further investigate the reported correlation between NP-acquisition and serum IgG levels, and the impact of ethnicity.

Methods. Anticapsular IgG concentrations measured one month after 3 PCV7/PCV13 doses (age = 7 months); and NP-acquisition collected at ages 7, 12, 13, 18 and 24 months enabled serotype specific analyses of 1410–1530 subjects. A logistic regression model assessed the rate of new acquisitions as a function of the logarithm of IgG concentrations, and was then adjusted by ethnicity.

Results. New NP-acquisition rates decreased as IgG concentrations increased for all studied serotypes ($p < 0.001$ for 6A, 14, 23F; $p = 0.010$ for 6B; $p = 0.089$ for 19F; Figure 1). There were significant differences in the model between Bedouin and Jewish populations for all serotypes (covariate p-value, ≤0.007) except for serotype 4, where acquisition was low (9/1530). Despite higher acquisition rates in Bedouin children than in Jewish children, serotype-specific immune responses were similar across ethnic groups. Decrease in rates of NP-acquisition by increasing IgG concentrations within each ethnic group, seemed similar across the groups for most serotypes (Figure 2).

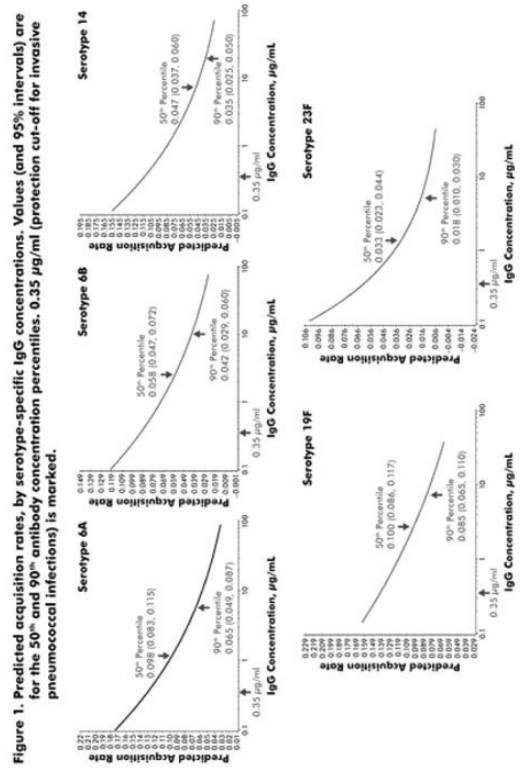

Figure 1. Predicted acquisition rates, by serotype-specific IgG concentrations. Values (and 95% intervals) are for the 50th and 90th antibody concentration percentiles. 0.35 µg/ml (protection cut-off for invasive pneumococcal infections) is marked.

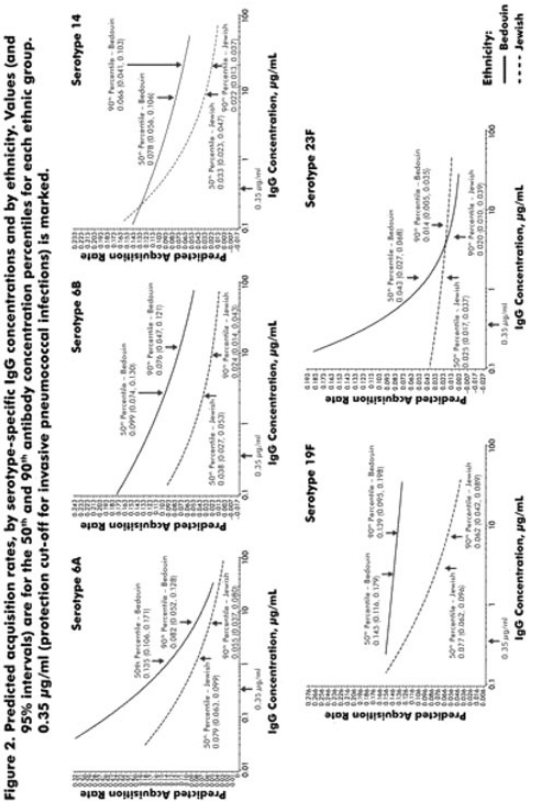

Figure 2. Predicted acquisition rates, by serotype-specific IgG concentrations and by ethnicity. Values (and 95% intervals) are for the 50th and 90th antibody concentration percentiles for each ethnic group. 0.35 µg/ml (protection cut-off for invasive pneumococcal infections) is marked.

Conclusion. NP-acquisition decreased with increasing anti-capsular serum IgG for all common serotypes and serotype 6A. Despite different NP-acquisition rates observed between the ethnic groups, the dynamics of NP-acquisition reduction by increasing IgG concentrations were similar in the majority of serotypes studied, and seemed similar across ethnic groups.

Disclosures. **R. Dagan**, Pfizer: Consultant and Speaker's Bureau, Grant recipient; MSD: Consultant, Grant recipient; GSK: Consultant and Speaker's Bureau, Speaker honorarium **C. Juergens**, Pfizer: Employee and Shareholder, Salary **J. Trammel**, inVentiv Health Clinical: employee of CRO contracted by Pfizer to perform the analyses for this study, Salary **S. D. Patterson**, Pfizer Vaccines Clinical Research: Employee, Salary **W. C. Gruber**, Pfizer: Employee and Shareholder, Salary **D. A. Scott**, Pfizer: Employee and Shareholder, Salary

1107. Could Disparities in Childhood PCV Adherence Become Disparities in Pneumococcal Disease Rates Under a Reduced Schedule?

John M. Mclaughlin, PhD, MSPH; Verna L. Welch, PhD, MPH; Edward Power, PhD, MBA; Gregg Sylvester, MD, MPH; Pfizer Vaccines, Collegeville, PA

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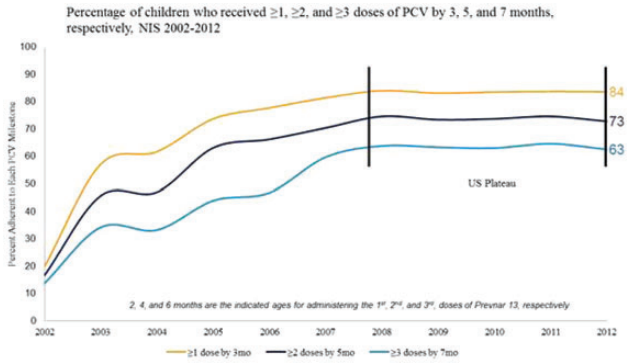
Background. ACIP recommends that PCV13 be given to children as a 3-dose (d) primary series at 2, 4, and 6 months (m) with a booster dose at 12-15m. This 4d (3 + 1) schedule is associated with remarkable declines in vaccine-type childhood pneumococcal disease. Recently, however, ACIP discussed reducing this 4d schedule to a 3d schedule—forgoing either the 6m or 12-15m dose. While this 3d schedule has been a success in other developed countries that have national immunization programs with high levels of adherence, childhood PCV adherence rates in the US are lower. Moreover, US PCV adherence appears to have plateaued, and significant racial and socioeconomic disparity still exists.

Methods. Data from the 2002-2012 National Immunization Survey (NIS) and 2013 IMS Health database were evaluated to assess adherence to the ACIP-recommended US childhood PCV immunization schedule.

Results. NIS data showed that adherence decreased at each subsequent primary series milestone (Figure). At 19-35m, the overall proportion of US children receiving 4 doses of PCV increased from 54% in 2005 to 82% (only 75% at age 19m) in 2012. Rates varied by state and city with Indiana and New York City reporting the lowest 19-35m, 4d PCV adherence (73%) in 2012. According to IMS data, US 4d 2013 PCV adherence rates remained <80% at 24m, with lower rates for children aged 12-15m (12m: 45%; 15m: 66%; 18m: 74%; 24m: 77%). In 2012, compared to whites, 19-35m, 4d PCV adherence for African American children was worse (84% vs 77%). Similarly, compared to those at or above poverty, those below poverty had worse adherence (85% vs 77%).



Conclusion. A recent cost-effectiveness study concluded that a US switch to a 3d PCV schedule would have considerable cost savings, but would likely result in more childhood disease. The study also stressed that any dose reduction must be coupled with a significant increase in PCV adherence. This suggestion appears unrealistic given that US adherence rates have leveled-off since 2008. Finally, more assurance is needed that, under a reduced schedule, racial, socioeconomic, and geographic disparities in PCV coverage will not correspond with disadvantaging poor or minority children in terms of disease burden. This consideration remains a dilemma for both the policymaker and clinician.

Disclosures. **J. M. Mclaughlin**, Pfizer Inc.: Employee, Salary **V. L. Welch**, Pfizer Inc.: Employee, Salary **E. Power**, Pfizer Inc.: Employee, Salary **G. Sylvester**, Pfizer Inc.: Employee, Salary

1108. Timing of Information-Seeking about Childhood Vaccines for Pregnant and Recently-Delivered Women

Sean O'leary, MD, MPH[1]; Sarah Brewer, MPA[1]; Jennifer Pyrzanowski, MSPH[1]; Juliana Barnard, MA[1]; Anna Furniss, MS[1]; Jason Glanz, PhD[2]; Amanda Dempsey, MD, PhD, MPH[1]; [1]The Children's Outcomes Research Program, Children's Hospital Colorado, Aurora, CO; [2]Kaiser Permanente Colorado, Denver, CO

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Background. Vaccine hesitancy is on the rise, yet little is known about when parents-to-be seek information about vaccines or about their preferred modes of learning about them. Our objectives were to assess among a sample of pregnant and recently-delivered women: 1) the timing of thinking about and seeking information about childhood vaccines, and 2) preferred modes of communication about vaccines.

Methods. A sample of women from 9 obstetrics practices in Colorado responded to an email survey administered January to February 2014 regarding decision-making about vaccines, timed so that about half the sample had delivered and half were still pregnant. Vaccine hesitancy was assessed using a validated scale. Women estimated how much they had been thinking about, and seeking information about, childhood vaccines in the prior few weeks. Preferred communication methods for receiving childhood vaccine information were also assessed.

Results. The response rate was 54% (231/425). Among respondents, 53% were pregnant and 47% had delivered. Overall, 2% were very vaccine hesitant and 16% were somewhat vaccine hesitant. Women who had delivered more often reported thinking about and for information about childhood vaccines than pregnant women (Figure 1). This finding was consistent in vaccine hesitant participants, in whom often or sometimes seeking vaccine information was more common after delivery (29% and 38%, respectively) vs while still pregnant (0% and 26%, p = 0.01). Figure 2 shows responses regarding seeking information based on expected or actual date of delivery; larger bubbles represent more respondents with a particular response option. Overall, most women preferred a conversation with their child's doctor over other forms of childhood vaccine information (Figure 3).

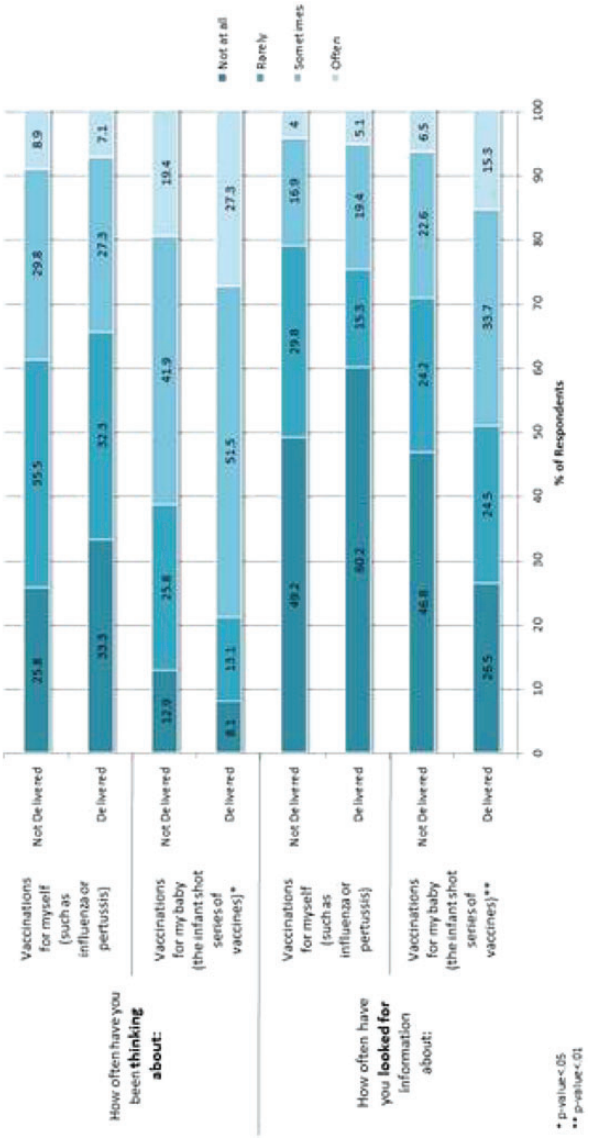
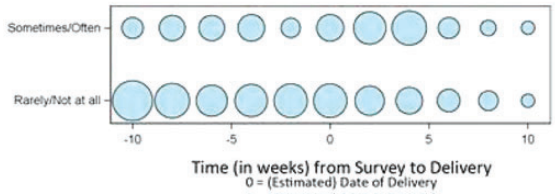
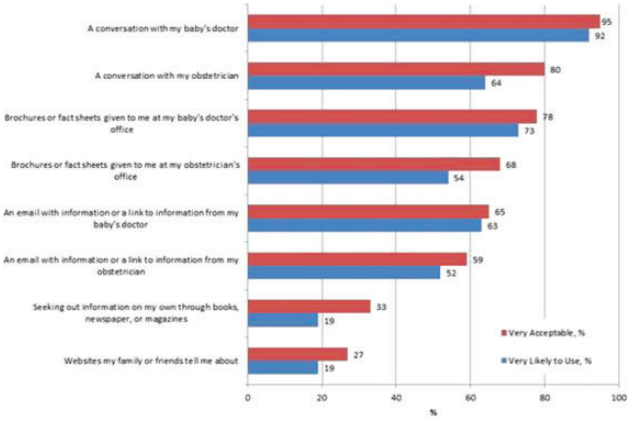


Figure 2 - Frequency of Seeking Information About Infant Vaccines.



Time (in weeks) from Survey to Delivery
0 = (Estimated) Date of Delivery



Conclusion. Pregnant and recently delivered women prefer receiving childhood vaccine information from their child's doctor over their obstetrician and are thinking about and seeking information about childhood vaccines more after their child is born than during pregnancy. Two to 4 weeks after delivery appears to be the time when the most women seek vaccine information. Such information is useful for developing interventions to address the growing problem of vaccine hesitancy.

Disclosures. **A. Dempsey**, Merck: Consultant, Consulting fee

1109. Knowledge and Attitudes of Pregnant Women Towards Recommendations for Immunization During Pregnancy

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Background. Tetanus, diphtheria and acellular pertussis (Tdap) and influenza vaccination is recommended during each pregnancy to prevent serious illness in pregnant women and young infants. National data show that uptake is suboptimal. We evaluated knowledge and acceptance of vaccination recommendations among pregnant women.

Methods. Prospective, convenience survey of pregnant women presenting for routine, antenatal care at the Pavilion for Women, Texas Children's Hospital, Houston.

Results. 796 of 825 (96.5%) of women invited to participate completed surveys. The mean age of participants was 30.2 (range 18-45) years. Self-identified race/ethnicity was 45% white, 26% Hispanic, 13% black, 12% Asian and 4% mixed or other. Most women had college degrees (84%) and private health insurance (83%); 17% had preconception doctor visits. The mean gestation at participation was 28.5 (range 3-41.8) weeks with 4.8%, 37.8% and 57.4%, in the 1st, 2nd and 3rd trimesters, respectively. Women used a number of sources for pregnancy information (personal contacts, healthcare providers [HCP], print, audiovisual and online media) but 89.1% cited a HCP as the most trusted source, and for 85.8% it was their physician. Most avoided smoking, alcohol (99% each) and certain foods (78.2%) for fetal health; 92.6% intended to breastfeed. 668 (84%) knew that vaccines can be given during pregnancy. 77% and 61% knew that influenza and Tdap, respectively, were recommended. 659 (83%) were willing to receive vaccines during pregnancy if recommended by their doctor. Factors impacting the decision to be vaccinated included safety for baby, safety for mother and being sufficiently informed, scoring 4.7, 4.5 and 4.2, respectively, on a 5-point scale. Factors considered less important were extra time taken (2.6), cost (1.9) or fear of needles (1). Women in the 3rd trimester were more accepting of vaccines than those earlier in gestation (87% vs 78%; P= 0.003). Serious illness in a prior infant or current multiple gestation did not affect willingness to receive vaccines.

Conclusion. Pregnant women are willing to accept vaccines in pregnancy if recommended by their physician and if sufficient discussion of safety and rationale occurs. Strong healthcare provider recommendation, as is proven for pediatric vaccination, is essential to optimizing uptake of vaccines during pregnancy.

Disclosures. **C. M. Healy**, Sanofi Pasteur: Grant Investigator, Research grant; Novartis: Grant Investigator and Scientific Advisor, Consulting fee and Research grant

1110. Identification of Formulations and Vaccine Schedules of a Trivalent Group B Streptococcus Vaccine for Further Development in Non-pregnant and Pregnant Women

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Background. Group B Streptococcus (GBS) is a primary cause of infant sepsis and meningitis. As maternal anti-capsular (GBS) antibody is protective, maternal immunization could protect newborns. Here, the safety and immunogenicity of various doses, schedules and adjuvants of a trivalent GBS glycoconjugate vaccine (Novartis) were evaluated in non-pregnant women (clinicaltrials.gov NCT01150123).

Methods. In a phase Ib, single-centre, randomized, observer-blind, placebo-controlled study, 678 healthy 18–40 year-old non-pregnant women were enrolled in two cohorts. Each cohort was randomized to 9 groups, to receive either placebo, or 1 or 2 doses (day 1 and 31) of one of 4 formulations of trivalent GBS vaccine: 5 or 20 µg of each glycoconjugate for serotypes Ia, Ib and III, with or without $AlOH_3$ (cohort I); or with half or full doses of MF59® (cohort II). Solicited local and systemic reactions and adverse events were assessed. Antibodies were measured by ELISA at days 1, 61 and 361.

Results. Relatively low antibody levels (all serotypes) were found at baseline, similar in all groups, and remained unchanged throughout the study after placebo. Vaccination significantly increased antibody levels. In cohort I groups Geometric Mean Ratios (Day 61:Day 1) were 19–45, 23–47 and 15–36 for serotypes Ia, Ib and III, respectively; 70–93%, 50–74%, and 46–73% of groups achieving levels ≥ 1 µg/mL. There were no clear differences between 5 and 20 µg doses (except for a trend to higher responses with 20 µg vs 5 µg in women with no detectable antibodies at baseline), 1 or 2 injections, or use of $AlOH_3$. In cohort II, no added benefit of MF59® adjuvant was observed. Across all subjects, antibodies waned by Day 361, but remained significantly higher than placebo.

No vaccine-related serious adverse events were reported; adverse events were mostly mild to moderate. Local reaction rates were higher with vaccine than placebo, and increased with $AlOH_3$ and MF59®. Systemic reaction rates were comparable across all groups.

Conclusion. GBS vaccine was immunogenic and well-tolerated in non-pregnant women. No clear added benefit was observed from higher dosage, two injections or adjuvants, but a trend towards higher responses was observed with 20 µg vs 5 µg in women with undetectable baseline antibody.

Disclosures. **G. Leroux-Roels**, Novartis Vaccines: Investigator, Consulting fee **C. Maes**, Novartis Vaccines: Investigator, Consulting fee **J. Willekens**, Novartis Vaccines: Investigator, Consulting fee **F. De Boever**, Novartis Vaccines: Investigator, Consulting fee **R. De Rooij**, Novartis Vaccines: Employee, Salary **L. Martell**, Novartis Vaccines: Employee, Salary **L. Bedell**, Novartis Vaccines: Employee, Salary **F. Wittke**, Novartis Vaccines: Employee, Salary **K. Slobod**, Novartis Vaccines: Employee, Salary **P. M Dull**, Novartis Vaccines: Employee, Salary

1111. The Evaluation of the Results of Postexposure Rabies Prophylaxis in a Turkish State Hospital

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Session: 131. Vaccines: Rabies, CMV, Combined
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Background. The aim of this study was to understand the use and distribution of human rabies post exposure prophylaxis (PEP) vaccination in Izmir.

Methods. A retrospective analysis of the files of all patients who consulted for rabies PEP at the Infectious Diseases Clinic of Karsiyaka State Hospiltal in Izmir, Turkey, between January 2013 and June 2013 was conducted.

Results. PEP data were evaluated in 1314 patients. Males (57.2%) accounted for significantly more PEP events than females (42.8%) ($P < 0.005$). The mean age of the cases was 32.11 (0-89) years old. The number of patients with cat bites or scratching (49.6%) was similar with dog bites (47.8%) ($P > 0.5$). The mean admission time for PEP was 0.70 days. Post exposure treatment was provided throughout the year with a higher number during the spring and summer months. Fifty-five percent (n = 723) of the patients received an incomplete course of vaccine (<5-doses of vaccine intramuscular). The most common injury sites were right and left hands (16% and 14%). Lower

limb/buttock injuries were significantly higher in children than adults, but the adults sufferred significantly more severe injury. The majority of dog bite injuries were washed with soap and irrigated with water or saline and 92% of the cases received PEP.

The compliance with the protocol of five injections was 45%. In 40% of the patients, PEP discontinued after the third injection. Thirteen percent of the cases abandoned PEP after the first injection. Eighty-five percent of cats and 79% of the dogs were unclaimed. Sixty-five of the owned cats and 42% of the owned dogs were unvaccinated. The history of previous contact with suspected animals was reported in 9% of the cases and 78% of them had PEP history. PEP wasn't discontinued for adverse effect in any cases. The most common adverse effect were pain at site of administration (5.8%), headache (4.4%), and arthralgia (2.5%).

Conclusion. Because the frequency of stray animals in developing countries is more, the risk of trauma due to suspected animal bites is common. Control of stray animals and more effective PEP program are important approaches in prevention of human rabies.

Disclosures. **All authors:** No reported disclosures.

1112. A Phase III Study of the Safety, Tolerability and Immunogenicity of an Investigational Combination Vaccine against Diphtheria, Tetanus, Pertussis (DTaP5), Polio (IPV), *Haemophilus influenzae* type b (Hib; PRP-OMPC), and Hepatitis B (HepB) in US Infants

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Session: 131. Vaccines: Rabies, CMV, Combined
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Background. Combination vaccines simplify vaccination visits and improve coverage and timeliness. DTaP5-IPV-Hib-HepB is an investigational, fully-liquid, combination vaccine designed to protect against 6 diseases.

Methods. In this multicenter, open-label, comparator-controlled, Phase III study, healthy infants were randomized 2:1 to receive one of the following immunization regimens:

	Age	
Group	2, 4 and 6 mo.	15 mo.
1	DTaP5-IPV-Hib-HepB Prevnar 13 (PCV13) RotaTeq (RV5)	Daptacel (DTaP5) PedvaxHIB (PRP-OMPC) Prevnar 13 (PCV13)
2	Pentacel (DTaP5-IPV/Hib) Recombivax HB (HepB)[†] Prevnar 13 (PCV13) RotaTeq (RV5)	Daptacel (DTaP5) ActHIB (PRP-T) Prevnar 13 (PCV13)

[†]Dose not given at 4 mo.

Results. All infants received HepB in the first month of life. A total of 981 subjects were vaccinated in Group 1 and 484 in Group 2. In a per-protocol analysis, immune responses to all DTaP5-IPV-Hib-HepB antigens 1 month after dose 3 were non-inferior in Group 1 as compared to Group 2, with the exception of anti-filamentous hemagglutinin (FHA, a pertussis antigen) GMTs (46.59 vs 72.28, ratio 0.64 [95% CI 0.59, 0.70]). Vaccine response rates for FHA were non-inferior to control. After the toddler dose, Group 1 was non-inferior to Group 2 for all pertussis antigens. Group 1 response to concomitant RV5, measured as anti-rotavirus IgA GMT 1 month after dose 3, was also non-inferior.

Solicited adverse event rates after any dose were similar in both groups, with the exceptions of increased injection-site erythema (48.8% vs 42.2%, difference 6.5% [1.1, 11.9]), increased fever (47.4% vs 34.4%, difference 13.1% [7.7, 18.3]), and decreased appetite (48.9% vs 43.3%, difference 5.6% [0.2, 11.0]) in Group 1. Most adverse events were mild-to-moderate and did not lead to subject withdrawal. Fever was not associated with hospitalization or seizures.

Conclusion. The safety and immunogenicity of DTaP5-IPV-Hib-HepB is comparable to the analogous licensed component vaccines. Decreased anti-FHA GMTs and increased injection-site reactions and fever are unlikely to be clinically significant. DTaP5-IPV-Hib-HepB provides a new hexavalent option for pediatric combination vaccines, aligned with recommended US immunizations.

Disclosures. **G. S. Marshall**, Merck: Investigator, Research grant and Research support **G. Adams**, Merck: Investigator, Research grant and Research support **M. Leonardi**, Merck: Investigator, Research grant and Research support **M. Petrecz**, Merck: Employee and Shareholder, Salary **S. Flores**, Merck: Employee and Shareholder, Salary **A. Ngai**, Merck: Employee and Shareholder, Salary **J. Xu**, Merck: Employee and Shareholder, Salary **G. Foglia**, Sanofi Pasreur: Employee, Salary **A. W. T. Lee**, Merck: Employee and Shareholder, Salary

1113. Safety and Efficacy of a Cytomegalovirus Glycoprotein B (gB) Vaccine in Adolescent Girls

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Session: 131. Vaccines: Rabies, CMV, Combined
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Background. Cytomegalovirus (CMV) is a leading cause of congenital infection and an important target for vaccine development.

Methods. This randomized double blind trial (NCT00133497) was conducted in 5 USA sites. CMV seronegative girls between 12 and 17 years of age received 20 µg of CMV glycoprotein B with MF59 or saline by the IM route at 0, 1 and 6 months. Subjects were followed for 24 months after the last vaccination for safety, immunogenicity and efficacy. Blood and urine were obtained prior-to and one month following each vaccination then every 3 months for evidence of CMV infection based on PCR and / or seroconversion to non-vaccine CMV antigens measured by ELISA. Vaccine efficacy was estimated using Cox Proportional Hazards model with p-values calculated using a 2-sided log-rank test.

Results. 402 CMV seronegative subjects were enrolled and vaccinated (195 vaccine, 207 placebo) based on an assumption of a 20% attack rate in the placebo group and 8% in the vaccine group. The vaccine was generally well tolerated although local and systemic adverse events were significantly more common in the vaccine group. The vaccine was immunogenic inducing gB antibody (measured by ELISA) in all vaccine recipients and a gB geometric mean titer of 13,400 (95% CI: (11,436 – 15,700) after 3 doses of vaccine. Overall, 48 CMV infections were detected (21 in vaccine, 27 placebo). In the per protocol population (124 vaccine, 125 placebo) vaccine reduced the incidence of CMV infections after 3 vaccinations from 14 in the placebo group to 8 in the vaccine group (efficacy 43%; 95% CI: -36; 76, P =0.20). Using the modified intent to treat population (3 doses, regardless of timing of vaccinations; 164 vaccine, 170 placebo) the vaccine reduced the number of CMV infections from 18 in the placebo to 11: (efficacy 38%; 95% CI: -31; 72, P = 0.20). The most significant difference was after 2 doses, administered as per protocol; vaccine: 13/164, placebo: 24/172 (efficacy 45%, 95% CI: -9; 72, P = 0.08). The failure to show a significant reduction may have been influenced by the lower than anticipated attack rate.

Funding: NIH/DMID

Conclusion. The vaccine was safe and immunogenic. Although the decrease in CMV infection in the vaccine group did not reach significance the results are consistent with a previous study (Pass et al NEJM 360:1191, 2009) using the same formulation.

Disclosures. **K. Edwards**, Novartis: Grant Investigator and Scientific Advisor, Research grant **S. Pichon**, Sanofi Pasteur: Employee, Salary

1114. Variability in Pediatric Rotavirus Disease in the Post-Vaccine Era

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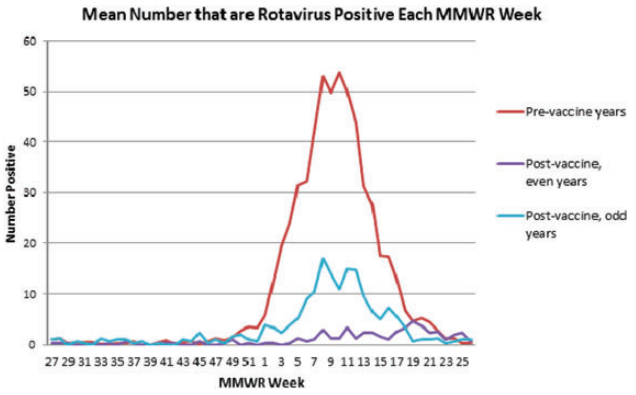
Background. Marked declines in pediatric rotavirus (RV) disease have been observed beginning in 2008 after implementation of RV vaccination. Biennial variations in RV have been observed but are not understood. We reviewed our pre- and post-vaccine era data to better understand these differences.

Methods. Stool samples submitted for RV testing to the Children's Healthcare of Atlanta microbiology laboratory were tested by SA Scientific Rota Test from July 2000 – June 2006 and Remel RV Xpect rapid antigen from July 2007 – June 2013. Each RV season was defined as MMWR week 27 of the previous calendar year through week 26 of the selected year. The 2007 season (July 2006 – June 2007) was excluded as a transitional year. The pre-vaccine seasons included 2001-2006, the post-vaccine seasons included 2008-2013. Given biennial variation, we divided seasons into even (2008, 2010, 2012) and odd (2009, 2011, 2013). Samples from subjects ≥ 18 years and duplicates were excluded. Vaccination history was collected from the Georgia Registry of Immunization Transactions and Services for subjects ≥8 months and born after January 1, 2006.

Results. A total of 20,013 tests were performed, of which 3,423 (17%) were not eligible. RV was identified in 3,456 of 11,430 (30%) tests pre-vaccine and in 690 of 5,160 (13%, p <0.0001) tests post-vaccine. The prevalence and seasonality of RV is demonstrated in the Figure. RV was detected about 4 weeks later post-vaccine (MMWR week 15.2 vs 10.8, p < 0.0001). The delay in even seasons was more pronounced than that of the odd seasons (MMWR week 19.5 vs 14.2, p <0.0001). Children with RV were older in the post- than the pre-vaccine seasons (3.1 vs 1.6 years,

$p < 0.0001$). Those with RV were older in the even than the odd seasons (3.2 vs 2.6 years, $p = 0.01$). Overall, 14% of RV positive subjects ≥8 months of age were fully vaccinated for RV with no difference between even and odd seasons (11% vs 16%, $p = 0.2$).



Conclusion. The marked decline in RV disease continued during the post-vaccine era with significant differences in the biennial burden and seasonality. The biennial increases in RV occurred among older children that were not fully vaccinated. Improving infant RV vaccination rates could impact the biennial seasonality of RV in the post-vaccine era.

Disclosures. **All authors:** No reported disclosures.

1115. Impact of a Publicly Funded Rotavirus Vaccine in Quebec, Canada

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Session: 132. Vaccines: Rotavirus
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Background. Rotavirus (RV) is the leading cause of severe gastroenteritis (GE) in young children. In November 2011, the province of Quebec, Canada implemented a publicly funded RV vaccination program. To assess its impact, trends in passive RV laboratory detection from 2006-2013 and Emergency Department (ED) visits for GE at two pediatric centres were evaluated.

Methods. We used the virology laboratory databases from Montreal Children's Hospital (MCH) and Centre hospitalier universitaire de Sherbrooke (CHUS) for RV ELISAs and ED data of GE visits between July 2006 and June 2013. For virology laboratory data from July 2012 to June 2013 only MCH data were evaluated because of changes in diagnostic algorithm at CHUS. The % positive RV ELISAs over time and season duration was assessed using a 5-week moving average. We defined season start and end as the first 2 and the last 2 consecutive weeks where the % positive RV tests were ≥ 10%, respectively. GE burden was determined by review of ED visits for GE from July 2006 – June 2013. A year was defined from July – June. We stratified the % of ED visits for GE per total ED visits by age.

Results. MCH and CHUS combined have >90,000 annual ED visits; >3,000 of which are for GE. From July 2006 to June 2012, 784 of 6140 non-duplicate RV ELISAs were positive: post-vaccination program, 5.1% were positive (2011-12), compared to 15.9% (2006-09) ($p < 0.001$). At MCH, 3.05% were positive in 2012-13. Compared to 2006-09, 2012-13 saw a greater decrease in the proportion of positive tests (80.1%) compared to the decrease in number of tests ordered (43.6%) ($p < 0.001$) at MCH. Prior to the vaccine program, RV seasons started between December and February, peaked in March or April and ended in May. In 2011-12, the season started in March, peaked in April, and ended in May. At MCH in 2012-13, the season lasted 3 weeks in May. In children <5 years old, ED GE visits decreased from 6.2% in 2006-09 to 5.3% in 2012-13 ($p < 0.001$).

Conclusion. Implementation of a publicly funded RV vaccination program had a major impact on the epidemiology of RV infections in Quebec. The RV season started later and was shorter than usual, peak positives were fewer, and ED visits for GE decreased.

Disclosures. **C. Quach**, GlaxoSmithKline: Grant Investigator, Research grant

1116. Rotavirus in Adults in the Post-Rotavirus Vaccine Era

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Session: 132. Vaccines: Rotavirus
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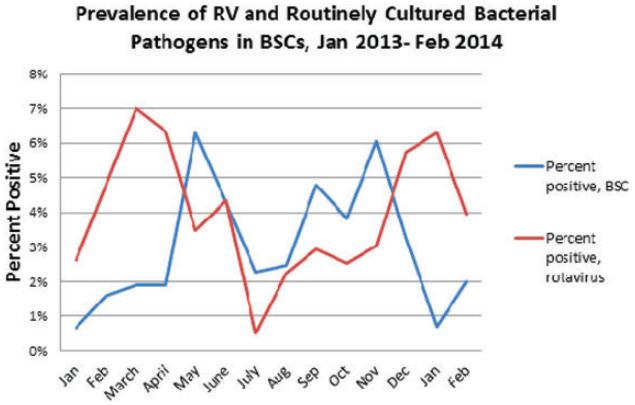
Background. Rotavirus (RV) has been increasingly recognized as a pathogen of adults. Data from the pre-vaccine era suggested that the seasonality of RV mirrored that of children with most cases occurring in the winter and spring. Implementation of pediatric RV vaccination has resulted in declines in the prevalence of RV in both children and adults but with marked biennial variability. The seasonality, prevalence, and clinical characteristics of adult rotavirus disease in the post-vaccine era are poorly understood.

Methods. Residual stools were collected January 1, 2013 – Febuary 28, 2014 from specimens submitted for bacterial stool culture (BSC) to Emory Healthcare Microbiology Laboratory in Atlanta, GA. Duplicate specimens, those from subjects <18 years or hospitalized for ≥72 hours were excluded. BSCs were tested retrospectively for RV by Rotaclone® EIA to determine the prevalence of RV. The prevalence, seasonality, and clinical characteristics of those with RV were compared to those with routinely cultured bacterial pathogens (e.g., *Salmonella, Shigella, Campylobacter, Aeromonas*). Shiga toxin testing results were excluded since these were not routinely performed until July 2013.

Results. A total of 3,080 BSCs were sent of which 386 (13%) did not meet eligibility criteria. Of the 2694 eligible BSCs, 2062 (77%) were saved and available for RV testing, and 82 (4.0%) of these had RV detected. In contrast, routinely cultured bacterial pathogens were identified in 61 eligible and saved specimens (3.0%). The prevalence and seasonality of RV and these bacterial pathogens combined is demonstrated in the figure. Compared to those with bacterial pathogens identified, those with RV were older (mean of 52 vs 43 years, $P < 0.003$), more frequently admitted (56% vs 31%, $p < 0.004$), but less likely to have traveled internationally (5% vs 16%, $p < 0.05$).



Conclusion. In this convenience sample of BSC samples from adults that was collected primarily during a peak pediatric rotavirus year (2013), winter-spring seasonality was observed. The prevalence of RV in adults was similar to the combined prevalence of all other routinely cultured bacterial pathogens. Those with RV were older, more frequently admitted, but had less international travel.

Disclosures. **All authors:** No reported disclosures.

1117. The Acute Febrile Illness Surveillance Study in Puerto Rico: Findings from the First Two Years

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Session: 133. Viral Infections: Epidemiology
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Background. Dengue has been endemic in Puerto Rico for four decades, but little is known about other acute febrile illnesses (AFI) on the differential diagnosis of dengue. To study this, an AFI surveillance study was implemented at a Sentinel Enhanced Dengue Surveillance Site consisting of a teaching hospital and a small rural hospital in Puerto Rico.

Methods. Outpatients with fever or history of fever for <7 days were enrolled with informed consent and followed through their illness. Serum and nasopharyngeal swabs were collected and tested by PCR and immunodiagnostic methods as appropriate for the four dengue viruses (DENV-1-4), influenza virus A (Flu A), influenza virus B (Flu B), five other respiratory viruses (ORV) including adenovirus, respiratory syncytial

virus, metapneumovirus, and parainfluenza viruses 1 and 3, 122 enteroviruses (Entero), *Leptospira* spp. (Lepto), and *Burkholderia pseudomallei* (Burk).

Results. From May 7, 2012 through May 6, 2014, 5,207 of 23,627 AFI patients seeking care were enrolled; 31.3% were hospitalized, 50.2% were female, and the median age was 12.0 years (range: 0-103 years). Half (49.3%, 2,567) of all enrolled patients had a pathogen detected; 963 (37.5%) were DENV, 794 (30.9%) Flu A and B, 675 (26.3%) ORV, 48 (1.9%) Entero, 8 (0.3%) Lepto, and 2 (0.1%) Burk. In addition, 77 (3.0%) co-infections were confirmed by PCR; nearly half (34, 44.2%) were DENV co-infections and most (31, 91.2%) were PCR positive for DENV and a respiratory virus. Almost all (95.1%) of the 719 DENV PCR positive cases were DENV-1; 33 DENV-4 and two DENV-2 cases were detected. Dengue patients were slightly older than other enrolled patients (median age 15.0 vs 10.0 years) but similar in age to influenza patients (median age 15.0 vs 17.0 years). Dengue patients were more likely to be admitted than other enrolled patients (OR 2.33, 95%CI 2.02-2.70) and influenza patients (OR 3.26, 95%CI 2.62-4.06).

Conclusion. Most AFIs were caused by either a DENV, a viral respiratory pathogen (Flu A, Flu B or ORV), or an enterovirus. Leptospirosis and melioidosis cases were sporadic and focal; study of these diseases may require additional study sites in high risk areas of the island. Reasons for why dengue cases were more likely to be hospitalized will be studied further and data for the first two years will be presented.

Disclosures. **All authors:** No reported disclosures.

1118. Respiratory syncytial virus among children under age 5 years with viral acute lower respiratory infections in Guatemala

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Session: 133. Viral Infections: Epidemiology
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Background. Hospital-based estimates of respiratory syncytial virus (RSV) frequency have ranged between 60% and 96% among children aged <5 years with viral acute lower respiratory infections (ALRIs) in South American countries, but limited information is available about the frequency of RSV among children with viral ALRIs in Central America. We thus aimed to estimate the frequency of RSV among children aged <5 years with viral ALRIs in Guatemala.

Methods. We collected nasopharyngeal swabs for immunofluorescence viral testing of all children aged <5 years admitted to the Pediatric Emergency Department of Roosevelt Hospital (Guatemala City, Guatemala) with standard clinical symptoms of ALRI (e.g., cough, tachypnea, and wheezing) between January 2013 and September 2013. The results of nasopharyngeal swabs were supplemented with demographic and clinical data abstracted from medical records. We estimated the overall and subgroup-specific (age [<6 months, ≥6 months] sex, and season [wet season since May to October, dry season since November to April]) frequency and corresponding 95% confidence limits (CL) of RSV among children with viral ALRIs

Results. Our study population comprised 157 children with ALRIs, 87 children where positive for virus. The median age at admission was 5 months (interquartile range = 2 – 12 months) and 68% were male. RSV was detected in (74) 85% of children with viral ALRIs (95% CL: 77%, 93%). This frequency varied little by age (<6 months = 87%, 95% CL: 76%, 97%; ≥6 months = 83%, 95% CL: 72%, 95%), sex (male = 83%, 95% CL: 73%, 93%; female= 89%, 95% CL: 77%, 100%), or season (wet season: 88%, 95% CL: 76%, 99%; dry season = 84%, 95% CL: 74%, 94%). 97% of the Children with RSV requiered hospitalization, 69% required oxygen supplementation (SatO2 <92%), and 11% mechanical ventilation support. The clinical presentation of the patients was classified as Severe ALRIs: tachypnea, costal retraccions, nasal flaring eg. in the 58% of all cases.

Conclusion. The estimates from our hospital-based study in Guatemala suggest a high frequency of RSV among children aged <5 years with viral ALRIs. Our findings may be useful for raising awareness about the burden of RSV in Central America, but future studies in other Central American countries are necessary to provide context for our findings.

Disclosures. **All authors:** No reported disclosures.

1119. Respiratory Viral Infections in a Cohort of Patients with Hematological Malignancies

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Session: 133. Viral Infections: Epidemiology
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Background. Assess the prevalence of respiratory viruses, clinical course and outcomes of patients with hematological malignancies (HM) and acute onset of respiratory tract infection (RTI).

Methods. Patients with HM and acute onset of RTI from Instituto Nacional de Cancerologia in Mexico City were assessed. RTI symptoms, neoplasia and its treatment, comorbidities, lymphopenia, neutropenia, respiratory support, intensive care and outcomes were evaluated. Nasopharyngeal specimens were collected and tested by Multiplex RT-PCR (Anyplex ™RV16, Seegene) for RSV A & B, INFA & B, PIV 1,23 & 4, AdV, MpV, CoVOC43, 229E & NL63, RV A/B/C, EV and HboV 1/2/3/4. A descriptive analysis was conducted.

Results. 95 patients were included from February 2013 to February 2014, 58 (61.1%) male, mean age 39 ± 16.3 years. Forty-five (47.3%) had leukemia, 29 (30.5%) lymphoma, 14 (14.7%) multiple myeloma, and 7 (7.4%) other malignancies. Four (4.2%) were recipients of stem cell transplant; 20 (21.1%) were obese. Twenty-three (24.2%) had < 500 neutrophils, and 12 (12.6%) were on severe lymphopenia. Thirty three (34.7%) were positive for one virus; 36 (37.9%) had viral co-infection, 26 (27.3%) were negative. The most frequently identified viruses were: rhinovirus (36%), RSV (19%), influenza AH1N1 (18%) and influenza A (16%). In spring and early summer, the viral activity was very low. During the rainy season, an increase on activity was observed, being MpV and rhinovirus the predominant viruses. At the beginning of the autumn, the number of RTIs increased, with a predominance of RSV (n = 6). Between December and February, the number of RTIs increased by 3 times, being influenza the most common virus; AH1N1 (n= 17), was the predominant serotype. Forty-five (47.4%) patients developed pneumonia, 12 (26.6%) required respiratory support. Seventeen patients (17.9%) died, 7 (41.2%) related to RTI, 3 with influenza and 3 with RSV.

Conclusion. RTIs in patients with hematological malignancies were frequent, 47.4% developed pneumonia. Viral co-infection was common (37.9%). Attributable mortality to pneumonia was more frequent in patients with influenza or RSV. Seasonality was similar to other reports from the Northern Hemisphere.

Disclosures. **All authors:** No reported disclosures.

1120. The Impact of Influenza Vaccination in Patients with Cancer on Subsequent Disease during the 2013-2014 Influenza Season

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Background. Patients with cancer may experience higher morbidity and mortality from influenza infection. Influenza vaccination is universally used for prevention; however, effectiveness in patients with cancer may be suboptimal but its impact on severity of illness is yet to be determined.

Methods. A phone survey for cancer patients with laboratory confirmed influenza (LCI) was carried out during the influenza season 2013-2014 to determine impact on clinical outcomes including hospitalization, intensive care unit stay and death.

Results. A total of 105 out 139 adults with LCI participated in the phone survey at a rate of 77%. A total of 47 (45%) were vaccinated and 58 (55%) were not and their baseline characteristics were similar. Median age was 57 years old (21 - 88) while 61% were male and 59% were Caucasians. Most common underlying conditions were hematopoietic cell transplant (51%), solid tumors (19%) and leukemia (14%). On multivariable analysis, patients who progressed to pneumonia were more likely to be neutropenic, were older, had delay in diagnosis from symptoms onset, and did not receive oseltamivir at upper respiratory tract infection stage (all $p < 0.05$). Vaccination status had no significant impact on progression to pneumonia or mortality.

Conclusion. In our cohort, almost half of the patients who had influenza were vaccinated. Interestingly, influenza vaccination during the current season did not have an impact on the severity of illness including incidence of pneumonia, hospitalization or mortality rates in our cancer patients. Although not determined in this study, vaccination may have protected our cancer patients from acquiring influenza.

Disclosures. **All authors:** No reported disclosures.

1121. Do Viral Diagnoses in Primary Care Precede and Predict Those Obtained in Secondary Care: A Temporal Trend Comparison Study

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Background. Children with respiratory tract infections (RTIs) form a large proportion of primary care (PC) consultations. In secondary care (SC), high levels of viral activity can lead to increased pressure on already limited resources. Current national RTI surveillance systems are not at present used to provide local 'early-warning' systems to provide real-time indicators to predict when SC may experience increased pressure. This study investigates if viruses isolated from children presenting to Bristol PC with RTI precede and predict the same viruses isolated from children in local SC.

Methods. The PC dataset was sourced from the NIHR funded 'TARGET' study, including throat swabs from Bristol children presenting to PC with acute RTI during August 2011-May 2013. Viral detection results from SC respiratory samples from the

same age group were retrospectively sourced for children with a Bristol postcode, presenting simultaneously to a local hospital. Influenza A&B, respiratory syncytial virus (RSV), human metapneumovirus, parainfluenzaviruses, adenovirus, rhinovirus and enterovirus were studied. Time series graphs were generated using weekly numbers of positive samples and proportion of respiratory samples positive.

Results. 596 and 949 samples were analysed in PC and SC respectively. 'Flu A: (PC n = 26 (4.3%), SC n = 23 (2.4%)) demonstrated a seasonal pattern, with two periods of increased activity simultaneously observed in December 2011-April 2012, and January 2013-May 2013. 'Flu B: (PC n = 30(5.0%), SC n = 9(1.0%)) demonstrated one peak of increased activity, again simultaneously, from December 2012. RSV: (PC n = 58 (9.7%), SC n = 216 (23.0%)) demonstrated two peaks in PC and SC around December in both 2012 and 2013. Graphical analysis of further viruses will be presented.

Conclusion. To our knowledge this is the first study to investigate if there is potential for PC virus surveillance as an 'early-warning' utility for a city. Preliminary analyses suggest that PC is unlikely to offer a predefined indicator to local SC services. Although this study was limited by small numbers of positive samples, some viruses isolated in Bristol PC follow the same temporal patterns as those in SC, suggesting that either PC or SC data could be used for real-time surveillance of circulating viruses causing children to require PC and SC.

Disclosures. **All authors:** No reported disclosures.

1122. Increase in Influenza-Like Illness in the Spring of 2014 Associated with *Human Metapneumovirus*

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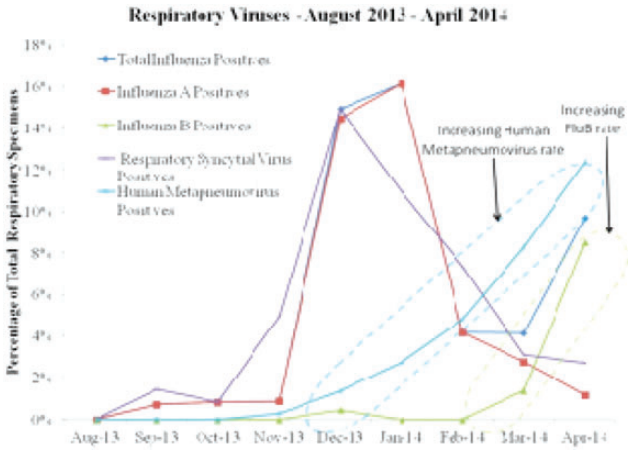
Background. Beginning in March 2014, our emergency department (ED) surveillance system detected a significant increase in the number of patient visits with influenza-like illness (ILI). The percentage of ED patients with ILI crossed the imminent (10%, +2 standard deviations (SD) above the baseline 5%) and widespread (12.5%, +3 SD) thresholds during March and April of 2014, respectively. This was assumed to be related to the spring appearance of influenza B.

Methods. ILI surveillance in the ED was conducted by a unique electronic surveillance system, GUARDIAN, which utilizes natural language processing of the patient's entire ED record. This markedly increases the sensitivity of detecting symptoms of ILI. Respiratory specimens from patients in the ED were obtained at the discretion of the ED provider. Respiratory viruses in the specimens were identified by a qualitative nucleic acid multiplex test (RVP FAST) Luminex Corporation. Descriptive and bivariate analyses were conducted to describe the identified increases in ED ILI rates during March and April 2014.

Results. The review of the results of respiratory specimens sent from patients in March and April 2014 revealed a significant increase in specimens with *human metapneumovirus*(HMPV) when compared to the prior two months (10.2% vs 3.4% p< .001).



Of the specimens submitted during March and April, 4.7% were positive for influenza B and 10.2% were positive for HMPV (p< .001). Forty-six distinct patient specimens were positive for HMPV. Five were outpatients and not admitted. Two patients also had *coronavirus* and one had *rhinovirus.* Seventeen of the 41 were admitted to pediatrics. Thirty-four of the patients admitted were seen in the ED, 13 of which were pediatric patients. Twenty-six of the 34 (74.3%) patients had ILI, 12 were children and 14 were adults.

Conclusion. A sensitive electronic ILI surveillance system and the use of a qualitative nucleic acid multiplex test for respiratory viruses allowed us to quickly recognize an increase in ILI related to serious respiratory infections due to HMPV.

Disclosures. **All authors:** No reported disclosures.

1123. Clinical manifestations and complications of hospitalized patients with severe H1N1 influenza infection during the winter of 2013 -2014

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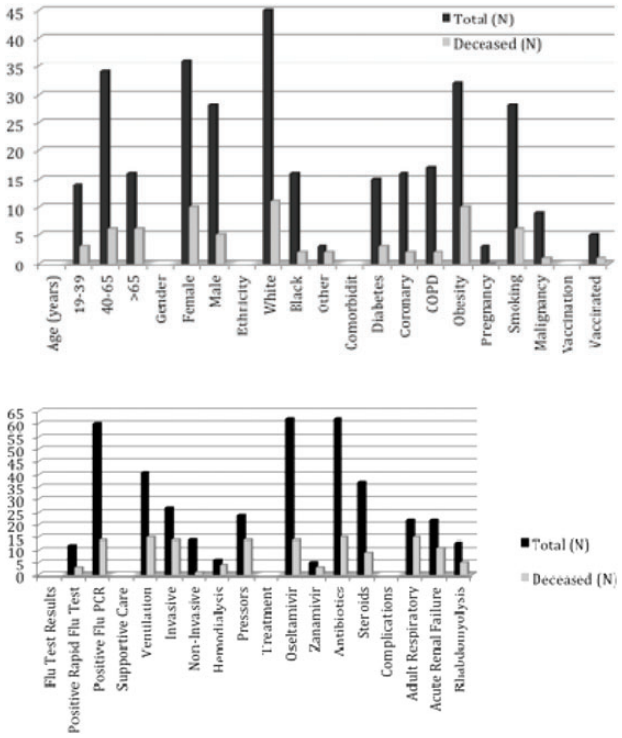
Background. The 2013 - 2014 influenza season showed widespread influenza like activity associated with significant morbidity and mortality. 2009 pH1N1 predominated and accounted for 96% of reported influenza A viruses.

Methods. Demographic, clinical, laboratory and outcome data from all adult patients admitted with severe H1N1 influenza were collected during 2013-14 influenza season.

Results. We identified 64 adult patients (44% male). Median age was 55.5 years (70% white). Common comorbidities included COPD (27%), CAD (25%), Obesity (50%) and smoking history (43%) (Figure 1). Median time from symptom onset to hospitalization was 5 days. Most common presentation was cough (75%), fever (73%), shortness of breath (72%) and myalgia (70%). In the emergency room, 58% had tachycardia, 16% were hypotensive and 33% had oxygen saturation less than 90% on room air. Among 60 patients that had a positive H1N1 PCR, 54 has a concomitant rapid flu test within 24 hours; only 8 was positive with Sensitivity of 17%. Pathogens commonly co-detected by PCR were: *MRSA* (17%), *Pneumococcus*, *Hemophilus Influenza* and *pseudomonas* (5%) and RSV in 3%. Chest radiographs were negative in 34% and showed pneumonia in 66%. CT chest was done in 24 patients showing multilobar involvement with 33% had Extensive Bilateral Infiltrates. Steroids given in 57% and did not affect outcome. 42 patients admitted to the ICU. 42% needed Mechanical ventilation. Median duration of ICU stay and ventilation was 8 and 6 days respectively. Fatality rate was 23%; 27% had no risk factors for severe influenza infection. Most common complications were adult respiratory distress syndrome (34%) and acute renal failure (34%) (figure 2). Hemodialysis used in 6% of those who developed renal failure. Of 26 patients with known vaccination status, only 5 were vaccinated.



Conclusion. Patients with severe pH1N1 infection were most likely middle age, obese with history of smoking. They presented late in the disease most commonly with respiratory distress. Significant number needed ICU admission, mechanical ventilation and pressers. It was associated with significant complications and high fatality rate. In addition, rapid influenza testing had very low sensitivity, which calls for PCR testing in all hospitalized pa

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1124. Clinical characteristics of adult patients with influenza B and A infections during 2013/2014 flu season

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Background. Human infection caused by influenza B virus (IFV-B) has been known to be less severe than that caused by influenza A virus (IFV-A). Although more recent studies did not find any significant differences between the clinical features of patients with IFV-B and those with IFV-A, clinical data are still lacking on this subject, especially in adult patients.

Methods. This study was performed in Chung-Ang University Hospital, Seoul, South Korea. An adult (>15 years of age) patient, who received a rapid influenza antigen detection test or a respiratory virus multiplex reverse transcriptase PCR test between January and March 2014 and was influenza-positive, was included in this study.

Results. In comparisons for 137 admitted patients (A in 90 and B in 37), baseline characteristics of the IFV-B group did not differ from those of the IFV-A group. Initial clinical symptoms were similar between the two groups, except more frequent sputum production in the IFV-B group (82.6% vs 61.1%, $P = 0.01$). Development of pneumonia was not different between the two groups (15.6% in IFV-A vs 21.3% in IFV-B, $P = 0.40$). Oxygen therapy, antiviral therapy, and mechanical ventilation was similarly performed between the two groups, whereas vasoconstrictors were more commonly used in the IFV-B group (6.4% vs none, $P = 0.04$). Intensive care unit admission was more common in the IFV-B group (10.6% vs 2.2%, $P = 0.047$), whereas in-hospital mortality (none in IFV-A vs 2.3% in IFV-B, $P = 0.34$) and the mean days of hospital admission (11.3 days vs 9.7 days, $P = 0.56$) were not different between the two groups. In comparisons for patients of outpatient deparment (OPD) (A in 121 and B in 105), mean age was higher (41.6 years vs 35.3 years, $P = 0.001$), and sputum production (72.4% vs 41.3%, $P < 0.001$) and sore throat (82.9% vs 70.2%, $P = 0.03$) were more common in the IFV-B group, whereas the median number of hospital visit were not different between the two groups (1 vs 1, $P = 0.44$).

Conclusion: In adult patients with influenza infection, a few clinical features were more prominent in IFV-B than IFV-A both for admitted and OPD patients, whereas clinical outcomes were not different. IFV-B infection was not milder than IFV-A.

Disclosures. **All authors:** No reported disclosures.

1125. Viral Infections In Outpatients With Medically Attended Acute Respiratory Illness During the 2012-13 Influenza Season

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Background. Respiratory tract infections are a major cause of primary care visits, yet only a portion is tested to determine the causative organism. This study examined the distribution and characteristics of viruses responsible for outpatient visits during the 2012-2013 influenza season.

Methods. Individuals presenting for outpatient visits with acute (<7 days) respiratory illness were swabbed and assayed for presence 18 viruses using a multiplex reverse transcriptase polymerase chain reaction method. Surveys provided clinical and demographic characteristics.

Results. Among 935 patients, 563 (60.2%) tested positive for single virus infections, 85 (9.1%) tested positive for ≥1 virus and 287 (30.7%) were negative for all tested viruses. Fever and fatigue were significantly more frequently associated with solo influenza detection while wheezing was significantly less frequently reported among those with only CoV ($P = 0.01$). Most frequently co-detected viruses were influenza A (38 times), respiratory syncytial virus (25 times), influenza B (9 times); corona virus, human rhinovirus, adenovirus, human metapneumovirus, and parainfluenza virus also co-occurred. The percentages of single, multiple and no viruses detected varied by age. For children <18 years, the percentages of single virus, multiple viruses, and no virus detected were 63%, 14%, and 23%, respectively; whereas for younger adults 18-49 years, the percentages were 58%, 8%, and 34% and for older adults the percentages were 61%, 5%, and 32%, respectively ($P < 0.001$). Co-detections were more common than single infections in children than older adults (≥65 years; $P = 0.01$) and less frequent in households without children than in households with children ($P = 0.003$). Co-detections were less common if sore throat was present ($P = 0.01$) but did not vary by other symptoms. Compared with individuals with single viral infections, those with co-detections missed fewer days of school (1.1 vs 2 days; $P = 0.04$) or work (2 vs 3 days; $P = 0.03$). These groups did not vary on other measures of illness severity.

Conclusion. In this study of outpatient medically attended acute respiratory illnesses, co-infections were infrequent but varied by demographic and household characteristics.

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1126. Comparison of influenza Activity Determined through Community- vs Hospital Laboratory-based Surveillance

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Background. Current surveillance for influenza focuses on laboratory testing, medically attended visits for influenza-like illness (ILI)/acute respiratory illness (ARI) and hospitalizations. In this study, we compare influenza activity detected through community-based surveillance using mobile text message responses and specimen acquisition to hospital-based laboratory data.

Methods. Community-based surveillance for respiratory viruses including influenza was conducted from January 2013 to March 2014 in the Washington Heights neighborhood served by Columbia University Medical Center (CUMC) in New York City. A random sample within an existing cohort of households was enrolled to receive text messages twice weekly to identify members with symptoms of ILI/ARI. Nasal swabs were obtained from individuals with ILI/ARI and tested by multiplex RT-PCR (FilmArray Panel). Hospital laboratory results (inpatients, emergency department and other) obtained at CUMC and analyzed using the same RT-PCR panel over the same period were assessed. Correlation between influenza activities determined through community- vs hospital laboratory-based surveillance was calculated and epidemiologic curves of influenza activity created. Strain specific influenza activity was compared using chi-squared tests.

Results. In community-based surveillance, 286 households were enrolled (1385 participants, mean: 4.8 members/household). Of 756 specimens tested 85 (11.2%) were positive for influenza. In laboratory-based surveillance, 21,247 specimens were tested and 3143 (14.8%) were positive for influenza. Influenza activity detected through community-based surveillance was significantly correlated with that from hospital laboratory testing (Pearson coefficient 0.98, $p < 0.01$, **Figure 1**). Influenza B activity was significantly higher in community-based surveillance (47.6% vs 36.8% while influenza A H3 was detected more in laboratory surveillance (41.4% vs 27.4%) ($p = 0.04$, **Figure 2**).

Figure 1: Community versus laboratory surveillance for Influenza activity

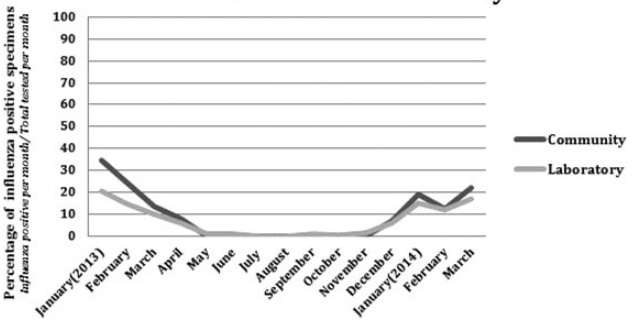
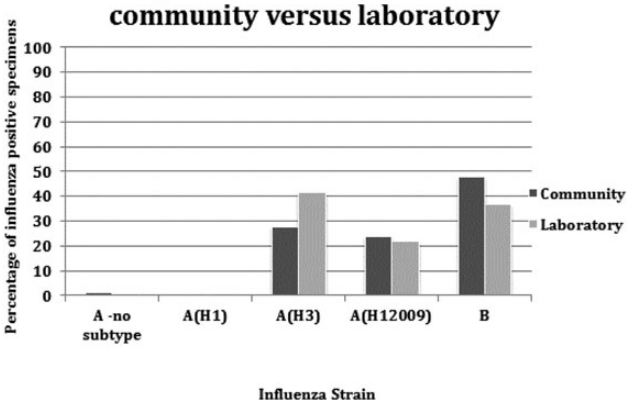


Figure 2: Influenza strains community versus laboratory



Conclusion. Community- and laboratory-based surveillance for influenza activity showed similar trends but differed by strain. Further work will assess epidemiology, disease burden and utility of community-based surveillance for other respiratory viruses.

Disclosures. **All authors:** No reported disclosures.

1127. Seroconversion for Cytomegalovirus in a Canadian Cohort of Pregnant Women

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Background. Cytomegalovirus (CMV) is the leading cause of congenital infection and non-genetic sensorineuronal hearing loss in children. CMV primo-infection occurring during pregnancy has the highest risk of symptomatic infection in the newborn. There are no recent data on the incidence of CMV infection during pregnancy in Canada.

Methods. This study used serum samples and questionnaire data collected as part of the 3D Pregnancy and Birth Cohort Study (Quebec, Canada, 2010-2013) designed to investigate the effect of a range of prenatal factors on birth outcomes. Consent allowed for subsequent use of data and biobanked biological specimens. Women who had serum banked from both the end of the first trimester and the third trimester were included. Serum CMV IgG antibodies were determined. Women who were seronegative in early pregnancy had their late serum tested to determine conversion rates. Associations between independent variables and seroprevalence were assessed using logistic regression, and associations with seroconversions, by Poisson regression.

Results. Of 1938 subjects tested in early pregnancy, 1156 (59.6%) were seronegative for CMV, and 35 seroconverted (3.0%) by the end of pregnancy. The seroconversion rate was 2.0 (95% CI 1.4-2.8) per 10,000 person-days at risk or 5.7 (95% CI 4.0-7.9) per 100 pregnancies assuming a 280-day gestation. Maternal factors independently associated with seropositivity were working as a daycare educator or a kindergarten teacher (OR= 5.0, 95% CI 1.8-13.9), first language other than French or English (OR = 4.0, 95% CI 2.7-5.5), being born outside Canada or USA (OR = 4.0, 95% CI 2.9-5.3), lower education (primary or secondary vs university, OR = 2.6, 95% CI 1.8-3.7), and having had children (OR 1.3, 95% CI 1.1-1.7). Among initially seronegative pregnant women, those born outside Canada or USA were at higher risk of seroconversion (RR = 3.1, 95% CI 1.3-7.3).

Conclusion. Nearly 60% of pregnant women in this cohort were susceptible to CMV in early pregnancy. Overall seroconversion rates approaching 6% are of concern with seronegative women born outside Canada and the USA being at higher risk; targeted interventions may be needed in this group. Further data are needed on the effectiveness of public health prevention strategies.

Disclosures. **All authors:** No reported disclosures.

1128. Association between Cytomegalovirus Seropositivity or Titres and Cardiovascular Disease: Systematic Review and Meta-Analysis of Prospective Evidence

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Background. Established risk factors for cardiovascular disease (CVD) do not fully explain CVD risk. Cytomegalovirus (CMV) has been linked to development of CVD among transplant recipients, but its association with CVD in immunocompetent adults is not established.

Methods. Embase®, Medline® and Web of Science® were searched in April 2014. Titles, abstracts and full-text articles were screened and meta-analysed using *a priori* criteria.

Results. Of 2,658 titles screened, 25 prospective studies met criteria for synthesis. All included studies defined CMV exposure using serological tests with a clinically important CVD outcome, but varied substantially regarding potential bias, confounding, and sample size. Random-effects meta-analysis of studies examining CMV seropositivity and CVD revealed a null association in both 13 population-based studies (effect estimate, 0.99; 95% CI, 0.87–1.12) and in 10 studies of patients with previous history of CVD (1.13; 1.00–1.27). However, in the three population-based studies that examined CMV antibody levels and CVD, there was an indication of increased risk in CVD among participants with higher titres, with the most methodologically robust study reporting an adjusted hazard ratio (95% CI) of 1.21 (1.04–1.41) for participants in the highest tertile of titres vs seronegative subjects.

Conclusion. There appears to be a modest increased risk in CVD associated with higher CMV antibody levels. Given high burden of CVD and high seroprevelance of CMV among adults worldwide, this association is of potential public health relevance. Further research examining this association in other cohorts, and prospective studies correlating CMV antibody levels with direct measurements of active infection are necessary.

Disclosures. **All authors:** No reported disclosures.

1129. Varicella in Belgium: a National One year Prospective Survey

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Background. Varicella is a worldwide endemic infection self-limited in the vast majority of cases. However, serious complications are described in otherwise healthy people that add to a significant societal burden of disease. In many countries, varicella universal mass vaccination (vUMV) has now been implemented for years. Nevertheless, vUMV remains debated in Europe and few data are available on the real burden of the infection and the potential benefits achievable by national vaccination campaigns. We propose here to assess the burden of varicella over the whole Belgian area through analysis of due hospitalized cases during a one-year period.

Methods. Pediatric varicella-related hospitalized cases were actively collected (prospectively then retrospectively) through a national network from November 2011 to October 2012. Inclusion criteria were either acute varicella episode or related complications up to 3weeks after the rash.

Results. 101 hospitals participated, covering 97.7% of the total pediatric beds available in Belgium. 553 children were recorded with a median age of 2.1 years. Incidence of pediatric varicella-due hospitalizations reached 29.5/ 10^5 people-year with the highest impact among the 0-4y old (global incidence and odds of hospitalization: 79/ 10^5 people-year and 1.56/100 varicella-cases; respectively). Only 16% of the cohort had underlying chronic condition. 65% of children had ≥1 complication justifying their admission, 49% were bacterial super-infections and 10% neurological disorders. Many children were also hospitalized for anorexia and dehydration. Incidence of complicated hospitalized cases was 19/ 10^5 people-year. Only one fourth of children received acyclovir but 58% were under antibiotics. ICU admission and surgery were required in 4% and 3%, respectively. One child died from severe bacterial sepsis (mortality and fatality rates: $0.5/10^6$ and 0.2%; respectively) and 1% had sequelae at discharge.

Conclusion. Varicella demonstrated a substantial burden of disease in Belgian children, especially among the youngest. Our thorough nation-wide study, run in a country without vUMV policy, offers recent data to fuel the debate over vUMV in Europe.

Disclosures. **P. Lepage**, GSK: Consultant, Research grant

1130. An Administrative Data-Based Study on the Association Between Psychological Stress and Herpes Zoster: Might the Conventional Wisdom Be Wrong?

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Background. It is a commonly-held belief that herpes zoster (HZ) can be provoked by psychological stress. We used data from a large national dataset to investigate this contention.

Methods. We used medical claims data from 2002-2011 Truven Health MarketScan® Commercial Databases to evaluate the possible association of psychological stress with HZ in adults aged ≥25 years. We defined stress as an abrupt death or catastrophic health event occurring in a previously-healthy spouse (i.e., an age-matched co-beneficiary of the opposite gender). We used self-controlled case series methods to assess for increases in HZ events during a 3-month risk window following stress as compared to a 3-month control window (days 120-30) prior to stress. To control for changes in health seeking that might occur in persons experiencing stress, we also used Poisson regression to assess for increases in HZ as a proportion of all outpatient health care services during the risk as compared to control window. Finally, we used mental health visits (anxiety states [ICD-9 300.0 and 300.0x]; acute stress reaction [ICD-9 308 and 308.x]; adjustment reaction [ICD-9 309.xx])as a positive control to validate our case definition of stress, applying Poisson regression to test whether the proportion of these visits increased during the risk window compared to the control window.

Results. Among 39,811 persons experiencing stress, 137 developed HZ during the observation period. The incidence of HZ was not increased during the risk window, whether assessed as incidence rate ratio (0.76; 95% CI, 0.54-1.06), or as ratio of proportion of all outpatient health services (0.99; 95% CI, 0.70-1.39). The risk of HZ was not increased when stratifying by age, in different risk windows ranging from 1 to 3 months, or among persons whose stress was the abrupt death of their spouse (an extreme subset of our case definition for stress). Patients experiencing stress did have increased utilization of mental health services (i.e., our positive control), assessed as the ratio of proportion of all outpatient health services (1.87; 95% CI 1.67-2.10).

Conclusion. Our study did not find an association between psychological stress and HZ. Administrative data have limitations but we used novel methods to strengthen our conclusions.

Disclosures. **All authors:** No reported disclosures.

1131. Parechovirus and Human Herpes Virus-6 in the Cerebrospinal Fluid of Infants Clinically Tested for Enterovirus or Herpes Simplex Virus

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Background. Human parechovirus (HPeV) and human herpes virus-6 (HHV-6) are commonly acquired in the first six months of life and associated with central nervous system infection. Their prevalence in the cerebrospinal fluid (CSF) of infants tested for enterovirus (EV) and herpes-simplex virus (HSV) is unknown.

Methods. All stored CSF samples from EV or HSV testing in infants less than six months of age at Children's Hospital Colorado between January 1, 2010 and December 31, 2011 were tested for HPeV, HHV-6, EV, and HSV by PCR. Cases were categorized according to primary microbiologic diagnosis. Clinical characteristics and epidemiological data were collected using blinded, retrospective electronic chart review.

Results. Of the 239 infants tested, 106 (44.3%) had a microbiologic diagnosis made in the clinical setting with an additional 15 (6.3%) diagnosed following standardized testing for HPeV, HHV-6, EV, and HSV. There were 29 cases of EV (12.1%), 7 cases of HPeV (2.9%), 5 cases of HHV-6 (2.1%), and 5 cases of HSV (2.1%) identified. Twenty four infants (10%) had serious bacterial infections, though no bacterial co-infections occurred within the HPeV, HHV-6, EV, or HSV groups. All HPeV cases occurred in infants less than 2 months of age between July and October. Infants with HPeV had a median maximum temperature of 39ºC (Interquartile range (IQR): 38.9-39), median fever duration of 3 days (IQR: 2-3) and median peripheral white blood cell count of 5.2 x 10^3/μL (IQR:3.6-6.3). HHV-6 cases occurred in infants with median age of 50 days (IQR: 20-136) without seasonality. The typical sepsis evaluation involved four days of hospitalization, three days of intravenous antibiotics, and one to two days of intravenous acyclovir.

Conclusion. Five percent of infants less than six months of age undergoing testing for EV or HSV have HPeV or HHV-6 in their CSF, increasing the diagnostic yield by 15%. Targeting testing of HPeV towards febrile infants less than 2 months of age with leukopenia in the late summer to early fall, and HHV-6 towards older infants may increase this yield. Further research is needed to determine the impact that a standardized approach to testing for these four viruses will have on rates of hospitalization, exposure to antimicrobials, and health care costs in infants with suspected sepsis.

Disclosures. **All authors:** No reported disclosures.

1132. Seasonal Incidence of Medically Attended RSV and Influenza Illness in Children 6-59 Months Old

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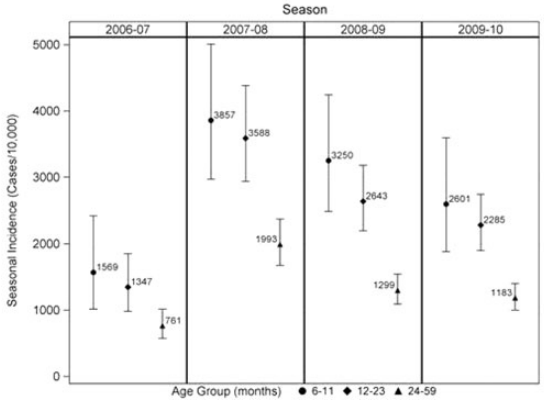
Background. Respiratory syncytial virus (RSV) and influenza are major causes of seasonal respiratory illness in children. The incidence of medically attended, laboratory confirmed illness with these pathogens is not well documented. We estimated the seasonal incidence of medically attended RSV and influenza in a Wisconsin community cohort of children 6 to 59 months of age during 4 seasons (2006-07 through 2009-10).

Figure 1. Seasonal respiratory syncytial virus incidence (cases per 10,000) and 95% confidence intervals by age group in a community cohort of children 6 to 59 months old.



Methods. Children with medically attended acute respiratory illness (MAARI) were prospectively enrolled during annual studies of influenza vaccine effectiveness; enrollment occurred for 10-12 weeks and included the period of peak influenza and RSV activity. Respiratory swabs were tested for RSV and influenza by multiplex RT-PCR. Results from enrolled children were used to estimate RSV and influenza cases among non-enrolled children with MAARI in three age groups: 6-11, 12-23 and 24-59 months. Results for the enrollment period were weighted to estimate seasonal incidence (week 40 to 18) based on the statewide proportion of RSV and influenza cases that occurred outside the enrollment period.

Results. There were 2800 to 3073 children in the community cohort each season; 627 (27%) of the total 2326 enrolled children with MAARI had RSV and 235 (10%) had influenza. Overall seasonal incidence (cases per 10,000) among children 6-59 months old was 1725 (95% CI, 1609-1850) for RSV and 702 (95% CI, 549-896) for influenza. RSV incidence was higher than influenza in every age group and season; it was highest among children 6-11 months old (2863) and 12-23 months old (2473) (figure 1). Influenza incidence did not differ significantly by age group.

Conclusion. RSV incidence was higher than influenza in every season and age group. Children 6-23 months old had a higher incidence of both RSV and influenza compared to those aged 24-59 months. The burden of RSV is high in young children and points to the ongoing need to develop safe and effective preventive interventions.

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1133. Consequences of Late Presentation for HIV Care in Mexico, 2007-2013

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Background. In Mexico, there is a limited number of studies describing the characteristics of hospitalized HIV-infected patients and exploring the risk factors for mortality in the era of antiretroviral therapy (ART).

Methods. 85% of the data were collected from a prospective database and 15% were collected retrospectively. All HIV-infected patients hospitalized from April 2007 to February 2013 were included in the study. Poisson Logistic regression was used

Results. 1310 HIV-infected patients were included in the study and 91 were excluded due to incomplete clinical data. Median age was 33 years (interquartile range (IQR) 28-40); 94% were male; and median CD4 T cell count was 54 cells/mm^3 (IQR 23-125). 300 patients were receiving ART on admission (21%); 237 died (18%). Hospitalizations were due to opportunistic infections in 1032 patients (79%): 475 had PCP (48%); 94 had TB (19%); 107 had cryptococcosis (10%); 88 had Kaposi's sarcoma (9%); 70 had cytomegalovirus (7%); 66 had *Mycobacterium avium complex* (6%); 50 had histoplasmosis (5%); and 203 had unidentified acid-fast bacillus (20%). In addition, 277 had bacterial confection (21%); 79 had Hepatitis B (6%); 53 had syphilis (4%); and 30 had Influenza (3%). *Median length of hospital stay was* 15 days (IQR 9-22). By using univariate analysis, mortality had a negative association with higher CD4 T cell counts (HR 0.7, CI 95% 0.6-0.8, $p < 0.001$); and a positive association with older age (HR 1.2, CI 95% 1.0-1.4, $p = 0.04$). ART use on admission had a weak association with de*creased mortality* ($p = 0.06$). In the multivariate analysis these factors were not associated with mortality, but renal failure, low platelet counts and respiratory failure remained as risk factors for mortality (HR 1.7, 95% CI 1.1-2.6, $p = 0.01$; HR 1.23, 95% CI 1.06-1.43, p= 0.005; HR 5.6, CI 95% 3.6-8.5, $p > 0.001$ respectively).

Conclusion. 80% of the patients were admitted on stage C3 of HIV-infection and 79% were without ART. Mortality was associated with poor clinical condition (renal failure, low platelet counts and respiratory failure). The fact that ART was not protective against mortality was probably due to late presentation for HIV care in most of the patients. Health policies should focus on early presentation for HIV care.

Disclosures. **All authors:** No reported disclosures.

1134. Characteristics of Hospital-Acquired Influenza in Adults in Southern Ontario, 2005-2012

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Background. Influenza poses a particular threat to vulnerable hospitalized patients. We reviewed the characteristics of hospital acquired influenza identified by surveillance in Toronto from 2005 to 2012.

Methods. The Toronto Invasive Bacterial Diseases Network has performed population based surveillance for laboratory confirmed influenza associated with

hospitalization in south central Ontario since the 2004/5 influenza season. Eligible patients were those with influenza identified by EIA, DFA, culture, and/or RT-PCR who either required hospitalization for the illness associated with the positive test, or were admitted to an acute care hospital when the specimen was obtained. Acute care hospital acquired influenza (HAI) was defined as influenza with symptom onset >72 hours after hospital admission.

Results. Between January 2005 and May 2012, 3130 adult influenza cases were identified, of which 318 (10%) were HAI. Of these, 268 were Influenza A (54 H1N1, 112 H3N2, and 103 not subtyped) and 50 were Influenza B. The median rate of HAI was 1.15 per 100,000 patient days (range 0.47-1.93) with no discernible trend. 22% of cases were associated with declared hospital outbreaks. Compared to community acquired cases, patients with HAI were older (70 vs 66 years old, $p < 0.01$), more likely to have prior chronic illness (95.3% vs 90.6%, $p < 0.01$), and more likely to be infected by influenza A (84% vs 77%, $p < 0.05$). At diagnosis, only 40% of hospital acquired cases met the CDC definition for Influenza-like illness. Patients with hospital acquired influenza were more likely to require ICU admission (26% vs 20%, $p < 0.001$) and more likely to die within 15 days of diagnosis (18% vs 9%, $p < 0.001$). Median time from admission to onset of symptoms was 12 days (range 3-209 days). 192/318 (60%) patients were treated with antibiotics, and 217/318 (68%) with antivirals (compared to 84% and 59% in community acquired cases, respectively). Median time from symptom onset to antiviral therapy was 48 hours.

Conclusion. Hospital acquired influenza has atypical presentations and results in a significant number of ICU admissions and deaths. Our surveillance identified only a fraction of cases. Active surveillance studies are needed to further define clinical criteria for influenza testing, and to identify cases occurring after hospital discharge.

Disclosures. **A. Mcgeer**, Hoffman LaRoche: Grant Investigator, Investigator and Scientific Advisor, Research grant and Research support; GSK: Grant Investigator, Investigator and Scientific Advisor, Research grant and Research support; Novartis: Grant Investigator, Investigator and Scientific Advisor, Research grant and Research support; Sanofi Pasteur: Grant Investigator and Scientific Advisor, Research grant and Research support

1135. High rates of self-reported alcohol use in HIV/HCV co-infected and HIV mono-infected patients in a Southeastern U.S. Cohort

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Background. Alcohol use among HIV and hepatitis C virus (HCV) co-infected patients may influence uptake of newer HCV treatment and impact outcomes. Using a Rapid electronic Survey Tool (ReST), we characterized alcohol use in a cohort of HIV/HCV co-infected and HIV mono-infected patients. We hypothesized that co-infected patients would use less alcohol due to education and other healthcare interventions related to alcohol's known effects on liver disease progression.

Methods. The retrospective cohort included patients who attended ≥2 clinic visits at the Vanderbilt Comprehensive Care Clinic, had HCV testing, and completed ≥1 ReST survey between 2008 and 2011. The ReST was administered at each clinic visit to quantify alcohol and drug use in the last 7 days by self-report. Incidence rate ratios (IRR) for alcohol and drug use were obtained by negative binomial regression adjusting for HIV/HCV co-infection, age, race, sex, antiretroviral therapy (ART) use, and HIV risk factor (injection drug use [IDU], men having sex with men [MSM], or other).

Results. Among 2,448 patients, 15% had HIV/HCV co-infection, and 87% had ReST data from ≥1 visit. Compared to HIV mono-infected, HIV/HCV co-infected patients were older ($p < 0.001$), more likely to be female ($p = 0.01$), more likely to identify IDU as their primary HIV risk factor (39% vs 3%, $p < 0.001$), and had a lower mean CD4 nadir (187 vs 228, $p < 0.001$). Forty three percent of co-infected patients reported alcohol use in the last 7 days vs 48% of mono-infected ($p = 0.13$). Only cocaine use differed significantly between co-infected and mono-infected patients (12% vs 5%, $p < 0.001$). In adjusted analysis, alcohol use was more frequent among MSM (IRR 1.7, $p < 0.001$), but was not associated with co-infection (IRR 1.0, $p = 0.7$). Cocaine use was reported more frequently among persons with an IDU HIV risk (IRR 2.4, $p = 0.005$), but also was not associated with co-infection (IRR 1.3, $p = 0.3$). Both alcohol (IRR 0.8, $p < 0.001$) and cocaine use (IRR 0.4, $p = 0.03$) were less frequent among those prescribed ART.

Conclusion. Reported use of alcohol in the last 7 days was high in both HIV mono-infected and HIV/HCV co-infected patients in this cohort. Alcohol use is likely to affect future HCV treatment decisions and outcomes even with the availability of more effective therapies.

Disclosures. **All authors:** No reported disclosures.

1136. Surveillance of Acute Flaccid Paralysis (AFP) in the Republic of Korea during 2012-2013

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Background. Acute flaccid paralysis (AFP) is described as sudden onset of flaccid paralysis in one or more limbs in children and mainly caused by polioviruses. AFP surveillance was managed by World Health Organization (WHO) for standard progress of poliomyelitis eradication.

Methods. This study aimed to investigate clinical and etiological characterization of paralysis cases through a nationwide AFP surveillance during 2012-2013. The AFP surveillance was conducted through reporting and laboratory testing according to the WHO recommendations.

Results. In total of 178 case of AFP between 2012 and 2013, none of case was confirmed poliomyelitis. The non-polio AFP rate were 1.24 in 2012 and 1.11 in 2013 (non-polio AFP cases/100,000 children <15years, respectively). The patients aged < 5 years accounted for the largest proportion (69.1%) of the cases. The analysis of the temporal distribution showed that occurrences were distributed randomly throughout the year, with the highest occurrence from May to July (73 cases; 41.0%). The major clinical manifestation of AFP was meningoencephalitis (71 cases; 39.9%) and the Guillain-Barré Syndrome (22 cases; 12.4%). Non-polio enterovirus (NPEV) infection was diagnosed in 81 patients (45.5%), the major genotype was EV 71 (55 cases; 67.9%). In addition, present study demonstrated that while patients with AFP are not infected with wild poilovirus, they are highly positive for EV.

Conclusion. The AFP surveillance systems comply with WHO-specified epidemiological and laboratory performance standards. Therefore this surveillance was important report for our knowledge of epidemic characteristics, clinical symptom associated with AFP in Korea.

Disclosures. **Y. S. Yoon**, Korea Centers for Diseases Control and Prevention: Member, Educational support **H. Kim**, Korea Centers for Diseases Control and Prevention: Employee, Educational support **S. W. Lee**, Korea Centers for Diseases Control and Prevention: Member, Educational support **J. Y. Hyeon**, Korea Centers for Diseases Control and Prevention: Member, Educational support

1137. Epidemiology and Persistence of Human Rhinovirus Infections in Childcare

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Background. Human rhinoviruses (HRV) are the most common cause of respiratory illness in adults and children. Use of molecular technology has allowed for enhanced detection of HRV and differentiation between infections with different HRV genotypes. We aimed to describe HRV shedding patterns in symptomatic and asymptomatic children attending childcare.

Methods. Children ages 5 weeks to 30 months were prospectively enrolled from three large childcare centers located in Fort Lewis, WA. Nasopharyngeal swabs were collected at enrollment and at onset and weekly during respiratory illness episodes until symptoms resolved. Nasal samples were tested by PCR for HRV and other respiratory viruses and HRV genotype was determined by sequencing the 5' non-coding region. Extended shedding was defined as consecutive positive swabs at least 7 days apart.

Results. During the study period, 225 children were enrolled. A total of 127 children provided an asymptomatic nasal swab at enrollment, with 52 (41%) having HRV present. HRV was detected during 223 out of 455 prospectively-captured illnesses; 123 children had HRV detected during at least one illness. HRV detection persisted for at least 7 days in 28% of all HRV illnesses (n = 62; mean duration 16 days among those with extended shedding). Only 5 of 62 illnesses with extended shedding (8%) had multiple HRV genotype groups identified in different swabs. Respiratory illness symptoms, including fever and cough, were similar regardless of the duration of shedding. HRV illnesses accompanied by other coinfecting respiratory viruses were more likely to have extended shedding compared to illnesses with HRV alone (mean 7 vs 1 days, respectively; $p < 0.001$). Children under 9 months of age shed for a mean of 4 days longer than older children ($p = 0.03$).

Conclusion. We found that extended shedding occurred in over a third of all incident HRV infections. Risk factors for HRV extended shedding include young age and respiratory viral coinfections. In most cases, shedding was not due to subsequent infection with multiple HRV genotypes. This extended shedding may provide an explanation, especially in young children, for the high rates of asymptomatic detection of rhinovirus that has been previously reported.

Disclosures. **J. A. Englund**, Gilead: Consultant and Investigator, Consulting fee and Research support; Chimerix: Investigator, Research support; Roche: Investigator, Research support; GlaxoSmithKline: Consultant, Investigator and Member, DataSafety Monitoring Board, Consulting fee, Payment for DSMB participation and Research support; Ansun Biopharma: Investigator, Research support; MedImmune: Grant Investigator, Research support; Seattle Children's Hospital: Investigator, Research support

1138. Human Adenovirus (HAdV) Blood Viral Detection is Associated with Higher Viral Load in Immunocompetent Pediatric HAdV Respiratory Samples

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Background. Detecting HAdV in the respiratory tract (RT) by molecular methods can provide sensitive and rapid results. However, HAdV can persist in lymphoid tissues and represent incidental detection. We previously reported that HAdV PCR threshold cycle (Ct) of < 35 was associated with higher culture isolation rates from a RT sample. We hypothesized that HAdV detection in the blood (viremia) is more common in acute HAdV infection with high viral load (VL) compared to those with low VL in the RT. We sought to determine the frequency of HAdV viremia when respiratory HAdV is detected in immunocompetent pediatric patients.

Methods. Children presenting to the Emergency Department (ED) or inpatient units and testing positive for HAdV- using semi-quantitative real-time PCR from the RT (Ct <40) were prospectively enrolled from August 2013 to March 2014. The standard respiratory PCR panel includes respiratory syncytial virus, parainfluenza, influenza, metapneumovirus, rhinovirus and HAdV. HAdV PCR was also performed on whole blood or plasma. Mann-Whitney, chi-square or Spearman for correlation was used as appropriate.

Results. HAdV was positive from RT specimens in 269 patients of which 96 (36%) were enrolled. HAdV was detected from blood in > half of patients (50/96, 52%). RT HAdV VL were significantly higher in those with HAdV viremia compared to those without viremia (Ct median 26.9 vs 36.9, $p < 0.0001$). Viremia rates were significantly higher in patients with respiratory specimens having Ct ≤35 vs those with Ct of 35-40 (78% vs 24%, $p < 0.0001$). Semi-quantitative VL in RT specimens were positively correlated with VL in blood ($r = 0.3641$, $p = 0.011$). HAdV was co-detected with ≥1 other respiratory virus in 133/269 (49%). HAdV RT viral load was significantly higher in children with HAdV alone vs co-infection (Ct median: 29.6 vs 36.0, $p< 0.001$).

Conclusion. HAdV viremia is common in the setting of HAdV RT infection. HAdV VL in the RT is positively correlated with VL in blood. A positive HAdV PCR result in RT samples should be interpreted with caution as it may represent incidental shedding when patients have low VL, especially with viral co-infection, suggesting incidental shedding of HAdV.

Disclosures. **All authors:** No reported disclosures.

1139. Risk of influenza after Previous Acute Respiratory Illness in a Cohort of Households with Children

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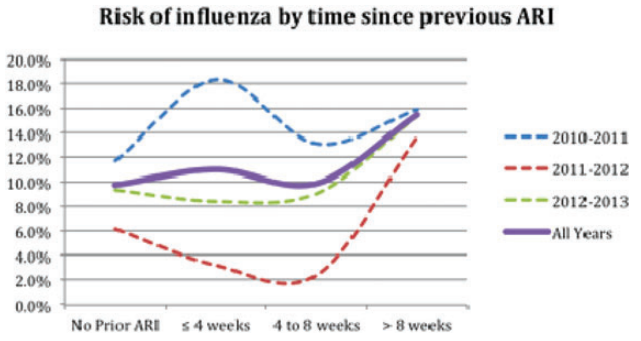
Background. Understanding interactions between the agents that cause respiratory infections can provide valuable insights into pathogenesis of acute respiratory illness (ARI). Viral-bacterial interactions are well studied, particularly influenza and *S. pneumoniae*. Recent studies have suggested viral competition and innate immunity as mechanisms of viral-viral interactions, though these studies are less common.



Methods. We used prior ARI as a proxy for specific respiratory pathogens to examine potential interaction between previous infection and the risk of influenza over 3 years of observation in a prospective cohort of households with children. Regression models used robust standard errors to account for clustering within individuals.

Results. For those with a prior ARI, risk of influenza tended to increase as the time between illnesses increased, though some variability was observed across study years (figure). Previous ARI at any point (RR: 1.29 95% CI 1.03-1.62) and onset of ARI greater than 8 weeks prior to current illness (RR: 1.55 95% CI 1.17-2.01) were significantly associated with an increased risk of influenza compared to those with no previous ARI. However, after adjusting for calendar time between illness onset and peak influenza transmission the association was attenuated for all outcomes and was reversed for those with prior ARI at any point (RR: 0.79 95% CI.0.63-0.98). In fully adjusted models, the risk of influenza was significantly lower for illnesses with an ARI that began 4-8 weeks prior to the current illness (RR: 0.63 95% CI 0.43-0.93) compared to those without a previous ARI.

Conclusion. The observed increase in risk of influenza with any prior ARI appears to be driven by illnesses that occurred more than 8 weeks before the onset of the influenza illness. However, this finding could also be due to underlying susceptibly that is not captured by high-risk health conditions. Significantly lower risk for those with an ARI that began between 4 and 8 weeks prior to the current illness may imply competition among pathogens that cause ARI and warrants further study. Additional analyses will examine interactions among specific viruses specific. These results suggest that calendar time is an important confounder when examining the effects of respiratory pathogen interaction on virus specific outcomes.

Disclosures. **A. Monto**, Sanofi Pasteur: Consultant and Grant Investigator, Consulting fee and Grant recipient; GSK: Scientific Advisor, Consulting fee

1140. Data on Measles, Mumps, Rubella, and Varicella Immunity; using Locally Derived Seroprevalence by Birth Cohort to Determine Risks for Vaccine Preventable Diseases during International Travel

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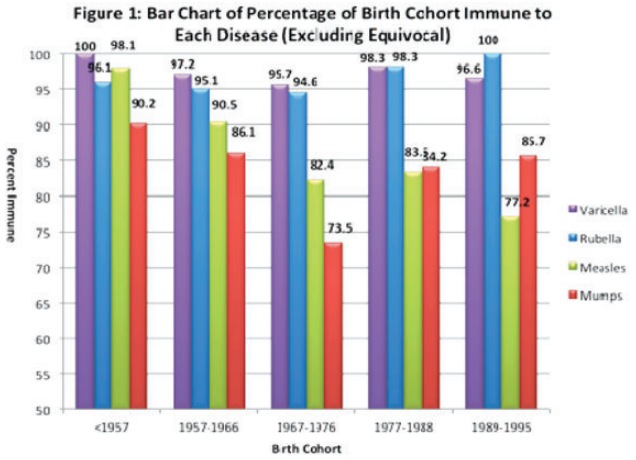
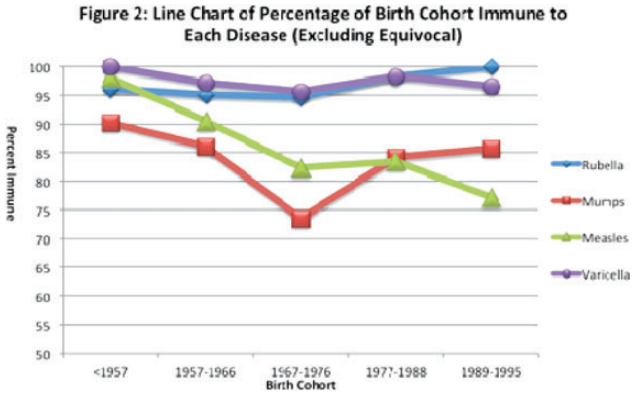
Background. Even after dramatic reductions in the prevalence of measles, mumps, rubella and varicella in the United States, there continue to be outbreaks of these diseases, stressing the need for ongoing immunization and pre-traveling counseling.

Most prior studies of seroprevalence for these viral diseases are often based on national surveillance data. It is therefore important to get a clearer understanding on the local level of immunity so that more focused recommendations can be made for our patient population.





Methods. Leftover, non-duplicate outpatient serum samples obtained in Lehigh Valley Pennsylvania were tested for IgG antibodies using commercially available enzyme immunoassays to mumps, measles, rubella, and varicella. Samples were collected sequentially, and de-identified. Five birth cohorts were created and 460 samples were

collected as follows: <1957 (52), 1957-1966 (109), 1967-1976 (117), 1977-1988 (121), and 1989-1995 (61).

Results. Results are summarized in Figures 1 and 2. Overall seroprevalence (excluding equivocal results) for measles, mumps, rubella, and varicella were (%): 85.8, 82.8, 96.6, and 97.4. There was a significant association between seroprevalence and birth cohort for measles ($p = 0.010$) and mumps ($p = 0.037$) only. Pairwise comparisons of the cohorts found that for measles there was a significant difference between the <1957 vs 1967-1977 ($p = 0.005$) cohort and the <1957 vs 1989-1995 ($p = 0.001$) cohort. Additionally, the overall seroprevalence for our study sample was significantly different than national seroprevalence results for rubella, mumps, and measles.

Conclusion. Our study on local seroprevalence showed dramatically lower immunity rates to measles and mumps than prior national seroprevalence studies have shown. The rates in many of the later birth year cohorts were significantly lower than rates reported necessary to sustain herd immunity. The results of this study show the tremendous value in determining seroprevalence on a local basis. We will use these results to alter our approach to assessing travelers and others in our clinics based on their birth year.

Disclosures. **All authors:** No reported disclosures.

1141. 2013-2014 Resurgence of 2009 Influenza A (H1N1) Infection among Adults: Has the Epidemiology and Clinical Severity of Disease Changed?

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Background. For the first time since the 2009 pandemic, 2009 Influenza A (H1N1; pH1N1) emerged in 2013-2014 as the predominant influenza A subtype in the US. We analyzed adult cases of pH1N1 from 2009-2014 to describe how the epidemiology and clinical severity of disease has changed over time.

Methods. Established in 2009, the Acute Respiratory Infection Consortium (ARIC) Natural History Study is an observational, longitudinal study of influenza-like illness (ILI) among military beneficiaries at five US military treatment facilities. Individuals age 18-65y with ILI onset <72h were eligible. Clinical symptoms and physical findings were ascertained at enrollment. Nasal/throat swabs were collected at baseline and tested by influenza PCR.

Results. From 2009-2014, 161 enrollees were positive for influenza. Of these, 143 (88%) were influenza A, including 71 pH1N1 cases (50%). Twenty-six pH1N1 cases were enrolled in the 2013-2014 influenza season. The age of pH1N1 cases was higher in the current season compared to the previous four seasons (median 35y vs 27.6y, respectively; $P < 0.01$). Cases in 2013-2014 had lower severity of cough (median score 2 vs 3; $P = 0.04$) and composite systemic symptom score (mean score of chills, muscle, headache, fatigue, and dizziness; median 1 vs 1.6; $P = 0.01$) than cases from the previous four years. The proportion of pH1N1 cases receiving pH1N1-containing vaccine in the season of enrollment varied from 22.2% in 2009-2010 to 73.1% in 2013-2014. In 2013-2014, 19 (66%) of 29 pH1N1 cases had received seasonal influenza vaccine >14 days prior to illness: 8 (42%) received quadrivalent and 11 (58%) received trivalent vaccine. Quadrivalent vaccine recipients were younger than trivalent vaccine recipients (mean 29.1y vs 44.3y; $P = 0.004$), with similar doses of influenza vaccine received in the past 5 years. No significant differences in clinical severity were observed in the two vaccination groups.

Conclusion. Middle-aged adults were more affected during the resurgence of pH1N1 in 2013-14, while the highest incidence of pH1N1 2009-10 was among those <25y. Symptom severity of pH1N1 infection appears to have lessened over time.

Disclosures. **All authors:** No reported disclosures.

1142. Critically Ill Children Hospitalized with an Acute Respiratory Viral Infection: Characterizing ICU severity

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Background. Acute respiratory viral infections (ARVI) are a common public health problem with a significant global health care burden. There is no comprehensive data on which viral pathogen or pathogens are associated with the highest severity in children with ARVI requiring intensive care. We characterized the severity of critical illness secondary to ARVI in a Pediatric Intensive Care Unit (PICU). We hypothesized that no single virus would consistently correlate with a greater severity of illness.

Methods. We performed a retrospective chart review of children ≤18 years of age with a respiratory viral infection and a positive PCR test (Respiratory Viral Panel, Biofire) requiring PICU admission in a 23-bed New York City PICU between 2010-2013. We described and analyzed the clinical characteristics of infected children. The institutional review board of Weill Cornell Medical College approved conduct of this study with a waiver of informed consent.

Results. Our PICU admitted 2957 patients during the study period, of which 245 (8%) tested positive for a viral pathogen. The average age was 3.08 years (0.04-19.45), compared to an average age of 3.48 years for the general PICU population. Most patients with a positive viral assay also had an underlying medical condition (78%). 103 patients (42%) with a respiratory virus were intubated and 27 patients (18.6%) had a tracheostomy, compared to 221 (7.5%) and 81 patients (2.7%) respectively in the general PICU population during the same period. Rhinovirus was the most common pathogen, comprising 55% of our cohort. RSV comprised 13%. Regarding severity, adenovirus ($p = 0.06$) and parainfluenza ($p = 0.01$) were associated with a longer length of stay in both the PICU and hospital. Additionally, 67% of children with adenovirus required mechanical ventilation vs only 29% of children with RSV, though these results did not achieve statistical significance.

Conclusion. Our data suggests that while no single virus was responsible for an overall greater severity of illness, parainfluenza and adenovirus trended towards this; further study is needed. Overall, respiratory viruses have a considerable pediatric healthcare and critical care burden.

Disclosures. **All authors:** No reported disclosures.

1143. GenMark ESensor Respiratory Viral Panel in an Inpatient Pediatric Population

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Background. Respiratory viruses cause significant morbidity and hospitalization among children. Recent advances in diagnostics have improved the ability to identify viral pathogens, avoiding prolonged hospitalization and unnecessary antibiotic use. A molecular diagnostic test was recently FDA approved (eSensor XT-8 with GenMark Dx).

Methods. The standard of care to identify respiratory viral pathogens at our large pediatric referral facility utilizes Direct Fluorescent Antibody (DFA), with viral culture on DFA-negative specimens. GenMark probe testing was added to standard-of-care testing for a total of 300 samples from inpatients during the 2012-13 respiratory season. 200 samples negative by DFA/culture and 100 positive by either DFA or viral culture were used. Clinical data were collected. Length of stay was only calculated for those ≤ 21 days (n= 268), to exclude hospitalizations unlikely related to viral illness.

Results. The eSensor RVP identified viral nucleic acids in 74.1% of samples, compared to 22.5% from standard of care, thus tripling the diagnostic yield. Results by virus are listed in the table. There was no association with longer hospitalization or higher acuity among subjects with multiple viruses detected, or with influenza or RSV alone. Longer length of stay and higher acuity was only associated with Coronavirus. OC43 was the most common coronavirus identified (71%) and these associations remained significant. Younger subjects were more likely to have RSV, HRV, and > 1 virus.

Subject Characteristics by Virus

Virus	N	Age (years) mean	Length of Stay (days) mean	p-value	Higher Acuity	p-value
Influenza A	6	3.8	5.8	0.7	1.4%	0.4
Influenza B	11	3.1	3.8	0.3	4.2%	0.8
RSV	26	1.7	5.9	0.3	8.3%	0.3
PIV	10	3.3	3.9	0.3	2.8%	0.4
hMPV	25	2.2	4.6	0.5	11.1%	0.9
HRV	42	1.9	4.3	0.2	18.1%	0.9
ADV	7	4.1	2.7	0.1	2.8%	0.9
Corona	34	3.4	7.3	**0.004**	25.0%	**0.004**
OC43	24	3.5	7.4	**0.011**	18.1%	**0.012**
> 1 virus detected	72	1.9	5.2	0.9	26.4%	0.4

Conclusion. The improved sensitivity of the eSensor RVP identifies many more infections than current standard of care. Coronavirus, especially OC43, could potentially represent a more virulent pathogen, associated with both prolonged hospitalization and higher acuity. Detecting > 1 virus in a hospitalized child is not predictive of higher acuity illness or longer hospitalization.

Disclosures. **D. W. Kimberlin**, GSK: Grant Investigator, served as study site for clinical trials conducted by GSK (all monies went to university), Grant recipient; Gilead: Grant Investigator, served as study site for clinical trials conducted by Gilead (all monies went to my university). Grant recipient **M. N. Prichard**, GenMark: Investigator, Mark Prichard received research funds from GenMark to defray costs associated with the study. and Research support

1144. Healthcare Acquired Crimean Congo Hemorrhagic Fever in Turkey 2002-2012 - Low Risk of Transmission in Routine Diagnostic Laboratory Practice

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Background. Healthcare-related transmission of Crimean Congo Hemorrhagic Fever (CCHF) is a well- recognised hazard. We reviewed a decade of experience in Turkey, where CCHF is endemic, to determine the relative contributions of transmission in near patient settings and in diagnostic laboratories.

Methods. Physicians managing patients provided retrospective case details from clinical and public health records and details of their local infection control practices relevant to CCHF. Only virologically/serologically confirmed cases were included.

Results. 7192 cases of CCHF were notified to the Ministry of Health (MoH) in 2002-2012, with 359 deaths (5 %), of which 4 were identified as nosocomial. The details of 37 confirmed healthcare-related cases were obtained from 7 centres, including 27 (73%) women, with 3/37 (8.1%) overall mortality. 16 (43%) were physician trainees, 15 nurses, 2 physician specialists, 2 medical students and 2 other staff. The main routes of injury were needlestick in 28/37 (75.7%), other defined blood/secretion exposure in 8 (21.6%) and unidentified in 1 case. Post exposure ribavirin prophylaxis was administered after 18/28 (75.6%) needlestick and 0/9 other exposures. No possible or probable laboratory-related infections were noted. An estimated minimum of 20,000 samples from CCHF patients were analysed in routine haematology and biochemistry laboratories nationally in this period. The 7 reporting institutions are regional infectious disease centres, where CCHF cases are managed with standard blood and secretion precautions and staff are trained in safe sharps disposal. No special precautions are taken in routine haematology and biochemistry labs to handle diagnostic samples from CCHF patients in special cabinets.

Conclusion. Healthcare-related transmission of CCHF is dangerous but the incidence in Turkey is lower than in other reports, involving an estimated total of 50-60 staff in 7192 admissions (<0.1%) in a decade. Those at greatest risk are ward-based staff performing invasive procedures including cannulation and venepuncture, and these staff especially need adequate training and protection. Our data suggest that there is very little hazard from processing haematology and biochemistry blood samples while following routine laboratory procedures.

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1145. 2009 H1N1 Compared to Post-pandemic H1N1 Influenza Among Pediatric Inpatients

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Background. The novel influenza A H1N1 strain emerged in 2009, contributing to significant morbidity and mortality. It is not known whether the current H1N1 strains cause the same severity of illness. The aim of this study was to compare the burden of disease from H1N1 influenza during the 2009 pandemic year to the subsequent years (2010-2014) and to identify whether the same risk factors for severe disease exist.

Methods. A retrospective cohort study of inpatients admitted to Children's Hospital Colorado with respiratory specimens positive for influenza from May 1, 2009 to November 30, 2009, and December 1, 2010-April 12, 2014 was conducted. Data regarding patient demographics, clinical symptoms and signs, comorbidities and outcomes were compared to data previously obtained for the 2009 H1N1 pandemic influenza strain.

Results. There were 328 inpatients with H1N1 during the 2009 pandemic, and 120 during the post-pandemic years. 90% of all post-pandemic H1N1 was observed during the 2013-2014 influenza season. 39% of patients with post pandemic H1N1 were completely vaccinated against influenza. Compared to the post-pandemic years, there were more Hispanic, black and native-American patients with H1N1 admitted (P <0.02 for all) and more patients with an underlying medical condition (P < 0.0001) during the pandemic year.

Older patients were more likely to be admitted to the ICU for both pandemic and post-pandemic groups (median age 6.5 years and 4.9 years respectively, P =0.19). For patients admitted to the ICU, there was higher antibiotic use during the pandemic year (82% vs 58%, P = 0.013). While a higher proportion of patients were admitted to the ICU during 2010-2014, 43/120 (36%) vs 84/328 (26%), P = 0.024, patients with 2009 H1N1 were more likely to be intubated (P =< 0.0001), have mental status changes (P= 0.0005), hypotension (P = 0.05) and have ARDS (P = 0.017) compared with the post-pandemic strain.

Conclusion. H1N1 represented the majority of influenza cases over the last influenza season. While there were higher rates of ICU admission among inpatients with post-pandemic H1N1, there appears to be decreased illness severity compared with the pandemic H1N1 patients, including lower intubation rates, hypotension, ARDS and mental status changes.

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1146. Prevalence of blood borne viruses in the dialysis unit, Mubarak Al-Kabeer Hospital, Kuwait

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Background. Due to the lack of recent data in Kuwait, it was decided to investigate the prevalence of HBV, HCV and HIV, among dialysed patients in the dialysis unit at the Mubarak Al-Kabeer Hospital.

Methods. Between January 1–December 31, 2012, a total of 1,369 blood samples were received by the virology unit from adult patients on dialysis at Mubarak Al-Kabeer Hospital.

HBV, HCV and HIV were screened. A positive screening result is followed by a confirmation method.

SPSS software (version 17.0 for Windows; SPSS, Chicago, IL) was used for all statistical analyses. For categorical variables, χ^2-test or Fisher's exact was used.

Results. A total of 1369 blood samples were collected over a one year period with a total number of 588(43%) females and a total number of 781 (57%) males. Seven hundred and forty four (54.3%) samples were received from Kuwaitis and 625 (45.7%) samples from non-Kuwaitis (table).

The prevalence of BBV in the dialysis unit in relation to gender and nationality with calculated p-value

	HBV	HCV	HIV
N (%)		Negative	
Gender:	1346 (98.3%)	1277 (93.3%)	1362 (99.5%)
Male	762 (97.6%)	709 (90.8%)	776 (99.4%)
Female	584 (99.3%)	568 (96.6%)	586 (99.7%)
Nationality:	736 (98.9%)	708 (95.2%)	740 (99.5%)
Kuwaiti	610 (97.6%)	569 (91%)	622 (99.5%)
Non-Kuwaiti			
N (%)		Indeterminate	
Gender:	6 (0.4%)	6 (0.4%)	5 (0.4%)
Male	4 (0.5%)	5 (0.6%)	3 (0.4%)
Female	2 (0.3%)	1 (0.2%)	2 (0.3%)
Nationality:	4 (0.5%)	1 (0.1%)	2 (0.3%)
Kuwaiti	2 (0.3%)	5 (0.8%)	3 (0.5%)
Non-Kuwaiti		5	
N (%)		Positive	
Gender:	17 (1.2%)	86 (6.3%)	2 (0.1%)
Male	15 (1.9%)	67 (8.6%)	2 (0.3%)
Female	2 (0.3%)	19 (3.2%)	0 (0.0%)
p-value	*0.018*	*0.001*	*0.608*
Nationality:	4 (0.5%)	35 (4.7%)	2 (0.3%)
Kuwaiti	13 (2.1%)	51 (8.2%)	0 (0.0%)
Non-Kuwaiti	*0.020*	*0.012*	*0.557*
p-value			

Conclusion. The calculated prevalence for HBV, HCV and HIV are 1.2%, 6.3% and 0.1%, respectively. The prevalence of HBV among males was significantly higher when compared to females. HCV prevalence among males is significantly higher when compared to females. The prevalence of HBV among non-Kuwaitis was significantly higher when compared to HBV prevalence among Kuwaitis. HCV prevalence among non-Kuwaitis was significantly higher when compared to HCV prevalence among Kuwaitis. The prevalence for HIV in the dialysis is relatively low when compared with HBV and HCV. Therefore, screening for HIV is best when based on a risk assessment of individual patients.

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1147. Factors Associated with Spontaneous Resolution of HCV Infection in Untreated Individuals, Philadelphia

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Background. Hepatitis C virus (HCV) affects approximately 3.2 million individuals in the United States. An estimated 70% of HCV-infected individuals suffer from chronic infection. The specific factors associated with spontaneous clearance of HCV in the remaining 30% of individuals remains poorly defined. This study uses surveillance data to highlight differences between those who spontaneously clear HCV infections and those who are chronically infected in a large urban area.

Methods. The Philadelphia Department of Public Health (PDPH) collects clinical and risk factor data from patients and providers as a part of an enhanced surveillance project. Surveillance data from January 1, 2013 – May 31, 2014 was used to compare those with RNA-positive chronic HCV cases to individuals with resolved infection (currently RNA-negative). Demographics, active risk factors (injection drug use (IDU), tattoos, incarceration, many lifetime sex partners and being a man who has sex with men) and passive risk factors (organ/blood transfusion, needle stick, and hemodialysis) were compared.

Results. Of the 739 HCV patients investigated, 84 (11%) had resolved infections without receiving treatment. These 84 individuals were less likely to be male (42% vs 62%, p-value = 0.0007), black (19% vs 47%, p-value < 0.0001), and were younger (median: 31 years vs 49 years, p-value <0.0001) than those with chronic infections. Chronically infected individuals were more likely to be in care for HCV (61% vs 35%, p <0.005) and have histories of IDU (54% vs 23%, p-value <0.0001) or incarceration (54% vs 16%, p-value <0.0001).

Conclusion. Our findings support prior studies showing that African-Americans and males are less likely to show spontaneous clearance of HCV. The association between high risk behavior and reduced HCV clearance may be partially explained by reinfection with new viral strains, though further studies are warranted. By defining the mechanisms underlying viral control, it may be possible to utilize robust surveillance data to target individuals for treatment and/or care using risk and demographic indicators. The use of new medications for HCV treatment with this enhanced targeting technique may allow for additional clearance of HCV infection in non-resolved patients.

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1148. Characterization of Patients with Hepatitis B and C Infection at an Urban Hospital, 2006-2013

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Background. Since the CDC now recommends routine Hepatitis C screening among baby boomers, identifying patients with this infection has become a public health imperative. In Washington, DC an area with high HIV and injection drug use prevalences understanding the disease burden of both Hepatitis B and C is critical due to the impact of co-infection. Despite this, the prevalence of Hepatitis B and C had not been previously assessed at our hospital. Given the absence of these data we assessed the demographics and volume of persons with Hepatitis B and C patronizing our facility.

Methods. The hospital health information system was queried for hospital patients with Hepatitis B and C diagnosis codes from 2009-2013 irrespective of site of service and reason for presentation. This list was further stratified to include persons presenting for either hospital or emergency department (ED) admission. Demographic data and primary, secondary and tertiary diagnosis codes were identified for each patient. Univariate analysis was conducted to epidemiologically characterize Hepatitis patients seeking hospital-based care.

Results. Over the 5 year period, 5,129 visits for 4,201 individual patients occurred among patients with Hepatitis B and C. The median age was 54 (range 17-91), 63% were male, 76% were publically-insured and 13% were from correctional settings. Over 95% were African-American and 68% resided in Southeast, Washington, DC. Because treatment for Hepatitis B and C were not available at our institution, no data were available for treatment status. Primary, secondary and tertiary diagnoses were largely related to chronic medical conditions rather than Hepatitis.

Conclusion. The prevalence of Hepatitis B and C infection in Southeast Washington, DC is significant. Given the need to expand testing and treatment for these diseases, strategies are needed to ensure availability and access to care for this population. In addition, this population was largely insured through public insurance programs which suggests public policy will be needed to support the cost of care for this group.

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1149. High prevalence of Hepatitis B infection among pregnant mothers attending Antenatal clinics in Hospitals in Gulu District, Northern Uganda

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Background. Newborn infants acquiring Hepatitis B Virus (HBV) infection through peri-natal transmission have a greater than 95% chance of becoming chronic carriers compared to 5% for infections acquired during adulthood. 50%of the carriers will die of liver complications. Subsaharan Africa bears a big brunt of the mortality attributed to HBV, but there is limited data on HBV burden and infectivity among pregnant mothers in Uganda. We aimed to determine HBV infection prevalence among pregnant women attending antenatal clinic (ANC) in the two major Hospitals in Gulu District, Northern Uganda and to determine Hepatitis B e antigen (HBeAg) positivity as a surrogate measure of risk of infectivity for vertical transmission

Methods. A cross sectional study was done among pregnant women attending ANC at Lacor and Gulu Hospitals. Demographic, clinical history and examination data was collected by trained midwives. They were also tested for serum HBsAg using ELISA. HBsAg positive women were also tested for HBeAg. Data was analyzed using SPSS version 17, comparing proportinos using chi square and reporting p values.

Results. Of 397 women studied, 47 (11.8%) tested positive for HBsAg. Of these 47 women, 4 (14.7%) were HBeAg positive. The highest HBsAg positivity rate was seen in women aged 20 years or less (20%) compared to those above 20 years old (8.7%), OR 2.2 (CI 1.29-3.78), p = 0.005. HBsAg positivity was associated with high levels of leucocytes, p = 0.046 but there were no significant difference between the HBsAg positive and negative by liver enzymes, Hemoglobin level, neutrophil or mean WBC count. HIV positivity was not a predictor of HBV positivity

Conclusion. There is a high prevalence of Hepatitis B infection among pregnant women coming for care in Gulu and Lacor Hospitals (11.8%). Although high, this is lower than the regional prevalence of 17-22%, possibly stressing the fact that there is more early childhood transmission. A significant number of these mothers are HBe Ag positive (14.9%) and may be at an even increased risk of transmitting infection to their unborn babies, signifying need to vaccinate HBV exposed babies at birth for HBV, which is not yet a standard practice in Uganda.

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1150. The Disease Burden of Chronic Hepatitis C in Turkey

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Background. Hepatitis C virus (HCV) disease burden and the impact of new potent direct acting antivirals (DAAs) in Turkey are currently unknown. We examined HCV-related disease progression to quantify the burden of disease from a Turkish perspective.

Methods. Using a modeling approach, we quantified the HCV-infected population and associated disease progression through 2030. The HCV-infested population was characterized using published literature, Turkish government reports including year-end 2013 and estimates from a panel of country experts. We developed three treatment strategies to analyze the changes in burden of HCV infection: treatment of patients >F3 with new DAAs (restricted treatment), treatment of all patients with new DAAs (unrestricted treatment) and increased diagnosis and treatment for the elimination of HCV.

Results. The viremic prevalence is estimated to have peaked in 1998 (601,000 individuals), and to decline 40.2% by 2030 (359,000 cases). However, the number of cases of compensated (n = 74,500) and decompensated (n = 9.480) cirrhosis, HCC (n = 4,170), and liver-related deaths (n = 3,670) will peak between 2028-2032.

Compared to the base case, under restricted treatment HCV related mortality will decrease 7% by 2030. Under unrestricted treatment, HCV related mortality will decrease 22% by 2030. Elimination was achieved through aggressive treatment and diagnosis wherein mortality was decreased by 77%.

Conclusion. Prevalence of HCV infection in Turkey has been declining for the last 15 years; however, the prevalence of HCV-related liver disease, morbidity and mortality is increasing. This analysis may facilitate the development of strategies for HCV care and management in Turkey.

Disclosures. **All authors:** No reported disclosures.

1151. *Geographic Distances Between Patients and Providers for Hepatitis C Virus Infection Testing*

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Background. To address the lack of US specialists available to care for the estimated 2.7 million persons with chronic hepatitis C virus (HCV) infection, CDC supports training of primary care providers and technology to offer remote treatment options. We evaluated the distance patients travelled to visit the provider ordering HCV tests.

Methods. A new private-public partnership allowed for preliminary analysis of LabCorps testing records conducted during February – July 2012. HCV-related tests consisted of antibody, nucleic acid (RNA and genotype) and host IL28B tests. We calculated the frequency and distribution of tests by test type, and the ratio of number of tests and unique providers by provider specialty. We used SASHELP.zipfile to estimate the distance between the center of the patient zipcode and the center of the provider zipcode to compare median distances by provider specialty and US state.

Results. CDC received records from 1,112,105 tests conducted by LabCorps during the 6 month period. Of these, 83% (926,805) were antibody tests, 16% (178,020) were nucleic acid tests, and <1% (7,276) were IL28B tests; 981,078 tests ordered by 120,721 providers had complete information. The test to provider ratio was 8.1 overall and was higher for infectious diseases (23.7) and hepatology (26.1) specialists compared with primary care providers (family practice, 6.4; general practice, 6.6; internal medicine, 7.3). For 571,356 records, the median distance between patient and provider zipcodes was 12.1 miles. The median distance patients travelled did not differ by type of test; 12.0 miles for an antibody test and 12.4 miles for a nucleic acid test. However, the median distance to see a primary care provider was shorter (internal medicine 8.0 miles, general practice 10.0 miles, and family practice 11.5 miles) compared to the median distance travelled to see a gastroenterologist or hepatologist (12.4 miles, and 22.7 miles, respectively).

Conclusion. Patients were closer in proximity to primary care providers and if these can be trained to test and provide care and treatment, then more infected persons could be helped.

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1152. Burden of Hepatitis C Virus and Infective Endocarditis in Community and Inmate Hospitalized Patients in Massachusetts

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Background. Increasing rates of ED visits and hospitalizations secondary to opiate abuse have been observed by the MA DPH. Despite these trends, there is a relative lack of data on hospitalizations related to infectious complications of injection drug use, including Hepatitis C Virus (HCV) and infective endocarditis (IE) in the public health or corrections setting.

Methods. We performed a retrospective review of electronic medical records of patients who were discharged from Lemuel Shattuck Hospital, a MA public health facility that provides care to inmates and community patients. We collected information on discharges from the hospital in 2004, 2008 and 2011 including patients' age, race, gender and incarceration status, and presence of ICD-9 codes for HCV, IE and opioid abuse.

Results. There were a total of 3969 discharges; 83% of patients were male, 55% inmates, and 55% white. 24% of patients were admitted more than once. Mean age increased from 46.0 (2004) to 47.6 (2008) and 47.7 (2011; ANOVA, p = 0.001). The proportion of discharges with HCV ICD-9 codes increased from 2004 (21.6%) to 2008 (23.9%) and 2011 (26.3%; p= 0.003). The proportions of discharges with IE and opioid abuse also increased. Inmate discharges with HCV and opioid abuse increased, but not inmate discharges with IE.

Trends in Discharges with ICD-9 Codes for HCV, IE and Opioid Abuse

	2004	2008	2011	P value
All Discharges (n=3969)	1396	1228	1345	
HCV (n=949)	301 (21.6%)	294 (23.9%)	354 (26.3%)	0.003
IE (n=170)	38 (2.7%)	68 (5.5%)	64 (4.8%)	0.008
Opioid Abuse (n=298)	51 (3.6%)	111 (9.0%)	136 (10.1%)	>0.001
Inmate Discharges (n=2202)	790	676	736	
HCV (n=485)	149 (18.9%)	159 (23.5%)	177 (24.0%)	0.01
IE (n=44)	12 (1.5%)	21 (3.1%)	11 (1.5%)	0.99
Opioid Abuse (n=87)	19 (2.4%)	31 (4.6%)	37 (5.0%)	0.008

P value calculated through Chi-Squared Test For Trend in Proportions

Conclusion. Our data show an increasing burden of hospitalizations at a public health facility in people with a history of HCV, IE and opioid use. Increasing rates of HCV and IE are the likely downstream infectious complications of a local epidemic of opiate abuse and transition to injection drugs. These data inform future public health, hospital and corrections departments resource allocations into HCV and substance abuse treatment programs.

Disclosures. **A. Kim**, Abbvie Pharmaceuticals: Scientific Advisor, Consulting fee; Gilead Sciences: Investigator and Scientific Advisor, Consulting fee and Research grant; Bristol-Myers Squibb: Investigator, Research grant

1153. Epidemiology and Trend in hepatitis A hospitalizations in the United States, 2002 – 2011

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Background. Hepatitis A virus infection is a mild disease in children, but illness severity increases with age, particularly in persons with chronic liver disease. An effective vaccine is available, and vaccination of all children aged 12–23 months and of adults with chronic liver disease is recommended. The purpose of this study is to assess changes in hospitalization rates in the last decade and describe characteristics of persons hospitalized for hepatitis A.

Methods. We used data from the National Inpatient Survey (NIS), the largest population-based hospital inpatient care database available in the United States. Hospitalizations with hepatitis A as the primary diagnosis were identified by the ICD-9 code 070. To develop national estimates we used discharge weights provided by NIS, to extrapolate the NIS sample to the total hospitalizations nationwide. The study period was divided into time intervals: 2002-2003, 2004–2005, 2006–2007, 2008-2009 and 2010-2011.

Results. Rates of hospitalization for hepatitis A as the primary diagnosis decreased proportionally across all regions from 0.72/100,000 to 0.29/100,000 ($p < 0.0001$) during 2002–2011. Mean age increased from 37.6 years to 45.5 years ($p < 0.0001$) during the same time period. Percentages of hospitalizations for hepatitis A that were covered by Medicare increased from 12.4% to 22.7% ($p < 0.0001$). The percentage of comorbid medical conditions also increased from 2002-2003 to 2010-2011; specifically, non-alcohol related liver diseases (from 5 to 13%), alcohol-related liver disease (from 2 to 5%), other liver disease (from 6 to 18%), ischemic heart disease (from 5 to 9%), and hypertension (from 17 to 27%). There was no significant change in length of stay or in-hospital deaths.

Conclusion. Hospitalization rates for hepatitis A illness declined from 2002–2011, and the characteristics of persons hospitalized for hepatitis A disease have shifted to those who are older and more likely to have comorbid medical conditions. Although there are fewer hospitalizations, persons who are hospitalized were sicker in 2011 compared to 2002. Hepatitis A vaccination of persons with liver disease or cardiovascular diseases should be prioritized to prevent poor outcomes from hepatitis A disease.

Disclosures. **All authors:** No reported disclosures.

1154. Host and Pathogen Genetics Modulate HSV-1 Severity

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Background. HSV-1 infection has a wide severity spectrum in the immunocompetent host, from asymptomatic seropositivity to frequent orolabial lesions. To gain insight into virus and host genotype contributions to disease phenotype, we evaluated HSV-1 genotypes and immunity in mono- (MZ) and dizygotic (DZ) twins.

Methods. HSV-1 seropositive twin pairs collected daily oral swabs for quantitative HSV-1 PCR and kept symptom diaries for 60 days. Associations of shedding rates were assessed by estimating correlations. We categorized the viral strain as identical or different in each pair with DNA available for genotyping from both. The identity and breadth of HSV-1 antigens recognized by circulating CD4 T-cells were determined using a complete HSV-1 ORF (open reading frame) set. CD4 T-cell responses were scored as present or absent to each ORF. We used a bootstrap method to estimate the distribution of agreements in ORF responses between individuals.

Results. We enrolled 29 MZ and 22 DZ twin pairs. The overall shedding rate was 10.3% of days (median 9.3%; range 0-47%). There was a positive correlation between shedding rates within twin pairs ($r = 0.33$, $p = 0.015$) but not among unrelated individuals ($r = -0.086$; $p = 0.5$). Genotyping showed that 15/14 twin pairs had the same/different HSV-1 strain, respectively. The correlation for shedding rates in all twin pairs was higher in those with the same virus ($r = 0.55$, $p = 0.033$) vs different ($r = -0.169$, $p = 0.56$). 8 MZ pairs were analyzed for CD4 T-cell responses. The median number of ORFs recognized per person was 19 (range 6-35). The bootstrapped mean percent agreement in ORF response between unrelated pairs was 71% ($5^{th}/95^{th}$ percentile, 67%/75% respectively). The percent agreement between the original 8 pairs of MZ twins was 77% ($p = 0.003$ for difference from bootstrapped dataset).

Conclusion. A relationship between HSV-1 shedding and host genotype is supported by our observation of a higher correlation in HSV-1 shedding between twin pairs than between unrelated individuals and similar CD4 T-cell responses between MZ twins. These data and the higher correlation in shedding rates among twins with the same vs different virus suggests that both viral and host genetics contribute to HSV-1 severity.

Disclosures. **A. Wald**, Aicuris: Consultant, Consulting fee; Genocea: Investigator, Research support; Agenus: Investigator, Research support; Vical: Investigator, Research support

1155. Origin of the dengue virus outbreak in Martin County, Florida, USA 2013

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Background. Dengue virus (DENV) is the most important mosquito-transmitted virus worldwide. DENV is also increasing in transmission and range. This is evidenced in the United States by two outbreaks in South Florida. The question of whether these two Florida outbreaks were caused by the same DENV strain has implications for surveillance and control. If the two viruses are similar, then that would suggest that a single introduction had spread to multiple areas in Florida due to movement of people/mosquitoes within the state. If the two viruses are distinct, that would suggest a new introduction of DENV in Florida from outside the USA. Control and surveillance measures to address these two scenarios would differ in focusing on local vs international transport. In this study, we report clinical findings from an index case and phylogenetic analysis of the E gene region from the infecting DENV.

Methods. A 56 year-old male gutter installer was evaluated August 2013 with generalized body aches and flulike symptoms. Two other employees were admitted with similar symptoms. He was seen in the Emergency room and discharged on oseltamivir. He was readmitted the following day with a temperature of 102 degrees F and a diffuse skin rash. His physical examination was remarkable for a faint macular papular rash. His WBC was 0.9 with Neutrophils 16%, Bands 32%, Lymphocytes 34%, Monocytes 10%. His platelets were 23K. His ALT was 552, AST 270, Total Bilirubin 0.6. Influenza antigen was negative. His cultures were negative for CMV, EBV, and HIV. DENV IgM was confirmed positive five days later after his symptoms improved but IgG was negative. His platelets normalized as well as his LFTs prior to discharge.

Results. Sequencing results from virus amplified from this patient indicate that the 2013 Martin County DENV-1 strain is distinct from the 2009-2010 Key West DENV-1 and that it is most closely related to viruses from a recent expansion of South American DENV-1 strains into the Caribbean.

Conclusion. The phylogenetic analysis of our index patient demonstrates a distinct virus from the 2009-2010 outbreak in Key West. This suggests a new introduction of DENV in Florida from outside the US and warrants immediate Control and Surveillance policy for the Florida - Caribbean port of entry.

Disclosures. **All authors:** No reported disclosures.

1156. Clinical syndromes associated with Kaposi Sarcoma Herpesvirus lytic replication: Comparing features of KSHV Inflammatory Cytokine Syndrome, Multicentric Castleman Disease and Hemophagocytic Lymphohistiocytosis

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Background. Kaposi Sarcoma Herpesvirus (KSHV) is the causative agent for Kaposi Sarcoma (KS), Primary Effusion Lymphoma (PEL) and Multicentric Castleman Disease (MCD). The recently described entity KSHV Inflammatory Cytokine Syndrome (KICS) shares features of systemic inflammation with MCD but lacks the characteristic pathology.

Methods. Symptomatic patients with plasma KSHV DNA > 4 log copies/mL were identified at Harborview Medical Center in Seattle, WA. They were categorized according to the National Cancer Institute HIV/AIDS Malignancy Branch working case definition of KICS and Hemophagocytic Lymphohistiocytosis (HLH)-2004 criteria. KSHV DNA was measured by an in-house PCR assay for ORF73; Interleukin-6 (IL-6) by sandwich immunoassay (Viracor-IBT); and Immunohistochemistry by monoclonal antibody for LANA-1.

Results. In a 1 year period, we treated 3 patients with inflammatory syndromes associated with KSHV lytic replication. All were HIV infected, with CD4 counts 506, 216 and 230 cell/μL, HIV plasma RNA 5.0, 2.3, 1.9 log copies/mL, with antiretroviral therapy used by the latter 2 patients. Each had fever > 40°C, fatigue and respiratory or neurologic symptoms. Labs revealed marked thrombocytopenia, anemia, hypoalbuminemia and elevated plasma CRP (100, 147, 94 mg/L), IL-6 (n/a, 243, 94, normal < 17 pg/mL) and KSHV PCR (7.2, 4.8, 6.1 log copies/mL). Radiography showed diffuse lymphadenopathy (3/3), splenomegaly (2/3) and pleural effusion (1/3). Patient 1 had reactive hyperplasia on lymph node (LN) biopsy, was diagnosed with HLH and treated with cyclosporine and dexamethasone; patient 2 had KS with non-specific MCD-like changes (figure), was diagnosed with KICS and treated with valganciclovir and rituximab + doxorubicin (val + R-Dox); and patient 3 had flare of MCD and was treated with val + R-Dox. All patients are alive at mean (range) 204 (23 – 373) days with median 1 relapse.

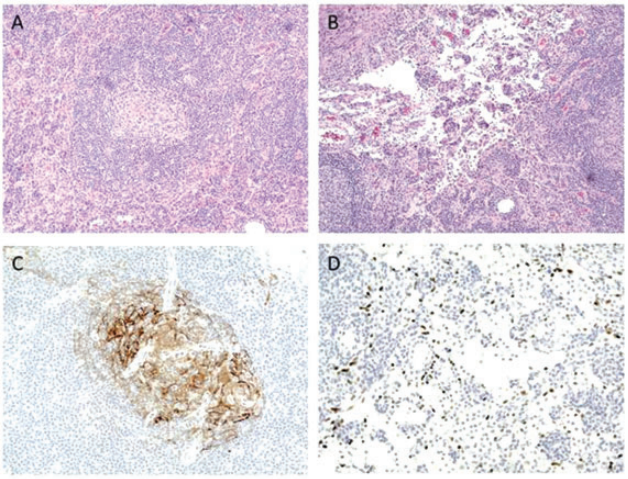

Figure: Lymph node biopsy of patient 2 showing early KS (B,D) and reactive, MCD-like changes (A,C). (A) H&E showing atretic follicles and "onion-skinning" of mantle zone cells, (B) H&E showing vascular proliferation consistent with early KS, (C) Immunohistochemistry D2-40 highlights dendritic cells and penetrating vasculature in atretic follicles, and (D) Immunohistochemistry for KSHV latent nuclear antigen.

Conclusion. KSHV can cause critical illness by an IL-6 mediated inflammatory process clinically similar to severe sepsis or HLH. KICS and MCD are different by subtle findings on pathology and diagnostic uncertainty persisted after applying the case definition. Antiviral, immunomodulatory and cytotoxic chemotherapies were used with good outcome in these 3 patients.

Disclosures. **All authors:** No reported disclosures.

1157. Crucial Parameter of the Outcome in Crimean Congo Hemorrhagic Fever: Viral Load

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Background. Crimean Congo hemorrhagic fever (CCHF), which is endemic in our country, is the widest spread of the viral hemorrhagic fevers. In our study relation of viral load with mortality and clinical and laboratory findings were evaluated retrospectively.

Methods. A total of 126 patients that were treated in our clinic with diagnosis of CCHF between 2008 and 2013 were included in the study. Routine laboratory parameters were taken from hospital records whereas measurement of CCHF viral load were performed from serum samples conserved at -80°C with Real Time PCR.

Results. In our study, mortality rate was 11.1%. The most important prognostic factor was found to be viral load with a mean of $8{,}3x10^7$ copy/ml in patients who survived and $4{,}6x10^9$ copy/ml in patients who died. As viral load increases PT and aPTT times significantly extend; INR, AST, ALT, CPK, LDH, and creatinine levels rise and the probability of bleeding and seizure significantly increase. Any of the patients who had viral load greater than $2x10^9$ copy/ml survived.

When cut-off value that can estimate the prognosis is calculated, probability of survival is found to be significantly reduced where viral load > $1.03x\ 10^8$ copy/ml. Patients were categorized according to their viral load with a cut-off value of 10^8 copy/ml. While no significant differences were found for frequency of fever, myalgia, nausea and vomiting and abdominal pain; patients with 10^8 copy/ml or higher viral load had diarrhea, headache and unconsciousness significantly more frequently. Among clinical findings; bleeding, seizure and haemodialysis were significantly more frequent in patients with viral load 10^8 copy/ml or higher ($p < 0.05$). WBC, haemoglobin, and platelet counts were significantly lower in patients who had 10^8 copy/ml or higher viral load whereas AST, ALT, CPK, LDH, creatinine levels, PT and aPTT time, D-dimer levels and INR were found to be significantly higher among same patients. All blood product transfusions were significantly used more in patients who had viral load > 10^8 copy/ml.

Conclusion. Our study has the largest number of patients among studies which evaluate viral load on CCHF. As in all other studies, our study shows that viral load is the most effective parameter on mortality and as viral load increases survival rate significantly decreases.

Disclosures. **All authors:** No reported disclosures.

1158. Significance of HIV Viral Load and CD4 Count on Kaposi Sarcoma in the Era of Highly-Active-Antiretroviral Therapy

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Background. Approximately 20% of patients with HIV will have Kaposi Sarcoma (KS) and about half will die within 3 months of diagnosis. Incidence and outcomes of KS have traditionally been linked to CD4 counts <350. More recently, KS has been increasingly described in higher CD4 counts and variable presentations in the era of Highly-Active-Antiretroviral-Therapy (HAART). No studies have established the role of Viral Load (VL) on KS. The goal was to determine the effect of CD4 count and HIV VL on KS presentation and outcomes.

Methods. Retrospective review of KS patients with HIV admitted over 12 years (2000-2012). KS patients without HIV infection were excluded. Patients were divided into 4 groups based on CD4 count (>200 or < 200) and VL (>100,000 or <100,000). Groups were analyzed with regards to KS severity (good vs poor risk), extent (soft-tissue vs visceral), receipt of HAART and survival (<3 months vs >6 months). Statistical analysis was done via Chi-Square.

Results. 43 patients were included. KS affected predominantly young (30-40yrs), male (93%) HIV patients with VL >100,000 (85%) and CD4 counts <200 (53.4%). Patients with VL >100,000 had a statistically significant increased incidence of visceral involvement (96%, $p < 0.001$) and more severe disease (71.9% poor risk). No statistically significant difference between receipt of HARRT and survival was seen between patients with viral load >100,000 and < 100,000. Patients with CD4 counts <200, showed a trend towards less severe disease (66.7% with good risk), increased survival (59.4% survived > 6 months) and less use of HAART (20%). Although, these differences were statistically insignificant.

Conclusion. HIV VL of >100,000 is correlated with increased severity and extent of KS. Though statistically insignificant, CD4 counts <200 showed a trend for less severe disease and increased survival despite less use of HAART. Larger prospective studies are warranted to elucidate on these differences.

Disclosures. **All authors:** No reported disclosures.

1159. BanLec, a banana lectin, is a potent inhibitor of Middle East respiratory syndrome coronavirus in *in vitro* assays

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Session: 135. Viral Infections: Treatment and Prevention
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Background. Middle East respiratory syndrome coronavirus (MERS-CoV) continues to cause human infections with multiple clusters two years after the onset of the epidemic. Though mild cases have been recognized, the infection is severe in those with comorbidities and >30% of patients die from the infection. Our recent structure-based development of a fusion inhibitor is one of the few treatment options for MERS and it led us to hypothesize that other existing antivirals that block cellular entry may also be active against MERS-CoV. BanLec is a jacalin-related banana lectin that has potent anti-HIV activity through binding to glycosylated viral envelope proteins and blocking cellular entry. We assessed the anti-MER-CoV activity of BanLec in cell culture assays.

Inhibitory effect of BanLec on MERS-CoV replication

Cell line[a]	EC_{50}	EC_{90}	EC_{99}	CC^{b}_{50}	SI[c]
Vero	3.99±0.22	7.95±0.21	8.84±0.20	>10	>2.51
Calu-3	4.82±0.48	8.95±0.40	9.88 ± 0.39	>10	>2.07
HK2	4.58±0.005	8.74 ± 0.17	9.67 ± 0.21	NA	NA

[a]EC_{50} was determined by CPE inhibition assay in Vero and Calu-3 cells, and by PRA in the HK2 cells

[b]NA, not available

[c]Selectivity index = CC_{50}/EC_{50}

Methods. The anti-MERS-CoV activity of BanLec was assessed by cytopathic effect (CPE) inhibition, viral yield reduction, and plaque reduction (PRA) assays in Vero, Calu-3, and/or HK2 cells. The cytotoxicity of BanLec was also assessed.

Results. The CC_{50} of BanLec was >10 nM in Vero and Calu-3 cells. CPE was completely absent in Vero and HK2 cells infected with MERS-CoV on 3 dpi with 30.00 nM of BanLec. In Calu-3 cells, CPE was completely absent at 90.00 nM of the drug. The EC_{50} of BanLec ranged from 3.99-4.82 nM (table). The mean viral loads reduced by 7.13, 3.40, and 3.63 $\log_{10}$ copies/ml in Vero, Calu-3, and HK2 cells respectively (Figures 1A, 1B and 1C). The highest percentage of plaque reduction at a concentration of >10 nM of BanLec were 100% and 59.5% in Vero cells and HK2 cells respectively (Figures 2A and 2B).

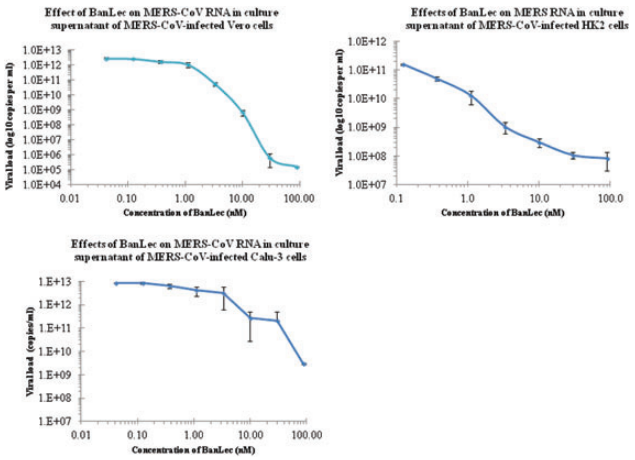


Fig. 2A Inhibitory effect of BanLec on MERS-CoV in MERS-CoV-infected Vero cells by plaque reduction assay

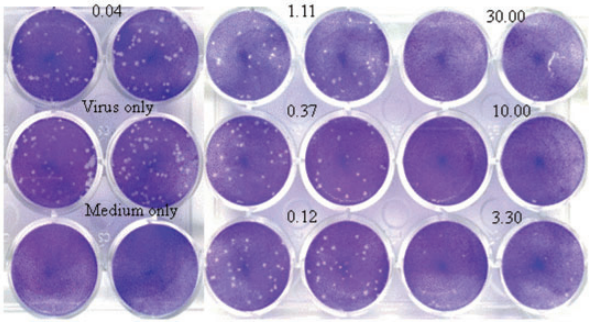
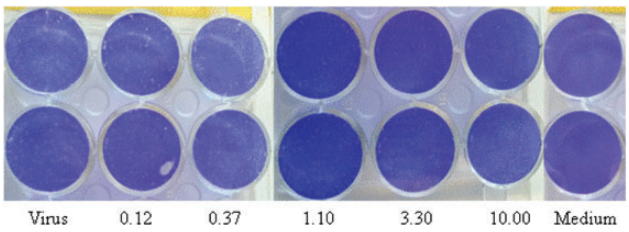


Fig. 2B Inhibitory effect of BanLec on MERS-CoV in MERS-CoV-infected HK2 cells by plaque reduction assay



Conclusion. BanLec exhibits potent *in vitro* anti-MERS-CoV activity. The detailed mechanism and *in vivo* correlation of its antiviral activity should be further tested in animal models. The potential advantages of using BanLec for MERS include its high stability and the prospect of using it as a topical treatment or prophylaxis for exposed patients.

Disclosures. **D. Markovitz**, Novartis Vaccines: Collaborator, Consultant and Grant Investigator, Research grant, Speaker honorarium and patenting the use of the modified lectin for purifying vaccine antigens

1160. Compliance of rabies post exposure prophylaxis and rabies vaccine application problems

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Background. In our country and around the World rabies remains important due to mortality rates and lack of specific treatment. Of patients who were admitted to our

clinic with suspicion of rabies contact (post exposure) vaccination compliance scheme and side effects aimed to be assessed.

Methods. In our study, patients applying to our clinic since September 8, 2009 through April 4, 2014 were included. A retrospective study was performed to scan the file. Incompliance of rabies post exposure prophylaxis; delaying vaccination dates, missing the vaccination and refusing the treatment.

Results. The study included 685 patients, of 53.4% were male. The age range was 1-86. 88.7% of the post exposure rabies cases applied in the first 48 hours, 11.3% in 2-15 days. 52% of cases were with cat exposure, 46% were with dog exposure. Exposure to animals living on the streets were 58.3%, exposure to owned but unvaccinated animals were 16.6%. 89,2% of the patients had rabies vaccine and / or rabies antiserum. 74 of the patients (10.8%) could not demonstrate good compliance with the planned scheme rabies vaccine (table). In these cases, 16 individuals completed vaccination schedule with delay. Only in a child case, fever observed after the first dose of vaccine. Serious adverse reaction was not observed.

Characteristics of cases of rabies post exposure prophylaxis our service

Category	Subcategory	N(%)
Application time	0-48 hour	598 (88,7)
	2-7 day	65 (9,6)
	7-15 day	11 (1,6)
Contact type	Bite	375 (54,9)
	Scracth	278 (40,7)
	Other	16 (4,4)
Type of animal	Dog	316 (46,1)
	Cat	356 (52)
	Other	13 (1,9)
Treatment schema	1+1 (0. and 3. Day)	15 (2,2)
	2+1+1	32 (4,7)
	5 doses vaccine and/or Ig	624 (91,1)
	Other	14 (2,1)
Compliance	Well	610 (89,2)
	Lately vaccinated	16 (2,3)
	Not completed dose	41 (6)
	Reject to offer the vaccine	6 (0,1)

Conclusion. 11,3% of the cases applied 48 hours later, 10,8% did not comply with given vaccination scheme. Therefore we assume that a public awareness should be build about rabies post exposure prophylaxis and compliance of case or case relatives for vaccination against rabies.

Therefore it is necessary to inform the theme of rabies in the community, when it is applied after contact with the patients and their relatives, the risk of rabies vaccine given as much detail as possible about the need to improve compliance with the scheme is evaluated.

Disclosures. **All authors:** No reported disclosures.

1161. Use Specific Quaternary Ammonium Formulations for controlling the spread of Noroviruses in Institutions

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Session: 135. Viral Infections: Treatment and Prevention
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Background. Noroviruses have caused numerous outbreaks in health care environments and in other institutions (schools, hotels, cruise ships, etc.). They survive well on surfaces and have a low infectious dose. Selection of proper disinfectants and cleaning tools are critical in controlling the spread of these viruses. Quaternary ammonium compounds (QAC) are active ingredients for many common disinfectants used in the households and institutions. Successful application depends upon selecting the proper formulation for the target organism(s), the specific need (i.e., fomite, hand sanitizer), and application (spray, disposable wipe).

Methods. We evaluated the application of QAC's registered by the EPA for efficacy against norovirus in different settings for controlling their spread. QAC formulations known to be effective against noroviruses were first evaluated in the laboratory to confirm their effectiveness. QAC-based formulation wipes delivered a more controlled dose of QAC to the treated surface. The first intervention involved an elementary school in which QAC wipes were used in six class rooms to wipe the children's desk tops at the end of the school day over a period of three months. The occurrence and concentration of norovirus on classroom surfaces was compared to an equal number of classrooms which did not use wipes.

Results. Norovirus was commonly detected on classroom surfaces during the winter in classrooms that did not use QAC wipes. The concentration of norovirus was statistically significantly lower (by 99.9%) in the classrooms using the wipes. In addition, absenteeism rates were statiscally significantly less in the classrooms using the wipes. In a second intervention we assessed the impact of cleaning dormitories which were closed after an outbreak of norovirus. Norovirus was detected on 73% of the surfaces tested in the dorm rooms after the outbreak. A onetime use of QAC wipes by cleaning crews resulted in the virus being detect on fewer than 30% of the surfaces.

Conclusion. The results indicate that QAC–based formulations known to be effective against norovirus can result in decreased exposure to noroviruses (and related viruses such as SARS) in venues such as schools and offices where close contact with others facilitates rapid disease spread.

Disclosures. **C. Gerba**, Consumer Specialty Products Association: Consultant, Consulting fee

1162. Self-administration of intranasal influenza vaccine: immunogenicity and volunteer acceptance

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Background. Military personnel in congregate settings are at increased risk for influenza. In an epidemic, a mass vaccination strategy would maximize force health protection. Self-administration of live attenuated influenza vaccine (LAIV) with minimal healthcare worker supervision may be a means to achieve deployment readiness while sparing the use of human resources.

Methods. A phase IV, open-label, randomized controlled trial to evaluate the immunogenicity and acceptance of self-administered (SA) LAIV was conducted at two military hospitals over two influenza seasons (2012-2014). SA subjects were randomized to either individual self-administration or self-administration in a group setting (groups of 5 or 10 subjects each). Control randomized subjects received healthcare worker-administered (HCWA) LAIV. Serum was collected pre-vaccination and 28 (±7) days later for anti-hemagglutinin (HAI) antibody. The primary endpoint was immunogenicity (geometric mean titer, GMT) non-inferiority between SA and HCWA groups. Subjects were surveyed on preferred method of administration.

Results. A total of 1077 eligible subjects consented and were randomized (529 SA, 548 HCWA). Subject characteristics, including age, sex, race, study site, and beneficiary status were similar between groups, though SA subjects were younger, more likely to be white and on active duty. The per-protocol analysis included 1024 subjects (501 SA, 523 HCWA). The post-vaccination GMT by vaccine strain and by study group (HCWA vs SA) was as follows: A/H1N1 (45.8 vs 48.7, respectively; $p = 0.43$), A/H3N2 (45.5 vs 46.4; $p = 0.80$), B/Yamagata (17.2 vs 17.8; $p = 0.55$). Seroresponse (post-vaccination titer >1:40) rates to A/H1N1 and A/H3N2 components were high (~67%), while seroresponse rates to B components were lower (~25%). Seroresponse did not differ by method of administration. Baseline preference for method of administration was similar between groups, with majority expressing no preference. After vaccination, the majority (62%-66%) of SA subjects preferred SA; this proportion did not differ by individual or 5- and 10- subject groups.

Conclusion. LAIV immunogenicity was similar for HCWA and SA. SA was well-tolerated and preferred to HCWA among those who experienced SA.

Disclosures. **All authors:** No reported disclosures.

1164. Effectiveness of Live Attenuated Influenza Vaccine and Inactivated Influenza Vaccines in Active Duty Members of the US Military

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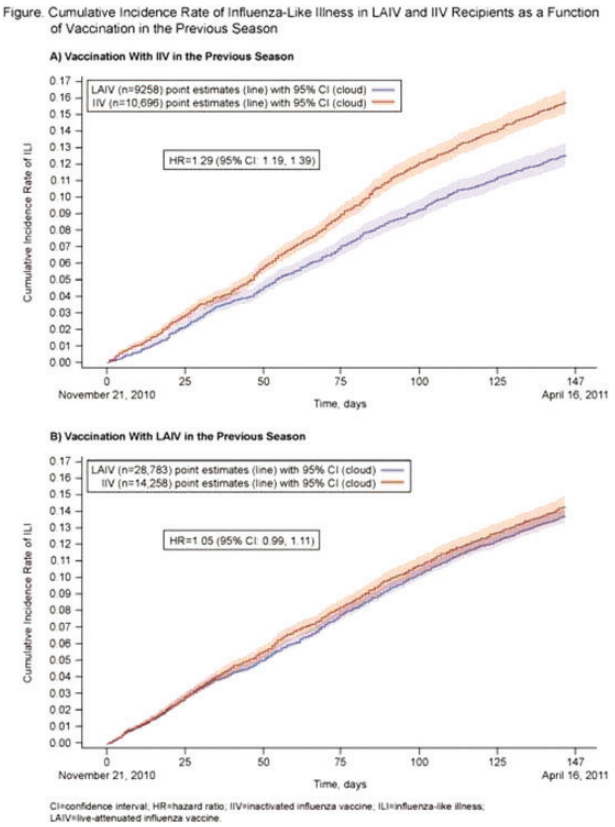
Background. Most studies assessing the relative effectiveness of live attenuated influenza vaccine (LAIV) and inactivated influenza vaccine (IIV) in adults have demonstrated that vaccines were similarly effective or IIV was more effective. Studies have suggested that relative effectiveness may vary by season and population characteristics. This study evaluated effect modifiers of the relative effectiveness of LAIV vs IIV against influenza-like illness (ILI) in adults vaccinated in the US military during 2010–2011.

Methods. Active duty members of the US military aged 18–49 years, stationed in the contiguous United States were followed from November 21, 2010 (start of the influenza season) until occurrence of ILI, season end (April 16, 2011), or censoring event, whichever came first. To help ensure comparability of LAIV and IIV recipients, individuals with asthma, chronic bronchitis, emphysema, shortness of breath, diabetes mellitus, HIV infection, or pregnancy were excluded. Data were obtained from the Department of Defense Military Health System database, a relational database containing longitudinal data on demographic characteristics and medical encounters of service members.

Results. A total of 90,084 LAIV recipients and 50,098 IIV recipients were identified. Cumulative incidence rates of ILI are presented in the Figure. The risk of ILI during the influenza season was higher among IIV recipients (14.0%) than among LAIV recipients (12.6%), yielding a hazard ratio (HR) of 1.12 (95% CI: 1.09, 1.16). LAIV relative effectiveness vs IIV was greater among those vaccinated with IIV in the prior season (HR: 1.29 [95% CI: 1.19, 1.39]) than among those vaccinated with LAIV in the prior season (HR: 1.05 [95% CI: 0.99, 1.11]. No other significant effect modification was observed as a function of gender, class of age, exposure to tobacco, or other baseline characteristics.

This study was sponsored by MedImmune.



Conclusion. The type of influenza vaccine received in the prior year was a significant effect modifier of the LAIV relative effectiveness vs IIV in adults, with LAIV relative effectiveness higher among IIV recipients in the prior season. The validity and generalizibility of this finding will be examined in data from additional seasons.

Disclosures. **H. Caspard**, MedImmune: Employee, Salary **A. Steffey**, MedImmune: Independent Contractor and Shareholder, Consulting fee **N. M. Sicignano**, MedImmune: Collaborator, Research support **C. S. Ambrose**, Astrazeneca: Employee, Salary

1165. Efficacy of Live Attenuated Influenza Vaccine Upon Revaccination of Children

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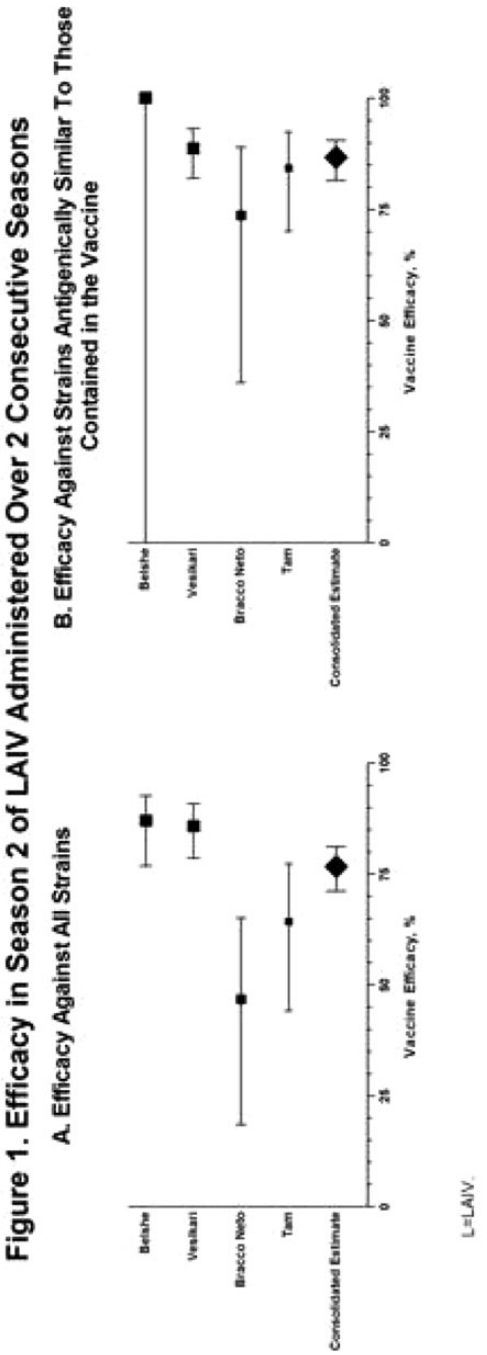
Background. Recent observational studies yield conflicting results regarding the effectiveness of repeated influenza vaccination. This meta-analysis evaluates the efficacy of live attenuated influenza vaccine (LAIV) in children upon revaccination. LAIV is approved for children ≥24 months of age. This study was sponsored by MedImmune.

Methods. All randomized double-blind clinical trials that evaluated the efficacy against laboratory confirmed cases of influenza of LAIV vs placebo in children in 2 consecutive influenza seasons were reviewed. LAIV consisted of $10^{6.5-7.5}$ median tissue culture infectious doses of each of the 3 influenza strains (A/H1N1, A/H3N2, and B) and was administered as 2 doses in season 1 and 1 dose in season 2.

Results. Four published studies were identified; 6090 children aged 18 months to 7 years in season 2 were included in the analysis. Efficacy in season 2 of LAIV administered over 2 consecutive seasons was 76.7% (95% CI: 71.2%, 81.2%; **Fig1A**) against all strains and 86.7% (81.5%, 90.5%; **Fig1B**) against antigenically similar strains. In the absence of revaccination, residual efficacy in season 2 of LAIV administered in the prior season was 40.7% (22.6%, 54.6%) against all strains and 56.4% (37.0%, 69.8%) against antigenically similar strains. Among LAIV recipients in season 1, the additional efficacy of LAIV administered in season 2 was 27.6% (0.8%, 47.2%) against all strains and 58.4% (28.3%, 75.9%) against antigenically similar strains. LAIV administered over 2 consecutive seasons was also compared with LAIV administered in season 2 only: the 2 strategies were equally efficacious against all strains (relative efficacy: 0.0% [-49.1%, 28.5%]); against antigenically similar strains administration over 2 consecutive seasons was more efficacious than administration in season 2 only (relative efficacy: 53.9% [17.4%, 74.3%])



Conclusion. No reduction in vaccine efficacy was observed with LAIV administered over 2 consecutive seasons, with overall efficacy rates greater than 75%. The efficacy of LAIV over 2 consecutive seasons was also similar to or higher than the efficacy of LAIV administered in season 2 only.

Disclosures. **H. Caspard**, MedImmune: Employee, Salary **C. S. Ambrose**, Astrazeneca: Employee, Salary **T. Heikkinen**, AstraZeneca/MedImmune: Collaborator, Presentation at ESPID 2012 Congress and Scientific Advisor, Consulting fee and Speaker honorarium **R. B. Belshe**, MedImmune: Consultant, Grant Investigator and Scientific Advisor, Consulting fee, Research grant and Speaker honorarium

1166. Evaluation of Drug-Drug Interaction between Daclatasvir and Methadone or Buprenorphine/Naloxone

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Background. Daclatasvir (DCV) is a potent hepatitis C Virus (HCV) NS5A replication complex inhibitor with pangenotypic (1-6) activity *in vitro*. Methadone (MET) and buprenorphine (BUP) are opioid medications to treat opioid addiction; patients on HCV therapy may require MET or BUP treatment. The effect of DCV on the pharmacokinetics (PK) of MET or BUP/naloxone (NLX) was assessed in subjects on stable MET or BUP.

Methods. An open-label, 2-part study assessed the effect of steady-state oral administration of DCV on the PK of MET (Part 1, P1) or BUP/NAL (Part 2, P2). Safety/tolerability and pharmacodynamics (PD, opioid withdrawal scales/overdose assessment) were also assessed. Subjects (P1, N = 14; P2, N = 11) received daily single-dose oral MET (40-120mg) or BUP/NLX (8/2-24/6mg) based on their prescribed stable dose throughout, in addition to DCV (60 mg QD) on Days 2-9. Serial PK sampling occurred predose and postdose until 24 hrs on Day 1 (MET/BUP) and Day 10 (MET/BUP/DCV). Non-compartmental PK were derived. Geometric mean ratios (GMR) and 90% confidence intervals (90%CI) for MET/BUP/norBUP C_{max} and AUC_{TAU} were derived from linear mixed effects models.

Results. Subjects were aged 19 to 39 years, mostly white (P1, 93%; P2, 100%) and male (P1, 71%; P2, 91%). All subjects completed the study. No clinically meaningful effect was demonstrated as the GMR and 90% CIs fell within the pre-specified interval (P1, 0.7-1.4; P2, 0.5-2.0: table). DCV coadministration was well tolerated: overall, 6 [43%] subjects had AEs (all mild and resolved without treatment). DCV had no clinically significant effect on the PD of MET or BUP/NLX.

	With DCV *Adj. Geo. Mean*	W/O DCV *Adj. Geo. Mean*	GMR *(90%CI)*
R-MET[a] **C_{max}**, *ng/mL*	103.6	96.6	1.07 (0.97,1.18)
AUC_{TAU}, *ng•h/mL*	1699.6	1569.8	1.08 (0.94,1.24)
BUP C_{max}, *ng/mL*	3.3	2.5	1.30 (1.03,1.64)
AUC_{TAU}, *ng•h/mL*	25.1	19.2	1.31 (1.15,1.48)
NORBUP C_{max}, *ng/mL*	3.1	1.8	1.65 (1.38,1.99)
AUC_{TAU}, *ng•h/mL*	42.6	26.4	1.62 (1.33,1.96)

[a]S-MET and total MET results similar Exposures were normalized to lowest dose of MET or BUP.

Conclusion. Steady-state administration of DCV 60 mg QD had no clinically meaningful effect on the PK of MET or BUP/NLX and was generally well tolerated, suggesting that no dose adjustments will be required.

Disclosures. **T. Garimella**, Bristol-Myers Squibb: Employee, Salary **R. Wang**, Bristol-Myers Squibb: Employee, Salary **W. L. Luo**, Bristol-Myers Squibb: Employee, Salary **P. Wastall**, Bristol-Myers Squibb: Employee, Salary **H. Kandoussi**, Bristol-Myers Squibb: Employee, Salary **C. Hwang**, Bristol-Myers Squibb: Employee, Salary **R. Bertz**, Bristol-Myers Squibb: Employee, Salary **M. Bifano**, Bristol-Myers Squibb: Employee, Salary

1167. Clinical Presentation and Risk Factors for Cytomegalovirus Colitis in Adult Immunocompetent Patients

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Background. Cytomegalovirus (CMV) colitis is a common manifestation of CMV end-organ diseases, which has been usually described in immunocompromised hosts. Recently, it is recognized that we also occasionally experience it among immunocompetent patients. To get relevant data about clinical presentation, prognosis, and risk factors for development of CMV colitis in immunocompetent hosts, we analyzed all cases that occurred during a 19-year period in our center.

Methods. A case-control study was performed to identify risk factors of CMV colitis in immunocompetent hosts. The electronic medical records were reviewed in individuals who admitted and were diagnosed with CMV colitis during the period of January 1995 through February 2014 at a tertiary care university hospital. Two non-CMV colitis patients with age and sex matching were selected to each case patient as controls.

Results. A total of 51 patients with CMV colitis were included and compared with 102 control patients. Renal disease on hemodialysis, neurologic disease, rheumatologic disease, ICU care, and exposure to antibiotics, antacid, steroid, and RBC transfusion within 1 month prior to diagnosis of colitis were associated with CMV colitis in the univariate analysis. Among them, steroid use (OR 9.95, 95% CI 1.95-46.66) and RBC transfusion (OR 30.85, 95% CI 5.70-167.06) within 1 month were identified to be independent risk factors for development of CMV colitis in the multivariate analysis. 30-day mortality was 7.8% without any attributable mortality.

Conclusion. Steroid use and RBC transfusion within 1 month prior to diagnosis of colitis were independent risk factors for development of CMV colitis in immunocompetent hosts.

Disclosures. **All authors:** No reported disclosures.

1168. Use of First Positive *Cytomegalovirus* (CMV) PCR Determination to Differentiate a Viral Blip From Established CMV Infection in Transplant Recipients

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Background. CMV infection frequently complicates the course after solid organ or haematopoietic stem cell transplantation. A pre-emptive strategy relies on regular screening with CMV PCR of recipients to diagnose and promptly treat the infection while still asymptomatic. The PCR technology is known in HIV to also identify isolate positive reads – so called blips – that do not require medical intervention. Whether such viral blips exist also for CMV in the transplant setting remains unknown. We wanted to determine the prevalence and risk factors for developing viral blips while screening transplant recipients with CMV PCR in our cohort.

Methods. In a large unselected cohort of transplant recipients, consecutive situations were identified characterised by a triplicate of CMV PCRs during follow-up where the 1st PCR was undetectably low, the 2nd was positive and the interval between the 2nd and 3rd PCR was < 8 days apart. The situation was defined as either a viral blip or an established infection depending on whether the 3rd PCR was again undetectably low or still positive, respectively. Using logistic regression, the impact of the following factors on the % of situations being classified as blips were investigated: viral load of the 2nd PCR, type of transplantation, CMV IgG serostatus of donor and recipient, and use of treatment.

Results. Of a total of 402 scenarios fulfilling criteria above, 126 were classified as blips (31%). The proportion of blips was higher the lower the viral load of the 2nd PCR (table); the adjusted odds ratio (OR) of a blip (vs 2nd PCR just positive = 273 IU/mL) was 0.12 ([0.04-0.4] p<0.001), and 0.03 ([0.003-0.2] p<0.001)) when viral load was 2,730-9,100 or > 9,100 IU/mL, respectively, whereas OR was comparable with the group just positive if viral load levels was 273-2,730 IU/mL. The results were unaffected by use of anti CMV treatment.

Table. Distribution of blips at different CMV viral loads stratified for type of transplantation and risk of CMV infection according to CMV IgG status*

Viral load of first positive CMV PCR (IU/mL)**	% of situations classified as viral blips (N=402)					
	Total (N=402)	Type of Transplantation		Risk of CMV according to CMV IgG status*		
		SOT (N=172)	HSCT (N=230)	High Risk (N=194)	Intermediary Risk (N=189)	Low Risk (N=18)
273	47% (32/68)	39% (11/28)	53% (21/40)	32% (9/28)	59% (20/34)	50% (3/6)
>273-910	35% (48/136)	33% (17/52)	37% (31/84)	37% (24/65)	34% (22/64)	29% (2/7)
>910-2,730	40% (40/100)	39% (12/31)	41% (28/69)	31% (14/45)	45% (23/51)	75% (3/4)
>2,730-9,100	10% (5/49)	8% (2/25)	13% (3/24)	9% (2/22)	12% (3/26)	0% (0/1)
>9,100	2% (1/49)	3% (1/36)	0% (0/13)	0% (0/34)	7% (1/14)	0% (0/1)

* Based on Donor (D)/ Recipient (R) CMV IgG status (positive (+) or negative (-)) pre-transplantation. High risk is associated with D+/R- for solid organ transplantation (SOT) and D-/R+ for hematopoietic stem cell transplantation (HSCT). D+/R+ is associated with intermediary risk for both transplantation types; low risk is associated with D-/R+ for SOT and with D+/R- for HSCT.
**Corresponding to the 2nd PCR of the PCR triplicate (see methods section); 0.91 IU/mL corresponds to 1 copy/mL

Conclusion. Viral blips are frequent while screening transplant recipients with CMV PCR, in particular if the viral load of the first positive PCR is low. Our findings imply that in asymptomatic patients, a first positive CMV PCR viral load < 2,730 IU/mL should be confirmed before initiation of antiviral therapy, as otherwise more than 40% of patients will receive unnecessary antiviral medication.

Disclosures. **All authors:** No reported disclosures.

1169. Peramivir Safety in Hospitalized Influenza

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Background. Peramivir is a parenteral neuraminidase inhibitor (NAI) with potent in vitro activity against all influenza sub-types. Although oseltamivir is widely used for the treatment of influenza, a need still exists for an effective and safe parenteral treatment. Peramivir has been studied as a single dose treatment in acute uncomplicated influenza.

Methods. A total of 2217 subjects were enrolled in five randomized, double-blind trials in acute uncomplicated influenza with either placebo or oseltamivir

controls. A total of 1411 subjects received peramivir, 485 by intramuscular injection and 926 by intravenous infusion. A bioequivalence study demonstrated equivalent systemic exposure for IM and IV administration. An integrated analysis of adverse events (AE) was performed by treatment group. Since peramivir dose varied (150-600 mg), the results in the table include only subjects receiving the proposed dose of peramivir 600 mg.

Results. AEs had a similar frequency across arms. Serious AEs (SAEs) and AEs leading to study discontinuation (AELTSD) were rare. AELTSD were mainly infection, GI or rashes. The most common AEs in peramivir treated subjects were diarrhea, decreased neutrophils, hyperglycemia, and positive urine protein. The only AE with ≥2% difference over placebo was decreased neutrophils. Mean decreases in neutrophil counts were similar: peramivir -2.1 x 10^3/μL, placebo -2.0 x 10^3/μL, oseltamivir -2.5 x 10^3/μL. Neutrophils < 500/mm^3 occurred in 0.4% peramivir, 0.2% placebo and 0.6% oseltamivir treated subjects. No AEs in peramivir treated subjects occurred at ≥2% difference over oseltamivir. AEs occurring at ≥2% difference over peramivir in oseltamivir treated subjects were decreased neutrophils, nausea, vomiting, and decreased monocytes.

Acute Uncomplicated Influenza	Peramivir 600 mg (N=664)	Placebo (N=441)	Oseltamivir (N=365)
AEs (%)	48.3	51.0	48.8
SAEs (%)	0	0.5	0.5
AELTSD (%)	0.9	0	1.4

Conclusion. Peramivir's safety profile was similar to placebo and AEs were consistent with the underlying influenza. Nausea and vomiting, which may be factors in discontinuation of oral oseltamivir, occurred at a lower incidence in peramivir treated subjects compared to placebo. Parenteral peramivir has excellent tolerability and no unique safety risks.

Disclosures. **S. Dobo**, BioCryst: Employee and Shareholder, Salary **J. Elder**, BioCryst: Consultant, Consulting fee **P. Collis**, BioCryst: Employee and Shareholder, Salary **W. Sheridan**, BioCryst: Employee and Shareholder, Salary

1170. Outcomes of Peramivir for Avian Influenza Virus(h7n9):a Single-Center Experience

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Background. During 2013 spring, the reported avian influenza virus (H7N9) human infection was initially started in Shanghai, with 132 confirmed cases including 44 deaths in China. The purpose of this study is to evaluate the outcome of IV peramivir on H7N9 human infection.

Methods. Data on demographics, clinical presentation and hospital course, comorbid conditions, dosing and dates of antiviral medications administered were abstracted from medical records, pharmacy medication records and autopsy reports by staff at the SPHCC using the same standardized case report form. Comparative analysis was performed for patients received peramivir and patients treated with osetamivir.

Results. Of 18 confirmed H7N9 patients, 13 (72%) received oseltamivir, 5 (28%) cases received IV peramivir as a second antiviral. The median age for peramivir treatment group (P group) was 71 year-old, while the oseltamivir treatment group (O group) was 68.5 year-old. Clinical complications in both group included pneumonia or acute respiratory distress syndrome requiring mechanical ventilation (P group vs O group: 100% vs 61%), ECMO (P group vs O group: 60% vs 0%), and death (P group vs O group: 80% vs 15%). In P group, the median days of undetectable H7N9 RNA copy number was range from 3-17 days post peramivir; 1 out of 5 late peramivir-treated cases recovered and discharged. There was no noticeable adverse drug reaction in P group.

Conclusion. These findings indicate that IV peramivir may be an additive option for critically ill H7N9-infected patients. The use of peramivir merits further study to assess clinical effectiveness and safety.

Disclosures. **All authors:** No reported disclosures.

1171. The development of influenza virus variants with reduced susceptibility following peramivir treatment: an analysis of clinical and post-marketing experience

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Background. Peramivir is a neuraminidase inhibitor (NAI) with potent in vitro activity against all virus sub-types. It has been commercially available in Japan since 2010 and to date more than 1 million patients have received peramivir following approval. Influenza A/H1N1 viruses containing an H275Y mutation in the neuraminidase gene that confers resistance to oseltamivir have been previously shown to result in reduced sensitivity to peramivir.

Methods. The peramivir clinical development program included over 2,800 subjects with laboratory-confirmed influenza infection in 10 phase 2 and 3 studies. The activity of single dose peramivir treatment in the outpatient setting and repeat dose treatment in hospital studies was evaluated. Phenotypic analysis of paired baseline/post-treatment virus isolates was attempted for all subjects with culturable virus and genotypic analysis of the NA gene (and hemaglutinin [HA] gene in a subset) was conducted on viruses from subjects with prolonged virus shedding or with increased 50% inhibitory concentration (IC_{50}) for peramivir. A surveillance study conducted in Japan since 2010 assessed the prevalence of circulating strains with resistance to peramivir.

Results. Baseline 50% inhibitory concentration (IC_{50}) data was available for over 2300 subjects. Over 1200 subjects were selected for sequence analysis, and partial or complete sequence data was available for 1122 subjects. The only treatment-emergent mutation associated with peramivir exposure detected in more than 1 subject was an H275Y mutation in influenza A/H1N1, which was identified in 13 subjects. Data from postmarketing surveillance in Japan following the approval of peramivir (RAPIACTA™) have identified no novel mutations in circulating seasonal influenza strains that are associated with loss of susceptibility to peramivir.

Conclusion. Loss of sensitivity to peramivir in clinical isolates appears to be associated primarily with development of an H275Y mutation in the NA gene. The incidence of development of treatment-emergent H275Y substitutions in response to treatment with peramivir appears to be low.

Disclosures. **P. Collis**, BioCryst: Employee and Shareholder, Salary **P. Zoeteweij**, BioCryst: Research Contractor, Research support **H. Bunschoten**, BioCryst: Research Contractor, Research support **R. Taylor**, BioCryst: Employee and Shareholder, Salary **Y. Babu**, BioCryst: Employee and Shareholder, Salary **W. Sheridan**, BioCryst: Employee and Shareholder, Salary

1172. Virological Efficacy of Peramivir Administration in Children with Influenza

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Session: 135. Viral Infections: Treatment and Prevention
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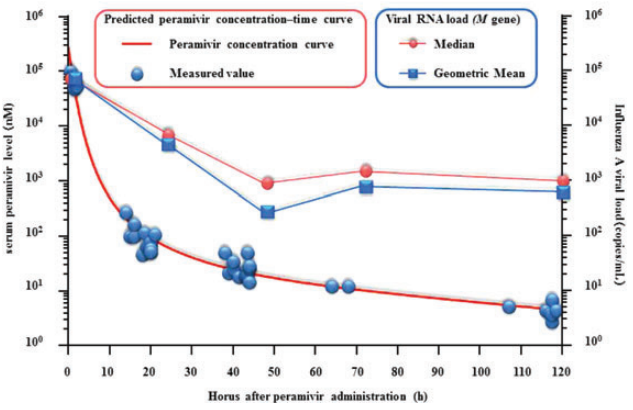
Background. Peramivir is only one option which can be intravenously administered to control influenza. In this study we estimated the virological efficacy of peramivir administration in children.

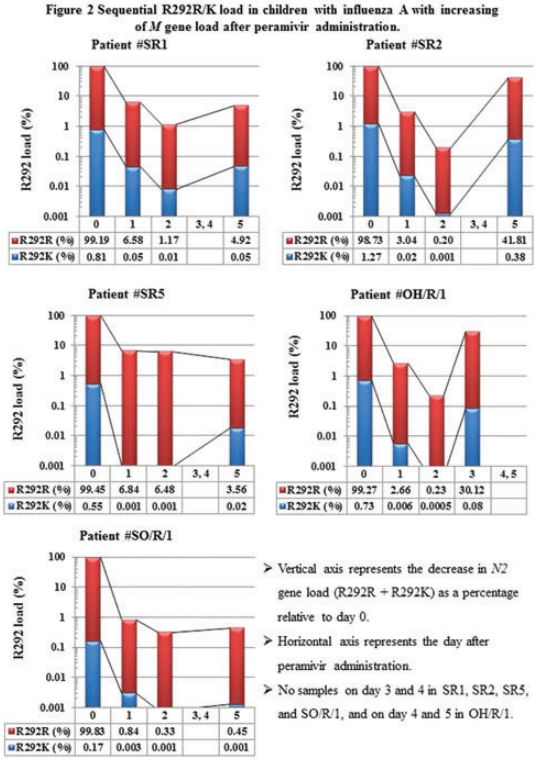
Figure 1 Predicted peramivir concentration–time curve and sequential influenza A viral load



Methods. Sequential serum samples and nasal swabs were collected before and after administration of a single 10 mg/kg dose of peramivir from 15 hospitalized children who had been diagnosed with influenza A or B using a rapid antigen test. We measured the serum concentration of peramivir, determined the sequential virus copy number of the *M* gene, and the population of E119E/V and R292R/K at the *N2* gene by quantitative real time RT-PCR. The isolated viruses were analyzed using a chemiluminescence-based neuraminidase inhibition assay to determine IC_{50} and IC_{90} values of peramivir.

Results. Among the 15 children, 10 and 3 were diagnosed with influenza A (H3) and B, respectively, based on the positive results of the real time RT-PCR. The serum peramivir concentrations measured at 0.5, 1, and 1.6 hour after the initial doses were 97,746.7, 79,628.5, and 58,587.1 nM, and on days 1, 2, 3, and 5 were 97.0, 27.4, 12.0, and 4.4 nM, respectively. Although the viral load of influenza A decreased to 10^{-2} of that before peramivir administration by day 2, the viral load in 5 children increased after day 3 (Figure 1). No E119V substitution was detected, and the percentage of R292K did not increase during the observation period in these 5 children (Figure 2). Peramivir administration did not reduce the viral load of influenza B as much as it

lowered that of influenza A. The IC_{50} values of type A and B influenza were within 0.15–0.2 nM and 1.27–1.47 nM, respectively.



Conclusion. For influenza A, the viral load increased after day 3 of peramivir administration without a change in susceptibility and an increase in the prevalence of resistant strains, indicating that the peramivir concentration in the respiratory airways was below the concentration required to inhibit neuraminidase activity after day 3 of peramivir administration. For influenza B, it was found that the effectiveness of peramivir was low within the early days after peramivir administration. Therefore, peramivir readministration should be considered at 48 hour and 24 hour after the first administration in severe cases with influenza A and B, respectively.

Disclosures. **All authors:** No reported disclosures.

1173. Long-term Immunogenicity and Safety of an Investigational Herpes Zoster Subunit Vaccine in Older Adults

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Session: 135. Viral Infections: Treatment and Prevention
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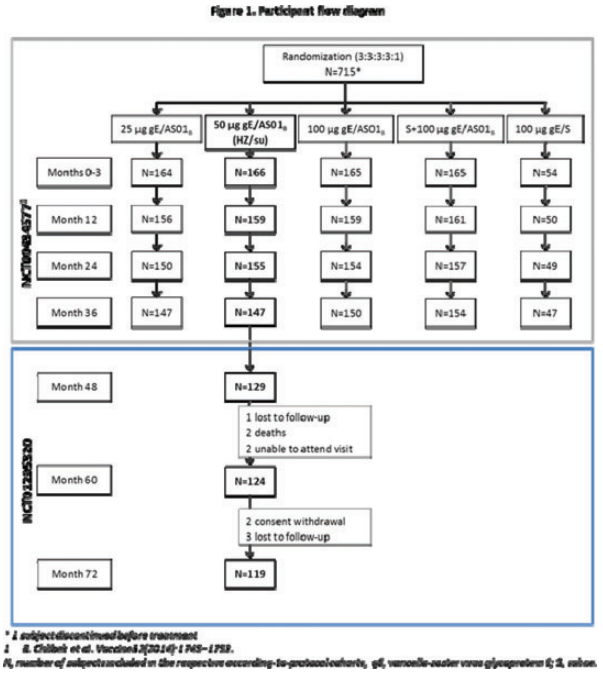
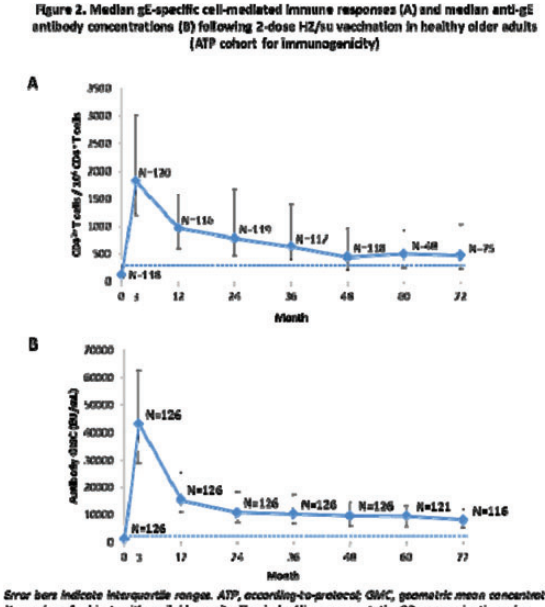
Background. An investigational subunit vaccine containing varicella-zoster virus glycoprotein E (gE) and the $AS01_B$ Adjuvant System is being evaluated for the prevention of herpes zoster (HZ) in older adults. A phase II clinical trial evaluating different formulations of the candidate vaccine (containing 25 µg, 50 µg, or 100 µg gE; adjuvanted with $AS01_B$) was conducted in adults ≥60 years of age, and showed that all 2-dose adjuvanted vaccine formulations elicited robust cellular and humoral immune responses in older adults, for up to 3 years post-vaccination. The 50 µg gE formulation (HZ/su) was selected for further clinical development. In order to gain insight into the potential of this investigational vaccine to provide long-term protection against HZ, we assessed the persistence of the vaccine-induced immune responses for up to 6 years post-vaccination in subjects who received 2-doses of HZ/su.

Methods. This phase II, open-label, multicenter, single group trial conducted in the Czech Republic, Germany, Sweden and the Netherlands (NCT01295320) followed 129 subjects who had received 2 doses (2 months [M] apart) of HZ/su (50 µg gE + $AS01_B$) during the previous trial (NCT00434577). Vaccine-induced immune responses (frequencies of antigen-specific $CD4^+$ T cells expressing ≥2 activation markers measured by intracellular cytokine staining after *in vitro* stimulation with gE and serum anti-gE antibody concentrations measured by ELISA) from these subjects were evaluated at 48, 60 and 72 M after the first HZ/su dose. Serious adverse events (SAEs) were recorded from M48 to M72.



Results. Participant flow is shown in Figure 1. 6 years after the 2-dose vaccination with HZ/su, gE-specific cell-mediated immune (CMI) responses and anti-gE antibody concentrations had decreased, but remained higher than pre-vaccination values (Figure 2). M72 gE-specific CMI response median values were 3.8 times higher than pre-vaccination values. No vaccine-related SAEs were reported from M48 to M72.



Conclusion. Persistence of immune response was observed for up to 6 years after 2-dose vaccination with HZ/su in healthy older adults. No safety concerns were identified.

Disclosures. **H. Lal**, GlaxoSmithKline Vaccines: Employee and Shareholder, Salary **L. Rombo**, GSK: Investigator, Research support **T. F. Schwarz**, GlaxoSmithKline: Board Member, Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium **G. Plassmann**, GSK: Investigator, Investigator duty **J. H. Richardus**, Glaxo Smith Kline: Grant Investigator, Grant recipient **G. Catteau**, GSK: Employee, Salary **T. Heineman**, GSK Vaccines: Employee and Shareholder, Salary

1174. Comparing the Duration of Treatment for Cytomegalovirus Infection Pre and Post Quantitative Nucleic Acid Test Standardization: Does Use of a More Sensitive Assay Lead to Longer Treatment Duration?

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Session: 135. Viral Infections: Treatment and Prevention
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Background. Cytomegalovirus (CMV) quantitative nucleic acid testing (QNAT) has now been standardized with the use of the World Health Organization (WHO) calibration standard. In a pilot study, we observed that the pre-defined threshold of 5,000 copies/ml using an old laboratory-developed test (LDT) was equivalent to 1,810 IU/ml using the WHO-calibrated commercial assay (WHO-CA). With a lowest limit of quantification of 137 IU/ml, the WHO-CA was more sensitive than LDT. We hypothesized that the increased assay sensitivity may lead to longer duration of antiviral therapy for CMV infection in solid organ (SOT) and hematopoietic stem cell transplant (HSCT) patients.

Methods. Medical records of SOT and HSCT patients with CMV were reviewed during October 2011 to March 2014. Patients were divided in two groups based on CMV QNAT for diagnosis and monitoring (i.e., LDT vs WHO-CA). Descriptive statistics were used to assess the data. Length of therapy was non-normally distributed and analyzed by comparison of medians.

Results. A total of 118 transplant patients were studied; 59 each in LDT and WHO-CA groups. There was equal distribution of age and gender between the groups. The mean age of patients was 53 years (range, 18-72); 70 (59%) were male. There was no difference in the type of transplant: the LDT group included 32 (55%) SOT, 23 (39%) allogeneic HSCT, 2 (3%) autologous HSCT, and 2 (3%) umbilical cord transplant recipients, while the WHO-CA included 34 (58%) SOT, 22 (37%) allogeneic HSCT, and 3 (5%) umbilical cord transplant recipients. There was no significant difference in type of CMV infection: in LDT group, there were 32 (54%) with asymptomatic disease, 12 (20%) with syndrome, and 15 (26%) with tissue-invasive disease, while in WHO-CA group, there were 32 (54%) with asymptomatic disease, 8 (14%) with syndrome, and 19 (32%) with tissue-invasive disease. There was a strong trend towards shorter median length of antiviral treatment for the WHO-CA group (33 days [range, 5-113]) compared to the LDT group (39 days [4-191]; p = 0.06).

Conclusion. In this large cohort of SOT and HSCT patients, use of a more sensitive QNAT did not prolong duration of treatment for CMV infection and disease. A trend towards shorter length of therapy was observed using WHO-CA CMV QNAT.

Disclosures. **All authors:** No reported disclosures.

1175. *In Vitro* Antiviral and Synergistic Effects of Thiazolides and Oseltamivir Carboxylate Against Human Influenza A and B Viruses

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Session: 135. Viral Infections: Treatment and Prevention
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Background. The impact of influenza virus infection on humans whether measured by morbidity, mortality, or economic costs, is clear and significant. While two classes of antiviral drugs are available for prophylaxis and treatment of influenza, antiviral resistance development can limit the effectiveness of these drugs. Thiazolides, such as nitazoxanide (NTZ) and its active metabolite tizoxanide (TIZ), have been found to have broad antimicrobial activity. As the antimicrobial effect of the thiazolides appears to be mediated by a cell-specific rather than a virus-specific mechanism, the potential for resistance development through viral mutational adaptation is thought to be low. Consequently, NTZ and its derivatives may serve as valuable alternatives or adjuncts to conventional antiviral therapy provided that they demonstrate inhibitory activity against human-lineage influenza A and B viruses.

Methods. In this study, we examined the *in vitro* antiviral activity of NTZ and TIZ against four human-lineage influenza A viruses, including two oseltamivir carboxylate (OC) resistant strains, and one influenza B virus. To obtain antiviral concentration-response curves, monolayer cultures of Madin Darby Canine Kidney (MDCK) cells were inoculated with influenza virus. After 1 hr of incubation, NTZ and TIZ were added at concentrations ranging from 0.05 to 0.4 mM. Subsequently, antiviral activities of TIZ in combination with OC were evaluated *in vitro* using a modified plaque reduction assay. Antiviral EC_{50} for each compound alone and in combination was determined and the fractional inhibitory concentration (FIC) was calculated.

Results. Both NTZ and TIZ inhibited replication of all viruses tested with 50% effective concentrations (EC_{50}) ranging from 0.06 to 0.25 mM and from 0.05 to 0.13 mM, respectively. The FIC values obtained for the influenza A viruses tested were suggestive of synergism (0.972 +/- 0.251) of this drug combination.

Conclusion. The results indicate that NTZ and TIZ exhibit antiviral activity against several contemporary strains of human influenza A and B virus *in vitro* and might act synergistically with OC. Further investigation is currently being conducted to determine the efficacy of NTZ and TIZ in human patients and to determine synergistic effects *in vivo*.

Disclosures. **G. Landolt**, Romark Laboratories: Research Contractor, Research support **L. Bentsen**, Romark Laboratories: Research Contractor, Research support **D. Bush**, Romark Laboratories: Research Contractor, Research support **C. Hong**, Romark Laboratories: Research Contractor, Research support

1176. Analysis of the Primary Antiretroviral Drug Resistance among HIV-1 Naý¨ve Patients in a Tertiary Hospital in Saudi Arabia

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Session: 135. Viral Infections: Treatment and Prevention
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Background. To determine the prevalence of resistance-associated mutation in individuals at tertiary care facility hospital to knowledge of local resistance data and help to follow treads in the prevalence of resistance and result in a better understanding of the current HIV epidemic.

Methods. In a retrospective study in HIV Clinic affiliated with KFSHRC-Jeddah branch, dat analysis on genotypic resistance testing was performed in untreated HIV-positive patients before administration of first-line highly active antiretroviral Therapy (HAART).

Results. Between January 2008 and December 2013 resistance testing was performed in 37 therapy- naý¨ve individuals. HAART was initiated in all 37 patients who were included into the study. Two-third were males, the most common mode of transmission was heterosexual sex. The mean CD4-cell count was 83.3 cells/mm^3, mean viral load was 10.614 log copies/ml. Resistance-associated mutation were detected in 33 patients (89.1%), 13.5% showed mutations indicating nucleoside reverse transcriptase inhibitors (NRTI) resistance (V118I, M184I), 16.2% showed non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance (V90I, A98G, K103N), and 32.4% showed protease inhibitor (K20I, K20R, M26I, Q58E, L10I, I13V, L63P, H69K, L89M, I93L, I15V, D60E, G16E, L36T, T74S), respectively. Multi-class-resistance was found in 27%. No significant difference in distribution of the parameters age, sex, duration of HIV diagnosis CDC stage, CD4-cell count and viral load, between group with and without resistance was identified.

Conclusion. The prevalence of primary resistance resistant virus strains can be estimated at 89.1% in chronically infected HAART-naý¨ve HIV-patients in KFSHRC-Jeddah branch. The majority of these cases show PI-associated resistance. Resistance NRTI, NNRTI, as well as multi-class-resistance is of low prevalence. No risk factor of predictive value can be indicated for the diagnosis of resistance mutations in the individual. In conclusion, routine genotypic resistance testing in untreated HIV-positive patients should be performed before administration of first-line HAART in this population.

Disclosures. **All authors:** No reported disclosures.

1177. Relapse in patients with chronic hepatitis B infection treated with oral antivirals (nucleotide / nucleoside), after treatment discontinuation

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Session: 135. Viral Infections: Treatment and Prevention
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Background. The aims of treatment in chronic hepatitis B (CHB) are suppression of HBV replication and the prevention of liver diseases. Nucleoside (nucleotide) analogues (NA) are oral antiviral drugs used for treatment of chronic HBV infection. Therewithal, they cause regression in liver fibrosis and allow histological healing. The duration of treatment with oral antiviral drugs is still unclear. In this study, we investigated the frequency of relapse in patients with CHB after cessation NA.

Methods. Chronic hepatitis B (HBeAg negative or positive) patients whose NA treatments were discontinued for any reason were included to the study. Relapse was accepted as the HBV viral load over 2,000 IU/ml or ALT levels two fold higher than the normal level in patients whose HBV DNA levels were undetectable or ALT levels were in normal ranges for the last three outpatient follow-up during the cessation of NA oral antivirals. In patients whose HBV DNA level was detectable but suppressed during the cessation of NA oral antivirals, increase of HBV DNA level to pretreatment levels was accepted as relapse.

Results. Thirty eight patients were included to our study whose NA treatments were discontinued for any reason. Fifteen patients used tenofovir, 14 used entecavir, 7 used lamivudin, and 2 used adefovir. During the cessation of drugs, HBV DNA levels were undetectable in 30 patients; while 8 patients had detectable HBV DNA levels. Before the treatment, the numbers of patients with HBeAg positive and negtaive were 21 (55.3%) and 17 (44.7%), respectively. The reasons for cessation of NA drugs in patients were as follows; in 17 patients with his own request, in 16 patients with doctor's request, in 4 patients because of pregnancy and in one patient because of HBsAg seroconversion. In patients who discontinued treatment with undetectable HBV DNA relapse was observed in 23 of 30 patients and in 7 of 8 patients with detectable HBV DNA, viral load increased to pretreatment levels after cessation of NA drugs. Fulminant hepatitis was not obsereved in any of the patients with relapses.

Conclusion. In patients using oral antiviral treatment, cessation of NA oral antivirals was found to be associated with high virologic relapses.

Disclosures. **All authors:** No reported disclosures.

1178. Comparison of the Accelerated and Standard Vaccination Schedules Against Hepatitis B in Healthy Adults

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Session: 135. Viral Infections: Treatment and Prevention
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Background. In our country, premarital screening for hepatitis B (HB) virus infection is systematic. Immunization against HB virus is indicated for partner at risk. The aim of this study was to compare the immune response and the compliance of an accelerated (A; days 0, 7, 21) and standard (B; days 0, 30, 180) HB vaccination schedules.

Methods. A prospective study was performed between January 2007 and January 2013. Recombinant HB vaccine was given as 20 micrograms intramuscularly. The anti-HBs antibody was determined 30 days after completion of the third vaccine injection in both groups. A seroprotective titer was defined as 10 IU/L. The non-responders received new monthly doses of vaccine (maximum 3 doses). The anti-HBs antibody was determined 30 days after each injection.

Results. Our study included 466 (117 men, 349 women) healthy adults. The mean age was 28 ± 6 years. Three hundred ninety nine (84.3 %) assigned to schedule A and 73 (15.7%) to schedule B according to the delay between the first consultation and the marriage. One month after the third dose, 56% (schedule A) and 59% (schedule B) of the subjects were seroprotected. The compliance with four doses was significantly better in schedule A rather than schedule B ($p = 0.004$). Anti-HBs geometric mean titers were higher in group B than in group A ($p = 0.009$). After four doses of vaccine, the seroprotective rate was 82% and 91.2 % for schedule A and B respectively. At the end of the protocol, the seroprotective rate was 99.4% and 100% for schedule A and B respectively ($p = 0.4$).

Conclusion. A 3-week HB vaccination schedule confer good and early protective immunity. Therefore it seems to be a good preference for last minute immunization in premarital examination.

Disclosures. **All authors:** No reported disclosures.

1179. Implementing Hepatitis C Treatment Programs in Comprehensive HIV Clinics: The Health Resources and Services Administration (HRSA) Special Projects of National Significance (SPNS) Hepatitis C Treatment Expansion Initative

Todd Wills, MD[1]; Martha Friedrich, PhD[1]; Jeffrey Beal, MD[2]; Charurut Somboonwit, MD[1]; Sean Mcintosh[1]; Anthony Bork[1]; Melinda Tinsley, MA[3]; Adan Cajina, MS[3]; Pamela Belton[3]; Jessica Xavier, MPH[3]; Rupali Doshi, MD, MS[4]; Renetta Boyd[3]; Natalie Solomon, MPH[3]; [1]Division of Infectious Disease and International Medicine, University of South Florida College of Medicine, Tampa, FL; [2]Mental Health Law and Policy, University of South Florida, Tampa, FL; [3]HRSA Special Projects of National Significance, Rockville, MD; [4]HRSA HIV/AIDS Bureau, Rockville, MD

Session: 135. Viral Infections: Treatment and Prevention
Friday, October 10, 2014: 12:30 PM

Background. Mortality and morbidity from underlying liver disease in HIV/HCV coinfected patients remains high. Successful linkage to and retention in HCV treatment for HIV/HCV coinfected patients has been historically poor, with correspondingly low HCV treatment success rates. In an attempt to address both clinical, training, and workforce related issues regarding this problem, The Hepatitis C Treatment Expansion Initiative was funded by the Health Resources and Services Administration - Special Projects of National Significance branch from 2010-2014.

Methods. Twenty-nine demonstration site comprehensive HIV clinics were funded for two years to implement one of four clinic-selected models of HCV care, including: integrated HCV care, designated HCV clinic sessions, HCV care delivery by a primary provider with expert back-up, and referral to an outside specialist for care. An Evaluation and Technical Assistance Center (ETAC) assisted all sites with project implementation, patient-level medical consultation as-needed, monthly didactic and case-based teleconferences, and in-person annual site visits and grantee meetings. Quantitative outcomes measured included number of patients linked to and retained in treatment and the number of treated patients achieving a sustained virologic response (SVR) for each clinic. Qualitative data about model designs were also analyzed.

Results. 223 patients entered HCV treatment across all clinic sites over the course of the project. Of those, 195 (87.4%) completed treatment and 99 (44.4%) achieved an SVR. No statistically significant difference in treatment success was identified based on the model of care delivery selected. Qualitative analysis of clinic models through structured interviews and surveys revealed a benefit for clinics that identified a dedicated patient tracker to ensure linkage to and retention in care. Additionally, surveys of demonstration clinic staff including clinical and program personnel revealed increased confidence in initiating care based on the availability of ongoing clinical technical assistance.

Conclusion. A dedicated interdisciplinary effort to implement an HCV treatment program within an HIV clinic can improve treatment implementation and completion rates compared to historical rates in similar populations.

Disclosures. **T. Wills**, Gilead Sciences: Research Contractor, Research grant **C. Somboonwit**, Gilead Sciences: Speaker's Bureau, Speaker honorarium

1180. Predictors of Sustained Virological Response in Cancer Survivors with Hepatitis C Virus Infection Receiving Antiviral Therapy

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Session: 135. Viral Infections: Treatment and Prevention
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Background. No evidence-based information is available on the use of antiviral therapy (AVT) in cancer patients (pts) infected with hepatitis C virus (HCV). We sought to determine the predictors of sustained virological response (SVR) 24 weeks after AVT in these patients.

Methods. Records of HCV-infected pts with history of any type of cancer seen at MD Anderson Cancer Center from 2008-2011 were reviewed retrospectively. Cancer survivors (those with cancer in remission for at least 6 months) with HCV treated with AVT were further evaluated. Baseline characteristics of pts who achieved SVR were compared to those who did not achieve SVR. Categorical variables were compared using Chi-square test or Fisher's exact test. Continuous variables were compared using Wilcoxon rank-sum test. Logistic regression modeling was used to determine predictors of SVR.

Results. Ninety-eight HCV-infected cancer survivors received AVT during the study period. The most common previous cancer was non-Hodgkin's lymphoma (19%). Among the 78 pts with known treatment outcome, 27 (35 %) achieved SVR. AVT analyzed consisted of either a combination of interferon (IFN) and ribavirin (85%) or standard IFN monotherapy (15%). When compared to those who had SVR, more pts who failed AVT were males (44% vs 65%; $P = 0.09$), blacks (4% vs 29%; $P = 0.007$), had more genotype 1 infection (6% vs 69%; $P < 0.001$), higher baseline ALT (mean IU/L, 43 vs 71; $P = 0.009$), higher baseline AST (mean IU/L, 46 vs 77; $P = 0.006$), more leukopenia (total WBC count < 4,000 cells/μL) (4% vs 25%; $P = 0.05$) and neutropenia (absolute neutrophil count < 1,500 cells/μL)(0% vs 16%; $P = 0.09$). There was no statistically significant difference between those who achieved SVR and those who failed AVT with respect to type of previous cancer, baseline HCV RNA levels, CD4 count, body mass index, hepatitis B core antibody positivity, and cirrhosis. Only few pts were tested for IL28B polymorphism. After exact logistic regression analyses, those without genotype 1 infection (OR, 7.2; 95% CI 2.2-55.6; $P < 0.001$) had higher odds of achieving SVR.

Conclusion. AVT is feasible in cancer survivors, with genotype 1 infection being a major predictor of antiviral failure. More efficacious AVTs are needed in this emerging special population of HCV-infected pts.

Disclosures. **All authors:** No reported disclosures.

1343. Noninvasive Infection Detection in Mechanically Ventilated Adults via the Breath Delta Value

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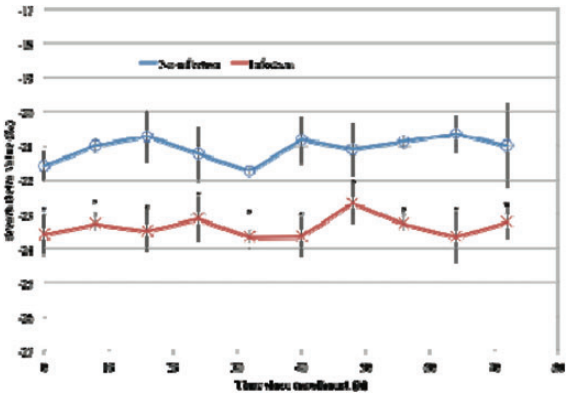
Session: 187. Biomarkers of Immune Responses
Saturday, October 11, 2014: 12:30 PM

Background. The breath delta value (i.e., $^{13}CO_2/^{12}CO_2$ or BDV) is a non-invasive marker for altered metabolism due to infection. Infection detection is achieved by monitoring stable isotopes of carbon in exhaled CO_2 termed the BDV. Exhaled breath samples may be taken non-invasively from the ventilator exhaust and isotopic CO_2 analyzed. Animal studies and a pilot study in the pediatric intensive care unit (ICU) indicate that the BDV may be an indicator for the onset of infection. We report here the variation in the BDV in critically ill mechanically ventilated adults with and without infection.



Breath delta value over time in critically ill mechanically ventilated adults with and without infection. Data are reported as the average, and error bars represent the standard error of the mean. Asterisks denote significant differences with $p<0.05$.

Methods. Subjects were given the standard of care, and breath was sampled every 8 hours for 72 hours. BDV was determined using the Canary BDV monitor (Isomark,

LLC, Madison, WI) currently under development and not yet cleared by the FDA. Infection was defined as either clinically diagnosed sepsis and/or pneumonia. Trends were analyzed using the mixed procedure accounting for autocorrelation of repeated measures (SAS version 9.2, SAS Inst. Cary, NC). Differences were considered significant with $p < 0.05$.

Results. The table shows the demographics of the subjects. The figure shows the BDV trends over time. The trends remained stable over time and did not increase or decrease significantly from the first sample. The BDV from subjects with an infection was significantly lower than subjects without infection at all time-points. The mean BDV was -21.07‰ (0.19 SEM) in subjects without infection and -23.39‰ (0.18 SEM) in subjects with an infection.

Demographics

Age (yrs)	63 (45-89)
Sex	7M 8F
Race	100% Caucasian
Height (m)	1.74 (0.04)
Weight (kg)	108 (8.0)

Conclusion. The BDV is significantly lower in critically ill mechanically ventilated adults with an infection than in similar subjects without an infection. These data suggest that BDV may be a marker for infection in critically ill mechanically ventilated adults. Further testing is underway, to determine if the BDV is a useful marker for the onset of infections in the ICU.

Breath delta value over time in critically ill mechanically ventilated adults with and without infection. Data are reported as the average, and error bars represent the standard error of the mean. Asterisks denote significant differences with $p < 0.05$.

Disclosures. **J. Boriosi**, Isomark, LLC: Grant Investigator, Research support **D. Butz**, Isomark, LLC: Grant Investigator, Member and Shareholder, Salary

1344. Rapid Detection of Neonatal Immune System Activation

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Background. Inter alpha inhibitor proteins (IAIP) are natural serine protease inhibitors that play a crucial role in modulating host response to inflammatory insults. Necrotizing enterocolitis (NEC) and spontaneous intestinal perforation (SIP) are serious morbidities affecting premature infants with overlapping features. It is important to distinguish them earlier as etiology and therefore management may differ. We examined if blood levels of IAIP differ in infants with NEC compared to those with SIP and matched controls.

Methods. Prospective observational unmasked study. Blood and clinical data were collected serially at and after presentation from infants diagnosed with NEC, SIP and matched controls admitted to NICU of Women and Infants Hospital. Infants with NEC were diagnosed by Bell's staging criteria (≥ stage 2 or 3). Infants with SIP were diagnosed by clinical and radiological findings. Controls were matched for gestational age, gender and weight. IAIP levels were measured via a competitive enzyme-linked immunosorbent assay which has a sensitivity of 50 mcg/ml, intra-assay variability (coefficient of variation, CV) of <3% and inter-assay CV of <7%. Mean biomarker levels were subjected to ANOVA and Student Newman Keuls analysis.

Results. There were 28 infants studied in three groups.Mean ± SD IAIP levels measured serially on days 1, 3 and 5 after initial presentation in infants with NEC (170 ± 40, 201 ± 19 and 239 ± 24 mcg/ml) were significantly lower than those with SIP (269 ± 64, 377 ± 84 and 326 ± 47 mcg/ml respectively) ($p < 0.05$).

	NEC (n=5)	SIP (n=6)	Controls (n=17)	P Value
Gestational age, weeks*	$27^5 \pm 3^4$	$26^4 \pm 1^5$	$27^5 \pm 2^6$	0.64
Age at presentation, days*	12.2±11.5	8.1±4.8	10.2±7.1	0.11
Birth weight, grams*	1025±705	825±243	1067±570	0.69
Gender, male %	20%	66%	35%	0.25
IAIP at presentation, mcg/ml*	139±21	319±72	276±110	0.01

*Mean±SD

Conclusion. IAIP levels are decreased in states of immune system activation. As a biomarker, IAIP may assist in early detection of NEC and distinguish NEC from SIP. This distinction at presentation may lead to earlier effective treatments and improved outcomes including long term neurodevelopmental sequelae. Since IAIP correlates with disease progression, it may serve as a surrogate to monitor response to therapy in NEC.

Disclosures. **Y. P. Lim**, ProThera Biologics: Employee, Research grant and Salary

1345. ASO and DNase Titers in Patients with Streptococcal Skin Infections in the Dalbavancin DISCOVER Program

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Background. Elevated values of anti-Streptolysin O (ASO) and DNase-B antibody titers are known to be consistent with antecedent group A streptococcal infections, especially acute streptococcal pharyngitis, acute rheumatic fever or acute glomerulonephritis, but not much is known about their association with streptococcal skin infections. We evaluated the presence of elevated ASO/DNase-B titers in patients enrolled in 2 global phase 3 clinical trials comparing dalbavancin alone to vancomycin/linezolid for the treatment of patients with acute bacterial skin and skin structure infections (ABSSSI).

Methods. Cultures obtained at a local laboratory at baseline were sent to a central laboratory for species identification. ASO and DNase-B titers were measured at baseline and Day 28. ASO titers were considered elevated if there was a 4 fold increase from baseline or if the titer was >200 kIU/L at any time.

Results. 52/107 (48.6%) of patients with a positive DNase and elevated ASO titer had a positive streptococcal culture compared to 91/499 (18.2%) of those with a negative titers ($p < 0.001$).

	ABSSSI patients with a positive streptococcal culture at baseline	ABSSSI patients without a positive streptococcal culture at baseline					
		No positive streptococcal culture at Baseline	P value	Any non-streptococcal positive culture	P value[1]	No positive culture	P value[2]
Elevated ASO titer	77/145 (53.1)	148/472 (31.4)	<.001	136/437 (31.1)	<.001	6/27 (22.2)	0.003
Elevated DNase-B antibody	84/151 (55.6)	112/480 (23.3)	<.001	107/446 (24.0)	<.001	5/27 (18.5)	<.001
Elevated ASO and DNAse-B antibodies	52/143 (36.4)	55/463 (11.9)	<.001	53/430 (12.3)	<.001	2/27 (7.4)	0.003

[1]p value calculated for patients with a positive streptococcal culture vs those with a positive non-streptococcal culture
[2]p value calculated for patients with a positive streptococcal culture vs those with negative cultures

Conclusion. A higher proportion of patients with documented streptococcal skin infections had elevated ASO and/or DNase-B titers than patients who did not have streptococci isolated from cultures at baseline. ABSSSI patients with an elevated ASO and DNase titer are more likely to have a streptococcal etiology for their infection but additional investigation to improve its sensitivity and specificity is warranted.

Disclosures. **S. Puttagunta**, Durata Therapeutics: Employee and Shareholder, Salary **M. Dunne**, Durata Therapeutics: Employee and Shareholder, Salary

1346. Protective Properties of the Fusion PspA Protein Vaccine against Pneumonia Caused by *Streptococcus pneumoniae* with Five Different PspA Clades in Mice

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Background. An increase in the appearance of non-vaccine serotypes in both children and adults with invasive pneumococcal disease (IPD) after introduction of pneumococcal conjugate vaccine represents a limitation of this vaccine.

Methods. In this study, we generated three recombinant pneumococcal surface protein A (PspA) proteins consisting of PspA families 1 and 2, and examined for the reactivity of antisera raised in mice by these PspA fusion proteins with CpG oligonucleotides plus aluminum hydroxide gel. The protective effects of immunization with PspA fusion proteins against pneumococcal pneumonia caused by strains with five different clades were also examined in mice.

Results. PspA3 + 2 induced antiserum showing the high bindings of PspA-specific IgG to all of five challenge strains with different clades in a flow cytometry, although PspA2 + 4 or PspA2 + 5 induced antiserum showing a low binding of PspA-specific IgG to clade 3. We next examined the protective effects of PspA fusion proteins against pneumonia caused by five strains with different clades. Immunization with PspA3 + 2 afforded significant protections against pneumonia caused by five strains with different clades in mice, but immunization with PspA2 + 4 or PspA2 + 5 failed to protect mice from pneumonia caused by strains with clades 1 and 3. The binding of PspA-specific IgG was examined for 68 clinical isolates from adult patients with IPD by antisera raised by three PspA fusion proteins. Immunization of mice with PspA3 + 2 induced antiserum with a high binding capacity to clinical isolates expressing clades 1-4, but not clade 5.

Conclusion. Our results suggest that PspA3 + 2 vaccine has an advantage over PspA2 + 4 or PspA2 + 5 in terms of a broad range of cross-reactivity with clinical isolates and of a cross-protection against pneumococcal pneumonia in mice.

Disclosures. **All authors:** No reported disclosures.

1347. Evaluation of Circulating sCD200 (OX-2), High Sensitive C-reactive Protein and Sedimentation Rate in Diabetic Foot Patients

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Background. CD200 (OX-2) is a novel immune-effective molecule, both cell membrane bound and also existing in a soluble form in serum (sCD200), which acts to regulate inflammatory and acquired immune responses. Recently, our study group showed that sCD200 in serum and blister fluid in a patient with bullous pemphigoid and anti-IgE therapy impact on those levels. We therefore planned this study to evaluate the serum sCD200 levels of diabetic foot and compare it with that of healthy controls. We also analyzed the association between the serum sCD200 levels and the clinical severity of the disease in diabetic foot patients.

Methods. The study was performed with 32 diabetic foot infection patients and 25 healthy control patients. sCD200 concentrations were quantified by using ELISA kit.

Results. We found that sCD200 levels in diabetic foot patients were higher than control group (124.79 ± 4.22 vs 21.57 ± 1.11 [mean ± SEM], $p < 0.0001$). However there is no correlation between sCD200 levels and the Hba1c levels, blood glucose levels (pre/postprandial) and BMI these markers. The hs-CRP levels and sedimentation rates were higher in patient group ($p < 0.0001$, $p < 0.005$ and $p < 0.0001$ respectively).

Conclusion. To the best of our knowledge, this is the first study to assess serum sCD200 in diabetic patients with the late complication of diabetic footinfection.We investigated evidence for possible correlations between serum CRP levels, hs-CRP, and HbA1c, pre-prandial glucose levels BMI, WGS, and sedimentation rate. The sCD200 levels did not correlate with any of these markers.

Disclosures. **All authors:** No reported disclosures.

1348. Immune response to endothelial cell growth factor is elevated during acute Lyme borreliosis but not in post-Lyme disease syndrome

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Background. Lyme disease is caused by spirochetes of the *Borrelia burgdorferi* species complex. Some of the symptoms of Lyme disease are thought to result from the body's immune response during infection. Recently, immune reactivity to endothelial cell growth factor (ECGF), a self-antigen, has been reported to be elevated in patients with Lyme disease. As such, the ECGF protein has been proposed as an autoantibody target in manifestations that are thought to involve infection-induced immune-mediated mechanisms, including refractory Lyme arthritis and post-Lyme disease syndrome (PLDS).

Methods. We aimed to evaluate this hypothesis through analysis of antibody response to recombinant human ECGF in serum from 90 individuals with a range of early to late manifestations of Lyme disease, including single EM, multiple EM, early neurologic, late neurologic, arthritis, and refractory arthritis, as well as 93 PLDS patients, 25 post-Lyme healthy individuals, and 30 healthy individuals without a history of Lyme disease. In addition, ECGF's potential as a target of *B. burgdorferi* cross-reactive antibodies in Lyme disease was examined through competition experiments.

Results. In comparison to non-Lyme healthy individuals, Lyme disease patients with multiple EM ($p < 0.001$), early neurologic ($p < 0.001$), late neurologic ($p < 0.001$), arthritis ($p < 0.001$), and refractory arthritis ($p < 0.05$) manifestations displayed significantly increased antibody reactivity to ECGF. There was not a significant difference in anti-ECGF antibody reactivity between PLDS patients and post-Lyme healthy individuals. Antibodies from rabbits immunized with *B. burgdorferi* whole protein extract did not cross-react with ECGF. Patient serum antibody reactivity to ECGF could not be inhibited by competition with *B. burgdorferi* proteins.

Conclusion. Our data indicate that antibody reactivity to ECGF is elevated throughout the course of acute Lyme disease, with the highest levels occurring after the dissemination of infection. However, immune response to ECGF is not specifically associated with refractory Lyme arthritis or with post-Lyme disease syndrome. In addition, the anti-ECGF antibody response in Lyme disease does not appear to be a result of cross-reactivity.

Disclosures. **All authors:** No reported disclosures.

1349. Gene Expression Profiles Discriminate Between Young Children with Human Rhinovirus (HRV) Symptomatic Infection vs Asymptomatic Detection

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Background. HRVs are among the most common causes of respiratory infections in humans. However, rates of up to 50% HRV detection have been found in asymptomatic children. We evaluated the value of gene expression profiles to differentiate asymptomatic detection from symptomatic HRV infection in young children.

Methods. Whole blood samples from children <2 years old (n = 114) were obtained at four study sites (Columbus, OH; Dallas, TX; Turku, Finland; and Malaga, Spain). Children were classified into: 1) HRV- healthy controls (HC; n = 22); HRV+ asymptomatic (n = 16); HRV+ outpatients (n = 18); and HRV+ inpatients (n = 58). RNA samples were hybridized into Illumina arrays. We used R software package and ComBat script to correct for batch effects and GeneSpring software and modular analyses for analyses.

Results. Statistical group comparisons ($p < 0.05$, Benjamini-Hochberg and 1.25x fold change filter) identified 402 differentially expressed genes between HC and HRV+ inpatients (HRV biosignature), which was validated in an independent group of subjects. The HRV biosignature was then applied to all study groups (114 patient samples) using unsupervised hierarchical clustering which identified 2 main patient clusters (C): C1 composed of HC and the majority of asymptomatic HRV+ subjects 15/16 (94%) and C2 with HRV+ inpatients and the majority of outpatients 15/18 (83%). Class prediction using support vector machine (SVM) identified 57 genes that classified HC vs HRV+ inpatients with 97% accuracy and HRV+ outpatients vs HC with 93% accuracy. Modular analysis showed a gradual increment on the up-regulation of innate immunity genes and a gradual reduction in the down-regulation of adaptive immunity genes between HRV+ inpatients, outpatients and asymptomatic children, respectively. Indeed, the latter group showed no modular differences compared with HC.

Conclusion. Symptomatic HRV infection induced a robust and reproducible biosignature. On the other hand, transcriptional profiles of children with asymptomatic HRV+ detection were comparable to those of HC. Transcriptomic profiling represents a useful tool to discriminate between clinically irrelevant pathogen detection and true infection.

Disclosures. **All authors:** No reported disclosures.

1350. Urine ß-defensin 2 Concentration Increases during Urinary Tract Infection

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Background. The urinary tract, apart from the urethral meatus, is usually sterile despite its close proximity to enteric flora. Antimicrobial peptides (AMPs) are components of innate immunity and play an important role in maintaining urinary tract sterility. Human ß-defensin 2 (BD2) is an AMP described in the urinary tract, but its role during urinary tract infection (UTI) is not well defined. The objective of this study was to evaluate whether urine BD2 concentration increases during UTI in children.

Methods. We prospectively collected urine samples from Emergency Department patients aged ≤18 years in whom urine culture (UC) was performed for any clinical indication. Demographic, clinical, and culture data were obtained by review of the medical record. Urine creatinine (Cr) concentration was measured by a colorimetric assay. Urine BD2 concentration was measured by enzyme-linked immunosorbent assay and was normalized to urine Cr concentration to account for dilution. Culture-positive (UC_{pos}) was defined as UC yielding ≥50,000 CFU/mL of a uropathogen. Other UC results were considered culture-negative (UC_{neg}).

Results. The cohort comprised 43 patients, 34 (79%) of whom were female. Median age was 9.6 years (IQR 3.8-16.7). At presentation, 15 (35%) patients had fever and 21 (49%) had vomiting and/or flank pain. UC was positive in 14 patients and negative in 29 patients. The UC_{pos} and UC_{neg} groups were similar in the above demographic and clinical characteristics. Urine was obtained by catheterization in 9 (21%) and clean catch in 34 (79%). Pyuria and/or leukocyte esterase was present in 13 (93%) UC_{pos} patients and 10 (34%) UC_{neg} patients. *Escherichia coli* was the most common bacterium isolated, accounting for 12 (86%) of 14 positive UC. Urine BD2 concentration was significantly higher in UC_{pos} than UC_{neg} patients, with median BD2 concentrations of 82.25 pg/mg Cr (IQR 0-190.2) in UC_{pos} patients compared to 0 pg/mg Cr (IQR 0-61.27) in UC_{neg} patients ($P = 0.0299$).

Conclusion. Urine BD2 concentration is significantly higher in UC_{pos} than UC_{neg} patients. This indicates that increased BD2 expression is a component of the innate immune response to UTI. Further study should define the precise role of BD2 during UTI, evaluate its performance as a diagnostic UTI biomarker, and elucidate its dynamics throughout the course of a UTI.

Disclosures. **All authors:** No reported disclosures.

1351. Prevalence and Age-Related Acquisition of Antibodies against Group A Streptococcal M-Related Proteins

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Background. Group A streptococcal (GAS) infections are common in children but less common in adults. Immunity against type-specific M proteins of GAS protects against subsequent infection with the same M type. The relative resistance of adults

to infection has been attributed to immunity to multiple M types, among other factors. An additional explanation is immunity to cross-protective GAS antigens that provides broader protection later in life. M-related proteins (Mrp) of GAS are expressed by 83% of GAS isolates and they contain protective epitopes. Unlike M proteins, Mrp's are highly conserved and are grouped into three structurally related families represented by Mrp2, 4, and 49. In the current study we evaluated the prevalence and age-related acquisition of Mrp antibodies in children.

Methods. Serum samples from 356 subjects (ages 1-16) were obtained from the clinical laboratories of a pediatric hospital. Purified, recombinant N-terminal peptides of Mrp2, Mrp4, and Mrp49 were used to assess Mrp antibody levels by ELISA. Human Mrp antibodies were purified by affinity chromatography and used in bactericidal tests.

Results. Significant levels of antibodies against any of the three Mrp's were observed in 175/356 serum samples (49%). Mrp4 antibodies were the most prevalent (145/356), followed by Mrp 2 (88/356) and Mrp49 (73/356). There was a clear association between the subjects' age and prevalence of antibodies against all three Mrp's ($r = 0.32$, $p < 0.001$). Significant age-related trends were also observed for antibody levels against each individual Mrp peptide. Mrp4 antibodies affinity purified from human serum resulted in 99% killing of heterologous serotype M28 GAS.

Conclusion. Mrp antibodies are prevalent and are acquired in an age-related manner. Purified human antibodies against Mrp4 were strongly bactericidal. Taken together with our recent studies showing that Mrp's have relatively conserved sequences comprising three structurally related families and that all three contain opsonic epitopes, our results suggest that Mrp antibodies in combination with M antibodies may contribute to the relative resistance to GAS infections later in life. These findings also have implications for the development of broadly protective GAS vaccines.

Disclosures. **J. Dale**, Vaxent, LLC: Board Member, Member and Shareholder, Equity

1352. Progression of Lyme Disease to Later Stages is Associated with Antibody Response Towards the Membrane-Proximal Domain of the VlsE Protein of *Borrelia burgdorferi*

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Background. Lyme disease is associated with a robust B cell response to the VlsE lipoprotein of *Borrelia burgdorferi*. Epitope mapping analyses have shown the IR6 region within the variable domain and specific sequences in the N- and C-terminal invariable domains of VlsE to contain the major immunogenic regions. However, antibody reactivity against immunodominant epitopes of VlsE has not been systematically analyzed during the various stages of infection.

Methods. Here, we examined serum samples from 90 patients with a range of early to late manifestations of Lyme borreliosis for antibody reactivity to the three major epitope sequences of VlsE. These included amino acid sequences 274-298 (IR6 epitope), 21-44 (N-terminal epitope), and 336-349 (C-terminal epitope) of the VlsE protein from *B. burgdorferi* B31. In addition, antibody response to a recombinantly generated protein containing the entire membrane-proximal domain of VlsE and its associated epitopes as a contiguous sequence was examined.

Results. Antibody reactivity to the IR6 region of VlsE was found to vary little between cohorts of patients representing early disseminated to late manifestations of Lyme disease. In contrast, antibody responses towards the specific N- and C-terminal epitopes of VlsE, as well as the recombinant sequence representing the entire membrane-proximal region, were predominantly absent during early Lyme disease and became highly elevated in late manifestations.

Conclusion. The data help to elucidate the evolution of humoral immune reactivity to VlsE during the course of *B. burgdorferi* infection, demonstrating the development of a divergent antibody response towards distinct epitopes of a single protein. The results may be consequential to gaining an understanding of the epitopes' potential involvement in a mechanism of immune evasion by the spirochetes.

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1353. The Induction of Endotoxin Tolerance is Associated with the Activation of Mitochondrial Biogenesis in THP-1 Cells

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Background. In sepsis monocyte immune deactivation is associated with increased mortality and susceptibility to secondary infections. There is increasing evidence of mitochondrial depletion and dysfunction, including impaired respiration and oxidative stress, in monocytes in sepsis. Survival and recovery of cellular function following sepsis has been associated with the induction of mitochondrial biogenesis. Using endotoxin tolerance (ET), whereby repeated exposure to lipopolysaccharide (LPS) produces diminishing inflammatory responses, as a model of monocyte deactivation we investigated the link between immunity, respiration and mitochondrial biogenesis.

Methods. THP-1 cells, a human monocytic cell line, were pre-incubated with 100ng/ml LPS from *Escherichia coli* 026:B6 for 0, 2, 6, 24, 48 and 72 hours. The ability of THP-1 cells to respond to a second inflammatory stimulus was then assessed in addition to measurements of oxygen consumption, oxidative stress and mitochondrial biogenesis.

Results. Pre-incubation with LPS produced a change in THP-1 cell immune phenotype consistent with ET. In response to a second inflammatory stimulus there was reduced release of pro-inflammatory cytokines but increased anti-inflammatory cytokine release and phagocytosis. LPS exposure also resulted in evidence of early oxidative stress with recovery associated with the activation of antioxidant defences. Significant increases in mitochondrial DNA copy number and expression of mitochondrial transcription factor A following exposure to LPS suggest that mitochondrial biogenesis is induced during ET. In addition, after LPS exposure there was an increase in THP-1 cell oxygen consumption due to mitochondrial adenosine triphosphate generation.

Conclusion. In association with a shift towards an anti-inflammatory phenotype there is evidence of the induction of mitochondrial biogenesis and anti-oxidant defences in ET THP-1 cells. Further investigation into the potential co-regulation of these pro-survival responses may provide important insights into the mechanisms of immune deactivation and cellular recovery in human monocytic cells following inflammatory insults in diverse conditions including sepsis.

Disclosures. **All authors:** No reported disclosures.

1354. Toll-like Receptor Agonists Alter the CD8$^+$ T Cell Response Hierarchy in Neonates During Respiratory Syncytial Virus Infection

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Background. CD8$^+$T cells clear respiratory syncytial virus (RSV) during infection and, as a component of the adaptive immune response, develop memory for more rapid responses upon subsequent exposure. In neonates, this process is compromised, thus we propose to define age-dependent innate immune mechanisms that influence the T cell response in order to advance vaccine design for neonates.

Methods. Intranasal RSV infection of CB6F1 adult hybrid mice generates a strongly dominant RSV-specific CD8$^+$ T cell response to a K^d- restricted peptide (SYIGSINNI) from the M2 protein of RSV, and a numerically subdominant response to a RSV epitope from the M protein (NAITNAKII, $D^bM_{187\text{-}195}$). Neonatal mice, however, generate a more co-dominant response to these two epitopes as determined by flow cytometry. To define the role of antigen-presenting cell (APC) in driving the T cell response, Toll-like receptor (TLR) agonists that active APC were administered at the time of RSV infection.

Results. TLR agonist treatment of neonatal mice resulted in a more adult-like CD8$^+$ T cell response hierarchy indicating a critical role for APC in driving T cell responses. Conventional dendritic cells (cDC) are important professional APC in the lung. Evaluation of cDC during RSV infection demonstrates age-dependent differences in the number of cDCs, with diminished costimulatory capacity in neonates. TLR agonist treatment at the time of RSV infection of neonates increased expression of costimulatory molecules, CD80 and CD86, on two subsets of cDC, the CD103$^+$DC and CD11b$^+$DC. Partial blockade of CD80 and CD86 during RSV infection of neonates treated with a TLR agonist reversed the T cell response hierarchy back to a co-dominant response, indicating the importance of cDC costimulatory molecule expression. Surprisingly, during RSV infection, both CD103$^+$DC and CD11b$^+$DC are able to effectively present antigen to CD8$^+$ T cells to stimulate proliferation, in contrast to other infection models that characterized CD11b$^+$DC as poor stimulators of CD8$^+$T cells.

Conclusion. The unique age-dependent changes in immunity seen in RSV infection, and the ability to modify both CD103$^+$DC and CD11b$^+$DC to alter the character of RSV-specific CD8$^+$ T cell responses can be used to develop vaccines that target the youngest and most vulnerable in the population.

Disclosures. **All authors:** No reported disclosures.

1355. Th1 responses in persons with disseminated coccidioidomycosis depend on serology titer and time from diagnosis but Th17 responses are persistent

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Background. Development of a T helper lymphocyte type-1 (Th1) response characterized by release of cytokines such as interleukin-2 (IL-2) and interferon-γ (IFN-γ) has been associated with a good outcome in coccidioidomycosis. Recent data have also suggested that T lymphocytes producing the interleukin-17 (IL-17) family of cytokines (Th17) may play a role in modulating that immunity.

Methods. A cross-sectional analysis of adult subjects with coccidioidomycosis was performed. Approximately 5 mL of heparinized whole blood was obtained by venipuncture from each subject and incubated for 18 hr with 20 μg/mL of the coccidioidal antigen preparation T27K. The plasma supernatant analyzed for concentrations of IL-2, IFN-γ and IL-17.

Results. Nineteen subjects with non-meningeal coccidioidomycosis and 6 healthy coccidioidal immune and 6 healthy non-immune donors were recruited. In those with disseminated coccidioidomycosis, levels of IL-2 and IFN-γ were equivalent to those from healthy, immune donors and significantly above healthy non-immune donors ($P < 0.01$). However, both IL-2 and IFN-γ were significantly lower among disseminated patients if the coccidioidal serology titer was ≥1:8 compared to less than this ($P<0.03$). Moreover, IL-2 levels were significantly higher in those diagnosed >1 year compared to those diagnosed earlier ($P = 0.04$). IL-17 levels were significantly higher in the disseminated group than either immune or non-immune donors ($P < 0.03$) and did not change with either serologic titer or time from diagnosis.

Conclusion. These data suggest that the Th1 response in disseminated coccidioidomycosis responds to treatment and control of disease over time. However, the Th17 appears to be persistent and not dependent on either serologic response or time from diagnosis.

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1356. HMGB-1/RAGE Signaling and Cytokine Activation in Adults Hospitalized for Active Tuberculosis

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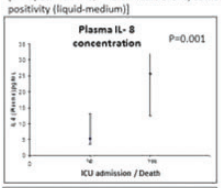
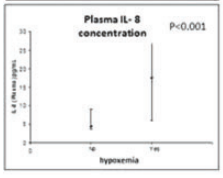
Background. This study aims to evaluate the clinical significance of high-mobility group box 1 (HMGB-1) / advanced glycation end-products (RAGE) signaling pathway and cytokine activation in active tuberculosis (TB), and its associated inflammasome cascade (NALP3, Caspase-1). Funding: Research Fund for the Control of Infectious Diseases, Hong Kong SAR, no. 11100272.

Correlations between clinical/microbiological variables and plasma cytokine concentrations

	TB severity score [1]		Duration of hospitalization, day		Time-to-fever resolution, day		Time-to-culture positivity, day [2]		Semi-quantitative AFB smear result	
Plasma concentration	r	P-value	r	P-value	r	P-value	r	P-value	r	P-value
IL-6 (pg/mL)	+0.207	0.065	+0.359	0.001	+0.272	0.015	-0.445	0.007	+0.264	0.024
IL-8 (pg/mL)	+0.317	0.004	+0.407	<0.001	+0.137	0.230	-0.335	0.046	+0.247	0.035

[r = Spearman *rho*; * TB clinical severity score (adapted from: Wejse C *et al.* Scand J Infect Dis. 2008;40:111) ; * time-to-culture positivity (liquid-medium)]





Final logistic regression model showing explanatory variables associated with ICU/death (n=8)

Variable	Adjusted OR (95% CI)	P-value
Age, per 20 yr	3.50 (0.94, 13.10)	0.063
Sex, male	0.19 (0.02, 2.00)	0.190
Comorbidity	1.32 (0.17, 10.42)	0.793
IL-6 (pg/mL)	1.01 (0.97, 1.04)	0.726
IL-8 (pg/mL)	1.12 (1.01, 1.24)	0.027*
IL-18 (pg/mL)	1.00 (1.00, 1.00)	0.116
HMGB1(ng/mL)	1.30 (0.93, 1.83)	0.131

Final logistic regression model showing explanatory variables associated with hypoxemia (n=21)

Variable	Adjusted OR (95% CI)	P-value
Age, per 20 yr	2.93 (1.35, 6.36)	0.007
Sex, male	0.16 (0.03, 0.81)	0.027
Comorbidity	0.90 (0.23, 3.49)	0.881
IL-6 (pg/mL)	1.00 (0.97, 1.02)	0.701
IL-8 (pg/mL)	1.13 (1.03, 1.23)	0.007*
IL-18 (pg/mL)	1.00 (1.00, 1.00)	0.422
HMGB1(ng/mL)	1.25 (1.01, 1.56)	0.044*

[Comorbidity, Charlson index; adjusted OR, per unit increase of IL-8, HMGB1]

Methods. A prospective, case-control study was performed. Adults aged ≥18 years hospitalized with laboratory-confirmed, active pulmonary TB (n = 80) were compared to age-and-gender matched healthy controls (n = 45). Plasma concentrations of interleukin (IL)-6, IL-8, IL-18, IL-10, IL-12p70, IL-1 ≤], TNF- ≤ \, HMGB-1, and soluble RAGE were measured using Cytometric Bead Array and ELISA. Expression of transmembrane RAGE on monocytes and dendritic cells was measured by flow cytometry. Cellular NALP3 mRNA expression was quantified using real-time PCR.

Results. Elevated plasma concentrations of IL-6, IL-8, IL-18, and HMGB-1 were found in patients with active TB. There was increased expression of transmembrane RAGE, together with up-regulated NALP3 expression and Caspase-1 activity. Plasma soluble RAGE was depleted. High IL-8 and IL-6 levels were associated with ICU admission/death, hypoxemia, and mycobacterial load (Figure). IL-8, IL-6, HMGB-1, and NALP3/Caspase-1 expressions correlated with durations of fever and hospitalization, and TB severity score (HMGB1 vs fever duration, Spearman's *rho* +0.272, $P = 0.015$). Plasma IL-8 and HMGB-1 levels independently associated with hypoxemia, and ICU admission/death, adjusted for patient characteristics (hypoxemia, HMGB1 adjusted OR 1.25, 95%CI 1.01-1.56, $P = 0.044$).

Conclusion. HMGB1/RAGE signaling and pro-inflammatory cytokines (e.g., IL-8) may play important roles in pathogenesis of active TB.

Disclosures. **All authors:** No reported disclosures.

1357. Viral Diversity and Neutralizing Antibody Responses in Infants with Symptomatic Congenital CMV Disease receiving Antiviral Therapy

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Background. Congenital cytomegalovirus (cCMV) is the most common congenital infection and an important cause of childhood sensorineural hearing loss (SNHL). Extensive genetic diversity among CMV strains, infection with multiple CMV strains, and strain-specific neutralizing antibody responses appear to be common. However, the association between virus diversity and strain-specific antibody responses is not known.

Methods. Residual samples were available from 8 infants with symptomatic cCMV enrolled in the NIAID's CASG 109 study, a PK study of valgancyclovir. Subjects received 6 weeks of antiviral therapy from enrollment. Blood samples obtained at enrollment (less than 3 weeks of age) and 6 months later were analyzed for genotypes of glycoproteins gB, gH and gN. Neutralization response was measured in sera at enrollment using gN recombinant viruses. A 3-fold difference in neutralizing titers against at least two gN recombinant viruses was considered evidence of strain specific response.

Results. All 8 patients had >1 CMV genotype detected at either enrollment or 6 months. At enrollment, all subjects had >1 strain detected, with a range of 2-4 strains per subject. At follow up, the number of strains for each patient ranged from 1 to 3. Five of the 8 subjects had fewer genotypes detected at 6 month follow-up compared to enrollment. Two subjects had the appearance of new strains after 6 months.

All subjects had detectible neutralization response against all 4 recombinant gN viruses (titers >400) within the first month of life. Strain-specific neutralizing responses were detected in 5 children. Although not statistically significant, lower neutralizing titers were observed in 5 children who were infected with ≤ 2 gN genotypes compared to those with greater virus diversity (mean titers, 3800 vs 4500).

Conclusion. All study infants were infected with multiple CMV strains and most had strain-specific neutralizing antibody responses. Overall the viral diversity decreased over time. It is unknown at this point if the changes in viral diversity are related to antiviral treatment. Studies are ongoing to determine strain specific neutralization over time and the association between virus diversity and antibody responses in a larger cohort randomized to longer antiviral treatment times.

Disclosures. **D. W. Kimberlin**, GSK: Grant Investigator and served as study site for clinical trials conducted by GSK (monies went directly to my university), Grant recipient; Gilead: Grant Investigator and served as study site for clinical trials conducted by Gilead (monies went directly to my university), Grant recipient

1358. Evaluating the Accuracy of Combining two Biomarkers to Differentiate Viral and/or Bacterial Immune Response in Patients with Acute Febrile Respiratory Infection

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Background. To determine the accuracy of combining two biomarkers, C-reactive protein (CRP) and Myxovirus A (MxA), to identify an immune response to viral and/or bacterial infection in patients presenting with suspected pharyngitis or lower respiratory tract infection (LRTI) as compared to confirmatory microbiological, radiological, and laboratory testing.

Methods. A prospective single center, blinded, clinical feasibility trial was performed at Beth Israel Deaconess Medical Center – a Harvard Medical School teaching hospital – from December 2012-August 2013. Patients with presumed acute febrile respiratory infection consistent with suspected pharyngitis or LRTI were enrolled, as well as age matched controls. Qualifying patients with a clinical diagnosis of pharyngitis or LRTI had oropharyngeal samples sent for viral respiratory polymerase chain reaction (PCR) testing and routine bacterial cell culture. Patients with suspected LRTI also had sputum cultures and a chest x-ray. A venous blood sample was collected, WBC count measured, and an enzyme-linked immunosorbent assay (ELISA) was then used to measure CRP and MxA levels.

Results. The study enrolled 60 patients, 23 with definitive microbiological confirmation of disease (8 enrolled with presumed pharyngitis and 15 with presumed LRTI) as well as 22 controls. The 15 remaining subjects had no definitive microbiological confirmation of disease. A low CRP cut off of 15 mg/L and high CRP cut off of 80 mg/L combined with the presence or absence of MxA levels greater than 40 ng/ml, led to the correct identification of a combined total of 95% (21/22) of the patients negative for infection, 93% (13/14) of bacterial infections, and 78% (7/9) of viral infections [Figure 1].

Conclusion. In isolation, neither CRP (elevated primarily in bacterial infection) nor MxA (elevated primarily in viral infection) alone is sensitive or specific at identifying both viral and/or bacterial infection. However, by simultaneously examining low and high levels of CRP, each in combination with the presence of elevated MxA, it is possible to successfully classify patients with bacterial vs viral etiology of infection. Further validation is warranted for this promising approach.

Disclosures. **R. Sambursky**, Rapid Pathogen Screening, Inc.: Board Member, Employee and Shareholder, Salary **N. Shapiro**, Beth Israel Deaconess Medical Center: Collaborator and Investigator, Research support

Lower Respiratory Tract Infections (N=32)					
N=10	ELISA values (range)				
Bacterial infection	CRP (mg/L)	High CRP	120	Mean	62.9
		Low CRP	7		
	MxA (ng/ml)	High MxA	20.9	Mean	9.1
		Low MxA	0		
N=5	ELISA values (range)				
Viral infection	CRP (mg/L)	High CRP	56	Mean	24.1
		Low CRP	2.4		
	MxA (ng/ml)	High MxA	148	Mean	80.3
		Low MxA	10.7		
N=17	ELISA values (range)				
Negative	CRP (mg/L)	High CRP	15	Mean	3.5
		Low CRP	0.5		
	MxA (ng/ml)	High MxA	18.3	Mean	2.1
		Low MxA	0		

Upper Respiratory Tract Infections (N=13)					
N=4	ELISA values (range)				
Bacterial infection	CRP (mg/L)	High CRP	120	Mean	110
		Low CRP	100		
	MxA (ng/ml)	High MxA	19.7	Mean	6.1
		Low MxA	0		
N=4	ELISA values (range)				
Viral infection	CRP (mg/L)	High CRP	100	Mean	48.7
		Low CRP	6.1		
	MxA (ng/ml)	High MxA	147.4	Mean	107.8
		Low MxA	52.3		
N=5	ELISA values (range)				
Negative	CRP (mg/L)	High CRP	8	Mean	4.5
		Low CRP	0.1		
	MxA (ng/ml)	High MxA	0	Mean	0
		Low MxA	0		

Combined (N=45)					
N=14	ELISA values (range)				
Bacterial infection	CRP (mg/L)	High CRP	120	Mean	75.5
		Low CRP	7		
	MxA (ng/ml)	High MxA	20.9	Mean	8.3
		Low MxA	0		
N=9	ELISA values (range)				
Viral infection	CRP (mg/L)	High CRP	100	Mean	35
		Low CRP	2.4		
	MxA (ng/ml)	High MxA	148	Mean	92.5
		Low MxA	10.7		
N=22	ELISA values (range)				
Negative	CRP (mg/L)	High CRP	15	Mean	3.7
		Low CRP	0.1		
	MxA (ng/ml)	High MxA	18.3	Mean	1.6
		Low MxA	0		

1359. Circulating Cytokines in Pregnant Women Infected with *Toxoplasma gondii*

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Background. Toxoplasmosis during pregnancy can result in severe neurological damage or death of the fetus or newborn. Immunopathology has been suspected as mechanism of disease. We recently published cytokine profiles in pregnant women infected with Toxoplasma from USA and Colombia and were surprised that a number of cytokines were down regulated in the US cohort (JID 2014 Mar 23). In this study we investigated profiles of 51 cytokines in 15 pregnant women before and after they became infected with Toxoplasma.

Methods. A Luminex (Affymetrix, Santa Clara, CA) human 51-plex assay was performed at the Human Immune Monitoring Center at Stanford University. Plates were read using a Luminex 200 instrument with a lower bound of 100 beads per sample per cytokine. Each sample produces a median of florescent intensities (MFI) and are measured in duplicate. Statistical analysis: Separately by patient, after centering/scaling, a smooth, curve for log (MFI) on time since infection was estimated per cytokine via empirical Bayes shrinkage of -spline coefficients across cytokines.

Results. Sparse clustering on pooled smoothed data across time points (including interpolated values) and patients gave an optimal six-cluster solution for 49 cytokines. IFN-, TNF-, VCAM1 and IL17F contributed most heavily to cluster separation. The two most prevalent clusters across patients and time points were distinct in that most of the 49 cytokines were upregulated in one (immune state 2, 36% of data, Figure 1) and downregulated in the other (immune state 3, 40% of data, Figure 2). Prevalence of each cluster was regressed on time since infection using a piecewise linear generalized linear mixed model. Prevalence of immune state 2 decreased prior to infection and rose after infection, while prevalence of immune state 3 decreased after infection (Figure 3).

Conclusion. Cytokine profiles in pregnant women before and after Toxoplasma infection are reported here for the first time. Upregulation and downregulation are the result of host-parasite interactions in their balancing act to fight the parasite, prevent immunopathology and survival of both

Disclosures. **All authors:** No reported disclosures.

1360. Streptococcal Toxic Shock Syndrome due to Beta-hemolytic Streptococci : Clinical Features and Cytokines/ Chemokines Analysis of the Cases

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Background. Beta-hemolytic Streptococci including *S. pyogenes* cause acute infections, including severe infections such as necrotizing fasciitis and streptococcal toxic shock syndrome (STSS). Although these infections progress rapidly and have high mortality rate, precise mechanism of pathogenesis remains obscure. Here, we conducted a prospective study to explore the pathogenesis of STSS in terms of bacterial and host factors.

Methods. Since January 2013 until March 2014, patients diagnosed as STSS due to β-hemolytic Streptococci were prospectively screened. Serum sample on admission was collected for measuring a variety of cytokines(IFN-γ, TNF-α, IL-1β, IL-6, IL-8, IL-12, IL-17, G-CSF, IL-10, IL-4) and chemokines(MCP-1, IP-10) levels. Bacterial strains from blood culture were categorized by Lancefield grouping and analyzed for *emm* type, *speA, speB, speC*, and *speF*.

Results. Nine patients were diagnosed as STSS. Mean age was 66-years old. Eight patients revealed cellulitis over lower extremities, of which five patients suffering from necrotizing fasciitis. Average period from onset of the symptoms to hospital visit was 2 days and mortality was 55.6%, despite intensive treatment including high amount of PCG/CLDM administration. Seven strains were categorized as group A and two were group B. There were two *emm* type 12, other strains revealed different type. All strains were negative for *speA,* and positive for *speB and,speF. SpeC* was positive among 50% of strains. Mean white blood cell count and creatine kinase level were 9522/μL and 2652 IU/L, respectively. Impressively, TNF-α and IL-1β were not elevated at all, but IFN-γ was slightly elevated (mean 288 pg/mL). Relatively large amount of IL-6, IL-8 and G-CSF were produced (mean 12967, 2433, 2328 pg/mL, respectively). Meanwhile, abundant amount of MCP-1 and IP-10 were observed (11026, 20682 pg/mL, respectively).

Conclusion. There are few reports that present immunological analysis along with clinical/bacterial features of STSS patients. Our results indicated reduced production of Th-1 type cytokines and increased production of MCP-1 and IP-10 might be prominently involved in STSS pathogenesis.

Disclosures. **Y. Ishii**, Toho Univesity Shool of Mediicne: Employee, Salary **K. Tateda**, Toho Uneiversity School od Medicine: Employee, Salary

1361. Innate Pulmonary Response to Community-Acquired Pneumonia (CAP) in Patients with Chronic Obstructive Pulmonary Disease (COPD): Results from the Community-Acquired Pneumonia Inflammatory Study Group (CAPISG)

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Background. Patients with COPD have chronic airway inflammation characterized by increased cytokine levels and neutrophil activation. It is not well defined if these chronic inflammatory changes in the airway may impair the innate pulmonary response during an episode of CAP. The objective of this study was to compare cytokine production and neutrophil function in patients with CAP with and without COPD.

Methods. Blood samples were collected from 40 patients diagnosed with CAP upon admission to the hospital. The plasma levels of 10 different cytokines and chemokines were measured, as well as the peripheral blood neutrophil function. Patients were grouped according to the presence of COPD [CAP-COPD (+) vs CAP-COPD (-)]. The Mann-Whitney U test was used to compare cytokine and chemokine levels between the CAP-COPD (+) and CAP-COPD (-) groups.

Results. A total of 14 CAP-COPD (+) and 26 CAP-COPD (-) patients were enrolled. Median (interquartile range) CD35 expression was 163 (111) in CAP-COPD (+) and 127 (101) in CAP-COPD (-) ($P = 0.238$). CD66b expression was 62 (44) in

CAP-COPD (+) and 63 (24) in CAP-COPD (-) ($P = 0.847$). Ph-Sa was 837 (810) in CAP-COPD (+) and 913 (880) in CAP-COPD (-) ($P = 0.713$). H2O2 production was 536 (480) in CAP-COPD (+) and 726 (406) in CAP-COPD (-) ($P = 0.494$). The cytokine and chemokine levels didn't show significant differences between groups.

Conclusion. The innate pulmonary response during an episode of CAP measured by cytokine production and neutrophil function is not different in patients with or without COPD. These data support the clinical concept that COPD is not a risk factor to poor outcomes in patients with CAP.

Disclosures. **All authors:** No reported disclosures.

1362. Procalcitonin and Interleukin-6: Biomarkers of Cancer and Infection

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Background. Procalcitonin (PCT) and Interleukin-6 (IL-6) have emerged as biomarkers for different inflammatory conditions, including cancer and infection. The purpose of the study was to evaluate the role of PCT and IL-6 as biomarkers of cancer and its progression in a large cohort of patients with and without infection.

Methods. This prospective, observational study included residual plasma samples collected from febrile and non-febrile cancer patients, and control subjects without cancer. Levels of PCT and IL-6 were determined by Kryptor compact bioanalyzer and ELISA respectively.

Results. We identified a total of 1064 patients, including 575 febrile cancer patients, 410 non-febrile cancer patients, and 79 non-cancer individuals. The median PCT level was lower in control subjects (0.029 ng/ml) compared to cancer patients with stage I-III disease (0.127 ng/ml) ($p < 0.0001$) and stage IV disease (0.190 ng/ml) ($p < 0.0001$). It was also higher in febrile cancer patients (0.310 ng/ml) compared to non-febrile cancer patients (0.1 ng/ml) ($p < 0.0001$). PCT was also higher in febrile cancer patients with sepsis or bacteremia (0.490 ng/ml) compared to those without microbiological documented infection (0.310 ng/ml) ($p = 0.003$). Median IL-6 level was significantly lower in the control group (0 pg/ml) than in non-febrile cancer patients with stages I-III (7.376 pg/ml) or stage IV (9.635 pg/ml) ($p < 0.0001$), but did not differ in patients with stage IV cancer from those with stage I-III.

Conclusion. Our results suggest a potential role for PCT and IL-6 in predicting cancer in non-febrile patients. PCT is also useful in detecting cancer and its progression in non-febrile patients. However, in febrile cancer patients, PCT predicts bacteremia or sepsis.

Disclosures. **I. Raad**, Atellas: Grant Investigator, Grant recipient Pfizer: Consultant, Consulting fee

1363. The Iowa Disinfection Cleaning Project: Opportunities, Successes and Challenges of a Structured Programmatic Intervention in 56 Hospitals

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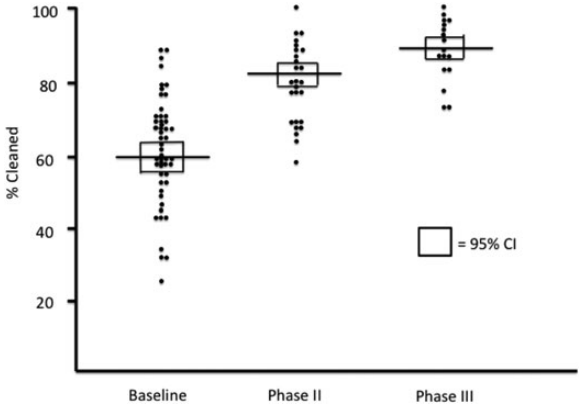
Background. Studies have shown that cleaning thoroughness improves when infection preventionists (IPs) use a fluorescent marker to objectively assess cleaning and give environmental services (ES) staff feedback. We evaluated whether this program could improve cleaning efficacy across a state.



Methods. We evaluated the efficacy of disinfection cleaning of 14 standardized environmental surfaces after patient transfer or discharge before and after an intervention in 56 Iowa hospitals (15-415 beds). We used a fluorescent targeting system ($DAZO^-$) to objectively quantify cleaning. IPs covertly marked surfaces and used UV light to assess pre-intervention (baseline) cleaning efficacy. IPs again assessed cleaning after ES staff saw a standardized educational presentation (Phase II) and after IPs fed back cleaning efficacy results to ES staff (Phase III). We used interviews and questionnaires to obtain information on facilitators and barriers for the project.

Results. At baseline, the fluorescent target was removed from 60% (95% CI = 56.7 to 64.4) of 15,658 standardized environmental surfaces during terminal cleaning were considered cleaned (figure). 41 hospitals completed Phase II interventions and reached a cleaning efficacy of 83% (95% CI = 77 to 84.3). 20 hospitals provided ≥ 1 cycle of performance feedback to ES staff (Phase III). These hospitals achieved a cleaning efficacy of 89% (95% CI = 84.6 to 93.1). 6 hospitals that maintained the program beyond the planned study period had a cleaning efficacy of > 90% after 38 months. IPs at 20 hospitals that completed Phase III noted that: All ES staff valued the program (20); senior management were enthusiastic (11, 55%); ES now defined their work as improving patient safety (10, 50%).

Conclusion. ES departments achieved high cleaning efficacy (mean 89%) with a standardized programmatic intervention using a fluorescent marker, an education program and objective feedback of performance to ES staff in 20 hospitals that completed Phases I-III. Unfortunately, 50% of hospitals could not finish the study because resources were limited. Our findings support the value of monitoring environmental cleaning as recommended by CDC in 2010 but to reap these benefits, hospitals must provide appropriate resources for such programs.

Disclosures. **P. Carling**, Ecolab: Patent License and Speaker's Bureau, Consulting fee and Licensing agreement or royalty

1364. Enhanced Terminal Room Disinfection: A Qualitative Summary of Perspectives from Environmental Services (EVS) and Nurse Managers

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Background. The hospital environment is an established cause of healthcare-associated infections (HAI). Enhanced terminal room disinfection, including the use of UV-C emitting devices and/or bleach, has been proposed as a method to reduce the risk of HAI caused by environmental contamination, but implementation of these methods is poorly described. We characterized the perceptions of EVS and nurses regarding enhanced disinfection strategies.

Methods. We administered surveys to EVS supervisors and nurse (RN) unit managers at the 9 hospitals in the BETR Disinfection study to assess perceptions about delays in room cleaning, odor, streaking, and other unintended consequences based on type of terminal room disinfection method employed (quaternary ammonium (reference group), quaternary ammonium with the UV-C emitting device, bleach alone, or bleach with UV-C). We compared responses a) during the use of quaternary ammonium vs bleach and b) with and without UV-C. Proportions were compared using the 2-tailed chi-square test.

Results. 335 survey answers were provided from 137 EVS staff (77% response rate) and 198 nurse managers (61% response rate). EVS supervisors, housekeepers, and RN managers all perceived an increase in room cleaning/decontamination delays with the use of UV-C than without UV-C (EVS: 52 vs 27%, p = 0.006; housekeepers: 45 vs 29%, p = 0.07; RN: 47 vs 34%, p = 0.023). RNs received more complaints from staff concerning odor with UV-C than without (62 vs 40%, p = 0.005). EVS supervisors received more complaints about delays from RNs (70 vs 42%, p = 0.002) and bed control (58 vs 40%, p = 0.04) with the use of UV-C than without UV-C. Regardless of cleaning strategy, EVS believed that delays in the Emergency Department were the primary cause of delays in hospital room turnover, whereas RNs perceived that room disinfection was the principal source of delay. RNs felt that rooms were not cleaned consistently with either disinfectant (59% each, p = 0.90) and that rooms were not cleaner with UV-C (58 vs 61%, p = 0.65). Over one-third of RNs believed that room disinfection with any strategy frequently interfered with the timely care of patients.

Conclusion. The successful implementation of enhanced terminal room disinfection strategies must address the barrier of perceived increases in cleaning/disinfection times among both EVS and nursing.

Disclosures. **D. J. Weber**, Clorox: Consultant, Consulting fee; Johnson and Johnson: Consultant, Consulting fee; Germitec: Consultant, Consulting fee **W. Rutala**, Clorox: Consultant, Consulting fee; ASP: Consultant, Consulting fee **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

1365. Identifying Opportunities to Improve Environmental Hygiene in Multiple Healthcare Settings

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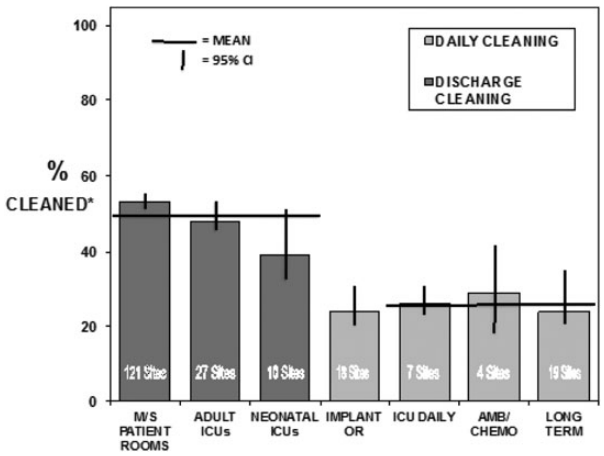
Background. Near-patient surfaces play a role in transmission of pathogens in healthcare settings. Thus, disinfection cleaning is an important infection prevention intervention. Our previous studies objectively documented opportunities to improve environmental cleaning in acute care hospitals. We used the same evaluation system to analyze cleaning practice in a range of defined healthcare venues.

Methods. Trained healthcare professionals, primarily infection preventionists and hospital epidemiologists, in 140 facilities (121 acute care hospitals and 19 long-term care facilities) covertly evaluated disinfection cleaning practice using a fluorescent targeting system (DAZO®) to objectively quantify cleaning compliance of standardized sets of near-patient surfaces that had a high risk of transmitting pathogens between patients and healthcare workers. The objects chosen were specific to the particular venue evaluated. **Results** were expressed as the percentage of surfaces marked with the fluorescent target that were cleaned (DAZO® removed).

Results. As summarized in the figure, thoroughness of discharge cleaning of 52,931 objects in 4,243 medical/surgical and ICU rooms averaged 49% (95% CI = 48.1 to 51.0). Thoroughness of daily cleaning of: 3,657 objects in 271 implantation operating rooms was 24%; 1,160 objects in 84 adult ICU rooms was 26%; 3,680 objects in both common areas and patient rooms in long-term care facilities was 24%; and 610 objects in 38 ambulatory clinic treatment areas was 20%. While potentially overestimated as a result of a Hawthorne effect, daily cleaning, which averaged 25%, was significantly less thorough than discharge cleaning (p = <.0001).



Conclusion. The thoroughness of disinfection cleaning was surprisingly similar in the 129 facilities evaluated. Covert evaluation of disinfection cleaning of both inpatient and outpatient care areas consistently revealed opportunities for practice improvement. These findings were also similar to affiliated studies in Canada and Australia and they provided an objective basis for subsequent successful process improvement projects in all sites that implemented structured programs to enhance the thoroughness of cleaning practice.

Disclosures. **P. Carling**, Ecolab: Patent License and Speaker's Bureau, Consulting fee and Licensing agreement or royalty **S. S. Huang**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product

1366. Assessment of the Overall and Multi-drug Resistant Organism (MDRO) Bioburden on Environmental Surfaces in Healthcare Facilities

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Background. There is increasing need to understand the role of high-touch environmental surfaces in transmission of MDROs. Despite the likelihood that bacteria are unevenly spread over large surface areas and transmission risk is proportionate to bioburden, previous studies sampled small areas (<100 cm^2) qualitatively. Sampling large surface areas (>1,000 cm^2) quantitatively, we sought to establish overall and MDRO bioburden levels on high-touch surfaces in various healthcare settings after routine (RC) or terminal cleaning (TC).

Methods. From 11 inpatient healthcare facilities in 4 states, surface samples were collected from high-touch sites in MDRO isolation rooms after RC or TC using a standard sampling protocol. Two composite samples were collected from each room and a third composite was collected from *C. difficile* isolation rooms only. Composite 1 included the TV remote, telephone, call button and bed rails. Composite 2 included the room door handle, IV pole and over-bed table. Composite 3 included the bathroom (door handle, flush handle and grab bars) or toileting site (portable commode/bedpan). Samples were processed, the overall bacteria and MDROs (MRSA, VRE, *A. baumannii*, *K. pneumoniae*, and *C. difficile*) were quantified, and results from RC and TC rooms were compared.

Results. A total of 360 composite samples were collected from 166 rooms (113 RC and 53 TC). The mean and range of overall bacteria and MDROs recovered is shown in the table. MDROs were recovered from 45% (74/166) of rooms; VRE was the most recovered MDRO (19%, 32/166). Higher bioburden was significantly associated with RC rooms (p < 0.0001) and composite 1 (p = 0.0003). A room bioburden level >1,281 CFU/100 cm^2 increases the risk of recovering any MDRO from the room (RR = 2.02, p < 0.0001).

Room Type	Overall Bacteria Mean CFU/100 cm^2 (Range)	MDRO Mean CFU/100 cm^2 (Range)
RC	5,780 (≤1–147,000)	480 (≤1 - 13,000)
TC	790 (≤1–7,800)	23 (≤1–59)

Conclusion. RC MDRO rooms, specifically surfaces close to the patient (composite 1), are more likely to have higher bioburden which may increase the risk of recovering an MDRO. In an effort to prevent transmission of MDROs from the environment it is important to assess an unsafe level of bioburden on surfaces and to determine the adequacy of cleaning methods.

Disclosures. **All authors:** No reported disclosures.

1367. A Prospective Longitudinal Study of Transmission of Multidrug Resistant Organisms (MDROs) between Environmental Sites and Hospitalized Patients – Interim Analysis of the *TransFER* Study

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Background. Contaminated hospital surfaces may be sources for bacterial transmission. However, the nature and efficiency of bacterial transmission between patients and surfaces in hospital rooms remain unknown. We describe the dynamics and quantity of MDRO transmission between surfaces and patients admitted into newly-cleaned hospital rooms.

Methods. We performed a prospective cohort study enrolling patients admitted to newly-disinfected hospital rooms at a tertiary care medical center and a community hospital. Samples from patients and room surfaces were cultured and analyzed to describe the level of colonization of 4 MDROs (MRSA, VRE, MDR Acinetobacter and C. difficile [Cdiff]) at scheduled intervals during hospitalization in the same room (day of enrollment, day 3, day 7, weekly thereafter, and on discharge). Rodac plates were used to sample 8 specific surfaces in patient rooms using previously-published methods. Patient specimens were collected from anterior nares, pharynx, axillae, rectum, and if available, from wounds, indwelling devices and feces.

Figure. Example Transmission of *C. difficile* (*Cdiff*) from Environmental Surfaces to Patient and to Surfaces of a New Room. Numbers in Parentheses indicate Colony-Forming Units (CFUs).

Results. Data from 40 enrolled patient-room pairs were examined in this interim analysis. At enrollment, 5 (13%) of patients were colonized and 26 (65%) rooms were

contaminated with one of the four MDROs. VRE and bathroom floors were the most commonly implicated organism and surfaces, respectively. Four (80%) patients had persistent colonization with the same organism throughout the hospitalization. By Day 3, 22 (58%) rooms had MDRO contamination. Of these, 12 (55%) rooms were newly contaminated while 10 (45%) rooms had residual surface contamination with organisms identified on enrolment (day 1). There were 4 (10%) apparent transmission events: 2 were patient-to-environment transfer events (Cdiff and VRE) and 2 were environment-to-patient transfer events (Cdiff and MRSA) (Figure).

Conclusion. Patients and surfaces in disinfected and cleaned rooms were frequently colonized with MDROs. These organisms persist in patients and on surfaces. Transmission of MDRO between patient and room surfaces occurred in 10% of hospitalizations. Molecular identification and related studies are underway. Future research should study interventions to interrupt this bi-directional transmission cycle.

Disclosures. **W. Rutala**, Clorox: Consultant, Consulting fee; ASP: Consultant, Consulting fee **D. J. Sexton**, UpToDate: Editor, Royalties; National Football League: Consultant, Consulting fee and Educational grant; Cubist: Grant Investigator, Grant recipient; Johnson and Johnson: Consultant, Consulting fee

1368. Assessment of Environmental Cleanliness in Outpatient Clinics

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Background. Environmental contamination appears to be a risk factor for acquisition of hospital-associated pathogens. Although the environment is likely a source of transmission of pathogens in settings other than acute care hospitals, few data are available on environmental contamination in non-hospital settings. This project sought to evaluate the cleanliness of high-touch surfaces in outpatient clinics.

Mean relative light units (RLU) and colony forming units (CFU) on 5 surfaces by time period

Period	Surface	Mean RLU	Mean CFU
Prior to clinic opening	Chair	835	48
	Chair Arm	710	49
	Computer Table	284	13
	Counter	75	1
	Exam Table	238	15
Noon	Chair	831	56
	Chair Arm	3127	126
	Computer Table	772	10
	Counter	255	5
	Exam Table	701	38
After clinic closing	Chair	504	59
	Chair Arm	975	66
	Computer Table	539	18
	Counter	464	3
	Exam Table	752	13

Methods. Three clinics (total of 81 patient care rooms) in a large outpatient complex adjacent to a 621-bed academic medical center participated in the project. Five patient care rooms in each clinic were evaluated during 3 time periods on a single day (prior to clinic opening, noon, and after clinic closing). Five high-touch environmental surfaces in each room were sampled using the Clean Trace ATP system (3M St. Paul, MN), which measures ATP using relative light units (RLU). Swabs were simultaneously collected for culture to determine the number of colony forming units (CFU) on each surface.

Results. A total of 208 environmental surfaces were sampled. Mean RLU and CFU for each surface and time period are shown in the table. Mean composite RLUs prior to clinic opening, at noon, and after clinic closing were 388, 1025, and 628, respectively. There was significant correlation between RLU and CFU measurements across all 3 clinics over all time periods for every environmental surface.

Conclusion. Significant environmental contamination is present on high-touch surfaces in outpatient clinics, likely due to the lack of standardized cleaning protocols in this setting. The chairs, which were not routinely cleaned, were shown to harbor large amounts of ATP and bacteria. Horizontal surfaces had low RLU values prior to clinic opening, but became contaminated throughout the day. The results of this quality improvement project highlight the need to enhance environmental cleanliness in the outpatient setting.

Disclosures. **M. E. Rupp**, 3M: Consultant and Grant Investigator, Consulting fee and Research grant

1369. Legionella(L) Risk Associated with Ice Machines (IM) in Hospitalized Patients at University of Pittsburgh Medical Center Presbyterian (UPMC-P)

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Background. L is common in many environments (soil, water (W), etc.) but only multiplies at 20°C-50°C. Therefore, L preventative measures such as Copper (C)/Silver (S) ionization are directed at warm W systems and have been in place at UPMC-P since 1984. Ion levels are monitored monthly with prescribed protocols for low levels and/or + faucets. In October 2013 a transplant patient developed respiratory failure thought to have recurrent hospital acquired pneumonia (HAP). Despite therapy the patient died. A bronchoalveolar lavage grew *L. pneumophilia (P)* not sero 1. The objective of this study was to investigate a L HAP.

Methods. All hot W sources in patient's care area (7 faucets and 4 showers – all negative) were cultured. Adequate C/S levels were confirmed and L surveillance increased. The patient had been ordered NPO with ice and had a witnessed aspiration. The IM cultured + for LP NOT serogroup 1 and a fluorescent L species. Over the next month 2 immunocompetent cases were identified. They were no identified commonalities except NPO with ice orders and witnessed aspiration. W sources and ice from patients' care areas were culture negative. Ice from 16 IMs (4 of which had W reservoir (R)) and 10 additional WRs were cultured All IMs were sanitized using CDC defined methods and in-line 0.2 μ W Filters were placed to prevent entry of L. Overall 47 clinical care IMs and 15 WRs were cultured for L.

Results. See the table.

Lm(multiple serogroup/species)	ICE (%)	WR	TOTAL
Pre	3/16 (19)	1/16 (7.1)	4/32 (16.4)
Post	2/47 (4.3)	0/1 (0)	2/47 (4.3)

1/6 IM was replaced, sanitized, filtered, and weekly cultured negative X 4. 5/6 + IMs were sanitized/filtered. 1/5 was repetitively + and required disassembly to identify issues unique to that IM. Issues identified that facilitated growth/resistance to disinfection.

- Thermal element (generator) adjacent to the WR generated temps as high as 94.8^0 F.
- Maintenance process was directed at descaling, not disinfecting
- Some IM components remained + due to lack of contact with the disinfectant
- IMs should be routinely chlorinated and descaled.
- Small pore filters may prevent introduction of L into IM.
- Routine sanitizing, filtering, and culturing of patient care IMs is likely necessary to prevent L colonization/infections in susceptible hospitalized patients.

Conclusion. L amplification can occur in IM WR at increased temperatures due to proximity of the generator.

Disclosures. **All authors:** No reported disclosures.

1370. Microbiological Safety and Environmental Efficacy of Disposable Bedside Cool-Mist Humidifiers

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Background. Bedside room humidifiers can harbor pathogens, and have been linked to nosocomial outbreaks. Our hospital policy requires humidifiers to be filled only with sterile water and discarded after 3 days. This study explores potential risks and benefits of humidifiers when adhering to the policy.

Methods. Cool Mist humidifiers (Kaz 4100) filled with sterile water were placed in an empty patient room for 5 days. Daily humidity and temperature readings were obtained from a sensor on the bed (1 meter from the humidifier, within the vapor vector). The experiment was duplicated 22 times: 15 using humidifiers and 7 control runs with no humidifier. The reservoir was sampled daily; 0.5 mL of water was inoculated onto blood agar plates (TSA with sheep blood) and incubated for 7 days at room temperature. On days 3-5, blood agar settle plates were placed at 1, 3, and 5 meters from the humidifier within the vapor vector. Plates were exposed for 1, 5, and 10 minutes at each distance. Statistical analysis was performed with SAS.

Results. We found a significant difference between humidifier and control experiments in both room humidity (38% and 25%, respectively, $p < 0.001$) and temperature (75.2°F and 73.9°F, respectively, $p = 0.003$). There were also significant differences between summer and fall/winter humidity and temperature readings ($p < 0.001$). When controlling for season, the humidifier effect on temperature disappeared, but the effect on humidity remained significant ($p = 0.006$). In multivariable analysis, a higher number of colonies grew from reservoir cultures and settle plates in summer than in fall/winter ($p = 0.002$). Contamination appeared as early as day 1, increased with experiment day ($p = 0.003$), and accelerated after day 3. Settle plate colony count diminished with increasing distance from the humidifier ($p < 0.001$). Further controlling for

temperature and humidity did not affect these results. Organisms that grew included skin flora and molds.

Conclusion. Humidifiers had a modest effect on room humidity, but became contaminated over time despite the use of sterile water. Contamination with potential pathogens spread in vapor may pose a risk to immunosuppressed patients, particularly during the summer. This risk is only partially mitigated by replacing humidifiers after three days.

Disclosures. **All authors:** No reported disclosures.

1371. Ambulatory Dialysis Unit Surface Decontamination: Roles for Enhanced Environmental Service Resources and Antimicrobial Surfaces

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Background. Hospitalization for infection in hemodialysis patients increased 43 percent between 1993 and 2011. Reducing the burden of healthcare-acquired infection pathogens on healthcare surfaces is a major infection control strategy. We developed an intervention bundle designed to reduce surface contamination on key areas within a large, urban ambulatory dialysis unit.

Methods. The intervention bundle included enhanced environmental service (ES) resources (increased staffing and implementation of a cleaning checklist for the entire unit) as well as installation of antimicrobial copper components (sinks, light switch plates and glove box holders) in one section of the unit. Pre- and post-intervention implementation, we measured contamination of dialysis stations, sinks, light switch plates, and glove box holders. All surfaces were sampled with a tryptic soy agar contact plate. Plates were incubated overnight at 37°C and colonies were counted. Contamination was reported either as colony forming units (CFU) per surface or the percentage of plates positive for contamination (% Positive). All data was reported as mean CFU or % Positive ± standard error of the mean.

Results. ES interventions significantly reduced the % Positive rate of dialysis stations relative to pre-intervention measurements (78.5 ± 2.2 and 89.3 ± 5.7, respectively; $p < 0.0236$). For copper surfaces, when compared to pre-intervention measurements, ES interventions significantly reduced surface mean CFUs on glove box holders (19.59 ± 17.04 and 3.57 ± 0.69, respectively; $p = 0.048$). Installation of copper sinks significantly reduced mean CFUs relative to pre-intervention and non-copper, ES intervention sinks (5.91 ± 1.94, 74.94 ± 24.64, 60.12 ± 14.16, respectively; $p < 0.0001$). The % Positive rate was also significantly lower on copper sinks relative to pre-intervention and ES intervention sinks (55, 100, 100, respectively; $p < 0.0001$).

Conclusion. Enhancement of ES resources lead to a reduction in the % Positive rate of dialysis stations and the total contamination on glove box holders. Installation of copper sinks lead to a dramatic reduction in both the frequency and total surface contamination.

Disclosures. **All authors:** No reported disclosures.

1372. Quantification and Bioburden of High Frequency Touch Surfaces (HFTS) in ICU Patient Rooms

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Background. Contaminated environmental surfaces serve as reservoirs of pathogens causing health care-associated infections by transient carriage on hands of healthcare personnel (HCP). We chose to quantify contact of high frequency touch surfaces (HFTS) by HCP using direct observation and assessed bioburden on these before and after direct contact.

Methods. Direct observation was conducted in a total of 10 ICU rooms (medical and surgical). Number of touches by discipline were quantified for two four hour periods per room. Quantitative environmental microbiologic samples of each HFTS were collected prior to and after disinfection and then 24 +/-2 hours after first sample. Relation between number of touches on a particular surface and bioburden were analyzed using non-parametric Spearman Rank Correlation Coefficient. Differences in touch frequency and bioburden between MICU and SICU were assessed using Kruskal-Wallace test.

Results. In the SICU, mean number of touches/shift were computer mouse/keyboard (115.6), bed rail (65.4), infusion pump (63.2), mechanical ventilator controls (41.4) and door knob (21.4). MICU touch means were: bed rail (148.2), ventilator controls (73.8), nurse server (55.4), infusion pump (45.8) and handwashing station (24.8). Mean number of touches/nursing shift were (294.6) followed by respiratory therapist (69.6), visitor (54.0), physician (28.6), and patient care assistant (23.5).

MICU had a greater total bioburden than SICU ($p = 0.0123$). Bioburden (CFU / in ^{2}) was only significantly higher at 24 hours after initial disinfection ($p < 0.0001$). Post-hoc test correcting for multiple comparisons showed that pre cleaning cardiac monitors had less bioburden than other surfaces ($p = 0.0260$). Ventilator controls had more bioburden pre and 24 hours post cleaning ($p = 0.0182$ and $p = 0.039$). The only pathogen cultured from any surface was *Enterococcus* species and the nurse server in MICU had significantly higher concentration compared to others ($p = 0.0026$).

Conclusion. Computer mouse/keyboards, bed rails and mechanical ventilators were touched most often/shift of 14 different HFTS. Level of contamination correlated with frequency of touches but only at 24hrs after initial disinfection. Targeted disinfection of HFTS is an important infection control measure.

Disclosures. **R. Olmsted**, Ethicon: Speaker's Bureau, Speaker honorarium; Premier Inc.: Consultant, Consulting fee

1373. A Multi-Disciplinary Approach to Improve Room Cleanliness across a Large Academic Medical Center Using Adenosine Triphosphate Technology

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Background. The hospital environment poses a substantial risk for transmission of pathogens. Assessing cleaning efficacy is difficult and often relies on a subjective visual check. A multidisciplinary approach is required to evaluate and improve hospital cleanliness. However, an objective, reliable quality indicator is needed as an outcome metric to assess the cleanliness of the environment. Technology is available to detect adenosine triphosphate (ATP), a substance present in organic matter, which can generate a measure of cleanliness.

Figure 1. Surface pass rates by week

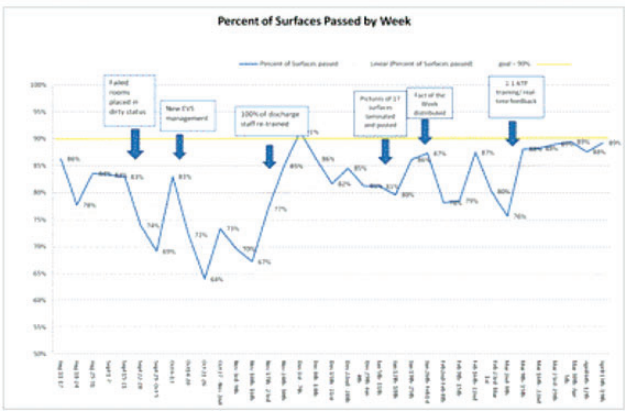
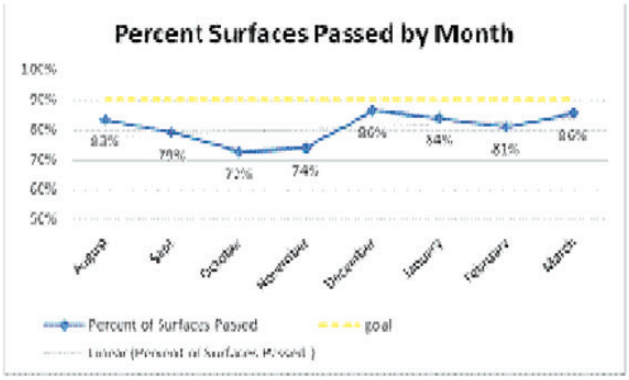


Figure 2. Surface pass rates by month

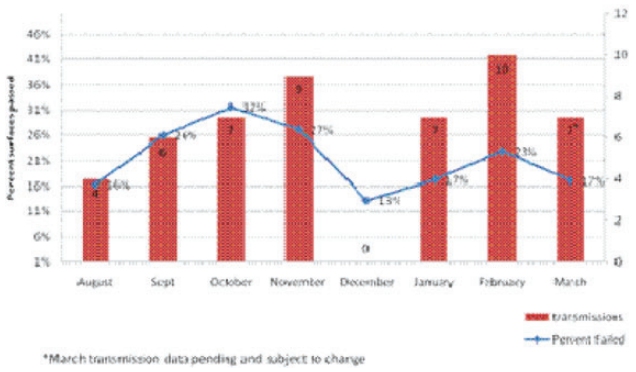


Methods. From August 2013-March 2014, we swabbed 30 discharge-cleaned rooms per week using the ATP technology in six nursing units, selected based on historical multi-drug-resistant organism (MDRO) transmission data. Up to 17

high-touch surfaces were sampled per room. The 3M Clean-Trace luminometer™ quantifies organic material on each surface. A reading below 250 RLU is considered a clean surface. If more than 30% of surfaces per room fail, recleaning is required. Metrics included: percentage of surfaces that fail, room fail rate, percent fails by surface, percent fails by unit, room fail rate, and MDRO transmission in relation to surface fails. Nursing, Infection Prevention, and Environmental Services management were responsible to test rooms. The data were used to formulate intervention strategies.

Results. Weekly data showed an improvement over time trending towards the goal of 90% (figure 1) Over eight months, the average monthly clean surface rate increased from 77% pre-intervention to 84% post-intervention (figure 2). We also saw a relationship between multi-drug resistant organism (MDRO) transmission and room cleanliness (figure 3). Intervention strategies included retraining EVS staff on appropriate cleaning practices, posting pictures of high-touch surfaces, distributing a "fact of the week," weekly data feedback, and performing real-time ATP process with the EVS staff that cleaned the room.

Figure 3. Surface fail rate in correlation with MDRO transmissions



Conclusion. The ability to assess cleaning performance with an objective, reliable metric, and analyze the data by individual touch point and staff accountability, led to improved cleanliness, reduced MDRO transmission risk, and enhanced collaboration efforts among Nursing, IP and EVS.

Disclosures. **All authors:** No reported disclosures.

1374. Environmental Cleaning at the Cornerstone of Decreasing Healthcare Acquired Infections, Including *Clostridium difficile*

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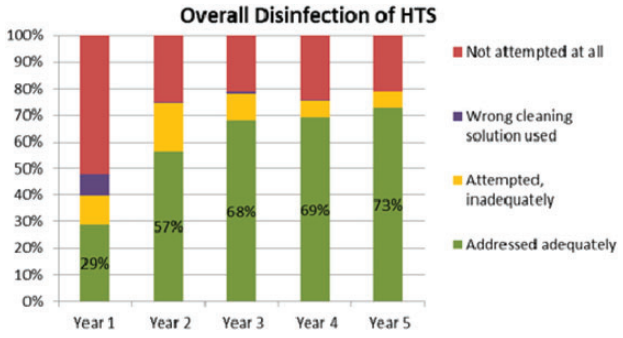
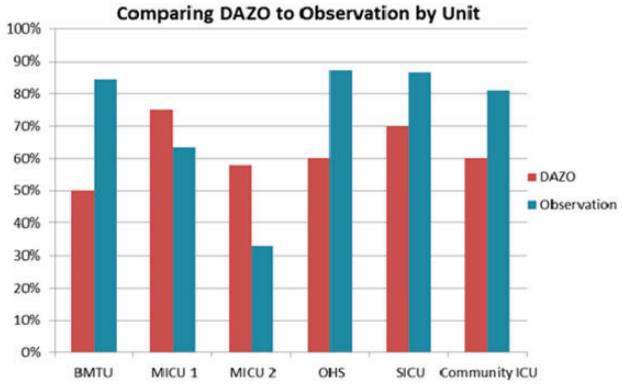
Background. Healthcare associated infections lead to > 90,000 deaths in the US. During routine patient care, the room is contaminated with microbes and it is recommended to be disinfected routinely. In the CDC guidelines for environmental infection control in health-care facilities, there is little guidance on how to monitor compliance. The objective of this study was to observe environmental services (ES) cleaning of patient rooms over multiple years, implement objective modalities for monitoring room cleaning and assess if improved cleaning could impact healthcare onset *C. difficile* infections (HO-CDI).

Methods. In this study, direct observations of ES workers were done in *real-time* comparing the cleaning process from start to finish with the ES policy on patient care units with the highest rates of HO-CDI with a focus on high touch surfaces (HTS). Cleaning of HTS was graded as adequate, attempted but inadequate, wrong solution used or not attempted at all. Observations were done at baseline, after in-service education with ES promoting manufacturers' recommendations and CDC guidelines, post-intervention with real time feedback, and after transition to a private third party ES company in the last year. During the last year fluorescent target technology via the DAZO method was used to compare to direct observations.

Results. Cleaning of 383 rooms was observed over 5 years. In year 1, 29% of HTS were cleaned adequately, 11% were attempted but inadequate, 8% had the wrong solution used and 52% were not attempted at all. After ES education in year 2, HTS cleaning rates improved to 57%, 18%, 0% and 25%, respectively. In years 3 and 4, these rates improved to 68%, 10%, 1% and 21% respectively. In year 5, observations showed consistency with 73% of HTS cleaned adequately, 6% attempted but inadequate, 0% had the wrong solution used and 21% not attempted at all. HO-CDI rates alone did not appear to be impacted for those years with well-delineated HO-CDI.





Conclusion. Real time observation is one method to monitor compliance with disinfection of HTS in patient care rooms, and sustainable improvements may be seen with ongoing ES staff education. DAZO confirmed similar results by minimizing the Hawthorne effect.

Disclosures. **All authors:** No reported disclosures.

1375. Reduction of Bacterial Air Burden During Routine Patient Care by a Novel Mobile Air Purification System (PhotoxAir)

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Background. Airborne transmission of pathogens such as *Mycobacterium tuberculosis*can result in the rapid spread of disease. This project assessed the ability of PhotoxAir, a novel mobile air purification system (MAPS) based on photocatalytic oxidation, to minimize the bacterial air burden during routine patient care in an emergency department (ED).

Methods. Fifty patients admitted to the ED underwent air sampling in their respective rooms during routine care activities. One six-stage Andersen Air Sampler each was placed at the head and foot of a patient's bed and at the exit/entrance doorway. The MAPS was positioned near the foot of the bed. All samples were collected on blood agar plates. Baseline air burden was assessed for 20 minutes without MAPS activated, followed by a wash-out phase with MAPS activated (eight total air exchanges per room), and a 20 minute air sampling with MAPS activated. Colony-forming units (CFUs) were counted and summed for each location. Significance was assessed using the signed Wilcoxon rank-sum test.

Results. A significant reduction in bacterial CFUs was observed from baseline to MAPS use. The greatest decrease was seen at the head of the bed (-7 CFUs; -54%; $p < 0.001$) followed by the foot of the bed (-4.5 CFUs; -47%; $p < 0.001$) and the exit (-3.5 CFUs; -27%; $p < 0.001$). The room total (sum across all sampling locations) also showed a significant reduction (-15 CFUs; -46%; $p < 0.001$) under MAPS use.

Conclusion. The MAPS significantly reduced the bacterial load observed under routine care in an ED setting. The foot of the bed and the exit showed smaller decreases probably affected by higher traffic/activity patterns in these areas as compared to the head of the bed. Application of this new, mobile technology promises to reduce the airborne pathogen burden, and decrease exposure risk providing a safer environment for patient care.

Disclosures. **J. Stehle Jr.**, PhotoxAir: Investigator, Research support and Salary **M. Blevins**, PhotoxAir: Investigator, Research support and Salary **J. Turner**, PhotoxAir: Investigator, Research support and Salary **N. Pajewski**, PhotoxAir: Investigator, Research support and Salary **W. Bischoff**, PhotoxAir: Investigator, Research support and Salary

1376. Contaminated surfaces in the Outpatient Clinics and Emergency Departments as a source for Healthcare associated Infections

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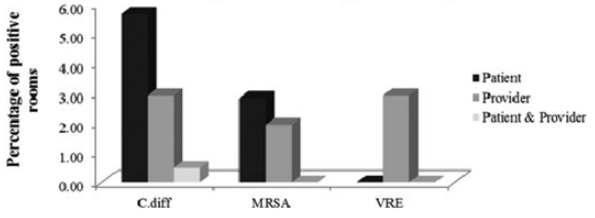
Background. Outpatient clinics and emergency departments may be underappreciated sources for transmission of healthcare-associated infections. High turnover of patients and the lack of adequate disinfection procedures allows for healthcare-associated pathogens to contaminate healthcare workers and patients.

Methods. We collected 104 outpatient and emergency department room samples from 10 hospitals. Samples were cultured from patient high touch surfaces (blood pressure cuff, exam table, and call button) and provider high-touch surfaces (work station, keyboard, and mouse) in each room. Samples were cultured for methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and *Clostridium difficile* (C.diff) contamination.

Results. Of the 10 hospitals, 5 (50%) had C.diff contamination in the outpatient setting. 6% of patient high touch surfaces were positive for C.diff, whereas 3% of provider high-touch surfaces were contaminated with C.diff. MRSA and VRE contamination was less frequent in the outpatient setting with 5% of rooms exhibiting contamination with MRSA and 3% exhibiting contamination with VRE.

Figure 1. Percentage of rooms positive



Conclusion. The outpatient setting may play an important role in the transmission and acquisition of hospital acquired pathogens. There seems to be a need to establish practice guidelines for effective disinfection of outpatient clinics and emergency departments.

Disclosures. **All authors:** No reported disclosures.

1377. Evaluating a New Paradigm for Comparing Surface Disinfection in Clinical Practice

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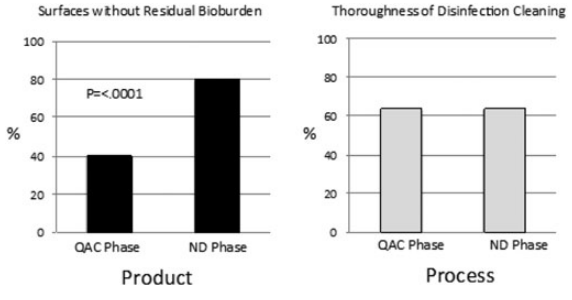
Background. Despite an increasing understanding of the importance of near patient surfaces in the transmission of healthcare associated pathogens, there remains a need to define the relative clinical effectiveness of disinfection interventions.

Methods. A unique system for quantifying bioburden reduction while monitoring the possible impact of differences in cleaning thoroughness was used to compare the clinical effectiveness of a traditional quaternary ammonium compound (QAC) and a novel parecetic acid/hydrogen peroxide disinfectant (ND) as part of terminal room cleaning. Process, the thoroughness of cleaning, was evaluated by fluorescent marker (DAZO) removal. Product, the potency of the disinfectant used, employed aerobic dip slides to assess bioburden removal.



Results. As a result of QAC cleaning, 93 of 237 (40%) of cleaned surfaces confirmed by fluorescent marker (DAZO) removal were found to have complete removal of aerobic bioburden. During the ND phase of the study, bioburden was removed from 211 of 274 (77%) of cleaned surfaces. Since there was no difference in the thoroughness of cleaning with either disinfectant (65.3% and 66.4%) the significant ($p < .0001$) difference in bioburden reduction can be attributed to better cleaning efficacy with the ND (Figure).

Conclusion. In the context of the study design, the ND was 1.93 times more effective in removing bacterial burden than the QAC ($p < .0001$). Furthermore, the study design represents a new research paradigm in which two such interventions can be compared by concomitantly and objectively analyzing both the product and process variables in a manner that can be used to clinically define the relative effectiveness of all surface disinfectants. This study design will also permit effectively defining the relative clinical efficacy of cleaning and disinfecting materials of non-touch disinfection technologies and self-disinfecting surfaces. Such studies may then begin to objectively clarify best practices for decreasing the risk of pathogen transmission from contaminated surfaces to patients through the use of various cleaning modalities and chemistries while providing guidance for more in-depth clinical studies of cost benefit issues and healthcare associated pathogen transmission prevention.

Disclosures. **P. Carling**, Ecolab: Patent License and Speaker's Bureau, Consulting fee and Licensing agreement or royalty **A. Thomasser**, Ecolab: Employee, Salary

1378. *Clostridium difficile* (CD) hospital acquired infection (HAI) Rates unaffected by switch from Bleach (B) to Hydrogen Peroxide (H2O2) and Peracetic acid (PA) Based Disinfectants – The New Smell of Clean

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Background. CD continues to plague patients who are frequently exposed to healthcare settings, remaining the 3rd mostly common HAI, reaching historically high prevalence levels. Because CD is a spore former, the microorganism is particularly resistant to disinfection. Until recent years options for sporocides have been limited to sodium hypochlorite (B) based products. Though sporicidal, B based products are caustic to the environment (i.e., furniture, mattresses, equipment, etc.) and leaves a salt precipitate. In recent years, H2O2 based products have received Environmental Protection Agency approval for use in healthcare settings. Some products are combined with PA which decreases contact time (≤ 5 minutes) by disrupting cell wall permeability. H2O2/PA use has been limited because of its vinegar odor. This study was done to determine if an H2O2/PA product was acceptable for use in healthcare and assess CD HAI rate after disinfectant change.

Period	Disinfectant	Dates	#CDI-Ais	Patient-days	CDI-AI Rate	Slope (m)	Y-Intercept (b)
1	B	1/06 – 11/12	313	562,571	5.5	-0.0001	-2.1
W	B->H2O2/PA	12/12– 7/13	28	59,712	4.7	-0.0001	-17.8
2	H2O2/PA	8/13 - 4/14	29	60,708	6.4	-0.000002	-0.7

Methods. CD HAI rates were compared over 2 periods (Ps) across the same patient care areas. P1 (B) = January 2006–November 2012. Washout (W) includes 8 months where both products were used. P2 (H2O2/PA) = August 2012–April 2014

H2O2/PA implementation:

1.CD Environmental Services (EVS) staff educated on the use of H2O2/PA.

2.All staff, including Admin. were engaged.

3.Infection Preventionists (IPs) and EVS promoted H2O2/PA products.

4.Ongoing education provided to staff on efficacy, safety, and smell, "the new smell of clean".

5.EVS, clinical staff and patient feedback was noted

Results. During P2, overall perception of less damage to the environment, odor appreciated but diffused quickly, and environment cleaner. HA CDI rates were not significantly different after switching to H2O2/PA products (OR = 0.86, CI,0.61-1.2, p = 0.43). WP CD HAI rate was similar to P1 and P2.

- IPs, EVS and Admin. were instrumental in promoting the new smell of clean.
- To date there has been no damage to furniture or equipment, there is no precipitate to remove and the patient care area appears cleaner.
- Despite the change in smell, staff were accepting of the H2O2/PA product.

Conclusion. H2O2/PA products were not associated with a significant increase in CD HAIs.

Disclosures. **All authors:** No reported disclosures.

1379. Evaluation of an Enclosed Ultraviolet Radiation Device for Disinfection of Mobile Handheld Devices

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Background. Mobile handheld devices (MHDs) are ubiquitous in healthcare settings, both for personal use and for delivery of patient care. In hospitals, MHDs are frequently contaminated with pathogenic bacteria, but seldom cleaned. Because wiping

MHDs with disinfectants can negatively affect screen quality, there is a need for new disinfection methods that are rapid and effective against a wide range of healthcare-associated pathogens.

Methods. The Sky™ 6Xi device (Daylight Medical, Inc.) is an enclosed box with a conveyer belt that delivers ultraviolet-C radiation in close proximity to MHDs (e.g., iPad™, Tablet PCs, cell phones), moving devices at a speed of 0.4" per second. We examined the efficacy of the device against methicillin-resistant *Staphylococcus aureus* (MRSA) using a modified ASTM International method. To assess "real-world" efficacy, we cultured MHDs of healthcare staff before and after use of the device.

Results. The Sky™ 6Xi device reduced recovery of MRSA by 5.10 $\log_{10}$CFU and was only modestly affected by organic load. Of 50 healthcare staff MHDs cultured, 46 (92%) had positive aerobic colony counts vs 9 (18.0%) after use of the device ($P < 0.001$); the mean aerobic count on MHDs decreased from 46.5 to 0.4 colony forming units (CFU) ($P < 0.001$) after use of the device. Of the 50 MHDs cultured before use of the device, 4 (8%), 2 (4%), and 2 (4%) were contaminated with MRSA, *C. difficile*, and Gram-negative bacilli, respectively; all were culture negative after use of the device. No adverse effects on MHD surfaces were observed after repeated exposure to the device. The device required approximately 15 seconds to disinfect a standard cell phone and 50 seconds to disinfect an iPAD™.

Conclusion. The Sky UV device is a novel technology that is effective for safe and rapid disinfection of healthcare-associated pathogens from MHDs.

Disclosures. **C. J. Donskey**, GOJO: Consultant, Consulting fee

1380. Spores on Wheels: Effectiveness of a Peroxyacetic Acid Based Cleaner Disinfectant Solution for Disinfection of Wheelchairs

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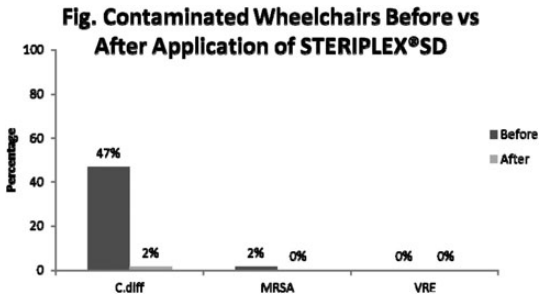
Background. Wheel chairs are high-touch surfaces that frequently become contaminated with healthcare-associated pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and *Clostridium difficile*.. Because these items are frequently shared between patients, there is a need for effective and efficient disinfection methods. STERIPLEX® SD is an EPA-registered cleaner and disinfectant with sporicidal activity for use on hard and soft surface.



Methods. We tested the hypothesis that spraying wheel chair surfaces in healthcare facilities with peroxyacetic acid disinfectant using an electrostatic sprayer would reduce bacterial burden on surfaces that are challenging to clean with other solutions. To evaluate efficacy in our facility, we treated 64 wheelchairs (95 sites) in patient rooms, escort services, and outpatient clinics with STERIPLEX® SD with sampling before and after application.

Results. On wheelchairs, application of STERIPLEX® SD resulted in reduction of C.diff (30/64; 47% vs 1/64; 2%). Wheels were more frequently contaminated with C. diff (13/31; 42%) than the body of the wheelchair (7/35; 20%). Positive body cultures were reduced from 20% to 0% and positive wheel cultures were reduced from 42% to 3% following application of STERIPLEX® SD. MRSA was recovered on 1 of 64 wheelchairs and VRE was not recovered from any wheelchairs.

Conclusion. Our results provide evidence that spraying wheelchairs with a peroxyacetic acid solution may be a simple and effective means to reduce contamination with healthcare-associated pathogens. It appears that decontamination and the potential of wheelchairs as a reservoir for healthcare-associated pathogens is under-valued and may be a significant source of contamination to patient, staff, and visitors.

Disclosures. **All authors:** No reported disclosures.

1381. Impact of OxyCide™ Use on Environmental Contamination and Infection Rates Compared To Standard Cleaning Practice

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Background. The aims of this study were to compare the standard cleaning practice to cleaning using OxyCide™, a novel, sporicidal, one-step disinfectant concentrate on environmental contamination and hospital-acquired infections (HAIs).

Methods. A cross-over study was conducted using 1 medical-surgical and 1 intensive care unit. In the intervention group, OxyCide™ was used for routine cleaning of all patient rooms. In the control group, standard cleaning was conducted using Virex II 256- quaternary ammonium compound and Dispatch for *C. difficile* rooms; and Virex II alone for other rooms. The study period was 13 months. Using moist cotton swabs, qualitative environmental cultures were collected after terminal cleaning from selected rooms of discharged patients with *A. baumannii* or *C. difficile*; and quantitative samples were collected from occupied rooms. Standard laboratory procedures were used. HAIs were tracked throughout the study period.

Results. A total of 4,105 patients were cared for on study units during the study period, accounting for 20,932 patient days. After terminal cleaning, 747 samples were collected from 69 rooms (27 *C. difficile* and 42 *A. baumannii*). There was no growth from 331 swabs collected in the control group and 2/416 swabs (0.5%) from the intervention group grew (1/270 for A. *baumannii* and 1/146 for *C. difficile*).

216 swabs were collected from high touch objects in 36 occupied patient rooms (18 in each group). 18/108 (17%) samples from the control group grew, as did 20/108 (18.5%) from the intervention group ($p = 0.85$).

There were a total of 122 unit-acquired infections, 24 device-related infections, 15 unique patients with *A. baumannii* and 25 with *C. difficile*. The rate of HAI was 6.6 in the control arm and 4.8/1,000 patient days in the intervention arm ($p = 0.09$); of device-related infection was 1.6 and 0.6/1,000 patient days, respectively ($p = 0.04$); of *A. baumannii* was 0.7 and 0.7/1,000 patient days respectively ($p = 0.98$); and of *C. difficile*, was 1.0 and 1.4/1,000 patient days, respectively ($p = 0.36$).

Conclusion. Use of OxyCide™ was associated with decreased device-related hospital infections when compared to standard cleaning with quaternary ammonium compound +/- bleach. Recovery of environmental pathogens was low in both study arms.

Disclosures. **K. Kaye**, Ecolab: Grant Investigator, Grant recipient

1382. Antimicrobial efficacy of Corning® Gorilla® Glass 3 under laboratory conditions

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Background. The use of cellular phones and tablet computers has become widespread in the clinical environment. These hand-held devices can be contaminated with microorganisms and be a potential source for transmission of pathogens between healthcare workers and patients. We assessed the antimicrobial activity of silver-impregnated Corning® Gorilla® Glass 3 (Corning Incorporation, USA) against common nosocomial pathogens. This antimicrobial glass can be installed on display panels in mobile electronic devices.

Methods. Approximately 10^4 cfu bacteria (MRSA, *Klebsiella pneumoniae*) suspended in low-level organic soiling (0.03% bovine serum albumin) was inoculated onto a control (without silver) or test (antimicrobial) glass surface (25 cm^2) and covered with a microscope glass slide. After the appropriate contact time (0.25, 30, 60 minutes and 3, 5, 24 hours) each test area was sampled with a pre-moistened cotton swab, plated on Columbia blood agar and incubated at 37°C for 24hours prior to reading. Tests were replicated six times.

Results. MRSA and *K. pneumoniae* recovered from the antimicrobial glass surfaces in the presence of low-level soiling was statistically significantly less ($p = 0.02$ and $p < 0.001$, respectively) than from control glass after 30 minutes contact time. The antimicrobial glass surface reduced MRSA contamination by 2.81$\log_{10}$ demonstrating 99.8% reductions after 3 hours contact time and to below the detection limit (2 cfu/25cm^2) within 24hours. Contamination with *K. pneumoniae* was reduced by 3.19$\log_{10}$ (99.96% reduction) within 3 hours contact-time and reduced to below the detection limit on antimicrobial glass surface after 5 hours contact time.

Conclusion. Under laboratory conditions, silver-impregnated antimicrobial glass (Corning® Gorilla® Glass) can effectively reduce MRSA and *K. pneumoniae* contamination from treated glass surfaces even under low-level soiling and without mechanical cleaning. The reduction of bacteria from items such as tablet devices will reduce the likelihood of these surfaces becoming potential reservoirs for bacterial transmission in the clinical environment.

Disclosures. **M. Muzslay**, Corning Incorporation: Investigator, Research support **S. Ali**, Corning Incorporation: Investigator, Research support **P. Wilson**, Corning Incorporation: Consultant, Research support

1383. Survey of Hospital Practices Regarding Use of Chlorhexidine Gluconate Bathing for Prevention of Healthcare-Associated Infections

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Background. Bathing of hospital inpatients with chlorhexidine gluconate (CHG) has been shown to reduce the risk of acquisition of multidrug-resistant infections

(MDROs) and development of healthcare-associated infections (HAIs). We conducted a survey to characterize the use of CHG bathing as a tool for infection prevention at a variety of hospitals.

Methods. An electronic survey was sent to all members of the Society for Healthcare Epidemiology of America Research Network in October 2013. **Results** were analyzed using basic descriptive statistics and Chi-square tests for association.

Results. Ninety-four hospitals responded to the survey (response rate, 33.8%); eighteen (20%) responding hospitals were located outside of the U.S. Seventy-six (80.9%) hospitals had implemented CHG bathing in at least one unit. The only hospital characteristic associated with implementation of CHG bathing was location in a metropolitan setting ($p < 0.01$). Hospital locations where CHG bathing was performed include some intensive care units (ICUs) (26 [34.2%]), all ICUs (40 [52.6%]), some non-ICU units (29 [38.2%]) and hospital wide (13 [17.1%]). The most frequent reasons for implementation of CHG bathing were response to evidence-based recommendations (60 [78.9%]) and higher than desired HAI rates (33 [43.4%]). The majority of hospitals (50 [67.7%]) used CHG cloths rather than CHG soap and water, and some type of monitoring for compliance with CHG bathing occurred in most hospitals (55 [72.4%]). Among the 18 hospitals where CHG bathing was not performed, the most frequent reasons included cost (7 [38.9%]) and lack of support from hospital leadership (5 [27.8%]).

Conclusion. The majority of hospitals we surveyed had implemented CHG bathing in at least one unit. Among hospitals that had implemented CHG bathing, there was substantial variability in practice, including inpatient units where CHG bathing was performed, what type of CHG product was used, and how compliance with CHG bathing was monitored. Standardized recommendations could be helpful in developing more consistent practices and persuading hospital leadership at hospitals where CHG bathing has not been implemented.

Disclosures. **All authors:** No reported disclosures.

1384. High Level Disinfection Failure in Gastrointestinal Scopes with Elevator channels – Is it time to switch to Ethylene oxide (ETO) Sterilization?

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Background. CRE infections are a challenge in health-care. Carbapenem-resistant (CR) Klebsiella pneumoniae (KP) is the species most commonly encountered in the US and resistant to most antimicrobials. Infections have been associated with high rates of morbidity and mortality. In 2012, CRKP incidence increased from 0.24 to 0.33; many patients had an Endoscopic Retrograde Cholangiopancreatography (ERCP) prior to (+) clinical culture. An investigation indicated that after high level disinfection the 5/31 (16%) ERCP scopes were positive for organisms consistent with GI flora. 1 ERCP grew both Carbapenem susceptible (CS) and CRKP, 1 Endoscope (EUS) grew Carbapenem sensitive Klebsiella Pneumoniae (CSKP). A decision to routinely disinfect scopes with an elevator channel with High level Disinfection (HLD) followed by Ethylene oxide (ETO) was made. The scope washer was changed as per scope manufacturer recommendation. The objective of this study was to determine if the new scope washer would be able to successfully achieve HLD.

Methods. A new scope washer was introduced in 2012. A maximum of 30 scopes were to undergo culture post HLD and prior to ETO. Initially targeted scopes were for patients who had undergone an ERCP and had a history of CRKP colonization/infection. The study would terminate if a positive culture was identified as this would show that the new scope washer could not consistently HLD scopes.

Results. Over 2 months 6 scopes were cultured. 4/6 grew commensals, 1 scope was negative and 1 scope grew and ESBL KP.

- To ensure adequate disinfection, ETO should be considered for use with scopes with elevator channels (ERCP/EUS) scopes will be Ethylene oxide gas sterilized (ETO) after every patient use
- Routine scope culturing should occur to ensure proper cleaning and HLD
- No additional healthcare associated infections noted since cleaning/HLD has been combined with ETO.

Date	Scope Number	Biopsy Port	Water Channel	Elevator	Patients Cultures
11/18/12	1	Viridans strep	Micrococcus		07/06/13 CR KP in Blood
11/25/12	2	No Growth	S viridians & Coag Neg Staph	Coag Neg Staph	09/01/13 CR KP in wound
11/25/12	3	S viridans & Coag Neg Staph	S viridans	No Growth	10/04/11 KP in BAL
11/27/12	4	Micrococcus	No Growth	No Growth	09/08/08 KP in Urine
11/27/12	5	S viridans & Micrococcus	S viridans		06/30/13 KP in Urine
01/07/13	6	KP(ESBL) & E. coli & E. faecium	No Growth		12/25/13 ESBL KP in Urine

Conclusion. GI pathogens can be recovered post HLD even after a switch to the manufacture recommended scope washer.

Disclosures. **All authors:** No reported disclosures.

1385. Association between Storage Interval and Contamination of Reprocessed Flexible Endoscopes in a Pediatric Gastrointestinal Procedural Unit

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Background. The maximum safe storage interval after endoscope reprocessing remains unknown. We sought to assess the association between storage interval and scope contamination to inform the need for scope reprocessing prior to patient use.

Methods. We conducted a study in two phases. First, we cultured 9 gastrointestinal (GI) endoscopes (6 gastroscopes, 2 duodenoscopes, 1 colonoscope) that had been in storage for >7 days since reprocessing. Each scope had 3 cultures: the external surface (using a sterile swab moistened with sterile saline for the suction/biopsy ports and scope handle); the insertion tube (using sterile gauze moistened with sterile saline); and the internal channels (flushed with sterile saline, then brushed with a sterile brush). Second, after reprocessing these scopes, we hung and cultured them prospectively in a similar fashion at 1, 2 and 4 week intervals without patient use. All specimens were cultured for bacteria and fungi. We defined clinically relevant contamination as >100 CFU/mL.

Results. In phase 1, the median hang time was 69 days (range, 8-555). Three of 27 cultures (11.1%) from 3/9 scopes were positive, all with nonpathogenic flora at ≤100 CFU/mL (10 CFU/mL coagulase-negative staphylococcus [CoNS] from biopsy/suction ports at 69 days, 100 CFU/mL *Micrococcus* from surface insertion tube at 69 days, 100 CFU/mL CoNS from channel flush/brush at 85 days). Median hang time was not statistically different between scopes with positive and negative cultures ($P = 0.68$). In phase 2, 4 of 69 prospective cultures (5.8%) from 3 scopes were positive, all at ≤100 CFU/mL. At 7 days, 1/27 (3.7%) was positive (90 CFU/mL CoNS from biopsy/suction ports); at 14 days, 2/27 (7.4%) were positive (100 CFU/mL CoNS from surface insertion tube and 10 CFU/mL *Candida albicans* from flush/brush); at 28 days, 1/15 (6.7%) grew 3 organisms (10 CFU/mL CoNS, 10 CFU/mL viridans streptococci, 10 CFU/mL *Neisseria subflava*) from biopsy/suction ports.

Conclusion. No endoscopes demonstrated clinically relevant contamination at hang times ranging from 7-555 days, and most scopes remained uncontaminated up to 28 days after reprocessing. Our data suggest that properly cleaned and disinfected GI endoscopes could be stored safely for at least 4 weeks, and potentially longer, before patient use.

Disclosures. **All authors:** No reported disclosures.

1386. Chlorhexidine Bathing of Hospitalized Patients: Beliefs and Practices of Nurses and Patient Care Technicians, and Potential Barriers to Compliance

Andrea Green Hines, MD[1]; Suzanne Nuss, PhD, RN[2]; Mark E. Rupp, MD[1,3]; Elizabeth Lyden, MS[4]; Kate Tyner, RN[3]; Angela Hewlett, MD, MS[1,3,4]; [1]Division of Infectious Diseases, University of Nebraska Medical Center, Omaha, NE; [2]The Nebraska Medical Center, Omaha, NE; [3]Department of Infection Control and Epidemiology, The Nebraska Medical Center, Omaha, NE; [4]College of Public Health, University of Nebraska Medical Center, Omaha, NE

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Background. Bathing hospitalized patients daily with chlorhexidine gluconate (CHG) has been adopted by many institutions as a measure to reduce healthcare-associated infections. Although nursing policy states that CHG is to be used for all inpatient bathing in our institution, compliance rates vary significantly between units. This quality improvement project sought to assess beliefs, practices and potential barriers that influence nurses and patient care technicians (PCT) and may impact compliance rates with daily CHG bathing.

Methods. An 11 question survey was distributed via e-mail to all inpatient nurses and PCTs at an academic medical center with 621 licensed beds. Paper copies of the survey were distributed to the units with poor response rates.

Results. A total of 401 surveys were returned, representing approximately 39% of the nurse and PCT work force. Eighty-eight percent of the respondents correctly identified that CHG is to be used instead of regular soap for all inpatient bathing as part of our institution's nursing policy. Patient refusal and lack of time were indicated as the major barriers to daily bathing of patients (74% and 62% of respondents, respectively). A larger proportion of PCTs indicated that CHG bathing was very/extremely important to the care and outcomes of their patients compared to nurses (73.1% vs 60.7%, p= .0493), and that CHG bathing had high/essential priority (78.7% vs 49.5%, p = <.0001). A larger proportion of PCTs identified patient reluctance/refusal as a barrier to daily bathing compared to nurses (87.5% vs 70.3%, p = .0007), and lack of supply availability as a barrier to daily bathing (14.6% vs 5.6%, p = .0076). A larger proportion of nurses identified lack of patient care support as a barrier to daily bathing compared to PCTs (47% vs 31.3%, p = .0064).

Conclusion. CHG bathing compliance rates are likely impacted by multiple factors, including the beliefs and attitudes of the nursing staff, as well as perceived or true barriers. Recognition of these issues is of utmost importance in order to influence practice. Results from this project will be utilized to create targeted educational interventions in an attempt to increase compliance with CHG bathing.

Disclosures. **M. E. Rupp**, Mölnlycke Health Care: Research Contractor, Research support

1387. Effectiveness of a Sporicidal Disinfectant Spray for Disinfection of Hospital Privacy Curtains

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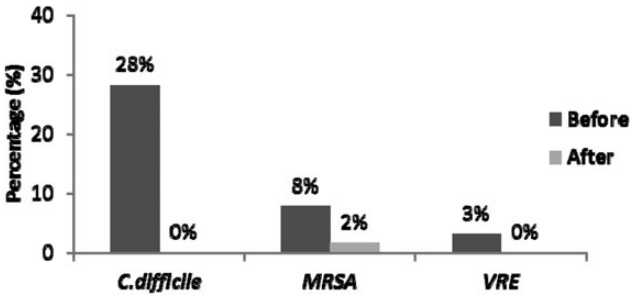
Background. Hospital privacy curtains are high-touch surfaces that frequently become contaminated with healthcare-associated pathogens, including methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), and *Clostridium difficile*. There is a need for effective and efficient methods to disinfect privacy curtains. We hypothesized that STERIPLEX® SD, an EPA-registered cleaner and disinfectant with sporicidal activity, would be effective for disinfection of curtains when applied via electrostatic sprayer as a touchless spray product.

Fig. Contamination of Privacy Curtains Before versus After Application of STERIPLEX® SD



Methods. In the laboratory, we examined the efficacy of STERIPLEX electrostatic spray vs a 1 to 10 dilution of household bleach for disinfection of *C. difficile* spores on 3-cm circular sections of privacy curtain with an exposure time of 3-minutes. In hospital rooms, cultures for MRSA, VRE, and *C. difficile* were collected from 1 x 2 foot sections of privacy curtains before vs after electrostatic spraying with STERIPLEX.

Results. In laboratory testing, STERIPLEX was as effective as bleach for disinfection of *C. difficile* spores on sections of curtain in the absence of organic load (>4 $\log_{10}$-colony-forming unit [CFU] reduction), and more effective than bleach in the presence of organic load (>4 vs 2 $\log_{10}$CFU reduction; $P < 0.01$). Of 64 curtains cultured, 19 (30%) were contaminated with one or more pathogens at baseline vs 1 (2%) after application of STERIPLEX ($P < 0.001$). The figure shows contamination frequency by pathogen. Repeated applications of STERIPLEX did not result in visible damage to curtains.

Conclusion. Hospital privacy curtains were frequently contaminated with healthcare-associated pathogens, including *C. difficile* spores. Spraying curtains with STERIPLEX could provide an effective and efficient means to disinfect privacy curtains.

Disclosures. **All authors:** No reported disclosures.

1388. Eradication of Medically Important Multidrug Resistant Bacteria and Fungi Using PurpleSun Inc. Multivector UV Technology

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Background. Hospital associated infections are important causes of morbidity and mortality that cost the nation billions of dollars per year. Although major advances in infection control practice have reduced the frequency of hospital-associated infections, thousands of lives continue to be lost. New strategies and technologies are clearly needed in order to reduce the incidence of these infections. We tested the modular Ultraviolet-C light (UVC) disinfection unit from PurpleSun Inc. The unit can be used in wide areas, as well as configured for disinfecting critical objects such as patient beds, operating tables, and med-carts. The modularity allows for deployment anywhere at anytime, without the inconvenience of leaving the immediate patient room or healthcare work environment.

Methods. Three isolates of each following resistant bacterial pathogens and pathogenic fungi were used in the study: methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus faecium* (VRE), ESBL *Escherichia coli* (EC), carbapenemase-resistant *Klebsiella pneumoniae* (KPC), multidrug-resistant *Pseudomonas aeruginosa* (PA), *Acinetobacter baumannii* (AB), *Clostridium difficile* (CD), *Candida albicans* (CA), *C. glabrata* (CG), *C. parapsilosis* (CP), *C. krusei* (CK), *Aspergillus fumigatus* (AF), *Fusarium solani* (FS), and *Scedosporium apiospermum* (SA). Plates containing two different sizes of inoculum 1-5 ´ 10^3-10^4 or 1-5 ´ 10^1-10^2were exposed to UV energy at different times (s) and locations in the UV field, according to the design of the study.

Results. Full clearance of the organism from the plates was achieved at 15 s of exposer for MRSA and PA. Clearance of VRE, EC, CG, CP, CK, FS, and SA was achieved after 30 s of exposure. KPC, AB, CA, and CD demonstrated no growth after 60 s of exposure to the UVC. The longest time, 120 s, was required to clear AF. The rate of clearance of organisms from the plates didn't depend on inoculum size.

Conclusion. The study demonstrated that UVC disinfection unit eradicates tested resistant bacteria and pathogenic fungi effectively and rapidly. Inoculum size did not affect rate of kill of tested organisms. This study provides foundation for the future testing of the UVC disinfection unit in the clinical environment.

Disclosures. **All authors:** No reported disclosures.

1389. Molecular Characterization of Environmental *Escherichia coli* Isolates from Public Restrooms in the Minneapolis-St. Paul Area

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Background. Extraintestinal pathogenic *E. coli* (ExPEC) is a major human pathogen. Clarification of the modes of transmission of ExPEC within the population is a public health priority.

Methods. We previously reported our recovery of 26 *E. coli* isolates from 1120 total environmental samples, as collected from 56 diverse public restrooms in the Minneapolis-St. Paul area (IDWeek 2013, abstract #39914). Here, PCR, DNA sequencing, and pulsed-field gel electrophoresis (PFGE) were used to further characterize these isolates as to major *E. coli* phylogenetic group, virulence gene (VG) profile, ExPEC status (presence of ≥ 2 of 5 key VGs), sequence type (ST), and pulsotype.

Results. Overall, the 26 *E. coli* isolates from public restrooms were distributed fairly evenly by phylogenetic group, i.e., B2 (27%), D (27%), A (23%), and B1 (23%). Nine isolates (35%) qualified as ExPEC. Compared with the 17 non-ExPEC isolates, the 9 ExPEC isolates were more commonly from group B2 (56%, vs 12%: P = .03), had a higher prevalence of 13 VGs other than those used to define ExPEC status (i.e., *iha, sat, cdtB, fyuA, iroN, ireA, traT, iss,* ibeA, *ompT,* usp, *malX*, and H7 *fliC),* and had much higher VG scores (median, 10 [range 6-13] vs 2 [range 0-8]: P < .001). Two isolates represented the classic ExPEC lineages ST95 (group B2; O1/O2:K1:H7) and ST69 (group D; "clonal group A"). All PFGE profiles were unique (≤ 80% similar) except for two pairs of indistinguishable profiles, within each of which the paired isolates were from the same or adjacent (mens vs womens) restrooms. The ST95 strain's PFGE profile closely matched those of multiple ST95 clinical isolates in a large private PFGE database.

Conclusion. Public restrooms are contaminated sporadically with ExPEC, some of which exhibit extensive VG profiles, represent classic human-associated STs, and by PFGE closely resemble known human pathogens. Such public restroom-source ExPEC, which likely reflect human fecal contamination, could contribute to ExPEC transmission within the population.

Disclosures. **All authors:** No reported disclosures.

1390. Effectiveness of a Hydrogen Peroxide Cleaner Disinfectant Spray for Disinfection of Soft Surfaces in Hospitals

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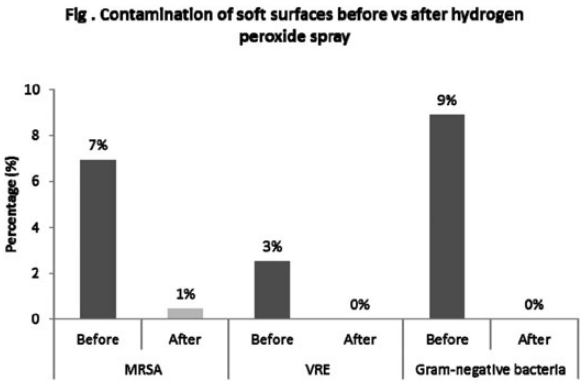
Background. Soft surfaces in hospitals frequently become contaminated with healthcare-associated pathogens, but are not amenable to cleaning and disinfection with many products commonly used on hard surfaces. Clorox Healthcare Hydrogen Peroxide Cleaner Disinfectant containing 1.4% hydrogen peroxide is Environmental Protection Agency-registered for disinfection of hard and soft surfaces and is safe to apply as a spray.

Methods: We tested the effectiveness of the hydrogen peroxide applied as a spray with no mechanical wiping for disinfection of soft surfaces. In the laboratory, we assessed killing of vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) on vertical polyester carriers. In two hospitals, we evaluated the hydrogen peroxide spray for disinfection of 300 soft surface sites in patient rooms, physical therapy areas, and outpatient clinics.

Results. On polyester carriers, the hydrogen peroxide spray resulted in a ≥6 $\log_{10}$ colony-forming unit (CFU) reduction in VRE and MRSA with a 1 minute contact time; effectiveness was not significantly reduced by the presence of organic load. On soft surfaces in patient care areas, the hydrogen peroxide spray significantly reduced total aerobic and facultative colony counts (mean CFU recovered, 276 before vs 0.6 after application; $P = .0001$). Recovery of MRSA, VRE, and gram-negative bacilli was common from soft surfaces and was reduced or eliminated by the spray.



Conclusion. A hydrogen peroxide cleaner disinfectant was effective for disinfection of soft surfaces when applied as a spray with no mechanical wiping. Spray application of this solution could provide an efficient and effective means to disinfect soft surfaces in healthcare settings.

Disclosures. **All authors:** No reported disclosures.

1391. Policies for prevention of influenza transmission in health care facilities in Japan

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Background. Seasonal influenza is prevalent during the winter months in Japan, but policies for prevention of influenza transmission in health care facilities are unclear.

Methods. An observational study was performed using a questionnaire mailed to 3,597 acute care facilities (ACFs) and 146 long-term care facilities (LTCFs) in Japan during September and October 2013. Information was collected about influenza vaccination policies for health care personnel (HCP), prophylactic administration policies for anti-influenza drugs, sick-leave policies for HCP who present with influenza-like illness, and policies regarding outbreaks.

Results. A total of 841 forms (788 ACFs and 53 LTCFs) were returned. Almost all facilities administered influenza vaccine to HCP (99% of ACFs and 98% of LTCFs). Up to 80% of ACFs and 68% of LTCFs administered prophylactic anti-influenza drugs to patients, depending on the situation. Fifty-two percent of ACFs and 58% of LTCFs did not administer prophylactic anti-influenza drugs to HCP; however, the remaining facilities administered the drugs to HCP depending on the situation. Only 78% of ACFs and 74% of LTCFs had a sick-leave policy for HCP who had influenza-like illness. HCP could take sick leave in 87% of ACFs and 83% of LTCFs. Forty percent of ACFs and 72% of LTCFs answered that HCP could take sick leaves regardless of profession, whereas 56% of ACFs and 28% of LTCFs answered that HCP in only some types of employment could take sick leaves. Thirty-three percent of ACFs and 40% of LTCFs had criteria for notification of influenza outbreaks to the public health institute and 64% of ACFs and 51% of LTCFs answered that they had no criteria for notification. Only 10% of ACFs and 15% of LTCFs had criteria for requesting infection control support against influenza outbreaks, whereas 87% of ACFs and 77% of LTCFs had no such criteria.

Conclusion. This study is the first systemic review of influenza prevention policies in ACFs and LTCFs in Japan. The results identified gaps in influenza prevention policies among healthcare facilities in Japan. Re-evaluation of seasonal influenza prevention policies, particularly in prophylactic anti-influenza drug administration and sick leaves in Japan on a consensus basis, is imperative to promote HCP and patient safety.

Disclosures. **All authors:** No reported disclosures.

1392. Differences in Perceived Influenza Risk in a University Student Population

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Background. The CDC recommends all healthy adults receive seasonal influenza vaccine. University students belong to a demographic with lower vaccination rates despite extensive sharing of spaces known to increase transmission of airborne disease.

Methods. Starting September 2013, we recruited 741 undergraduates (35% men, 65% women) at the University of Wisconsin-Madison to use our smartphone app (*OutSmart Flu*) to report symptoms of influenza-like illness. As part of this initiative, 566 (76.4%) users completed a baseline survey that asked about influenza knowledge, perceived susceptibility and severity of influenza, and attitudes towards hand hygiene and vaccination. Using a Health Belief Model framework, we examined these influenza risk perceptions, which are predictors of prevention practices such as vaccination and hand washing.

Results. Men and women had different influenza risk perceptions. Men were more likely than women to report not feeling at risk for influenza [OR = 1.86, p= 0.02]. In the context of an influenza illness, as compared to women, men were more likely to believe their symptoms would not to be serious [OR = 1.65, p = 0.04], that they would not need to seek medical care [OR = 1.89, p = 0.02], and believe symptoms would last less than a week [OR = 2.13, p < 0.001]. Further, men were less likely than women to believe hand washing would protect against influenza [OR = 3.53, p = 0.024], and more likely to find it difficult to wash their hands more often [OR = 3.15, p = 0.003]. We asked students to rate the priority of hand washing in each of 10 specific situations; women were more likely than men to prioritize hand washing in every case [all p < 0.05]. All students incorrectly identified 11 or less seconds as a sufficient duration of proper hand washing (the CDC recommends 20 seconds). Men and women did not differ in beliefs regarding vaccine efficacy or ease of vaccine seeking. Overall, 65.0% of students surveyed reported receipt of the previous year's seasonal flu vaccine (2012-13), and 74.5% of students believe that they have previously had the flu.

Conclusion. Male students may have elevated risk for influenza because their risk perceptions may lead to lower hand hygiene and vaccine uptake as compared to women. It may be important for flu prevention messaging to university students be gender-specific.

Disclosures. **All authors:** No reported disclosures.

1393. Utilizing Automated Microscopy Analysis to Detect Heteroresistant Subpopulations among *P. aeruginosa* susceptible To Ciprofloxacin

Connie Price, MD[1,2]; Steven Metzger[3]; Alena Shamsheyeva[3]; Ben Turng[3]; David Howson[3]; [1]University of Colorado-Denver, Denver, CO; [2]Infectious Diseases, Denver Health Medical Center, Denver, CO; [3]Accelerate Diagnostics Inc., Tucson, AZ

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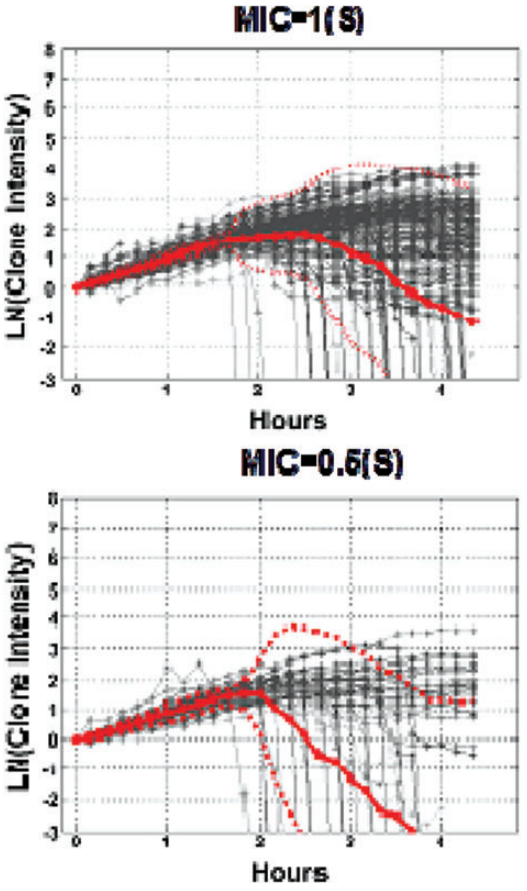
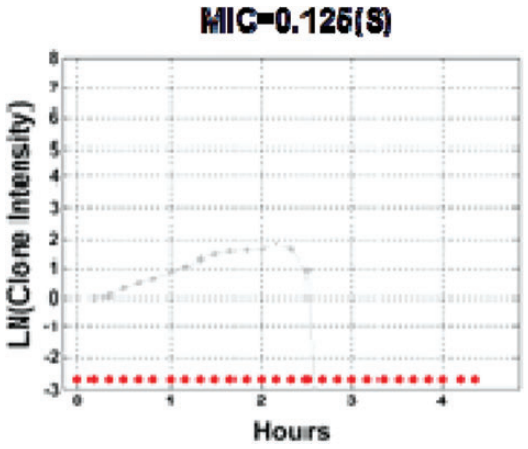
Background. Heteroresistance is defined as resistance to certain antibiotics expressed by a subset of a microbial population that is generally considered to be susceptible by traditional in-vitro susceptibility testing. Various factors may subsequently lead to the proliferation of the resistant sub-population and the emergence of a fully resistant microbial strain. Detecting heteroresistance is challenging with standard culture based methodologies. Here we have utilized Multiplexed Automated Digital Microscopy (MADM) to demonstrate heteroresistant growth of ciprofloxacin-susceptible *Pseudomonas aeruginosa* in the presence of 2 µg/mL ciprofloxacin.





Methods. A total of 35 clinical *P. aeruginosa* isolates with MIC < 2 by to frozen broth micro-dilution (BMD) testing per CLSI standards were evaluated in this study. A 0.5 McFarland aliquot of each isolate was diluted 200-fold then introduced into independent flowcells of a disposable multichannel cassette. Electrokineticconcentration immobilized cells on the transparent lower surface of each flowcell channel (5 minutes). Immobilized cells were challenged with a single concentration of ciprofloxacin (2 µg/mL) prepared in cation-adjusted Mueller Hinton broth with 0.85% agar. Automated microscopy with image analysis software scanned and analyzed growth rates from changes in the mass of each progenitor cell as it grew into a clone of daughter cells (4.5 hours). A growth control was also performed. A plot of clone intensity vs time was constructed for each MIC result defined by BMD.

Results. A time-lapse plot of individual growing clones of ciprofloxacin-susceptible *P. aeruginosa* exhibited a surprising degree of growth rate dispersion at MIC ≥0.5, with a large percentage of those clones demonstrating continued growth after 4 hours in the presence of 2 µg/mL ciprofloxacin (figure).

Conclusion. MADM was able to demonstrate heteroresistant growth of susceptible *P. aeruginosa* in the presence of 2 µg/mL ciprofloxacin. Conventional susceptibility testing does not adequately characterize minority clone expression. Further studies are required to evaluate the clinical implications of heteroresistance in an era in which rates of antimicrobial resistance are increasing alarmingly worldwide.

Disclosures. **C. Price**, Accelerate Diagnostics, Inc.: Collaborator, Grant Investigator and Scientific Advisor, Research support **S. Metzger**, Accelerate Diagnostics, Inc.: Employee, Salary **A. Shamsheyeva**, Accelerate Diagnostics, Inc.: Employee, Salary **B. Turng**, Accelerate Diagnostics, Inc.: Employee, Salary **D. Howson**, Accelerate Diagnostics, Inc.: Consultant, Consulting fee

1394. Validation of Rosco Diagnostica Diffusion Discs for Identification of Carbapenem Resistance Mechanisms in a Clinical Laboratory

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Background. There is increasing need for clinical laboratories to reliably detect and differentiate carbapenem resistance mechanisms. We evaluated the performance of two methods for the detection of Klebsiella pneumoniae carbapenemase (KPC): the Rosco KPC/Metallo-beta-lactamase and OXA-48 Confirm Kit, a disc diffusion method for in vitro identification of bacteria producing carbapenemases and the modified Hodge test.

Methods. Bacterial test strains were selected from previously identified beta-lactam and carbapenem resistant clinical isolates, including KPC producing strains confirmed by blaKPC PCR . Carbapenemase detection was performed with Rosco discs using 0.5 McFarland suspension of each isolate on Mueller Hinton agar. Modified Hodge test was performed using 10ug meropenem discs. Plates were incubated overnight at 35°C in ambient air and read independently by two blinded investigators When discrepancies in interpretation occurred, the tests were repeated by a third blinded investigator. Test characteristics of the two methods were calculated using PCR as the reference standard.

Results. Fifty-two bacterial strains (20 KPC positive and 32 KPC negative) were tested. Sensitivity of the Rosco discs and modified Hodge test for identification of KPC was 95%. Specificity of the Rosco discs (positive synergy test with boronic acid), using the manufacturer's cutoff of ≥4 mm increase in the zone size was 87.5% for KPC. By increasing the cutoff to ≥5 mm, the specificity of the Rosco kit increased to 93.8% without any decrease in sensitivity. Hodge test specificity for KPC was 71.9%; positive results were also observed for 2 ampC, 1 extended-spectrum beta-lactamase, 3 metallo-beta-lactamase, and 2 OXA-48-like producing strains.

Conclusion. The Rosco KPC/Metallo-beta-lactamase and OXA-48 Confirm Kit had equivalent sensitivity and superior specificity for identification of KPC compared to the Hodge test. We propose a modification of interpretation of test results to further improve specificity. An added advantage of the Rosco kit is its ability to differentiate between classes of carbapenem resistance mechanisms.

Disclosures. **K. Singh**, Quidel Corporation: Scientific Advisor, Consulting fee

1395. Reporting of Unit-Specific, Culture Site-Specific Antimicrobial Susceptibility for Gram-Negative Bacteria: Identification of Significant Differences in Susceptibility, Intervention to Guide Empiric Therapy and Impact on Antimicrobial Consumption

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Background. Previous studies have described variances in antimicrobial susceptibility between patient care areas within the same institution. CLSI suggests consideration of segregating antibiogram results, including by patient location, specimen type, or clinical condition. However, the clinical impact of reporting antimicrobial susceptibility by combining unit and collection site-specific data is not well described. Our previous work using this novel antibiogram demonstrated significant differences in susceptibility results when combining unit and culture site specific data. Based on these data, we recommended cefepime (as good as a carbapenem) for ICU sepsis. We analyzed impact of this recommendation on antimicrobial consumption, and subsequent trends of selected gram-negative resistance patterns within high antimicrobial pressure units to aggregated hospital data.

Methods. All clinical isolates from January 2010 - December 2013 of gram negative organisms that were obtained from sterile site inpatient cultures at a large academic medical center were analyzed. Sterile sites included blood or lower respiratory tract. Differences between units for site-specific data were compared using Chi-square or Fisher's exact test. We analyzed trends in susceptibility and also antimicrobial consumption per 1,000 patient days before and after our recommendation (guiding clinicians to use cefepime as a carbapenem sparing agent given similar susceptibilities).

Results. Susceptibility results were statistically different between the hospital-wide results and ICU-specific, site-specific antibiogram results for all comparisons involving our 3 most commonly used b-lactams for all four years analyzed. Statistical difference was also observed when comparing specific ICUs to each other, and to aggregate results. Although intial cefepime use did increase after our recommendation, utilization rebounded to baseline.

Conclusion. Reporting susceptibility by both unit- and collection site-specific data allows for increased insight into antimicrobial resistance. This method may be useful for therapeutic decisions for empiric therapy and increased knowledge of resistance patterns within specific patient care areas but dissemination of data must be sustained to impact prescribing practices.

Disclosures. **All authors:** No reported disclosures.

1396. In Vitro Susceptibility of Common Urinary Tract Pathogens to Fosfomycin

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Background. Urinary tract infections (UTI) are common in both outpatient and inpatient settings. Urinary pathogens are increasingly resistant to many commonly used antimicrobial agents. Fosfomycin is an approved agent for UTI, however, there are few recent large-scale susceptibility surveys. Here we report a prospective survey of in vitro susceptibility of urinary isolates to fosfomycin at a tertiary care institution.

Methods. Bacterial strains isolated from urine from September – December, 2013 were collected from the clinical laboratory at the Jackson VA Medical Center. Isolates were tested using Vitek ® 2 system and specifically with fosfomycin using E test according to CLSI protocol. MICs were interpreted according to CLSI breakpoints where such standards are published, otherwise, MICs are reported in mg/mL.

Results. A total of 198 unique isolates were included: Enterobacteriaceae - 132, *Pseudomonas aeruginosa - 22*, *Enterococcus* spp. - 22, *Acinetobacter baumanii* - 3, *Stenotrophomonas maltophila - 1*, *Staphylococcus* spp. – 9, ESBL - 9. CLSI breakpoints for fosfomycin are established only for *E. coli* and *E. faecalis*. For these, 98% of *E. coli* and 94% of *E. faecalis* isolates were susceptible. For ESBL- producers eight were *E.coli* and one was *Klebsiella pneumonia*. Only one ESBL *E. coli* was resistant to fosfomycin. MIC_{50} and MIC_{90} for Enterobacteriaceae isolates were 4 and 96 respectively. MIC_{50} and MIC_{90} for *P. aeruginosa* isolates were 128 and >1024 respectively. Interestingly, of eight unique isolates of *Morganella morganii*, all demonstrated resistance to fosfomycin, with MICs >1024. Glucose non-fermentative organisms in this study (*Acinetobacter, Stenotrophomonas*) had MICs at or above 96 mg/mL.

Conclusion. Fosfomycin is an effective yet under-utilized treatment for UTIs caused by Enterobacteriaceae, including ESBL-producers. An exception to this is *M. morganii*, which appears to be intrinsically resistant to this agent. Further large surveys are needed to confirm this observation. Fosfomycin appears to be highly active against the two most common *Enterococcus* species found in UTIs in humans. The activity of fosfomycin against *Pseudomonas* is not predictable and use of fosfomycin to treat UTIs with this pathogen should be guided by in vitro testing.

Disclosures. **All authors:** No reported disclosures.

1397. Characterization of Carbapenem Resistant Gram Negative Bacilli Isolated in a Tertiary Care Hospital: Epidemiology and Treatment Outcome

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Background. To describe the epidemiology of carbapenem resistant Gram negative bacilli isolates and clinical outcome associated with these infections at a tertiary care centre in Mumbai.

Methods. Carbapenem resistant isolates were collected from January 2013 to April 2013. Identification and antimicrobial susceptibility testing were performed using Vitek 2 analyser (Biomerieux Ltd.). Carbapenemase production was confirmed by Modified Hodge test and EDTA-disk synergy test was used to screen MBL production. PCR was performed on certain isolates for molecular identification. Clinical and microbiological outcomes were evaluated.

Results. 100 clinically significant isolates of carbapenem resistant Gram negative bacilli identified were: *Acinetobacer spp.* (52), E*nterobacteriaceae spp.* (33), and *Pseudomonas aeruginosa* (15). Source of isolate: Blood (42), tracheal aspirate (31), tissue/wound/drainage (19), and urine (8). Colistin had maximum in vitro activity, with 98% against *Acinetobacter*, 97% against *Enterobacteriaceae* and 100% activity against *Pseudomonas aeruginosa*. Positivity of Modified Hodge's test was 93% and that of EDTA-disk synergy test was 64%. Previous exposure to antibiotic was seen in 97% of patients [BL/BLI (75%) and Carbapenem (45%)]. In 30 out of 42 patients; source of bacteremia was associated with central line venous catheter. MBL production was detected in 94.1% isolates and 64.7% were positive for AmpC β-lactamase production. All 15 isolates carried $bla_{\text{OXA-23}}$ and bla_{VIM}, of these 3 also carried bla_{NDM}gene. Successful treatment outcomes were seen in 5 out of 6 patients with bacteremia in colistin monotherapy and 100% (12 patients) with colistin-carbapenem combination therapy. Colistin-non carbapenem combination showed improved clinical response compared to colistin-carbapenem combination against *Acinetobacter* isolates carrying $bla_{\text{OXA-23}}$ and bla_{VIM}.

Conclusion. Increasing prevalence of carbapenem resistance in *Enterobacteriaceae* is a worrisome trend. Treatment options are compromised, limited to colistin which has its own limitation. Stringent protocols such as antibiotic policies and resistance surveillance programs are mandatory to curb these bacteria.

Disclosures. **All authors:** No reported disclosures.

1398. Comparative Effectiveness of the Three Most Popular Automated Identification and Susceptibility Platforms for Testing Multidrug-resistant and Carbapenemase-producing Organisms

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Background. Although several publications have compared the performance of the Vitek-2 (Biomerieux), Phoenix (Becton Dickinson), and the Microscan Walkaway (Siemens), most included a smaller number of number of drug-organism combinations, and none reported in their methodology a true tri-partite (same day/same plate) comparison. Such a comparison allows simultaneous inoculation from one culture to minimize operator and culture growth biases.

Methods. The Multidrug-resistant organism Repository and Surveillance Network (MRSN) circumvented these biases and conducted the first reported tri-partite comparison study. Analysis included >20,000 drug-organism combinations of *Acinetobacter baumannii, Klebsiella pneumoniae*, *Pseudomonas aeruginosa, Escherichia coli,* and methicillin-resistant *Staphylococcus aureus* from 2003-2013**.**

Results. We found all machines performed to the manufacturers' performance standards. However, the Phoenix produced the least number of total susceptibility errors, and the Vitek-2 was the most reliable source for organism identification. Furthermore, susceptibility error rates were dependent on the drug-organism combination, with the most errors occurring with *E. coli* and *K. pneumoniae*and select carbapenems or cephalosporins, particularly cefepime. Microscan had the greatest number of susceptibility errors for testing MRSA.

Conclusion. The Phoenix offers the most reliable antibiotic susceptibility testing results, while the Vitek-2 correctly identifies the organism more often than the other machines. The cost associated with sample processing is slightly higher on the Phoenix platform relative to the Vitek-2. Microscan costs are approximately half of the other two platforms. In addition to being the first same day/same plate comparison, this comparison also includes the largest number of antibiotic-organism combinations.

Disclosures. **All authors:** No reported disclosures.

1399. Laboratory Characterization and Epidemiology of Carbapenem-Resistant Enterobacteriaceae (CRE) in Hennepin and Ramsey Counties, Minnesota, 2012-2013

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Background. Infections caused by CRE are a serious public health threat due to limited treatment options and increased morbidity and mortality. Detecting the presence of specific carbapenemases helps describe trends, inform infection prevention and control strategies, and define CRE test practices for clinical and public health laboratories.

Methods. CRE surveillance is conducted in Hennepin and Ramsey Counties; cases are defined as *E. coli*, *Enterobacter spp., and Klebsiella spp.* isolates from sterile sites or urine that are nonsusceptible to a carbapenem (excluding ertapenem) and resistant to all tested 3rd generation cephalosporins. CRE isolates were submitted to MDH during 2012-2013 and characterized by modified Hodge test (MHT), Carba NP test (CNPT), and polymerase chain reaction for KPC, NDM, VIM, IMP, and OXA-48 carbapenamases and SHV, TEM, and CTX-M extended-spectrum beta-lactamases (ESBLs).

Results. 73 CRE cases were identified; 63 isolates were submitted and characterized in this analysis. Species represented were *E. coli* (9), *E. cloacae* (14), *E. aerogenes* (26), and *K. pneumoniae* (14). Urine (59) was the most common source followed by blood (2) and other sterile sites (2). 34 (54%) isolates were cultured outside of the acute care setting. 21 (33%) isolates were KPC positive; none were NDM, VIM, IMP, or OXA-48 positive. 19 (90%) KPC-CRE isolates were also positive for ESBL genes; 17 were positive for both SHV and TEM. 11 (26%) KPC-negative CRE carried ESBL genes; 8 were positive for CTX-M. A single *E. cloacae* isolate was both CNPT and MHT positive, but negative for carbapenemase genes tested. All KPC-positive isolates were positive for both CNPT and MHT. Another 6 *Enterobacter spp.* were weak-to-strongly MHT positive, CNPT negative, and carbapenemase gene negative.

Conclusion. KPC was the only carbapenemase identified among MN isolates, occurring in one-third of CRE submitted. Notably, KPC-positive isolates were typically accompanied by ESBL genes. We found the CNPT to be a useful method for clinical and public health laboratories to detect carbapenemase production, and more accurate than the MHT due to exclusion of non-carbapenemase CRE phenotypes prevalent in *Enterobacter spp.* The CNPT also has the potential to detect novel carbapenemases.

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1400. Clinical and Microbiological Analysis of *Staphylococcus lugdunensis* isolates at UCLA

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Background. Staphylococcus lugdunensis (SLUG) can cause serious infection. SLUG is more often penicillin susceptible (PS) than other coagulase negative staphylococci. The Sanford Guide suggests penicillin as a treatment option for β-lactamase negative SLUG infection. This study evaluated antimicrobial susceptibility test (AST) results for SLUG isolated from 2008-2014. Retrospective review of clinical features and treatment decisions for 31 penicillin-susceptible (PS) and 31 penicillin- resistant (PR) SLUG was also performed.

Methods. AST was performed by Clinical and Laboratory Standards Institute broth microdilution and induced cefinase β-lactamase tests. Clinical features of 62 patients with cultures positive for SLUG were documented through retrospective chart review.

Results. Among 574 SLUG isolates, the percentages susceptible were: 55% for penicillin, 94% for oxacillin, 99% for trimethoprim-sulfamethoxazole (T/S) and 100% for vancomycin. Chart reviews for 62 patients revealed 22 had bacteremia, 1 osteomyelitis, 36 skin and soft tissue infections (SSTI). For the 16 patients with bacteremia and documented consolidative therapy, 10 were treated empirically with vancomycin, and 5 remained on vancomycin after AST was reported. 2 were de-escalated to oxacillin or cefazolin, and for 3, treatment was discontinued. Documented consolidative therapy (table) for bacteremia included 1/4 with a PS isolate treated with ampicillin and 5/15 with an oxacillin-susceptible isolate treated with oxacillin or a first generation cephalosporin. In contrast, almost half of patients with SSTI were treated with oxacillin or a first generation cephalosporin, and a third with T/S.

Documented consolidative therapy for SLUG infections.

Antimicrobial	No. patients (% with susceptible isolates) Bacteremia/Osteomyelitis (n=16)	SSTI (n=30)
Ampicillin	1 (25)	0 (0)
Oxacillin / 1st gen ceph	5 (31)	12 (46)
Vancomycin	5 (30)	0 (0)
Ciprofloxacin	3 (18)	0 (0)
T/S	0 (0)	10 (34)
Other	2 (n/a)	8 (n/a)

Conclusion. Disparity between AST results and penicillin and oxacillin utilization for the treatment of SLUG infections was found. Rapid identification and further education regarding penicillin and oxacillin susceptibility in SLUG may aid in expanded use of these antimicrobials for SLUG infections.

Disclosures. **R. M. Humphries**, Affinity Biosensors: Investigator, Research support

1401. Multicenter Retrospective Study on *Streptococcus pneumoniae* Serotypes isolated from Adult Patients with Invasive Pneumococcal Disease in Latin America

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Background. *Streptococcus pneumoniae (Sp)* is the leading vaccine-preventable killer in adults worldwide. The aim of the study was to describe serotype distribution in cases of invasive pneumococcal disease (IPD) in adults and to establish the percentage of isolated serotypes included in the formulation of available pneumococcal vaccines PCV13 and PPSV23.

Methods. Observational and retrospective study. We analyzed 542 *Sp* strains isolated from sterile fluids in adults >18 years between January 1, 2010 and December 31, 2012. Three Latin American countries participated in the study, number of strains per country: Argentina (111), Brazil (179 plus 125 IPD cases published by SIREVA 2010-2012) and Mexico (127). Serotyping was performed using Quellung reaction. Serotype distribution and percentages covered by PCV13 and PPSV23 were estimated and stratified by age group: 18-29; 30-49; 50–64 and ≥ 65 years. Categorical variables were summarized as percentages; quantitative variables were expressed as mean .p < 0.05 was considered statistically significant. STATA statistics program version 11.1 was used.

Results. 57.7% of patients were men, mean age was 51.23 years (SD 18.27). Bacteremic pneumonia was the most common manifestation of IPD (58.33 %). Serotypes 3 (8.40%), 12F (7 %), 19A (6.6%), 7F (6.4 %), and 14 (4.8%) were the most prevalent. Serotypes 3 (8.65%) and 7F (7.27%) predominated in pneumonia. The percentage of serotypes covered by PPSV23 and PCV13 were overall 78.8% and 54.2% (difference 24.6%), in patients 50-64y 80.6% and 56.9% (difference 23.7%) and in adults ≥ 65y 79.04% and 54.5% (difference 24.54%) respectively (Table 2).

Percentage of IPD caused by serotypes included in PPSV23 and PCV13, by country

Country	Number of strains	PPSV23	PCV13	Δ (Difference)
Overall	542	78.8%	54.2%	24.6% (p<0.01)
Argentina	111	84.7%	57.8 %	26.9 % (p<0.01)
Brasil	304	77.9 %	51.1 %	26.8 % (p<0.01)
Mexico	127	76.38 %	61.4 %	14.98 % (p<0.01)

Conclusion. In the 3-year study period, vaccine serotype coverage in adults was 78.8% for PPSV23 and 54.2% for PCV13. Most common serotypes were 3, 12F, 19A and 7F. Continued surveillance of adult IPD in Latin America is warranted.

Disclosures. **All authors:** No reported disclosures.

1402. Multicenter Clinical Evaluation of the Novel Alere i Strep Isothermal Nucleic Acid Amplification Test

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Background. Rapid detection of group A beta-hemolytic streptococcus (GAS) is used routinely to help diagnose and treat acute pharyngitis. However, available rapid antigen detection tests for GAS have a relatively low sensitivity of about 70-90%. An isothermal nucleic acid amplification test utilizing simple equipment that offers highly sensitive, rapid results at the point-of-care can reduce the need for follow-up testing and time to notification – leading to appropriate antibiotic therapy.

Methods. To evaluate the performance of the new Alere™ i Strep A isothermal nucleic acid amplification test to detect GAS in comparison to bacterial culture as a reference standard.

Results. 484 assays were performed on prospectively collected throat swab specimens. In comparison with bacterial culture, the overall sensitivity and specificity of the Alere™ i Strep A assay was 95.9% and 94.6%, respectively. Discrepant results were adjudicated by real-time polymerase chain reaction (RT-PCR), resulting in an improved sensitivity and specificity of the Alere™ i Strep A assay of 98.7% and 98.5%, respectively. Tests initially interpreted as invalid (n = 23) by Alere™ i Strep A were repeated and results of the second test were considered the final result. A total of 14 assays (~3%) had a final result interpreted as invalid.

Conclusion. The Alere™ i Strep A isothermal nucleic acid amplification test is a robust point-of-care test for GAS detection in children and adults due to high sensitivity and specificity coupled with available results in less than 10 minutes. Rapid and accurate diagnosis of GAS leads to appropriate antibiotic therapy to prevent rheumatic fever and potentially other invasive infections.

Disclosures. **D. Cohen**, Alere: Grant Investigator, Grant recipient **W. Gluckman**, Alere: Investigator, Grant recipient **A. Parekh**, Alere: Grant Investigator, Grant recipient

1403. Evaluation of Diatherix Laboratories TEM-PCR: a novel multiplex diagnostic panel for detection of bacterial and viral respiratory pathogens

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Background. A broad array of pathogens causes influenza-like illness (ILI). Knowing etiology aids treatment and prevention. Novel multiplex diagnostic panels have been developed. Evaluating their performance on clinical isolates is warranted.

Methods. An observational study of febrile ILI among otherwise healthy subjects (0-65y, majority outpatient) is ongoing at five US military hospitals. Nasopharyngeal specimens are tested by single reaction PCR for influenza, human rhinovirus (HRV), and adenovirus. A subset of 403 specimens (78 influenza PCR-positive, 54 HRV PCR-positive, 10 adenovirus PCR-positive, 263 influenza-, HRV- and adenovirus PCR-negative) was tested by a target-enriched multiplex PCR (TEM-PCR) panel for 13 bacterial and 10 viral respiratory pathogens (Diatherix Laboratories, Inc.; Huntsville, AL).

Results. Of 403 specimens, 387 were evaluated by TEM-PCR with 259 (67%) positive for at least one virus. Compared to single reaction PCR, the sensitivity/specificity of TEM-PCR was as follows: influenza A (94%, 99%); influenza B (65%, 99%); HRV (68%, 90%); adenovirus (40%, 100%). Viral detection rates were: HRV, n = 61 (16%); Influenza A, n = 51 (13%); Coxsackie/Echovirus, n = 45 (12%); Coronavirus, n = 42 (11%); RSV, n = 40 (10%); Parainfluenza, n = 32 (8%); Human Metapneumovirus, n = 18 (5%); Influenza B, n = 17 (4%); Adenovirus, n = 4 (1%); Bocavirus, n = 1 (0.3%). Decreased TEM-PCR panel sensitivity can be explained by suboptimal sample volume used for nucleic acid extraction.

A total of 304 (75.4%) specimens were positive for at least one bacterium. Bacterial detection rates were: pneumococcus (37.4%); *Staphylococcus aureus* (28.7%); *Haemophilus influenzae* (26.4%); *Moraxella catarrhalis* (23.2%). Influenza A detection was not associated with detection of pneumococcus, *S. aureus*, or *H. influenza*e. Influenza B detection was associated with detection of *H. influenzae*, while specimens positive for RSV were also positive for pneumococcus.

Conclusion. The sensitivity and specificity of the Diatherix panel for detecting Influenza A, the most clinically relevant of the viral pathogens, was high. It is unknown whether bacterial co-detection represents colonization or co-infection. Multiplex panels improve diagnostic yield for ILI.

Disclosures. **L. Malone**, Diatherix Laboratories, Inc.: Employee, Salary **E. Grigorenko**, Diatherix Laboratories, Inc. Employee, Salary

1404. *Brucella suis* Bacteremia Misidentified as *Ochrobactrum antropii* by Vytek 2 Automated System

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Background. Accurate and rapid identification of *Brucella spp.* is necessary to provide appropriate treatment to the patient and take measures to prevent laboratory-acquired infections.

Methods. In January 2013 a 67-year-old man was admitted to our institution with a 3-day history of fever up to 39°C and fatigue. His medical history was significant for mitral valve replacement in 2010. The patient had close contact with pigs by keeping them as pets at home. On the day of admission two sets of aerobic blood cultures (BC) were obtained, becoming positive after 72 hs of incubation. The isolated organism

was a non-motile gram-negative coccobacillus identified as *O. anthropi* by Vytek 2 system. In order to establish the clinical significance of this isolation in the setting of a work up for possible prosthetic infective endocarditis (IE), repeated BC were taken on days 3 and 5 of admission, all of them resulting positive for the same organism. No vegetations were seen in the transesophageal echocardiogram. A diagnosis of definite IE was made based on the presence of 2 major criteria (six positive BC taken >12 hs apart, plus 6/6 positive BC) and 2 minor criteria (predisposing cardiac condition and fever > 38°C).

Results. Due to the rareness of the isolated pathogen, the adverse clinical outcome while on treatment for *O. antropii,* and the strong epidemiological data, patient's serum was tested for the presence of Brucella antibodies with microagglutination test, complement fixation test and enzyme linked immune-sorbent assay (ELISA) confirming the diagnosis of acute brucellosis. BC bottles were sent to a reference laboratory where the isolates were identified as *B. suis* biovar 1 by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism, thus confirming the misidentification of *B. suis* as *O. antropii* by Vytek 2.

Conclusion. *B. suis* can be misidentified using Vytek 2 system. Previous reports have described erroneous identification of *Brucella spp.* by API 20NE, RapID NF Plus and MicroScan systems. Countries where brucellosis is endemic need to be aware of this possibility. A high index of suspicion based on epidemiological and clinical data is essential not only to make accurate diagnosis and provide adequate treatment but also because *Brucella spp.* requires special handling to prevent unintentional exposure.

Disclosures. **All authors:** No reported disclosures.

1405. Antimicrobial Susceptibility of Obligate Anaerobes Isolated from Military Trauma Patients

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Background. Despite reports of high levels of antimicrobial (abx) resistance among obligate anaerobic bacteria, susceptibility testing is not routinely utilized to direct clinical care. This study clarifies distribution of obligate anaerobe susceptibility patterns in a combat-related trauma population.

Methods. We utilized all initial unique isolates of obligate anaerobes collected as part of the Trauma Infectious Disease Outcome Study September 2009-May 2013. Susceptibility testing was performed using CLSI agar dilution method. Tested abx included beta-lactam/beta-lactamase inhibitors (amp/sulb, pip/tazo), cephalosporin (cefoxitin), carbapenems (ertapenem, imipenem, meropenem), clindamycin, metronidazole, moxifloxacin, tigecycline, and linezolid. Resistance was defined by CLSI criteria except for tige which utilized FDA criteria and no criteria exists for linezolid.

Results. 48 patients with 63 unique anaerobic isolates were included (15 (24%) *B. fragilis*, 16 (25%) *B. non-fragilis*, 11 (17%) *Clostridium* spp., *12 (19%) Finegoldia* and *Peptostreptococus* spp., and *9 (14%) P. acnes).* For *Bacteroides* spp, the 4 most active agents were metro (90% susceptible), pip/tazo (93%), imipenem (95%) and tigecycline (95%) with an $MIC_{50/90}$ of 4/8 mcg/ml for linezolid. 100% of *Clostridium* spp isolates were susceptible to amp/sulb, pip/tazo, ertapenem, meropenem, metro, and tige with a $MIC_{50/90}$ of 4/16 mcg/ml for linezolid. 100% of *Finegoldia*, *Peptostrepcoccus* and P. acnes isolates were susceptible to amp/sulb, pip/tazo, cefoxitin, ertapenem, imipinem, meropenem, and tige with a linezolid MIC_{90} of 0.5 for *P. acnes* and 2 for the other isolates. 6(10%) of the isolates were resistant to 3 or more classes(excluding tige and linezolid) of abx and (of those 6 isolates, 5 were *Bacteroides* spp.), 3 (5%) isolates to 4 or more classes (all *Bacteroides* spp.). One *B. fragilis* isolate was resistant to all abx tested except for tige. Of the 45 isolates that had prior exposure to 82 abx with anaerobic activity, 19 (23%) combinations of drug and bacteria demonstrated resistance.

Conclusion. This study reveals high levels of resistance among some obligate anaerobes. Further studies are warranted to evaluate risk factors for resistance and to determine if *in vitro* susceptibilities correlate with clinical outcomes.

Disclosures. **All authors:** No reported disclosures.

1406. Next Generation Diagnostic Test for Lyme Disease

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Background. Current serodiagnostic tests for Lyme disease lack sensitivity and specificity for detecting B. burgdorferi infection in the early stages of the disease. To address these deficiencies, we fabricated a recombinant chimer- based diagnostic assay for Lyme disease using highly antigenic Borrelia proteins that we have identified in multiple genospecies of Borrelia spp.

Methods. Using protein arrays, we identified 48 key antigenic proteins from the B. burgdorferi strains that we used to construct 16 sets of chimeric proteins each containing three of the Borrelia antigens. Recombinant proteins were printed onto nitrocellulose-coated FAST glass slides. Proteome chips were probed with serum from 54 patients with early untreated Lyme disease.

Results. Although there were sample-specific responses, there was a subset of proteins recognized in common by a majority of the sera. The majority of sera recognized 9 highly antigenic Borrelia chimeras using IgM secondary antibody and 7 chimeras using IgG secondary antibody for a total of 11 individual proteins. Furthermore, each of these 11 chimeric antigens had a specificity of ^{3} 99% using normal sera and sera from patients with other chronic infections or autoimmune diseases. The sensitivity of our protein array was 80% with IgM + IgG secondary antibody for the early untreated Lyme sera. In comparison, the sensitivity was 44% for standard 2-tiered testing for these same early Lyme patients. Thus, the sensitivity of our assay far exceeds that of commercially available Lyme disease assays in patients in the early stages of the disease Among the 52 healthy controls from areas in which Lyme disease is endemic, none had positive results with our assay. For the potential cross reactive patients 11 of 83 samples had positive IgM or IgG antibody responses in our assay. Thus, the overall specificity for the array assay was 100% for normal controls and 87% in Sick-non-Lyme patients.

Conclusion. Given these exciting results, we are now poised to develop a standardized sensitive and specific single-tier Lyme disease assay of recombinant chimeric Borrelia proteins that will potentially have a wide range of coverage and specificity against Lyme disease.

Disclosures. **All authors:** No reported disclosures.

1407. Highly accurate diagnosis of scrub typhus using conventional PCR against *Orientia tsutsugamushi*

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Background. Scrub typhus is an acute febrile disease caused by *Orientia tsutsugamushi*. Delays in diagnosis and antibiotic administration can cause fatal complications. Therefore, a rapid and early diagnosis is critical.

Methods. We evaluated the clinical usefulness of the conventional PCR (C-PCR) amplification of the 16S ribosomal RNA gene using specifically designed primers. We examined blood specimens from 115 adult patients confirmed to have scrub typhus and 52 patients confirmed to have non-scrub typhus. All the patients were 18 years of age or older and visited Chosun University Hospital from 2007 to 2008 due to acute febrile disease within four weeks of onset. To evaluate the clinical usefulness of this new method, we compared its diagnostic accuracy to that of the following methods: C-PCR targeting the 47-kDa, 56-kDa, and groEL genes; nested PCR targeting the 47-kDa and 56-kDa genes; and real-time PCR targeting the 47-kDa gene.

Results. Using primers designed by the authors to amplify the 16S ribosomal RNA gene, C-PCR detected *O. tsutsugamushi* infection with a sensitivity of 86.8% and a specificity of 100%. C-PCR amplified the 47-kDa, 56-kDa, and groEL genes with lower sensitivities of 3%, 8%, and 61%, respectively. Nested PCR amplification of the 47-kDa and 56-kDa genes showed sensitivities of 81% and 80%, respectively, whereas real-time PCR of the 47-kDa gene exhibited a sensitivity of 76%. These results were subsequently confirmed; ROC curves provided statistical evidence that 16S ribosomal C-PCR using the authors' primers was the best method.

Conclusion. C-PCR amplification of the 16S ribosomal RNA gene using the authors' primers is simple, clinically useful, and has excellent diagnostic accuracy.

Disclosures. **All authors:** No reported disclosures.

1408. Evaluation of *Legionella* Diagnostic Testing by Urinary Antigen, Culture, and PCR

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Background. Infection by *Legionella* is associated with pulmonary disease that can range in severity from mild respiratory symptoms to fatal pneumonia. The goal of this retrospective study was to evaluate multiple diagnostic methods recommended for Legionairres' Disease and examine the circumstances surrounding positive tests.

Methods. The clinical database was searched for *Legionella* urinary antigen (UAG), culture (CUL), and polymerase chain reaction (PCR) ordered March 2010 to December 2013 at Cleveland Clinic. Each test could be ordered individually, or CUL and PCR could be ordered as a single set (CUL + PCR). UAG was performed by the *Legionella* Urinary Antigen EIA (Binax) and the laboratory developed PCR was run on the LightCycler (Roche) using *Legionella pneumophila* primers and probes. For cases where all 3 test methods were performed and at least one was positive, the medical record was reviewed for relevant clinical and epidemiologic factors.

Results. A total of 22,345 tests were ordered during the 4-year period. Excluding repeat testing, 16,808 unique tests were ordered (12,569 UAG, 643 CUL, 492 PCR, and 3,104 CUL + PCR). There were 363 unique positive results (336 UAG, 7 CUL, 12 PCR, and 8 CUL + PCR). For 24 patients, all 3 test methods were ordered: 10 (42%) cases were positive by all 3 methods; 9 (38%) positive by UAG and PCR only; 4 (17%) positive by UAG only; and 1 (4%) positive by CUL and PCR only. Initial presentation included pneumonia (n = 23, 96%), diarrhea (n = 10, 42%), and hyponatremia (n = 4, 17%). All cases were believed to be community acquired, and all except 1 were consistent with *Legionella* pneumonia. This patient had a prior *Legionella* infection and tested positive

by UAG only. Most of the patients (n = 13, 54%) were immunocompromised, and 17 (71%) showed resolution of symptoms with single-agent, definitive antibiotics. Most patients (n = 22, 92%) showed clinical improvement (2 patients expired).

Conclusion. The positivity rate for all *Legionella* test methods is low (≤2.7%). Although CUL is the only method that will detect species other than *L. pneumophila*, this did not occur for any of 717 cultures performed. There was good correlation between UAG and PCR. Cases positive for UAG-only may indicate prior infection or inadequate specimen provided for PCR and CUL.

Disclosures. **All authors:** No reported disclosures.

1409. The Use of Liquid Chromatography-Mass Spectrometry (LC-MS) for the Diagnosis of Community-Acquired Pneumonia

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Background. Community-acquired pneumonia (CAP) is one of the leading causes of morbidity and mortality worldwide. Early diagnosis is important for the appropriate use of antimicrobials. In this study, we sought to determine whether plasma metabolite profile can distinguish patients with CAP and those without CAP.

Methods. We acquired and compared the plasma metabolite profile of 143 patients suffering from CAP and 97 controls without CAP using Ultra-High-Performance Liquid chromatography coupled with Quadrupole-Time-of-Flight Mass Spectrometry (UHPLC-QTOFMS) and statistical methods using multivariate analysis, including Volcano Plot, principal component analysis (PCA) and partial least-squares discriminant analysis (PLS-DA).

Results. Unsupervised method using PCA showed clear clustering of CAP cases and controls in the plasma profile (Figure 1). Supervised method using PLS-DA showed 98% accuracy in confusion matrix to differentiate CAP cases and controls in the plasma profile (Figure 2).

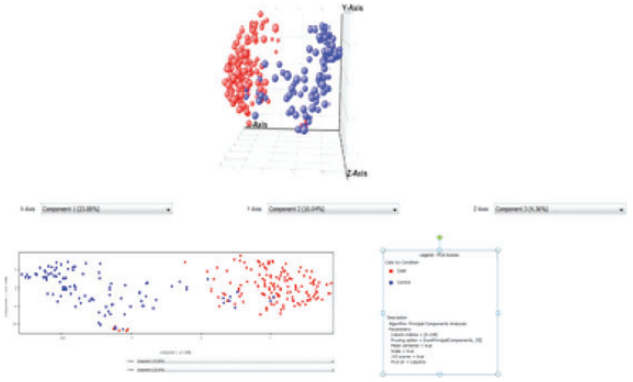

Figure 1. Plasma metabolite profile can distinguish patients with CAP from those without CAP.

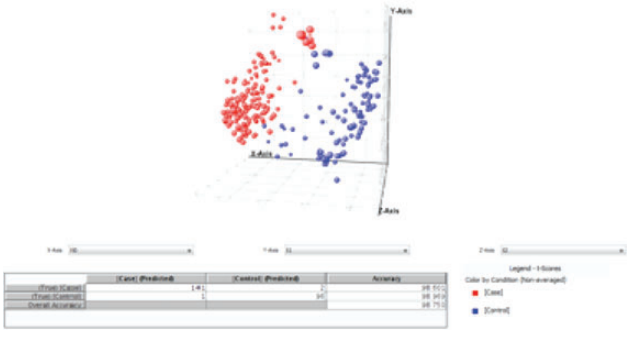

Figure 2. Partial least squares-discriminant analysis (PLS-DA) was used to generate the classification results summarized as visual output that can separate CAP case and control plasma samples.

Conclusion. Plasma metabolite profile can distinguish patients with CAP from those without CAP.

Disclosures. **All authors:** No reported disclosures.

1410. Evaluation of the FilmArray for Rapid Identification of Pathogens from Cerebrospinal Fluid (CSF) in Children

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Background. Meningitis is a severe infection that causes significant morbidity and mortality. Rapid etiologic diagnosis is critical to initiation of appropriate therapy. A molecular system to rapidly identify bacteria, viruses, and fungi causing meningitis could improve the medical management of this infection in children.

Methods. The FilmArray® Meningitis / Encephalitis Panel (FA ME; BioFire Diagnostics, Inc., Salt Lake City, UT) performs automated nucleic acid purification and multiplex PCR to identify 17 bacterial, viral and fungal pathogens directly from CSF. We performed a retrospective study of 120 children <= 18 presenting to our children's hospital with concern for meningitis. Conventional CSF testing (culture and/or viral testing) was ordered at the discretion of the treating physician. FA studies on archived CSF, using a research use only version of the panel, were performed at the University of Utah. FA ME results were compared to conventional testing.

Results. The median age of children in the study was 6 months (range 0-237 months). 18 children had positive CSF cultures, of which 11 grew true pathogens. Nine were included on the FA ME panel. FA detected 8/9 cultured panel bacteria, and also detected bacteria in 6 additional specimens (table). The median CSF WBC count in children with positive cultures was 391; median WBC for children with positive FA ME testing was 1749. This difference is related to low CSF WBC in samples culture-positive for presumed contaminants. Only 4 children had viruses detected by conventional methods, including PCR of blood or CSF. FA ME detected viruses in 16 samples, including 4 also positive for bacteria.

Pathogen	Identified by Conventional Testing (n)	Identified by FilmArray (n)
S. pneumoniae	3	4
S. agalactiae	1	2
N. meningitidis	1	1
H. influenzae	3	4
E. coli	1	3
K. pneumoniae/C. koseri	1/1	0/0
Presumed contaminants (skin flora)	7	0
HSV/HHV6/EBV/CMV/VZV	0/1/1/0/0	1/8/5/0/0
Enterovirus/Parechovirus	2/0	2/1

Conclusion. The FilmArray ME panel is a sensitive tool for the rapid identification of pathogens from CSF and may identify causative pathogens not detected by conventional testing. Improved detection of pathogens from CSF using FilmArray has the potential to improve treatment and outcomes for children with meningitis.

Disclosures. **K. Hanson**, BioFire Diagnostics, LLC: Collaborator, Co-investigator on NIH grant, Principal Investigator **A. Hemmert**, BioFire Diagnostics: Employee, Salary **M. A. Poritz**, BioFire Diagnostics: Employee, Salary **A. J. Blaschke**, BioFire Diagnostics LLC: Collaborator and Scientific Advisor, Co-Investigator on NIH grant, Principal Investigator, Consulting fee and Licensing agreement or royalty

1411. Utilization of PCR to Characterize Vaginal Flora in a Longitudinal Study of Recurrent Bacterial Vaginosis

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Background. Bacterial vaginosis (BV) is the most common vaginal infection for women of reproductive age and is associated with pre-term labor and HIV acquisition. It is characterized by a shift in the vaginal flora from commensal lactobacillus to diverse facultative and anaerobic species. Treatment is oral or topical antibiotics, after which up to 80% of patients experience recurrent disease within 6 months.

Methods. We performed a longitudinal study on symptomatic BV patients, obtaining vaginal specimens at 3 visits: initial diagnosis, 10-14 days and ~1 month later. BV was diagnosed based on signs and symptoms (Amsel's criteria) and Nugent score (Gram-stained vaginal smears). DNA was extracted from vaginal specimens and analyzed by real-time PCR to quantify the presence of BV-associated microbes and commensal lactobacillus species.

Results. Initial diagnosis of BV by either Amsel's criteria or Nugent score was strongly correlated with the presence and quantity of *Gardnerella vaginalis*, *Atopobium vaginae*, BVAB2 and *Megasphaera* and reduced presence of commensal lactobacillus species. When evaluated 10-14 days later, treatment was successful in 78/82 patients (95%) and was associated with the eradication of *Megasphaera* type 1 in 54/55 (98%) and type 2 in 21/21 (100%) patients. In contrast, *G. vaginalis*, *A. vaginae* and BVAB2 persisted in 54/75 (72%), 36/69 (52%) and 19/58 (33%) patients, respectively, although their median concentrations decreased by ~3 logs. Frequency of colonization with the commensal lactobacillus species *L. crispatus*, *L. gasseri* and *L. jensenii* all increased after treatment; from 17% to 32%, 7.7% to 12% and 10% to 25%, respectively. Twenty-nine patients (37%) would go on to experience recurrent disease at their 3rd visit, ~ 1 month after diagnosis. However, neither persistence of BV-associated microbes nor colonization with commensal lactobacillus species after treatment was associated with disease recurrence.

Conclusion. Successful treatment of BV is associated with profound changes in the vaginal flora that can be characterized by PCR. Recurrent disease in this population was not associated with treatment failure and the recovery of commensal lactobacillus species was not protective. Future studies will evaluate additional factors contributing to disease recurrence.

Disclosures. **D. Hilbert**, Medical Diagnostic Laboratories: Employee, Salary **S. Balashov**, Medical Diagnostic Laboratories: Employee, Salary **M. Adelson**, Medical Diagnostic Laboratories: Employee, Salary **E. Mordechai**, Medical Diagnostic Laboratories: Employee, Salary **J. D. Sobel**, Medical Diagnostic Laboratories: Board Member, Consulting fee **S. Gygax**, Medical Diagnostic Laboratories: Employee, Salary

1412. Impact of Culture Yield and Detection of Multi-Drug Resistant Organisms from CT-guided Abscess Drainage despite Prior Antibiotics

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Background. Culture information obtained from CT-guided abscess drainage is used to direct therapy decisions. However, these cultures are often performed after antibiotics have been initiated and the effect of this on culture yield is unclear. The WHO describes increasing antibiotic resistance as a major global threat and so we also sought to determine the prevalence of MDROs in our population of patients with abscesses. Our objectives were to evaluate the yield of cultures obtained from CT-guided abscess drainage despite prior antibiotics, the prevalence of multi-drug resistant organisms (MDROs) and their impact on antibiotic management.

Methods. This retrospective study evaluated 300 patients who underwent CT-guided aspiration or drainage for suspected infection (November 2011 - September 2013) at a single academic medical institution. Patient imaging and clinical characteristics were evaluated by an Abdominal Imaging fellow. Culture results and antibiotic therapy were evaluated independently by an Infectious Diseases fellow. Statistical analysis was performed using the Kruskal-Wallis, Fisher exact and χ^2 tests.

Results. 17 patients were excluded due to lack of pre-procedure antibiotics or cultures being sent. 283 patients constituted the final cohort, with average age of 55 and M:F ratio of 53:47. Leukocytosis was present in 165/283(58%) and fever in 64/283 (23%). Cultures were positive in 208/283(74%) with change in management in 184/283(65%). Patients with positive cultures had a shorter median time difference between antibiotic initiation and drainage than those with negative cultures (1.0 vs 3.7 days, $p < 0.001$). Change in management included change of antibiotics in 70/186 (38%), narrowing therapy in 97/184 (49%) and cessation of antibiotics in 17/184 (9%). ID consultation was significantly correlated with change in therapy ($p < 0.006$). MDROs were cultured in 51/283 (18%). Detection of MDROs was significantly correlated with change in therapy ($p < 0.002$).

Conclusion. Despite prior antibiotics, CT-guided drainage has a high yield of positive cultures, which have an impact on antibiotic therapy decisions. MDROs were detected in 18% of cases and this finding increased the likelihood of changes to antibiotic therapy.

Disclosures. **All authors:** No reported disclosures.

1413. Factors Associated with Pertussis Testing: Potential Disparities in Case Ascertainment

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Background. In the U.S., pertussis incidence is now at the highest rates in over a half-century. Detection and treatment of pertussis cases is critical to control the current epidemic. A better understanding of provider testing practices will inform efforts to improve case ascertainment.

Methods. We conducted a retrospective case-control study of children ≤18 years who presented to a primary care clinic within the Children's Hospital of Philadelphia network between July 2011 and September 2013. Case patients (tested by pertussis PCR) were matched by date to control patients (seen for cough illness but not tested for pertussis). Logistic regression was used to compare children who were and were not tested for pertussis.

Results. Pertussis PCR was obtained from 6797 children (544 positive, 8.0%); 6236 untested controls were identified. On bivariate analysis, age group ($p < 0.001$) and race ($p < 0.001$) differed significantly by testing status, but sex, ethnicity, and insurance payor did not. Children tested for pertussis were less likely to have asthma (42.2% vs 57.8%, $p < 0.001$) or documented fever (3.9% vs 5.7%, $p < 0.001$), but were more likely to have ≥1 visits in the prior month (54.0% vs 41.1%, $p < 0.001$) and to have been seen at an urban clinic site (36.2% vs 24.7%, $p < 0.001$). Virtually all patients were up-to-date for pertussis vaccine (96%), and pertussis vaccine status did not differ between groups. Children tested for pertussis were more likely to have last received pertussis vaccine ≥3 years ago (33.5% vs 31.1%, $p = 0.004$). On multivariate analysis, pertussis vaccine ≥3 years ago, ≥1 visit in the past month, and visiting an urban primary care center were associated with testing for pertussis (ORs [95% CI]: 1.19 [1.06-1.34], 1.67 [1.55-1.79], and 2.38 [2.16-2.63], respectively). Lower likelihood of pertussis testing was associated with age 1-6 years, black race, history of asthma, and fever (ORs [95% CI]: 0.83 [0.74-0.94], 0.55 [0.49-0.61], 0.71 [0.66-0.77], and 0.57 [0.48-0.68], respectively).

Conclusion. Pertussis testing practices varied by both patient and provider factors, with clinic site having the greatest effect. Racial disparities may also exist. Standardization of testing practices might improve pertussis case ascertainment.

Disclosures. **All authors:** No reported disclosures.

1414. Case of *Brucella spp* misidentification and resulting laboratory staff exposure in a large academic hospital in central New Jersey

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Background. Brucellosis is a zoonotic infection that causes a clinical syndrome of fever, malaise, and arthralgia in humans. It is contracted by ingestion of contaminated animal products in endemic areas or via aerosolization. High risk individuals for occupational exposure (veterinarians and lab personnel) are routinely advised to take precautionary measures when exposed to suspected cases of *Brucella spp (Br)*. Brucellosis is the most common laboratory acquired infection and is a potential bioterrorism agent.

Methods. A 45 year old male presented with drenching sweats, arthralgia, and 25lb weight loss that began 2 months after visiting family in Mexico. Blood culture Gram stain revealed weakly staining gram positive cocci, which were identified as *Staphylococcus hominis.* Despite antibiotic therapy and initial improvement, his symptoms relapsed and on readmission to the hospital blood cultures were positive for the same organism. Infectious work up with TEE, bone marrow smear, and HIV and tuberculosis screens were all negative. A blood culture isolate sent to the state public health laboratory was identified as *Br* by PCR. Misidentification of *Br* as *S. hominis* by a commercial assay has not been reported in the literature.

Results. 55 staff members were exposed to the *Br* isolate in the laboratory, 23 with high risk exposure by direct contact with or direct roles in preparation of lab specimens. All tested staff had negative baseline serology for *Br* antibodies and were offered post exposure prophylaxis with doxycycline and rifampin for 21 days. Thirty two of 55 exposed staff completed post exposure prophylaxis therapy (20/23 high risk staff including 1 known pregnant staff member, and 12/32 low risk staff). Serial serologic testing in all exposed individuals at 2, 4, 6, and 24 weeks remained negative for all tested individuals (27 patients missed ≥1 serial serologic test). There were no reports of symptoms or illnesses at the time of discovery or in sequential follow up. The case patient received 5 weeks of rifampin and doxycycline.

Conclusion. Commercial lab assays may misidentify *Br*. A high level of clinical suspicion is needed in non-endemic areas to correctly identify this organism and ensure safe handling of specimens to prevent laboratory exposures.

Disclosures. **All authors:** No reported disclosures.

1415. A Quality Improvement Initiative to Decrease Unnecessary Streptococcal Antigen Testing in an Urban Pediatric Emergency Department

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Background. Acute pharyngitis is a common complaint in the pediatric emergency department (ED). Group A beta-hemolytic streptococcus (GAS) accounts for 15-30% of childhood pharyngitis. Previous investigation revealed that 64% of

streptococcal testing performed in our ED during peak season was not clinically indicated. The objective was to optimize diagnostic and treatment decisions in children with pharyngitis in the ED using quality improvement (QI) methods.

Methods. The first plan-do-study-act (PDSA) cycle included a multi-tiered educational approach (daily huddles, lecture, and closed circuit television) of nurses, physicians, and nurse practitioners targeting recent testing guidelines and the current hospital testing protocol. Demographics, clinical features, and rapid antigen test (RADT) results were collected from 20 patients weekly from March 1, 2014-April 30, 2014. Adherence to the current protocol was determined by chart review and compared to pre-intervention data.

Results. A total of 128 patients had RADT testing; 45 (35%) were positive. Reflex throat culture was positive in 11 (13%) of the negative RADT isolates. Of those with a positive RADT, 25 (56%) patients did not meet testing criteria; 19 (76%) had viral symptoms (e.g., cough, congestion, rhinorrhea), 10 (40%) had no sore throat, and/or one (4%) were <3 years old. Of those with a negative RADT, 62/82 (75%) patients did not meet testing criteria; 48 (77%) had viral symptoms, 28 (45%) had no sore throat, and/or four (6%) were <3 years old. No decrease in unnecessary testing was seen between the pre-intervention and post-intervention time frames (p = 0.43). Antibiotics were prescribed for three (4%) patients with negative RADT and culture result. Twenty-nine patients (23% overall) who did not meet testing criteria, but had a positive RADT (n= 25) or culture (n = 4), received an antibiotic.

Conclusion. The majority of GAS testing in our ED continues to be unnecessary, and 25% of patients received unnecessary antibiotic treatment. Educational interventions targeting all healthcare providers did not change clinical testing decision-making. The next QI intervention will include implementing a new GAS testing protocol for the ED and ordering restrictions.

Disclosures. **All authors:** No reported disclosures.

1416. Serial Procalcitonin for Assessment of Hospital Mortality in Critically Ill Patients Including Recipients of Solid-Organ Transplantation (SOT) with Infection or Infection-Like Syndrome

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Background. The role of procalcitonin (PCT) in infection diagnosis and predicting treatment response among critically ill SOT recipients is not certain. Here, we sort to assess diagnostic feasibility of PCT in our hospitalized patients.

Methods. Critical care unit patients with SOT (n = 32) were compared with patients who had no history of transplantation (n = 174) between April 2012 and December 2013. Standard guidelines were used for diagnosis of infection, treatment response and outcomes. Chi-square and Mann Whitney U test were used for statistical analysis. PCT values are shown as ng/ml.

Results. SOT recipients were a) younger (age 56 vs 69 years; P < 0.01), b) had undergone major surgery (56% vs 22%; p < 0.01), c) had less cardiovascular and d) chronic pulmonary disease (25% vs 53% [p < 0.01] and 6% vs 28% [p = 0.02], respectively). Chronic liver disease was common (63% vs 10%; p < 0.01) and critical unit stay was longer in SOT group (14 vs 6 days; p <0.01). Whereas, fewer transplant recipients had cancer (3% vs 26%; p < 0.01) and received chemotherapy recently (0% vs 14%; p = 0.03). The APACHE score and hospital mortality (18 vs 17 [p = 0.6] and 16% vs 25% [p = 0.3], respectively) were comparable. The table shows PCT values were higher in patients with microbiologic infection diagnosis. In 78 evaluable patients, including 10 SOT recipients in whom serial PCT measurements were performed, rising vs declining/unchanged PCT levels were associated with a significant risk of hospital mortality (odds ratio 7.5; 95% confidence interval, 2.38-23.86).

	SOT (N=32)		Non-SOT (N=174)		
	N	PCT median	N	PCT median	*p* value
Microbiologic infection diagnosis	14	6.98 (0.14-197.0)	94	0.94 (0.05-172.70)	0.02
Gram positive infections	5	5.49 (1.05-48.66)	41	0.92 (0.05-73.10)	0.04
Gram negative infections	11	8.48 (0.38-197.0)	64	0.85 (0.05-172.73)	0.01
Bacteremia	8	10.23 (0.38-197.0)	22	0.85 (0.05-172.73)	0.04
Lung infection	3	1.05 (0.42-40.77)	50	1.16 (0.05-73.10)	0.7
Clinical Infection diagnosis	13	0.87 (0.05-39.08)	69	0.55 (0.05-726.70)	0.3
No infection suspected	5	0.38 (0.11-1.62)	11	0.21 (0.05-12.72)	0.7
Mortality	5	2.59 (0.38-5.49)	44	1.38 (0.05-44.07)	0.7

Conclusion. A rising PCT level in critically ill patients may be an important predictor of poor outcome and needs further evaluation.

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1418. By the Book: Inconsistent Compliance with Clinical and Laboratory Standards Institute's Antibiogram Guidelines in Community Hospitals

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Background. Knowledge of local drug resistance is critical for management of infectious diseases. Community hospitals' compliance with Clinical and Laboratory Standards Institute (CLSI) guidance for creation of cumulative antibiograms is uncertain.

Methods. This is a descriptive cohort study of antibiogram reporting practices in 32 community hospitals enrolled in the Duke Infection Control Outreach Network. We requested 2012 cumulative antibiograms from each facility. Microbiology personnel were sent a voluntary, electronic survey on antibiogram preparation practices. Data on reporting practices and compliance with CLSI guidance were compiled using descriptive statistics.

Results. 32 of 42 (76%) hospitals (median [IQR] bed size 210 [124-280]) participated by providing antibiograms; 21 of 42 (50%) also provided survey responses. The median [IQR] isolate numbers of common species were as follows: *E. coli* 914 [768-1429], *P. aeruginos*a 129 [88-184], *S. aureus* 341 [206-615]. Twelve (38%) antibiograms specified methods used for compiling data and exclusion of duplicates. Eight (25%) reported species with >30 isolates only; 3 (13%) of the 24 who did not follow the 30-isolate rule included a footnote to indicate impaired statistical validity. Twenty (63%) reported at least 1 pathogen-drug combination not recommended for primary or supplemental testing per CLSI (e.g., *E. coli* and tigecycline). Thirteen (41%) reported methicillin-resistant and susceptible *S. aureus* separately. Of the 23 facilities that reported susceptibilities for *S. pneumoniae,* 12 (52%) used meningitis and non-meningitis breakpoints. Complete compliance with CLSI guidance was observed in 3 (9%) antibiograms. Survey respondents' self-assessment of full or partial compliance with CLSI guidelines was reported by 50% and 17%, respectively. 33% reported uncertainty or unfamiliarity with CLSI guidance.

Conclusion. Full compliance with CLSI guidance for hospital antibiograms was uncommon, largely due to small isolate numbers. Uncertainty about CLSI guidance was common. Alternate strategies, such as regional antibiograms using pooled data, and educational outreach efforts are needed to provide reliable local drug susceptibility estimates for community hospitals.

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1419. Comparison of Systemic Inflammatory Response Syndrome (SIRS) Criteria in Children with Viral vs Bacterial Infections

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Background. Pediatric sepsis remains a major cause of morbidity and mortality in the U.S. Prompt recognition and goal-directed therapy early in the sepsis cascade result in improved outcomes. There is a growing interest in the use of early warning systems (EWS) to quickly identify rapidly deteriorating patients. One concern is that a pediatric sepsis alert would trigger excessively in children with viral infections. The purpose of this investigation was to identify the potential utility of an EMR-based EWS for pediatric sepsis, based international consensus criteria for pediatric systemic inflammatory response syndrome (SIRS).

Methods. Charts were obtained for 250 children with positive blood cultures (excluding contaminants), 917 children with PCR-confirmed respiratory syncytial virus (RSV), and 97 children with PCR-confirmed influenza virus during a 2.5-year period at Virginia Commonwealth University Medical Center. Of these charts, a convenience sample of 15 from the RSV group, 15 from the influenza group, and 30 from the bacterial group were randomly selected for further review. Records were assessed for the number of SIRS criteria met, from 24 hours prior to and up to 48 hours after the positive microbiologic result. Comparisons between bacterial and viral groups were carried out using Fisher's exact test.

Results. There were 77% (n = 23) children in the bacterial group vs 63% (n = 19) in the viral group who met ≥2 SIRS criteria (p = 0.40). Likewise, there were no differences between groups meeting ≥3 SIRS criteria (63% (n = 19) bacterial vs 43% (n = 13) viral; p = 0.20) or groups meeting no SIRS criteria (23% (n = 7) bacterial vs 37% (n = 11) viral; p = 0.40). However, more children in the bacterial group (40% (n = 12)) had organ dysfunction than those in the viral group (7% (n = 2)), (p = 0.0048).

Conclusion. Any pediatric sepsis EWS algorithm will have to take into account the large number of children with viral infections that meet SIRS criteria in order to minimize unnecessary testing and treatment.

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1420. An Early Warning System to decrease Necrotizing Enterocolitis (NEC) severity.

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Background. Clinical symptoms and signs of early intestinal dysfunction and stage I Necrotizing Enterocolitis (NEC) are non-specific but may be important to identify to decrease risk of disease progression and associated morbidity and mortality. *Hypothesis:* Early signs of NEC are related to intestinal feeding intolerance, intestinal ileus, and later cardiorespiratory signs and symptoms which can be used in a scoring warning system impact on progression to severe NEC.

Methods. Prospective analysis of clinical health signs and symptoms of inborn infants <1500gms from October 2012-October 2013 included clinical categories of CNS (lethargy), Cardiac (change in heart rhythm and blood pressure), Respiratory (change in apnea and respiratory rate), and Gastrointestinal (change in residuals, emesis abdominal fullness or girth). Infants with change in clinical symptoms and score $\geq$ to 5 were evaluated by abdominal radiographs for early intestinal pattern abnormality (ileus, dilated loops, loss of gas pattern). Analysis also included retrospective application of score tool of all infants with NEC in previous 3.5 years. Regression analysis was performed with SAS and JMP statistical tool.

Results. The symptoms and signs most associated with Stage I NEC (early stages of NEC) were cardio respiratory with signs of abdominal and feeding intolerance as later finding associated with later stages of NEC development. The clinical score was associated with decreased incidence of stages II-III NEC and NEC mortality. Use of the scoring tool increased number of xrays as well as 1 day greater of antibiotics without adverse effects on growth and LOS.

Conclusion. Cardiorespiratory symptoms precede gastrointestinal symptoms and may serve as an early warning sign for intestinal dysfunction and development of early stages of NEC. Based on these findings we are developing a mobile scoring tool (iPad application) for early identification of changes in cardiorespiratory baseline symptoms to assist in management of the high risk preterm infant.

Disclosures. **N. Sheth**, megnih llc: Shareholder, Salary

1421. Characteristics of Patients Referred to a Pediatric Infectious Diseases Clinic with Unexplained Fever

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Background. Case series from the 1970s-90s, focusing on children meeting *a priori* definitions of fever of unknown origin (FUO), established the classic diagnostic categories of infectious, inflammatory, neoplastic, and miscellaneous conditions. These studies also suggested that the proportion of children with no definitive final diagnosis was increasing over time. Few U.S. studies since then have revisited the FUO construct, and none has provided broader insight into children referred with unexplained fever *per se*.

Methods. Patients referred to a pediatric infectious diseases clinic for unexplained fever from January 1, 2008-December 31, 2012 were identified in a database of outpatient visits. Records were abstracted for demographic, clinical, and laboratory data, and descriptive analyses were performed.

Results. Of 4586 visits, 309 were of unique patients with the terms "fever," "febrile" or "FUO" in their diagnosis. After exclusions, 221 remained in the study group. By history, ten patients were not truly having fever. Fifty-nine (27%) were referred with prolonged fever. Of these, 11 had diagnoses that were apparent at initial visit. The remaining 48 patients were classified as having FUO; their median age was 5.6 years (IQR 2.1-11.1), median duration of reported fever was 30 days (21-60), and 71% reported daily fevers. Fifteen (31%) patients with FUO had a definitive diagnosis established—10 infectious, 3 inflammatory, 1 neoplastic, and 1 miscellaneous. Thirty-three (69%) never had a definitive diagnosis established. Of 152 patients with recurrent fevers, 92 (61%) had an intermittent fever pattern; 84 (91%) of these had no specific diagnosis made or were thought to have sequential, self-limited viral illnesses. Of 60 patients with a periodic fever pattern, 20 were thought to have periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome, 1 had familial Mediterranean fever, and 39 had no specific diagnosis made.

Conclusion. Most children referred with unexplained fever ultimately had either self-limited illnesses or no specific diagnosis established. Serious diagnoses were unusual, suggesting that such diagnoses rarely present with unexplained fevers alone, or that, when they do, the diagnoses are made by primary care providers or other subspecialists.

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1422. Evaluation of an Intervention to Decrease Blood Culture Contamination Rates in the Emergency Department

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Background. Blood cultures are commonly done in hospitals to work up fever. Positive blood cultures indicate either bacteremia, or false positive blood cultures from contamination with bacterial skin flora through improper technique. False positive blood cultures are associated with unnecessary hospitalization and/or extended length of stay with consequent financial burden. False positive blood culture rates in Emergency departments (ED) are often twice as high as on the medical wards (7% vs 3% at our institution, Sentara Norfolk General Hospital (SNGH)). We present the results of an intervention to decrease false Positive blood culture rates at the SNGH ED.

Methods. A pilot study with kits containing sterile gloves, masks, and blood culture supplies were introduced into the SNGH ED in July 2013, as well as training including new instructions to have two staff members present when drawing blood cultures, and prohibiting drawing blood cultures from pre-existing lines. False positive blood culture rates were measured in the weeks preceding and the weeks following this intervention.

Results. In the 12 weeks following the intervention, the average false positive blood culture contamination rate in SNGH ED was 2.7% out of 1354 blood culture samples. In the 6 months preceding the intervention, the blood culture contamination rates ranged from 5.2% to 10.7% each month, with an overall rate of 7.6% out of 3240 blood culture samples. This calculates to a greater than 60% reduction in false positive blood culture rates after the intervention (p value <0.0001 using Fischer's exact test).

Conclusion. Blood culture kits and educational training on proper technique resulted in significant reduction (> 60%) in the false positive blood culture rate in the SNGH ED. Studies at other institutions have suggested that reducing the false positive blood culture rate could decrease costs by preventing unnecessary hospitalizations and administration of unnecessary antibiotics, as well as helping to prevent the development of multi-drug resistant organisms. Further studies at SNGH are necessary to precisely describe the financial and other benefits of the described intervention.

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1423. Clinical Utility Of Incubating Anaerobic cultures 2 vs 5 Days

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Background. Clinical microbiology references suggest that cultures for anaerobic bacteria should be incubated for 5 days (d); however, little data exist to support this recommendation. A Quality Assurance (QA) study performed in our laboratory in 1992 revealed that most anaerobes were detected within 2 d and that the incremental yield of 5 d of incubation was negligible. We have repeated this analysis using contemporary reagents and methods to reevaluate the relative yield of anaerobes after 2 d vs 5 d of incubation. In addition, we assessed the clinical utility of the identification of isolates grown after 2 d of incubation.

Methods. We performed an 8 month prospective QA study between August 1, 2013, and March 31, 2014. Specimens from sterile body fluids; wounds, tissues, abscesses, aspirates and operative specimens were inoculated to appropriate media, and placed into chambers with anaerobic atmosphere generated by the Anoxamat system. Cultures were incubated for 2 d before being examined. Cultures that showed no growth after 2 d were re-incubated for an additional 3 d and then re-examined at 5 d. Chart review was performed on anaerobic cultures that were positive only after 5 d.

Results. A total of 2107 anaerobic cultures were processed during the study period, of which 177 specimens (8.3%) grew anaerobes. Only 2 (1.2%) were positive at 5 d and not at 2 d; 175/177 (99.4%) anaerobes were detected after 2 d of incubation. *Propionibacterium acnes* was isolated from the 2 positive specimens that grew only after 5 d of incubation. One of the 2 *P. acnes*isolates, which was from brain tissue, was judged to be clinically important. Thus, 1 of 177 clinically important anaerobic cultures (0.6%) would have been missed with a 2 d incubation protocol.

Conclusion. Our results generally confirm observations from two decades ago. We conclude that the great majority of anaerobic cultures will show growth within 2 d of incubation. Rarely, particularly for *P. acnes,*longer incubation (e.g., 5 d) is needed. Infectious Diseases physicians should be aware of incubation protocols in their Microbiology labs and may wish to request extended incubation when clinically indicated. In an era of cost containment, in-house QA studies can enhance cost effective microbiology.

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1424. Cost-Effectiveness of 30- Compared to 20-Milliliter Blood Culture Draws: A Retrospective Study

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Background. The importance of blood volume for detection of BSIs has been well documented. Recently, improved diagnostic sensitivity (7.2%) was demonstrated for 30 vs 20 ml blood cultures (BCs) in adults. Arguably, increased BC volumes can improve patient care. In addition, hospitals receive higher reimbursement for patients with documented septicemia, providing a potential financial incentive for 30 ml BCs. We have attempted to determine the cost-effectiveness of 30 ml vs 20 ml BCs using a combination of published and retrospective data from our institution.

Methods. Data from 20 ml BCs drawn at RWJUH from January 1, 2012 to March 31, 2012 were reviewed retrospectively and positive cultures were categorized as representing true infection, contamination, or unknown significance based on published criteria. The RWJUH Medical Record and Accounts Receivable Departments provided actual Medicare reimbursement (MR) data for patients with selected ICD-9 diagnostic codes. Costs of reagents, equipment, and phlebotomist and technologist time and effort were obtained from the Microbiology Laboratory. These data were used to provide an estimate of the expected annualized increase in MR and costs associated with conversion to 30 ml BCs.

Results. Based on our calculations, the projected mean MR for 464 annual primary BSIs was $24,808 per episode. An expected 7.2% increase in the number of primary BSIs detected using 30 ml BCs would result in an additional 34 annual cases and MR of $843,479. Comparative MR data where septicemia was a complication of another diagnosis were available for 4 ICD-9 codes: laparoscopic cholecystectomy, disorders of the biliary tract, simple pneumonia and cellulitis. Mean MR for each such episode (704 annually) was projected to be $9667. A 7.2% increase in secondary BSIs would result in detection of 50 additional annual cases and an increased MR of $483,350 annually. The annual cost to the hospital associated with conversion to 30 ml BCs was estimated to be $73,402. Taken together, the net profit to the hospital would be estimated to be $1,253,427 for conversion from 20 ml to 30 ml BCs.

Conclusion. Using results suggest that conversion to 30 ml BCs may not only improve care by detecting more BSIs but may also substantially increase MR to the hospital.

Disclosures. **All authors:** No reported disclosures.

1425. Financial Impact of Pediatric Blood Culture Contamination: Is There Room for Improvement?

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Background. Blood cultures (BC) are integral in clinical practice to detect pathogens and guide antibiotic therapy. Contaminated BC are a problem in many emergency departments (ED) and rates have been reported as high as 11%. Increased BC contamination leads to unnecessary use of antibiotics, repeat testing, and increased healthcare costs. The rate of isolation of true pathogens from BC is directly related to the volume of blood collected and inadequate blood volumes have been linked to isolating contaminants. The objective of this study is to assess the financial impact of BC contaminants and the association with blood volume.

Methods. Retrospectively reviewed medical records of children who had BC obtained in the Pediatric ED over a 19-month period (January 1, 2012 to July 31, 2013). Positive BC were further analyzed to determine if isolated organisms were contaminants. Associated healthcare charges (ED visits, admissions, antibiotics and laboratory testing) were calculated. The associations between BC volume and contamination were assessed using chi-square test.

Results. There were 8916 pediatric BC specimens obtained during the 19-month period. There were 461 (5.17%) positive BC: 336 (72.9%) contaminated and 125 (27.1%) true positive. The total charges for the 336 contaminated BC was almost 5 million dollars ($4,780,781) with a median of $12,950 per patient. Of the 461 positive BC, 406 (88%) contained inadequate volume. Contaminated BC were more likely to contain inadequate volume compared to true positive BC (odds ratio [OR] 3.93, 95%CI: 2.20-7.00) ($p < .0001$, chi-square test). Among children 12 months of age or younger, contaminated BC had 4.5 times higher odds of containing inadequate volume compared to true positive BC (OR 4.53, 95% CI: 1.34-15.24).

Conclusion. Contaminated BC lead to a substantial increase in healthcare costs and inappropriate antibiotic use. A major factor contributing to isolating BC contaminants is inadequate blood volume, especially among infants. Future research is ongoing to assess the impact of implementing volume guidelines at our children's hospital on reducing BC contamination and healthcare costs.

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1426. Correlation of Cytomegalovirus Viral Load between a Laboratory-Developed Test and a WHO-Calibrated Commercial Assay in Transplant Recipients

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Background. Quantitative CMV nucleic acid testing (QNAT) is the standard laboratory method for the diagnosis and treatment guidance of CMV infection in transplant recipients. Until recently, QNAT using laboratory developed tests (LDT) have not been standardized and results are not directly comparable. Recently, the first WHO International Standard for CMV QNAT (WHO-QNAT) has been released, and clinical laboratories are now calibrating their QNAT to this standard. Our objective is to correlate the viral load measurements between an FDA-approved WHO-QNAT assay and a LDT used by three different clinical laboratory sites.

Methods. Plasma samples were quantified for CMV viral load by LDT and WHO-QNAT at three different clinical laboratories of a single institution during the summer of 2013. Spearman's correlation coefficients (ρ) and Lin's concordance correlation coefficients (CCC) were used to compare the viral load levels obtained with WHO-QNAT and LDT. LDT results were transformed into binary result categories based on a pre-defined threshold of 5,000 copies/mL (trigger for antiviral therapy), and WHO-QNAT levels were evaluated using logistic regression and ROC analysis, from which optimal cut-points and sensitivity/specificity (sens/spec) values were obtained.

Results. A total of 431 clinical plasma samples were tested by both LDT and WHO-QNAT assays: 123 samples at Lab A, 202 at Lab B, and 106 at Lab C. Combining all data, the optimal viral load equivalent of the pre-defined threshold of 5,000 copies/mL was 1,200 IU/mL (based on WHO-QNAT), with sens/spec of 82.9%/90.2%. For individual sites, the pre-defined threshold was equivalent to 1,810 IU/mL at Lab A (sens/spec 100%/92%), 1,200 IU/mL at Lab B (sens/spec 82%/88%), and 326 IU/mL at Lab C (sens/spec 90%/82%). For Lab A values, the correlation between assays was modest (ρ= 0.777) and concordance was poor (CCC = 0.304). Similar results were observed for Lab B (ρ= 0.793, c = 0.330) and Lab C (ρ= 0.758, CCC = 0.248).

Conclusion. Despite using a similar LDT, viral load equivalence to the FDA-approved assay varies among clinical laboratories, possibly due to differences in patient population and other aspects of viral load testing. Understanding factors that contribute to these variations will optimize the ongoing efforts of standardizing testing for CMV viral load.

Disclosures. **All authors:** No reported disclosures.

1427. High specificity of OraQuick® rapid HIV-1/2 antibody testing during dengue infection

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Background. OraQuick® is a rapid test with high specificity demonstrated in non-dengue endemic settings. However reports of false positive OraQuick® results in the context of dengue infection suggest poor specificity in settings where dengue and HIV co-exist, home to 2.5 billion people. We performed a cross-sectional study across three Singapore hospitals to assess the specificity of OraQuick® for HIV-1/2 antibody detection in patients with dengue infection.

Methods. Adult participants meeting WHO 2009 criteria for probable dengue (fever >37.5°C plus two other clinical or haematological criteria) were identified at hospital outpatient clinics from April 2012-July 2013. Eligible participants were asked to give informed consent to complete a questionnaire on HIV risk factors as well as HIV-1/2 antibody testing by OraQuick® and HIV-1 RNA testing by PCR. Other laboratory data were collected from electronic health records contemporaneously. Dengue testing was by Dengue Duo NS1Ag + Ab Combo kits. Confirmed dengue was defined as NS1-positive and probable dengue as IgM-positive.

Results. Of 152 eligible patients, 82 consented to inclusion in the study. Fifty-two of these had dengue; 43 confirmed and 9 probable cases. The mean age was 38.6 years and 38 (73%) were male. Forty-five (86.5%) were Chinese and three were Indian and Malay (5.8% each). The mean duration of fever at presentation was 5.8 days (range 1 to 14). Thrombocytopenia (23/51, 54.9%), leucopenia (49/51, 96.1%) and transaminitis (16/20, 80%)were common. Thirty-three had been sexually active in the last month, all with opposite sex partners, and eleven without a condom. All patients with dengue had a negative OraQuick® result corresponding to a specificity of 100%. HIV-1 RNA was not detected by PCR in any of the specimens. OraQuick® test kits were a mean 656 days from their expiry date at the time of use (range 477 to 764 days, IQR 603 to 728 days).

Conclusion. OraQuick® has high specificity in the context of dengue infection. It can be used to exclude HIV-associated illness as a cause of fever in dengue endemic settings. It should be noted that there are insufficient data in this study to assess the sensitivity of OraQuick® for acute HIV.

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1428. Impact of Rapid Influenza PCR Testing on Inpatient Clinical Outcomes

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Background. Early diagnosis of influenza leads to improved infection control and early initiation of antiviral therapy. Rapid antigen testing is limited by poor sensitivity. Few data exist to evaluate the effect of rapid polymerase chain reaction (PCR) testing on patient outcomes.

Methods. A retrospective cohort study of 150 consecutive hospitalized patients from two respiratory viral seasons was performed using chart review to compare baseline sociodemographic characteristics as well as clinical outcomes before (Season 1: 2012) and after (Season 2: 2013) implementation of a rapid RSV/influenza PCR test vs previous send out PCR testing at the University of Washington and Harborview Medical Centers.

Results. The majority of hospitalized patients with testing performed had comorbid conditions, including 73 (24%) with underlying pulmonary disease. A total of 156 (52%) patients reported influenza vaccination. Influenza was detected in 9 (6%) patients in Season 1 and 31 (21%) in Season 2. The median time between sample collection and reporting of results in Season 1 was 28 vs 2 hours in Season 2 ($P < 0.001$). In Season 2, empiric therapy with oseltamivir was more likely to be initiated (42% in Season 1 vs 59% in Season 2; $P = 0.004$), and antiviral duration was shorter in patients who were influenza negative (1.4 days in Season 1 vs 0.73 days in Season 2; $P = 0.05$) compared to Season 1. No difference was found in hospitalization duration (11 days vs 12 days; $P = 0.56$) or antibiotic use (83% vs 81%; $P = 0.55$) between the two seasons.

Conclusion. Despite a significant decrease in time to result with the implementation of rapid influenza PCR testing, no difference was observed in frequency of antibiotic use or duration of hospitalization. Initiation of oseltamivir was more frequent though overall duration of antiviral therapy was shorter in patients who tested influenza negative by rapid testing in Season 2. This suggests that unnecessary antiviral use may be decreased with implementation of rapid testing for influenza in an inpatient setting.

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1429. Nasopharyngeal Carriage of Potential Bacterial and Viral Pathogens in Hospitalized Patients with Respiratory Symptoms

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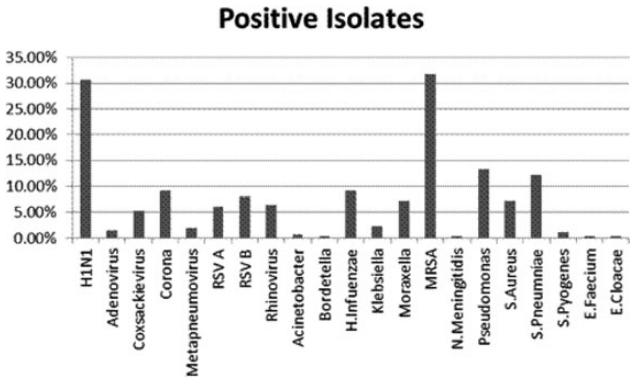
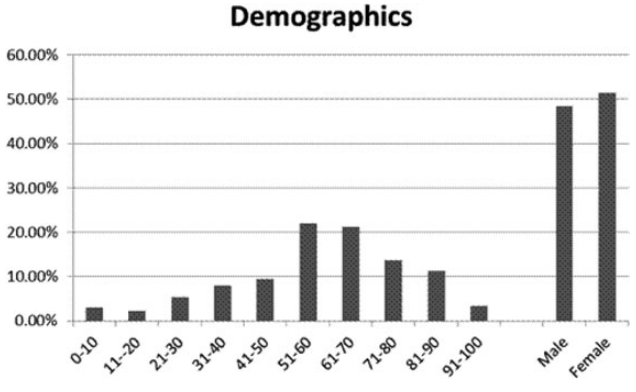
Background. To determine the frequency of detecting potentially pathogenic bacterial and viral gene targets in respiratory specimens collected from symptomatic patients during the 2013-2014 influenza season.

Methods. A retrospective study involving 264 hospitalized patients with respiratory symptoms. Respiratory samples were obtained and screened for 22 different viruses, 16 bacteria, and 5 genetic drug resistance targets using a Target Enriched Multiplex Polymerase Chain Reaction.

Results. We enrolled 264 hospitalized patients. Age range of 1-100 years with mean age of 57 years, 48.5 % male and 51.5 % females, 25% had both viral and bacterial gene targets detected while 17% had more than one bacterial target detected and 9% had more than one viral target detected. Positive viral targets were found in 57.2% subjects, of these: 54% were H1N1, 24.5% RSV, 11.2% rhinovirus, 15.9% coronavirus, and 9.3% Coxsackie virus. Positive bacterial targets were found in 65%, majority of which were *Staphylococcus aureus* (60%), *Moraxella* (11%), *Pseudomonas* (20%), *Streptococcus Pneumoniae* (19%) and *Hemophilus Influenzae (14%)*. MRSA accounted for 81.5 % of *S. aureus* and 12 % of those were PVL gene positive. Positive H1N1 samples were found in 30.68% subjects. Of all the H1N1 positive subjects; 59 % were females, 23 % were 51-60, 22% were 61-70 and 16% were 31-40 years. Of all the MRSA positive, 58 % were females, 32% were 61-70. 17% were 51-60, 14% were 71-80 and 11% were 81-90 years. Of all the H1N1 positive patients 25 % had co detection of MRSA, 9 % *Pseudomonas* and 11% *Streptococcus Pneumoniae*. Out of the co positive bacterial isolates 17% had co detection of MRSA and *Pseudomonas*. Out of the co positive viral isolates 16% had co detection of H1N1 and Rhinovirus





Conclusion. Hospitalized patients with respiratory symptoms admitted during the influenza season 2013-2014 showed high rate of H1N1 detected of 30%, it showed co-detection of viral and bacterial targets, female were more commonly infected . Those with other viral infection were commonly RSV and coronavirus. Detection of MRSA target was high in our patient population whether been carrier or infected. H1N1 and MRSA were detected more common in elderly.

Disclosures. **All authors:** No reported disclosures.

1430. Development of Qualitative HCV RNA Testing on Dried Blood Spots as an Adjunct Screening Tool to Identify Active Hepatitis C Infection

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Background. Tackling hepatitis C infection has been identified as a strategic priority for Public Health England. Increased awareness, testing and referral for treatment are among the initiatives introduced as part of a public health strategy. The use of rapid tests among persons at increased risk of HCV infection is currently advocated to facilitate enhanced surveillance. Screening with dried blood spots (DBS), using finger-prick capillary blood, combines ease of testing in a community setting with minimum sample requirement and therefore is an ideal tool for those who are difficult to bleed or refuse venepuncture.

Methods. Screening for blood borne viruses using DBS was developed in our laboratory to test individuals from high risk populations, including prisoners. Blood spots were eluted using a specific buffer and tested in semi-automated assays for the presence of hepatitis B surface antigen (HBsAg) as well as antibodies against human immunodeficiency virus (HIV) and hepatitis C virus (HCV). In addition, elution of dried blood spots was modified to allow a qualitative detection of HCV RNA using RT-PCR.

Results. The lower limit of detection for HCV RNA in DBS was determined to be 1 x 10^3IU/mL. Over a six month period from June - November 2013, 5005 individuals were screened for hepatitis C using DBS in an 'opt-in' programme. Of those screened, 537 (10.7%) were found to be HCV antibody positive. In addition, screening for hepatitis C RNA on DBS was done in 458 of these HCV-antibody positive individuals, of which 258 had detectable HCV RNA (62.8%), indicating active infection.

Conclusion. Qualitative detection of HCV RNA from dried blood spots is sensitive enough to be used as an additional screening tool in high risk and difficult-to-reach populations. A positive RNA result indicates active infection and enables

immediate referral of patients for specialist care, thus avoiding delay and possible loss to follow-up of patients that are consequent on having to obtain a second sample.

Disclosures. **All authors:** No reported disclosures.

1431. Comparison of two multiplex PCR techniques for the study of respiratory viruses in Mexican children with pneumonia

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Background. Respiratory tract infections are the main cause of morbidity and mortality worldwide. Diagnostic methods have evolved through time and now there are techniques available to detect multiple viruses in one sample. The aims of the study were to identify respiratory viruses in nasal washings from children younger than 5 years old admitted with pneumonia at 6 hospitals from 6 cities in Mexico and to perform a diagnostic test evaluation between 2 multiplex PCR techniques for the detection of respiratory viruses.

Methods. 310 nasal washings from children younger than 5 years old with clinical and/or radiological diagnosis of pneumonia were included. Nucleic acid was extracted, and amplified by two methods: xTAG RVP (Luminex Molecular Diagnostics, Toronto, Canada) and Anyplex II RV16 (Seegene, Seoul, Corea). The respiratory viruses detected were: RSV A and B, INF A and B, PIV1, 2, 3 and 4, AdV, MpV, CoV OC43, 229E and NL63, RV A/B/C, EV and HBoV1/2/3/4. The gold standard was a construct (the same result with both techniques, and those with discrepancies were sequenced). Virus frequencies, sensitivity, specificity, positive predictive value and negative predictive value were calculated.

Results. The viruses detected were in order of frequency: 43.1% RSV A, 22.9% RV/EV, 7.2% ADV, 6.5% INF A, 3.9% MpV, 2.9% HBoV, 2.6% PIV 3, 2.3% RSV B, 2.3% PIV 4, 2.3% CoV NL63, 1.9% PIV 1, 1.3% PIV 2, 0.9% INF B, 0.9% CoV OC43, 0.6% CoV 229E and 0.3% CoV HKUI.

Overall Anyplex II RV16 had a higher sensitivity (90% vs 78.9%) and specificity (97.4% vs 59.4%) compared to xTAG RVP. Anyplex II RV 16 was more sensitive in detecting AdV (100% vs 52.2%), INF A (83.3% vs 53.3%), RSV A (97.8% vs 69.9%) and CoV OC45/HUK1 (100% vs 50%) compared to xTAG RVP, respectively. xTAG RVP was more sensitive in detecting PIV (95% vs 80%), RSV B (80% vs 71.4%), RV/EV (86.9% vs 83.1%) and MpV (90% vs 83.3%) compared to Anyplex II RV 16, respectively.

Conclusion. The 3 most frequent pathogens detected in children with pneumonia were RSV, RV and PIV (1/2/3/4). Overall, Anyplex II RV16 had a higher sensitivity and specificity than xTAG RVP for the diagnosis of multiple respiratory viruses. Although, xTAX RVP is more sensitive to detect PIV, RSV B, RV and MpV.

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1432. Diagnostic Performance of a Multiplex PCR Assay for Meningitis in an HIV-Infected Population in Uganda

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Background. Meningitis remains a worldwide problem, and rapid diagnosis is essential to optimize survival. Delay in diagnosis leads to excess morbidity, mortality and healthcare costs related to unnecessary empiric treatment and isolation procedures.

Methods. From January-April 2014, cerebrospinal fluid (CSF) from 39 HIV-infected persons with suspected meningitis in Kampala, Uganda was collected at time of diagnosis (n = 18) and among persons with cryptococcal meningitis at therapeutic lumbar punctures (n = 53). Standard bacterial, mycobacterial and fungal CSF diagnostics were performed on site. Cryopreserved CSF specimens (200 mcL) were then analyzed on the FilmArray™ System using a Meningitis/Encephalitis PCR panel (BioFire Diagnostics, Salt Lake City, UT; research use only). The panel targets 16 common pathogens: 6 bacterial, 8 viral, and *Cryptococcus neoformans/gattii* speciation. Operators were blinded to microbiology results. We assessed the diagnostic performance of the panel.

Results. The FilmArray™ multiplex PCR panel detected *Cryptococcus* in the CSF of all patients diagnosed with a first episode of cryptococcal meningitis by quantitative fungal cultures (n = 14) with 100% sensitivity and specificity. In second episodes, the FilmArray™ system was able to differentiate between fungal relapse (n = 2) vs paradoxical immune reconstitution syndrome (IRIS) and/or sterile cultures (n = 4). In patients receiving antifungal therapy, FilmArray™ predicted follow up culture sterility with 67% negative predictive value. The first possible case of *C. gattii* meningitis in Uganda was detected. EBV was frequently detected in this HIV-infected population regardless of whether or not they had active cryptococcal infection [77% with (n = 35) and 100% without (n = 4) cryptococcosis]. Other pathogens detected included CMV (n = 3), HSV-2 (n = 2), HHV-6 (n = 2), VZV (n = 1), *Streptococcus pneumoniae* (n = 1).

Conclusion. The FilmArray™ multiplex PCR panel offers a promising platform for the rapid diagnosis of CNS infections. PCR testing appears to be particularly useful in cryptococcal disease, distinguishing species, predicting culture sterility, and differentiating IRIS from culture-positive cryptococcal relapse in patients with recurrent symptoms.

Disclosures. **J. Cloud**, BioFire Diagnostics, LLC: Employee, Salary **A. Hemmert**, BioFire Diagnostics: Employee, Salary **S. Bellamkonda**, BioFire Diagnostics, LLC: Employee, Salary **C. Oswald**, BioFire Diagnostics, LLC: Employee, Salary **E. Lo**, BioFire Diagnostics, LLC: Employee, Salary

1433. Diagnosis of Latent Histoplasmosis Using Interferon-γ Release Assays

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Background. Histoplasmosis is the most common endemic mycosis in the US. Infection is often mild in healthy individuals, in part due to effective interferon-gamma (INFγ) Th1 immune response. In those with immune suppression (organ transplantation or TNFa inhibition), reactivation infection can be severe or fatal. We hypothesize that development of better methods to diagnose latent histoplasmosis will enable development of better prevention and treatment strategies. Here, we present proof-of-concept that latent histoplasmosis can be diagnosed by INFγ-release assays (IGRA), similar to recent advances with TB diagnostics.

Methods. Healthy volunteers from endemic areas with and without known latent histoplasmosis were recruited to provide blood as potential cases and controls. Peripheral blood mononuclear cells (PBMCs) were harvested, separated, counted and used in assays to measure IFNγ release after exposure to multiple *Histoplasma* antigen preparations, using ELISA and ELISpot, with phytohemagglutinin (PHA) as a positive control. Antigen-specific spot-forming units or concentration of IFNγ (pg/mL) were calculated for cells tested. One volunteer with known latent histoplasmosis had a very robust response and was used for optimization and reproducibility studies.

Results. Screening of volunteers identified PBMCs from 2 cases exhibiting robust responses to yeast cell lysate (YCL) from *H. capsulatum* strain G217B, with less response to YCL from a different strain and C-antigen. Assay optimization produced reproducible measurements of approximately 100 spot-forming units/10^5 cells with ELISpot and measureable quantities (25-50 pg/mL) of IFNγ released by ELISA. Positive responses were reproducible with repeated assay and differential blood draws. Controls with no known exposure or latent disease demonstrated no response to *Histoplasma* YCL.

Conclusion. This study provides proof of concept that latent histoplasmosis is detectable by measurement of INFγ expressed in and/or released from reactive T-cells after exposure to *H. capsulatum* antigens. Optimization of such assays could better enable development of IGRAs for diagnosis of latent infection, enabling therapeutic strategies to prevent reactivation of histoplasmosis in individuals with impending immune suppression.

Disclosures. **K. A. Marr**, Astellas: Consultant and Scientific Advisor, Consulting fee; Merck: Consultant, Consulting fee; Pfizer: Consultant, Consulting fee

1434. Clinical Effectiveness of Fungal Blood Cultures: A 10-year Retrospective Analysis

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Background. Invasive fungal infections cause substantial morbidity and mortality. Fungal specific blood cultures have been proven effective in isolating fungal isolates but their clinical impact is unclear. This study evaluates the clinical utility of fungal blood cultures in an integrated healthcare network of 22 hospitals over a 10 year period.

Methods. Intermountain healthcare (IHC) has used the BACTEC MYCO/F Lytic fungal blood culture bottle in acute care settings for the past 10 years. IHC's electronic data warehouse was used to identify all fungal blood cultures performed from 2004 through 2013. Results of standard blood cultures (BACTEC Plus Aerobic/F) performed within 7 days of fungal cultures were obtained for the same time period. Positive fungal blood cultures were considered 'matched' if standard blood cultures grew the same organism or 'unmatched' if standard cultures were performed and did not grow the same organism.

Results. From 2004 through 2013, 7,759 fungal blood cultures were performed. Ordering of fungal blood cultures tripled from 407 cultures in 2004 to 1193 cultures in 2013. Of the 7,759 fungal blood cultures, 97 were positive for fungal species (1.25%), representing 64 unique infection episodes; 42 matched cases and 22 unmatched cases. *Candida sp.* made up similar amounts of matched and unmatched cases (86% and 90%, respectively). Matched cases had on average more concomitant blood cultures performed (8.42 cultures vs 4.46 cultures, $p < 0.01$) within 7 days of the index fungal blood culture. Unmatched Candida cultures were most likely due to sampling variation and not due to culture technique. In the unmatched group, 3 infection episodes were due to non-Candida organisms; 1 was deemed a contaminant, 1 was identified via non-culture techniques, and 1 episode was identified with fungal blood culture.

Conclusion. Over a 10 year period, we found that fungal blood cultures had little impact on clinical care and contributed to the management of only 1 patient. Eliminating the use of fungal blood culture is unlikely to negatively impact patient care and would reduce healthcare cost.

Disclosures. **All authors:** No reported disclosures.

1435. Development and Validation of a Diagnostic Real-time PCR Assay for the Rapid and Accurate Detection of *Pneumocystis jirovecii* from Bronchoalveolar Lavage Fluid Samples

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Background. *Pneumocystis jirovecii* causes severe interstitial pneumonia called Pneumocystis pneumonia (PcP) among immunocompromised patients. Laboratory diagnosis of PcP currently relies on direct microscopic examination of respiratory specimens. The purpose of this study was to develop and validate an in-house PCR Assay for the rapid, reliable, and accurate detection of *Pneumocystis jirovecii* from bronchoalveolar lavage fluid (BALF) samples.

Methods. This study analyzed 92 BALF samples sent to Calgary Laboratory Services (CLS) between May 2011 and September 2012 for detection of *P.jirovecii*. DNA from the BALF samples was subjected to an in-house real-time PCR assay targeting the mitochondrial large subunit ribosomal RNA gene. **Results** were compared to the existing gold standard immunofluorescence assay (IFA) at CLS. Discrepant positive PCR samples were sent to St. Paul's hospital (SPH, Vancouver) for repeat PCR testing through their in-house PCR assay. Test characteristics were re-calculated using a modified gold standard that defined a positive test as one that was positive through both PCR assays in an immunocompromised patient.

Results. Results: 54% of the samples were derived from immunosuppressed patients. The immunosuppressed samples included those with HIV (18%), malignancies (28%), solid-organ transplants (46%), hematopoietic stem cell transplant (4%), and others (4%). 13 of the 92 samples tested positive with the IFA at CLS. The in-house PCR assay identified an additional 7 positive samples, besides confirming the positivity of the previous 13 samples. Using the IFA as the available gold standard, the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of the PCR assay was 100%, 91%, 65%, and 100% respectively. The 7 additional positive samples were subsequently confirmed as true positives through an independent PCR assay at SPH. Using the modified gold standard, the sensitivity, specificity, PPV, and NPV of PCR assay were all 100%. In comparison, the IFA had a sensitivity, specificity, PPV and NPV of 65%, 100%, 100%, and 91%, respectively

Conclusion. The in-house real-time PCR assay aids in the rapid and accurate diagnosis of PcP from BALF samples, with a considerable increase in sensitivity as compared to the currently existing IFA at CLS.

Disclosures. **All authors:** No reported disclosures.

1436. An Optimized Procedure for Extracting DNA from Non- tuberculosis Mycobacteria for Genome-scale Epidemiologic Investigations

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Background. In the U.S., non-tuberculosis Mycobacterium (NTM) lung infections far exceed those caused by *M. tuberculosis*. Due to the technical difficulties inherent in isolating high quality genomic DNA for full genome sequencing of NTM, the availability of whole NTM genomes is severely limited. Our objective was to overcome these burdens by optimizing currently available, but inadequate, extraction protocols and provide more fully sequenced genomes to be used for epidemiologic and pathogenic investigations of NTM.

Methods. All accessible and relevant protocols available in PubMed were examined and tested. Mycobacterium genomic DNA was extracted from cells grown on Lowenstein-Jensen slants at 37°C. Cells were both chemically and mechanically lysed prior to two rounds of phenol- chloroform, followed by chloroform extraction, according to the methods of Kaser *et al,* 2010. DNA was further purified by ethanol precipitation and the Zymoclean DNA clean and concentration kit (Irvine, CA) before quantification, using the Qubit 2.0 florometer (Life Technologies) and sequencing using the Illumina MiSeq sequencing platform.

Results. Sufficient high quality nucleic acid material was extracted and underwent full genome sequencing. Eight draft genomes of clinically relevant NTM isolates were generated in three days. Sequence reads were assembled with Newbler (Roche Diagnostics Corp.; Branford, CT) and comparative genomics were performed using Geneious (Biomatters Lim.; Auckland, New Zealand). All but one isolate were identified as *Mycobacterium abscessus* and carried the *erm* erythromycin resistance gene. Of the eight, one isolate cannot be speciated given its 16S sequence is an identical match to three 16S database sequences, each with unique species designations. All isolates belonged to a different multi-locus sequence type (MLST), indicating that they are not related. None have MLST matches to the only two publically available *M. abscessus* NCBI reference genomes suggesting that they are novel in comparison.

Conclusion. The protocol described herein is accurate, fast, and cost effective for genome scale epidemiology and comparative genomics of NTM. Using it, we doubled the number of whole NTM genomes available in Genebank in less than oneweek.

Disclosures. **All authors:** No reported disclosures.

1437. Utility of Xpert MTB/ RIF (CB-NAAT) for Diagnosis of Tuberculosis in a Tertiary Care Centre in Mumbai, India

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Background. Xpert MTB/ RIF is a fully automated diagnostic test which simultaneously detects tuberculosis and rifampicin drug resistance within few hours. As India is a high TB burden country this can help in appropriate treatment decision on the same day. The test has been strongly recommended by WHO (October 2013) as initial diagnostic test in pulmonary and extrapulmonary (CSF, conditional for lymph node and other tissues) tuberculosis.

Methods. All the specimens from patients suspected to have tuberculosis sent to the laboratory for Mycobacterial smear; culture and XpertMTB/RIF from December 2013 to March 2014 were considered for the study. Culture positivity was considered gold standard for comparison of the results.

Results: A total of 236 specimens - pulmonary (sputum, BAL) and extrapulmonary (lymphnode, CSF, tissues etc.) were received in the laboratory. Of these, 63 (27%) were pulmonary samples and 173 (73%) were extrapulmonary (EP) specimens. Mycobacterium tuberculosis was grown in 16% of pulmonary and 9% of EP specimens by culture. 29% of pulmonary and 12% of EP specimens were positive by XpertMTB/RIF. Among 9(45%) pulmonary and 10(60%) EP specimens; smear was negative but XpertMTB/RIF was positive. Rifampicin resistance was seen among 11% of pulmonary and 38% of EP specimens. Among 3% of EP (CSF, Lymphnode, Liver aspirate) specimens which were smear negative; XpertMTB/RIF showed rifampicin resistance. See the table for sensitivity and specificity of ZN Smear and XpertMTB/RIF.

Sensitivity and Specificity of ZN Smear and XpertMTB/RIF.

	Sensitivity in %	Specificity in %
Smear: Pulmonary	55%	70%
Smear: EP	50%	35%
XpertMTB/RIF Pulmonary	90%	100%
XpertMTB/RIF EP	75%	80%
Smear & XpertMTB/RIF: Pulmonary	100%	100%
Smear & XpertMTB/RIF:EP	86%	80%

Conclusion. Cartridge based XpertMTB/RIF is a useful test for initial screening of both pulmonary and extra pulmonary specimens. Rapid results can help in taking vital treatment decisions.

Disclosures. **All authors:** No reported disclosures.

1438. Detection and Differentiation of *Babesia microti* and Other Pathogenic *Babesia* Species by a Single-Amplicon, Dual-Probe Real-Time PCR Assay

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Background. Babesiosis is an emerging zoonotic disease caused by infections with the apicomplexa, *Babesia*. Babesiosis is most frequently acquired through bites with infected ticks but may also be transmitted through blood transfusion or vertical infection. In the U.S., most human infections are caused by *Babesia microti*, but infections

with *Babesia duncani* (previously WA-1) and the unnamed taxon MO-1 are increasingly recognized. Microscopic examination of blood films, the reference method for diagnosis of babesiosis, is labor intense, only enables genus-level identification, and may pose difficulties distinguishing *Babesia spp.* from *Plasmodium falciparum*. Most available real-time PCRs only detect *Babesia microti*. Thus, we developed a multiplex, real-time PCR for detection and differentiation of *Babesia microti* (channel 1) and other human pathogenic *Babesia spp.* (channel 2).

Methods. A 190bp segment of the 18S rRNA gene (18S) was amplified with a common set of PCR primers and detected by two different probes: (1) *Babesia microti*, (2) other *Babesia spp.* of human relevance. Test performance was established with 39 whole blood specimens from patients with known *B. micro*ti infections diagnosed by microscopy ($n = 8$) and PCR ($n = 31$). Whole blood was also spiked with *B. duncani* organism (ATCC PRA-302) and plasmids covering the 18S target of MO-1, *B. divergens*, and EU-1.

Results. Analytical sensitivity for both channels was between 285-435 copies/mL (8-13 copies/reaction). All positive whole blood samples produced the expected results. Positive patient specimens had a mean of 2.6E + 08 copies/mL (range 2.5E + 03 to 1.2E + 10). No cross-reactivity was observed with 56 other human pathogens, including the 5 relevant *Plasmodium spp.*, *Trypanosoma cruzi,* and *Leishmania infantum*.

Conclusion. The incidence of babesiosis has increased in recent years and previously unrecognized species have been shown to cause human infections. We describe the first multiplex, real-time PCR assay for sensitive detection of all *Babesia* species of known human relevance using an innovative single-amplicon, dual-probe design. Given the highly conserved 18S target, this assay will enable us to identify and monitor circulation of unusual *Babesia* species by subsequent 18S sequencing.

Disclosures. **B. Couturier**, Gen-Probe: Collaborator, Kits supplied for study **R. Schlaberg**, Epoch Biosciences: Collaborator, Research reagents

1439. Clinical Correlation between CLSI vs EUCAST Criteria of *Candida* Species in Military Trauma Patients

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Background. *Candida* is associated with infection and high mortality in combat-related injured patients. This study clarifies *Candida spp.*distribution, susceptibility patterns compared between CLSI and EUCAST criteria, risk factors for resistance, and outcomes by non-susceptibility (NS) status in a military trauma population.

Methods. We utilized all initial unique and serial (≥ 7days between same species) *Candida* isolates collected as part of the Trauma Infectious Disease Outcome Study (June 2009-October 2013). Sensititre YeastOne[R] (YO-9) plates were used for broth microdilution susceptibility testing. Demographic and trauma-related data, source of *Candida* isolate, infection vs colonization, and antifungal exposures before initial and between serial isolates were obtained. Susceptibilities were defined by CLSI and EUCAST criteria.

Results. 127 patients with 131 unique *Candida* isolates were included. There were 102 (78%) *C. albicans* (*Ca*) and 29 (22%) non-albicans isolates: 10 *C. tropicalis (Ct)*, 7 *C. glabrata (Cg)*, 6 *C. parapsilosis (Cp),* 2 *C. dubliensis* and *C. lusitaniae*, and 1 *C. kefyr* (*Ck*) and *C. pelliculosa (Ce)*. Source of isolate included 63 (48%) pulmonary, 37 (28%) wound, 17 (13%) blood, 9 (7%) other, and 5 (4%) intra-abdominal. By CLSI, 6 isolates were NS: 1 *Ct* resistant (R) to anidulafungin (AF) and fluconazole (FC) and intermediate (I) to micafungin (MF) and caspofungin, 2 *Cg* R to itraconazole and FC, and 1 *Ck* R to amphotericin. NS by CLSI was associated with non-albicans spp. ($p < 0.05$). By EUCAST, 68 (52%) isolates were NS: 52 R (44 *Ca,* 1 *Cg,* and 7 *Ct*), 6 I to AF and MF (all *Cp*), 9 R to posaconazole (all *Ct*), 1 R to voriconazole (*Ct*), 4 R (2 *Cg,* 1 *Ce*, 1 *Ct*) and 6 I to FC (5 *Cg*, 1 *Ct*). In univariate analysis EUCAST NS was associated with infection, non-albicans spp., mold infection, wound site, prior antifungal exposure, and less time between culture and death. In multivariate analysis, only mold infection, non-albicans spp., and prior antifungal exposure remained significant. NS by CLSI, EUCAST, and discordance between CLSI and EUCAST interpretations were not associated with death or infection.

Conclusion. CLSI and EUCAST breakpoints offer different interpretations of susceptibility patterns, especially for echinocandins, without evidence of difference in infection rates or mortality.

Disclosures. **All authors:** No reported disclosures.

1440. Central Venous Catheter Retention and Mortality in Children with Candidemia: A Retrospective Cohort Analysis

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Background. Candidemia causes significant morbidity and mortality among hospitalized children. Prompt removal of a central venous catheter (CVC) is often recommended for adults with candidemia to decrease the likelihood of persistent and metastatic infection, but pediatric specific data are limited. We investigated the association of CVC retention and 30-day all cause mortality in a pediatric specific cohort.

Methods. We performed a retrospective cohort study of inpatients (age 0 to <19 years) with candidemia at the Children's Hospital of Philadelphia between 2,000 and 2012 who had survived and retained their CVC at least one day beyond the blood culture being positive for yeast. A structured data collection instrument was used to retrieve clinical and laboratory data. A discrete time failure model was used to assess the association of CVC retention and 30-day all cause mortality. CVC exposure was not considered until the day after the culture was known to be positive for a *Candida* species. We adjusted for age and the complexity of clinical care prior to onset of candidemia. Complexity of clinical care included recent exposure to immune suppressive agents, recent requirement for parenteral nutrition, and admission to the ICU at time of blood culture.

Results. Of the 436 incident cases of candidemia, 289 (64%) had a CVC in place at the time of blood culture and survived at least one day after candidemia onset. Among these 289 patients, 30 (10%) died within 30 days of candidemia diagnosis. CVC retention was significantly associated with an increased risk of death on a given day (OR: 2.53, 95% CI: 1.07 to 5.98).

Conclusion. Retention of a CVC was associated with an increased risk of death after adjusting for age and complexity of care at candidemia onset. These results need to be interpreted with caution, as there is likely persistence of unmeasured confounding. However, given the negative association between catheter retention and death, our data suggest that early CVC removal should be strongly considered in pediatric patients with candidemia.

Disclosures. **T. Zaoutis**, Merck: Investigator, Research grant, Consultant, Consulting fee; Pfizer: Consultant, Consulting fee; Astellas: Consultant, Consulting fee

1441. Risk factors and Treatment outcomes of Candida Ocular Infection in Candidemia Patients: Analysis of 845 cases over a 15-year period

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Background. The incidence of hospital-acquired candidemia has risen dramatically during the last few decades. Among the complications of invasive candidiasis, ocular involvement in candidiasis is one of the devasting complications because of blindness. The aim of this study was to find out the incidence, clinical presentation and risk factors of candida ocular infection.

Methods. We conducted a retrospective case review of all patient with candidemia who had ophthalmologic examination from July 1998 to August 2013. Ocular involvement of candida defined as *candida* chorioretinitis and endophthalmitis. *Candida* chorioretinitis is retina and choroid involvement without vitreal involvement. *Candida* endophthalmitis defined as chorioretinitis with extension into the vitreous with characteristic fluffy balls. Severe visual loss was defined as visual acuity which was checked less than 0.1, moderate visual loss was defined less than 0.5. Group of candida ocular infection was compared with non-involvement group.

Results. We studied 845 patients with candidemia. Of 845 patients, 77 had ophthalmologic examination. Ocular candidiasis was diagnosed in 16 patients (16/77, 20.7%) and endopthalmitis (n = 5) or chorioretinitis (n = 11). *Candida albicans* (13, 81.3%) was the most frequent microorganism in ocular candidiasis. 4 (13.8%) eyes had severe visual loss and 11 (37.9%) eyes had moderate visual loss. Visual loss were occurred in 7 (7/21, 33.3%) eyes in chorioretinitis and 8 (8/8, 100%) eyes in endophthalmitis. In an univariate analysis, neutropenia, parenteral nutrition, catheter related blood stream infection, time to start treatment > 72hr and *c. albicans* were risk factors for candida ocular infection ($P = 0.004$, $P = 0.03$, $P = 0.011$, $P = 0.028$ and $P = 0.045$ respectively). In a multivariate analysis, neutropenia, parenteral neutrition and catheter related blood stream infection were significantly associated with candida ocular infection ($P = 0.007$, $P = 0.038$, $P = 0.017$ and $P = 0.048$ respectively).

Conclusion. Candida ocular infection occurred in 20.7% of patients with candidemia. High rate of moderate to severe visual loss were shown in this study (15 of 29, 51.7% per eye). Neutropenia, parenteral neutrition and catheter related blood stream infection were significant risk factors of candida ocular infection.

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1442. Clinical Epidemiology of *Candida* Colonization and Infection in Military Trauma Patients from Iraq and Afghanistan

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Background. Combat-related injured patients have high rates of mold wound infections (MWI) with mortality rates of 7.8%. This is the first study to examine the risk factors, epidemiology, and outcomes of *Candida* infections and colonization in US military patients injured in Iraq and Afghanistan.

Methods. Between June 2009-May 2013, from a population of 5,694 patients from the Trauma Infectious Disease Outcome Study (TIDOS), all initial unique and serial (≥7 days between same species) *Candida* isolates were included. Clinical information associated with *Candida* isolates was evaluated.

Results. 127 (2%) patients with 131 unique *Candida* isolates were included. 99% of patients were male with a median age of 23 and an infection severity score (ISS) of 22. 90 (71%) injuries were due to explosive device blasts, 22 (17%) to gunshot wounds (GSW) and 89% of patients were initially hospitalized in Afghanistan. There was a median of 7 days (minimum-maximum, 1-127) from injury to initial *Candida* isolate. 102 (78%) of unique isolates were *C. albicans*. The 29 (22%) non-albicans isolates included 10 *C. tropicalis*, 7 *C. glabrata*, and 6 *C. parapsilosis*. Isolation of non-albicans *Candida* spp. was associated with prior antifungal exposure, blood isolates (BI), and wound isolates (WI) in multivariate analysis ($p < 0.01$). 74 (56%) isolates were associated with infection [32 WI, 16 BI, 17 pulmonary (PI), 4 intra-abdominal (IA), 5 other] while 57 (44%) isolates were colonizers (5 WI, 1 IV-catheter, 46 PI, 1 IA, 4 other). Only 7 of 127 patients had recurrent *Candida* of the same species cultured ≥7 days after initial isolation, including 6 *C. albicans* (3 serial WI, 1 serial IA isolate, 1 IA followed by WI, and 1 BI followed by WI) and 1 had *C. parapsilosis* from a WI followed by BI. Patients with *Candida* isolation had a 7.1% mortality rate compared with 1.4% from the overall TIDOS population. There was no attributable mortality to *Candida* infection. 20% also had mold infection and 21% multidrug-resistant bacterial infection which were not significantly associated with death.

Conclusion. Military trauma patients have high rates of *Candida* infection and colonization. While this is not associated with attributable mortality, its presence is associated with a similar mortality rate to invasive MWI.

Disclosures. **All authors:** No reported disclosures.

1443. Candida Bloodstream Infection in Left Ventricular Assist Device Recipients

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Background. Left ventricular assist devices (LVADs) are being increasingly used as bridge-to-transplant and destination therapy for end-stage heart failure that is refractory to medical management. Fungal infections, especially due to Candida species, are uncommon in LVAD recipients but require special consideration in regards to management interventions.There is limited data on clinical presentation and outcome of infections due to Candida species in LVAD recipients.

Methods. We retrospectively reviewed hospital records of 247 patients who underwent LVAD implantation at Mayo Clinic campuses in Minnesota, Arizona and Florida, from January 2005 to December 2011. Demographic and clinical data of patients that developed infection due to Candida species were extracted.

Results. Of the 247 patients with LVADs, 7 (2.83%) developed infection with Candida species. The median age of seven patients was 70 years (range, 53-75 years). All patients presented with Candida blood stream infection (BSI).

The causative Candida species included C. albicans (5)and C. glabrata (2).

One patient underwent LVAD exchange and two patients underwent heart transplantation. Five of the seven BSI were non-LVAD-related, one was LVAD-related, and one was associated with LVAD pump/cannula infection. Patients received intravenous fluconazole (1), caspofungin (2), amphotericin (1), anidulafungin (1) and a combination of caspofungin and fluconazole (2). The average duration of anti-fungal therapy was 4.24 weeks (range, 1week to 8.5 weeks). Two patients received lifelong antifungal suppression with oral fluconazole.

Only two of the patients were alive (both had undergone orthoptic heart transplant). Average survival in this cohort of LVAD recipients with Candida BSI was 6 months (0.3 -10.5 months) from the time of candidemia.

Conclusion. Despite non-LVAD source of BSI in majority of cases, candidemia in LVAD recipients portends poor long-term survival. Only patients who had undergone heart transplantation survived beyond 6 months

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1444. Comparative effectiveness of fungicidal vs fungistatic therapies for the treatment of pediatric candidemia

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Background. Patient-level review of adult clinical trial data concluded that echinocandin therapy for treatment of candidemia was associated with a decreased mortality rate. Limited data are available comparing options for systemic antifungal therapy in children. We compared the effectiveness of fungicidal vs fungistatic agents as definitive therapy for pediatric candidemia on 30-day all-cause mortality.

Methods. All pediatric inpatients (> 6 months and <19 years of age) diagnosed with candidemia between 2000 and 2012 at the Children's Hospital of Philadelphia were retrospectively identified. Clinical and laboratory data were abstracted using a structured data collection tool. Candidemic patients were included in the final data analysis if they received the same antifungal agent for two consecutive days following candidemia onset. Amphotericin products and echinocandins were categorized as fungicidal and fluconazole as fungistatic. A propensity score model was used to generate inverse probability weights for receiving a fungicidal agent. These inverse weights were included in a weighted logistic regression model to compare 30-day mortality in fungicidal vs fungistatic recipients.

Results. Among 203 children with candidemia that received the same antifungal agent for two consecutive days after culture was known positive, 151 (74.4%) received either amphotericin (n = 134) or caspofungin (n = 17) and 52 (25.6%) received fluconazole. Overall, 18 (8.9%) patients died within 30 days. In the weighted logistic regression model there was no statistically significant difference in mortality between patients that started on a fungicidal agent as compared to fungistatic therapy (OR: 2.19, 95% CI: 0.42 to 11.48).

Conclusion. In a propensity score weighted model, initiation of definitive therapy with a fungicidal agent did not result in a significant decrease in 30-day mortality. These data suggest that both fungicidal and fungistatic agents can be considered as definitive therapy for pediatric candidemia. The results should be interpreted with caution given the small sample size and resultant wide confidence intervals. Larger pediatric cohort studies are needed to further compare antifungal therapeutic options and outcomes.

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1445. T-Cell Exhaustion in *Candida* Blood Stream Infections

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Background. Despite appropriate therapy, *Candida* Blood Stream Infections (CBSI) are still associated with a mortality rate of 39%, much higher than most bacterial infections. Clinical trials of antifungal prophylaxis in high risk patients in intensive care have not shown it to be effective. In animal models, immune exhaustion has been implicated in worse outcomes of invasive infection. Use of immunomodulators that reverse the immune exhaustion can improved survival from CBSI in animal models. We examined the possibility that immune exhaustion may contribute to *Candida*infection in humans.

Methods. Patients were included in the study if they had a CBSI. Control subjects were patients who were admitted to the intensive care unit following trauma or major surgery who did not have fungal infections. Exclusion criteria for both groups were coinfection with HIV, Hepatitis B or C, use of high dose immunosuppressives, age <18 years, hematologic malignancy, and lymphocyte count less than 100 cells/ microliter X 10^3. Blood was collected and analyzed via flow cytometry for expression of cytokines, including CD28, PD-1, PDL-1 and IL-7.

Results. 14 patients with a CBSI, and 9 control patients were studied. The CD4-positive T cells from patients with CBSI were less likely than controls to express CD28, an important costimulator for T cell activation, (58% vs 84%, $P = 0.01$). In addition, CD8 positive T cells from patients with CBSI were more likely to express PD-1 (32.4% vs 21.2, $P = 0.04$), and PDL-1 (18.2% vs 3.0%, $p > 0.01$); this combination of cell surface marker expression is associated with cell exhaustion and eventually apoptosis. PDL-1 expression in CD4 positive T cells was also increased but it was not statistically significant (15.9% vs 6.7%, p= 0.44). IL-7 expression also appears to be reduced in CD4 and CD8 positive cells from patients with CBSI but that was not statistically significant in our preliminary data (P values of 0.27 and 0.15, respectively).

Conclusion. These findings are consistent with an immunosuppressive phenotype in immune effector cells in patients with CBSI. Combined with previous animal data, this suggests that T cell exhaustion may be an important feature of CBSI and raises the possibility that blocking T-cell exhaustion could lead to improved outcomes in invasive candidal infections.

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1446. Fungemia due to Uncommon *Candida* species in Patients with Cancer: Increasing Incidence, Frequent Resistance and High Mortality rates

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Background. Bloodstream infections (BSI) with uncommon *Candida* species (UCspp: other than *albicans, glabrata, krusei, parapsilosis*, *tropicalis*) in cancer patients are not well-characterized. We evaluated the epidemiology and *in-vitro* susceptibility patterns, as well as factors associated with all-cause mortality.

Methods. We identified all episodes of BSI due to UCspp between 1998 and 2013 in our cancer center. Electronic medical records were reviewed for demographic, clinical, laboratory data and all-cause mortality.

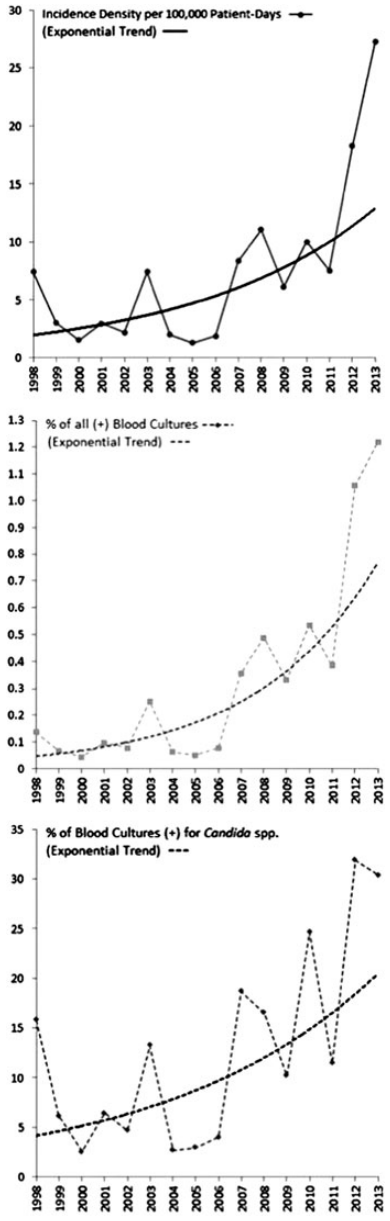

Figure 1: Increasing incidence of BSI from UCspp in cancer patients

Results. *Candida* species were isolated from 1,395 blood culture specimens during the study period; of those, 191 (68 patients) were due to UCspp. The overall incidence-density was 7.4 episodes per 100,000 patient-days. The incidence of BSI from UCspp and their proportion relative to all positive blood cultures and all episodes of candidemia increased significantly between 1998 and 2013 (Incidence density, Poisson-regression for trend $P < .0001$; Proportion, Cochran-Armitage for trend $P < .0001$, Figure 1). Forty-two patients had leukemia (62%) and 43 (63%) were neutropenic (ANC < 500/mcL). *C. guilliermondii* was the most common species isolated (28, 41%), followed by *C. lusitaniae* (19, 28%), *C. kefyr* (13, 19%), *C. famata* (7, 10%), and *C. dublinensis* (1, 1.5%). Thirty-seven patients (54%) had an intra-abdominal source (recent abdominal surgery, peritonitis, gastrointestinal GVHD, or biliary sepsis). Thirty-seven patients (54%) had breakthrough infections, most frequently while being treated with an echinocandin (21 patients, 57%). *C. kefyr* (82%) and *C. lusitaniae* (21%) isolates frequently had caspofungin MICs above the epidemiological cutoff values. *C. guilliermondii* was more frequently resistant to voriconazole (24%) than other species. The crude 30-day mortality rate was 59% and was significantly associated with ICU stay on the date of candidemia (adjusted hazard ratio [aHR] 4), persistent (>7 days, not recovered) neutropenia (aHR 3), and high APACHE II score (aHR 2.8).

Conclusion. The incidence of BSI from UCspp is increasing in patients with cancer. Uncommon *Candida* species are frequently resistant to azoles and echinocandins, and associated with breakthrough infections and high mortality rates.

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1447. Intra-abdominal Candidiasis: Description of an Under-appreciated Disease and a Case Report of Rapid Diagnosis by Whole Blood T2Candida Assay

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Background. Intra-abdominal candidiasis (IAC) is less well-recognized than candidemia. Diagnosis is made by deep tissue culture. Non-invasive, non-culture assays would improve diagnoses.

Methods. We performed a 2-year, observational study of patients (pts) with proven IAC. T2Candida assay was performed as part of a clinical trial.

Results. IAC was the most common invasive candidiasis (IC) at our center (52% *vs* 35% for candidemia). IAC (n = 122) was primary (spontaneous or dialysis-associated) in 15% of pts. Secondary IAC resulted from surgery (45%), perforation (30%), transmural colitis (16%), and other causes (9%). Pts with post-surgical IAC had procedures of colon (51%), small bowel (24%), liver/biliary (15%) and esophagus (10%). Perforations involved small bowel (63%), G-tube (25%) and colon (11%). Antifungal breakthrough infection occurred in 11%. 50% of pts had abscesses (IAA), 42% peritonitis and 8% peritonitis + IAA. Pathogens were *C. albicans* (58%), *C. glabrata* (23%), *C. parapsilosis* (8%) and *C. tropicalis* (4%); 65% of pts were co-infected with bacteria. Mortality was 23%, and higher for pts with perforation (50% *vs* 11%; p = 0.04). 27% of survivors required prolonged antifungal therapy and/or repeated surgeries. 38% of pts did not initially receive an antifungal agent; 50% of these pts developed persistent IAC, and 20% died. Overall, only 12% of pts had (+) blood culture. Recently, a liver transplant patient with IAA receiving voriconazole prophylaxis was diagnosed with *C. albicans* infection by T2Candida assay, a non-culture, whole blood detection system with limit of detection = 1 CFU/mL. The diagnosis was confirmed 7 days later by culture of surgically-drained IAA fluid. Multiple blood cultures were negative.

Conclusion. IAC was the most common IC at our center, and was associated with high mortality, need for repeated surgeries, and antifungal breakthrough infections. Clinicians could not reliably identify pts who were cured with surgical drainage alone, indicating that all pts require antifungal therapy. Blood cultures have extremely poor sensitivity. The whole blood T2Candida assay may result in more rapid diagnoses and initiation of antifungal therapy against IAC and other types of IC (turn-around ~4 hrs), with low false-positivity.

Disclosures. **C. Clancy**, T2 Biosystems: Investigator, Site investigator in clinical trial; Pfizer: Grant Investigator, Research grant; Merck: Grant Investigator, Research grant; Astellas: Grant Investigator, Research grant **M. H. Nguyen**, Pfizer: Grant Investigator, Research grant; Merck: Grant Investigator, Research grant; Astellas: Grant Investigator, Research grant.

1448. Nosocomial Bloodstream Infections Due to *Candida* spp. at a Tertiary Care Center in Lima, Peru: Species Distribution and Clinical Features

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Background. *Candida* sp. has become one of the major worldwide pathogens in nosocomial bloodstream infections. In recent years, reports from multiple parts in the world show this trend consistently. Our series describes the clinical epidemiology and presentation of candidemia at a Peruvian referral hospital.

Methods. Prospective study at a large tertiary care hospital in Lima, Peru. *Candida* sp. isolates identified by hospital laboratory between July 2012 and December 2013 (18 months) were included in the present study. Microbiological and clinical information was collected for each isolate.

Results. Seventy four episodes of candidemia were reported during the study period. *Candida* was the fourth most common pathogen isolated from blood cultures. The median age of patients with candidemia was 58 years (0–100), and 43 (58.1%)

of them were males. Ten (13.5%) episodes occurred in children (5.4% younger than 1 year, and 8.1% between 1 and 18 years), thirty (40.5%) episodes in adults between 19 and 60 years old, and 34 (45.9%) episodes in elderly subjects. The overall incidence was 1.18 cases per 1,000 admissions. In 69 of 74 isolates, the laboratory identified the species of candida. Non-*albicans* candidas were predominant (69.6%), although *C. albicans* was the most common species (30.4%), followed by *C. tropicalis* (24.6%), *C. parapsilosis* (18.8%), *C. glabrata* (11.6%), *C. guilliermondii*(2.9%). Isolates recovered were most commonly from the ICU (n = 17, 23.1%), followed by cultures from surgical wards (n = 12, 16.9%). Recent surgery (n = 29, 39.2%), and hemodialysis (14, 18.9%) were the most frequent associated conditions, with fever the most common clinical finding in 52 cases (70.3%). Forty-seven cases (63.5%) in this series received antifungal treatment based on blood culture finding. Eleven patients (14.9%) received empirical treatment. The overall 30-day survival was 56.8% (treated subjects, 68.1%; not-treated patients, 37%, p = 0.0094).

Conclusion. Candidemia is a frequent finding in nosocomial bloodstream infection at our institution, a large, urban hospital in a middle income country. The incidence, mortalitiy and species distribution is comparable to that found in other Latin American, North American and European centers. A large proportion of our cases came from non-ÍCU settings, but this is probably related to the low number of ICU beds at this hospital.

Disclosures. **All authors:** No reported disclosures.

1449. Clinical Prediction Model for Candidemia in Pediatric ICU Patients: Failure to Validate

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Background. Candidemia is associated with significant morbidity and mortality and pediatric intensive care unit (PICU) patients with candidemia are at particular high risk for death. A clinical prediction rule for early detection of candidemia in the PICU was previously derived at a single center. Multi-center validation is necessary prior to routine application.

Methods. Patients <19 years of age with candidemia were identified prospectively from six pediatric institutions (January 1, 2005-December 31, 2009). Cases were matched to two controls in the same PICU by incidence density sampling. Conditional logistic regression was performed to evaluate the association of candidemia with the previously derived predictor variables.

Results. Ninety-six patients with candidemia were identified with a median age of 4 years (range 43 days to 18 years) and matched to similar controls. The proportion of predictors of candidemia for cases and controls varied significantly by study site (table) and only the presence of a central venous catheter was associated with candidemia (OR: 9.6; 95% CI: 3.4-27.3).

Conclusion. Our multi-center study did not validate the previously derived prediction rule due to significant variability in predictors across hospitals and time. Consideration should be given to including biomarkers in future prediction rules.

Disclosures. **T. Zaoutis**, Merck: Investigator, Research grant, Consultant, Consulting fee; Pfizer: Consultant, Consulting fee; Astellas: Consultant, Consulting fee

1450. Impact of Body Surface Decolonization on Bacteriuria and Candiduria in a Cluster-Randomized Trial of Intensive Care Units

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Background. Bacteriuria commonly precedes UTI, and is often treated with antibiotics, especially in ICU patients. The impact of body surface decolonization on bacteriuria and candiduria is unknown.

Methods. Secondary analysis of a 3 arm cluster randomized trial of 43 hospitals (74 adult ICUs). Arms included 1) MRSA screening and isolation, 2) targeted decolonization: screening, isolation, and decolonization of MRSA carriers with chlorhexidine (CHG) and mupirocin, and 3) universal decolonization: no screening, all patients decolonized. Protocol included CHG cleansing of the perineum and proximal 6" of urinary catheters. Outcomes included high-level (HL) bacteriuria (>50K colony forming units (CFU)/ml) with uropathogens, HL candiduria (>50K CFU/ml), and any bacteriuria with uropathogens. Gender analyses were pre-specified. Proportional hazards models assessed differences in reductions across arms comparing18-month intervention to a 12-month baseline, clustering by hospital.

Results. There were 48,390 patients in the baseline period; 74,256 patients in the intervention period. Hazard ratios (HR) for HL bacteriuria were 1.02 for screening/isolation, 0.88 for targeted decolonization, and 0.87 for universal decolonization (P = 0.26), with no gender-specific reductions (Men: Screening/isolation: HR = 1.09; targeted decolonization: HR = 1.01; and universal decolonization: HR = 0.78; P = 0.12). HRs for HL candiduria were 1.1 for screening/isolation, 0.99 for targeted decolonization, and 0.83 for universal decolonization (P = 0.05), and was due to reductions in men in the universal decolonization arm (Screening/isolation: HR = 1.21; targeted decolonization: HR = 1.01; and universal decolonization: HR = 0.63; P = 0.02). Bacteriuria with any CFU/ml was also reduced in men in the universal decolonization arm (Screening/isolation: HR = 1.01; targeted decolonization: HR = 1.02; and universal decolonization: HR = 0.74; P = 0.04).

Conclusion. Universal decolonization of ICU patients was associated with significant declines in candiduria and any bacteriuria among men, but not women, in a secondary analysis of a large cluster randomized trial. Reductions in HL bacteriuria were not significant, although similar point estimate reductions were seen in men.

Disclosures. **S. S. Huang**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **E. Septimus**, Sage and Molnlyke: received product, provided product for ABATE study; AHRQ, CDC, NIH: Grant Investigator, Grant recipient **M. K. Hayden**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **K. Kleinman**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **T. Avery**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **J. Moody**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **J. Hickok**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **J. Lankiewicz**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **A. Gombosev**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **R. E. Kaganov**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **K. Haffenreffer**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **J. Jernigan**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **J. Perlin**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product **R. A. Weinstein**, Sage Products: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed Product; Molnlycke: Conducting clinical trial for which contributed product is being provided to participating hospitals, Contributed product

1451. Breakthrough Candidemia in Children on Prophylactic Micafungin

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Background. The echinocandins are the newest class of antifungals approved for prophylaxis and treatment of candidemia and invasive candidiasis. However, no report has described breakthrough candidemia (BC) in children taking prophylactic micafungin (MCFG).

Methods. We identified all patients with candidemia at our institution between January 2008 and April 2014 and conducted a case-control study according to whether patients were on prophylactic MCFG (≥3 doses) or not. Patients' demographics, microbiological data, choice of antifungals, and outcomes were extracted from electronic medical records and statistically analyzed.

Results. There were 26 patients (median age: 48 months, 42% male) with candidemia during study period. Of these patients, 8 patients (median age: 46 months, 38% male) had been on prophylactic MCFG. This represented a breakthrough rate of 2.7% (8/292) during the study period, with a median duration of MCFG administration of 24 days (maximum 274 days). The causative strains of BC were *Candida(C.) parapsilosis* in 7 patients and *Candida* sp. in 1 patient. Minimum inhibitory concentration of MCFG was ≤ 1 μg/ml (susceptible) in all eight isolates. Median duration of MCFG exposure was 19 days (5 – 51 days) prior to the onset of BC. Seven patients (88%) were immunocompromised, including 3 (38%) liver transplant recipients and 1 (12%) allogeneic bone marrow transplant patient. The case control study identified that the use of immunosuppressants including steroids was found to be the only independent factor associated with BC patients (7/8; 88%), compared to non-BC patients (4/18, 22%) ($p = 0.008$, odds ratio 0.041[95%CI 0.004-0.437]). History of transplantation (4/8 [50%] vs 1/18 [6%], $p = 0.020$), and a previous use of antifungals (6/8 [75%] vs 5/18 [28%], $p = 0.038$) were found to be significant by univariate analysis only. Meanwhile, association of *C. parapsilosis* with BC was not statistically significant. (7/8 [88%] vs 8/18 [44%], $p = 0.084$)

Conclusion. The majority of causative strains of BC were *C. parapsilosis* in this study. Immunocompromised patients on immunosuppressants may develop BC caused by MCFG-susceptible strains, even on prophylactic MCFG. Further investigations of patients diagnosed with BC are warranted.

Disclosures. **All authors:** No reported disclosures.

1452. Emergence of Echinocandin and Multi-drug Resistant *Candida glabrata* Bloodstream Infection: Data from a Large Multi-site Population-Based Candidemia Surveillance Program

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Background. *Candida glabrata* (*Cg*) is the second most common cause of candidemia in the United States. Echinocandins are first-line treatment for *Cg* due to substantial resistance to azoles. Echinocandin resistance, concomitant with azole resistance, is concerning due to limited treatment options. We describe the epidemiology of echinocandin-resistant ER and multi-drug resistant (MDR) (resistant to fluconazole and echinocandins) *Cg* using data from a population-based surveillance program.

Methods. CDC's Emerging Infections Program conducts surveillance for candidemia in four metropolitan areas (7.5 million people, 67 hospitals). We identified *Cg* cases occurring during 2008-2014; medical records were reviewed and all isolates underwent broth microdilution antifungal susceptibility testing. We defined ER and MDR *Cg* based on 2012 CLSI MIC breakpoints. Independent risk factors for ER *Cg* were determined by logistic regression.

Results. Of 1,211 cases of *Cg* infection, 55 (4.5%) were ER *Cg,* of which 21 (1.7%) were MDR *Cg*. In 2008, 6 of 167 (3.6%) *Cg* were ER, compared to 16 of 177 (9.0%) in 2013 ($p = 0.003$). Compared to echinocandin-susceptible cases, ER *Cg* cases were more likely to be young (median age: 50 vs 61 years; $p < 0.001$), have received echinocandins in the previous 14 days (10.6% vs 1.4%; $p < 0.001$), have had a prior episode of candidemia (42.6% vs 8.1%; $p < 0.001$), have been hospitalized in the previous 90 days (76.6% vs 57.1%; $p = 0.009$), and have a central line (91.3% vs 74.9%; $p = 0.012$). Previous exposure to echinocandins (OR 9.1, 95% CI 3.6-27.1) and a prior episode of candidemia (OR 6.5, 95% CI 3.6-12.0) remained significantly associated with ER *Cg* in multivariate analyses, which included age as a covariate. Of 55 cases with ER *Cg,* 28 (50.9%) did not have the above-mentioned risk factors; 22 had been hospitalized in the prior 90 days or been admitted from a long-term care facility, leaving 6 (10.9%) without known prior healthcare exposure.

Conclusion. We document the emergence of ER and MDR *Cg*. Previous echinocandin exposure and candidemia episode are important risk factors, although the presence of ER and MDR *Cg* without these exposures suggests possible exogenous acquisition. Microbiology laboratories should consider routine antifungal susceptibility testing of *Cg*.

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1453. Epidemiology of *Candida dubliniensis* in Central Kentucky

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Background. *C. dubliniensis* is an uncommon *Candida* species first identified as causing candidiasis in HIV patients and later found in the oral cavities of patients with diabetes mellitus and cystic fibrosis. During the validation of the Bruker MALDI-TOF system at a tertiary care hospital in Central Kentucky, a more than 5-fold increase in the number of *C. dubliniensis* isolates was noted. Since little is known of the epidemiology of this yeast in the US, this epidemiologic study was initiated.

Methods. This was an IRB approved, retrospective chart review study. This study included all of the patients from whom *Candida*species were isolated from clinical specimens over a one-year period (January - December 2012). Data were also collected using a SUNQUEST Epi report to determine the base-line prevalence of yeasts for 2009 and 2011.

Results. *Candida* species were isolated from a total of 2039 patients from January-December 2012. *C. dubliniensis* was isolated from 56 patients in 2012, compared to only 9 and 11 patients during 2009 and 2011 respectively. The majority (79%) of 2012 isolates of *C. dubliniensis*was isolated from oral/respiratory specimens with 7% being cultured from urine, 5% from stool, 5% from blood and 4% from other specimen types.

In contrast, *C. albicans*was isolated from 1129 patients, representing the predominant yeast for 2012. Forty-five percent were cultured from oral/respiratory sources, 27% from urine, 7% from stool, 3% from blood and 18 % from other specimen types.

During 2012, the distribution of *Candida* species isolated from clinical specimens was 55% *C. albicans*, 25% *C. glabrata*, 8% *C. tropicalis,* 9% other yeast with *C. dubliniensis*representing less than 3% of all yeast isolates detected.

Conclusion. *C. dubliniensis* is more likely to be associated with specimens collected through the mouth (oral/respiratory tract) when compared with *C. albicans* ($p < 0.001$) and may reflect colonization rather than disease. Although the prevalence of *C. dubliniensis* was only 2.7%, this amounted to a 5-fold increase in the number of isolates detected This is likely reflective of improved screening and diagnostic accuracy of the MALDI-TOF instrument during the 2012 validation period, rather than an actual emergence of the organism in Central Kentucky.

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1454. Antifungal Susceptibility Patterns of a Global Collection of Fungal Isolates and Polysorbate-80 Effect on the Susceptibility of the Antifungal Classes

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Background. The importance of antifungal surveillance was highlighted by the increasing resistance among certain species and breakthrough infections. We evaluated 1,846 fungal clinical isolates against 9 antifungals using CLSI reference broth microdilution methods (BMD). Additionally, 1,206 isolates were tested using polysorbate-80 (P-80).

Methods. 1,846 isolates collected in 2013 (31 countries) were tested by CLSI BMD and interpretive criteria. Echinocandins (EC), amphotericin B (AMB) and fluconazole (FLC) were also tested using 0.002% P-80 supplemented broth. Isolates were identified using MALDI-TOF MS and/or DNA sequencing.

Results. EC, AMB and FLC were active against common *Candida* spp. (Table). EC-resistance ranged from 0.0 to 2.8% (anidulafungin for *C. glabrata* [CGLA]). 11.9 and 11.6% of the CGLA and *C. tropicalis* were resistant to FLC, respectively. Two *A. fumigatus* displayed elevated MIC values for itraconazole (≥4 μg/mL). All *C. neoformans*had MIC < epidemiological cutoff values for azoles. P-80 lowered the MIC values for EC for all species, but not for FLC. AMB MIC values were lower and ranges broader (0.03-0.5 μg/mL) when compared with reference BMD (0.5-2 μg/mL).

Organism (no. tested [no. tested with P-80])	MIC/$MEC_{50/90}$ for CLSI BMD (with P-80) Anidulafungin	Caspofungin	Amphotericin B	Fluconazole
C. albicans (712 [475])	0.015/0.06 (≤0.008/≤0.008)	0.03/0.03 (≤0.008/≤0.008)	1/1 (0.06/0.12)	0.12/0.25 (0.25/0.25)
C. glabrata (252 [156])	0.06/0.12 (0.015/0.015)	0.03/0.06 (≤0.008/≤0.008)	1/1 (0.12/0.12)	8/64 (4/32)
C. parapsilosis (215 [149])	2/2 (1/2)	0.25/0.5 (0.06/0.06)	1/1 (0.12/0.25)	1/2 (1/4)
C. tropicalis (155 [90])	0.015/0.03 (≤0.008/≤0.008)	0.03/0.03 (≤0.008/≤0.008)	1/1 (0.06/0.12)	0.5/32 (0.5/1)
C. krusei (49 [29])	0.06/0.06 (0.03/0.03)	0.12/0.25 (0.03/0.03)	1/2 (0.25/0.25)	32/64 (32/64)
A. fumigatus (142 [94])	≤0.008/0.03 (≤0.008/≤0.008)	0.03/0.03 (≤0.008/≤0.008)	2/2 (0.25/0.5)	-/-

Conclusion. EC and azoles were potent against yeasts and moulds. P-80 use broadened MIC ranges for AMB; however, differences in the growth patterns in RPMI + P-80, requirement for new QC ranges and a possible effect in cell growth reported previously in bacteria might be an impediment to the use of P-80 for antifungal BMD testing.

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1455. Histoplasmosis-induced Hemophagocytic Syndrome: A Case Series

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Background. Sparse clinical data exist regarding the course and outcomes of histoplasmosis-associated hemophagocytic lymphohistiocytosis (HLH) in adults. Data from this decade are limited to case reports. The objective of this study is to describe the clinical features, treatment, and outcomes of patients with histoplasmosis-associated (HLH) at our institution in the past decade.

Methods. We performed a retrospective chart review study of all inpatients at Parkland Memorial Hospital diagnosed with HLH associated with *Histoplasma capsulatum* from 2003-2013.

Results. Eleven cases of histoplasmosis-associated HLH over this time period were available for review. 9 of 11 cases were males (82%) with a mean age of 46.8 years. 9 had AIDS with a CD4 <100 cells/mm^3, one was a renal transplant, and the last had no immune compromise. The most frequently seen HLH criteria were splenomegaly (n = 10), fever (n = 10), and a ferritin >500 ng/dL (n = 8). The urine *Histoplasma* antigen was positive in every patient examined (n = 9/11), and most antibodies for *Histoplasma* were positive if checked (n = 4/5). Blood culture and bone marrow yielded the highest positive cultures (64% and 54% respectively). Four of the HIV patients were on HAART at diagnosis. A majority of patients received liposomal amphotericin B during their hospital stay (n = 9) with average duration of treatment being 11 days. Five patients received immunosuppressive treatments during admission, including prednisone and IVIG. Five patients died within 30 days (45.5%), and seven within 90 days (63.6%). Of the 5 patients that received immunosuppression, 4 died (80%), whereas in the group not given additional immunosuppression (n = 5), only 2 died (20%).

Conclusion. We describe the largest case series to date of HLH related to histoplasmosis. Clinicians should consider this diagnosis in HIV+ and other immunocompromised patients in endemic areas with the clinical features described. Histoplasmosis-associated HLH among adults remains a lethal disease of highly immune compromised patients.

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1456. Histoplasmosis in Nonendemic Areas: The HIV Factor

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Background. *Histoplasma capsulatum* is endemic in certain areas of the United States, in Central and South America as well as some parts of Eastern Europe, Africa and Southeast Asia. Histoplasmosis may occur outside endemic areas but at much lower frequency. Miami, Florida, in the US, is not considered an endemic area for histoplasmosis. In our hospital, we care for a large number of patients with Human Immunodeficiency Virus (HIV) infection, and have identified several cases of histoplasmosis.

Methods. Retrospective review of patient's clinical and laboratory records at our institution from October 2003 to March 2012, with diagnosis of HIV infection and histoplasmosis. The diagnosis of histoplasmosis was confirmed by positive cultures and/or positive urine antigen in addition to manifestations of histoplasmosis.

Results. A total of 22 patients met the criteria for the diagnosis of histoplasmosis. We identified 17 (77%) male, and 5 (23%) female patients. Of the 22 case patients, 19 were from Latin America, and 3 from the US. Of the 22 patients, 22 (100%) were also HIV infected, and 11 (50%) have the diagnosis of histoplasmosis within 3 months of their diagnosis with HIV infection. None of these 11 patients were on antiretroviral therapy. Of the 22 patients, 19 (90%) had CD4 count < 50 cells/μL. The most common symptoms were fever in 17 (77%), weight loss in 13 (59%), chills in 11 (50%), cough in 8 (36%), and skin rash in 6 patients (27%). Of the 22 cases, 16 (72%) had positive urine antigen reported; 5 (23%) had positive blood cultures, and the organism was seen in 7 (32%) skin biopsies, 5 (23%) lymph node biopsies, 5 (23%) bone marrow aspirate, and 3 (13%) peripheral smears. Of the 22 patients, 5 (23%) died during the admission, and all have multiple organs involved. Of the 22 patients, 4 (18%) were re-admitted within 24 months the initial diagnosis with relapse of histoplasmosis due to non-compliance with their ARV and/or histoplasmosis therapy. Eleven (25%) were doing well two years after their diagnosis.

Conclusion. Histoplasmosis should be considered in the evaluation of patients with advanced HIV infection in non-endemic areas. Patients diagnosed with histoplasmosis outside the endemic areas should be evaluated for HIV infection. Prompt diagnosis and initiation of therapy should improve outcomes even in patients with advanced disease.

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1457. Febrile Illness at a State Correctional Facility — Illinois, 2013

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Background. On August 29, health authorities were notified that 42 state prison inmates had become ill during the preceding 48 hours, with fever, headache, cough, and dyspnea. A respiratory virus was suspected, and the prison was placed on lockdown. During the following week, 50 additional inmates became ill. We aimed to identify a source and prevent further infections.

Methods. We recommended laboratory testing for viruses, bacteria, and fungi; abstracted medical charts; interviewed inmates and staff; and conducted an environmental assessment. Cases were defined as illness in an inmate, including >2 of the following: temperature >100°F, chills, headache, chest pain, shortness of breath, cough, myalgia, or fatigue with onset after August 12.

Results. Eighty-five inmates met the case definition, three of whom required hospitalization. Testing for 21 viral and bacterial respiratory pathogens was negative. Of the 82 symptomatic inmates who submitted blood or urine, 78 (95%) tested positive for acute histoplasmosis (64 had positive antigen; 69 had positive antibody). Seventy-one of the 78 (91%) were housed in Cellblock X. Two weeks prior to the outbreak, two trees and their root systems directly outside Cellblock X had been removed for security reasons. These trees were roosting sites for some of the thousands of European starlings found nightly within prison grounds.

Conclusion. Acute histoplasmosis can mimic a respiratory virus outbreak and should be considered in endemic areas. Disturbance of soil contaminated with the fungus *Histoplasma capsulatum,* which thrives in soil contaminated with bird droppings, likely aerosolized fungal spores and caused this large outbreak. To decrease the risk for future histoplasmosis cases, the prison should limit starling roosting sites by removing other facility trees without disturbing their roots.

Disclosures. **All authors:** No reported disclosures.

1458. A Multi-center Laboratory Investigation of Coccidioidomycosis Enzyme Immunoassay Reproducibility in Patients with Confirmed Disease and Controls

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Background. Coccidioidomycosis or Valley Fever (VF) is a respiratory fungal infection endemic to the southwestern United States (US) with rising reported incidence rates over the last decade causing public health concern. Arizona VF surveillance is based predominantly on laboratory testing, including enzyme immunoassay (EIA), making VF EIA reproducibility and validity critical for determining disease burden. To evaluate the laboratory reproducibility of VF EIA results, we compared EIA IgM and IgG results from two different manufacturers [Immuno-Mycologics, Inc. – Premier *Coccidioides* EIA (Immy) and Meridian Biosciences, Inc. – *Coccidioides* Antibody EIA (Meridian)] using sera from the same patients divided among three laboratories.

Methods. Serum samples from 150 patients with laboratory (immunodiffusion and/or complement fixation) and clinical evidence of VF and 50 de-identified serum specimens (controls) from healthy individuals without travel to endemic areas, (presumed negative for VF), were blinded and distributed frozen to three laboratories after retrospective selection by the Kern County Department of Public Health. **Results** were analyzed for concordance and percent agreement as a primary outcome. EIA sensitivity and specificity were calculated as secondary outcomes.

Results. Percent agreement for EIA IgM and IgG combined among the three labs was 85.5% for Immy (90% for IgM and 89% for IgG) and 70.5% for Meridian (67% for IgM and 81%, for IgG alone). Of note, Meridian IgM EIA results were positive for 13 of 50 controls in one laboratory. Sensitivity for EIA IgM and IgG combined was 68.5% for Immy and 72.4% for Meridian; specificity was 99.3% for Immy and 91.3% for Meridian.

Conclusion. Percent agreement of EIA IgM and IgG among laboratories varies depending on the brand of EIA test kit used. One laboratory appears to have an increase in false positive EIA IgM results with the Meridian EIA test kit, which might explain reports of decreased specificity associated with the Meridian EIA IgM test kit described in the literature. Further studies looking at differences between laboratory methods for both test kits at different laboratories, including the wash step, are needed to determine the etiology of the discordant results.

Disclosures. **All authors:** No reported disclosures.

1459. Adjunctive Corticosteroid Therapy in the Treatment of Coccidioidal Meningitis

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Background. Coccidioidal meningitis is a morbid condition with severe consequences including stroke or the development of hydrocephalus. Adjunctive corticosteroid therapy has been examined in the treatment of other CNS infections and has shown a survival benefit in the treatment of tuberculous meningitis. We sought to determine if any benefit was observed in those given corticosteroid therapy during treatment of coccidioidomycosis associated cerebrovascular accident (CVA).

Methods. As part of a multicenter retrospective study all patients with coccidioidal meningitis were identified and underwent chart review. Clinical variables including demographic data, patient symptoms and exam findings, serum coccidioidal CF antibody titers, CSF results, and the onset of a CVA attributed to their diagnosis of coccidioidomycosis were abstracted. The use of corticosteroids as adjunctive therapy was included for dose, duration, and the presence of additional CVA symptoms after starting corticosteroids.

Results. One-hundred five patients with coccidioidal meningitis were identified and all were included for analysis. A CVA occurred in 18/105 (17%) patients. Fifteen patients received corticosteroids as adjunctive therapy, while three received only standard antifungal treatment. Dexamethasone was the most commonly prescribed corticosteroid and the majority of patients received 10mg followed by 4mg four times daily (9/15). All three patients without adjunctive therapy experienced a second CVA, while only 1/15 (7%) receiving adjunctive treatment experienced a second CVA. This difference was highly significant (P = 0.0049). There was no difference in time to discharge, AEs, or patient mortality at 90 days.

Conclusion. Adjunctive corticosteroid therapy reduced the rate of recurrent CVA in patients with coccidioidal meningitis and was well tolerated with few adverse events. Those with coccidioidomycosis associated CVA may benefit from a corticosteroid taper.

Disclosures. **B. Spellberg**, GlaxoSmithKline, Adenium, Spero Therapeutics, Anacor, Synthetic Biologics, Novartis: Consultant, Consulting fee **R. H. Johnson**, Astellas Pharma US: Speaker's Bureau, Speaker honorarium; Forest Phamaceuticals: Speaker's Bureau, Speaker honorarium; Pfizer Inc.: Investigator, Research support; Chevron: Grant Investigator, Grant recipient

1460. Disseminated Pericardial *coccidioidomycosis*: A Case Series and Review of the Literature

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Background. Extra pulmonary manifestations of *coccidioidomycosis* have been reported to have an incidence of 4.7% of recognized and 0.2% of total infections. Among these cardiac disease and especially pericardial dissemination has not been well reported in the literature. Five cases of pericardial disease with *coccidioidomycosis* at Kern Medical Center are described.

Methods. We queried Kern Medical Center database of 1771 patients with *coccidioidomycosis* spanning between the years 1992 and 2014. Cases were selected based on an Institutional Review Board approved chart review.

Results. Five cases were encountered. Of the five, four were African American, one was Filipino. The average age was 30.2 ranging from 23 to 52. All patients were male. Three were oil field workers. Tachycardia was present in all cases. The Complement Fixation titers ranged between 1:32 to >1:512 upon presentation. Echocardiography was performed on all which showed ejection fraction ranging between 30% to 75%. Two cases had moderate to large pericardial effusions and both underwent pericardial window placement. Cultures from pericardial fluid were negative. Three cases had constrictive pericarditis of which two underwent pericardiectomy, with one postoperative mortality. Other case was treated medically. Medical treatment on all cases was initiated with lipid preparation of amphotericin B with average duration of 16 weeks followed by azole therapy mainly with posaconazole.

Conclusion. Pericardial *coccidioidomycosis*is a serious form of dissemination with significant risk of morbidity and mortality and requires aggressive multidisciplinary approach and treatment. African American ethnicity and male sex are possible risk factors.

Disclosures. **R. H. Johnson**, Astellas Pharma US: Speaker's Bureau, Speaker honorarium; Forest Phamaceuticals: Speaker's Bureau, Speaker honorarium; Pfizer Inc.: Investigator, Research support; Chevron: Grant Investigator, Grant recipient

1461. Testing of Cerebrospinal Fluid 1,3 Beta-D-Glucan for the Diagnosis of Fungal Meningitis Associated with Contaminated Methylprednisolone Injections

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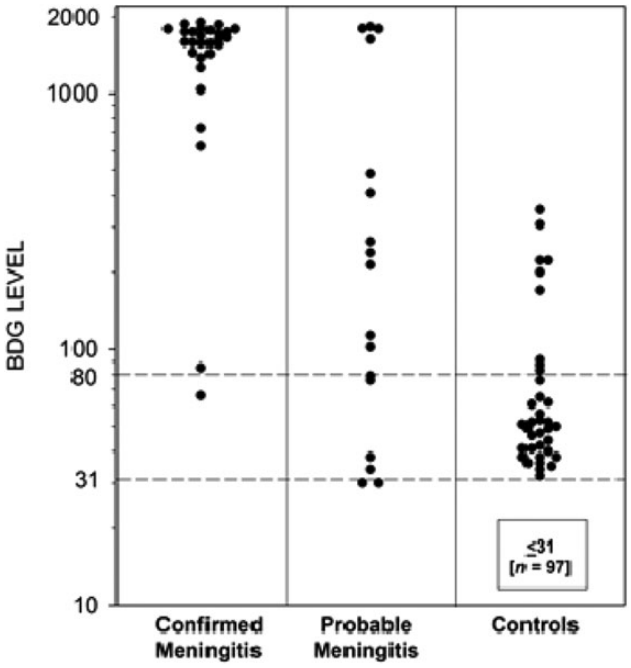
Background. The prompt diagnosis and treatment of fungal meningitis is critical, but culture is insensitive. (1,3)-beta-D-glucan (BDG) is FDA-cleared for serologic diagnosis of invasive fungal disease. (Fungitell assay, Associates of Cape Cod Incorporated). However, BDG is not cleared for testing cerebrospinal fluid (CSF) and the appropriate cutoff is unknown. We aim to validate the accuracy of CSF BDG for the diagnosis of fungal meningitis among patients exposed to contaminated methylprednisolone acetate (MPA).

Methods. A case-control study was conducted at St. Joseph Mercy Hospital and Vanderbilt University from November 2013 – February 2014. Patients were included if they received a contaminated MPA injection. Cases were classified as probable or confirmed meningitis according to Centers for Disease Control and Prevention guidelines. Controls were defined as persons exposed but not diagnosed with disease**.** CSF BDG testing was performed according to the package insert for serum and validated using Clinical Laboratory Standards Institute procedures (MiraVista Diagnostics).

Results. Of 233 patients, 45 had meningitis (28 confirmed), 53 had spinal/paraspinal infection (19 confirmed), and 135 did not develop disease. The figure depicts CSF BDG results from those with confirmed meningitis, probable meningitis, and controls. Using the manufacturer's cutoff (BDG $\geq$ 80 pg/mL), the sensitivity and specificity were 96% (95% CI 80-100%) and 93% (95% CI 87-97%) for confirmed meningitis and 84% (95% CI 70-93%) and 93% (95% CI 87-97%) for probable meningitis. The Receiver Operating Characteristic analysis identified the optimal cutoff for confirmed meningitis to be $\geq$ 500 pg/mL (sensitivity 93% [95% CI 76-99%], specificity 100% [95% CI 97-100%]); for probable meningitis to be 66 pg/mL (sensitivity 91% [95% CI 79-98%],specificity 92% [95% CI 87-96%]).



Conclusion. Our results suggest that CSF BDG is both a highly sensitive and specific test for diagnosis of fungal meningitis associated with contaminated MPA injections. Further study is needed on the diagnostic utility of CSF BDG for other types of fungal meningitis.

Disclosures. **L. Wheat**, MiraVista Diagnostics: Employee, Salary **T. Summons**, MiraVista Diagnostics: Employee, Salary **M. Durkin**, MiraVista Diagnostics: Employee, Salary

1462. Bronchoalveolar Lavage Lateral-Flow Device Test for Diagnosing Invasive Pulmonary Aspergillosis in ICU patients: a multicenter study

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Background. In invasive pulmonary aspergillosis (IPA) timely diagnosis is a key factor for successful treatment. Galactomannan testing from BAL represents a current gold standard. However, turnaround time and availability remain limitations of galactomannan (GM) testing. These limitations may be overcome by the Lateral- Flow Device (LFD) test, a single sample point-of-care test for native BAL testing that is based on the detection of an Aspergillus extracellular glycoprotein antigen by monoclonal antibody JF5. This study evaluates the LFD test by using bronchoalveolar lavage (BAL) samples from patients at intensive care units (ICU).

Methods. A total of 129 BAL samples from intensive care unit patients without hematological malignancies or solid organ transplantation (95 from Graz 24 from Innsbruck, 10 from Vienna) were included between July 2012 an March 2014 in this study. 22 ICU patients (16 from Graz, 4 from Innsbruck, 2 from Vienna) had probable or proven IPA. Diagnostic accuracy of LFD test for probable/proven IPA was evaluated. Clinical findings, fungal cultures and BAL GM were used for IPA grading (cut-off 1.0).

Results. Sensitivity and specificity were 73% (Graz 75%, Innsbruck 50%, Vienna 100%) and 91% (Graz 88%, Innsbruck 95%, Vienna 75%), respectively. PPV and NPV as well as diagnostic odds ratio of LFD test for probable/proven IPA were 62%, 94%, 25.9 (95%CI 8.3-81).

LFD resulted negative in 6 patients with probable IPA. BAL GM was tested in four of those patients and revealed levels of 3.4, 0.84, 0.74 and 0.2. In a total of three patients (including the latter with a BAL GM below the cut-off) BAL culture grew Aspergillus fumigatus.

Conclusion. The LFD test of BAL specimens is performed easily and provides accurate and rapidly available results. Therefore, this new point-of-care test may be a very promising diagnostic approach for detecting IPA in BAL specimens from ICU patients.

Disclosures. **C. Thornton**, Olmedica: Shareholder, Salary

1463. Immune Reconstitution Inflammatory Syndrome (IRIS) in Neutropenic Patients with Invasive Pulmonary Aspergillosis (IPA) during Neutrophil Recovery

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Background. Limited data on the incidence and clinical characteristics of IRIS in neutropenic patients with IPA were available.

Methods. During 6-year period, adult patients with neutropenia who met probable or proven IPA by the EORTC criteria were retrospectively enrolled. IRIS was defined as new appearance or worsening of radiologic pulmonary findings temporally related to neutrophil recovery with evidence of a decrease 50% in serum galactomannan index titers.

Results. Of 150 patients, 35 (23%, 95% CI 17% - 31%) developed IRIS during neutrophil recovery. IRIS was associated with shorter neutropenic period, controlled underlying hematologic disease, less immunosuppressant use, and voriconazole use (table). The 30- and 90-day mortalities were lower in patients with IRIS than those with non- IRIS (table). In the subgroup analysis of 53 patients who had progressive disease during the neutrophil recovery, 35 (66%, 95% CI 53% -77%) were classified as IRIS group. The 30- and 90-day mortalities was higher in patients with non-IRIS who had progressive disease during the neutrophil recovery than in those with IRIS (9% vs 39%, $P = 0.02$ and 31% vs 72%, $P = 0.005$, respectively).

Clinical characteristics and outcomes of neutropenic patients with and without immune reconstitution inflammatory syndrome following initiation of antifungal therapy for invasvie pulmonary aspergillosis

	IRIS (n=35)	Non-IRIS (n=115)	*P*
Age, median years (IQR)	55 (46-64)	52 (41-61)	0.39
Male gender	24 (68.6)	70 (60.9)	0.41
Underlying disease/conditions			
Acute leukemia	28 (80)	87 (76)	0.59
Aplastic anemia	1 (3)	12 (10)	0.30
Lymphoma	2 (6)	8 (7)	>0.99
Receipt of HCT	9 (26)	42 (35)	0.24
Prior corticosteroid use	7 (20)	39 (34)	0.12
Prior immunosuppressant use	3 (9)	30 (26)	0.03
Controlled state of underlying disease	11 (31)	18 (16)	0.04
Length of neutropenic period, median days (IQR)	29 (19-50)	40 (23-87)	0.04
Peak galactomannan index, median value (IQR)	1.4 (0.7-3.4)	1.5 (0.7-3.6)	0.86
Antifungal therapy on diagnosis day of IPA			
Amphotericin B	17 (49)	69 (60)	0.23
Voriconazole	15 (43)	29 (25)	0.045
Outcome after diagnosis of IPA			
30-day mortality	3 (9)	38 (33)	0.004
90-day mortality	11 (31)	67 (58)	0.005

Conclusion. IRIS occured in about one quarter of neutropenic patients with IPA, was associated with voriconazole use. In addition, it appears to be a good prognostic factor.

Disclosures. **All authors:** No reported disclosures.

1464. The Marijuana Threat in Leukemia Patients

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Background. Cannabis has evolved from being an illicit psychotropic drug, to now being recommended by many oncologists as an appetite stimulant and antiemetic. Marijuana contamination with molds such as *Aspergillus*, *Mucor* and *Fusarium* has been reported. Molds causing a nodular pneumonia, and bronchiolitis miliary micronodular pattern, both related to smoking marijuana have been well described in the literature. However, the detrimental effect of marijuana smoking in immunocompromised populations has been overlooked.

Methods. We reviewed four leukemia patients at Moffitt Cancer Center with chest imaging findings attributed to marijuana use. Summarized characteristics included patient's underlying malignancies, clinical presentation, absolute neutrophil count (ANC) at the time of diagnosis, antifungal prophylaxis used, imaging findings and the treatment offered.

Results. Of the four patients, two had acute lymphocytic leukemia (ALL) and two had acute myelogenous leukemia (AML). The two ALL cases were post induction chemotherapy at the time of diagnosis and were on fluconazole prophylaxis. They were found to have nodular pneumonia on CT-scan of the chest suspicious for mold infection. The lesion was cavitary in one patient who had just resolved 1 week of neutropenia. They both received voriconazole and showed resolution of the nodules on repeat CT-scan of the chest. Patients with AML had a miliary nodular pattern on chest imaging studies. The first patient was neutropenic with a productive cough. He had a positive galactomann test and showed progression of his lesions while on micafungin prophylaxis, followed by complete resolution on voriconazole. The second AML patient was not neutropenic at the time of diagnosis. He was started on posaconazole along with chemotherapy. Unfortunately, He expired 2 months later from disseminated *Fusarium* infection.

Conclusion. We reviewed four cases of nodular pneumonia in leukemic patients who admitted using marijuana and were not receiving anti-mold prophylaxis. Dramatic loss of the fourth patient, and the radiographic resolution on adequate anti-mold therapy in the first three cases confirmed our suspicion. This case series highlights the need to consider anti-mold prophylaxis in patients with leukemia and anticipated neutropenia who smoke marijuana.

Disclosures. **All authors:** No reported disclosures.

1465. Pigmented Mold Endocarditis – Case Series and Review of the Literature

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Background. Pigmented mold endocarditis (PME) is an uncommon infection. Despite aggressive surgical and antifungal treatment, mortality remains high. A better understanding of the epidemiology and treatment of PME is needed.

Methods. We identified PME cases from the University of Alabama at Birmingham (UAB) mycology laboratory from 1994-2012 and queried MEDLINE from 1968-2012. Cases that met the Modified Duke Criteria for definite or possible IE were included. Cases in which PME was the result of disseminated infection in immunocompromised hosts were excluded. Demographics, clinical data, treatment and outcomes were extracted.

Results. A total of 44 cases (3 from UAB, and 41 from MEDLINE) were identified and included in the analysis. Mean age was 51.7 years; 30 (68%) were males. 24 (55%) were classified as PVE, 13 (30%) NVE and 5 (11%) as cardiac device infective endocarditis. The most common predisposing factor identified was a prior cardiac procedure (32/44); the median time from the procedure was 113

days. Other predisposing factors such as solid organ transplantation (31%), stem cell transplantation (15%), chronic intravenous access (23%), IVDA (15%) and HIV (8%) were prevalent in the NVE subgroup but otherwise uncommon. 30/44 had fever, and 21/44 had an audible murmur. An embolic event prior to diagnosis was common (28/44); mean events 1.6. The most common fungi were: *Scedosporium apiospermum* 13/44, *Phialemonium curvatum* 5/44 and *Exophiala dermatitidis* 4/44. Two of 7 and 1 of 4 isolates had high MIC's to amphotericin B and voriconazole, respectively. Echocardiography was performed in 31 of 44 patients; it identified vegetations in 23/31, valvular regurgitation in 7/31 and an intra-cardiac mass in 5/31. Blood cultures were positive in 20 (54%) of 37 cases. The crude survival was 32% (14/44); 25% (1/4) in the medical management and 41% (12/29) in the combined medical and surgical management subgroups. Recurrence was common (10/44).

Conclusion. PME is a rare disease, but it should be considered in the differential diagnosis of culture negative PVE and culture negative NVE in immunocompromised hosts, those with chronic venous access or IVDA. Lack of fever, multiple embolic events, large vegetations and positive blood cultures could be clues to the diagnosis. Mortality in PME is high and recurrence is common.

Disclosures. **J. Baddley**, Merck: Consultant, Consulting fee; Astellas: Scientific Advisor, Consulting fee; Pfizer: Data review committee, Consulting fee

1466. Primary Cutaneous Mold Infections in Hematologic Malignancy with a Review of the Literature

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Background. Opportunistic fungal infections, namely *Aspergillus* and *Candida*, followed by *Fusarium*, *Rhizopus*, *Mucor*, and *Alternaria* spp are an important cause of morbidity and mortality in patients with hematologic malignancies. Cutaneous mucormysosis infections are extremely rare, and the incidence, survival outcomes, and factors associated with survival within hematologic malignancies are not clear.

Methods. We present a case of a neutropenic patient with underlying aplastic anemia who developed primary cutaneous gangrenous mucormycosis following a cat bite. The literature was reviewed for all cases of primary cutaneous fungal infections in immunosuppressed patients reported in the English literature utilizing the PubMed database from 1980-2012 with the search terms "primary," "cutaneous," "fungal," "infection" and "cancer." The review yielded 50 cases of primary cutaneous fungal infections in patients with hematologic malignancies with few cases excluded. Survival outcomes were investigated with clinical correlates as to provide a basis for comparison.

Results. In the 51 cases identified, 66.7% were neutropenic upon presentation, and 54.9% were male with an average age of 32 years. *Aspergillus spp* (33.3%) was the most cited followed by *Rhizopus* spp (19.6%). Overall mortality rate was 29.4% and was observed more frequently in patients with neutropenia (60%) and without surgical intervention (73.3%). Survival rate was higher (35.3%) for cases utilizing both antifungal and surgical intervention. The antifungal with the highest survival rate was amphotericin B and its formulations (58.8%).

Conclusion. Neutropenia within hematologic malignancies demonstrate a risk for developing severe cutaneous fungal infections of which primary cutaneous mucormycosis can carry significant mortality. Combination antifungal therapy and surgical debridement appears be associated with higher survival outcomes and warrants further investigation.

Disclosures. **All authors:** No reported disclosures.

1467. Delaying Diagnostic Procedure Significantly Increases Mortality in Patients with Invasive Mucormycosis

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Background. Invasive mucormycosis is an uncommon but increasing, life-threatening fungal infection. Effective therapy is represented by the combination of surgery and antifungal agent administration and early initiation of the therapy is necessary for favorable outcome. However, the disease is difficult to diagnose and mortality reaches 40% even if treated adequately, and clinical data on clinical course are limited.

Methods. We retrospectively reviewed histologically proven cases of invasive mucormycosis in two tertiary care referral hospitals from 2004 to 2013. The clinical and laboratory data were analyzed for all patients.

Results. We reviewed total of 28 patients who were histologically diagnosed as invasive mucormycosis. Overall survival was 60% (n = 17). The time from onset of symptom to diagnostic procedure proved to be associated with mortality (P <0.001). In addition, time from onset of symptom to initiation of antifungal therapy was associated with a poor outcome in our study (P = 0.032). On multivariate regression analysis, delayed diagnostic procedure (more than 10 days after onset of symptom) was an independently significant predictor of mortality (odds ratio = 13.28, 95% confidence interval, 1.07-164.62; P= 0.044).

Conclusion. Mucormycosis is a destructive fungal infection that is associated with a high mortality, ranging from 40 to 100 % depending on disease form. When a clinician suspects an invasive mucormycosis infection, early diagnostic procedure done within 10 days from the onset of symptom and early initiation of antifungal therapy will lead to successful management of the disease.

Disclosures. **All authors:** No reported disclosures.

1468. Detection of High CSF Levels of (1 → 3)-Beta-D-Glucan in Cryptococcal Meningitis

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Background. (1-3)-β-D-glucan (BDG) is a helpful diagnostic marker for many invasive fungal infections. However, BDG is not thought to be useful in diagnosing cryptococcosis. We evaluated the utility of cerebrospinal fluid (CSF) and serum BDG as an adjunct diagnostic tool for HIV-infected cryptococcal meningitis patients.

Methods. BDG concentrations were measured on cryopreserved CSF (n = 177) and serum (n = 109) of HIV-infected patients with suspected meningitis in Uganda and South Africa using the Fungitell® assay. Correlations between BDG concentrations and quantitative CSF cryptococcal cultures, CSF cryptococcal antigen (CRAG) titers, and 18 different CSF cytokine concentrations were assessed using non-parametric tests. Mixed models evaluated longitudinal changes in CSF BDG concentrations. Survival analyses evaluated BDG's relationship with mortality.

Results. The Fungitell® BDG assay provided 90% sensitivity (69/77) and 85% specificity (34/40) in CSF when compared to cryptococcal meningitis diagnosed by CSF culture or cryptococcal antigen at diagnosis (n = 117, 66% with *Cryptococcus neoformans*). Sensitivity in CSF improved to 98% (57/58) when initial fungal burdens were ≥10,000 CFU/mL. Median (IQR) CSF BDG concentrations at diagnosis were 346 (202-597) pg/mL in cryptococcal patients and 37 (20-46) pg/mL in patients without cryptococcosis. Baseline BDG concentrations correlated with CSF fungal burden (rho = 0.820, P < .001) and CRAG LFA titers (rho = 0.780, P < .001). BDG normalized rapidly after initiating antifungal therapy [-0.25 (95%CI: -0.31, -0.20) average change in $\log_2$BDG level per day of follow-up]. Baseline BDG concentrations correlated with MIP-1β and MCP-1 levels in CSF. Among cryptococcal meningitis patients, a BDG concentration ≥500 pg/mL was associated with increased 10-week mortality. The diagnostic performance of the BDG assay for cryptococcal meningitis was not as good in serum, where we observed 79% (37/47) sensitivity and 61% (38/62) specificity.

Conclusion. BDG is detectable in the CSF of HIV-infected patients with Cryptococcus, and may provide useful diagnostic and prognostic information. Further research is needed to clarify the role of BDG in the immunology and management of cryptococcal disease.

Disclosures. **M. Finkelman**, Associates of Cape Cod: Employee, Salary

1469. Posaconazole salvage treatment for invasive fungal infection : a single center experience with utilization of posaconazole oral suspension or delayed-released tablet

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Background. Posaconazole has a broad spectrum antifungal activity and it may be useful for salvage antifungal treatment for invasive fungal infection (IFI). The aim of this study was to evaluate the efficacy and outcomes of posaconazole salvage treatment (ST) in patients with IFI who were intolerant or refractory to other antifungal therapy with utilization of posaconazole oral suspension (os) or delayed-released tablet (tab).

Methods. A retrospective review of patients who were started on posaconazole ST for IFI at our institution between December 2007 and March 2014 was conducted.

Results. A total of 25 episodes of posaconazole ST for IFI in 23 patients were identified. Median age was 55 years and the majority of patients had hematologic disease (70%, 16/23). Classifications of 25 episodes of IFI were proven (12), probable (5), and possible (8). Etiology of 25 episodes of IFI included mucormycosis (7), *Paecilomyces variotii* (1), *Aspergillus fumigatus* (2), *Alternaria spp.*(2), and unspecified IFI etiology without positive culture (13). Reasons for posaconazole ST were : intolerance of previous antifungal therapy in 12 episodes, refractory IFI on previous antifungal therapy in 9

episodes, both intolerance and refractory IFI on previous antifungal therapy in 1 episode, and transition to long-term maintenance in 3 episodes. Posaconazole os and tab was used in 19 episodes and in 6 episodes, respectively. Duration of posaconazole ST ranged from 15 to 370 days with median 52 days. Posaconazole ST with tab (300mg twice daily loading on the first day and followed by 300mg daily) seemed to achieve favourable therapeutic posaconazole trough concentrations (range 0.9 – 5.8 ug/mL, median 2.0 ug/ml) compared to posaconazole os (800mg daily, range 0.1 – 3.6 ug/mL, median 1.0 ug/mL), P = 0.008. The overall successful posaconazole ST response rate was 64% (16 of 25 episodes from 3 tab recipients and 13 os recipients : 10 partial and 6 complete clinical and radiologic responses). There were 5 patients who died during the study period. However, only one death was attributed to the progression of IFI. Adverse events were noted in 4 patients with discontinuation of posaconazole in 3 patients.

Conclusion. Posaconazole ST may be used effectively for IFI. More studies are required to define the optimal antifungal therapeutic strategy.

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1470. Incidence and predictors of hypertension among adults with HIV initiating ART in southwestern Uganda

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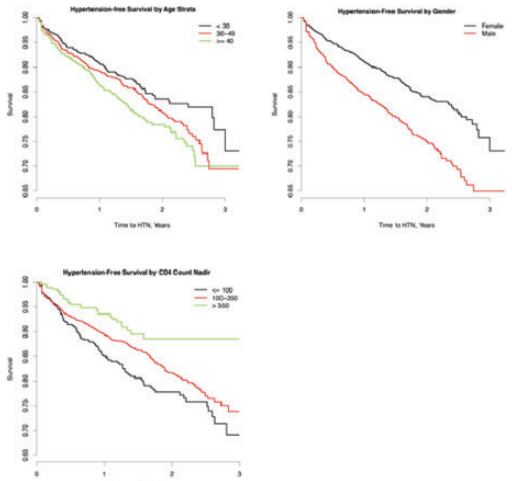
Background. Expanded access to anti-retroviral therapy (ART) in sub-Saharan Africa has increased life expectancy for people living with HIV (PLWH). In resource rich areas, there is evidence of increasing risk of non-communicable diseases among aging PLWH. Yet, there are limited data on the epidemiology of cardiovascular diseases in sub-Saharan Africa, which is home to approximately 90% of PLWH worldwide.

Methods. We abstracted sociodemographic and HIV-related clinical data (CD4 count, ART regimen) from adult patients initiating ART at the HIV clinic at Mbarara Regional Referral Hospital in Uganda from 2010-2012. Patients have a single blood pressure measured and recorded by a clinic nurse at each visit. Our outcome of interest was incidence of hypertension, defined as occurrence of 2 or more consecutive clinical visits with a systolic blood pressure >140mmHg and/or diastolic blood pressure recording of >90mmHg, or prescription for an antihypertensive medication. We calculated the crude incidence of hypertension by sex and age, and fit multivariable Cox proportional hazards regression models to determine predictors of incident hypertension.

Results. 3,400 patients initiated ART during the study period without a prior diagnosis of hypertension. Subjects attended a total of 22,783 clinic visits and contributed 3,996 person-years (median 396 days [IQR 170 – 628]). 67% were female and median age at enrollment was 32 years (IQR range 27 – 39). The incidence of hypertension was high in all age strata, and ranged from 87.9/1,000 py in females <30 years old to 157.7/1,000 py in males >40. In multivariable Cox proportional hazards models, male gender (AHR 1.86, 95%CI 1.47–2.35), increasing age (AHR 1.36, 95%CI 1.02–1.82 for those ≥40 vs those <30), nadir CD4 count (AHR 1.57, 95%CI 1.01–2.54 for those with a nadir CD4<100 vs >1350), and increasing body mass index (AHR 3.07, 95%CI 1.81–5.22 for BMI >30 vs <25) were associated with increased risk of hypertension.



Conclusion. Incident hypertension is common among PLWH initiating ART in rural Uganda. Notably, lower nadir CD4 count is associated with increased risk of hypertension, independent of gender and BMI. Increased attention to screening of and treatment for hypertension should be prioritized in people living with HIV on ART in the region.

Disclosures. **All authors:** No reported disclosures.

1471. A Pilot Study to Introduce Voluntary Medical Male Circumcision for HIV Prevention in Areas of High Prevalence of the Dominican Republic

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Background. Voluntary Medical Male Circumcision (VMMC) is an effective strategy to reduce the risk of HIV infection. Clinical trials conducted in Africa found that the procedure reduces the risk of HIV acquisition by approximately 60%. Studies conducted in the Dominican Republic (DR) suggest that acceptability of VMMC among men may be as high as 67% when information about the benefits is provided. The goal of this pilot study was to assess the acceptability, uptake, safety, for VMMC services in two areas of high HIV prevalence in the country.

Methods. Providers and study personnel received background information about the risks and benefits of VMMC. Physicians and nurses received theoretical and practical training on the surgical technique. Educational sessions were conducted in the community to inform men of the benefits and risks of VMMC. Each consenting participant completed a survey of demographics, sexual practices and knowledge about VMMC. One week after the surgery, participants returned for a postoperative visit for wound inspection. Descriptive statistics were generated and analyses were conducted to calculate rates and measures of central tendency.

Results. 454 men were circumcised using the Forceps Guided Method under local anesthesia. Median age of the cohort was 27 years. Fifty-seven subjects were excluded for medical or anatomical reasons. The rate of adverse events (AE) was 4.4% with no serious adverse events. All complications resolved promptly with treatment. Eighty seven percent of clients reported being very satisfied and 12.8% were somewhat satisfied with the outcome at the one-week postoperative visit.

Conclusion. Recruitment, uptake, and client satisfaction with VMMC in this pilot were high. The rate of AEs was low. Roll out of VMMC in targeted areas of the DR is feasible and should be considered. To our knowledge, this is the first time VMMC has been offered for HIV prevention to adult men outside of Africa.

Disclosures. **All authors:** No reported disclosures.

1472. Epidemiology of Meningitis in an HIV-infected Ugandan Cohort

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Background. There is limited understanding of the current epidemiology of meningitis amongst HIV-infected hospitalized populations in sub-Saharan Africa. Given limited resources, few diagnostics are performed. We sought to comprehensively evaluate the etiologies of meningitis in Uganda.

Methods. We conducted a prospective cohort study of HIV-infected adult inpatients admitted to Mulago National Referral Hospital in Uganda with suspected meningitis from November 2010 to October 2012. Intensive CSF testing was performed to evaluate for bacterial, viral, fungal, and mycobacterial etiologies. Test methods included standard CSF cell count, gram stain, AFB smear, bacterial and fungal cultures. Further testing included cryptococcal antigen, neurosyphilis VDRL,16s rDNA PCR for bacterial identification, and Plex-ID broad viral assay. Additionally, qPCR was used to detect HSV-1/2, CMV, EBV, VZV, *Toxoplasma gondii*, West Nile, Yellow Fever, Dengue, Chikungunya, and Zika virus, along with qRT-PCR for Enterovirus, and Xpert MTB/RIF assay.

Results. Cryptococcal meningitis accounted for 60% (188/314) of all causes of meningitis. Only 1.6% had bacterial meningitis. Of the 117 samples sent for viral PCR, 36% were EBV PCR positive, some with concurrent infections with cryptococcal meningitis, or other viruses. No samples were enterovirus or HSV positive. All arboviral studies were negative. Eight out of 63 (12.7%) CSF samples were positive by Xpert MTB/RIF assay. Among cryptococcal antigen negative patients, the yield of Xpert MTB/RIF assay in the CSF was 22% (8/36). After exclusion of cryptococcal meningitis and bacterial meningitis, 62% (44 of 71) with suspected meningitis and an abnormal CSF profile had no definitive diagnosis.

Results of Minnesota Department of Health testing

Etiology	Total (n=117)	Cryptococcal Meningitis (n=54)
EBV	42	21
EBV + CMV	3	2
CMV	2	0
JC virus	3	2
Toxoplasma	3	1
EBV + JC virus	3	2
EBV + VZV	1	0
CMV + Toxoplasma	1	0
BK virus	1	0
Enterovirus	0	0
Negative	58	26

Conclusion. *Cryptococcus neoformans* was the most common etiology of meningitis. The Xpert MTB/Rif assay was of potential promise. Exploration of new TB diagnostics along with diagnostic algorithms for evaluation of meningitis in resource-limited settings remains critical.

Disclosures. **All authors:** No reported disclosures.

1473. HIV in Pregnant Women in the Philippines: Revisiting Prospects for Universal Screening

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Background. The Philippines is one of nine countries globally with rapidly increasing rates of HIV infection. Annual reported cases have increased 34-fold in the last decade. A local prevalence study of 3,000 pregnant women in 1998 failed to find a single case of HIV. This study aims to determine whether universal HIV screening in pregnant women should be initiated in the light of the large number of newly-diagnosed cases.

Methods. Following institutional review board approval, adult pregnant patients at the Philippine General Hospital (PGH) were recruited into the study. PGH is the largest tertiary-care government hospital in the country and is a national referral center. 400 pregnant women were offered free HIV testing and 387 women qualified for the study. Demographics and risk factors for HIV were recorded and analyzed. Screening was done using ELISA/ECLIA testing (Abbott Architect HIV Ag/Ab) with Western blot for confirmation.

Results. Demographics and HIV risk factors are shown in the table. No pregnant women were found to have HIV. Two false positives occurred.

In order to better analyze risk factors for screening, we compared the demographics and risk factors of the study patients with the records of all (N = 4) pregnant HIV patients seen in our HIV clinic at PGH. Differences between HIV-positive vs HIV-negative pregnant women included more sexual partners (5 vs 2); higher rates of illicit drug use (50% vs 0.78%), sex with foreigners (50% vs 1.6%) STD rates (25% vs 3.9%), sex with illicit drug users (25% vs 3.1%), and receiving money for sex (50% vs 0.52%).

Demographics and risk factors (N=387)

Age (years)	Mean: 28.4 SD: 6.2	Range 19-46
Age of gestation (weeks)	Mean: 27.06 SD: 8.01	Range: 4 to 38
Number of partners (lifetime)	Mean: 1.92 SD: 1.61	Range: 1 to 20
History of sexually transmitted disease	Yes: 15 (3.88%)	No: 372 (96.12%)
Condom use	Yes: 65 (16.80%)	No: 322 (83.20%)

Conclusion. Universal screening for HIV in pregnant Filipino women is not supported by the findings of this study despite the tremendous increase in HIV prevalence in the Philippines. A larger sample size may be useful to strengthen this assertion. Targeted HIV screening of pregnant women, particularly female sex workers, drug users and those with multiple partners should be offered.

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1474. Genotypic Characterization of *pncA* Gene in Patients with Multidrug-resistant Tuberculosis from South Africa

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Background. Pyrazinamide (PZA) is an essential component of empiric first- and second-line TB treatment regimens. However, PZA drug susceptibility testing (DST) is difficult to perform phenotypically and not routinely available. Genetic mutations in the *pncA* gene of *M.tuberculosis* commonly confer PZA resistance, but limited data on the prevalence and diversity of these mutations are available from clinical populations of TB patients. We utilized *pncA* sequencing to estimate PZA resistance among MDR and XDR TB patients in KwaZulu-Natal province, South Africa.

Methods. We prospectively enrolled 206 MDR TB and 289 XDR TB patients from September 2011 to April 2014. Sputum collected from each participant underwent mycobacterial culture and DST for isoniazid (H), rifampin (R), streptomycin (S), kanamycin (Km) and ofloxocin (Ofx). We extracted DNA from pure Mtb isolates and performed targeted sequencing of the *pncA* gene, characterizing the proportion, frequency and structure of polymorphisms.

Results. To date, targeted sequencing has been completed for 266 unique isolates from 80 MDR TB (16 resistant to H&R only, 64 resistant to H,R,S) and 186 XDR TB participants (all resistant to all five drugs [H, R, S, Km, Ofx]. A mutation in the *pncA* gene was observed in 55 (69%) of MDR TB and 178 (96%) of XDR TB subjects. We found 31 distinct *pncA* mutations (figure); 20 different mutations were seen among MDR TB subjects, of which, only 7 were seen in more than one subject. Among XDR TB subjects, one mutation (insertion of cytosine after the 456 locus) was present in 133 (72%), consistent with the known genotypic clonality of the XDR cases in KwaZulu-Natal province.

Figure: Results of pncA gene sequencing of 266 XDR-TB and MDR TB isolates

S #	pncA mutation type	Frequency (no. of isolates)	
1	AGG(R)154GGG(G)	12 *(XDR-TB: 9; MDR-TB: 3)*	Mutations common to both MDR and XDR isolates
2	CAT(H)71TAT(Y)	9 *(XDR-TB: 5; MDR-TB: 4)*	
3	GCG(A)102GTG(V)	14 *(XDR-TB: 1; MDR-TB: 13)*	
4	GGT(G)132GCT(A)	2 *(XDR-TB: 1; MDR-TB: 1)*	
5	insA after 408	4 *(XDR-TB: 3; MDR-TB: 1)*	
6	insC after 456	141 *(XDR-TB: 133; MDR-TB: 8)*	
7	TTG(L)151TCG(S)	13 *(XDR-TB: 3; MDR-TB: 10)*	
8	WT	33 *(XDR-TB: 8; MDR-TB: 25)*	
9	459ΔCAGGGTGC	1	Mutations specific to MDR population
10	515 Δ T	1	
11	ACT(T)76ATT(I)	1	
12	CAT(H)137CGT(R)	1	
13	CTG(L)35CTA(L)	1	
14	CTG(L)35CTA(L), TTG(L)151TCG(S)	1	
15	GAG(E)91CAG(Q)	1	
16	GGT(G)97GAT(D)	1	
17	GGT(G)97TGT(C)	1	
18	insA after 407	1	
19	TCC(S)59CCC(P)	4	
20	TTC(F)58TCC(S)	1	
21	385ΔG, TTG(L)151TCG(S)	2	Mutations specific to XDR population
22	389ΔT	1	
23	ACC(T)153CACC(H)	1	
24	ACC(T)47ATC(I)	1	
25	AGG(R)154TGG(W)	1	
26	GTG(V)139GGG(G)	1	
27	insC after 456, CTG(L)35CTA(L)	1	
28	insG after 313	1	
29	insG after 515	12	
30	TAC(Y)34GAC(D)	1	
31	TCC(S)59CCC(P)	1	

Conclusion. Nearly 70% of MDR and nearly all XDR TB subjects had *pncA* mutations and likely PZA resistance in our cohort. A wide diversity of mutations was seen. Most mutations were singlets, suggesting acquisition of mutations de novo, perhaps due to empiric use. One specific mutation was common among XDR TB subjects, but it occurred in conjunction with a specific RFLP genotype associated with clonal expansion. Given the difficulty in determining PZA susceptibility, characterizing *pncA* mutations may provide important data for developing rapid genotypic PZA susceptibility assays in the future.

Disclosures. **All authors:** No reported disclosures.

1475. Hamsi scoring in the prediction of unfavorable outcomes in tuberculous meningitis: Results of multinational Haydarpasa-2 Study

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Background. The course of tuberculous meningitis is quite problematic since half of patients faces either permanent sequelae or mortality. Thus, predictive scoring of unfavorable outcome is of paramount importance in clinical decision making in TBM. Accordingly, we designed this multinational study, which provided the largest case series with microbiological confirmation ever known in the literature.

Methods. A total of 43 centers from 14 countries (Albania, Croatia, Denmark, Egypt, France, Hungary, Iraq, Italy, Macedonia, Romania, Serbia, Slovenia, Syria, and Türkiye) submitted data of confirmed TBM patients hospitalized between 2000 and 2012. Unfavorable outcome was defined as survival with significant sequel or death. To develop a risk score predicting unfavorable outcome, binary logistic regression models were constructed via 200 replicates of database by bootstrap resampling methodology. The final model was build according to the selection frequencies of variables. The severity scale included variables with arbitrary scores proportional to the predictive powers of terms in the final model. The final model was internally validated by bootstrap resampling.

Results. A total of 507 patient data were submitted among which 165 were presented unfavorable outcome. Eighty-six patients died while 119 sequelae were detected in 79 (16%) patients. The full model included 13 variables and finally age, nausea-vomiting, altered consciousness, hydrocephalus, vasculitis, immunosuppression, diabetes mellitus and neurological deficit remained in the final model. Arbitrary scores between one to three were assigned to the variables in the severity scale. The severity index (HAMSI) included scores between one to six. The distribution of mortality for the scores 1-6 were 3.4%, 8.2%, 20.6%, 31%, 30% and 40.1%, respectively.

Conclusion. Altered consciousness, diabetes mellitus, immunosuppression, neurological deficits, hydrocephalus, and vasculitis predicted the unfavorable outcome in HAMSI scoring and the cumulative score provided a linear estimation of prognosis. Consequently, we provided a strong model in the prediction of TBM outcome and accordingly.

Disclosures. **All authors:** No reported disclosures.

1476. Screening for Latent Tuberculosis Infection in Internationally Adopted Children in the era of Interferon-Gamma Release Assay (IGRA) Testing

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Background. Internationally adopted children are at 4-6 times the risk as US born children for latent Tuberculosis Infection (LTBI). Their diagnosis is complicated by confounding factors such as poor nutritional status and BCG vaccination. Pediatric recommendations are to screen with either an interferon gamma release assay (IGRA) or a tuberculin skin test (TST) upon arrival to the US. In children > 5 years of age who have received a BCG, IGRAs are more specific than the TST. However IGRAs in children <5years of age have been less well studied. We describe our experience in diagnosing LTBI in an International Adoption Clinic at a Children's Hospital in the era of IGRA testing.

Methods. Retrospective chart review of children evaluated at the Rainbow Babies and Children's Hospital International Adoption Clinic between January 2007-December 2012. Demographics, BCG status, TST and IGRA results at first and 6 month visit were collected. This study was approved by the University Hospitals IRB.

Results. 36 patients were included in the study. Mean age on arrival was 37.8 months. 23 children had both an IGRA and a TST performed, 6 patients only IGRA, 5 only TST, and for 2 patients no testing data was available. LTBI was diagnosed and treated in 15/36 patients. 13 had an initial TST placed (n = 12) or recently documented (n = 1) at the first visit, 9 of which had a positive TST. Six children were tested again or for the first time at the 6 month visit and all were positive. 4/6 had a conversion from an initial negative TST . 12/15 children had IGRA testing and only 2 were positive. These children were 2 siblings, > than 4 years of age, with no evidence of prior BCG whose mother died of TB disease. Only 6/15 children had evidence of BCG documented (visible BCG scar or documentation of the vaccine).

Conclusion. In internationally adopted children at our clinic, the result of a negative IGRA in the face of a positive TST did not influence the clinician's decision to treat for LTBI. The only 2 children with positive IGRA had significant family history for tuberculosis and were closer to the age in which the IGRAs have been better evaluated. More studies are needed to determine the best method of diagnosis of LTBI in this high-risk group and the role of IGRAs in this young population who is likely BCG vaccinated.

Disclosures. **All authors:** No reported disclosures.

1477. Factors affecting the early clinical response in due course of tuberculous meningitis treatment: Results of Haydarpasa-3 Study

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Background. Tuberculous meningitis (TBM) is the most severe form of tuberculosis. In our study, we aimed to assess the factors affecting the early clinical response including fever, mental alterations and headache in due course of TBM treatment.

Methods. In this study 506 adult TBM patients treated in 35 centers between 2000-2012 were evaluated and 88 patients with a complete set of radiological and clinical data were included. All of the patients had microbiological confirmation from the CSF. Early and late responders according to fever, headache and mental alterations were compared. In addition, cumulative comparisons were made for the disappearance of all findings of the classical triad.

Results. The mean age of the 88 cases included were 33,90 ± 16,41 years. All of these patients were survivors of TBM. The presence of vasculitis ($p = 0.029$, OR = 0.092 [%95 CI, 0.01-0.78]) and lower serum/CSF glucose rate ($p = 0.049$, OR = 52.571 [%95 CI, 1.01-2755.26]) were significant variables when early and late responders were compared. When early and late responder groups were compared for the normalization of conscious, hydrocephalus was the significant parameter ($p = 0.001$, OR = 0.123 [%95 CI, 0.04-0.42]). Accordingly hydrocephalus was of paramount importance on headache ($p = 0.029$, OR = 0.313 [%95 CI, 0.11-0.89]). When early and late responder groups were compared for the disappearance of all three findings according to median durations, hydrocephalus was found to be the significant parameter causing late responses ($p = 0.005$, OR = 0.189 [%95 CI, 0.06-0.61]). On the other hand, when the effects of clinical, radiological, laboratory, and therapeutic parameters were evaluated, vasculitis ($p < 0.001$), hydrocephalus ($p = 0.029$), and the use of ethambutol ($p = 0.008$) were found to be significant parameters in linear regression analysis. The presence of hydrocephalus was significantly associated with the extension of headache (21 vs 12, $p = 0.025$), extension of unconsciousness (19.5 vs 7, $p = 0.001$), and delays in clinical responses (21 vs 14, $p = 0.007$).

Conclusion. We found out that delayed start of antibiotics, hydrocephalus, and vasculitis. Hydrocephalus seems to be the principal factor affecting the normalization of the symptoms in TBM.

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1478. Dermatologic Manifestations in Live Attenuated Dengue Vaccines: A Skin Biopsy Study

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Background. Dengue fever is an important emerging disease and diffuse maculopapular rash is a characterizing clinical feature. Human dendritic cells (DC) are known targets for dengue virus (DV) infection and the etiology of the rash is hypothesized to be due to viral replication in DC or an immune mediated response. However, studies evaluating the presence of DV in dermal DC during wild-type infection and in one volunteer who received live attenuated dengue vaccine have been conflicting. In previous clinical trials of the TETRAVAX live attenuated tetravalent dengue vaccine (TDV), the majority of Caucasian subjects develop vaccine-induced rash (VIR). Examining VIR may provide important clues to the pathophysiology of wild-type infection.

Methods. In subjects without VIR, a single punch biopsy was performed. In vaccinees with VIR, three punch biopsies were done, two from rash site and one from non-rash site. Light microscopy was used to score the degree of inflammation and presence of Langerhans cells (LC), a subset of DC, by CD1a immunohistochemistry. VIR biopsies were also evaluated by dual immunofluorescence (IF) together with confocal scanning laser microscopy. 2H2 Ab for DV and CD1a for LC were used as double labels to demonstrate viral location. Data for neutralizing antibody response and viremia was collected.

Results. 12 subjects received TDV and 7 received placebo. VIR was found in 10 vaccinees (83.3%) and no placebos. Nine (90%) of those with VIR had inflammation

at the rash site, but not at non-rash sites. All VIR specimens demonstrated presence of DV within the dermis by IF. In 2 (20%) of subjects DV was detected in dermal DC, all others had extracellular virus. VIR was associated with viremia in 7(70%) of subjects with VIR, whereas 1 vaccinee without rash had viremia. Inflammation did not clearly correlate with higher numbers of DC or higher viremia.

Conclusion. Following TDV, DV is present in the skin of all vaccinees with VIR, which suggests systemic spread of virus. This is supported by the demonstration of viremia in 70% of subjects with VIR. Surprisingly, most DV was extracellular and not found in DC. VIR may be a clinical indicator of a robust immune response to vaccination. Correlation of VIR with antibody titer is ongoing.

Disclosures. **All authors:** No reported disclosures.

1479. Evaluation of Tularemia Courses: A Multicenter Study From Turkey

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Background. In this multicentric study, which is the largest case series ever reported, we aimed to describe the features of tularemia to provide detailed information.

Methods. This multi-center study pooled patients with any form of tularemia from 41 medical centers in Turkey. The study had a retrospective design and included patients treated between 2000 and 2013. No control groups were included for this study. Fatih Sultan Mehmet Training and Research Hospital's Review Board in Istanbul approved the study.

Results. Before the definite diagnosis of tularemia, tonsillitis (n = 653, 63%) and/or pharyngitis in (n = 146, 14%) were the most frequent the preliminary diagnoses. The most frequent clinical presentations were oropharyngeal (n = 832, 85.3%), glandular (n = 136, 13.1), oculoglandular (n = 105) forms. In 987 patients (95.5 %) the lymph nodes were reported to be enlarged, most frequently at the cervical chain [jugular (n = 599, 58%), submandibular (n = 401, 39%) periauricular (n = 55, 5%)]. Ultrasound imaging has shown hyperechoic and hypoechoic patterns (59% and 25% respectively). Granulomatous inflammation was the most frequent histological finding (56%). The patients were previously given antibiotics for 1176 episodes, mostly with beta lactam-beta lactamase inhibitors (n = 793, 76%). Anti-tuberculosis medications were provided in seven (2%) cases. The patients were given rational antibiotics for tularemia after the start of symptoms with a mean of 26.8 ± 37.5 days. Treatment failure was considered in 495 patients (48%). The most frequent reasons for failure were the production of suppuration in the lymph nodes after the start of treatment (n = 426, 86.1%), formation of new lymphadenomegalies under treatment (n = 146, 29.5%), and persisting complaints despite two weeks of treatment (n = 77, 15.6%). Fine-needle aspiration was performed in 521 patients (50%) as the most frequent drainage method.

Conclusion. In conclusion, tularemia is a long lasting, but a curable disease in this part of the world. However, the treatment strategy still needs optimization.

Disclosures. **All authors:** No reported disclosures.

1480. Distinguishing Anaplasmosis from Babesiosis Based on Initial History, Physical Examination, and Laboratory Data: Is It Possible?

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Background. Patients with presumptive diagnoses of tick-borne illnesses, including babesiosis and anaplasmosis are often treated for both diseases given their similar presentations in the preliminary stages of illness. This delay may expose patients to the side-effects of unnecessary treatment. During the year 2013, our endemic region saw a substantial increase in tick-borne illnesses. The aim of this study is to compare the presenting complaints, physical examination findings, laboratory values, and comorbidities for patients diagnosed with anaplasmosis or babesiosisin during this time of peak disease activity.

Methods. This cross-sectional study included patients with PCR-confirmed babesiosis or anaplasmosis diagnosed between January 1, 2013 and November 1, 2013. Data were collected from inpatient and outpatient electronic medical records. One-way analysis of variance was performed on continuous variables (age, duration of illness, laboratory data) and Fisher's Exact Test for categorical variables (sex, comorbidities, presenting signs/symptoms, Lyme disease coinfection). Statistical significance was assigned at $p < 0.05$.

Results. Of the 136 patients studied, 91 were diagnosed with anaplasmosis and 45 with babesiosis. Patients with anaplasmosis were statistically significantly more likely than those with babesiosis to present earlier to a physician or the ED following onset of symptoms (6.8 vs 4.2 days) and to have a lower serum sodium (136.4 vs 138.2), leukocyte count (4.5 vs 5.4), and total bilirubin (0.93 vs 1.40) on initial presentation. However, patients with babesiosis were significantly more likely to have a lower initial hemoglobin (12.0 vs 14.0) and hematocrit (35.1 vs 40.7), and a higher lactate dehydrogenase level (1794.5 vs 654.1). Patients with B. microti infection were significantly more likely to be coinfected with Borrelia burgdorferi compared with those infected with A. phagocytophilum (53.3% vs 7.7%), and to have a rash (15.6% vs 5.5%).

Conclusion. Our study shows key differences in the initial presentation, history, and laboratory values between patients with babesiosis vs anaplasmosis. This information may help to narrow and expedite therapeutic choices for patients.

Disclosures. **All authors:** No reported disclosures.

1481. Foodborne Outbreak of Human Brucellosis Caused by Ingested Raw Fetal Material of Cattles on Jeju Island

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Background. The first case of human brucellosis was reported in 2002 in South Korea, and followed by the incidence, it has been nationally increasing. However, bovine brucellosis, through the management of Animal and Plant Quarantine Agency, has not been discovered from 2003 to date on Jeju Island. Despite Jeju Island previously considered a clean area for bovine brucellosis, we experienced an outbreak of human brucellosis between 2012 and 2013.

Methods. We detected patients with human brucellosis between 2012 and 2013 on Jeju Island. The epidemiological, clinical, and microbiological data were collected. We tested for specimens in tissue from wound and blood using nested polymerase chain reaction (PCR) amplification of 16S ribosomal RNA (rRNA) and omp2. Serologic screening with standard tube agglutination (STA) test was performed on those who had a history of a contact with cattles.

Results. Between January 2012 and September 2013, 5 cases were identified on Jeju Island. Herein, the cases with Brucella abortus infection after ingested raw fetal materials of cattle at a folk restaurant are reported. All patients were male and immunocompetent. They were infected with brucella by a folk remedy that a raw fetal material would restore general conditions. Four cases were confirmed the isolation of brucella from blood. We investigated folk restaurants and detected a illegal distribution channel of raw fetal materials of cattle.

Conclusion. Because all patients developed zoonosis by a wrong folk remedy, we emphasize to enhance an educational program for awareness of zoonosis, active surveillance, detection and a control of illegal distribution channel for brucella infected animals in other areas.

Disclosures. **All authors:** No reported disclosures.

1482. Sentinel Surveillance of Respiratory Viral Pathogens in Border Areas of Western Cambodia

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Background. Little information is available about influenza and other common respiratory viruses in border populations in Western Cambodia, a region with relatively high incidence and highest mortality rate of H5N1 and future pandemic potential.

Methods. This out-patient surveillance system complements national surveillance using the same influenza-like-illness (ILI) case definition: > 1 years of age, fever (axillary $\geq 38.1^0$C), cough or sore throat, and fever onset within last five days without other diagnosis. Influenza real-time PCR was performed on combined nasal and throat swabs at 4 sentinel sites between May 2010 and December 2012. A subset of positive cases underwent antigenic analysis and antiviral susceptibility testing. All influenza PCR-negative ILI-specimens were cultured; a subset of culture-negative cases collected between May 2010 and April 2012 underwent RT-PCR for enteroviruses (EV), rhinoviruses (RV) and EV71.

Results. Among 586 ILI-patients (median age 5, 1-77 years), at least one respiratory virus was detected in 258 (44%) volunteers; 168 (29%) were positive by influenza PCR- 92 (55%) were flu A and 76 (45%) flu B. Among flu A, 48 (52%) were A/pH1N1, 43 (46%) A/H3N2 and one A/pH1N1 + B. Sixteen flu B isolates were B/Brisbane/60/2008 and four B/Malaysia/2506/2004. All 20 flu A and 16 flu B isolates tested were susceptible to oseltamivir and zanamivir. Influenza cases occurred almost exclusively in rainy season from June to November; vaccination coverage in 2010 and 2011 was ~ 20% responding to A/pH1N1(2009) pandemic and was zero in 2012 among study subjects. Viral culture

of 418 flu-PCR negative specimens detected adenovirus (5.7%), parainfluenza (3.8%), with no evidence of respiratory syncytial virus, metapneumovirus, coronavirus, or bocavirus. EV/RV RT-PCR detected 5.9% non-polio EV among 164 culture-negative specimens: coxsackievirus A4, A6, A8, A9, A12, B3, B4 and echovirus E6 and E9; no EV71 was found.

Conclusion. Influenza epidemiology in this sentinel surveillance showed similar trends as observed elsewhere in Cambodia. Ongoing surveillance for respiratory viruses including influenza and further research to clarify adenovirus and non-polio EVs as etiologic agents for acute respiratory infections is needed in Cambodia.

Disclosures. **All authors:** No reported disclosures.

1483. High Rate of Antibiotic Prescriptions for Outpatients with Influenza-Like Illness in Southern Sri Lanka

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Background. Acute respiratory illnesses, including influenza, account for a large proportion of ambulatory care visits worldwide. In the developed world, these encounters commonly result in unwarranted antibiotic prescriptions; data from more resource-limited settings are lacking.

Methods: Consecutive patients presenting to the Outpatient Department in the largest tertiary care hospital in southern Sri Lanka were surveyed for influenza-like illness (ILI). Patients meeting World Health Organization criteria for ILI– acute onset of fever ≥38.0°C and cough in prior 7 days—were enrolled. Consenting patients were administered a structured questionnaire, physical examination, and nasal/nasopharyngeal sampling for rapid influenza A/B testing (Veritor, Becton Dickinson).

Results were released to clinicians only in aggregate, as the test had not been formally approved for clinical use in Sri Lanka.

Results. We enrolled 311 patients with ILI from March-November 2013, with 54.7% (170) children ≤18 years and 55% (172) males. Approximately half (147, 47.2%) tested positive for influenza: 94 (30.2%) for influenza A and 53 (17.0%) for influenza B. On bivariable analysis, clinical features associated with influenza included pleuritic chest pain (26.5% vs 8.8%, $p < 0.001$), decreased appetite (83.0% vs 72.3%, $p = 0.026$), fatigue (87.8% vs 76.7%, $p = 0.012$), headache (85.0% vs 73.6%, $p = 0.014$), arthralgias (81.6% vs 62.9%, $p < 0.001$), and myalgias (81.6% vs 66.0%, $p = 0.002$). Most patients (253, 81.4%) were prescribed antibiotics, with no difference with regards to influenza status ($p = 0.320$). Commonly prescribed antibiotics included penicillins (164, 52.7%), first generation cephalosporins (64, 20.6%), and erythromycin (12, 3.9%). Patients prescribed antibiotics were more likely to be clinically diagnosed with a respiratory tract infection vs unspecified viral fever ($p < 0.001$), and to receive additional diagnostic tests (22.9% vs 10.3%, $p = 0.033$).

Conclusion. Approximately 50% of outpatients with ILI had confirmed influenza, but most were prescribed antibiotics. Improving access to low-cost, rapid diagnostic tests may decrease excessive antibiotic use, drug-related adverse effects, and healthcare costs. Rational prescribing of antibiotics in all settings is imperative given the rising global threat of antimicrobial resistance.

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1484. Detection of Respiratory Syncytial (RSV) and Influenza Viruses in Children with WHO Defined Pneumonia and Controls from Oshikhandass Village, Gilgit-Baltistan, Northern Pakistan from 2012-2014; Sensitivity and Specificity of Rapid Tests vs PCR

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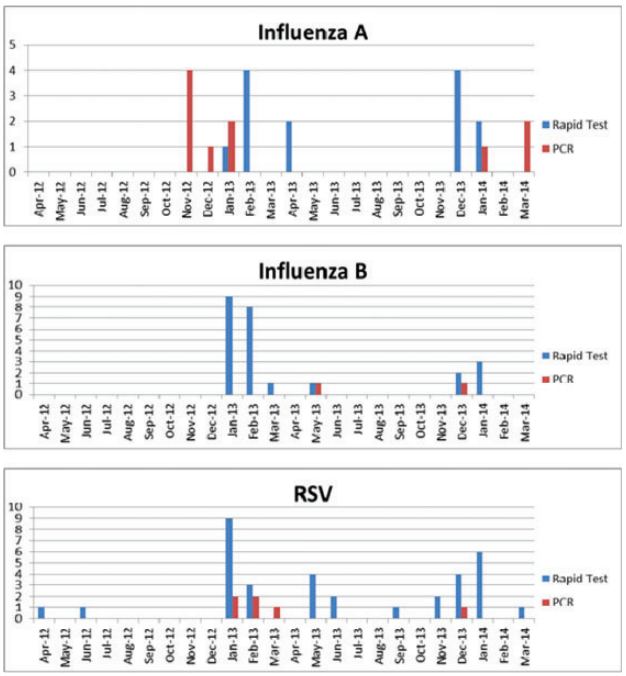
Background. Rapid viral diagnostic tests are commonly used to determine presumptive etiology of respiratory infections.

Methods. From 2012-2014, weekly surveillance of 1,176 children <5 years was conducted in Oshikhandass, a remote site with extreme winter and summer temperatures and 24 hours from reference labs. Nasopharyngeal (NP) swabs (Copan® Flocked Ultra Mini Tip) were collected from 233 children with WHO defined pneumonia and 66 controls for local rapid testing, followed by transport in PrimeStore® medium for PCR testing at reference labs. From April 2012-January 2013, rapid tests were conducted using QuickVue® and from January 2013-March 2014 using Sofia FIA®. The Luminex® platform was used from April 2012-November 2013 at AKU, Karachi, and the Taqman® Real Time PCR method from December 2013-March 2014 at NIH, Islamabad. Reported sensitivity/specificity for QuickVue® vs cell culture is 92/92% for RSV, 83/89% for Influenza A and 62/98% for Influenza B; for Sofia these are, 100/96%, 97/95% and 90/97%, respectively.

Results. Using PCR results as the gold standard, sensitivity/specificity of the various assays were compared. QuickVue® sensitivity was low for all 3 viruses. The number of influenza A and B positive results were too low to calculate sensitivity meaningfully. Sensitivity of the RSV Sofia® test was low when compared with Luminex® and Taqman®, while specificity for RSV was 74-94%, Influenza A 86-100% and influenza B 89-100%.

	QuickVue & Luminex N = 60		Sofia & Luminex N = 186		Sofia & Taqman N = 42	
	Sens	Spec	Sens	Spec	Sens	Spec
Inf A	0%	100%	0%	96%	100%	86%
	0/6	53/53	0/1	174/181	1/1	32/37
Inf B	N/A	100%	100%	91%	100%	89%
	0/0	59/59	1/1	164/180	1/1	33/37
RSV	0%	96%	37%	94%	26%	74%
	0/11	47/49	10/27	149/159	6/23	14/19

Conclusion. Possible reasons for poor sensitivity include low influenza circulation in the community and modest sample size. Other factors may be the inability to maintain controlled temperatures (15°C-30°C) for the kits and equipment in winter and summer month field conditions, and remoteness of reference labs. Development of diagnostic tests that maintain stability and function over extended time periods and within a wide range of temperatures is essential to provide reliable results for appropriate and timely management of respiratory illness in resource poor environments.



Positive rapid test and PCR results by month

Disclosures. **All authors:** No reported disclosures.

1485. Measles among immigrant children in Kirikkale, Turkey

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Background. Measles is still a leading cause of death among young children. For 2013, there were 31 520 measles cases reported in the European Region. Turkey is one of the nine countries where most of the cases were reported (7404 cases). According to the Ministry of Health (MH), all of these cases were outsourcing (mostly from Europe and Syria). Among all, 55, 1% of the cases were under 14 years of age and 36, 9% were

unvaccinated. Turkish MH organized an extensive vaccination campaign in refugee camps where Syrian children were living. However, out of 800,000 Syrian immigrants 600,000 don't live in these camps. Currently, receiving the vaccination within a recommended age period has become an important issue in many countries. A certain proportion of the target population lacking timely vaccination could contribute a measles outbreak, even if the overall coverage of that country was high.

Methods. This is a case-series of five measles cases followed between January 2014-February 2014.

Results. There are not many Syrian immigrants live in Kýrýkkale (a province in the middle of Anatolia) but, five measles cases (four were in 0-4 age group and one was 14 years old) were followed.Serological investigation confirmed the diagnosis of measles in all cases. They were all from the same extended family migrated from the South-East region of Turkey. This region is close to the Syrian border and also measles is still exists as a severe problem due to very low socioeconomic status. Common characteristics of our reported patients were being under nutrition, unvaccinated and living in the same crowded house.

Conclusion. Access to health care for medically uninsured immigrant children is a public health concern. Immigrant children are vulnerable to many risk factors and face a number of health problems related to their living conditions. The vaccination coverage of migrant children is much lower than that of local children, mainly as a result of migrants' high mobility, low socioeconomic status, lower level of knowledge and awareness about vaccination, and insufficient access to vaccination services. Therefore, to avoid outbreaks, it is crucial to attain high coverage levels by timely vaccination, thus, a systematic approach should be targeted to high-risk groups like immigrant and refugee children.

Disclosures. **All authors:** No reported disclosures.

1486. Geographic information system (GIS) mapping of endemic meningitis of 53 municipalities in three departments of Colombia

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Background. Application of new tools for epidemiological investigations, such as Geographical Information Systems (GIS), offers a new approach and possibilities for the eradication or control of infectious diseases. For this reason we developed epidemiological GIS-based maps for meningitis due to *Haemophilus influenzae* typo b (Hib), *Streptococcus pneumoniae* (Sp), *Neisseria meningitidis* (Nm) and *Mycobacterium tuberculosis* (Mt).

Methods. Surveillance cases data (2007-2011) were used to estimate annual incidence rates using reference population data, on above described meningitis (cases/1,000,000 pop) to develop the first maps of meningitis in the 53 municipalities of the coffee-triangle region of Colombia (departments Caldas, Quindio, Risaralda). GIS used was Kosmo® 3.1. Thematic maps were developed according municipalities, years and etiology.

Results. Between 2007-2011, 136 cases were reported (77 due to Mt, 31 Sp, 17 Nm and 11 Hib); for a cummulated rate of 55.68 cases/1,000,000 pop (31.52 Mt, 12.69 Sp, 6.96 Nm and 4.50 Hib). During that period, highest meningitis rates due to Mt, Sp, Nm and Hib were 80.54 cases/1,000,000 pop (2009, Pueblo Rico, Risaralda), 34.90 cases/1,000,000 pop (2007, Neira, Caldas), 26.02 cases/1,000,000 pop (2011, La Tebaida, Quindío) and 13.15 cases/1,000,000 pop (2011, Calarcá, Quindío), respectively.

Conclusion. Tuberculosis continue to be a significant cause of meningitis in this region of Colombia. GIS based disease surveillance was easily and rapidly implemented in this setting and should be useful in developing interventions, in addition to assessed socioeconomic and healthcare systems conditions for control and prevention.

Disclosures. **All authors:** No reported disclosures.

1487. Twenty years of experience in Hydatid Disease in Argentinian children

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Background. Hydatid disease (HD) is a zoonosis caused by larval forms of *Echinococcus granulosus,* and is the most frequent cause of liver cysts; however HD is one of the most neglected diseases. In Argentina, the pathology is endemic, with more than 300 new cases per year. The objective is to identify the epidemiology, clinical features, treatment, and outcome of children with HD admitted to a public tertiary care institution.

Methods. Observational study. Patients (p) ≤ 18 years old with *Echinococcus granulosus* infection based on WHO International diagnostic criteria were included. Epidemiology, clinical criteria, typical organ lesions by imaging techniques, histopathology, serology and parasitological studies were evaluated. Study period: from May 1993 to October 2013.

Results. Forty-five patients, most of them from rural areas, were included. Mean age at diagnosis was 7 years (range 3-17), 53% were male. Lungs and liver were the most common locations found in 48% and 42% respectively. Four patients (8%) had a cerebral and 1 p (2%) an ophthalmic cyst. In 38 patients (85%) only one organ was involved, and 14 patients (30%) had multiple cysts in one or more locations. Median time between symptom and diagnosis was 3 months (range 1-132). Clinical features depended on cyst location. Chronic cough and recurrent abdominal pain were the most frequent symptoms. Five p (11%) were asymptomatic, and 11 p (25%) only had fever. Specific serological tests were positive in 21 p (50%) and eosinophilia was seen in 11 p (25%), with a mean of 12.000/mm^3. Forty-one patients (92%) received anti-parasitic drug and surgical treatment. Total cystectomy was performed in 90%. Two p (4%) only required antiparasitic treatment because of the small cyst size. Complications were observed in 13 p (31%), with lung localization in 8 p (62%). Three p (6%) relapsed and required another surgery. None of patients died because of HD.

Conclusion. HD should be differentiated from other cyst types in patients coming from endemic areas, especially when located in the liver and or lung warranting adequate treatment. Lungs and liver are the most frequent organs involved. Surgery is necessary in the majority of cases.

Disclosures. **All authors:** No reported disclosures.

1488. Mapping malaria in municipalities of the Coffee-Triangle Region of Colombia using Geographic information system (GIS)

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Background. In other geographical settings, use of GIS for development of epidemiological maps in malaria has been extensively used, however not in the Coffee-Triangle region of Colombia, an area of three departments and 53 municipalities with endemic areas of disease for *P. vivax*, *P. falciparum* and *P. malariae*. Then, we developed such maps.

Methods. Surveillance cases data (2007-2011) were used to estimate annual incidence rates using reference population data, on above described etiological agents of malaria (cases/100,000 pop) to develop the first maps of malaria in the 53 municipalities of the coffee-triangle region of Colombia (departments Caldas, Quindio, Risaralda). GIS used was Kosmo® 3.1. Thirty thematic maps were developed according municipalities, years and parasite etiology, as well on uncomplicated and complicated cases.

Results. Between 2007-2011, 6582 cases were reported (6478 uncomplicated and 104 complicated) (77.8% from one department, Risaralda), for a cumulated rate of 269.46 cases/100,000 pop. Among uncomplicated cases, 5722 corresponded to *P. vivax* (234.25 cases/100,000 pop), 475 *P. falciparum* (19.45 cases/100,000 pop), 8 *P. malariae* (0.33 cases/100,000 pop) and 273 mixed (*P. falciparum/P. vivax*) (11.18 cases/100,000 pop). Highest rate was reported in the less developed and more rural municipality of one department (Pueblo Rico, Risaralda) with 5.77 cases/1,000 pop (717 cases in 2009).

Conclusion. Burden of disease is concentrated in one department (over 75% of the cases of the whole region). Use of GIS-based epidemiological maps allow to guide decisions-taking for prevention and control of a public health problem that still represents a significant issue in the region and the country, particularly in children.

Disclosures. **All authors:** No reported disclosures.

1489. Fulminant and Fatal: Two Strongyloidiasis Cases in HTLV-1 Patients

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Background. The Strongyloides hyperinfection syndrome is a well-known entity in patients with Human T-cell lymphotropic virus (HTLV-1). We present two cases of fulminant Strongyloidiasis in two unique HTLV patients in Bronx, NY. First case is a lethal infection in pregnancy and the second case had disseminated infection causing multi-organ failure.

Methods. Case 1: A 30 year old, 25 week pregnant patient from Haiti was admitted to the Obstetrics service for abdominal pain; presumptive diagnoses was abruptio placenta vs fibroid degeneration. She later developed acute hypoxic respiratory failure and septic shock. She had a still birth delivery, and died after one week in ICU. Respiratory and stool specimens showed *S.stercoralis* rhabditiform larvae. She was on antibacterials and Ivermectin, and was positive for HTLV-1. Autopsy findings reveal diffuse bronchopneumonia with bilateral hemorrhagic lungs, likely from *S. Stercoralis* hyperinfection and *E. coli*. Case 2: A 61 year old female from Jamaica presents with weight loss and altered mental status. She had fever, cachexia, ascites, severe electrolyte disturbances and anemia. Her course was complicated by acute hypoxic respiratory failure, septic shock and polymicrobial bacteremia (*Escherichia coli* and *Staphylococcus aureus)*. She developed skin changes thought to be necrotizing fasciitis on CT scan. Respiratory and stool microscopy were positive for *S. stercoralis,* and she was also positive for HTLV1. After treatment failure with oral Ivermectin, she was given oral then rectal Ivermectin mixed with

40% ethanol, and Albendazole. She improved with a prolonged course of Ivermectin. Patient had invasive *S.stercoralis* with cutaneous, respiratory, GI involvement causing polymicrobial sepsis.

Conclusion. These cases illustrate the mortality and morbidity of disseminated *S. stercoralis* in HTLV-1 co-infections. Pregnancy further enhanced the infection, which became rapidly lethal. In the second case, malnutrition and extensive GI involvement likely contributed to dissemination and caused treatment failure with standard Ivermectin treatment. Early consideration of Strongyloidiasis and HTLV-1 co-infections in patients from areas such as Caribbean and Japan, may reduce the morbidity of the infection.

Disclosures. **All authors:** No reported disclosures.

1490. Leptospirosis in the Coffee-Triangle Region of Colombia – mapping incidence and occupational aspects using Geographic information system (GIS)

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Background. There are few studies using GIS to mapping human leptospirosis. There are no detailed, municipality-level, epidemiological maps in Colombia neither in South America. Then, we developed such maps for the Coffee-Triangle Region of Colombia.

Methods. Surveillance cases data (2007-2011) were used to estimate annual incidence rates of leptospirosis using reference population data (cases/100,000 pop) to develop the first maps of disease in the 53 municipalities of the coffee-triangle region of Colombia (departments Caldas, Quindio, Risaralda). GIS used was Kosmo® 3.1. Five thematic maps were developed according municipalities and years. Using labor official information, an analysis between agriculture (cases among agriculture workers and harvested areas, available for 2008) with disease occurrence was done (linear regression).

Results. Between 2007-2011, 786 cases were reported (77.8% from one department, Risaralda), for a cumulated rate of 32.18 cases/100,000 pop. Highest rate was reported in the less developed municipality of one department (Pueblo Rico, Risaralda) with 1535.05 cases/100,000 pop (187 cases, 2009). Armenia (Quindio department capital city), reported 23.41 cases/100,000 pop (2011). In those patients with identified occupations, 33.3% were agriculture workers, finding a significant relationship between the number of cases in 2008 and the harvested area by municipality ($r^2 = 0.48$; $p = 0.0083$).

Conclusion. One of the 53 municipalities contributed with almost a quarter of the cases. Agriculture was significantly associated with the incidence. Use of GIS-based epidemiological maps allow to focus actions in prevention and control for risk zones for this disease that still represents a significant issue in the region and the country, particularly in agriculture workers.

Disclosures. **All authors:** No reported disclosures.

1491. Leptospirosis Mimicking Sepsis: A Multicenter Study

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Background. Leptospirosis is a common zoonotic infection in the world. Whether anicteric form of leptospirosis is a mild clinical course; icteric form of leptospirosis is severe clinical course which may sometimes result in mortality in the presence of the sepsis. The aims of our study were to evaluate clinical and laboratory findings of patients with leptospirosis according to jaundice and sepsis situations, and also to determine risk factors for mortality.

Methods. One hundred fifty seven patients were included to the study. The data between the dates of 1991-2013 from three different hospitals were retrospectively obtained from the formal records and laboratory findings. Patients firstly classified according to the presence of sepsis and non-sepsis then, they were divided into subgroups according to the presence of jaundice as icteric/anicteric. Clinical features and laboratory data were compared. Risk factors associated with mortality were determined.

Results. One hundred twenty nine (82%) of the patients were male. One hundred ten of the patients (68%) had signs of sepsis. Vomiting, abdominal pain, the presence of lung pathology also increased blood urea nitrogen and creatinine levels was significantly evident in sepsis group ($p = 0.046$, $p = 0.025$, $p = 0.003$, $p = 0.002$, $p < 0.001$, respectively). 99 of the patients (63%) were icteric and jaundice occurred more frequently in the sepsis group ($p = 0.115$). At the first admission to hospital, serum levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), total/direct bilirubin, potassium were higher in died patients than those of living ones ($p = 0.001$, $p = 0.003$, $p = 0.034$, $p = 0.036$, $p = 0.006$; respectively). Change in mental status ($p = 0.004$, OR:5.3, CI 95%: 1711-17042) and ALT elevation ($p = 0.030$, OR:1.004, CI 95 %: 1,000-1,008) were identified as independent risk factors for mortality.

Conclusion. The clinical and laboratory findings of leptospirosis are similar to sepsis. Elevation of serum transaminase and bilirubin levels and also presence of hyperkalemia has been associated with mortality in patients with leptospirosis. In areas where the disease is endemic; liver and kidney dysfunction is accompanied to the sepsis condition. So, leptospirosis should be investigated for the differential diagnosis.

Disclosures. **All authors:** No reported disclosures.

1492. Human Leptospirosis Trends: North Eastern Thailand, 2001-2012

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Background. Leptospirosis is an emerging public health problem globally. Since 1996, there has been a marked increase in number of reported leptospirosis cases and leptospirosis-associated deaths occurring annually in Thailand. The objective of this study was to determine the changing trend of this disease over time in Thailand.

Methods. Two prospective hospital-based studies conducted among adult patients with acute undifferentiated fever (AFI) admitted to Nakhon Ratchasima Hospital, Nakhon Ratchasima Province, North Eastern, Thailand in 2001-2002 and 2011-2012. Laboratory tests were performed to determine causes of this syndrome such as leptospirosis, scrub typhus, dengue infection. Incidence, clinical manifestations, and outcome of leptospirosis were compared between the two study periods.

Results. Two hundred and fifty eight patients were studied between July 2001 and December 2002, and 481 patients were studied between July 2011 and December 2012. During the first study period, leptospirosis (94 patients, 36.4%) and scrub typhus (61 patients, 23.6%) were two major causes of AFI. In the second period, scrub typhus (129 patients, 26.8%) was the most common cause of AFI, and leptospirosis was diagnosed in 63 patients (13.1%). Among patients with leptospirosis, proportion of male patients (89%), and median age were similar in both study periods. Most cases of leptospirosis were diagnosed between July and November. *Leptospira interrogan* serogroup Autumnalis was major infecting serogroup in both study periods. However, the case fatality rate of leptospirosis was significantly higher in 2011-2012 compared with the case fatality rate in 2001-2002 (19% vs6.4%, $p < 0.001$). Major cause of fatal leptospirosis was lung hemorrhage and multi-organ failure.

Conclusion. Number of leptospirosis has decreased over time. This trend is similar to reportable data for leptospirosis complied from passive surveillance of the Ministry of Public Health, Thailand. However, the case fatality rate of severe leptospirosis was increased. Severe lung hemorrhage associated with leptospirosis remained the major cause of dead.

Disclosures. **All authors:** No reported disclosures.

1493. Clinical features of Scrub typhus in Fukushima, Japan

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Background. Scrub typhus is endemic in Fukushima, where the highest number has been reported from 2006 to 2011 in Japan. The clinical and epidemiological features, phylogeneitc information have been reported in IDWeek 2012. The relationship between the clinical features and serotypes is not clear.

Methods. Observational clinical case series from 2008 to 2014, Retrospective chart review

Results. Total 42 cases (serotype Karp 18, serotype Kawasaki/Kuroki 24) of scrub typhus were confirmed as positive by real-time PCR analysis of eschars, and elevated specific IgM and IgG in the serum specimens in the year of 2008 to 2014. The clinical features categorized from type 1 to 4 based on two axes of characteristics: severity and presentation: triad (fever, rash and eschar) or atypical presentation without triad. Type 1 (mild/typical: 57% of 24/42) showed triad with stable clinical course, Type 2 (severe/typical: 5% of 2/42) presented with shock found to have bleeding tendency complicated with thrombocytopenia and DIC. Type 3 (severe/ atypical: 12% of 5/42) predominantly showed organ damage such as arrhythmia, syncope and meningoencephalitis. Type 4 (mild/atypical: 26% of 11/42) presented with the lack of triad, easily overlooked and resolved without treatment on occasion (5% of 2/42). Atypical cases with no eschar (14% of 6/42), no fever (10% of 4/42), no rash (5% of 2/42) are found in Type 4. In terms of serotype, Karp (43% of 18/42) in summer, Kawasaki/Kuroki (57% of 24/42) in late autumn are found with seasonal distribution.

Phylogenetic information by the gene sequences of the locus for the 56-kDa proteins showed that the two cases of Type 2 (severe/typical) are same as JP-1 (Karp). Serum type of Karp distributed from Type 1 to 4 (67, 11, 11 and 11%, respectively) and Kawasaki/Kuroki distributed also from Type 1,3 and 4 (50, 13 and 38%, respectively)

Conclusion. The clinical features of scrub typhus in Fukushima, Japan found to have diversity in severity, as well as both typical and atypical presentation. Serotype of Karp has wide clinical features from fatal to mild cases, and Kawasaki/Kuroki have also various features but non-fatal. The virulence of JP-1 in Type 2 should be noted. Atypical presentation of scrub typhus should be also mentioned as differential diagnosis of fever in this endemic area.

Disclosures. **All authors:** No reported disclosures.

1494. Scrub typhus among patients with acute undifferentiated febrile illness in a non-tropical, endemic area

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Background. Scrub typhus may be a life-threatening infection that usually presents as acute undifferentiated febrile illness (AUFI). Because of the similarity of clinical features and absence of sensitive point-of-care testing, however, clinicians have difficulty in differentiating scrub typhus from other etiologies among patients presenting with AUFI in acute healthcare settings.

Methods. This cross-sectional study included adult patients hospitalized with AUFI via the emergency department of a suburban Korean hospital between 2009 and 2013. AUFI was defined as any febrile illness with duration of ≤14 days, without any indication of localized infection at the time of initial presentation. Using epidemiological, clinical, and laboratory data, cases of scrub typhus, which were confirmed by indirect immunofluorescence antibody of ≥1:80 in a single serum or a ≥4-fold increase in paired sera, were compared with those of other AUFI etiologies. A multiple logistic regression model identified risk factors associated with scrub typhus to develop a clinical prediction rule (CPR) by summing up their regression coefficients. Its performance was checked by *c*-statistic.

Results. Of 382 AUFI cases, etiology was identified in 262 (68.6%): influenza (26.7%) was the most common cause, followed by acute hepatitis A (24.0%), scrub typhus (20.6%), hemorrhagic fever with renal syndrome (4.6%), primary bacteremia (4.2%), and *Plasmodium vivax* malaria (3.4%). Risk factors associated with scrub typhus included age of ≥65 years (simplified regression coefficient, 1), outdoor activity within the preceding 30 days (1), onset of the illness during the outbreak season of scrub typhus (2), myalgia (1), or eschar (1) ($P < 0.05$ for all). The *c*-statistic of CPR was 0.971 (95% CI, 0.951–0.991), and that with bootstrapping samples of 1,000 repetitions was 0.971 (95% CI, 0.952–0.990). For the cut-off value of ≥3, our CPR showed the sensitivity of 94.4% (95% CI, 83.7–98.6%) and specificity of 82.2% (95% CI, 76.2–87.0%).

Conclusion. Scrub typhus is one of the leading causes of AUFI in a non-tropical, endemic area. Our CPR can assist clinicians to identify immediately cases with scrub typhus among adult patients presenting AUFI in acute healthcare settings, with a high sensitivity and specificity.

Disclosures. **All authors:** No reported disclosures.

1495. Resistance of Fluoroquinolone in Orientia tsutsugamushi Due to gyrA Mutation in Scrub typhus

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Background. Scrub typhus is a mite-borne rickettsial disease caused by Orientia tsutsugamushi in endemic areas, and a public health concern for a population of over a million new cases emerging and a billion people at risk of infection. Although doxycycline remains the standard therapy, some reported effectiveness of levofloxacin as alternative regimen when treatment with doxycycline fails. However, there are clinical studies that quinolone is not effective in patients with scrub typhus. To clarify these discrepant results, we evaluated the genotype and mutation in gyrA associated with quinolone resistances.

Methods. This prospective observational study enrolled patients admitted to a tertiary hospital with scrub typhus from 2008 to 2012. 27 patients enrolled, and we obtained the gyrA gene of Orientia tsutsugamushi from 27 samples. With blood samples, we sequenced the quinolone resistance-determining region (QRDR), the target of fluoroquinolones, by nested polymerase chain reaction targeting the 56-kDa antigen gene.

Results. The genotype of samples were as followed; 7 Je-cheon strain, 5 Taguchi strain, 4 Boryoung strain, 3 Kanda strain, 3 Karp strain, 3 Pa-joo strain, 2 Ikeda strain. Irrespective of genotype, all 27 samples had the Ser83Leu mutation in the QRDR domain of gyrA gene, which is known to be associated with quinolone resistance.

Conclusion. Mutation of gyrA gene was identified in all DNA sample of O. tsutsugamushi, despite of genotype which enrolled for our study. These data provide evidence that O. tsutsugamushi has intrinsic resistance to fluoroquinolones, explaining treatment failures with such antibiotics in scrub typhus. Therefore fluoroquinolones should not be used for the treatment of scrub typhus, especially in severe cases.

Disclosures. **All authors:** No reported disclosures.

1496. Global Health Selective: A New Format for Introducing Topics in Infectious Diseases and Tropical Medicine for Medical Students at New York University School of Medicine

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Background. As demand grows for training in Global Health (GH) among medical schools, GH courses can offer new opportunities for teaching in infectious diseases and tropical medicine. Here, we describe a new selective taught at New York University School of Medicine (NYUSOM), aimed at introducing future physicians to fund of knowledge and clinical skills relevant to the practice of global medicine and research.

Methods. The course activities included patient case discussions in tropical medicine, clinical assignments in infectious diseases, literature review and journal clubs, microbiology workshops, and cultural competency and clinical skills simulation workshops.

Results. As a 4-week clinical clerkship, the GH Selective was completed by 39 students over three years. For each offering, 36 faculty members volunteered at least 216 hours of teaching hours from 10 NYUSOM departments. One half of the faculty involvement came from the Division of Infectious Diseases (Medicine); the Division of Infectious Diseases (Pediatrics); and the Department of Microbiology. Student feedback was overwhelmingly positive and the selective exceeded expectations.

Conclusion. GH course offerings provide a new vehicle for teaching relevant infectious diseases topics to medical students in innovative formats. The interactive, student-centered teaching employed in this course proved successful in introducing students to research-driven and culturally-sensitive GH care delivery.

Disclosures. **All authors:** No reported disclosures.

1497. Using Computer Vision and Depth Sensing to Measure Healthcare Worker-Patient Contacts and Personal Protective Equipment Adherence within Hospital Rooms

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Background. Determining if a healthcare worker (HCW) has practiced hand hygiene (HH) on entering or leaving a patient room is routinely performed by a variety of technologies; detecting potential HH opportunities within the room is more difficult. Our objective is to determine the feasibility of using computer vision and depth sensing to detect HH opportunities based on patient contacts, as well as determine personal protective equipment (PPE) adherence.

Methods. We used multiple Microsoft Kinects to track the 3-dimensional movement of HCWs and their hands within hospital rooms. We apply standard computer vision techniques to recognize and determine the position of fiducial markers attached to the patient's bed determin the location of HCW hands with respect to the bed. The only data saved is in the form of Cartesian (x, y, and z) coordinates from which we can recreate skeletal paths of HCWs with respect to the bed and the room.

To measure our system's ability to detect HCW-patient contacts we counted each time a HCW's hands entered a virtual rectangular box aligned with a patient bed. To measure PPE adherence, we identify the hands, torso, and face of each HCW on room entry, determine the color of each body area, and compare it to the standard color of gloves, gowns and face masks, respectively. Independently, we visually examined a ground truth video recording, producing a manual count for both contact and PPE adherence. We compared our system's results to ground truth.

Results. Overall, for touch detection the sensitivity was 99.7%, with a positive predictive value of 98.7%. For gowned entrances, sensitivity was 100.0% and specificity was 98.15%. For masked entrances, sensitivity was 100.0% and specificity was 98.75%, and for gloved entrances the sensitivity was 86.21% and specificity was 98.28%.

Conclusion. Using computer vision and depth sensing, we can estimate potential HH opportunities at the patient bedside and also estimate adherence to PPE adherence. Our approach can provide fine-grained estimates of how and how often HCWs interact directly with patients. Such approaches will help inform sub-room-level HH-monitoring efforts and other patient safety research.

Disclosures. **P. M. Polgreen**, GOJO Industries: Grant Investigator, Research grant and Research support

1498. Targeted Solutions to Increase Hand Hygiene

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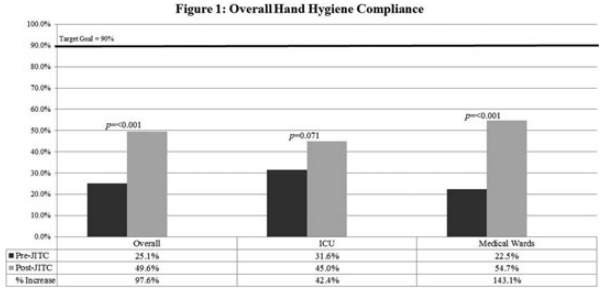
Background. Hand hygiene (HH) is a fundamental behavior for infection prevention. However, HH is commonly suboptimal, with compliance often only ~30-60%. In 2010, the Joint Commission Center for Transforming Healthcare launched the *Targeted Solutions Tool (TST) for Hand Hygiene* to aid institutions to increase HH compliance. Building on the principles and tools provided by the TST, we launched a HH Quality Improvement (HHQI) initiative on three pilot units.

Methods. Two medical wards and an ICU were in the HHQI pilot. A cadre of anonymous observers were trained and deployed for a two month period of covert baseline observations (n > 1,000) spanning all shifts/all days. Proper HH was defined as washing upon entry and exit from the patient environment. The second phase of the HHQI involved Just In Time Coaches (JITC) tasked to interact with staff on the pilot units, to coach noncompliant behavior, and to solicit the barriers to best practices. A team of JITCs seen as leaders in the organization, including nurse managers and medical directors, were trained and deployed on the pilot units.

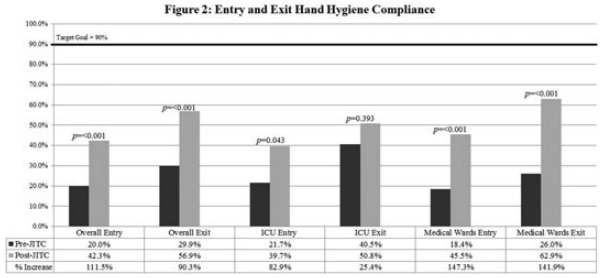
Results. Figures 1-3 show pre and post-JITC HH compliance overall by unit, upon entry and exit, and by healthcare worker type.

Figure 1: Overall Hand Hygiene Compliance



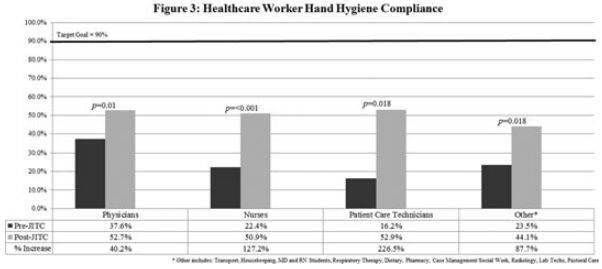
	Overall	ICU	Medical Wards
Pre-JITC	25.1%	31.6%	22.5%
Post-JITC	49.6%	45.0%	54.7%
% Increase	97.6%	42.4%	143.1%

Figure 2: Entry and Exit Hand Hygiene Compliance



	Overall Entry	Overall Exit	ICU Entry	ICU Exit	Medical Wards Entry	Medical Wards Exit
Pre-JITC	20.0%	29.9%	21.7%	40.5%	18.4%	26.0%
Post-JITC	42.3%	56.9%	39.7%	50.8%	45.5%	62.9%
% Increase	111.5%	90.3%	82.9%	25.4%	147.3%	141.9%

Figure 3: Healthcare Worker Hand Hygiene Compliance



	Physicians	Nurses	Patient Care Technicians	Other*
Pre-JITC	37.6%	22.4%	16.2%	23.5%
Post-JITC	52.7%	50.9%	52.9%	44.1%
% Increase	40.2%	127.2%	226.5%	87.7%

* Other includes: Transport, Housekeeping, MD and RN Students, Respiratory Therapy, Dietary, Pharmacy, Case Management Social Work, Radiology, Lab Techs, Pastoral Care

Conclusion. Baseline HH rates at our institution were suboptimal. Interventions with JITCs proved to be an effective tool to improve compliance and better understand barriers to best practices. JITCs found that HH noncompliance was largely due to many staff believing that HH was not required if they were entering a room not planning to have direct patient contact. Others believed gloves were an acceptable replacement for HH. While the goal is still 90% compliance, JITC was associated with statistically significant increases in HH rates early on during the pilot. It remains to be seen if this can be further improved and sustained, but the robust response to coaching indicates that firm emphasis on HH from leadership on the units can lead to rapid and significant improvements in compliance. Further efforts of the HHQI will include expanded institution wide JITC and education programs, as well as increasing the number of alcohol dispensers to facilitate proper HH. By facilitating appropriate behaviors while changing the culture of safety we hope to see greater sustained improvements in HH compliance.

Disclosures. **All authors:** No reported disclosures.

1499. Sustaining Hand Hygiene (HH) Near Perfect Compliance (C) with Just Culture (JC) – Accountability for Patient Care

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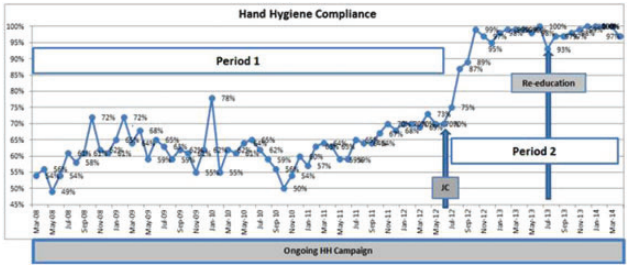
Background. HH is considered the most important way to prevent infections. Previous studies found deplorable Health Care Personnel (HCPs) HHC rates. Zero tolerance for HH nonC was adopted in 2003. Since then an ongoing HH campaign has been in place. HHC increased from 50% to 60% but peaked at 70%. In 2012 University of Pittsburgh Medical Center - Presbyterian (UPMC) HH campaign added JC, a system design to affect behavior. HCP are held accountable for conscious disregard for safety but not for system failures. HH nonC follows normal disciplinary process; verbal warning, written warning, final written warning, termination. JC was implemented in June 2012 and was associated with an immediate increased to near perfect HHC. Many investigators have reported success after HH initiatives but gains are often not sustainable. The objective of this study was to determine if neatly perfect HHC was sustainable after JC implementation.

Methods. ~800 standardized HH observations were collected monthly by 4 trained covert monitors (CoM). Rates were compared for 2 periods, pre intervention (P1) = March 2008-May 2012 and post intervention (P2) = June 2012 – April 2014. Biannual CoM training, education, and use of both soap and alcohol sanitizers were used in both periods. JC was implemented in June 2012. Education was provided initially and July 2013. Monthly HH observations were validated quarterly by external observers.

Results. See table.



HH C increased from a mean of 62.7 % (40,972/65,385) in P1 to 96.9% (18,321/18915) in P2, OR =0.05 (CI, 0.05-0.06, $p < 10^{-10}$) and has been ≥97% over the past 8 months. Overall 117 HCP received progressive disciplinary action; 112 verbal warnings, 1 written warning, 2 terminated, and 2 cases dismissed after JC deemed events to be secondary to system failure.

Conclusion. Incorporating a JC of patient safety with accountability and potential disciplinary action can drive HHC to near 100% and sustain near perfect HHC

Initiatives without accountability may increase HHC but gains are not sustainable

The acknowledgment of HH importance can become incorporated into the way work is done and system change can be achieved and sustained when JC system design is utilized.

Disclosures. **All authors:** No reported disclosures.

1500. Predictors of Hand Hygiene in the Emergency Department (ED): Impact of ED Crowding

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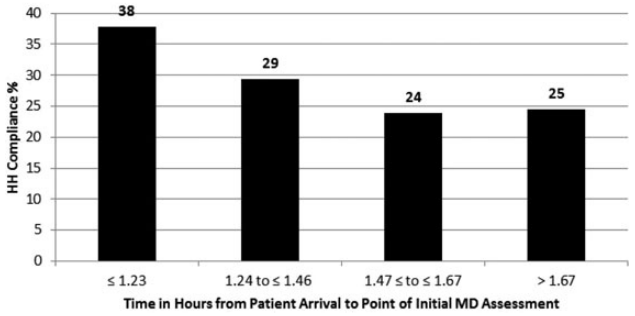
Background. Hand hygiene (HH) is not well studied in the emergency department (ED). In other settings, increased workload is associated with reduced compliance. We tested this hypothesis in the ED.

Methods. ED HH compliance was tracked at our facility by direct observation from January 2011 to October 2013. Daily ED patient volumes, staffing levels and mean time to MD assessment (TMDA) were used as measures of ED crowding. Predictors associated with compliance in univariate analysis ($p < 0.2$) were included in a multivariate logistic regression model.

Results. Average compliance was 29% (325/1116): 10% before aseptic procedures, 22% before patient/environmental contact, 26% after body fluid exposure and 37% after patient/environmental contact. Alcohol-based sanitizer was used 66% (215/325) of the time. Nurse staffing levels and patient volumes were not associated with compliance but TMDA was. Compliance was 38% for TMDA in the first quartile and 25% for TMDA in the fourth quartile (figure). Predictors of reduced compliance that remained significant ($p < 0.05$) in the multivariate model included: longer TMDA;

HH prior to patient/environmental contact or aseptic procedures (vs HH after contact); and professional designation of 'housekeeping' or 'other' (vs nursing).

Figure 1. Hand Hygiene Compliance by Quartiles of Mean Daily Time to MD Assessment



Conclusion. HH compliance in the ED was low. Soap/water are still used for 33% of HH. Increased TMDA and indication for HH were the strongest predictors of compliance. The drop in compliance seen with increasing TMDA indicates that ED crowding contributes to poor ED HH. Strategies to reduce the time required for HH in the ED (including optimal placement of dispensers or use of personal dispensers) and improve workflow practices are logical targets for improvement.

Disclosures. **All authors:** No reported disclosures.

1501. Inpatient Unit-Based Safety Culture Factors Associated with Sustained Hand Hygiene Compliance

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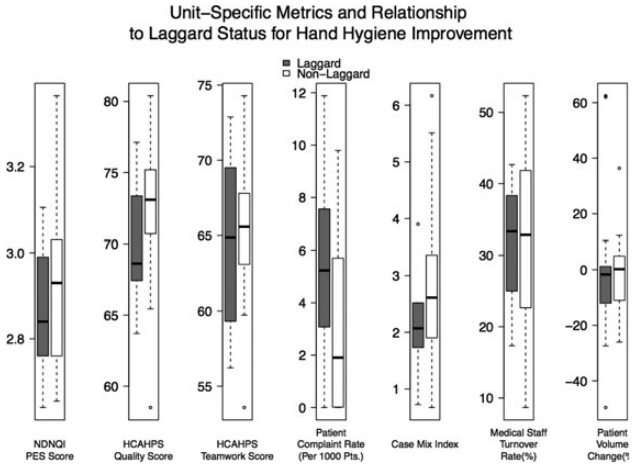
Background. Following institution of a hand hygiene (HH) program at an academic medical center, inpatient unit HH compliance increased from 58 to 92% over 3 years. The rate of improvement varied, with some units having early, sustained increases, and others exhibiting protracted improvement rates. We examined the association between patterns of HH compliance improvement and unit safety culture measures.



Methods. Adult inpatient units (N = 35) were categorized based on their pattern of HH compliance improvement (e.g., laggards = did not attain 90% compliance at three years; early adopters = achieved 80% compliance by year 1 and sustained high compliance during years 2-3; other = non-laggard/non-early adopter). Unit-based safety culture measures were collected, including nursing satisfaction scores (National Database of Nursing Quality Indicators [NDNQI]), patient ratings of quality and teamwork (Hospital Consumer Assessment of Healthcare Provider and Systems [HCAHPS]), and patient complaint rates. Case Mix Index (CMI), staff turnover rates, and annual changes in patient volume were also collected. Associations between each metric and laggard status were tested using a Mann-Whitney U test. Multivariate ordinal regression analysis was conducted using the outcomes of early adopter, laggard, or other and the variables of nursing satisfaction, CMI, patient complaint rate, and staff turnover rate.

Results. Laggard units had lower nursing satisfaction scores, lower patient ratings of quality, and a higher rate of patient complaints, although these differences were not statistically significant, potentially due to low sample size. Staff turnover rates, CMI, patient ratings of teamwork, and patient volume changes did not significantly differ between the groups. In the multivariate model, nursing satisfaction scores, CMI, and the patient complaint rate were, as a group, significantly associated with laggard status, (R-Squared = .35).

Conclusion. Uptake of HH compliance was associated with factors related to a unit's safety culture and teamwork. Staff turnover rates and patient volume changes were not associated with degree of uptake, suggesting that a strong unit culture may minimize the impact of such transitions on quality improvement programs.

Disclosures. **All authors:** No reported disclosures.

1502. Clean Hands Safe Hands: Behavioral Differences Between Doctors, Nurses and Allied Health Workers

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Background. Although hand hygiene (HH) is known to be central in reducing healthcare-associated infections, it is not consistently practiced. Audit reports in our hospital have shown that adherence rates have persistently been suboptimal at 50-60%. More importantly, the audits also showed differences in compliance rates between the healthcare workers (HCWs): physicians, nurses and allied health professionals (AH). Understanding why these differences are present may be key to designing better HH compliance strategies.

Methods. This is a cross-sectional study of physicians, nurses and AH in Tan Tock Seng Hospital Singapore using an anonymous questionnaire survey. Personal motivation and cognitive domains influencing HH compliance were assessed and compared between the three groups.

Results. We obtained 1064 valid surveys for analysis. Nurses reported the highest HH compliance (40.2% vs physicians 22.8%, AH 31.0%, $p < 0.01$) and motivation for improving their own HH compliance compared to the other groups (98.9% vs physicians, 96.5% and AH, 94.1%, $p < 0.01$).

Seven cognitive domains were identified from the survey: 1. Positive knowledge, attitude and behaviors (*kno*), 2. Personal motivators and enablers *(pers)*, 3. Emotional motivators (*emo*), 4. Need for external reminders (*ext*), 5. Barriers to HH (*bar*), 6. Preference for alcohol hand-rub (*alc*) and 7. Embarrassed if reminded (*emba*). Of these, *kno, bar, pers, ext* and *emo* were independently associated with good HH compliance. The domains *pers* and *ext* were also independently associated with the perceived ability to improve HH compliance (Table 1).

In a subgroup analysis of each HCW, we found that factors significantly associated with HH compliance were different between the groups (Table 2). In nurses, *pers* was positively associated with HH compliance, while *ext* was associated negatively. In physicians, *kno* was positively associated with compliance, while *ext, emba, bar* were negatively associated. Lastly, the AH group's HH compliance was only associated with *emo* (positive).

Table 1: Multivariate analysis. Factors associated **with *good hand hygiene compliance*** and ***the perceived ability to improve hand hygiene compliance.***

	Good HH compliance			Perceived ability to improve HH compliance		
Factors	Odds ratio	95% Confidence Interval	P-value	Odds ratio	95% Confidence Interval	P-value
Cognitive Domains						
Positive Knowledge, Attitudes, & Behaviors *(kno)*	1.44	1.23-1.69	< 0.01	0.76	0.47-1.23	0.27
Barriers to Hand Hygiene *(bar)*	0.83	0.72-10.95	< 0.01	1.26	0.76-2.07	0.37
Personal Motivators & Enablers *(pers)*	1.60	1.38-1.86	< 0.01	1.62	1.09-2.41	0.02
Preference for Alcohol Hand-rubs *(alc)*	0.90	0.79-1.03	0.13	0.91	0.61-1.35	0.63
Need for External Reminders *(ext)*	0.75	0.66-0.87	< 0.01	1.54	1.08-2.20	0.02
Emotional Motivators *(emo)*	1.62	1.4-1.88	< 0.01	0.67	0.44-1.02	0.06
Embarrassed if Reminded *(emba)*	1.03	0.90-1.18	0.46	1.05	0.70-1.57	0.82
Gender						
Male (vs. Female)	1.11	0.71-1.75	0.64	0.26	0.09-0.73	0.01
Profession						
Physician (vs. Allied Health)	0.67	0.38-1.19	0.17	3.26	0.84-12.62	0.09
Nursing (vs. Allied Health)	0.99	0.68-1.44	0.95	3.92	1.46-10.52	< 0.01
Years in profession						
>5 years (vs <=5 years)	0.98	0.73-1.32	0.89	2.78	1.04-7.39	0.04

Table 2: Multivariate analysis. Factors associated with good hand hygiene compliance in nurses, physicians and allied health professionals.

	Nurses			Physicians			Allied Health		
Factors	Odds ratio	95% Confidence Interval	P-value	Odds ratio	95% Confidence Interval	P-value	Odds ratio	95% Confidence Interval	P-value
Cognitive Domains									
Positive Knowledge, Attitudes, & Behaviors *(kno)*	1.01	0.96-1.06	0.76	1.66	1.28-2.16	< 0.01	1.07	0.97-1.18	0.20
Barriers to Hand Hygiene *(bar)*	1.00	0.96-1.05	0.97	0.65	0.51-0.82	< 0.01	0.93	0.84-1.03	0.16
Personal Motivators & Enablers *(pers)*	1.11	1.06-1.17	< 0.01	1.03	0.85-1.24	0.76	1.09	0.99-1.21	0.08
Preference for Alcohol Hand-rubs *(alc)*	0.93	0.86-1.01	0.06	0.94	0.69-1.28	0.70	0.89	0.78-1.03	0.11
Need for External Reminders *(ext)*	0.89	0.83-0.95	< 0.01	0.66	0.50-0.87	<0.01	0.91	0.78-1.06	0.21
Emotional Motivators *(emo)*	1.14	0.99-1.29	0.06	1.02	0.59-1.77	0.95	1.39	1.06-1.84	0.02
Embarrassed if Reminded *(emba)*	1.08	0.99-1.19	0.08	0.65	0.43-0.99	0.04	0.97	0.79-1.20	0.80
Gender									
Male (vs. Female)	0.91	0.46-1.79	0.78	2.22	0.62-7.99	0.22	1.07	0.42-2.76	0.89
Years in profession									
>5 years (vs <=5 years)	1.17	0.83-1.64	0.37	0.16	0.03-0.73	0.02	0.68	0.33-1.40	0.29

Conclusion. Our study has shown differences in socio-cognitive domains influencing HH compliance between groups of HCWs. Understanding these differences would permit a more targeted approach to improve HH compliance in hospitals.

Disclosures. **All authors:** No reported disclosures.

1503. Individual Accountability and Direct Feedback to Achieve and Sustain Good Hand Hygiene Performance

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Background. Hand hygiene (HH) is a fundamental infection prevention practice to prevent healthcare-associated infections and transmission of organisms, and is therefore a top patient safety priority. When our hospital initiated rigorous hand hygiene monitoring and data feedback in 2007, HH compliance was extremely low (20-30%). We planned and implemented a multi-faceted HH improvement program.

Methods. The Department of Hospital Epidemiology and Infection Control partnered with Executive Leadership, multi-disciplinary HH champions, hospital units and services, and a Hand Hygiene Task Force to implement a comprehensive hand hygiene program including Secret Shopper monitoring by trained observers, timely HH data feedback to units and services, unit- based monitoring and improvement efforts, and a HH Improvement Toolkit. When HH performance plateaued and further intervention was required, a Direct Feedback program was launched to provide reminders and education at the moment staff was observed missing a hand hygiene opportunity. Most recently, a HH accountability model was introduced holding staff accountable for individual HH compliance in a disciplinary model with escalating consequences for repeat offences.

Results. Hand hygiene compliance increased markedly after the introduction of direct feedback and the accountability model, reaching a record high of 97%. Performance has been sustained for 6 months, November 2013 through April 2014. High HH performance is seen across all services and provider types. There are 48 units on our Hand Hygiene Honor Roll for sustaining hand hygiene compliance of 90% or greater for 3 or more consecutive months. MRSA, VRE, and C. difficile transmission decreased and was temporally correlated with the HH compliance increase.

Conclusion. Hand hygiene improvement requires sustained effort and multi-faceted interventions over a number of years. Individual accountability and direct feedback were important additions to data monitoring and feedback to achieve culture change and sustained high HH performance. HH improvement is correlated with demonstrable decreases in MDRO transmission.

Disclosures. **All authors:** No reported disclosures.

1504. Implementing an Electronic Hand Hygiene Tracking Device at an Acute-Care Facility

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Background. With hand hygiene (HH) compliance seldom reaching 50% in healthcare, electronic compliance monitoring systems (ECMS) are supplanting the gold standard of monitoring with direct observation and feedback to increase compliance. We sought to determine the impact on HH compliance of an ECMS in an acute-care facility and to analyze theoretical constructs of health care workers (HCWs) and factors that impact program success and compliance improvement.

Methods. Pedometer-like ECMS devices were carried by 11 HCWs in a wing of a 117-bed acute-care hospital during a multi-phase study. Compliance was captured by direct observation and electronic recording through triggers installed in patient rooms and in touch-free dispensers. Feedback was disabled during Phase I, enabled during Phase II, and questionnaires were administered pre- and post-study. Comparisons of compliance between phases and according to work shift, in addition to questionnaire score differences, were calculated.

Results. During Phase I, HH compliance recorded by direct observation was 53.3% compared to 37.1% measured by ECMS. During Phase II, direct observation compliance decreased to 44.8% while ECMS increased to 50.8%. There was a statistically significant 22% increase in compliance from Phase I to Phase II. Timing of the work shift appeared to have a significant impact on compliance in Phase I where it was 40.4% during the day and 25.3% at night. However, compliance significantly increased in Phase II in all work shifts and, differences between work shift were no longer detected. Weekly quality checks for ECMS device accuracy were 93.6%, but verbatim questionnaire responses addressed concerns of accuracy and indifference to device use.

Conclusion. Despite a significant increase in HH compliance with ECMS, recruitment and retention of HCWs in the study was challenging, thus impacting sample size and leading to potential volunteer bias. Future studies may benefit from applying incentives, penalties or mandatory use of ECMS to sustain increased HH compliance. Developing a strong theoretical framework and identifying HH barriers and perceptions among HCWs prior to employing intervention may promote program success.

Disclosures. **S. Edmonds**, GOJO Industries: Employee, Salary **K. Fox**, GOJO Industries: Employee, Salary

1506. Variable Correlation Between Hand Hygiene Compliance and MRSA, VRE, and *C. difficile* incidence

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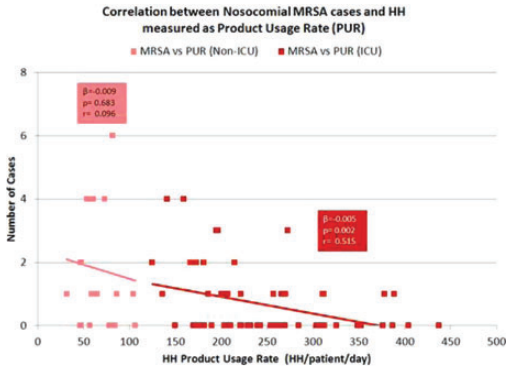
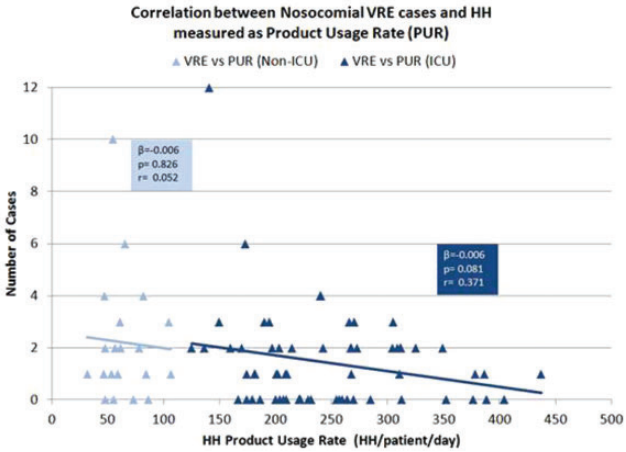
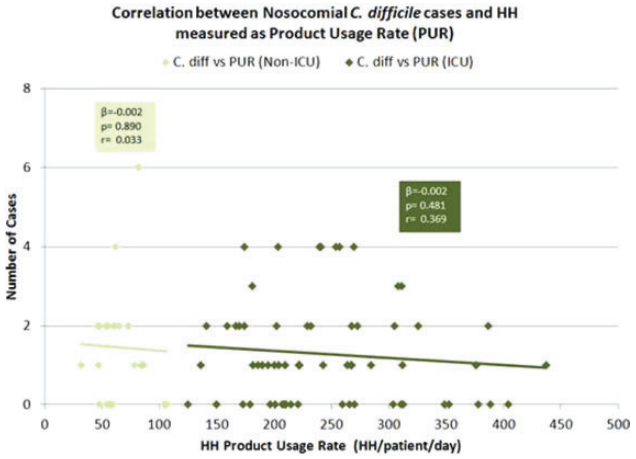
Background. Hand hygiene (HH) programs have been shown to reduce nosocomial infections but their relative impact on specific bacterial pathogens remains unclear. Understanding the effect of HH compliance on these pathogens may be important in prevention efforts. We sought to quantify the correlation between HH compliance and the incidence of MRSA, VRE and *C. difficile* at our institution.

Methods. A retrospective study was conducted using HH and MDRO data collected from January 2011 - March 2014. HH compliance was measured via product usage. Empty soap and alcohol hand rub containers are collected and counted weekly. HH events are calculated as the volume of product used divided by the standard aliquot per HH event. HH product usage rate (PUR) is calculated as the number of events per patient-days for each inpatient unit. All incident clinical and surveillance cultures positive for MRSA or VRE and nucleic acid amplification assays positive for *C. difficile*, obtained ≥2 calendar days after admission, were considered nosocomial cases. Only first cases per patient per organism were included. Number of cases and PUR were obtained for each unit and quarter, and then correlated using Pearson's correlation coefficient and generalized linear models controlling for unit type (intensive care unit [ICU] vs non-ICU), quarter.







Results. Eighty-three periods were included: 63 (75.9%) ICU periods and 20 (24.1%) non-ICU periods. PUR ranged from 31.8 to 437.0 HH/patient/day. The median was significantly higher in ICUs than in non-ICUs (231.8 vs 59.8, $p < 0.001$). There were significant negative correlations between MRSA and PUR ($r = 0.43$, $p < 0.001$) and VRE and PUR ($r = 0.25$; $p = 0.022$), but correlation was poor for *C. difficile* (figures). Adjusting for quarter and stratified by unit type, correlations for ICUs remained strong for MRSA ($r = 0.52$, $p = 0.002$) but weakened for VRE ($r = 0.37$, $p = 0.081$). Correlations for non-ICU units became non-significant.

Conclusion. HH compliance measured by product usage correlated well with MRSA cases overall and in ICU settings. VRE correlated more weakly and *C. difficile* correlated poorly. This ecological study suggests that the impact of HH over specific organisms is variable and may be related to the modes of transmission of each pathogen.

Disclosures. **All authors:** No reported disclosures.

1507. Impact of Electronic Compliance Monitoring in an Ambulatory Pediatric Orthopedic Clinic

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Background. Hand hygiene is one of the most crucial steps for preventing the transmission of illness; however rates of hand hygiene are persistently low. While most care occurs in ambulatory settings, there is little data on hand hygiene compliance rates in this environment. This study used an electronic hand hygiene compliance monitoring system to evaluate the impact of a comprehensive hand hygiene program on compliance rates in an ambulatory care clinic.

Methods. A compliance activity monitoring system was installed to monitor all exam room entries and exits in the clinic and all hand hygiene events from soap or sanitizer dispensers. Compliance was measured as number of events / number of entries and exits. Baseline measurements were taken without HCW knowledge from February 9, 2013-February 24, 2013. The intervention, which included implementation of a comprehensive hand hygiene program, ran from March 1, 2013-May 23, 2013. A post-study assessment from May 24, 2013-August 15, 2013 determined whether changes in compliance rates were sustainable. Pre- and post-study questionnaires assessed HCW knowledge, attitudes, and practices regarding hand hygiene. Appropriate statistical comparisons were made.

Results. There was a significant increase in the mean compliance rate from baseline to the intervention period, from 10.6% to 19.1%, representing an 80% increase. Additionally, the mean compliance rate in the post-study period was 13.6% which was significantly higher than the pre-study period, but a significant decline from the intervention period. Questionnaire data showed that HCWs perceived a significant increase in the amount of feedback they were given on their hand hygiene compliance, and observed a significant increase in the number of reminders to do hand hygiene.

Conclusion. Implementation of a hand hygiene program that includes a compliance activity monitoring system resulted in a significant, sustained improvement in hand hygiene compliance rates. However, sustaining increased rates after the intervention period continues to be problematic. Further research will help better understand how to sustain increased hand hygiene compliance rates over extended time periods and to determine the impact of the compliance monitoring system on clinical outcomes, including infection rates.

Disclosures. **S. Edmonds**, GOJO Industries: Employee, Salary **J. Kirk**, GOJO Industries: Employee, Salary

1508. Expected vs Actual WHO Five Moments Compliance among Paramedic Emergency Responders

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Background. WHO Five Moments (5M) is the gold-standard for the performance and measurement of Hand Hygiene (HH) compliance in hospital settings. Emergency responders practice in atypical environments where length patient transport time is often critical to clinical outcomes. To date however, there are no studies demonstrating the expected vs actual time spent on complying with WHO 5M performance indicators in the paramedic population.

Methods. HandyAudit® was used to collect HH compliance opportunities according to 5M among Paramedics at an urban, level-one trauma center in the USA Rocky Mountain Region. A total of 220 hours of direct HH observations were analyzed over two seasons (2012-2014) of the Respiratory Protection Effectiveness Clinical Trial (ResPECT). WHO 5M compliance was measured in time (hand washing= 50 seconds; alcohol rub = 25 seconds) according to expected and actual.

Results. A total of 106 paramedic-patient care transports were observed. Actual time spent on HH compliance was significantly lower than expected compliance. Expected compliance increases total time per patient 5.5-11 minutes depending on HH method implemented (table). Twenty-one HH observations occurred (12 Alcohol Rubs, 9 Hand Washing) in the external, non-patient care environment (i.e., staff break rooms), thus immeasurable in the context of WHO 5M due to HH performance location.

WHO 5 Moments		Expected	Actual
1. Before Patient Contact	Total HH Opportunities	1410	13
2. Before Aseptic Task	Hand Hygiene Performance		
3. After Body Fluid Exposure Risk	Hand Washing	N/A	0
	Alcohol Rub	N/A	13
4. After Patient Contact	Hand Hygiene Performance		
5. After Contact with Patient Surroundings	Hand Washing Time	1175 min	0
	Alcohol Rub Time	587 min	5 min, 25 sec
	Per Patient Transport		
	Hand Washing Time	11 min, 5 sec	0
	Alcohol Rub Time	5 min, 32 sec	3 sec

Conclusion. Paramedic WHO 5M compliance is suboptimal and education on WHO 5M performance indicators is needed. An emphasis that HH performance is to occur within the context of the patient environment is suggested in order to further increase WHO 5M compliance. Additionally, future HH research in the paramedic population for consideration is a paradigm shift model to account for unique workflow and access to HH issues.

Disclosures. **All authors:** No reported disclosures.

1509. Assessment of Hand Hygiene Practices And Usage of Alcohol-Based hand Sanitizer in Three Kenyan Hospitals, 2011-12

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Background. Hand hygiene (HH) by healthcare providers (HP) prevents healthcare-associated infections. Routine use of alcohol-based handrub (ABHR) increases HH adherence but can be cost-prohibitive. The World Health Organization (WHO) published methods for local production of ABHR to sustain supply and control costs in low-resource settings. The objective was to describe: 1) baseline HH adherence; 2) perceptions of locally-produced ABHR among HP; and 3) cost savings associated with local production of ABHR in 3 Kenyan hospitals.

Methods. Baseline HH adherence was defined as the number of successful HH events (HH with soap and water or ABHR) divided by the number of WHO-defined HH opportunities observed. Baseline HH adherence data was collected from December 2011 to May 2012 by trained observers in 16 wards. Differences in adherence by ward, HP type and before and after ABHR introduction were assessed using χ^2 tests. Nine focus groups were conducted with doctors, nurses, and other providers to assess perceptions of ABHR; transcripts were qualitatively coded using a standardized approach to describe key themes. ABHR was prepared in the hospitals using the published WHO formulation; data were collected from April 2012 to April 2013 and compared to the average wholesale cost of 8 brands of ABHR available to hospitals.

Results. Baseline HH adherence was 28%. ICU had the highest rates, while surgical and pediatric wards the lowest (figure). HH adherence significantly varied by HP type; doctors and clinical officers had the lowest adherence. Focus group respondents most often reported liking ABHR because it is fast and efficient to use and its perceived efficacy; dislikes included its smell and the residue it left on hands. Product availability was the dominant theme for sustainability, particularly "constant supply," "strategic placement" and "cheaper production." Production cost of ABHR was US$3.10 per liter compared to an average commercial purchase price of US$24.50. Throughout the pilot, 2166 litres of ABHR were used in the sites, with average monthly savings of $8503.

Figure 1: Baseline HH adherence 1st Dec 2011 to 31st May 2012

	Total # of Hand Hygiene Opportunities Observed	Overall Hand Hygiene Adherence (HH events/ opportunities)	Chi-square test of homogeneity (p-value)
Overall	5027	28%	
Ward			<0.0001
ICU	786	43%	
Medical	944	31%	
Specialty	1381	29%	
Pediatrics	1207	22%	
Surgical	709	15%	
Healthcare Personnel Type			<0.0001
Medical Officers	913	22%	
Clinical Officers	834	22%	
Nurses	1432	31%	
Students	708	31%	
Technicians#	153	32%	
Others*	987	32%	

#Technicians: Laboratory technician, Physical Therapist, Occupational Therapist
*Others include Nutritionists, patient attendants,

Conclusion. There is low HH adherence in Kenyan hospitals. Local production may provide a cost-saving sustainable source of ABHR that could improve HH adherence by Kenyan HP who like ABHR for its time-efficiency and perceived efficacy.

Disclosures. **All authors:** No reported disclosures.

1510. Improving healthcare worker hand hygiene adherence before patient contact: A contest between three Japanese tertiary care centers

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Background. Proper hand hygiene is an important strategy to prevent healthcare-associated infection. We previously showed low hand hygiene adherence among healthcare workers in four Japanese hospitals (adherence between 11% and 25%). In the current study, we evaluate the impact of a contest to improve hand hygiene practices of healthcare workers in three Japanese tertiary care centers.

Methods. Hand hygiene adherence was re-evaluated in three to four wards in each hospital - a surgical unit, a medical unit, an intensive care unit, and/or an emergency department – after a 6-month hand hygiene intervention. While all hospitals were provided guidance about the World Health Organization (WHO) multimodal hand-hygiene intervention, each hospital could tailor the intervention to their facility. Post-intervention hand hygiene adherence rates for each unit and hospital were compared to pre-intervention rates. Using the same methods as for pre-intervention, we focused on hand hygiene before patient contact. The hospital that achieved the highest hand hygiene adherence after the intervention was offered a prize consisting of 500,000 Japanese yen (approximately 5,000 USD) and a trophy, provided by an American collaborator not affiliated with any of the Japanese hospitals.

Results. A total of 2,982 post intervention provider-patient encounters were observed in 10 units across the three participating hospitals. Overall, the post-intervention hand hygiene adherence rate was significantly improved (18% pre- to 33% post-intervention; P < .001). Hand hygiene adherence was improved for both nurses (21% to 35%; P <.001) and physicians (15% to 30%; P <.001) post-intervention. Among those with appropriate hand hygiene, the use of alcohol-based hand rub increased significantly (67% pre- to 90% post-intervention; P < .001). The improvement in adherence rates varied considerably, however, by hospital (Hospital A +29%, Hospital B +5%, Hospital C +7%). Hospital A was the contest winner with 40% adherence post-intervention.

Conclusion. Use of a contest during implementation of a WHO-based multimodal intervention was successful in improving healthcare worker hand hygiene adherence rates in three hospitals in Japan. However, more work is required to improve hand hygiene compliance as rates remain low.

Disclosures. **All authors:** No reported disclosures.

1511. Correlation of Hand Hygiene Compliance Measured by Direct Observation with Estimates Obtained from Product Usage

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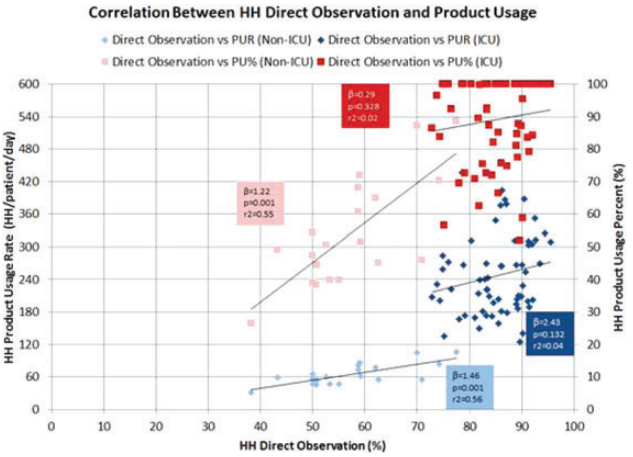
Background. Direct observation (DO) is the current standard for evaluating hand hygiene (HH) compliance but is labor-intensive and may overestimate compliance. Calculating HH rates indirectly by measuring product usage may be used to approximate HH compliance. We sought to characterize the correlation between HH by DO with product usage measured in two different ways.

Methods. HH data from January 2011 - March 2014 was included in the analysis. DO is performed by trained independent observers who record HH upon room entry/exit to obtain an average percent compliance (DO%). Observations are performed 3-4 times quarterly in intensive care units (ICUs) and 3-4 times yearly in medical/surgical units (non-ICUs). Empty soap and alcohol hand rub containers are collected and counted weekly. HH events are calculated as the volume of product used divided by the standard aliquot per HH event. HH product usage rate (PUR) is calculated as the number of events per patient-days for each unit and quarter. A standardized HH product usage percentage (PU%) is calculated using a standardized rate based on a study of room traffic (120 HH/patient/day for non-ICUs and 240 for ICUs). All 3 HH parameters were calculated by unit for each quarter. PUR and PU% were correlated to DO% using Pearson's correlation coefficient and generalized linear models controlling for unit type, fiscal year and quarter.

Results. Eighty-two periods were included, 62 (75.6%) ICU periods and 20 (24.4%) non-ICU periods. DO% ranged from 38.3% to 95.5% (median 83.3%); PUR ranged from 31.8 to 437.0 HH/patient/day (median 203.7); PU% ranged from 26.5 to 100% (median 86.7%). All 3 parameters were significantly higher in ICUs than non-ICUs. There was a significant positive correlation between DO% and PUR ($r = 0.74$, $p < 0.001$) and DO% and PU% ($r = 0.76$; $p < 0.001$). When stratified by unit type, adjusted correlations of DO% with PUR and PU% remained strong for non-ICUs ($p < 0.0001$) but not for ICUs (figure).



Conclusion. HH compliance by DO correlates well with HH by product usage measured by crude rates or standardized percentages. The latter allows presentation of data that is more easily interpreted by front-line staff. A weaker correlation in units with high HH compliance may highlight the need for more discriminating methods to measure HH compliance in top performers.

Disclosures. **All authors:** No reported disclosures.

1512. Commitment Instead of Compliance: A Secret of Success and Sustainability for the Hand Hygiene Program

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Background. For the past two decades, healthcare field has been overwhelmed with numerous patient safety initiatives. In the face of the ever-conflicting priorities,

it is common for organizations to rapidly implement and reallocate resources from one project to another shortly after implementation. In our experience in a multisite acute care community hospital, a consistent approach to maintaining dedicated resources for the Hand Hygiene program resulted in the significant and sustained improvement in Hand Hygiene over the five year period.

Methods. A program based champion model (one person from each of the hospital programs) was trained and allocated on the weekly bases to perform hospital wide auditing by direct observations. Just in time education and feedback by the auditors was given to healthcare providers for all the missed opportunities. A standardized provincial tool was used to collect and record observation data. The observation data was summarized using an access database and broadcasted hospital wide by-weekly, monthly and quarterly. An average of 1725 observations was collected on the weekly basis and broadcasted hospital wide. A year end data was reported publicly on hospital website. A positive reinforcement strategy was used to commend clinical areas with the best results. Certificates were handed by CEO to leaders of clinical areas that performed at or above the target level.

Results. The ongoing observations, feedback and attention to the hand hygiene resulted in a significant and sustained improvement. The target was raised and achieved three times over the five year period: year one and two target - 80% to 85%; year two and three target - 85% to 90%; year five target - 90% to 95%.

Conclusion. In five years since the beginning of the project, the adherence to Hand Hygiene increased to 95%. We were able to demonstrate that high priority patient safety initiatives require positive reinforcement and consistent ongoing effort over several years. The organizational commitment can be translated to the increased and sustained compliance over time.

Disclosures. **All authors:** No reported disclosures.

1513. Efficacy of Hand Hygiene (HH) Monitoring Technology: a Systematic Review

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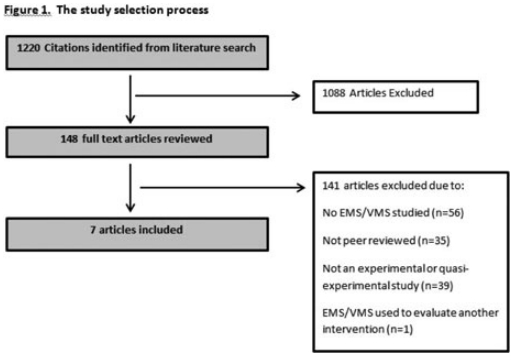
Background. Electronic and video monitoring systems (EMS/VMS) for healthcare worker HH may improve hand hygiene compliance (HHC) by providing feedback (FB) or real-time reminders (RTR). We conducted a systematic review to assess the efficacy of EMS/VMS in improving HHC.

Methods. MEDLINE and other databases were searched to 2013. Experimental and quasi-experimental studies of EMS/VMS were included if they measured directly observed HHC (1° outcome), HH frequency, HH product use, or system defined compliance (SDC). Risk of bias (ROB) was assessed using the Cochrane EPOC tool and a scale for quasi-experimental studies.

Results. Seven studies were included (Figure 1). Most (6/7) used SDC as their 1° HH outcome; 1 study used HH frequency and 1 used SDC and HH product use. SDC was defined differently for all EMS/VMS. No study measured HH prior to EMS/VMS installation. Most studies were on single wards (6/7) in acute care (6/7). The median (range) of study duration and HH opportunities were 24 weeks (2 to 91) and 194,150 opportunities (8,235 to 1,017,600). Studies are grouped by their mechanism of action: *EMS with RTR and no FB:* Two pretest-posttest studies evaluated use of voice prompts on room entry and/or exit. Both demonstrated improvement in SDC. Both were at high ROB. *EMS/VMS with FB and no RTR:* Two studies assessed the same VMS that provided continuous aggregate FB of SDC and found a sustained increase in SDC using a time series design. Both studies were at moderate ROB. One non-randomized controlled study assessed an EMS that provided aggregate FB on HH event rates. There was no difference in HH frequency in the control and intervention unit but baseline HH frequency was not measured and the study was at high ROB. *EMS with FB and RTR:* Two studies tested EMS that monitored room or zone entry/exit and provided healthcare workers with individual FB and vibratory RTR. A pretest-posttest study showed an increase in SDC but was at high ROB. An RCT showed a small, non-sustained increase in SDC and was at low ROB.

Figure 1. The study selection process



Conclusion. No study measured directly observed HHC or HH pre-installation. The only study at low ROB showed no sustained benefit. Before widespread implementation of a complex and expensive technology, efficacy should be demonstrated in well-designed studies at low ROB.

Disclosures. **All authors:** No reported disclosures.

1514. Targeting Behaviors Using Transtheoretical Model To Improve Hand Hygiene Adherence Among Intensive Care Unit Healthcare Workers

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Background. To evaluate the behavioral-based interventions to improve hand hygiene (HH) among Thai intensive care units (ICUs) healthcare workers (HCW).

Methods. A quasi-experimental study was performed at Thammasat University Hospital. Baseline HCW demographics, self-reported stage of HH behavior within the Trantheoretical Model (TTM), and observed HH adherence were examined. Pre-intervention period (P1) was from January 1, 2012 to December 31, 2012 and post-intervention period (P2) was from January 1, 2013 to December 31, 2013. Six ICUs were group randomized to one of three strategies: HH education by Infection Control Division every 3 months (S1); intensified HH interventions by study investigator (S2); and intensified HH interventions together with increasing alcohol hand rub at all bedsides, nursing stations, physician working stations, and procedure stations (S3). Intensified HH education included monthly education that emphasized HH adherence and impact on patient safety and weekly workgroup discussion exploring reasons for not performing HH among HCWs with different behaviors. Each strategy consisted of 2 ICUs.

Results. There were 125 HCWs from 6 ICUs (42 in S1; 41 in S2; 42 in S3) with 1,936 HH observations over both periods. During P1, 70 HCWs (56%) self-reported HH Maintenance, 26 HCWs (21%) reported HH Action, and 29 HCWs (23%) reported HH Preparation or less commitment. Most HCWs were nurses (75/125; 60%) and nurse assistant (25/125; 20%). Compared to P1, overall HH adherence in P2 improved in ICUs in S2 (65% vs 85%; P= 0.02) and S3 (66% vs 95%; $P = 0.005$), but not ICUs in S1 (68% vs 71%; $P = 0.84$). Improvement in HH adherence in ICUs in S2 was shown among HCWs who reported HH Preparation or lower commitment (21% vs 84%; $P < 0.001$), while improvement in HH adherence in ICUs in S3 occurred among HCWs who self-reported HH preparation or lower commitment stage (24% vs 89%; $P < 0.001$) and HH Action and Maintenance stages (78% vs 96%; $P < 0.001$).

Conclusion. Our findings suggest that HH intervention should be tailored to the HCWs self-reported HH commitment. Additional studies to translate behavioral theory into practice will further inform on sustainable improvement in HH adherence.

Disclosures. **All authors:** No reported disclosures.

1515. Perceptions and Barriers to Universal Gloving for Infection Prevention: A Survey of Healthcare Workers and Patients

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Background. Universal gloving (UG) for patient care is an infection prevention adjunct. We assessed healthcare worker (HCW) and patient perceptions/barriers to UG.

Methods. VCU Medical Center is an 865-bed academic medical center. A 12-item HCW and 10-item patient anonymous, voluntary, Likert scale survey was distributed by convenience sample. We compared responses between providers and patients.

Results. A total of 137 patient and 366 HCW surveys were completed. The largest barrier to UG is HCW inconvenience, 41% (n = 140).

Patients would be more satisfied with care under UG, 70% (n = 94).

Item	Nurse	Physician	P value
Gloves readily available (mostly/always)	100% (210/210)	100% (57/57)	NA
Perform hand hygiene (HH) before wearing gloves (mostly/always)	91% (191/210)	82% (47/57)	.07
Perform HH after wearing gloves (mostly/always)	95% (200/210)	88% (50/57)	.06
Gloves prevent spread of infection between patients (probably/definitely)	77% (161/209)	65% (37/57)	.06

continued.

Item	Nurse	Physician	P value
Gloves compromise HCW-patient relationship (probably /definitely)	8% (18/210)	12% (7/57)	.40
Gloving takes away from patient contact time (probably/definitely)	7% (15/210)	0% (0/57)	.05
UG should be mandatory (probably/definitely)	50% (106/210)	12% (7/57)	<.0001

Item	HCW	Patient	P value
HCWs perform HH before wearing gloves (mostly/always)	84% (300/357)	72% (98/136)	.003
HCWs perform HH after wearing gloves (mostly/always)	93% (331/357)	74% (100/135)	<.0001
Gloves compromises HCW-patient relationship (probably/definitely)	10% (37/357)	15% (21/136)	.12
Gloves prevent spread of infection between patients (probably/definitely)	76% (270/357)	77% (106/137)	.68
UG should be mandatory (probably/definitely)	43% (154/358)	79% (106/134)	<.0001

Conclusion. HCWs and patients believe that UG decreases cross transmission. Despite high glove availability and high rates of HH, HCWs perceive UG as inconvenient. Patients reported that HCW HH compliance was less than compliance as reported by HCWs. HCWs and patients feel that UG does not impact the HCW-patient relationship. Patients and nurses favor mandatory UG more than physicians. Hospitals advocating UG must overcome perceived inconvenience and ensure that high rates of HH are sustained.

Disclosures. **All authors:** No reported disclosures.

1516. Acquisition of *Clostridium difficile* on Hands of Healthcare Workers Caring for Patients with Active or Resolved *C. difficile* Infection

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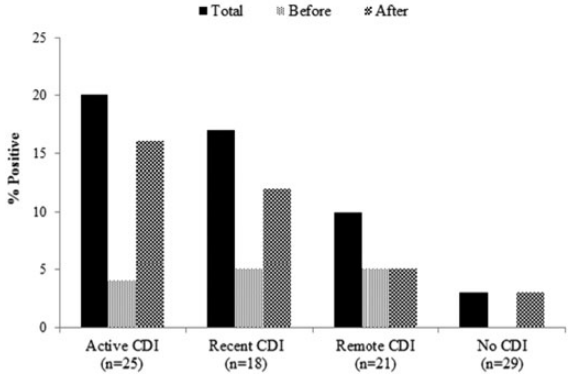
Background. Current practice guidelines for management of *Clostridium difficile* infection (CDI) recommend that contact precautions can be discontinued after diarrhea resolves. However, it is known that patients with CDI often continue to shed spores for several weeks after successful treatment. We hypothesized that healthcare workers frequently contaminate their hands while caring for patients with recently resolved CDI who are no longer in contact precautions.

Figure. Acquisition of *Clostridium difficile* on Hands of Healthcare Workers Caring for Patients



Methods. During a 4-month period, we cultured hands of healthcare workers for toxigenic *C. difficile* before and after providing care for patients with active CDI, recent CDI (within 6 weeks after end of treatment with no recurrent CDI symptoms), remote CDI (6-24 weeks after treatment), or no history of CDI; cultures after care were collected prior to hand hygiene. Healthcare workers wiped their hands with a sterile, pre-moistened gauze pad that was placed into a sterile specimen cup and cultured by broth enrichment. Bivariate analysis was used to identify factors associated with positive hand cultures.

Results. Hand cultures were collected during 93 encounters with 53 patients (1 to 3 healthcare workers per patient). As shown in the figure, acquisition of hand contamination was common when caring for patients with active or recent CDI, and less common when caring for patients with remote or no CDI. Factors associated with acquisition on hands included nursing job description and extensive interaction with patient and/or environment. Acquisition of spores on hands was common during care of CDI patients despite glove use.

Conclusion. Healthcare workers frequently acquired *C. difficile* spores on their hands while caring for patients with active or recent CDI. Hand contamination during care of CDI patients was common despite glove use, suggesting that hand washing with soap and water may be beneficial. Extending the duration of contact precautions may be a useful strategy to reduce transmission by patients with recent CDI.

Disclosures. **All authors:** No reported disclosures.

1517. Maintaining a near perfect Hand Hygiene (HH) and Isolation (Iso) Compliance (C) despite high Isolation Density

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Background. HH is among the most important way to prevent healthcare-associated infections (HAIs). There are a multitude of reasons why HHC is not perfect. In 7/12, UPMC – Presbyterian Campus (P) implemented measures to Just Culture (JC) system design to create an environment of accountability for HH practices. Previously

HHC rates averaged 62.7% but since JC implementation HHC rates have been nearly perfect (96.9%). In addition to HH practices, the Centers for Disease Control and Prevention (CDC) recommends that personal protective equipment (PPE) be worn for patients who require pathogen-specific isolation. A recent study (Dhar S. et al. ICHE 2014;35(3):213) suggested that when the proportion of patient in contact IsoDays increase, HHC and IsoC decreases. The objective of this study was to access whether HHC is influenced by Iso Density at UPMC-P.

Methods. HH is expected for all patient zone interactions. ~800 standardized HH observations were collected monthly (evenly distributed over 36 patient care areas) by 4 trained covert monitors (CoM). HH C is measured across all health care personnel (HCP) types for all WHO HH opportunities (some before, some after contact with the patient zone). Definitions:

PTDays - the # of days that in-patients are hospitalized and extracted from our medical healthcare record a

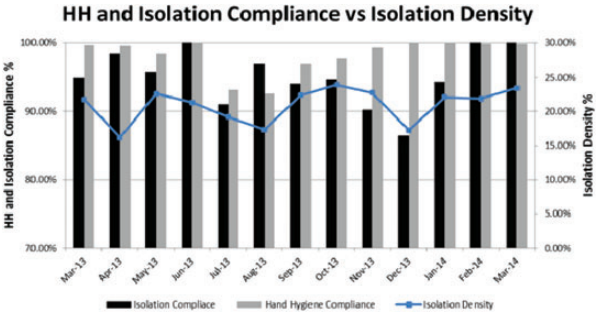
IsoDays - the # of PTDAYs spent in contact precaution and are determined using Theradoc software

Iso Density - the proportion of patient (PT) days that are spent in contact Iso (contact Iso Days)/PTDays)

IsoDensity better quantifies potential exposures and risk for transmission and was calculated monthly and compared to

HHC/IsoC over a 13 month period.

Results. See graphs.



	Mar-13	Apr-13	May-13	Jun-13	Jul-13	Aug-13	Sep-13	Oct-13	Nov-13	Dec-13	Jan-14	Feb-14	Mar-14
ISO Days	4115	2898	4223	3884	3621	3290	4130	4553	3856	3049	4205	3738	4317
Patient Days	18914	17938	18680	18208	18883	18995	18461	19032	16960	17679	19050	17082	18445
Isolation Density	22%	16%	23%	21%	19%	17%	22%	24%	23%	17%	22%	22%	23%
Hand Hygiene Compliance	100%	100%	98%	100%	93%	93%	97%	98%	99%	100%	100%	100%	100%
Isolation Compliance	94.93%	98.47%	95.73%	100.00%	91.04%	96.94%	94.03%	94.69%	90.27%	86.41%	94.32%	100.00%	100.00%

Conclusion. HH and IsoC were both high, often approaching 100%. Providers/IP programs should consider the potential for transmission if when developing infection control policies/practices. Iso Density had no effect on HHC or IsoC.

Disclosures. **All authors:** No reported disclosures.

1518. Hand Hygiene for Patients: an Initiative to Study and Promote Hand Hygiene Practice for Hospitalized Patients

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Background. Hand hygiene (HH) practice in hospitalized patients has not been widely studied. Patient HH (PHH) may affect the acquisition of hospital acquired infections (HAIs) by direct contact transmission. The healthcare worker (HCW) is the primary resource for PHH assistance and education. The acuity and mobility status of patients may be obstacles to HH. Preliminary surveys at our hospital showed HH education was provided 20% of the time and HH opportunities before meals and after toileting occurred < 50% of the time. A PHH study was implemented on 4 patient units to provide education coupled with pre-packaged alcohol wipes (AWs) at the bedside to improve PHH practice.

Methods. Patients were surveyed over a 1 month period concerning their HH practices for baseline data. HCWs were then in-serviced on the value of PHH and requested to educate all new patients. AWs (Sani Hands® 69.5% alcohol) were made available. Daily reminders and assisted opportunities for HH were encouraged. Dietary provided a reminder on meal trays for HH prior to eating. After implementation, follow-up surveys were collected for a 4 month period. Percent improvement was analyzed by Chi-square test. HAIs were followed pre- and post-intervention.

Results. PHH increased significantly post-intervention (table). *C. difficile* infections (CDIs) decreased (14 pre- and 9 post-intervention) with no reduction noted in other HAIs during the study.

Patient HH Survey Questions

	Pre-intervention (N=97)	Post-intervention (N=291)	Percentage Change	Chi-Square p-value
Verbal or written education provided	33/96 (34%)	188/291 (64%)	88.20%	<0.0001
Opportunity for HH provided	55/92 (60%)	251/291 (86%)	43.30%	<0.0001
Encouragement for HH: Prior to meals	51/92 (55%)	201/277 (72.5%)	31.80%	0.002
After toileting	66/94 (70%)	236/287 (82%)	17.10%	0.013
Before or after having visitors	21/87 (24%)	106/253 (41.8%)	74.20%	0.003
Before touching dressings or incisions	15/73 (20.5%)	92/194 (47.4%)	131.20%	<0.0001
After returning from testing or procedure	18/76 (23.6%)	88/214 (41%)	73.70%	0.007

Conclusion. PHH practice can be improved by providing education, the opportunity to clean hands with AWs and encouragement. Incidence of CDI may be influenced by improved PHH practice.

Disclosures. **All authors:** No reported disclosures.

1519. "Clean in, Clean out" initiative: Improving hand hygiene compliance among frontline healthcare personnel by observations of each other and immediate feedback

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Background. Hand hygiene (HH) has an important role in infection control and patient safety in healthcare facilities. The University of North Carolina (UNC) Hospitals has improved our HH compliance, but reached a plateau between 80-90% in recent years. To achieve further compliance we implemented our "Clean In, Clean Out" (CICO) initiative encouraging all healthcare personnel (HCP) to perform observations and provide immediate feedback of each other. Here we provisionally assessed the trends of HCP involvement in this program and HH compliance.

Methods. CICO has been conducted at UNC Hospitals, an 800-bed tertiary care facility since October 2013. Observations were performed of any HCP who entered or exited the patient's room. Providing immediate feedback to non-compliant HCP was encouraged. HCP reported their observations with dates, locations, and job classifications of observers using the mobile iScrub App or paper forms entered in a web-based survey tool. Unit and job classification based reports were provided at least monthly and each location maintained a visual display with real-time data available as charted by observers in their area. Areas with low compliance were required to develop specific action plans. CICO data between October 2013 and March 2014 were evaluated. Our compliance goal was ≥90%.

Results. A total of 46,064 observations were reported during six months. Overall, the number of unique observers increased from 758 in October to 1,026 in March. Increasing trends were observed in the overall compliance and average compliance among the units and job classes who had <90% compliance at the start of the program (Figure 1). The proportion of units which achieved 90% compliance doubled (95% CI 1.0-4.1, p = 0.04) from 20.5% (8/39) in October to 41% (16/39) in March. By job classes, housekeeping staff improved their compliance significantly by 21.5% (95% CI 13.9-29.1%, p < 0.0001) from 67.9% in October to 89.4% to March.

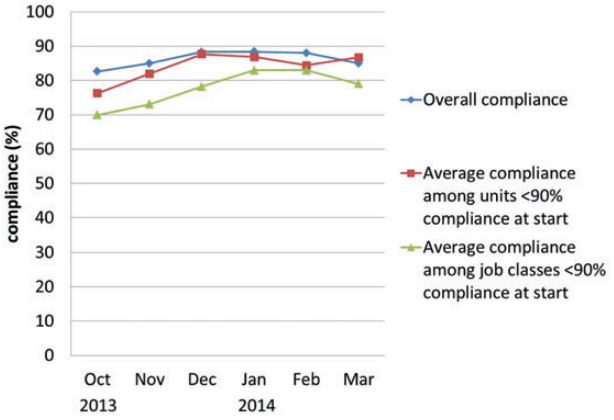

Figure 1. Trends in hand hygiene compliance during "Clean in, Clean out"

Conclusion. By involving more and different types of healthcare personnel in hand hygiene monitoring and feedback, CICO helped improve HH compliance among units and departments at low compliance levels. At the end of our 8 month implementation period, we will assess the impact of this intervention on the incidence of healthcare-associated infections.

Disclosures. **All authors:** No reported disclosures.

1520. Outcomes after Implementation of a Public Health Program for HIV Partner Notification in Edmonton, Canada

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Background. We evaluated the characteristics of newly reported HIV cases and their partners after implementation of HIV Partner Notification guidelines in Edmonton, Canada in April 2010.

Methods. All individuals newly diagnosed with HIV in Edmonton, Canada were interviewed by a Partner Notification Nurse (PNN) for sexual, needle sharing and perinatal contacts. Data collected on partners included whether they were located, tested, and test results. A descriptive analysis was performed on data collected from April 2010 to December 2013.

Results. There were 346 newly diagnosed HIV cases during this time period: 69.4%(n = 240) were male with a median age of 37 years (IQR 29-46). The majority of male cases were Caucasian (n = 134; 55.8%) with the primary mode of transmission being sex with men (MSM) (n = 142; 59.2%). The majority of female cases were Black (n = 48; 45.3%) and reported heterosexual transmission (n = 80; 75.5%).

Seventy per cent (n = 243) of HIV cases provided contact information. Cases reporting contacts were younger (35 years, IQR 28-44 vs 41 years, IQR 33-51, p < 0.001). Those who did not have sexual or IDU as the primary mode of transmission (e.g., vertical transmission) were less likely to report contacts (27.3% vs 71.6%, p = 0.004).

Information on 584 contacts was provided; the median number of contacts per case was 1 (IQR 1-3). The majority (92.6%; n = 541) of contacts were exposed through sex, 5.5% (n = 32) through needle sharing and 2.2% (n = 13) perinatally. 15.6% (n = 91) were previously HIV positive. Sixty nine per cent (n = 404) were eligible by place of residence for follow up by local PNNs; 85.7% (n = 347) of these contacts were located

and of these, 88.2% (n = 306) were tested resulting in 20 new cases of HIV. All new cases received HIV care; at baseline, 70% (n = 14) had normal CD4 counts (>350 x10^9/L), 5 cases had CD4 counts 200-350 x10^9/L and 1 case was below 200 x10^9/L.

Of the previously positive contacts, 81.3% (n = 74) were sero-positive prior to their exposure to the case. 18.7% (n = 17) were sero-positive after their last exposure to the index case.

Conclusion. HIV partner notification efforts, conducted by PNNs, resulted in the majority of named contacts being located and tested, including the identification of 20 previously undiagnosed cases of HIV.

Disclosures. **All authors:** No reported disclosures.

1521. Missed Opportunities for HIV prevention at an Integrated Hospital System in Bronx, NY

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Background. Early diagnosis of HIV remains an important challenge, especially in urban, underserved populations. Montefiore Medical Center (MMC) is an integrated delivery system in Bronx, NY, an area of high HIV prevalence. We hypothesize that patients may experience missed opportunities for early diagnosis, despite frequent encounters with the MMC system.

Methods. Retrospective chart review of 82 patients newly diagnosed with HIV in 2012 at varied MMC clinical sites. Data was collected via EMR databases. Missed opportunities were defined as > 1 prior health care encounter within 3 years of diagnosis in which HIV testing was not performed for those who had a prior negative test or no prior test. Descriptive statistics were used to analyze findings.

Results. Of the 82 HIV positive patients, 72% were male, and 80% Black or Latino. 62% of men identified as MSM; 91% of women were heterosexual. Median CD4 count was 326, (29% had CD4 < 200) and the median viral load was 16,490. 67% of patients were diagnosed at outpatient departments (OPDs) or emergency departments (EDs), and 35% had a prior negative HIV test. The most common presenting symptoms included: constitutional symptoms (24%), sexually transmitted infections (STDs) (17%), systemic or opportunistic infections (12%), and follow up after high-risk contact (10%); 21% were asymptomatic.

Among those with prior visits and previous negative HIV tests, 98% of prior visits occurred in EDs or OPDs. 23% of these presented with constitutional symptoms, 23% with STDs, 7% for routine care. The mean number of missed opportunities for testing in this group was 2.4.

Among those with prior visits and no prior HIV tests, 97% of visits occurred in EDs or OPDs. 32% presented with general primary care complaints, 17% with constitutional symptoms, and 14% with acute infections. The mean number of missed opportunities for testing was 3.8.

Conclusion. HIV positive patients continue to present late to care, with variable symptomatology, low CD4, high viral load, and commonly utilize OPDs and EDs, where missed opportunities for early diagnosis are common. Policies that address more systematic, and routine testing across healthcare delivery systems is needed to prevent transmission.

Disclosures. **All authors:** No reported disclosures.

1522. Knowledge and Perception of PrEP Among Two Cohorts of Infectious Disease Providers

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Background. The FDA recently approved tenofovir/emtricitabine as pre-exposure prophylaxis (PrEP) to prevent acquisition of HIV among adults. The CDC established guidance on prescribing PrEP. However, there is a paucity of data on how providers should implement PrEP into clinical practice, provider knowledge related to PrEP, and its cost-effectiveness.

Methods. A voluntary, anonymous survey was conducted to evaluate the current knowledge, attitudes, and perceptions of PrEP among two groups of primarily infectious disease providers. The link to the 34-question survey was emailed to both the Greater Washington Infectious Disease Society (GWIDS) and the Armed Forces Infectious Disease Society (AFIDS). This survey assessed provider demographics and the volume of HIV-infected patients in their practice in addition to their knowledge, prescribing patterns, and opinions regarding PrEP.

Results. There were 105 responses – 20 (19%) were members of GWIDS, 58 (55%) were members of AFIDS, and 27 (25.7%) were part of both groups. All were physicians, and 94% were adult infectious disease specialists. The majority (60%) of knowledge questions were answered incorrectly. Of the respondents, 36 (34.3%) spent >25% of their time in HIV care. Those who spent >25% of their time in HIV care had a significantly higher percentage of correct answers in the knowledge component of the survey. Sixty-two (67%) respondents felt that the current literature supports the use of PrEP, 12 (13%) did not think the literature supports its use, and 18 (19.5%) were undecided. When asked whether the cost of PrEP was considered justifiable, only 23 (25%) said yes, while 35 (38%) said no and 34 (37%) were undecided.

Conclusion. There is a significant amount of uncertainty that remains regarding the use of PrEP. This survey demonstrates that knowledge related to the use of PrEP is lacking and suggests training is warranted to ensure providers become familiar with CDC guidance. Given the lack of knowledge amongst providers who spent <25% of their time caring for HIV patients, organizations should consider restricting its use to providers who spend >25% of their time caring for HIV patients. Only a quarter of surveyed providers feel the cost is justified. Further research in this area is necessary to explore options for more cost effective methods of HIV prevention.

Disclosures. **All authors:** No reported disclosures.

1523. Attitudes and Interest Toward HIV Pre-Exposure Prophylaxis Among Participants Using HIV Non-Occupational Post-Exposure Prophylaxis

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Background. Many persons who present for non-occupational post-exposure prophylaxis (NPEP) remain at increased risk for HIV acquisition because of recurrent practices. Limited data exist regarding facilitators and barriers to transitioning from non-occupational post-exposure prophylaxis (NPEP) to pre-exposure prophylaxis (PrEP) for ongoing HIV prevention in this population.

Methods. Participants enrolled in an observational study of co-formulated Tenofovir/Emtricitabine/Elvitegravir/Cobicistat for consensual NPEP were administered a survey to assess perceptions about and interest to use PrEP at day 14 (D14) and day 90 (D90) of an NPEP study at a large urban community health center between May, 2013 and March, 2014. Proportions were calculated for categorical variables. A Chi-square test or Fisher's exact test was used to measure differences in responses.

Results. Of the 33 participants that completed the D14 and D90 visits for the NPEP study, 87% participants completed the D14 and D90 surveys, all of whom were men. Their mean age was 34.6, and most were Caucasian (79.3%) and men who have sex with men (86.2%). Most (65.5%) had heard of PrEP as of D14. Among 23 who reported having a primary care provider, 34.8% did not feel comfortable talking to their provider about PrEP, the most common reason (62.5%) being that they did not feel comfortable discussing sexual practices with them. Respondents were more likely to report that they thought they could access PrEP via an STD clinic (75.9%; p = 0.008), an LGBT provider (86.2%; p = 0.0008), or an HIV provider (86.2%; p = 0.0008) than their primary care provider (41.4%). Most respondents (58.6%) expressed interest in starting PrEP at D14, which increased to 75.9% at D90 after completing NPEP (p = 0.162). Of those that completed the NPEP study thus far, 24.2% were referred to a PrEP program, accessing medication through a research study or a medical provider.

Conclusion. The majority of NPEP users reported a high interest in using PrEP, which tended to increase after completing their NPEP course. They perceived discomfort with discussing their sexual behavior with their PCP as a barrier to accessing PrEP compared to other clinical venues. Linkages should be strengthened between NPEP and PrEP programs.

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1525. Optimizing HIV Pre-Exposure Prophylaxis Implementation among Men Who Have Sex with Men in Toronto: A Dynamic Modelling Study

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Background. Once daily tenofovir/emtricitabine-based pre-exposure prophylaxis (PrEP) can reduce HIV acquisition in men-who-have-sex-with-men (MSM). To inform large-scale PrEP implementation, we examined the potential population-level impact and cost-effectiveness of different PrEP implementation strategies.

Methods. We developed a dynamic, stochastic compartmental model of HIV transmission among the ~57,000 MSM in Toronto, Canada, stratified by HIV infection (CD4), serostatus (known/unknown diagnosis), and sexual behaviour. Parameterization was performed using local epidemiologic data. We calibrated the model to observed data on annual HIV diagnoses (300-400), annual HIV-attributable deaths (40-65), and ART coverage among MSM (50-70%). Baseline annual HIV testing was 22%. Strategies examined included: a) uniform PrEP delivery vs targeting the highest-risk decile of MSM (avg. 36 partners/year); b) varying PrEP efficacy (44% to 99%); c) increasing HIV test frequency (Q3 to Q24 months). Outcomes included HIV infections averted and the incremental cost (in $CAD) per incremental quality-adjusted-life-years (QALYs) gained over 10 years.

Results. Use of PrEP among all HIV-uninfected MSM at 25, 50, 75, and 100% coverage prevented 832, 1387, 1693, and 1736 infections respectively, with costs per QALY increasing from $230,000 to $300,000. Targeted PrEP for the highest-risk MSM at 25, 50 75, and 100% coverage prevented 241, 452, 555, and 590 infections respectively, with costs per QALY ranging from $45,000-60,000 CAD. Maximizing PrEP efficacy prevented 424 infections with a cost per QALY of $32,000 (assuming PrEP in 25% of high-risk). HIV testing alone (Q3 months) averted 50% of infections with a cost per QALY of less than $10,000. However, increasing HIV testing frequency had minimal prevention impact. Maximizing PrEP efficacy increased the number of infections prevented. Assuming PrEP use in 25% of high-risk MSM with 99% efficacy and with Q3 month testing, a $32,000 cost per QALY was achieved.

Conclusion. Among those examined, the optimal implementation strategy for PrEP over the next 10 years in Toronto is to target high-risk MSM with strategies to maximize efficacy. Frequent HIV testing alone in high-risk individuals provides a substantial benefit.

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1526. PrEP implementation in Houston, TX among high-risk heterosexuals and MSM

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Background. HIV pre-exposure prophylaxis (PrEP) has been proven to decrease risk of HIV transmission; however, demonstration of effectiveness in clinical settings is needed. A comprehensive HIV Prevention Clinic at Thomas Street Health Center (TSHC) in Houston, TX was established in July 2013, merging biomedical and behavioral prevention in a free-standing HIV clinic.

Methods. Patients ≥18 years old presenting for confidential walk-up rapid HIV testing at TSHC who tested negative, were assessed for high-risk and, if appropriate, were invited to participate in the HIV prevention clinic, which provides counseling, condoms, and PrEP as appropriate. Retrospective chart review of clinic data assessed patient acceptance, successful linkage to care in prevention services, and retention in preventive services. Behavioral risk factors included sero-discordance, sexual orientation, injection drug use, or having multiple sex partners.

Results. Of the 477 HIV walk-up tests performed from July 2013 to May 2014, 52 patients (10.9%) were deemed at the highest risk by the HIV tester, and agreed to an appointment in the HIV prevention clinic. Over half the patients (52%) were women. Twenty-three patients (44.2%) had multiple partners. Forty-five patients (86.5%) were in a serodiscordant relationship, 10 patients (19.2%) were MSM, and zero patients reported injection drug use. Most patients (55.8%) relied on Harris Health System programs for subsidized cost of medical care and medication from pharmaceutical assistance programs. Nine patients (17.3%) had Medicaid and 4 patients (7.7%) had private insurance. Five patients (9.6%) eligible for PrEP declined the prescription. There were zero seroconversions. Two HIV positive patients were identified during baseline screening labs. Four patients were prescribed non occupational pre-exposure prophylaxis. In total, 36 patients (69%) attended their appointment, 19 patients (37%) completed at least one follow up appointment, and 12 patients (23%) started PrEP.

Conclusion. PrEP implementation for MSM and high risk heterosexuals in context of comprehensive preventive services is feasible in an urban HIV clinic. Like the treatment cascade, prevention efforts show a steep drop between patients initially deemed high-risk and those who are linked to and retained in care.

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1527. Longitudinal Trends in HIV Non-Occupational Post-Exposure Prophylaxis (NPEP) at a Boston Community Health Center Between 1997 and 2013

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Background. Although guidelines have recommended HIV non-occupational post-exposure prophylaxis (NPEP) for potentially HIV-exposed individuals for more than 15 years, there have been scant behavioral and clinical outcome data that reflect changes in management over that interval. Here, we assess secular trends among NPEP users presenting at one US center over the past 16 years.

Methods. A retrospective longitudinal study of electronic medical records of NPEP recipients between July 1997 and August 2013 was performed at a large community health center in Boston. Eligible participants were age ≥18 years, HIV-uninfected, and had sexual or non-occupational intravenous needle exposures. Logistic generalized estimating equation models were used to assess trends in NPEP prescriptions and factors associated with regimen completion.

Results. Data from 894 NPEP patients' charts were analyzed. Almost all patients were male (92.4%), 5.9% female, 1.7% transgender/genderqueer, and 88.1% men who have sex with men. Most patients (71.5%) were Caucasian, 10.9% Latino/Hispanic, and 7.1% African-American. The mean age was 33.9 years. NPEP use increased over time and increasingly entailed Tenofovir instead of Zidovidine-based regimens ($P < 0.001$); 19.3% had ≥2 NPEP visits. Of 1244 NPEP visits, exposures included: 92.7% consensual sex, 5.3% nonconsensual sex, and 1.1% intravenous needle exposure. Regimen completion was documented for 37.2%, non-completion in 6.2%, and unknown in 56.6% of visits. A known HIV-infected partner (AOR 2.00, 95%CI:1.11-3.60) and Tenofovir-based regimen (AOR 2.60, 95% CI:1.49-4.53) were associated with increased odds of completion. Three-drug regimens (AOR 0.44, 95% CI:0.25-0.77) were associated with decreased odds of completion compared to two-drug regimens. HIV incidence was 2.1 per 100 person-years (95%CI:1.5-2.9).

Conclusion. Many patients in this study demonstrated ongoing high-risk behavior, as manifested by recurrent NPEP and a high HIV incidence. Simpler and better-tolerated regimens are needed to optimize regimen completion. NPEP recipients may benefit from early HIV risk-reduction counseling and pre-exposure prophylaxis.

Disclosures. **All authors:** No reported disclosures.

1528. Ralteragir Containing regimen, for Post Exposure Prophylaxis (PEP), well tolerated in Health Care Workers (HCW)

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Background. HCW with occupational exposure to blood are at risk for HIV infection. To decrease the risk of HIV acquisition, antiretroviral drugs are used as PEP. Studies evaluating PEP after high-risk sexual activity demonstrate Truvada + Raltegravir (R) to be extremely well tolerated. Since 2005, the PEP regimen used for occupational exposure at our insititious (Henry Ford Health System) has been Truvada + Kaletra (K). The aim of this study was to demonstrate that a HCW PEP regimen of Raltegravir + Truvada has a high rate of completion and is well tolerated.

Methods. Eligible subjects were randomized in this prospective, open label, controlled study at a 1:1 ratio to either the R or K arms. Data collected at baseline, 2, 4, 6, 12 and 24 weeks post-exposure included laboratory chemistries, symptoms and side-effects. Symptoms reported in >10% of subjects were evaluated. Fishers exact test and student T test were applied to determine statistical significance.

Results. A total of 16 subjects (8 per study arm) were enrolled from February 2011 to February 2013.

One from each arm discontinued after finding the source patient to be HIV negative. There were 17 reports of side-effects in the K arm and 6 in R arm. At week 2, 8 subjects reported nausea, abdominal pain, diarrhea, flatulence, tiredness, anxiety/depression. Abdominal pain and diarrhea tended to be greater in the K arm vs R arm ($p = 0.096$ and $p = 0.035$ respectively). Symptoms at week 4 were not significantly different between the arms. There was no difference between the two arms regarding incomplete dosage at either week 2 or week 4 of therapy ($p = 0.441$). One Kaletra patient discontinued therapy after 19 days due to tolerance issues. The creatinine level was changed for the R arm, showing an average increase from 0.69 at baseline to 0.79 at week 4 ($p = 0.053$). There were no HIV seroconversions at week 24 post-exposure.

Conclusion. A Raltegravir containing regimen as occupational PEP is well tolerated with high completion rates by HCW.

Disclosures. **I. Brar**, Gilead: Investigator, Shareholder, Speaker's Bureau and Truvada for this study was provided, Research grant and Speaker honorarium; Merck: Funding and raltegravir was provided, Grant Investigator, Research support; ViiV: Investigator, Research grant

1529. Raltegravir Plus Tenofovir DF and Emtricitabine for Non-occupational Postexposure Prophylaxis (nPEP): African-Americans are at Higher Risk of Non-Completion of nPEP

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Background. Current guidelines recommended the use of antiretrovirals after non-occupational exposure to HIV. However recommended regimens are based on 2005 drug pipeline. Since then significant advances in antiretroviral therapy have been achieved. This study aimed to assess the safety and tolerability of tenofovir DF/emtricitabine/raltegravir for non-occupational post exposure prophylaxis after possible sexual exposure to HIV in a population of Houston, Texas.

Methods. Non-randomized, open label, prospective cohort pilot study. Volunteers were ≥18- years-old and had a potential sexual exposure to HIV (defined as vaginal, anal or other mucosal exposure to ejaculate rectal or cervicovaginal secretions from an

HIV-infected or high risk individual of unknown HIV status) within 72 hours. A 28-day course of raltegravir, tenofovir DF and emtricitabine was given to subjects. Adherence and side effects were assessed. Statistical analysis was done using SPSS. Significance was set at 0.005 and CIs at 95%.

Results. 103 individuals were enrolled in a 2 year period. 89% of the participants were male, and 65% identified themselves as men who have sex with men. The mean age of participant was 32 years old. 68% of the patients were white, 24% were African-American, and 9% of other racial origin. 21% of the volunteers identified themselves as Hispanics. 41% of the participants reported that they had sex with a known HIV-1 infected individual, 53% reported not having used a condom and the remainder report that the condom broke.

None of the volunteers who completed all study visits had HIV-1 seroconversion at the 6-month follow-up. 11% of patients reported that they missed doses of medication. Only Grade 1 side effects were reported (headaches 5.8%, fatigue 4.8%, nausea 3.9%, dizziness, flushing, constipation, loose stools, and bloating 1.9%). 83% of the volunteers completed 28-day nPEP and 53% completed all study visits. African-American were the race with the lowest rate of 28-days nPEP completion (60% vs 94%) ($p = 0.0016$).

Conclusion. Tenofovir DF, emtricitabine and raltegravir was a very well tolerated regimen with a high rate of adherence and treatment completion. Efforts on prevention strategies need to continue to focus on high risk groups, such as African-Americans.

Disclosures. **K. J. Vigil**, Merck: Research grant; Gilead: Research support (medications) **R. Arduino**, Merck: Speaker's Bureau, Speaker honorarium

1530. No Decrease in HIV Risk Behaviors among Clients Repeatedly Screened for HIV in a State-Funded Counseling, Testing and Referral Program: Missed Opportunities for Risk-Reduction Interventions?

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Background. Prior research suggests that the majority of clients screened for HIV in community-based testing programs have been previously tested, and that repeat testers are more likely to report high-risk behaviors compared to one-time testers. While a main goal of many HIV counseling, testing and referral (CTR) programs is to provide counseling regarding behavioral risk reduction, the effectiveness of such counseling has not been well-described. We undertook a longitudinal study of clients utilizing CTR programs in Wisconsin to evaluate the impact of existing programs for reducing risk among repeat testers.

Methods. Between January 2008 and December 2012, all clients receiving HIV testing at a publicly-funded CTR site completed a standardized risk behavior questionnaire. We analyzed data from the subset of clients who (1) were first-time testers and (2) returned for at least one subsequent test 12 months or more after their first test, to determine whether clients reduced their risk behavior during the year following their first HIV test. HIV risk was quantified as the number of risky behaviors reported on the risk questionnaire during the preceding 12 months. Changes in risk behavior between the first and second test date were examined using the Wilcoxon signed rank test.

Results. During the study period, 576 unique individuals received their first HIV test through CTR and later received at least one additional test 12 months later. Of these, 113 (19.6%) indicated fewer HIV risk behaviors during the year preceding the second test compared to year preceding their initial HIV test; 273 (47.4%) reported a greater number of HIV risk behaviors at the time of the second test; 190 (33%) reported no change in the number of risk behaviors. The mean number of HIV risk behaviors increased by 0.6 between the first and second test ($p < 0.001$). Compared to other risk groups, men who have sex with men (MSM) were more likely to report a decrease in risk behaviors at the time of the second test (35% vs 12.1%, $p < 0.001$). Five clients were newly HIV-positive at the time of repeat testing.

Conclusion. Most clients who repeatedly utilize CTR services continue to engage in risky behavior after receipt of a first negative HIV test. Effective approaches to promoting behavioral risk reduction are needed for repeat testers, particularly for non-MSM.

Disclosures. **All authors:** No reported disclosures.

1531. Universal Treatment for HIV Infection Dramatically Reduces the Prevalence of HIV Infections Compared to Test-and-Treat Strategies

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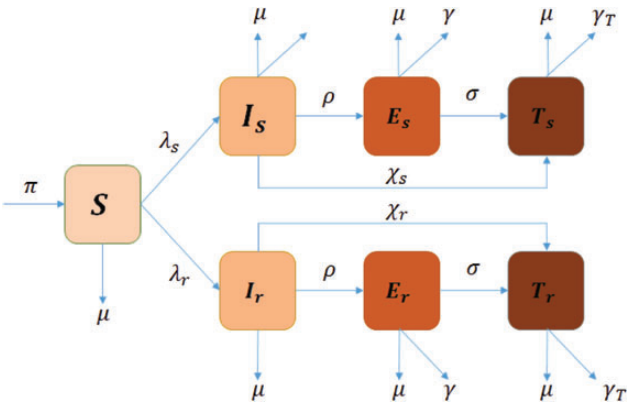
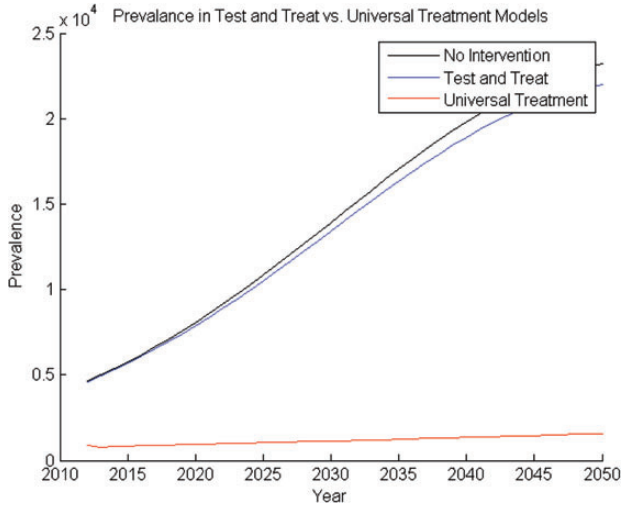
Background. HIV test and treat strategies aim to identify newly infected individuals and link them to care rapidly, resulting in modest reductions in prevalence. This contrasts with the dramatic prevalence reduction treating HIV-infected individuals in infection-discordant relationships. We modeled a comparison of prevalence reduction for a test-and-treat strategy vs universal treatment of all HIV-infected individuals with anti-retrovirals.

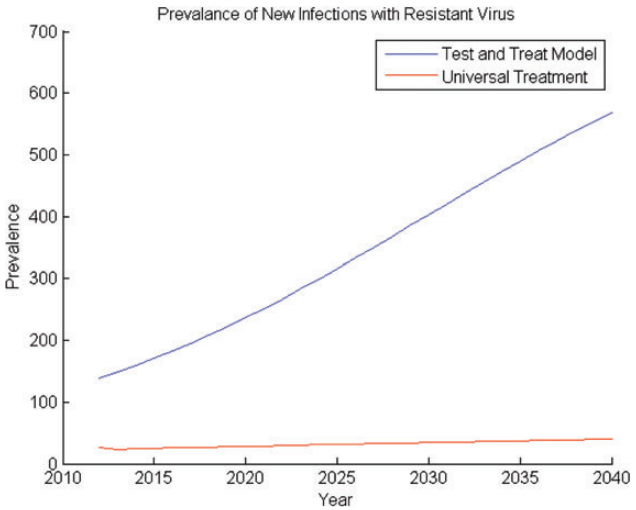
Methods. A simplified, idealized deterministic model is illustrated:



Individuals are uninfected (S), entering into this compartment at rate π. Individuals die at rate μ. Once infected (with λ as the "force of infection"), individuals enter compartment "I" (infected but unaware), become aware of their HIV infection (compartment "E") and once treated, enter compartment "T." The symbols χ, ρ, σ are rates changes between compartments. The "r" and "s" subscripts indicate compartments of with drug resistant or susceptible HIV.



The prevalence of new HIV infections: comparing test-and-treat (red curve) to universal treatment.



The prevalence of new infections with resistant virus in universal treatment models does increase, but is unusual.

Results. Simulation results are shown in the figures.

Further simulations demonstrate change in the "force of infection" or lambda value strongly determines prevalence

Simulations demonstrated that increasing the rate of early identification, decreasing the size of compartment "I," or even increasing the efficacy of test-and-treat strategies are less significant in reducing HIV transmission than universal treatment.

Conclusion. This simplified model demonstrates that preventing individuals from becoming infected is a more efficacious strategy than treating them once infected, no matter how aggressive the test-and-treat strategy. The prevalence of new infections with resistant virus is unusual, but does increase as a consequence of universal treatment of all HIV infections. Universal treatment of individuals with HIV should receive special emphasis to dramatically reduce prevalence of new HIV infections.

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1532. A Social Media-Based HIV Self-Test Program to Raise Community-Level Serostatus Awareness, Los Angeles

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Background. Up to half of all new HIV cases in Los Angeles may be caused by the 20-30% of men who have sex with men (MSM) with unrecognized HIV infection. MSM are at higher risk for being sero-unaware and might benefit from increased access to novel testing methods, such as the recently FDA-approved OraQuick® In-Home HIV Test.

Methods. An advertisement offering free HIV self-test kits was placed on Grindr™, a geosocial networking smartphone application popular with MSM, from April 17 to May 29, 2014, and was visible to users in Los Angeles. Those who clicked on the advertisement were linked to http://freehivselftests.weebly.com/ to indicate their selection for test delivery (via USPS® mail or Walgreens® voucher). Users were invited to participate in a study on testing experiences 2 weeks after test delivery. Eligible study participants were African American or Latino > 18 years old.

Results. In the first 19 days of the campaign, the website received 2,845 first time visitors (average number per day: 149), 218 (7.7%) of whom requested a test. Of those 218, 85 (39.0%) requested a test voucher and 133 (61.0%) requested test delivery by mail. Of the 81 visitors who were interested in and eligible for the study, 32 (39.5%) requested vouchers and 49 (60.5%) requested tests by mail.

Conclusion. Our findings demonstrate the potential of using modern information and communication technologies to engage hard-to-reach groups such as high-risk MSM in HIV testing. Further data collection will allow us to track kit use, assess testing behaviors, and identify new HIV cases with linkage to care and prevention services. Our methods could be used to assess whether a self-testing promotion system enhances the community-level of serostatus awareness and linkage to care and prevention services.

Disclosures. **All authors:** No reported disclosures.

1533. HIV Testing in a Primary Care Clinic: Missed Opportunities for Testing Older Adults

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Background. Older adults (age > 50 years) continue to represent 17% of the new HIV diagnoses each year in the U.S. and are often diagnosed later in the course of their disease. In 2010, 46% of the newly diagnosed HIV infected adults over 50 had AIDS within 12 months of their diagnosis. These realities led the authors to investigate how HIV risk assessment and testing practices within a primary care practice varied between older and younger patients.

Methods. 150 participants were recruited from the waiting room of an internal medicine clinic in a large academic medical center in New York City. Eligible subjects spoke English or Spanish, considered a medical provider in the clinic to be their primary doctor, and had attended at least two visits with their provider in the prior year. Participants completed a single computer-based survey that took less than 20 minutes in a private room. Data was analyzed using SPSS. Funding was available through a Pfizer Independent Research Grant.

Results. 148 participants (ages 21-91) completed the survey and were representative of the study clinic population. Older patients (> 50 years, N = 99) were compared to younger patients (N = 49). Older patients were less likely to have been previously tested for HIV (66.7 vs 87.8%, p = .0076) and to have had their medical provider recommend an HIV test (28.3 vs 55.1%, p = .0017). Older patients were less likely to have had medical provider discuss HIV risk behaviors with them including sexual activity (28.3 vs 55.1%, p = .0015), condom use (22.2 vs 53.1%, p = .0001), prior STIs (34.3 vs 63.3%, p = .0005), sexual abuse (17.2 vs 38.8%, p = .003), drug use (40.4 vs 69.4%, p = .0005), and incarceration (14.1 vs 34.7%, p = .003). Fewer older adults reported sex in the last year (53.5 vs 81.6%, p = .0009) but were twice as likely to have lost a main partner to death or illness (24.7 vs 10.2%, p = .038). Both groups reported similar numbers of lifetime sexual partners (15.2 vs 11.6, p = .65) and prior STIs (18.2 vs 16.3%, p = .76).

Conclusion. This study suggests providers continue to screen older adults significantly less often for HIV risk factors and are less likely to recommend risk based or routine HIV screening for older adults. Moving forward, prevention of the complications of late HIV diagnosis among older adults will require focus on routine HIV screening and risk based targeted screening for adults greater than 50 years of age.

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1534. Missed Opportunities for HIV Diagnosis in a New Orleans Area Health System

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Background. Patients often present to multiple healthcare facilities in the years preceding their initial HIV diagnosis. These 'missed opportunities' are the key to capturing the undiagnosed HIV positive individuals. New Orleans ranked 2nd in the nation for estimated HIV cases (43.0 per 100,000) followed by Baton Rouge (41.6 per 100,000). This study focused on the number of healthcare visits within the Ochsner Health System (OHS) where an HIV diagnosis could have been made in an HIV unaware individual.

Methods. Potential study subjects were identified from the positive HIV ELISA tests performed at OHS between January 1, 2011 and December 31, 2012. Charts were reviewed for the two years preceding diagnosis. The number of traditional (primary care) and nontraditional (all other) healthcare visits were recorded. Patients with indeterminate results and those with a previous HIV diagnosis were excluded.

Results. 17,677 ELISA tests were ordered, 159 positives were recorded, and 125 patients were identified as new diagnoses. Collectively, this population attended a total of 649 healthcare visits in the two years preceding their first HIV diagnosis.

45% of the sample was diagnosed with AIDS at the time of initial diagnosis or in the year immediately following (Table 2).

Table 1: Missed Opportunities and Diagnoses

	Total Missed Opportunities	Total Diagnoses Made	Rate of Diagnosis by Field
Primary Care Clinics	33.6%	26.4%	13.1%
Emergency/Urgent Care	28.2%	16.8%	10.3%
Specialty Care Clinics	19.0%	10.4%	9.6%
Surgical Specialties	11.1%	3.2%	5.3%
OBGYN Care	4.9%	6.4%	20.0%
Inpatient Care	3.1%	32.8%	67.2%
Blood Bank	NA	1.6%	NA

Table 2: AIDS Diagnosed Within One Year of Initial HIV Diagnosis (p=0.0092)

	HIV	AIDS	Total	% AIDS
OHS	69	56	125	44.8%
Louisiana	872	410	1,282	32%
USA	28,683	13,498	42,181	32%

Conclusion. A significant proportion of new HIV diagnoses were made at nontraditional healthcare facilities, supporting continued testing across all healthcare settings in order to decrease the undiagnosed, unaware population and minimize morbidity and mortality associated with late diagnosis.

Disclosures. **All authors:** No reported disclosures.

1535. Knowledge, Practice, and Attitudes of University of California San Diego Medical Students with Regard to HIV and HIV Screening

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Background. In 2006 the Centers for Disease Control and Prevention (CDC) recommended universal HIV screening for persons aged 13-64, but many providers have not integrated it into their practice. A pilot study was designed to assess HIV knowledge, current practice and attitudes of University of California San Diego medical students with regard to screening.

Methods. An anonymous online survey of 32 questions was distributed to students during early 2013. IBM SPSS Statistical Desktop version 21.0.0 was used for analysis of N = 132 respondents, with a statistical significance of $p < 0.05$.

Results. 93.3% (168/180) of respondents had not been informed of the 2006 CDC guideline for universal screening. Many of the respondents had knowledge deficiencies in HIV epidemiology, policy and infrastructure and high threshold for ordering HIV test. 65.6% (118/180) agreed that they would support universal opt-out HIV screening, however 52.8% (95/180) identified one or more barrier(s) to HIV screening in their practice training. The most common barrier was lack of knowledge or training (19.4% 35/180). Medical students who had never personally had an HIV test, had less experience with HIV patients, and had ordered fewer

HIV tests in the past 6 months were more likely to report barriers to universal testing.

Medical student perceived barriers to screening

	Pearson's X^2	p
Personal HIV test	10.569	0.005
HIV patient exposure	15.033	0.005
HIV tests ordered last 6 months	21.567	0.000
Perception of barriers	11.635	0.003

Multinomial bivariate and multivariable predictors of respondents with NO barriers to screening

	Bivariate OR (95% CI)	p	Multivariable OR (95% CI)	P
Perception of barriers	No 4.745 (1.81-12.43)	0.002	No 3.893 (1.31-11.56)	0.014
	Yes (ref)	–	Yes (ref)	–
HIV tests ordered last 6 months	[<5] 0.241 (0.09-0.64)	0.004	–	–
	[5-10] (ref)	–		
	[11-20] 3.182 (0.52-19.64)	0.213		
		0.416		
	[>20] 1.782 (0.44-7.18)			
Personal HIV test	Never 0.242 (0.09-0.59)	0.002	Never 0.275 (0.11-0.72)	0.008
	Yes (ref)	–	Yes (ref)	–

Conclusion. Medical students are largely unaware of the 2006 CDC HIV screening recommendations and universal HIV testing is not implemented. The most prevalent barrier to universal testing is lack of knowledge, which was evident in our data. Future interventions should focus on increasing HIV medical education and providing more clinical experience with HIV patient care.

Disclosures. **All authors:** No reported disclosures.

1536. Seek and Ye Shall Find: Successful Implementation of Hospital Laboratory-based 4th Generation HIV Screening

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Background. Acute HIV infection (AHI) contributes significantly to ongoing HIV transmission. In Washington, DC, an urban center with high HIV prevalence, the rate of HIV among men who have sex with men (MSM) is higher than other demographic groups. Furthermore, in Southeast DC, the region with the highest rates of poverty, chronic diseases and least access to healthcare services, HIV diagnoses are common among both heterosexuals and MSM. However, upon implementation of 4th generation HIV testing, AHI has been found exclusively among black MSM. We reviewed the presentation and clinical findings of these cases.

Methods. In November 2013, the Abbot Architect which detects HIV p24 antigen was installed in our hospital laboratory. To support HIV testing expansion, standardized clinical pathways were modified to include the addition of HIV serology to all standing order sets. In addition, HIV serology was added for all patients undergoing phlebotomy. The hospital laboratory HIV testing algorithm was modified to facilitate same day, on-site confirmation of positive results.

Results. Since November 2013, five cases of AHI have been identified in the emergency department. In four cases, AHI was not considered by the evaluating provider. All but one presented with a febrile illness. One patient left AMA and is lost-to-follow-up. Of the four remaining cases, the median age was 23 (range 20-26). The median CD4 at diagnosis was 376 (288-769). Median viral load was 3 million (range 750,000-8.6 million). All were able to determine the source and timing of their infection. Three elected to initiate antiretroviral therapy. Of those treated upon AHI diagnosis, viral suppression was achieved within 4 weeks of treatment initiation.

Conclusion. Identifying acute HIV infection within the timing of an emergency room visit is possible. However, emergency department providers must be educated to consider AHI, particularly among sexually-active MSM. Given the public health urgency to identify black MSM with AHI, access to and implementation of 4th generation testing technology in areas of HIV prevalence is imperative.

Disclosures. **All authors:** No reported disclosures.

1537. The AHKER Study: Assessing HIV Knowledge of Emergency Residents

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Background. Acute HIV infection, acute retroviral syndrome (ARVS), presents as a mononucleosis-like illness in up to two thirds of cases. 20% of people unknowingly infected with HIV are responsible for over 50% of new infections annually. A high index of suspicion is needed to screen for ARVS as there are no unique characteristics that distinguish it from other viral illnesses. We strive to determine Emergency Medicine residents' practice behaviors for considering ARVS in the presentation of an acute viral illness.

Methods. Two versions of an electronic survey was developed. Each had the same clinical vignette of a patient with symptoms suggestive of a viral illness; one version stated the patient's homosexual orientation (Sexual Orientation Qualifier "SOQ") while the other did not (No Qualifier "NQ"). The survey contained four sections including treatment options for the scenario, knowledge of ARVS symptoms, likelihood of ordering a rapid HIV test, and recommendations following a negative result. All U.S. based EM residency training programs were randomly assigned to receive one of the two versions of the survey. The survey link was sent to program directors with a request to forward it to their residents.

Results. 703 responses (414 NQ; 289 SOQ) were received from 101/158 EM programs (63% from NQ and 64% from SOQ). Knowledge of homosexual orientation resulted in greater use of HIV testing (14.8 NQ vs 56.4% SOQ $p<0.01$). >85% of respondents correctly identified the most common symptoms of ARVS however <27% were likely to order a rapid HIV test on patients with these symptoms (Table). 76% of respondents recognized a repeat HIV test was needed following an initial negative rapid test.

Likelihood of ordering a rapid HIV test

Patient Type	NQ	SOQ
Sexual assault victim	84%	85%
Female prostitute	84%	87%
IV drug user	78%	81%
Homosexual male	62%	73%
Rash, wt. loss & diarrhea	59%	53%
Positive chlamydia	61%	63%
Homosexual female	28%	31%
Fever, sore throat & swollen lymph nodes	25%	26%
Hypoxia, cough & dyspnea	24%	23%

Conclusion. EM residents do not consider ARVS in their differential diagnosis in patients with symptoms of viral illness, particularly in the absence of a high risk qualifier. This deficit in knowledge application may have significant negative public health consequences in the fight against HIV transmission.

Disclosures. **All authors:** No reported disclosures.

1538. Primary HIV Infection in an Adolescent Masquerading as Acute Pancreatitis

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Background. Acute pancreatitis is less common in children and adolescents than in adults, with etiology frequently including systemic disease, medications and trauma. Infectious etiology is reported to be as low as 8%. While it has been observed in the chronic course of HIV, acute pancreatitis rarely presents during primary HIV infection. We describe the second ever case of an adolescent presenting with acute pancreatitis masquerading as acute HIV infection.

Methods. Case: An 18 year old previously healthy male presented with subacute onset of fever, malaise and pharyngitis. One day prior to admission, he experienced severe abdominal pain, nausea and vomiting. Physical examination revealed an ill-appearing teenager with generalized lymphadenopathy particularly in the anterior and posterior cervical area. He had marked pharyngeal erythema with impressive exudates. Abdominal tenderness was notable for tenderness in the epigastric region and was without evidence of hepatosplenomegaly. Laboratory investigation revealed elevated lipase of 1024, leucopenia of 2.5 and thrombocytopenia of 128. Alcohol level was undetectable and liver function tests were otherwise unremarkable. Abdominal and chest xray imaging were unrevealing. An abdominal US revealed no evidence of cholelithiasis. Serologic EBV and CMV testing were negative for acute infection. Further history revealed unprotected anal intercourse 2 weeks prior with a new partner. An HIV antibody screen was negative however, given a high index of suspicion, he underwent HIV RNA PCR testing which revealed primary HIV infection with viral load of 77,586.

Results. Primary HIV infection is the time from initial infection until complete seroconversion. While often asymptomatic, 30-40% of patients experience a 'mononucleosis' type syndrome. Symptoms are non-specific and often attributed to other viral etiologies. While prior studies have revealed pancreatitis in advanced HIV, there are only 6 reported cases of primary HIV infection presenting as pancreatitis, one of which was in an adolescent.

Conclusion. Screening for HIV risk factors in high risk adolescents is crucial, however, in a patient like ours with acute pancreatitis, we recommend considering primary HIV infection as an etiology. Such patients should be tested with HIV RNA PCR.

Disclosures. **All authors:** No reported disclosures.

1539. The Changing Demographics of HIV Infection in the U.S. and the Caribbean and Central and South America

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Background. In the United States, the demographics of persons newly diagnosed with HIV are changing: an increasing proportion are younger (<25 years), particularly among men who have sex with men (MSM). It is unknown if similar trends are occurring in other regions of the world.

Methods. A retrospective analysis included HIV-infected adults (≥18 years of age) from 7 sites in the Caribbean, Central and South America network (CCASAnet) and the Vanderbilt Comprehensive Care Clinic (VCCC-Nashville, Tennessee). We sought to estimate the proportion of patients <25 years at HIV diagnosis by calendar year. A secondary analysis was repeated among MSM.

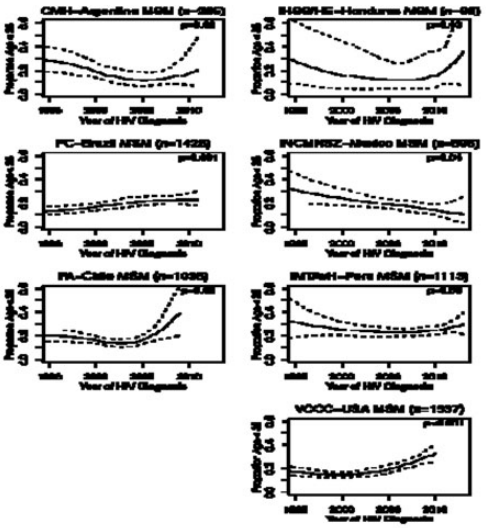

Figure 2. Trends in the proportion of patients <25 years of age at HIV diagnosis among men who have sex with men (MSM) according to site.

Results. 19,466 patients from CCASAnet and 3,746 from VCCC were included. Of these, 4650 (23%) and 1574 (40%) self-identified as MSM in CCASAnet and VCCC, respectively. Of those with a date of HIV diagnosis (80% and 95%, for CCASAnet and VCCC patients, respectively), 15% of CCASAnet and 19% of VCCC patients, were <25 years old. The proportion of VCCC patients <25 years at diagnosis changed over time ($p < 0.001$) and non-linearly ($p < 0.001$), ranging from <20% from 1998-2005, followed by an increase to 25% by 2010 (Figure 1). In contrast, the proportion of CCASAnet patients <25 years at diagnosis decreased significantly over time in Argentina, Haiti, Honduras, Mexico and Peru ($p<0.05$), with no change observed in Brazil and Chile ($p>0.05$). Although the proportion of MSM <25 years at diagnosis increased in VCCC since 2005 ($p < 0.001$), a similar change did not occur in CCASAnet, except in Brazil ($p = 0.002$) (Figure 2). Subjects <25 years at diagnosis were less likely to have AIDS at enrollment vs those >25 (29% vs 37% for CCASAnet, and 8% vs 14% for VCCC; $p < 0.001$ for both), and had higher $CD4^+$ (median $CD4^+$ 251 vs 180 cell/mm^3 in CCASAnet and 389 vs 306 cell/mm^3 in VCCC; $p < 0.001$ for both).

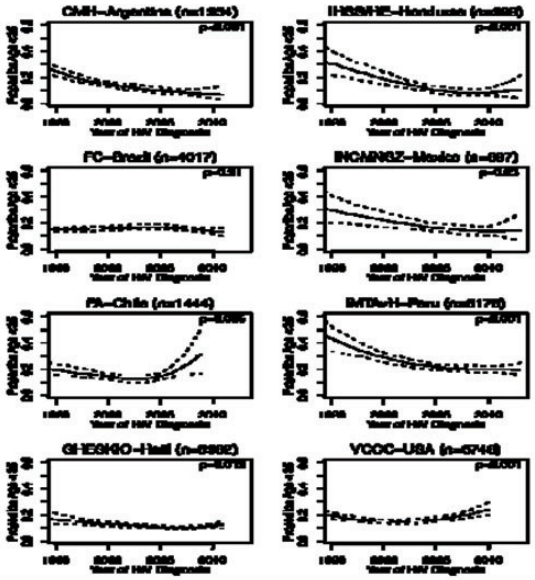

Figure 1. Trends in the proportion of patients <25 years of age at HIV diagnosis according to site.

Conclusion. Similar to the USA, in recent years the VCCC has had a greater proportion of newly diagnosed patients who are <25 years of age, both among the general population and MSM. Similar trends were not consistently observed in CCASAnet. Patients <25 years at HIV diagnosis in both cohorts were less immunocompromised. Differences in presenting risk factors should be explored, and prevention efforts tailored to young adults should be increased.

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1540. New Faces of HIV Infection: Differences between Younger and Older Persons Presenting for HIV Care in Nashville, Tennessee

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Background. Although annual rates of new HIV diagnoses in the U.S. have remained stable, incidence among younger individuals is increasing within certain groups. Although some characteristics of this younger cohort have been reported, we sought to compare persons newly engaged in care <25 years old with those ≥25 years at the time of first provider visit at a large Southeastern clinic.

Methods. This retrospective study identified new patients attending at least one provider visit at the Vanderbilt Comprehensive Care Clinic from October 2010 through June 2012. Those <25 years old at the time of first visit were compared with those >25.

Results. Of 281 persons, 25% were <25 years old at first visit (Table). Those <25 were more likely to be black, MSM, and to report a prior negative HIV test. Although days from positive test to first provider visit and baseline HIV RNA levels did not differ by age group, those <25 had a significantly higher median CD4 T cell count than those ≥25 years old. In a multivariate model, age <25 ($p = 0.01$) and female sex ($p = 0.02$) were associated with higher CD4 count at enrollment to care after adjustment for race/ethnicity, substance use, and MSM risk.

	Total (N=281)	>25 years (N=211)	<25 years (N=70)	P-value
Race/Ethnicity	138 (49)	113 (54)	25 (36)	0.03
White	122 (43)	80 (38)	42 (60)	(Black vs non-black p=0.001)
Black	16 (6)	14 (6)	2 (3)	
Hispanic	5 (2)	4 (2)	1 (1)	
Other				
Prior Negative Test	138 (49)	94 (45)	44 (64)	
Yes	74 (27)	61 (29)	13 (19)	
No	67 (24)	55 (26)	12 (17)	0.02

continued.

	Total (N=281)	>25 years (N=211)	<25 years (N=70)	P-value
Unknown Transmission Route	173 (62)	117 (55)	56 (80)	0.004
MSM	6 (2)	5 (2)	1 (1)	(MSM vs other p<0.001)
IDU	74 (26)	64 (30)	10 (14)	
Heterosexual	28 (10)	25 (12)	3 (4)	
Unknown				
Days from test to 1st visit, med (range)	61 (8-6894)	56 (8-6894)	69 (11-687)	0.25
Recent Hospitalization	62 (22)	54 (26)	8 (12)	0.02
Baseline CD4 count (cells/mL^3)	385 (176-549)	361 (111-530)	426 (342-595)	0.001

Data are N (%) or median (IQR) unless noted.

Conclusion. In a large Southeastern HIV clinic, 25% of new patients seen from 2010-mid 2012 were <25 years old. Those <25 were more likely to be black MSM. It is encouraging that despite being largely from underrepresented minorities, they did not have a longer time to presentation and had higher CD4 T cells. Further study is needed to better understand the changing dynamics of the U.S. HIV epidemic.

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1541. The Changing Molecular Epidemiology of HIV in the Philippines: Major Shift from Subtype B to CRF01_AE

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Background. The Philippines is one of only nine countries globally with rapidly increasing rates of HIV infection. Annual reported cases have increased 37-fold in the last decade. Sexual transmission still accounts for over 95% of cases, and a major shift from a heterosexual to men who have sex with men (MSM) transmission has occurred. Reasons for this remain unclear, but may include increased testing among MSMs, increased local transmission, and more aggressive strains of HIV. This study seeks to determine whether local molecular subtypes of HIV have changed over the last decade.

Methods. Following institutional review board approval and individual informed consent, 81 newly-diagnosed, treatment-naive HIV-positive patients at the Philippine General Hospital were interviewed and underwent genotyping of HIV RT and PR genes using WHO approved-protocols for HIV genotyping. Generated sequences were analyzed using the Stanford Drug Resistance Database. Demographics, sexual habits and CD4 counts at presentation were collected.

Results. The cohort had an average age of 29 years (range 19-51 years), CD4 count of 254 cells/mm3 (2-744 cells), and self-reported acquisition time of 2.42 years (0.17-8.17 years). All were male, and 79 were MSM. Genotype distribution was CRF01_AE (75%), B (22%), C (1%) and CRF01_AE/K (1%).

Pooled analysis of published data from samples collected from 1,985-2,000 showed that the majority of Philippine HIV infections were previously caused by subtype B (71%, N = 100), followed by subtype CRF01_AE (20%). Comparison with our cohort shows a highly significant shift in subtype ($p < 0.001$ by Chi-square)

Comparison of CD4 counts at presentation between CRF01_AE and B showed a significantly lower count (233 cells/mm3 vs 350 cells/mm3, $p = 0.03$ by T-test) despite no difference in age ($p = 0.15$), and self-reported time to acquisition ($p = 0.66$). This is consistent with previous reports that CRF01_AE is more aggressive, with faster progression to AIDS. While no viral loads were available for this cohort, CRF01_AE has been reported to have a higher rate of transmission. These two factors may partly explain the explosive increase in the number of new infections.

Conclusion. The molecular epidemiology of HIV in the Philippines has changed, with the more aggressive CRF01_AE now being the predominant subtype.

Disclosures. **All authors:** No reported disclosures.

1542. The Effect of Physical Proximity of HIV Testing Centers on HIV Testing Uptake in Northern Tanzania

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Background. HIV testing is crucial in curbing incidence, but testing behavior remains poorly understood. In the setting of a dramatic scale-up of rural HIV testing centers in Kilimanjaro, Tanzania, we assessed whether physical proximity to a facility offering HIV testing was associated with uptake.

Methods. Between June and July 2011, a random sample of 30 wards in the Moshi Municipal and Moshi Rural districts of northern Tanzania was selected, and self-reported HIV testing history was ascertained from 27 randomly selected heads of household from each ward. GPS coordinates were collected from all participating households and all government-registered HIV testing centers in the sampling frame. The association between testing center proximity and HIV testing history was measured using multivariable logistic regression.

Results. A total of 810 participants (62.8% female, median age 47.5 years) were interviewed, of which 428 (52.8%) had previously tested for HIV. Of HIV testers, 269 (62.9%) had not been tested in the past year. Distance from each household to the nearest HIV testing center, based upon available road data, ranged from 0.03 to 4.7km (median 1.21km). Although 294 participants (36.3%) cited "travel distance" as a major barrier to accessing healthcare, physical proximity to an HIV testing center was not associated with HIV testing on multivariable logistic regression analysis (adjusted odds ratio [AOR] 0.93, $P = 0.399$); the lack of association held when only rural wards were included in the model. Prior HIV testing was significantly associated with female gender (AOR 1.5, $P = 0.023$), younger age (AOR 0.96 per year, $P < 0.001$), and literacy (AOR 2.7, $P = 0.003$). Having children <5 years in the household was also highly associated with HIV testing (AOR 3.1, $P < 0.001$).

Conclusion. Despite availability of HIV testing facilities within 5km of all participants, still only about half had ever tested and proximity was not associated with uptake. High uptake among parents of young children suggests that provider initiated testing and counseling (PITC) during pregnancy remains key in enhancing uptake; PITC during other clinical encounters as well as targeted campaigns directed towards groups with low uptake may also be essential to promote universal testing.

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1543. Counting the Costs of Falsely Labeling Patients as HIV-Positive in Tahoua Region, Niger

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Background. At SIM Galmi Hospital in south-central Niger, we follow the national protocol for HIV testing, employing the Determine and ImmunoComb II kits in a serial approach. While this yields an expected sensitivity of 100%, specificity is only 91.5%, and conditions such as pregnancy increase the likelihood of a false positive result. Many Africans, especially pregnant women, are thus inaccurately labeled as HIV-positive, with diverse personal and societal costs.

Methods. We assessed 3957 persons diagnosed as HIV positive at our institution 2005-2011, and in a previous publication developed a protocol to identify 127 who were especially likely to be falsely labeled as HIV positive, based on CD4 and clinical criteria. This cohort included 75 pregnant women, the very population that yields the highest costs, as they are socially vulnerable and routinely started on ARVs. Through analysis and interviews with our HIV-positive population, we then attempted to quantify and assess the costs of false diagnoses.

Results. Considering 405 HIV positive diagnoses from 24,977 pregnant women screened at our institution in 2008-13, a 91.5% specificity suggests that 34 of these women were falsely labeled. Since pregnant women are routinely started on ARVs under the national PMTCT protocol, our center may annually draw $4957 in inappropriate ARV pharmaceutical costs alone. Beyond the programmatic financial burden, other costs are significant although harder to quantify. Women receiving an HIV diagnosis face challenges that can be psychological (for example, depression), physical (ARV and other medication side effects), professional (reduced job opportunities), social (shunning by her neighbors), and sexual (even divorce by a seronegative husband). The child may be viewed and treated unfavorably, and may be weaned more rapidly than necessary. Finally, the community and even health care workers lose trust in the accuracy of the diagnosis with repeated lab tests giving variant results.

Conclusion. Inaccurate HIV diagnoses, especially among pregnant women, result in extensive financial, physical, psychological, and societal costs, and represents a growing problem in the developing world. Our study highlights the importance of the employment of protocols and confirmatory laboratory testing to identify falsely labeled persons.

Disclosures. **All authors:** No reported disclosures.

1544. Describing the Local Context for HIV Screening in Tahaoua Region, Niger

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Session: 197. HIV 2: Testing and Changing Demographics
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Background. SIM Galmi Hospital is a Christian Hospital in the Tahoua Region of south-central Niger, where HIV prevalence is 1.0% across an area of 106,677 km^2 . In 2013 15,930 patients for HIV, and had over 3,000 consultations with HIV patients in follow-up.

Methods. We reviewed all HIV positive diagnoses over a five year period, with specific reference to the gender breakdown in each sub-region. Next, we interviewed 200 beneficiaries during routine follow-up visits, to determine how many had informed their spouse, and knew screening results for their spouse and children.

Results. 2433 new HIV diagnoses during the period 2005-2011 were identified as being from one of 9 sub-regions of our local Tahaoua region. Starting with the closest areas and working out, we found positives from Galmi (199, 71% female), Dogaraoua (496, 57% female), Madaoua (577, 57% female), Konni (525, 62% female), Illela (164, 43%), Bouza (247, 44% female), Tahaoua (184, 48% female), Keita (20, 15% female), and Abalack (21, 38% female). Gender disparities were striking. In the closest sub-regions, our new diagnoses were predominantly female, as we performed extensive prenatal screening. A significantly smaller percentage of diagnoses were women in the farther regions – likely because ailing women in the more distant departments do not have as much disposable income as their male counterparts.

Out of 200 patients interviewed, 157 were currently married, while 43 beneficiaries were single or divorced. We did not address non-marital sexual partners, as these are routinely denied within the culture. 117 had declared their status to their spouse, while 40 had not told their spouse. Out of these 117 who had informed a spouse, 98 spouses had been screened for the disease while 19 had not. We also inquired about children, and our survey respondents cited 60 children who had been screened for the disease. Of these 60, 18 had an HIV-positive child, a high number in a program with only 63 HIV positive children.

Conclusion. We have demonstrated that our hospital draws from a large catchment area, but with remarkable gender variations. Furthermore, we have identified a large group of potential new diagnoses close to home, in that' a full 25% of surveyed beneficiaries have not informed their spouse of their status.

Disclosures. **All authors:** No reported disclosures.

1545. Knowledge, Attitudes and Beliefs Regarding the Potential Impact of Health Care Reform on HIV-Infected Patients

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Session: 198. HIV 3: Cascade of Care
Saturday, October 11, 2014: 12:30 PM

Background. Public opinion of the Patient Protection and Affordable Care Act (ACA) has been divided. Polling of physicians and the general public about knowledge, attitudes, and beliefs towards the ACA has been conducted, but to date, no such studies have targeted HIV-infected patients. We report results of such a survey.

Methods. Sequential adult HIV-infected patients attending the University of Nebraska Medical Center HIV clinic between November 18, 2013 and March 31, 2014 were surveyed for demographics, knowledge regarding health care reform, and attitudes and beliefs regarding the ACA. Participants were English speaking and completed the surveys alone. A sample size of 371 was selected to allow for the estimation of confidence intervals for proportions with a precision of 5% or smaller. Chi-square tests were performed to assess differences in perception of benefit by patient characteristics and knowledge levels.

Results. 406 participants completed the survey. 50% reported full time employment and 50% reported annual income less than $20,000. 21% reported they have or will benefit from healthcare reform. 58% indicated they do not know whether they have/will benefit while 57% indicated they do not have enough information about the ACA to make informed decisions. 37% reported feeling they could not change jobs due to fear of change in health insurance. Four questions assessed patient knowledge of the ACA. Only 3% of participants correctly answered all four while 62% answered only one or zero questions correctly. Those who reported not knowing whether they had benefitted or would benefit from the ACA were significantly less knowledgeable about the ACA than those who reported they had benefitted or would benefit from the ACA ($p < 0.001$).

Conclusion. Very few HIV-infected patients have sufficient knowledge of the ACA and only 21% of patients feel they have benefitted or will benefit from the ACA. Compared to the general public, HIV-infected patients generally have less knowledge regarding the ACA and perceive less overall benefit, despite the fact that many are poised to benefit greatly. Targeted education and outreach are necessary to reduce the knowledge gap and empower HIV-infected patients to better understand and utilize their benefits.

Disclosures. **All authors:** No reported disclosures.

1546. HIV Patients' Knowledge, Beliefs, and Attitudes about the Patient Protection and Affordable Care Act

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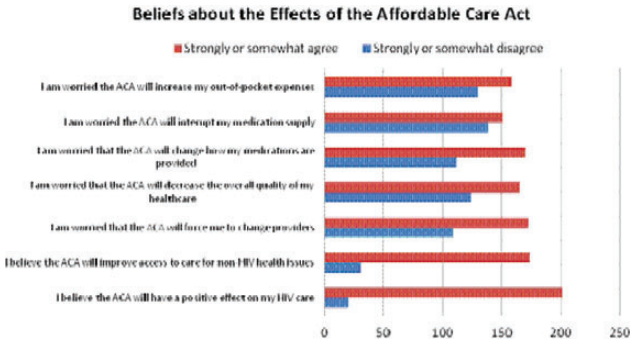
Background. The 2010 Patient Protection and Affordable Care Act (ACA) is designed to improve insurance coverage and access to healthcare for many people living in the United States. The ACA stands to uniquely impact persons living with HIV/AIDS (PLWH), many of whom are uninsured and reliant on Ryan White Care Act funded programs for coverage of their HIV care. Through the ACA, many PLWH have become eligible for expanded Medicaid coverage in participating states, or for private insurance coverage through the federal or state exchanges. We conducted a survey in order to explore PLWH's familiarity with and opinions about the ACA.

Methods. From January to April 2014, we administered a 35-question multiple-choice survey to patients presenting for follow-up HIV care at the Ruth M. Rothstein CORE Center in Chicago, IL. Demographic data, as well as data regarding knowledge, attitudes, and beliefs about the ACA, were collected and analyzed.

Results. A total of 289 respondents completed the survey: 202 (68.9%) were male, and 214 (75.1%) were black; respondents had been living with HIV for a median of 9.9 years. 86 (36%) were uninsured, 67 (28.3%) had Medicaid, and 50 (21.1%) had enrolled in County Care (an expanded Medicaid program in Illinois, in effect since January 2013). 246 (85.4%) of respondents had heard of the ACA, though only 108 (37.4%) felt they understood how the ACA would impact them personally. 143 (46.5%) respondents correctly answered questions assessing knowledge about basic aspects of the law. 201 (69.9%) feel the ACA will have a positive impact on the HIV care, and 60.2% feel it will increase access to care for their non-HIV health issues; however, 165 (57.1%) conflictingly worry that the overall quality of their healthcare will decrease. The greatest concerns regarding the ACA include fear of being forced to change providers (60.5%), and concerns about changes in how medications are supplied (58.8%).



Conclusion. Although most PLWH are aware of the ACA and have generally positive opinions on the law, there remains concern about the impact it may have on their future HIV care. Targeted education is needed in order to ensure PLWH can take optimal advantage of the expanded coverage opportunities available through the ACA.

Disclosures. **All authors:** No reported disclosures.

1547. Delayed Entry into Care in Younger HIV Infected Individuals

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Background. By 2010, young adults, age 13 to 24 years old, accounted for ~7% of persons living with HIV in the U.S. One in 4, new HIV infections in the U.S. occurred in young adults. Almost 60% of young adults with HIV are unaware of their status. South Carolina (SC) ranks amongst the top in new infections in young adults. The aim of this study is to compare characteristics and engagement in care in newly diagnosed HIV individuals in Richland County, SC between those who are <25 years (young adults) and ≥25 years at the time of diagnosis.

Methods. Baseline characteristics, time to engagement in care and time to undetectable HIV viral load (VL) were compared between individuals <25 years to those ≥25 years of age at HIV diagnosis. Means and standard deviations were calculated for all continuous variables and differences between individuals in the two age groups were assessed via two-tailed independent samples t-tests. Frequencies were calculated for all categorical variables and differences between the two age groups were assessed via χ^2 tests of independence.

Results. 231 new HIV diagnoses were identified of which 69 (29.9%) were <25 years at the time of diagnosis. Compared to the older group, the young adults were more likely to me male (61.7% vs 87%, $p = .001$) and report male sex with male (38.5% vs 79.7%, $p < .001$). There was no difference in race by age group. Compared to the older adults, the young adults had a higher proportion going to college (32.8% vs 64.7%, $p = .001$). Young adults reported more sexual partners in the past year (41% with >2 partners vs 16%, $p < .001$). The young adults had marginally higher rates of sexually transmitted infections (STI) at HIV diagnosis (23.1% vs 13%, $p = .06$). Young adults had a longer mean delay from diagnosis to first kept appointment, (12.9 weeks vs 9.0 weeks, $p = .04$). The young adults had a longer mean time to initiation of HIV medications (23.1 weeks vs 14.3 weeks, $p = .004$), and longer time to obtain an undetectable VL (7.6 months vs 5.4 months, $p = .03$).

Conclusion. Delayed entry into care, higher number of sexual partners and higher rates of STI in the younger individuals with newly diagnosed HIV are factors that may lead to the high rates of new infections in this age group. Prevention efforts need to be tailored to target this age group.

Disclosures. **All authors:** No reported disclosures.

1548. Laboratory Markers Overestimate Retention in HIV care

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Background. Patients who are retained in HIV care have a higher likelihood of viral suppression and increased survival. In some studies, laboratory markers have been used as surrogate markers for clinical visits. The purpose of this study is to determine the accuracy of these markers at predicting retention in care in an urban HIV clinic.

Methods. A retrospective cohort study was conducted using the medical records of patients who were newly diagnosed with HIV in the emergency department. Retention in care, congruent with the HRSA (Health Resources and Services Administration) definition, was defined as 2 clinical visits to an HIV provider separated by 3 months within a 1 year period. Retention by lab markers was 2 documented labs, either a CD4 count or an HIV viral load, separated by 3 months within the same 1 year period.

Results. Ninety-nine patients were newly diagnosed with HIV in the emergency department. By the HRSA definition 36 patients (36%) were retained at 1 year and 40 patients (40%) using the lab marker definition. The sensitivity and specificity of using lab markers to predict retention was 100% and 93.7% respectively. The positive predictive value (PPV) and negative predictive value (NPV) was 90% and 100% respectively. Lab markers predicted retention in 4 patients who did not meet HRSA definition of retention, but all patients who met the HRSA definition of retention were also retained by the lab criteria. Among the 99 patients, 56 were linked to the HIV clinic associated with our hospital, of which 63% (36) were retained at year 1 using the HRSA definition and 70% (39) using the lab marker definition. Using laboratory markers to predict retention among linked patients resulted in a sensitivity of 100% and a specificity of 85%. The PPV and NPV were 92% and 100% respectively.

Conclusion. Lab markers over estimate currently accepted definitions of retention, but the absence of lab markers was highly predictive for not being in care. Since multiple providers can measure these labs, the use of lab markers may be more representative of a patient's overall contact with the medical system. It is not unexpected that all retained patients met the lab definition since HIV providers measure CD4 counts and viral loads in routine disease monitoring.

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1549. Spectrum of Healthcare Engagement in an HIV Primary Care Clinic within the District of Columbia

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Background. The District of Columbia (DC) continues to have one of the highest rates of persons living with HIV within the US at 2.4% of its population. The VA Medical Center located in the DC (DCVAMC) has had 1,000 or more HIV-infected patients in care since 2008. We describe the proportion of patients with HIV diagnosis, in HIV care, on treatment and with viral suppression during 2008 through 2013.

Methods. A retrospective review of our clinic patients was made for the period 2008 through 2013 for those with HIV diagnosis and their age, gender, and race, those engaged in care based on clinic visit and HIV RNA testing, those on antiretroviral therapy (ART), and those with HIV suppression below the limit of detection. Mean CD4 count is given by calendar year.

Results. Percent of total HIV patients are given in each category except for mean age and CD4 count.

Parameter	2008	2009	2010	2011	2012	2013
Total HIV patients in DCVAMC	1,000	1,049	1,057	1,036	1,026	1,040
male	97%	97%	97%	97%	97%	96%
mean age (years)	51	51	52	52	53	53
African American race	80%	78%	79%	79%	77%	77%
Persons engaged in care	75%	77%	71%	82%	87%	91%
Persons with ART use	67%	67%	72%	77%	80%	84%
Persons with viral suppression	45%	54%	54%	59%	67%	72%
Mean CD4 (cells/mL)	354	362	390	421	457	484

Conclusion. During 2008 through 2013, our clinic patients achieved steady improvement along their continuum of HIV care based on persons engaged in care, on ART, and with viral suppression as well as higher mean CD4 counts within a metropolitan area with a high burden of HIV infection.

Disclosures. **All authors:** No reported disclosures.

1550. Can We Re-engage Patients with HIV Who Are Lost to Care? A Pilot Study in a Large Urban HIV Clinic

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Background. Secondary to broader HIV screening efforts and expanded treatment criteria for initiating antiretroviral therapy (ART), the number of patients requiring regular HIV care is increasing. After establishing care, one-third of patients become lost to follow-up (not seen in more than a 12 month period). We hypothesize that lost-to-care patients could be re-engaged in care with a brief, focused, patient oriented bundle intervention in two dedicated office visits.

Methods. We identified individuals who were not seen in more than 12 months from August 2012 to January 2014 in a large urban HIV clinic in Philadelphia, PA. Attempts were made to contact patients, and two separate dedicated office visits were scheduled in one month. We addressed reasons why patients were lost to care, evaluated insurance status, and arranged case management and psychiatric services. Patients' demographics and clinical information were reviewed.

Results. Fifty-nine consecutive patients were identified and evaluated. Median age was 44 years and median time from last visit was 32 months. More than half of patients (55.9%) completed two visits and 37 (62.7%) remained engaged in care (seen within a 6 month period after two visits). Most common reasons for lost to care were recent incarceration (42.4%), followed by substance abuse (22%). At the time of initial evaluation, nearly half (47.5%) were not taking ART. Patients who were using drugs or alcohol were less likely to remain engaged in care compared to others (30.8% vs 71.7%, P= 0.01). Patients who completed 2 visits in a one month period, were more likely to stay engaged in care (84.8% vs 34.6%, P <0.001), and were more likely to have a viral load <200 copies (86.4% vs 42.9%, P = 0.038) within a 6 month follow up period.

Conclusion. Our experience suggests that actively identifying patients who are lost-to-care and implementing two dedicated visits improved re-engagement in HIV care. If such a simple and low-effort intervention is done routinely, lost-to-care time can be decreased, potentially improving patient outcomes and decreasing secondary transmission. Additionally, addressing both the transition from incarceration to HIV care in the community and substance abuse may be high yield in retaining this high-risk population in HIV care.

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1551. The Patient-Centered Medical Home: A Reality for HIV Care in Nigeria

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Background. HIV care delivery in resource-limited settings (RLS) may serve as a new paradigm for chronic care in an environment where episodic acute care is the norm. Frameworks for evaluation of care systems are important to optimize clinic performance. The Patient-Centered Medical Home (PCMH) is one framework heralded for chronic medical care. Our objective was to adapt the PCMH framework for use in RLS, and evaluate the performance of HIV treatment programs in Nigeria according to this standard.

Methods. The study was conducted at comprehensive HIV treatment centers in the AIDS Prevention Initiative in Nigeria (APIN) network. In June of 2013, APIN coordinated 36 sites providing care and treatment to nearly 100,000 people living with HIV and AIDS. We adapted the 2011 National Committee on Quality Assurance PCMH standard for HIV care in RLS. We administered a 50-item survey to medical directors at all sites incorporating five key domains of the PCHM describing: 1) access and continuity, 2) patient population management 3) evidence-based care, 4) self care and community resource promotion, and 5) performance improvement.

Results. Thirty-three of 36 clinics completed the survey. Most clinics were public (86%) and in urban/semi-urban locales (65%). Seventy-nine percent had >5,000 patients in care. On a scale of 0-100, clinics scored highest in self-care and support 91% (range 63-100%), followed by patient population management 80% (72-81%), and performance improvement 78% (44-78%). Clinics scored lowest with the most performance variability in evidence-based care 65% (22-89%) and access/continuity 61% (33-80%). Average composite score across the domains studied was 74% (58-81%). Twenty-nine of 33 sites scored in the top 25th percentile for at least 1 domain. Factors including clinic type (public vs private vs faith-based), size, and urban or rural location did not statistically significantly predict composite scores.

Conclusion. HIV treatment programs in Nigeria performed quite well within the PCMH framework; 88% had a high score in at least one domain highlighting an opportunity to share best practices. Clinics showed greatest room for improvement on

access and continuity. The PCMH model may provide a useful framework for evaluating chronic HIV care delivery in RLS.

Disclosures. **All authors:** No reported disclosures.

1552. Predictors of poor retention in care among HIV-infected Patients receiving antiretroviral therapy in South Korea: results from a five-year retrospective hospital-based cohort

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Background. Several recent studies have shown that poor retention in care is associated with higher rate of antiretroviral therapy (ART) failure and worse survival. Identifying which patients are at greatest risk for not being retained is important to target intervention efforts to those groups. The objective of this study was to determine the risk factors for suboptimal retention in care among HIV infected adults receiving ART in Korea.

Methods. A five-year retrospective hospital based cohort study was conducted to assess the risk factors associated with suboptimal retention in care among HIV-infected patients initiating ART during 2002-2008. Patients who never return to hospital after loss to follow-up (LTFU) were traced to ascertain survival status. Retention in care was measured by hospital visit constancy (HVC) during the observation period after initiating ART. To determine the predictable factors for poor retention in care, we compared the demographic, psychosocial, and clinical characteristics between the patients with 100% HVC and the patients with ≤ 50% HVC, by using multiple logistic regression analysis.

Results. Among 247 patients initiating ART during 2002-2008, as of 5 years after ART initiation, 179 patients (72.5%) remained in care in the study hospital, 20 patients (8.1%) were transferred out to other hospitals, 9 patients (3.6%) died in the study hospital, and 39 patients (15.8%) were lost. Of the 39 patients initially categorized as lost, after tracing, 8 patients (20.5%) were known to have died and 31 patients (79.5%) were alive. When we compared 166 patients (67.2%) with HVC 100% with 33 patients (13.4%) with HVC ≤ 50%, in multivariate analysis, age at start of ART ≤ 30 years [odds ratio (OR), 4.08 vs > 50; 95% confidence interval (CI), 1.10-15.15, $P = 0.036$), no non-HIV related comorbidity [OR, 2.94 vs Charlson Comorbidity Index (CCI) ≥ 1; 95% CI, 1.02-8.49, $P = 0.046$], CD4 cell counts > 300 cells/μL at ART initiation (OR, 3.58; 95% CI, 1.33-9.65, $P = 0.012$) were significant predictable factors of poor retention in care during up to 5-year observational period after ART initiation.

Conclusion. Younger age, fewer non-HIV related comorbidity, and higher CD4 cell counts at ART initiation were significant risk factors for not being retained, highlighting the importance of special attention to these groups.

Disclosures. **All authors:** No reported disclosures.

1553. Burden of HIV on Hospitals in USA: Analysis of Nationwide Emergency Department Sample Data

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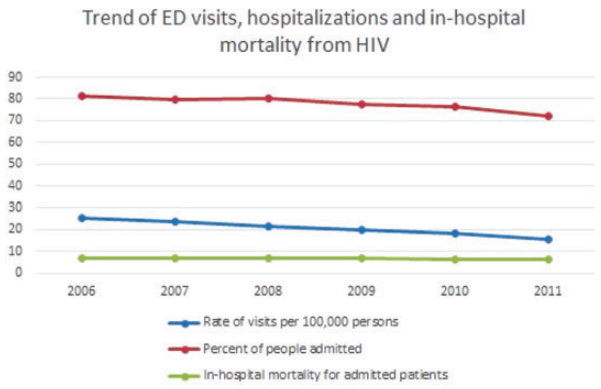
Background. Medical management for the HIV disease has made tremendous progress in the last decade with introduction of newer class of drugs and availability of combination pills making it possible to treat resistant and noncompliant patients respectively. However, the extent of burden of HIV on US hospitals is still not known. This study was done to determine the burden of HIV disease on USA healthcare and analyze the trend of disease from 2006-2011.

Methods. We queried Nationwide Emergency Department Sample data for all the patient visits with first listed diagnosis of HIV using Clinical classification software code 5, corresponding to International Classification Code 9 codes of 042, 042.0, 042.1, 042.2, 042.9, 043.0, 043.1, 043.2, 043.3, 043.9, 044.0, 044.9, 079.53, 279.10, 279.19, 795.71, 79.58 and V08. Data was extracted for the years 2006 to 2011. Admission rate to hospitals during Emergency Department (ED) visits and in-hospital mortality for admitted patients was calculated. SPSS was used for statistical analysis and $p < 0.05$ considered significant for the purpose of this study.

Results. We identified total of 379,332 ED visits with first listed diagnosis of HIV from 2006-11, with average admission rate of 78.36% and average in-hospital mortality during stay of 6.66%. Rate of patient visits to ED for first listed diagnosis of HIV decreased from 25.4 per 100,000 persons in 2006 to 15.7 per 100,000 in 2011. Hospital admission rates for ED visits declined from 81.28% to 72.25% ($p < 0.05$). In-hospital mortality for these admissions declined from 7.03% to 6.09% ($p < 0.05$)



Conclusion. Our study reveals that although ER visits, hospitalization and in-hospital mortality from HIV has decreased significantly from 2006-11 but still rate of hospitalization remains high with 3 out of 4 patients being admitted to the hospital with 6% mortality compared to national average of in-hospital mortality of 0.6% for Diabetes mellitus and 5% for myocardial infarction. It indicates there is still large unmet need for interventions in managements of HIV to reduce burden on healthcare.

Disclosures. **All authors:** No reported disclosures.

1554. Extremely High Level of Primary HIV Anti- Retroviral Therapy Drug Resistance in Naïve HIV Infected Patients in Uzbekistan

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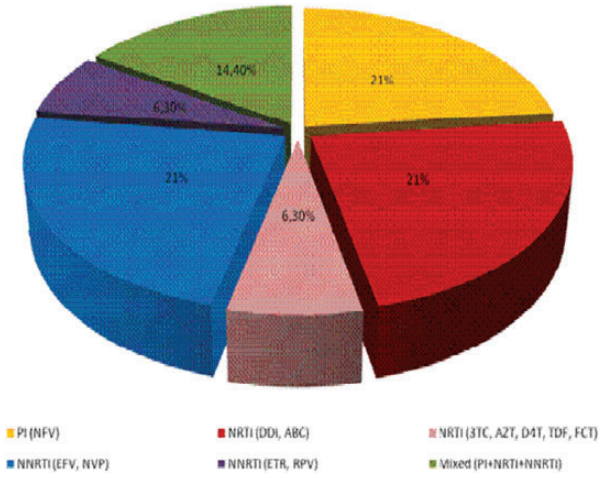
Session: 199. HIV 4: Treatment - Outcomes, Adherence, and Toxicities
Saturday, October 11, 2014: 12:30 PM

Background. Being a Global problem, the infection of HIV turned to be pandemic and remains very harmful and actual for treatment and vaccine searching studies. The antiretroviral therapy (ARVT) is still the most effective way to keep the level of HIV infected people lower and not to allow this infection more increasing. ARVT of HIV infected people started in 2006 in Uzbekistan; however, no laboratory monitoring of the ARVT effectiveness as well as a level of ARVT drug resistance among HIV infected treatment naïve people was controlled in this country. Firstly, we started our study to evaluate the level of primary drug resistance among HIV-infected not treated people.

Methods. Collected 48 samples from HIV-infected drug naïve patients were centrifuged and total RNA was extracted from blood plasma using QuiAmp RNA/DNA extraction kit (Quiagen, Netherlands). Both Nested PCR and cycle sequencing for Protease and two Reverse Transcriptase regions of HIV/RNA were performed using HIV-sequencing kit ("InterLabService," Moscow, Russia). Capillary sequence was performed using probes and manufacturers provided primers CEQ DTCS kit (Beckman Coulter, Germany).



HIV/ARVT drugs mutations rates

Results. The most sequenced samples from HIV-infected drug naïve patients had drug resistance mutations in both Protease and Reverse Transcriptase regions of HIV genome. Overall samples had 26 drug resistant strains from 48 sequenced samples (54%). That means the level of primary drug resistance mutations in our country is extremely high in comparison to other data reported earlier at least among former Soviet Union countries. Detailed data of ARVT drug resistance mutations in sequenced

HIV genome is presented on a diagram (figure 1). Mutations were mainly revealed in Protease and Reverse Transcriptase regions for Protease Inhibitors (PI – NFV) and Reverse Transcriptase Inhibitors (NRTI – DDI, ABC, AZT, D4T, 3TC and FTC; and NNRTI – EFV, NVP, ETR and RVP).

Conclusion. High level of HIV ARVT drug resistance rate is a signal for treatment scheme review and changing of the mainly using drugs in the area. However, it depends on the country possibilities and the drugs donating international projects. Further studies required for HIV ARVT efficacy monitoring and treatment adherence checking during therapy.

Disclosures. **All authors:** No reported disclosures.

1555. Factors Associated with the Selection of Initial Antiretroviral Therapy: Real-world Channeling

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Background. Over the last decade antiretroviral (ARV) regimens have become more effective and better tolerated yielding many options for use in first line therapy. Using data from the CNICS cohort, we explored factors associated with selection of the class of initial ARV regimen.

Methods. CNICS is a network of 8 HIV clinics situated at academic centers in the US. We classified all patients initiating HAART (3 or more drugs) between July 2009 and December 2012 as NNRTI, boosted-PI (PI/r), or raltegravir (InSTI). Measured factors suspected of being associated with regimen choice were explored individually and in 3 separate multivariable logistic regression models with regimen classification as the outcome variable. For each model the referent group was all patients whose initial HAART regimen was not in the classification being modeled.

Results. 1215 patients initiated HAART in the observation period. 650 regimens contained an NNRTI, 455 regimens contained a boosted-PI and 110 regimens contained raltegravir. Median age was 38 years; 34% Black, 57% White, 9% other; 19% Hispanic; 88% male; 67% MSM; 14% IVDU; 25% VL >100K; 16% HCV infected; and 65% had > 2 co-morbid conditions.

	Model 1: NNRTI	Model 2: PI/r	Model 3: InSTI
Age 37-47 vs 19-36	1.0 (0.7-1.3)	0.9 (0.7-1.2)	1.3 (0.8-2.2)
Age 48-75 vs 19-36	1.0 (0.7-1.4)	0.9 (0.6-1.2)	1.4 (0.8-2.4)
Female vs MSM	**0.5 (0.3-0.7)**	**2.1 (1.5-3.0)**	1.1 (0.7-2.0)
Heterosexual Male vs MSM	0.9 (0.6-1.3)	1.1 (0.8-1.6)	1.3 (0.8-2.3)
Prior ART Exposure	0.5 (0.2-1.2)	1.3 (0.6-2.9)	1.7 (0.6-4.7)
Liver-HCV Dx	**0.6 (0.4-0.9)**	1.3 (0.9-1.8)	1.4 (0.8-2.3)
Psych Depression Dx	**0.6 (0.5-0.8)**	**1.5 (1.2-1.9)**	**1.9 (1.2-3.0)**
Cardiovascular/ Cerebrovascular Dx	0.9 (0.5-1.6)	0.8 (0.4-1.6)	**2.7 (1.2-5.7)**
Diabetes Dx	0.9 (0.5-1.6)	0.9 (0.5-1.7)	1.7 (0.8-3.5)
Hypertension Dx	0.9 (0.7-1.2)	1.0 (0.7-1.4)	1.5 (0.9-2.4)

Conclusion. The choice of initial regimen is associated with several demographic and clinical factors, which is sometimes referred to as 'channeling.' In this study, patients with underlying psychiatric conditions were less likely to receive an NNRTI, while those with CVD were more likely to receive raltegravir. As more choices for HIV therapy become available, factors that impact initial regimen selection will likely become even more heterogeneous over time.

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1556. Quality Improvement of Antiretroviral Therapy Errors at University Hospital

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Background. University Hospital has more than 600 admissions of people living with Human Immunodeficiency Virus (PLWH) yearly. In an earlier study of antiretroviral therapy (ART) error, nearly half of PLWH admissions had at least one medication error, which could lead to increased drug resistance and treatment failure. Several interventions were introduced to reduce this high error rate including: physician and pharmacy education, utilization of computerized provider order management (CPOM) and ordering instructions and drug reference links in CPOM. This analysis evaluated the current state of medication errors after the implementation of these interventions.

Methods. A retrospective review of PLWH on ART administered during admissions from July 1, 2013 to December 31, 2013 was conducted. Medication errors were categorized as incomplete drug regimen, incorrect drug dosing, mismatched home ART (in HIV clinic patients whose records were available), and contraindicated drug-drug interactions. We also categorized medication errors by admitting specialty. The methodology was unchanged from our earlier study.

Results. A total of 315 admissions of PLWH were reviewed. Of these, 115 admissions (37%) had at least one medication error, an 18% relative error reduction. Of the 158 errors identified, incorrect drug dosing was the most common error (34%), followed by incomplete drug regimen (28%). Of note, there was a significant increase in co-administration of high dose histamine type 2 blockers and atazanavir (170% increase). Patients followed in the HIV clinic had similar ART error rates while inpatient as our prior study. Although, ART errors were again significantly reduced by infectious diseases (ID) consultation; the overall error rate reduction did not significantly change after these interventions. Again, surgical and medical services had the highest ART errors.

Conclusion. Overall, interventions such as additional education and guidelines can aid in reducing ART errors but they are not sufficient to eliminate them entirely. A more comprehensive approach is needed to prevent and reverse the detrimental consequences of ART errors in this community with such a high prevalence of HIV. We propose a dedicated infectious diseases and/or pharmacy stewardship that review ART on a daily basis.

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1557. Impact of HIV Pharmacist Reconcilation on Correction of Antiretroviral Prescription Errors Among Hospitalized HIV-Infected Patients

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Background. Antiretroviral therapy (ART) prescribing errors are common in hospitalized HIV-infected patients, which may cause patient harm and increase healthcare-associated costs. Previously, we retrospectively reviewed admissions from 2009-2011 and found a 35.1% error rate in ART prescribing, 35% of which were corrected within 24 hs. Subsequently, we developed a medication reconciliation process with an HIV pharmacist, and our institution implemented a unified electronic medical record (EMR).

Methods. We prospectively reviewed the medical records of HIV-infected patients admitted to the hospital for >24 hs between March 9, 2013 - March 10, 2014. An HIV pharmacist reconciled outpatient ART prescriptions with inpatient orders within 24 hs of admission. Errors were classified as omission; wrong drug; incorrect dose; drug-drug interactions (DDIs); and incorrect scheduling. Time to error correction was recorded. Error rates were compared to our retrospective evaluation and relative risks (RR) calculated. Logistic regression models were used to compare error rate with use of EMR, and proportion of errors corrected at 24 hs with prospective HIV pharmacist intervention, both compared to historical data.

Results. In 186 admissions for 105 patients, we identified 43 medication errors in 31 admissions (16.7%). The most common error was incorrect scheduling (42%), followed by drug omission and DDIs. All identified errors were corrected, 65% within 24 hs and 81.4% in 48 hs. Using a unified EMR decreased the risk of error occurrence compared to not using a unified system (RR 0.47, 95% CI: 0.34, 0.67). Logistic regression adjusting for gender and race found that errors were 61% less likely to occur using the EMR (95% CI: 40%-75%; $p < 0.001$). The second model, after adjusting for gender, race and total number of errors, found that errors were 9.4 times more likely to be corrected within 24 hs with pharmacist intervention ($p < 0.001$).

Conclusion. Use of an EMR decreased the error rate by more than 50% but the HIV pharmacist intervention was key to timely error correction. Two thirds of errors were corrected within 24 hs and no error was left uncorrected. Even with the implementation of an EMR, ART errors were common, but prospective HIV pharmacist intervention enabled rapid correction.

Disclosures. **All authors:** No reported disclosures.

1558. Clinico-demographic Profile and Treatment Outcomes of Pediatric Participants of a Large Outpatient HIV Clinic in Kigali, Rwanda

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Background. Pediatric patients make up 7.5% of the global population living with HIV infection and comprise 15% of incident cases worldwide each year (WHO). 91% of the 3.4 million children living with HIV at the end of 2011 reside in sub-Saharan Africa (WHO). They represent a challenging population to manage due to limited pediatric ARV formulations, poor healthcare resources, suboptimal medication adherence, societal stigma and neglect. Data on the demographics, clinical profile, and treatment outcomes of the pediatric HIV population is lacking in Rwanda.

Methods. Study was a retrospective chart review conducted from February 1, 2013 – January 31, 2014. The aim was to describe the demographics, clinical characteristics, and treatment outcomes of HIV infected pediatric participants (age <18 years) of a large outpatient HIV clinic in Kigali, Rwanda. Charts for review were selected by simple random sampling. Categorical demographic data and other categorical variables were expressed as simple frequencies and/or percentages of the whole. Continuous variables were expressed as median values with inter-quartile ranges or means with ranges as appropriate.

Results. 174 randomly selected charts were reviewed including 84 males and 90 females (sex distribution 1:1.1). Median age and CD4 count at the time of HIV diagnosis was 6 years (IQR 3-9 years) and 380 cells/uL (IQR 206-662 cells/uL) respectively. Nadir CD4 count was 272 cells/uL (IQR 148-416 cells/uL). Vertical transmission was the predominant mode of acquisition of HIV infection (70%). 46 out of 161 patients (28.6%) had WHO clinical stage 3 or 4 HIV disease at time of initial presentation to care. 68.2%, 27.2% and 4.6% of patients were on nevirapine (NVP), efavirenz(EFV) and lopinavir/ritonavir based regimens respectively. Average duration of ARV exposure was 83 months (range 8-135 months). 61/162 patients (37.7%) had HIV viral loads >400 copies/ml during their most recent viral load estimation.

Conclusion. Pediatric participants of the largest outpatient HIV clinic in Kigali, Rwanda frequently present late to care with advanced HIV disease and experience significant rates of virologic failure. More studies are needed to explore the causes of these observations.

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1559. Clinical and Immunologic Correlates of Pregnancy among HIV-infected Women in Care –United States (U.S.)

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Background. Women represent 25% of persons living with HIV in the U.S.; 80% are reproductive-age (15-44 years) when diagnosed and may consider pregnancy after HIV diagnosis. Clinical and immunologic factors associated with pregnancies among HIV-infected women have been understudied; such data may inform HIV care efforts.

Methods. We used data from the 2009 cycle of the Medical Monitoring Project (MMP), a cross-sectional survey of a representative sample of US HIV-positive adults in care. We included women diagnosed > 1 year before interview if aged < 45 years at diagnosis and compared women with and without ≥ 1 pregnancy after HIV diagnosis. We examined the association of pregnancy with years since HIV diagnosis and the following exposures during the 12 months preceding MMP survey: sexually transmitted disease (STD) screening, HIV/STD prevention conversations with providers, prescription of antiretroviral therapy (ART), documentation of viral suppression (≤ 200 copies/mL), and unprotected sex with a man of unknown or HIV-negative status. We computed unadjusted and adjusted prevalence ratios (APR) and 95% confidence intervals (CI) using logistic regression.

Results. Data were available for 939 respondents representing 94,718 HIV-positive women; 4.8% were currently pregnant or had been pregnant in the previous 12 months. Median age at diagnosis was 30.5 years; 60.1% were non-Hispanic black. Of respondents, 27% were screened for chlamydia or gonorrhea; 51% had HIV/STD prevention conversations with providers; 87% were prescribed ART, 66% achieved viral suppression; 16.9% reported unprotected sex with an HIV-negative man or man of unknown HIV status. Overall, 29.7% of women reported ≥ 1 pregnancy after diagnosis. Having ≥ 1 pregnancy since HIV diagnosis was more likely among women who were ≤ 19 years at HIV diagnosis (APR 7.8 CI 4.5 – 13.4); interviewed 5 -9 years since their HIV diagnosis (APR 1.4 CI 1.03 – 1.9); were virologically suppressed (APR 1.4 CI 1.2 – 1.7); and reported unprotected sex with a male of unknown or HIV-negative status (APR 1.5 CI 1.1 – 2.0).

Conclusion. These data suggest that interventions are needed to: 1) optimize viral suppression; 2) increase HIV/STD prevention conversations; and 3) incorporate reproductive health discussions as part of routine care for HIV-infected women.

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1560. Treatment responses and complications among HIV-infected patients who initiated antiretroviral therapy at the age of 50 years or older and those who are younger than 50 years at Maharaj Nakorn Chiangmai Hospital

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Background. Prevalence of HIV in adults aged ≥ 50 years is increasing. Responses to combination antiretroviral therapy (cART) in this population are variable. This study aimed to evaluate responses to cART and adverse effects after cART in HIV-infected elderly patients.

Methods. A retrospective cohort study was conducted among naïve HIV-infected adults initiating cART between January 2005 and December 2012 at Maharaj Nakorn Chiang Mai Hospital. We compared the demographic characteristics, responses to cART, and adverse effects after cART between patients who initiated cART at aged ≥ 50 years and aged < 50 years.

Results. 209 and 103 patients who initiated cART at aged < 50 years and ≥ 50 years were randomly selected from HIV cohort. Among patients aged ≥ 50 years, 63 were male (61.2%), the mean age was 54.5 years, the initial CD4 cells was 90 (IQR 32, 187) cells/mm^3, and the major route of transmission was heterosexual (97.1%). 27 (26.2%), 9 (8.7%), and 9 (8.7%) patients had underlying diseases of hypertension, diabetes, and dyslipidemia, respectively. Median time to reach CD4 cells of 350 cells/mm^3 was 30 months (IQR 18, 60), and 61/76 patients (80.3%) had undetectable HIV-1 RNA at 6 months after cART. Among patients aged < 50 years, 113 were male (54.1%), the mean age was 34 years, the initial CD4 cells was 80 (IQR 26, 220) cells/mm^3, and the major route of transmission was heterosexual (80.4%), followed by homosexual (18.2%). 13 (6.3%), 4 (1.9%), and 6 (2.9%) patients had underlying diseases of hypertension, diabetes, and dyslipidemia, respectively. Median time to reach CD4 cells of 350 cells/mm^3 was 30 months (IQR 18, 48), and 100/139 patients (71.9%) had undetectable HIV-1 RNA at 6 months after cART. There was no statistically significant different in gender, initial CD4 cells, time to reach CD4 cells of 350 cells/mm^3, and the proportion of people who had undetectable HIV-1 RNA at 6 months between groups. More patients among aged ≥ 50 years had underlying diseases. After receiving cART for at least 3 years, LDL and FBS were higher among patients aged ≥ 50 years.

Conclusion. We identified distinct differences in risk of transmission and underlying diseases between groups. However, immunologic and virologic responses to cART were not different. Blood cholesterol and sugar were higher among older patients after cART, although no relevant clinically significance.

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1561. The Relationship Between Self-reported Adherence and Efavirenz Blood Levels on the Appearance of HIV Viral Load Blips

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Background. Intermittent episodes of low-level viremia, termed "blips," can sometimes occur in HIV-infected persons on viral load (VL)-suppressive antiretroviral therapy (ART). The underlying causes of blips are not completely understood. We evaluated the association between self-reported adherence (SRA) and plasma drug levels in the U.S. Military HIV Natural History Study.

Methods. Participants experiencing blips on their initial single tablet ART regimen of efavirenz/emtricitabine/tenofovir (EFV/FTC/TDF) with available SRA data and repository plasma specimens on consecutive blip and non-blip dates were included. Blips were defined as a plasma VL ≥50 copies/mL, with values <50 copies/mL before and after the blip timepoint. SRA was categorized as < or ≥85% and assessed at both the blip and non-blip timepoints. Untimed plasma levels were measured for the EFV component of the regimen by high-performance liquid chromatography (HPLC) for the corresponding blip and non-blip timepoints. Random EFV levels below reported minimum trough concentration of 1 mcg/mL were considered subtherapeutic. SRA and EFV plasma levels were analyzed as categorical values < or ≥85% and above or below therapeutic threshold, respectively, by Chi-square test.

Results. A total of 116 participants met inclusion criteria. SRA was <85% for 6 of 232 (2.6%) timepoints, including 3 of 116 (2.6%) blip timepoints and 3 of 116 (2.6%) non-blip timepoints. Of the 232 specimens analyzed, 12 (5.2%) had EFV levels below threshold, including 5 of 116 (4.3%) blip and 7 of 116 (6.0%) non-blip timepoints. Among those with subtherapeutic EFV levels, adherence ≥85% was self-reported by 4 of 5 (80%) and 7 of 7 (100%) participants on blip and non-blip dates, respectively. There was no statistically significant association between SRA and EFV levels at either blip (P = 0.12) or non-blip (P = 0.11) timepoints.

Conclusion. The vast majority of participants experiencing blips had SRA ≥85%. Although studies have shown that suboptimal adherence results in reduced drug levels, we observed no association between SRA and untimed EFV levels in this retrospective study. This suggests that other factors, such as viral replication from reservoirs or VL assay variability, may be responsible for blip episodes.

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1562. The Influence of Co-infection with HCV on CD4 and B-cell Reconstitution in Human Immunodeficiency Virus (HIV)-infected Patients

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Background. HIV is associated with dysfunctional cellular and humoral immunity. The effects of co-infection with hepatitis C virus (HCV) on immune reconstitution are controversial. The utility of monitoring B-cell lymphocyte counts in HIV patients has not been well studied. In the present study, we compare the effect of antiretroviral therapy (ART) on CD4 and B-cell counts in HIV mono-infected (HIV + /HCV-) and HCV co-infected (HIV + /HCV+) patients.

Methods. Retrospective observational cohort of 160 HIV-infected patients (39 with HCV co-infection) who suppressed plasma viral load (VL) to undetectable levels within one-year of ART initiation. We reviewed baseline clinical and demographic variables, and CD4 and B-cell counts at two time points: prior to ART initiation and after 9-15 months of persistently undetectable VL (post-ART). A multiple general linear regression model was used to test for significant associations between predictor variables and change in B-cell counts after adjusting for pre-ART levels as well as covariates significant in the univariate analysis.

Results. The median absolute pre- to post-ART increase in CD4 and B-cell counts did not differ significantly between the 2 groups (table). In HIV + /HCV- and HIV + / HCV+ patients, the % increase in B-cell and CD4 count were strongly correlated (Spearman's R 0.58 and R 0.65, respectively, P < 0.001). In a multiple regression model adjusting for pre-ART B-cell count, HCV-co-infected patients experienced a not statistically significant 15% greater rise in B-cell counts, compared to mono-infected group (P = 0.08).

CD4 and B-cell increases after 9-15 months of persistently undetectable VL

	Parameter	HIV+/HCV-	HIV+/HCV+	P-value
CD4	Absolute Δ*	199.0 (115.0-342.0)	162.0 (79.0-237.0)	0.15
	% Δ**	98.8 (39.3-189.0)	64.6 (33.0-177.8)	0.20
B-cell	Absolute Δ	84.3 (22.6-200.4)	90.7 (15.1-201.7)	0.98
	% Δ	81.0 (24.6-203.8)	88.6 (5.3-233.9)	0.98

Median increase (IQR); cells/mL plasma; **% increase from pre-ART count.

Conclusion. In this cohort of patients with 9-15 months of suppressed viremia after ART initiation, HCV co-infection did not significantly influence the magnitude of reconstitution of CD4 or B cell counts. Changes in B-cell and CD4 count were strongly correlated. Our data provide support to recent guidelines against routine monitoring of B cell counts.

Disclosures. **All authors:** No reported disclosures.

1563. HIV Low-Level Viremia: It's Only a Matter of Time

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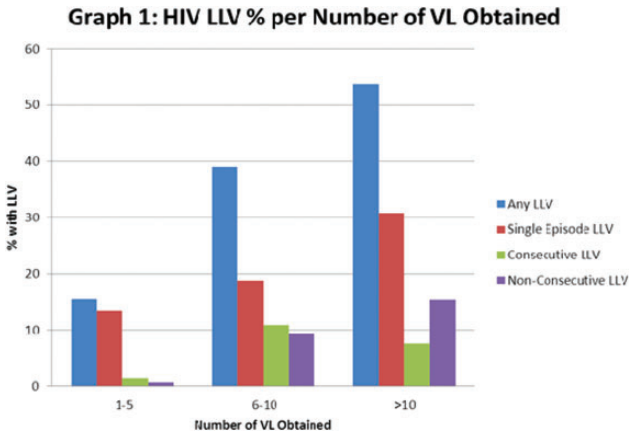
Background. Low-level viremia (LLV) has been studied previously, with the notion that LLV may lead to virologic failure necessitating a change in ART. We sought to characterize patients who achieve full virologic suppression and subsequently experience LLV, and to assess the clinician's response to these results.



Methods. 392 patient charts were retrospectively reviewed from the HIV clinic at TJUH. Patients were included in analysis if they were active in HIV clinic during the years 2007-2012, reported ART compliance, and achieved HIV viral load (VL) of <50 copies/mL on two consecutive occasions. Patients were categorized according to the total number of VL obtained during the study period (1-5, 6-10, >10). Any episode of LLV (VL > 50 copies/mL and < 1,000 copies/mL) was noted, and patients were further categorized as having single or multiple episodes of LLV. Those with multiple incidents of LLV were classified as having either consecutive or non-consecutive episodes. Any changes in ART were noted.

Results. 219 patient VL trends were analyzed. 165 patients had no evidence of LLV during the study period. 54 (24.6%) patients had at least one episode of LLV during the study period. Of 54 patients with LLV; 35 had a single episode, 9 had non-consecutive episodes, and 10 had consecutive episodes.

Frequency of any episode of LLV with regards to number of VL obtained occurred as follows: 1-5 VL; 16%, 6-10 VL; 39%, >10 VL; 53% (graph). Average magnitude of LLV was 162 copies/mL for single, 155 copies/mL for consecutive, and 122 copies/mL for non-consecutive episodes. No changes in ART were made as a result of LLV.

Conclusion. LLV occurs frequently and is of low magnitude. Single episodes of LLV occur most frequently, although additional episodes may occur either consecutively or non-consecutively. Occurrence of LLV, either single or multiple episodes, appears to be a function of time and frequency of VL measurement. In this urban, academic practice the clinicians made no changes in ART for any patient as a result of LLV.

Disclosures. **All authors:** No reported disclosures.

1564. Duration of Viral Suppression and objectively measured Antiretroviral Adherence as predictors of rebound Viremia in South Western Uganda

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Background. Relationships between antiretroviral (ART) adherence and virologic suppression are critical to understanding risk of treatment failure and drug resistance.

Methods. We used objective monitors to collect adherence data on adults taking ART during 2005-2011. CD4 and viral load were collected quarterly. Our primary outcome was rebound HIV-1 RNA viremia, defined by a detectable viral load following a previously undetectable viral load (<400 copies/mL). Our primary predictor was ART adherence, measured by: 1) average adherence, calculated by the number of pills taken divided by the number of pills prescribed; and 2) presence of three consecutive days of non-adherence. Secondary predictors were CD4 nadir and ART regimen. We used generalized estimating equations to fit regression models to assess for relationships between predictors and our outcome of interest.

Results. 399 participants contributed 2,837 intervals during the follow-up. Median nadir CD4 was 125 and median duration of suppression was 1.1 years. The most common regimen was AZT/3TC/NVP, used by 58% of subjects. Risk of rebound viremia was higher during the first year of suppression than after in all adherence strata (3.5% vs 1.9% for average adherence >90%, 5.3% vs 2.1% for average adherence 60-90%, and 14.2% vs 7.3% for average adherence <60%, P<0.06 for all categories). Compared to periods with average adherence >90%, we found increased odds of rebound viremia for adherence <60% during the first year (AOR = 6.0, P <0.001) and after (AOR = 3.4 P =0.003); but increased odds for adherence 60-90% during the first year only (AOR = 1.9, P = 0.04 vs AOR = 0.8, P =0.60). One or more 72-hour gap was associated with increased odds of rebound viremia during the first year (AOR = 1.8, P = 0.05) and after (AOR = 2.2, P = 0.03). CD4 nadir was not predictive of rebound viremia, and there were no significant interactions in these relationships by regimen.

Conclusion. In a cohort of PLWH on ART in rural Uganda, increasing duration of viral suppression was associated with reduced odds of viral rebound regardless of average adherence. Average adherence under 60% and one or more 72-hour treatment gaps are associated with increased risk of rebound viremia regardless of suppression time.

Disclosures. **All authors:** No reported disclosures.

1565. Identifying Optimal HIV Viral Load (VL) Thresholds for Predicting Antiretroviral Treatment Failure (TF) Using ROC Curve Analysis

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Background. Guidelines on HIV treatment differ in recommended VL thresholds indicative of TF. Improvements in VL assay sensitivity and worldwide scale-up of VL monitoring make it increasingly important to determine optimal VLs thresholds for guiding treatment changes. Receiver operating characteristic (ROC) curves can identify optimal VL thresholds which maximize sensitivity and specificity for predicting TF. The BRAVO study was a retrospective study, using the Roche COBAS® AmpliPrep/ COBAS® TaqMan® HIV-1 Test, v2.0, to explore thresholds of VL that might predict subsequent TF.

Methods. Longitudinal patient specimens were collected through the VERxVE study, a randomized, double-blind (DB) study in treatment-naïve patients treated with nevirapine immediate-release or extended-release (VIRAMUNE IR or XR), plus emtricitabine and tenofovir DF. Stored plasma samples from up to 24 timepoints (pre-treatment through 144 weeks of DB treatment), were tested with the Roche COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, v2.0. The BRAVO patient endpoints of TF (which differed from the primary VERxVE endpoints) were determined by two independent HIV physicians based on VL trajectories. A simple logistic regression model and ROC curves were created to determine the optimal VL thresholds for predicting TF at each study timepoint.

Results. Of 526 evaluable patient-series, 71 patients (13%) were TF by BRAVO criteria. By ROC curve analysis, a VL threshold of 95 copies/ml at week 24 maximized the

sensitivity (88%, 95% CI: 84-90%) and specificity (56%, 95% CI:41-70%) of predicting eventual TF [AUC (Area Under Curve):0.75]. Overall sensitivity and specificity were similar (overlapping 95% CIs for the sum of sensitivity and specificity) when compared to ROC curves for commonly used VL thresholds of 50 or 200 copies/ml.

Conclusion. ROC curve analysis identified a VL threshold that maximized sensitivity and specificity in predicting TF. Viral load thresholds of 50 or 200 copies/ml can also be used without a significant decrease in overall sensitivity and specificity. As VL assays may differ in sensitivity, ROC curve analysis can be help optimize the clinical utility of VL monitoring.

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1566. Factors Associated with 10 Years of Continuous HIV Viral Load Suppression on HAART

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Background. The principal goal of HAART is sustained viral load (VL) suppression resulting in immune reconstitution and a reduction in the risk of AIDS and death. We studied the factors associated with 10 years of continuous VL suppression on HAART in the US Military HIV Natural History Study.

Methods. We evaluated 5721 NHS participants, of which 276 (4.8%) met inclusion criteria. Participants with continuous VL suppression (CS, n = 149) were compared to those who experienced ≥1 virologic failure (VF, n = 127). All participants were required to have ≥1 VL determination each year for >10 years on HAART and no treatment interruptions >6 months. VL suppression (<400 c/mL) within 1 year was required for the CS group and maintained for >10 years on HAART. VF was defined as 2 consecutive VLs >400 c/mL after initial suppression. Factors associated with >10 years of VL suppression were evaluated by multivariate logistic regression.

Results. Compared to the VF group, CS participants at HAART initiation (HI) had higher median CD4 counts (375 cells/uL, IQR 256-499 vs 261 cells/uL, IQR 146-400; P < 0.001), lower VL (4.4 $\log_{10}$ c/mL, IQR 3.5-4.9 vs 4.5 $\log_{10}$ c/mL, IQR 3.8-5.0; P = 0.048), and were less likely to start treatment in the early HAART era (66 vs 90%, for years 1996-1999; P < 0.001). CS participants also had a lower proportion of antiretroviral (ARV) use prior to HAART (37 vs 83%; P < 0.001), used fewer HAART regimens (3, IQR 2-5 vs 7, IQR 4-9; P < 0.001), and had a lower proportion of new AIDS events by 10 years of HAART (5 vs 13%; P = 0.032). The factors associated with 10-year VL suppression by multivariate logistic regression included $\log_{10}$VL at HI (OR 0.60, 95% CI 0.39, 0.89; P = 0.013), ARV use prior to HI (OR 0.14, 95% CI 0.06, 0.31; P < 0.001), and number of HAART regimens used (OR 0.72, 95% CI 0.62, 0.82; P < 0.001). Demographic characteristics, prior AIDS, CD4 at HI, and self-reported adherence were not associated with 10-year VL suppression.

Conclusion. Sustained VL suppression is a key to long-term health in HIV-infected patients, as demonstrated by the lower proportion of AIDS events observed 10 years after HI. The current use of more potent and well-tolerated regimens may mitigate the negative factors of pre-HAART VL and prior ARV use encountered by treatment initiated in the early HAART era.

Disclosures. **All authors:** No reported disclosures.

1567. Simplification to elvitegravir/cobicistat/emtricitabine/tenofovir DF from ritonavir-boosted protease inhibitor plus emtricitabine/tenofovir DF maintains HIV suppression and improves fasting triglycerides at week 48

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Background. A higher triglyceride (TG) concentration is marginally independently associated with an increased risk of myocardial infarction in the D:A:D study. Patients switched to elvitegravir/cobicistat/emtricitabine/tenofovir DF (EVG/COBI/FTC/TDF) from ritonavir-boosted protease inhibitor (PI + RTV) plus FTC/TDF maintained high rates of virologic suppression at week 48 (94% vs 87%); and, overall had improvement in fasting triglyceride concentrations.

Methods. In the STRATEGY-PI study, fasting lipid parameters were measured at baseline and subsequent study visits. Subgroup analysis by PI examines the change from baseline (mg/dL) in fasting lipids and shifts in proportions of subjects with target lipid parameter by the National Cholesterol Educational Program (NCEP) category.

Results. 293 subjects switched to EVG/COBI/FTC/TDF; 139 continued PI + RTV (51 atazanavir [ATV], 60 darunavir [DRV], 23 lopinavir [LPV], 5 other PIs). Switching to EVG/COBI/FTC/TDF vs continuation of PI + RTV resulted in statistically significant decrease from baseline in fasting TG concentrations at week 48 (mean: -29 vs 1; p = 0.001), driven primarily by decreases in TGs when switched to EVG/COBI/FTC/TDF from LPV (mean: -59 vs -1; p = 0.003) or ATV (mean: -32 vs 5; p = 0.014). Proportions of subject with target TG by NCEP category at week 48 that were statistically different between groups are shown in the table. Changes in other fasting lipid parameters were generally small and not statistically different between groups except for a small increase in HDL (mean: 2 vs -1; p = 0.03) and decrease in total cholesterol (TC)/HDL ratio (mean: -0.2 vs 0.0; p = 0.029) for subjects who switched to EVG/COBI/FTC/TDF from DRV, and decreases in TC (mean: -24 vs 2; p = 0.002) and HDL (mean: -2 vs 6; p = 0.016) for subjects who switched to EVG/COBI/FTC/TDF from LPV.

Target Triglyceride (<150 mg/dL) by National Cholesterol Educational Program Category at W48

% (n)	EVG/COBI/FTC/TDF (n=250)	PI+RTV+FTC/TDF (n=112)	P Value
Baseline	63% (172)	64% (86)	0.94
Week 48	77% (206)	68% (80)	0.041
	EVG/COBI/FTC/TDF (n=49)	**LPV/RTV+FTC/TDF (n=23)**	
Baseline	34% (15)	33% (7)	0.92
Week 48	78% (35)	53% (10)	0.044

Conclusion. Switch to EVG/COBI/FTC/TDF maintained HIV suppression and improved fasting triglyceride concentrations, particularly in those switched from LPV or ATV.

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1568. Use of the Integrase Strand Transfer Inhibitor-Based Antiretroviral Regimen Elvitegravir/Cobicistat/Emtricitabine/Tenofovir Disoproxil Fumarate in a Predominantly African-American HIV Infected Population

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Background. Elvitegravir (EVG) is an integrase strand transfer inhibitor (INSTI) based drug for the treatment of HIV-1 infection, co-formulated with cobicistat (COBI), a CYP3A4 inhibitor, emtricitabine (FTC), and tenofovir disoproxil fumarate (TDF). The regimen consists of a single tablet, taken once daily. Two phase 3 clinical trials have established its efficacy and safety.

Methods. A retrospective chart review was conducted in a community HIV clinic for patients receiving treatment with EVG/COBI/FTC/TDF. Comparison analysis was conducted for African Americans (AA) and non-AA. Data was abstracted from 225 patient charts (190 AA, 29 non-AA). Six charts did not specify race. Four charts indicated patients opted not to begin therapy. Of the remaining 221 patients, there were 145 treatment experienced and 76 treatment naïve. Data was available for 144 ART experienced patients and 74 treatment naïve patients, and included GFR, HIV-1 RNA viral load, and CD4 cell count at baseline, 2 weeks, 3 and 6 months.

Results. There was no significant difference between the AA and non-AA groups with regards to GFR and HIV-1 RNA viral load. A higher CD4 cell count in the non AA group (P = 0.031, 691.71 ± 373.71 cells per μL vs 491.98 ± 345.55 cells per μL) at the 3 month interval was noted, but was insignificant at 6 months. ART experienced patients who achieved viral suppression prior to initiation of EVG/COBI/FTC/TDF, maintained suppression. Experienced patients, who were not suppressed were able to achieve viral suppression at either the three or six month interval. Viral load suppression was achieved in persons who were treatment naïve.

Conclusion. EVG/COBI/FTC/TDF is the first INSTI combination regimen approved for the treatment of HIV-1 infection and should be considered a viable treatment option regardless of ethnicity or treatment experience. This retrospective analysis provides real world data in a predominantly African-American population. Limitations pertained to patient adherence and difficulty with clinic follow-up. These challenges are inherent in treating a minority population with complicated socioeconomic factors and will be the focus of future quality improvement measures. However, patients prescribed EVG/COBI/FTC/TDF who were able to continue treatment as recommended, achieved or maintained viral suppression.

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1569. The effects of frequency of CD4 monitoring on clinical endpoints in clinically stable HIV-infected patients with viral suppression

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Background. Current treatment guidelines for HIV infection recommend CD4+ T lymphocyte (CD4) count monitoring every 6 to 12 months in patients with viral suppression. As clinically meaningful CD4 decline rarely occurs during viral suppression, routine CD4 monitoring may have a limited role in influencing care.

Methods. Among patients in a regional HIV observational cohort in the Asia-Pacific, those with viral suppression (2 consecutive viral loads <400 copies/mL) and a baseline CD4 count ≥200 cells/μL within 390 days of viral suppression who had CD4 testing every 6 months during viral suppression were analyzed. Study endpoints were occurrence of one CD4 count <200 cells/μL (single CD4 <200), confirmed CD4 count <200 cells/μL (confirmed CD4 <200; 2 results <200 cells/μL within a 6-month period), and clinical failure (a new or recurrent WHO stage 3 or 4 illness). A comparison of time to single CD4 <200 and confirmed CD4 < 200 at 6- and 12- month intervals was performed.

Results. Among 1538 patients who met the inclusion criteria, the rate of single CD4 < 200 was 3.45 per 100 patient-years, of confirmed CD4 < 200 was 0.77 per 100 patient-years, and of clinical failure was 0.57 per 100 patient-years. After 5 years of viral suppression, the cumulative probability of single CD4 <200 was 10%. The 5-year cumulative probabilities of confirmed CD4 <200 and clinical failure were lower than 10% (Figure 1). Patients with baseline CD4 between 200-249 cells/μL were significantly more likely to experience confirmed CD4 <200 compared with patients with higher baseline CD4 (hazard ratio 55.47 [95% confidence interval (CI) 7.36 – 418.20], p < 0.001 vs baseline CD4 ≥500). There was no significant difference in the time to confirmed CD4 <200 between the 6- and 12-month testing intervals (log rank = 0.335).

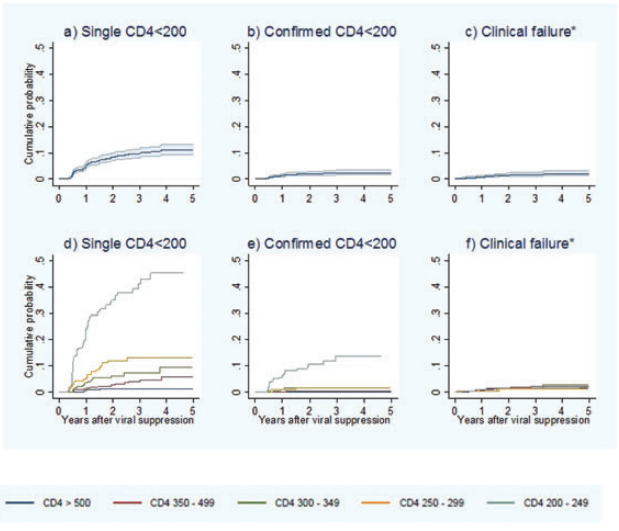

Figure 1. Cumulative probabilities during viral suppression of a) single CD4<200, b) confirmed CD4<200, c) clinical failure, d) single CD4<200 by baseline CD4 count, e) confirmed CD4<200 by baseline CD4 count, and f) clinical failure by baseline CD4 count.

Conclusion. Patients in our cohort with baseline CD4 <250 cells/μL were at greater risk of confirmed CD4 <200 during viral suppression compared with patients with higher baseline CD4. CD4 testing at 6-month intervals offered no benefit over annual testing in detecting confirmed CD4 <200. Annual CD4 monitoring in virally suppressed HIV patients with a baseline CD4 ≥250 cells/μL may be sufficient for clinical management.

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1570. Low rates of virologic failure among previously unmonitored patients in Malawi

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Background. Virologic monitoring for HIV-infected ART patients is largely unavailable in resource-limited settings. Undetected viremia may contribute to transmission and breed resistance. Treatment failure may be more common among patients who are not monitored for extended periods. We explored the prevalence of ART failure among previously unmonitored ART patients in Malawi.

Methods. Participants were enrolled from 5 hospitals and were eligible if they were ≥18 and had been on ART for 6 or 24 months or any 2-year period thereafter *or* if provider suspected failure. Virologic testing was done on dried blood spot cards using Abbott Real-Time HIV-1 Assay. Summary statistics were compared using independent group t-tests (continuous variables) and Pearson's $\chi 2$ tests (categorical variables). We used logistic regression to investigate the association between ART history, patient demographics, and virologic failure (viral load >5,000 cp/ml).

Results. Of 1,479 participants, 30% were male with an average age of 42 [SD: 10.2]. 64% were on ART ≤4 years (9% 6 months; 32% 2 years; 23% 4 years) and 22.9% had signs of clinical failure. 870 (68%) were classified as WHO stage 3/4 at ART initiation. Only 79 (5.3%) met virologic failure criteria. Proportion male (27.9% vs 29.9%, p = 0.70), on ART > 4 years (40.6% vs 31.7%, p = 0.12), with signs of clinical failure (26.9% vs 22.7%, p = 0.39), or WHO stage 3 or 4 at initiation (64.7% vs 68.4%, p = 0.52) did not differ between patients with virologic failure and those not failing. Failing participants were younger (37.8 vs 42.5, p<0.01). Holding sex, time on ART, clinical symptoms, and initiation WHO stage constant, increasing age was associated with decreased odds of treatment failure (OR:0.96, CI[0.93, 0.99]). Being on ART >4 years was associated with increased odds of failure (OR: 2.25, CI [1.27, 3.98]).

Conclusion. We observed an unexpectedly low prevalence of virologic failure among previously unmonitored patients. After controlling for factors that could contribute to treatment failure, younger patients and patients on ART >4 years were more likely to be failing. These results may suggest deficiency in adolescent adherence and adult ART care transitions. Despite being retained in care, our findings demonstrate the importance of virologic monitoring among patients on ART for extended periods, regardless of clinical symptoms.

Disclosures. **All authors:** No reported disclosures.

1571. Risk factors for Tenofovir-associated Renal Dysfunction in HIV-positive Patients

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Background. Risk factors associated with renal dysfunction in patients on tenofovir remain unknown and optimal monitoring is unclear. We investigated whether a urine protein-osmolality ratio would be a useful screening parameter.

Methods. This retrospective, single-center study of HIV-positive subjects investigated the relationship between three surrogates of renal function (eGFR, protein-osmolality (P:O) ratio and predicted 24hr proteinuria) and multiple risk factors for development of kidney dysfunction. Subjects were >18 years, on tenofovir with at least one urinalysis and serum creatinine performed between 2010 and 2013. Univariate regression analysis was used to analyze risk factors associated with development of proteinuria and abnormal eGFR during tenofovir therapy.

Results. Of 117 study subjects, 81% were male; 19% were African-American. The mean age was 45.1 ±11.8yrs; median tenofovir duration was 3.3yrs. Median CD4 count and HIV viral load at study initiation were 451 cells/μL and 62 copies/mL, respectively. 68% of subjects had an abnormal P:O ratio; 39% had abnormal predicted 24hr proteinuria and 9% had abnormal eGFR. After age adjustment, subjects on tenofovir > 5yrs had almost a four-fold increased risk of having had an abnormal P:O ratio than subjects on tenofovir for < 1yr (OR 3.9; 95% CI 1.2-14.0; p = 0.024). Increasing age was associated with an abnormal P:O ratio (OR 1.42, 95% CI 1.0-2.1, p = 0.048), 24hr protein >200 (OR 1.5; 95% CI 1.1-2.2; p = 0.01) and eGFR (OR 2.1, 95% CI 1.3-3.8; p = 0.048). Patients with hypertension were more likely to have abnormal eGFR (OR 3.8, 95% CI 1.1-12.9; p = 0.026). Neither abnormal P:O ratio nor abnormal predicted 24hr proteinuria were associated with an increased risk of abnormal eGFR.

Conclusion. Abnormal renal function, as measured by P:O ratio and proteinuria is common in HIV infected patients on tenofovir but rarely progressed to abnormal eGFR

during the study period. Duration of tenofovir use, age, diabetes and hypertension were risk factors for renal dysfunction in this study. Neither abnormal P:O ratio nor predicted 24hr proteinuria were associated with development of abnormal eGFR; serum creatinine remains the gold standard for monitoring renal function while on tenofovir.

Disclosures. **All authors:** No reported disclosures.

1572. Impact of Hyperbilirubinemia on Persistence and Adherence of Atazanavir among HIV Patients

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Background. Despite a favorable tolerability profile among the protease inhibitors, atazanavir (ATV) has been associated with hyperbilirubinemia (HBR). HBR is reversible upon ATV discontinuation and often asymptomatic but may sometimes lead to jaundice or scleral icterus. The goal of this study was to examine ATV persistence and adherence during the first year of therapy among HIV patients with and without HBR.

Methods. This retrospective analysis used medical and pharmacy claims and lab data from July 1, 2003-August 31, 2012 for commercial members from a large US managed care database. Included patients had ≥1 pharmacy claims for ATV (first claim = index date), were age 18 + , had ≥6 months of continuous enrollment prior to (baseline period, or b/l) and 12 months after (follow-up period, or f/u) the index date, and no b/l ATV use. HBR was defined by total bilirubin of ≥Grade 3 (>2.5x ULN) within 90 days of index; Non-HBR was defined as ≤Grade 2 (>1.5-2.5x ULN) in the 12-month f/u. Adherence was assessed using a medication possession ratio (MPR). Persistence was defined as the days on ATV until the earliest of discontinuation or end of the study period.

Results. Approximately one-third of the 3,268 ATV patients who met criteria had lab data available (131 HBR and 1,061 non-HBR). Mean age was 43.1 years, 82.6% were male, and 36.3% were treatment-naive. Patients in the HBR cohort were more likely to be male, have a bachelor degree or higher and be Caucasian compared to patients in the non-HBR cohort. Mean (SD) MPR (0.93 (0.10) vs 0.92 (0.11); $p = 0.22$) and persistence on ATV therapy (260 days (133) vs 241 (143); $p = 0.15$) in the f/u period were similar in the HBR and non-HBR cohorts. After controlling for demographics, socioeconomic status, b/l Charlson comorbidity index, and concomitant HIV medications while receiving ATV in multivariate analyses, differences in adherence and persistence between the two cohorts remained non-significant.

Conclusion. In this large US managed care database analysis of approximately 1,200 HIV-infected patients on ATV, patients with HBR ≥Grade 3 did not show significant differences in adherence or persistence of ATV in the first year of therapy vs those who developed ≤Grade 2 HBR. HBR does not appear to influence persistence with ATV in a real-world setting.

Disclosures. **L. Rosenblatt**, Bristol-Myers Squibb: Employee, Salary **H. Hardy**, Bristol Myers Squibb: Employee, Salary **T. Grasso**, Bristol Myers Squibb: Employee, Salary

1573. Use of protease inhibitors is associated with higher selenium levels in treated HIV infection

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Background. Selenium (Se) acts as a cofactor for several enzymes (selenoproteins) which have anti-inflammatory properties. In some studies, HIV-infected subjects have been found to be micronutrient deficient and it is known that Se can influence immune activation, inflammation and cardiovascular dysfunction.

Methods. We performed a cross-sectional study of HIV-infected adults on antiretroviral therapy (ART) with HIV-1 RNA ≤ 1,000 copies/ml to assess relationships between selenium (Se) levels and demographics, HIV-related factors, markers of inflammation and immune activation, markers of oxidative stress, as well as cardiovascular disease (CVD) risk measures. Spearman correlation analysis and linear regression were utilized.

Results. 147 subjects were included; 78% men, 68% African American, 8% with Hepatitis C, 63% current smokers. Median age was 46.2 years, BMI 26.7 kg/m^2 and eGFRcr 100 mL/minute per 1.73 m^2. Median known duration of HIV and cumulative duration of ART were 139 and 64 months. Median current and nadir CD4$^+$ counts were 613 and 179 cells/mm^3. 50% were on a protease inhibitor (PI) and 76% had HIV-1 RNA ≤ 48 copies/ml. Median Se level was 122 ng/ml. Demographics associated with higher Se included Caucasian race ($p < 0.01$), male sex ($p < 0.01$), lower BMI ($p = 0.02$) and lower eGFRcr ($p = 0.04$). Only current PI use ($p < 0.05$) was associated with higher Se. Markers of inflammation, monocyte or lymphocyte activation,and F2-isoprostanes were not associated with Se levels. In multivariable analysis, only Caucasian race ($p < 0.01$), being on a PI ($p = 0.03$) and lower BMI ($p = 0.01$) were independently associated with higher Se. Of the CVD risk measures studied, paradoxically, flow mediated dilation of the brachial artery was inversely correlated with Se ($\rho = -0.22$; $p = 0.007$); ($\rho = -0.17$; $p = 0.07$ for men; $\rho = 0.09$; $p = 0.62$ for women). This association did not remain significant after adjustment for usual CVD risk factors. Coronary artery calcification and carotid intima media thickness were not associated with Se levels.

Conclusion. In this ART-experienced group, only being on a PI was associated with higher Se levels with regard to HIV-related factors. Markers of inflammation, immune activation, and oxidative stress were not associated with Se in this group. Further study is warranted to better understand the effect of Se on endothelial dysfunction in HIV.

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1574. Safety Profile of HIV-1 Attachment Inhibitor Prodrug BMS-663068 in Antiretroviral-Experienced Subjects: Week 24 Analysis

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Background. BMS-663068 is a prodrug of BMS-626529, an attachment inhibitor that binds directly to HIV-1 gp120, preventing initial viral attachment and entry into the host CD4+ T-cell. AI438011 is an ongoing, Phase IIb, randomized, active-controlled trial investigating the safety, efficacy and dose–response of BMS-663068 vs atazanavir/ritonavir (ATV/r) in treatment-experienced (TE), HIV-1-positive subjects (sbj). At Week 24, response rates across the BMS-663068 arms were consistent with ATV/r.

Methods. Antiretroviral TE sbj (exposure to ≥1 antiretroviral for ≥1 week) with susceptibility to all study drugs (including BMS-626529 $IC_{50} < 100$ nM) were randomized equally to four BMS-663068 arms (400 or 800 mg, BID; 600 or 1200 mg, QD) and a control arm (ATV/r 300/100 mg QD), with tenofovir disoproxil fumarate (TDF) - + raltegravir (RAL). The complete safety profile through Week 24 is reported.

Results. In total, 251 sbj were treated (BMS-663068, 200; ATV/r, 51). No BMS-663068-related adverse events (AEs) led to discontinuation. Grade 2–4 drug-related AEs occurred in 17/200 (8.5%) sbj across the BMS-633068 arms; however, these events were mostly single instances and no dose-relationship was seen. Similarly, no noticeable trend for Grade 3–4 laboratory abnormalities was seen and Grade 3–4 hematologic changes and liver chemistry elevations were uncommon (neutropenia, 2.5%; AST/ALT elevations, 1% [n = 196]). In the ATV/r arm, Grade 2–4 drug-related AEs occurred in 14/51 (27.5%) sbj and were mostly secondary to gastrointestinal and/or hepatobiliary disorders. Serious adverse events (SAEs) occurred in 13/200 (6.5%) and 5/51 (9.8%) sbj receiving BMS-663068 and ATV/r, respectively; most were secondary to infections and none were related to study drugs. The most common AE reported for BMS-663068 was headache (28/200, 14%), occurring in 5/51 (10%) sbj in the ATV/r arm; in the BMS-663068 arms this was not dose-related. There were no deaths.

Conclusion. BMS-663068 was generally well tolerated across all arms, with no related SAEs or AEs leading to discontinuation and no dose-related safety signals. There were no trends for Grade 2–4 AEs or clinical laboratory abnormalities. These results support continued development of BMS-663068.

Disclosures. **C. Brinson**, Bristol-Myers Squibb: Investigator, employer received monies for conducting the trial, Contract Principal Investigator for clinical trials; Gilead: Board Member and Speaker, advisory board member, education board member, personal fees Investigator, Contract Principal Investigator for clinical trials; Boehringer Ingelheim: Investigator, Contract Principal Investigator for clinical trials; ViiV: Investigator, Contract Principal Investigator for clinical trials; GlaxoSmithKline: Investigator, Contract Principal Investigator for clinical trials; Shionogi: Investigator, Contract Principal Investigator for clinical trials; AstraZeneca: Investigator, Contract Principal Investigator for clinical trials; Pfizer: Investigator, Contract Principal Investigator for clinical trials; Janssen: Investigator, Contract Principal Investigator for clinical trials; Sangamo: Investigator, Contract Principal Investigator for clinical trials; Taimed: Investigator, Contract Principal Investigator for clinical trials; Theratechnologies: Investigator, Contract Principal Investigator for clinical trials; Serono: Investigator, Contract Principal Investigator for clinical trials; Achillion: Investigator, Contract Principal Investigator for clinical trials **J. Echevarría**, Bristol-Myers Squibb: Grant Investigator, Grant recipient **S. Treviño-Pérez**, Bristol-Myers Squibb: Grant Investigator, Grant recipient **J. R. Bogner**, All companies involved in antiretroviral therapy: Speaker's Bureau, Speaker honorarium **D. Stock**, Bristol-Myers Squibb: Employee and Shareholder, Salary **S. R. Joshi**, Bristol-Myers Squibb: Employee and Shareholder, Salary **G. J. Hanna**, Bristol-Myers Squibb: Employee and Shareholder, Salary **M. Lataillade**, Bristol-Myers Squibb: Employee and Shareholder, Salary

1575. A 28-day high-dose safety and pharmacokinetics study of raltegravir in healthy subjects

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Background. ISENTRESS (raltegravir, RAL) is licensed for 400 mg b.i.d. use. An investigational 1200 mg q.d. regimen for reformulated raltegravir (re-RAL) is under clinical development. This study assessed the safety and pharmacokinetics (PK) of a higher dose of re-RAL.

Methods. A double-blind, multiple-dose, randomized, fully domiciled study assessed the safety and PK of 1800 mg dose of re-RAL tablets (n = 18) or matching placebo (n = 6), given q.d. for 28 days in healthy subjects (18 to 55 years).

Results. There were no deaths and no serious adverse events. There were no clinically significant findings for vital signs or ECG data. A total of 23 subjects (95.8%) reported an adverse event (AE) that was related to the study drug [17 subjects (94.4%) after 1800 mg re-RAL and 6 subjects (100%) after matched placebo]. Two subjects withdrew their consent at Day 28 for personal reasons. No subjects discontinued the study due to AEs or changes in laboratory safety. Most common adverse events, reported in ≥6 subjects, included headache, myalgia, and abdominal pain. No subjects experienced ALT >5x upper limit of normal (ULN) in this study. One subject experienced ALT >3x ULN on Day 9 and another subject experienced ALT >2x ULN on Day 13, after 1800 mg re-RAL administration. No associated clinically significant symptoms were seen and the elevations stabilized or returned to normal without interruption of study therapy. Three subjects experienced CPK elevations which were rated severe in intensity and were considered related to the study drug. In two subjects, the first CPK elevations were detected at the post study visit held 2-weeks following completion of the dosing. While one subject showed asymptomatic increase in CPK level, CPK elevations in two subjects were symptomatic. RAL PK was comparable on Days 14 and 28. On Day 28, the mean values of RAL C_{max}, C_{24hr}, and $AUC_{0\text{-}24hr}$ were 29 μM, 88.5 nM, 74.5 hr. μM, respectively, as compared with 20.6 μM, 81.1 nM, and 59.5 hr.μM, respectively, at the 1200 mg dose being evaluated in Phase 3. There were no apparent relationship between PK and observed elevations in ALT or CPK.

Conclusion. Administration of 1800 mg q.d. doses of re-RAL was safe and well tolerated. Data from this study, in combination with other recently completed Phase I studies, support the continued development of the q.d. dosing regimen.

Disclosures. **R. Krishna**, Merck and Co.: Employee, Salary **M. Rizk**, Merck and Co., Inc.: Employee, Salary **V. Schulz**, Merck and Co., Inc.: Employee, Salary **J. Bruggencate-Broeders**, Merck and Co.: Employee, Salary **R. Liu**, Merck and Co: Employee, Salary **P. Larson**, Merck and Co.: Employee, Salary **K. Abou-Farha**, Merck and Co., Inc.: Investigator, Investigator for Merck Study

1576. Timing of Antiretroviral Therapy in Patients with Active Tuberculosis: a Systematic Review and Meta-analysis

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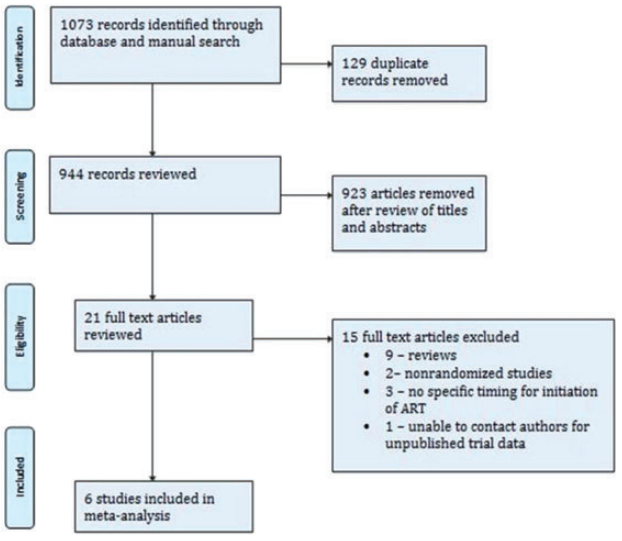
Background. Integration of antiretroviral (ART) and tuberculosis (TB) therapy has been shown to improve patients' outcomes, however optimal timing for initiation of ART during the treatment of active TB is unclear.

Figure 1: Study selection process



Methods. Systematic review and meta-analysis of randomized controlled trials using PubMed, EMBASE, Cochrane Library, CINAHL, clinicaltrials.gov, hand search from reference lists of identified papers

Randomized controlled trials (RCTs) comparing earlier within 4 weeks with later initiation at 8-12 weeks of ART during TB therapy in patients > 13 years of age co-infected with HIV and TB

Primary outcome was all-cause mortality at 48 weeks. Secondary outcomes were incidence of immune reconstitution inflammatory syndrome (IRIS), serious adverse effects (including change in ART regimen), HIV viral load and mycobacterial clearance.

Results. Data from six RCTs involving 2303 adolescent and adult patients was analyzed. Earlier initiation of ART (≤4 weeks) as compared to 8-12 weeks was associated with a non-significant decrease in overall mortality at 48 weeks (relative risk 0.81; 95% confidence intervals (CI) 0.63 to 1.05; p = 0.11), however there was a twofold increase in the risk of IRIS (RR 2.21; 95% CI 1.79 to 2.23; p > 0.001). In those with CD4 count less than 50 cells/μl, early ART was associated with a 43% lower risk of a new AIDS-defining illness or death (RR 0.57; 95% CI 0.38-0.86; p = 0.008).

Figure 2. Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

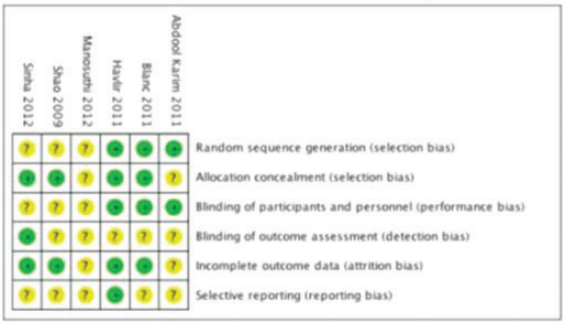
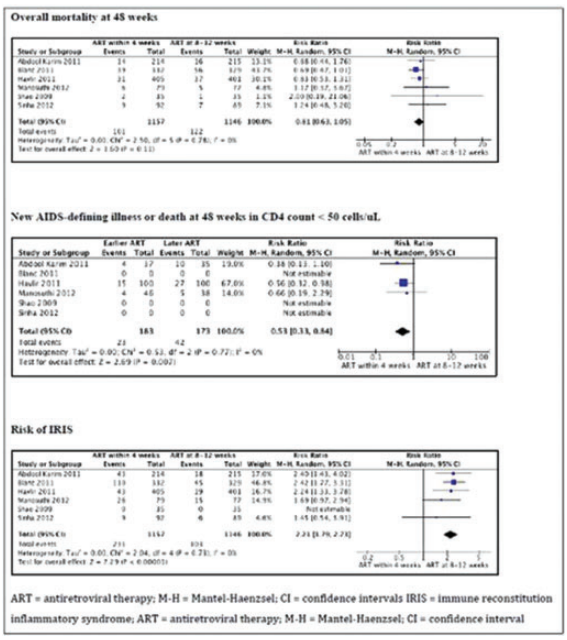


Figure 3. Pooled estimates of risk of outcomes with earlier vs. later initiation of ART



Outcomes	Number of studies	Number of participants	Relative risk	95% confidence interval	P value	Heterogeneity
All-cause mortality at 48 weeks	6	2303	0.81	0.63 to 1.05	0.11	$I^2 = 0\%$
Incidence of IRIS	6	2303	2.21	1.79 to 2.73	<0.001	$I^2 = 0\%$
Incidence of serious adverse effects	5	2122	1.00	0.94 to 1.08	0.41	$I^2 = 65\%$
Change in antiretroviral therapy	4	1486	2.46	1.16 to 5.22	0.02	$I^2 = 11\%$
Successful TB therapy	3	1271	0.04	-0.05 to 0.13	0.41	$I^2 = 65\%$
HIV RNA <400 at 48 weeks	4	1843	1.00	0.98 to 1.03	0.82	$I^2 = 0\%$
All-cause mortality at 48 weeks with CD4 count < 50	3	356	0.53	0.33 to 0.84	0.007	$I^2 = 0\%$

Conclusion. Earlier initiation of ART significantly lowers the risk of death or developing a new AIDS-defining illness in severely immunosuppressed patients with HIV and TB co-infection

Disclosures. **All authors:** No reported disclosures.

1577. In vitro polyfunctional CD4 T cell correlates of diagnostic tests for latent TB in HIV-infected subjects

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Background. Tuberculin skin test (TST) is a low cost means of determining the presence of latent tuberculosis (LTBI) in immunocompetent patients. However, few studies have examined the cytokine correlates of TB control in TST- vs TST+ subjects among HIV+ cohorts. This study examines TB-specific CD4 single cytokine and polyfunctional profiles of TST- and LTBI in HIV+ subjects.

Methods. HIV+ adults recruited in Kampala, Uganda were differentiated into 2 groups: LTBI (>5mm response to the tuberculin skin test (TST) and negative chest x-ray; n = 15), or TST- (TST <5 mm and chest x-ray; n = 15). Interferon gamma release assay (IGRA) was also performed for each subject. Multicolor flow analysis was performed on PBMC stimulated with either PPD or mitogen, and frequencies of IL-2, IL-17, IFN-γ and TNF-α secreting cells were determined within the memory subset of CD4 T cells. Polyfunctionality was determined using FlowJo and SPICE software.

Results. PPD-specific CD4+ T cell secretion of TNF-α and IFN-γ was higher in LTBI compared with TST- group ($p = 0.001$ and $p = 0.002$ respectively). In the IGRA+ group there was greater secretion of TNF-α compared with IGRA- though this difference was borderline ($p = 0.05$). IL-2, IFN-γ and TNF-α all correlated with clinical response in terms size of PPD-induced induration or IGRA. Frequency of polyfunctional cells among the TST+ group was greater than and IGRA+ ($p = 0.04$). TNF-α was the dominant cytokine in the TST+ group as 4/5 phenotypes of responding cells all generate either TNF-α alone or in combination with IFN-γ or IL-2. Both TNF-α and IL-2 were dominant among the single cytokine secretors in IGRA+ group. IFN-γ secreting cells are much more frequent in TST+ than IGRA+ subjects.

Conclusion. CD4+ T cell cytokine responses to TB-specific antigens were significantly higher in LTBI compared to TST- HIV+ adults. While IL-2, IFN-γ and TNF-α all appear to be correlates of LTBI, TNF-α is the dominant cytokine in this regard. Perhaps measurement of TNF-α secretors to diagnostic testing for latent TB could add sensitivity but may reduce specificity. Differences exist between polyfunctional cytokine profiles of TST+ and IGRA+ HIV+ individuals which may account for difference in test performance.

Disclosures. **All authors:** No reported disclosures.

1578. Clinical Features, Vaccine Status and *S. Pneumoniae* Serotypes among HIV-positive and HIV-negative Individuals Diagnosed with Invasive Pneumococcal Disease

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Background. HIV-positive persons have higher risk of Invasive Pneumococcal Disease (IPD) despite availability of HIV treatment and Pneumococcal polysaccharide (PPV23) vaccine. Clinical features, vaccine status and serotypes in IPD among HIV-positive and HIV-negative adults may help inform vaccine guidelines.

Methods. We examined HIV-positive and HIV-negative adult members of Kaiser Permanente Northern California (KPNC) diagnosed with IPD between 1996-2011. Cases were identified from a previously described cohort study of HIV-positive and demographically matched HIV-negative adults. IPD was defined as culture positive *S. pneumoniae* from normally sterile sites. We reviewed electronic medical records for demographics, comorbidities, vaccination, serotypes and compared these by HIV status with chi squared tests for categorical and t-tests for continuous variables.

Results. 109 HIV-positive and 75 HIV-negative adults were diagnosed with IPD. The HIV group was diagnosed with IPD at younger mean age than HIV-negative group (47 vs 54 years, $P < 0.001$). The HIV group had more obesity ($p = 0.036$) and less hypertension ($p = 0.027$) than HIV-negatives, but otherwise prevalence of comorbidities (e.g., smoking, asthma, cancer) was similar. HIV patients were more often vaccinated with PPV23 prior to IPD (56% vs 30.7%, $p < 0.001$).

Of cases serotyped (37 in HIV-positive, 36 in HIV-negative), there was a suggestion for a higher prevalence among HIV-positive cases of serotypes covered by both the existing PPV23 vaccine (83.8% vs 66.7%, $p = 0.11$), and the recently approved Pneumococcal conjugate vaccine (PCV13) (16.2% vs 8.3%; $p = 0.062$). The most common serotypes overall were 19A (n = 17; 23%), 7F (n = 6; 8%) and 22F (n = 6; 8%), with higher prevalence seen among HIV-positive cases for 19A (35.1% vs 11.1%; $p = 0.025$), but no difference for 7F ($p = 0.43$) or 22F ($p = 1.0$).

Conclusion. HIV patients with IPD were more likely to have been vaccinated with PPV23, suggesting this vaccine's reduced effectiveness in this population. The risk of IPD and associated serotypes among HIV-positive individuals should be closely monitored given the recent change in vaccine strategy to use both PCV13 and PPV23.

Disclosures. **M. Silverberg**, Pfizer: Grant Investigator, Grant recipient **R. Baxter**, GSK: Investigator, Research grant; Merck: Investigator, Research grant; Pfizer: Investigator, Research grant; Novartis: Investigator, Research grant; MedImmune: Investigator, Research grant; Sanofi Pasteur: Investigator, Research grant

1579. Administering Influenza Vaccine to Patients with Human Immunodeficiency Virus (HIV): Does Timing Matter?

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Background. Researchers have developed methods to predict the magnitude, timing, intensity and duration of the upcoming influenza season largely based on data from previous years. The Centers for Disease Control and Prevention (CDC) records peak months of flu activity annually. In recent flu seasons, the incidence of flu did not start to dramatically increase until mid-December. In the U.S., influenza risk is low in September and October, but begins to increase toward the end of November. The highest risk typically occurs from January through March. It takes 2-4 weeks to develop peak antibody titers after influenza vaccination. In the general population, once immunity to influenza has been acquired, it begins to wane over time. Patients who have human immunodeficiency virus (HIV) are at risk for rapid decline in protective immunity to influenza, thus rendering them more susceptible to influenza infection. It is known that antibody titers wane over time, but it is unclear if timing of influenza vaccination within the flu season affects the probability of an influenza infection later during the flu season. This retrospective analysis will explore the relationship between the occurrence of flu or influenza-like illness in HIV patients and the time after influenza vaccine was administered.

Methods. A retrospective chart review was conducted at VA San Diego Healthcare Systems from September 1, 2005 to May 31, 2013. Patients with laboratory confirmed influenza, diagnosed with influenza by a physician, or who retrospectively met criteria for influenza like illness (ILL) were included. Specific criteria for ILL included: fever (T > 100°F) and cough or sore throat in the absence of any other known cause.

Results. A total of 1176 patients were screened. If vaccinated early (n = 2773) (September 1-November 15) vs late (=1802) (on or after November 16) there was a higher incidence of flu, 30/2773 (1.1%) vs 7/1802 (0.4%), $p = 0.0105$. Vaccinated patients who developed flu were more likely to have symptoms later in the season (on or after January 16) 26/37 (70%) vs 11/37 (30%), $p = 0.0094$.

Conclusion. The results of this study can provide insight and guidance on timing and administration of influenza vaccination administration in HIV patients.

Disclosures. **All authors:** No reported disclosures.

1580. Sexual Health of HIV Infected Patients Attending KUMC ID Clinic

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Background. The aim of this study was to identify overall sexually transmitted diseases (STD) burden in HIV infected patients and determine compliance with sexual health screening and treatment based on CDC 2010 Guideline in our HIV clinic.

Methods. This is a retrospective cohort study of all adult patients attending at least 2 visits at the University of Kansas Medical Center outpatient infectious diseases clinic between October 1, 2010 and August 15, 2013. Syphilis, gonorrhea, chlamydia, genital warts, genital herpes, hepatitis A, B, C testing frequency, diagnoses and treatments were abstracted from the charts. Period prevalence, compliance with screening methods, frequency, and treatment were measured. Percentages below are calculated out of the total cohort.

Results. Of 241 patients included in the analysis, 197 (81.74%) were male, 43 (17.84%) were female, 1 (0.41%) was transgender, 136 (56.43%) were men who have sex with men, and mean age was 42.07 years. During the study period, 3 (1.24%) patients were diagnosed with gonorrhea, 3 (1.24%) had chlamydia, 34 (14.1%) had a positive syphilis test (RPR or EIA), 22 (9.13%) had positive hepatitis B surface antigen, 20 (8.3%) had positive hepatitis C antibodies, 26 (10.8%) had genital warts, 6 (2.5%) had genital herpes, and 4/43 (9.3%) women had positive cervical HPV DNA. At study entry, mean CD4 count was 403 cells/uL, and mean HIV viral load was 282,529 copies/mL. At STD diagnosis, mean CD4 was 352 cells/uL, and mean HIV viral load was 45,132 copies/mL. Testing per guideline occurred in 95.83% of patients for syphilis, 43.75% for chlamydia, 45% for gonorrhea, 90% for hepatitis A, 99.58% for hepatitis B and 96.25% for hepatitis C. Testing frequency per guideline occurred in 81.25% of patients for syphilis, 37.92% for chlamydia, 38.33% for gonorrhea. When STD was diagnosed, treatment was according to guideline for most patients.

Conclusion. Compliance with screening methods and frequency was adequate for syphilis and hepatitis, but screening for chlamydia and gonorrhea is suboptimal and can be improved.

Disclosures. **All authors:** No reported disclosures.

1581. Laboratory Evaluation of three HIV and Syphilis Combination Rapid Diagnostic Tests

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Background. Syphilis and HIV co-infection is increasingly common. In co-infected patients, syphilis can increase transmission of HIV by increasing viral shedding and

seminal viral load. Point of care tests for syphilis and HIV may reduce morbidity and transmission of these infections by increasing the number of patients identified and treated. This study evaluated three research-use only, rapid diagnostic tests (RDTs) that detect HIV and *Treponema pallidum* (TP) antibody simultaneously, in serum.

Methods. Serum from 150 patients, including 29 TP-/ HIV-, 22 TP + /HIV-, 35 TP-/HIV+ and 64 TP + /HIV+ were tested. Reference test were the Siemens Advia Centaur HIV 1/O/2 and the Serodia TP-PA. Specimens were tested in parallel by the 3 RDTs by a technician blinded to reference results. RDTs included MedMira Multiplo HIV/TP, Standard Diagnostics (SD) BIOLINE HIV/Syphilis Duo, and ChemBio DPP® HIV-Syphilis Assay. Specimens that yielded discordant or difficult-to-interpret results were repeated by both references and all 3 RDTs. Data were evaluated by summary statistics.

Results. Sensitivity and specificity of the RDTs as compared to reference methods are in the table. Repeat testing did not resolve any false negative (FN) or false positive (FP) results. All FN TP and HIV results observed by the RDTs were from HIV + /TP+ specimens. Faint TP reactions were noted for 16 MedMira, 10 SD and 6 ChemBio tests. Faint HIV reactions were observed in 2 MedMira, 3 SD and 2 ChemBio tests. Repeat testing yielded similarly difficult to interpret results. Kappa coefficient between the three RDTs was 0.95 for the HIV component and 0.93 for TP.

Performance of 3 RDTs, as compared to reference methods.

	HIV (% (95% Confidence Interval))		TP (% (95% Confidence Interval))	
	Sensitivity	Specificity	Sensitivity	Specificity
SD	96 (89-99)	100 (91-100)	93 (85-97)	100 (93-100)
ChemBio	97 (91-99)	98 (88-100)	95 (88-98)	100 (93-100)
MedMira	96 (89-99)	94 (83-98)	94 (86-98)	97 (88-99)

Conclusion. The 3 RDTs performed comparably, with excellent sensitivity and specificity. Further evaluation of these tests, using whole blood in the clinic, will aid in the determination of their performance as point-of-care tests.

Disclosures. **R. M. Humphries**, Affinity Biosensors: Investigator, Research support

1582. Don't ask, don't test? Rates of syphilis screening among urban HIV patients

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Background. HIV patients are at high risk for both acquiring and having complications due to syphilis. It is recommended by the IDSA and HIVMA that sexually active HIV patients have annual syphilis screening especially in high risk urban areas. We evaluated the compliance with syphilis screening in an urban Infectious Diseases clinic (IDC).

Methods. We evaluated adult HIV patients with > 2 visits to the IDC between January 1-December 31, 2011. Data were collected on age, gender, ethnicity, sexual orientation, documentation of sexual history during the study period, whether RPR testing was performed and results of RPR. Patients with and without RPR testing during the period were compared using χ^2 analysis, Student's t-test and logistic regression using SPSS vs 22.0. A p value <0.05 was considered significant.

Results. Among the 173 patients who met inclusion criteria, 122 (70.5%) were male, 115 (66.5%) were Black, 44 (25.4%) were White, 86 (49.7%) were men who have sex with men (MSM), 82 (47.4%) were heterosexual, 80 (46.2%) had recent sexual history documented and the mean age was 46.6 + 11.6. A total of 102 patients had an RPR test performed, including 93 (91.2%) screening tests and nine (8.8%) for either symptoms or syphilis exposure. Among those tested, 90 (88.2%) were negative and the median titer among positive tests was 2 (range: 2-512). Among the 12 positive RPR tests, nine (75%) were performed for screening. Patients who had RPR testing performed were younger (45.0 ± 11.5 vs 49.0 ± 11.3, p = 0.02) and had a sexual history obtained (75.3% vs 40.0%, p < 0.0001). Upon logistic regression analysis, after controlling for age, only asking about recent sexual history was predictive of syphilis testing (OR 4.16; 95% CI: 2.1-8.2).

Conclusion. The only factor predictive of compliance with syphilis screening guidelines was obtaining a sexual history during the study period. Increased emphasis on obtaining sexual history during routine care would likely result in increased appropriate syphilis screening.

Disclosures. **All authors:** No reported disclosures.

1583. Randomized, Active-duty U.S. Military Population-based NAAT Screening for Asymptomatic *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis* Infection using De-identified Urine Samples Received by the Navy Drug Screening Laboratory, San Diego

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Background. Sexually-transmitted infections (STIs) continue to disproportionately comprise the majority of infectious diseases reported within the Department of Defense; however, data predominantly represent symptomatic males, females identified during routine cervical cancer screening and other subsets of the U.S. military (e.g., recruits, recently-deployed personnel). To determine whether routine STI screening would be cost-effective, a more accurate prevalence estimate of *Neisseria gonorrhoeae* (NG), *Chlamydia trachomatis* (CT), and *Trichomonas vaginalis* (TV) from a randomized sample of U.S. active-duty military personnel is needed.

Methods. During the period 17 October to 29 November 2013, residual urine specimens randomly collected from San Diego regional Navy and Marine Corps commands and delivered to the Navy Drug Screening Laboratory (NDSL), San Diego, were set aside for STI testing. NDSL provides drug testing for U.S. Navy and Marine Corps units located west of the Mississippi River and in the Pacific Rim. All specimens received by NDSL were eligible if drug-negative and stored at room temperature for < 7 days prior to transfer to Gen-Probe (San Diego, CA) collection tubes. NAAT was conducted using the TIGRIS DTS Automated Analyzer system to detect NG, CT and TV rRNA using the APTIMA COMBO 2 (NG and CT) and APTIMA TV Assays. Rates were calculated to determine CT, NG, and TV prevalence.

Results. To date, 1,748 urine specimens have been tested for CT, NG, or TV. The prevalence rates of CT, NG, and TV were 3.5% (95% CI 2.6% - 4.4%, n = 61/1,737), 0.35% (95% CI 0.07% - 0.63%, n = 6/1,734), and 0.19% (95% CI 0.006% - 0.32%, n = 3/1,609), respectively.

Conclusion. CT prevalence (3.5%) is slightly less than previous asymptomatic rates reported among a non-random sample of U.S. military personnel (4.2%) and higher than U.S civilians (2.2%) screened in a population-based study. NG prevalence (0.35%) is similar to the reported prevalence among U.S. civilians (0.24%). Urine specimens randomly selected from active-duty military personnel as part of the required drug testing program will provide more accurate prevalence data for NG, CT and TV infections and can be used to inform cost and feasibility associated with implementing routine screening among male and female active-duty U.S. military personnel.

Disclosures. **All authors:** No reported disclosures.

1584. Gonorrhea and Chlamydia Testing in Routine Clinical Care of HIV-Infected Men Who Have Sex with Men

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Background. Men who have sex with men (MSM) are disproportionately affected by HIV and other sexually transmitted diseases (STDs) including *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis*(CT). Centers for Disease Control and Prevention STD Treatment Guidelines recommend screening sexually active MSM annually for urogenital and extragenital GC/CT, depending upon sites of exposure. Data on rates, correlates, and results of GC/CT testing among HIV+ MSM in routine HIV clinical care are limited.

Methods. A cross-sectional study at a university-based HIV clinic evaluated GC/CT testing among established patients in 2012, with primary focus on MSM. Patients were included if ≥19 years old, in care for >1 year, with at least 2 visits ≥90 days apart within the last year.

Results. Of 1,523 eligible patients (mean age 46 years; 59% MSM, 18% heterosexual men, 23% women; 53% African-American), 632 (41%) received GC/CT testing within the prior year. Testing was more prevalent among women than heterosexual men or MSM (67% vs 32% vs 35%). Among MSM (n = 890), 307 received GC/CT testing of which urogenital GC/CT testing was done in 32%, rectal in 9% and pharyngeal in 3%. Overall 15 patients tested positive for GC and 16 for CT; most were MSM (14/15 and 13/16 respectively). Among MSM receiving rectal testing (n = 77), 12% were GC and 16% CT positive. Of 9 positive rectal tests for GC in MSM, urogenital testing was also done in 6 [positive = 1]. Of 12 positive rectal tests for CT in MSM, urogenital testing was also done in 9 [positive = 2]. In multivariable analysis, factors significantly associated with increased GC/CT testing among MSM included African-American race (prevalence ratio, PR 1.30; 95% CI: 1.08-1.55) and self-reported sex without condom use (PR1.36; 95% CI: 1.07-1.73), while age (PR 0.93 per 5 year increase; 95% CI 0.89-0.97) and STD history (PR 0.81; 95% CI 0.69-0.97) were significantly associated with decreased testing.

Conclusion. Prevalence of GC/CT testing among MSM in routine HIV care was low, particularly extragenital testing. Most positive GC/CT results were from rectal testing in MSM, and corresponding urogenital tests were usually negative. Increased rectal GC/CT testing among HIV+ MSM would likely capture a significant number of undiagnosed GC and CT infections.

Disclosures. **All authors:** No reported disclosures.

1585. Implementation of Anal Dysplasia Screening with High Resolution Anoscopy in HIV-Positive Men at a U.S. Department of Defense Infectious Diseases Clinic: A Process Improvement Initiative.

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Background. As HIV-infected men live longer, rates of anal cancer have risen and antiretroviral therapy may not be protective. Anal human papillomavirus (HPV) infection prevalence has been estimated as high as 57% in HIV-negative men who have sex with men (MSM) and 88% in HIV-positive MSM populations. Approaches to screening and understanding of HPV-driven malignant transformation leading to anal cancer in this population are informed by experience with cervical cancer. We present data from the only Department of Defense Infectious Diseases (ID) anal dysplasia screening program.

Methods. Naval Medical Center San Diego ID clinic provides care to 600 HIV-positive men. In 2013, we began screening with anal Papanicolaou (Pap) smear and referred any abnormal results for high resolution anoscopy (HRA), performed by an ID attending. Anal Paps were repeated at the time of HRA. Using clinic records (paper and electronic), as well as information gathered from pre-procedural questionnaires regarding social history, data were compiled for each patient.

Results. To date, 78 patients have been evaluated with HRA. Average age was 42 years, duration of HIV infection 10 years, and CD4 nadir 284 cells/μL. Average CD4 nadirs were 400 cells/μL, 284 cells/μL, 285 cells/μL, 188 cells/μL for those with no dysplasia, Atypical Squamous Cells of Undetermined Significance (ASCUS), Low Grade Squamous Intraepithelial Lesion (LGSIL), and High Grade Squamous Intraepithelial Lesion (HGSIL), respectively. Of those with low grade cytology (ASCUS or LGSIL), 20% had high grade Anal Intraepithelial Neoplasia (AIN) II or III; negative predictive value of low grade cytology for AIN II or III was 77%. Of those with high grade cytology (HGSIL), 100% had AIN II or III, and one clinically early case of anal squamous cell carcinoma was identified.

Conclusion. In our first year, we've demonstrated the feasibility, utility, and importance of anal dysplasia surveillance in an HIV-infected population. Additional data are needed in order to link observation and intervention to clinical outcomes and will help to clarify natural history of dysplasia as well as help guide appropriate follow-up. Further, our experience provides a model to be considered by other ID and HIV clinics interested in starting anal dysplasia surveillance programs.

Disclosures. **All authors:** No reported disclosures.

1587. Prescription erectile dysfunction medication, sexual risk behaviors, and sexually transmitted infections among HIV positive men

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Background. Use of erectile dysfunction (ED) medication, particularly recreational use, has been associated with sexual risk behaviors and sexually transmitted infections (STIs). Data on prescription ED medication use, sexual risk behaviors and STI screening among HIV+ men are lacking.

Methods. A cross-sectional study at a university-based HIV clinic evaluated prevalence and correlates of ED medication prescription among established male HIV+ patients in 2011-12. Patients were included if ≥19 years old, in care for >1 year, with at least 2 visits ≥90 days apart within the last year. Multivariable (MV) log-binomial regression models were used to evaluate associations (prevalence ratio, PR with 95% confidence interval, CI) of patient characteristics with ED medication prescription.

Results. Of 1,170 HIV+ men, 269 (23%) were prescribed ED medication (mean age 50, 27% heterosexual and 73% MSM, 41% African American). Similar prevalence of ED medication prescription was observed for MSM (22%) and heterosexual men (26%). Among men on ED medications who took a survey regarding current sexual risk behavior, 181/234 (77%) reported multiple partners, 57/144 (40%) sex without condom use and 73/230 (32%) sex after alcohol/drug use. In MV analysis, age ≥ 50 years (PR = 1.5; 95% Cl 1.2-1.8), multiple sexual partners (1.9; 1.4-2.5), sex after alcohol/drugs (1.3; 1.0-1.7), and prior history of STI (1.4; 1.1-1.7) were significantly associated with ED medication prescription, while sexual orientation, race, insurance, substance use, and viral load were not. Annual protocol-driven syphilis testing was done in 253/269 (94%) of men on ED medication, with 9 (4%) positive for new infection. In contrast providers performed less annual testing for Neisseria gonorrhoeae (GC) and Chlamydia trachomatis (CT): 83/269 (31%), of whom 3 were GC positive and 1 CT positive. Among MSM on ED medication (n = 196), GC/CT testing was done in 55 (28%), of whom 54 received urogenital testing and 14 rectal testing.

Conclusion. In this cross-sectional study, ED medication prescription was significantly associated with sexual risk behavior in HIV+ men. Incidence of syphilis among men on ED medications was high. Screening for GC and CT needs to be increased, particularly rectal screening among MSM.

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1588. Prevalence of and Factors Associated with Hepatitis C Virus Testing and Infection Among HIV-infected Adults Receiving Medical Care in the United States

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Background. Hepatitis C Virus (HCV) infection causes substantial morbidity and mortality among HIV-infected persons. Representative prevalence estimates of HCV infection can help inform treatment efforts in the dawning era of highly effective anti-HCV therapy.

Methods. We used 2009 data from the Medical Monitoring Project, a nationally representative sample of U.S. HIV-infected adults in care, to determine prevalence of HCV testing and infection. We defined HCV testing as documentation of an HCV antibody or RNA test and HCV infection as a positive result. We used bivariate analyses and multivariate logistic regression to examine factors associated with HCV testing and infection.

Results. We estimated that 342,952 HIV-infected adults or 81% (95% confidence intervals [CIs]: 304,474—381,430; 79%–84%) were ever tested for HCV. Factors associated independently ($p < 0.01$) with testing included black race, recent HIV diagnosis, and history of AIDS. Among those tested, 21% (95% CI: 18-24%) were infected with HCV. Prevalence varied significantly by age (≥ 44 vs < 44 years: 27 vs 10%), men who have sex with women only (MSW) vs men who have sex with men (MSM) (33 vs 14%), public vs private insurance (28 vs 11%), income at or below poverty level vs not (28 vs 16%), homeless vs not (34 vs 20%), recent injection drug use (IDU) vs not (62 vs 20%), duration of HIV infection (≥ 10 vs <10 years: 27 vs 14%), and history of AIDS vs no AIDS (23 vs 17%). Factors associated independently with HCV infection included recent IDU (adjusted prevalence ratio [APR] 3.2; 95% CI 2.6–3.9), age >44 years (APR 2.2; 95% CI 1.7–2.7], MSW (APR 1.9; 95% CI 1.6-2.3), public insurance (APR 1.6; 95% CI 1.3–2.1), HIV diagnosed ≥10 years (APR 1.5; 95% CI 1.3–1.8), homelessness (APR 1.4; 95% CI 1.1–1.7), and income at or below poverty level (APR 1.3; 95% CI 1.1–1.5).

Conclusion. Current U.S. guidelines endorse baseline HCV screening for all HIV-infected persons and routine screening for those with IDU; however, almost 1 in 5 U.S. HIV-infected adults in care have never been tested. HCV infection prevalence varied among sub-groups. All HIV-infected adults, especially those in high-risk groups, should be tested for HCV to increase the number of persons aware of their HCV infection and eligible for potentially curative treatment.

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1589. Incidence and Risk factors of Hepatitis C Virus Infection among HIV Patients in a large HIV Clinic in South Korea

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Background. Increasing incidences of HCV infection in MSM with HIV infections were reported in the United States and Europe. However, there are few studies regarding the epidemiology of HCV in HIV infected patients in Asian countries.

Methods. To determine the risk factors of HCV infection, and the incidence of HCV in in HIV infected patients, a retrospective cohort study was performed. All HIV infected patients who visited Pusan National University hospital from January 2000 to October 2013 were identified from the computerized records. The patients with a negative baseline anti-HCV antibody who had subsequent anti-HCV antibody tests more than 6 months apart were included. Demographic and clinical data were reviewed, retrospectively. For analysis of risk factors, a multivariable logistic regression model was used.

Results. Among 996 HIV patients, 790 (79%) had baseline anti-HCV Antibody tests and 41 (5.2%) were positive for anti-HCV Ab. In a multivariable analysis, widowed or divorced marital status (adjusted odds ratio 2.67; 95% confidence interval 1.17-6.08, $P = 0.02$), HIV transmission by intravenous drug use (IDU) (aOR 66.08; 95% CI 16.31-267.69, $P < 0.01$) and blood exposure other than IDU (aOR 42.34; 95% CI 4.13-433.74, $P < 0.01$) were significantly associated with HCV infection in HIV patients. Of 330 patients with subsequent anti HCV Ab tests, were observed for 1527.94 person years and 4 patients (1 MSM and 3 IDU) had HCV seroconversion with incidence rate of 2.64/1,000 person years (PYs); 130.89/1,000 PYs in IV Drug user, 1.65/1,000 PYs in MSM, and 0/1,000 PYs in the heterosexual. Incidence rate of HCV was increased in recent 5 years [0 (2000 ~ 2,009) vs 4.58 (2010 ~ 2014)/1,000 PYs] although incidence of syphilis was constant [53.81 (2000 ~ 2009) vs 48.85 (2010 ~ 2014)/1,000 PYs]. All of the incident HCV infections were developed within recent 5 years. Among 34 patients with available HCV RNA results, 19 patients were positive for HCV RNA and genotype 1b (73%) was most common following 2a/2c (20%).

Conclusion. Incidence rate of HIV infected patients was 2.64/1,000 PYs. Widowed/divorced marital status, HIV transmission by intravenous drug use were independent risk factors for HCV infection in HIV patients. Although the seroconversion of anti-HCV was not frequent yet, the incidence of HCV infection is increasing in HIV infection in South Korea.

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1590. Hepatitis C Care among HIV Infected Patients in a Community Based Clinic

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Background. Improvements in the efficacy and safety of HCV treatments offer hope for HCV cure for many patients. HIV/HCV co-infected patients progress more often and more rapidly to significant liver disease, and thus stand to benefit from prompt treatment of HCV infection. Rates of hepatitis C treatment in patients enrolled in community-based HIV care programs are unknown.

Methods. We performed a retrospective cohort analysis of HIV/HCV co-infected adults enrolled in care in the Baltimore City Health Department Early Intervention Initiative program (a Ryan White HIV clinic based in two public sexually transmitted diseases clinics) between 2002 and 2012, with follow-up through March 2014. Data was gathered through retrospective chart review of the electronic medical and paper records.

Results. A total of 217 HIV/HCV infected patients were identified, of whom 102 were engaged in HIV care, defined as having at least two visits in different halves of the year. Patients were engaged in HIV care for a median of 3.6 years (IQR 2-6 years). HIV/HCV co-infected patients had a median age of 45 (IQR 39-50 years) at diagnosis and were predominately African American (89%) and male (79%). The median CD4 count was 422 (IQR 274-617). Fifty-six (55%) of HIV/HCV co-infected patients actively engaged in care were referred to a specialist for HCV treatment, of whom 37 (36%) attended at least one appointment; however, only 8 (8%) were treated for chronic HCV with a cure achieved in 4 (4%). Fifty-two (51%) had evidence of significant fibrosis of whom 16% had cirrhosis based on serum fibrosis markers (FIB 4 >1.44 and >3.25, respectively). Fifty-six (55%) patients in this cohort achieved virologic HIV suppression based on an HIV viral load <200copies.

Conclusion: In this urban community-based HIV clinic with significant HCV-related liver disease, rates of attendance for HCV specialty appointments and anti-HCV treatment were extremely low. Conversely, over half of co-infected patients achieved HIV viral load suppression. In the era of oral anti-HCV treatments, where a key predictor of treatment success will be treatment adherence, provision of HCV treatment and care by community HIV providers, who have demonstrated experience in maintaining patients on HIV therapy, may lead to higher rates of HCV treatment initiation and cure.

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1591. Hepatitis B outcome in coinfected HIV-HBV individuals in the tenofovir/emtricitabine era

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Background. Hepatitis B is an important public health issue in endemic areas, especially with the HIV epidemic. In the USA, hepatitis B and HIV coinfection represent approximately 6-10% of people living with HIV/AIDS. We report the experience with HIV-Hepatitis B-coinfected patients in our clinic

Methods. Of 1011 na•ve HIV patients enrolled at IDP from June 2004 to December 2011 who had available chart for review and who were started on antiretrovirals, those with HepBsAG+ were studied. Demographics, antiretroviral treatment and hepatitis B and HIV markers were abstracted. SAS9.2 was used for analysis. $p < 0.05$ was considered significant.

Results. There were 89HbsAg+ patients. Of those, 76(86%)were male, 73(82%) were black, and 58(65%) were men having sex with men or bisexuals. The age at HIV diagnosis was 34.4 years old. The majority 82 (92%) had a positive antigen at presentation to the clinic and 5 became positive during follow up. The baseline CD4 count was 87.16 + /-123 cells/mL. Among the 63(70%) with Hepatitis B viral load at baseline, 12(20%) had undetectable viral load and 32(51%) had high viral load (greater than 1 million). Among those, 48(55.2%) had an undetectable viral load at the last visit, and 7 (8%) developed immunity with HepBsAb + ; among the 22 who had a HBsAb checked at follow up, a third (7/22)were positive; 6 of the 7 was on tenofovir/emtricitabine and 1 on emtricitabine containing regimen . Among those who had undetectable HepB viral load, 83% were on tenofovir/emtricitabine, and 10% on a lamivudine or emtricitabine-containing regimen. Among the 5 patients who became HbsAg+ after enrolling in the clinic, all were male and 3 received HepB immunization. One had acute HepB and resolved, another developed chronic HepB and became immune, another transferred care, and 2 had no further follow up on their HepB.

Conclusion. In the late antiretroviral era, half of the chronic active hepatitis B coinfected patients had undetectable hepatitis B viral load at the last follow up and 8% developed immunity. Further studies with more uniform hepatitis B markers in follow up will help determine if a large proportion of chronically infected patients on dual hepatitis B therapy will develop immunity. Greater efforts are needed to ensure susceptible patients are immunized for Hepatitis B.

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1592. Impact of HAART on Incidence of Primary HIV-Associated Thrombocytopenia

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Background. Thrombocytopenia induced by HIV infection typically improves with highly active antiretroviral therapy (HAART); however, cases of primary HIV-associated thrombocytopenia (PHAT) continue to be reported in the literature. We examined the incidence of PHAT over 28 years in the U.S. Military HIV Natural History Study (NHS).

Methods. Retrospective NHS data from 1986 to 2013 including 5,697 participants were analyzed. PHAT was defined as subjects diagnosed with idiopathic thrombocytopenic purpura with a nadir platelet count < 100,000 cells/mm^3, and no other identifiable cause including known drugs and opportunistic infections. Subjects were excluded if coinfected with hepatitis B or C or diagnosed with cirrhosis, leukemia, and/or solid tumor malignancies. Variables included demographic data, platelet count, CD4 count, and HIV viral load (VL) at the time of PHAT diagnosis, and antiretroviral use. Time periods were categorized as pre-HAART (PH) 1986-1995, early-HAART (EH) 1996-2001, and later HAART (LH) 2002-2013. The relationship of CD4 count and VL with platelet count was studied. Descriptive statistics and mixed model linear regression with random intercept were used.

Results. A total of 218 participants met the case definition of PHAT. 86% of cases occurred prior to 2002. The incidence of PHAT per 1,000 patient years was 15.4, 4.5, and 1.9 during PH, EH, and LH respectively ($p < 0.001$). Median (IQR) CD4 count (cells/mm^3) at PHAT diagnosis was 156 (30, 406), 262 (148, 378), and 380 (255, 517) over the same three time periods ($p = 0.016$). Of the 67 patients with PHAT during the HAART eras, 33 (49%) were antiretroviral naïve. VL recorded within four months prior to nadir platelet count was available in 56 patients. Of these, viremia was detected in 54 (95%) participants, of which 29 (54%) were antiretroviral naive. Laboratory data collected during 1996-2013 in patients diagnosed with PHAT in the HAART eras showed strong correlation between log10 VL and platelet count ($p < 0.001$).

Conclusion. The incidence of PHAT has markedly decreased in the HAART era, although viremic individuals, including those with healthy CD4 cell counts, may be at risk. Further decline in incidence may be another benefit to current recommendations to begin HAART as early as possible.

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1593. Predictors of Mortality for HIV-associated Cryptococcal Meningitis

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Background. Cryptococcal meningitis (CM) is the common etiology of central nervous system opportunistic infection (OI) among HIV patients. The aim of the study was to determine clinical characteristics, laboratory parameters, outcome and factors associated with death among HIV-associated CM.

Methods. Retrospective study of HIV patients diagnosed with CM was conducted at Nakhonpathom hospital, a 500-bed tertiary care hospital in central Thailand during January 1, 2011 and September 30, 2013. Clinical features, outcomes and predictors of mortality were determined.

Results. There were 77 patients. The mean age was 39.3 ± 10.8 years and 34 (44.2%) were female. Fever and headache (85.7% each) were the most common presenting symptoms, followed by neck stiffness (55.8%), reduced conscious level (28.6%), focal neurological deficit (13.0%) and seizure (11.7%). Clinical triad of meningitis (fever, headache and neck stiffness) was seen in 44.2%. Median duration of symptoms before presentation was 7 (range 1-84) days. Median CD_4 count was 38 (range 4-420) cells/mm^3. Cranial imagings of 69 patients revealed 1 or more abnormalities in 33 patients (47.8%) including hydrocephalus (18 of 69 patients, 26.1%), meningeal enhancement (17 patients, 24.6%) and cerebral infarction (7 patients, 10.1%). Median CSF WBC count, protein and glucose were 5 (range 0-610) cells/mm^3, 69 (range 2-469) mg/dl and 39 (range 4-122) mg/dl, respectively. Normal CSF findings (WBC ≤ 5 cells/mm^3, protein ≤ 45 and sugar > 45 mg/dl) was documented in 11.8%. CSF india ink staining, CSF and serum cryptococcal antigen testings were discovered in 79.2%, 96.6% and 94.0%, respectively. In-hospital mortality was 32.5%. Factors associated with death were neck stiffness (OR 3.7, 95%CI 1.3-10.7), altered consciousness (OR 2.9, 95%CI 1.1-8.2) and CSF leucocyte count below 10 cells/mm^3 (OR 3.7, 95%CI 1.1-12.3). Increased CSF protein (above 45 mg/dl) was a protective factor among survivor (OR 0.3, 95%CI 0.1-0.9). Nevertheless, duration of illness, CD_4 count, CSF glucose and abnormalities of cranial imaging did not influence patients' outcomes.

Conclusion. CM is an important OI with high mortality. Neck stiffness, depressed conscious level, low CSF WBC count and low CSF protein value were a major determinant of outcome.

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1594. Invasive Sinonasal Aspergillosis in Patients with HIV Infection

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Background. Invasive sinonasal aspergillosis is a serious infection that occurs in immunocompromised hosts. Patients with HIV/AIDS represent a minority of such cases in the literature in comparison to those with neutropenia due to malignancy and chemotherapy, diabetes, and corticosteroid use. The purpose of this study is to describe the clinical manifestations and treatment outcomes of invasive sinonasal aspergillosis among patient with HIV infection.

Methods. A PubMed search was conducted for English-language articles using search terms relating to aspergillus, HIV/AIDS, sinusitis, and central nervous system infection.

Reference lists of those studies selected were also reviewed for eligible articles. Only those cases of aspergillosis originating from the paranasal sinuses were included in the analysis, in order to compare characteristics of invasion and outcome.

Results. Eighteen articles were found totaling 48 patients with HIV infection and invasive sinonasal aspergillosis. The average patient age was 37 (range 30 to 50), and 36 (75%) were men. Of the 38 patients in whom immunologic parameters were reported, all had AIDS and 32 (84%) had a CD4 count less than 50 at the time of diagnosis of aspergillosis. All cases were due to Aspergillus fumigatus among those that were reported. The most common symptoms were fever (35%), headache (32%), proptosis (29%) and facial pain (26%). Thirty-five patients had imaging data reporting sinus involvement, the most common of which were the maxillary and ethmoid sinuses (46% respectively) followed by the sphenoid sinus (26%). The most common intracranial site of invasion was the orbit and periorbit (46%). Thirty-two (89%) of 36 patients underwent surgery after diagnosis, while all patients received anti-fungal therapy. Two of 31 patients with reported data received itraconazole alone, while the remainder received amphotericin B either alone or in combination or consecutively with itraconazole. Among 44 cases with reported outcomes, the mortality was 91%.

Conclusion. Invasive sinonasal aspergillosis is a lethal infection in patients with advanced HIV/AIDS. Clinicians must consider this disease in HIV-infected patients presenting with fever, headache, and proptosis, and initiate early antifungal therapy and surgical debridement when appropriate.

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1595. Incidence of Kaposi Sarcoma and Associated Mortality in HIV-infected Adults, Fresno, California, 1998-2012

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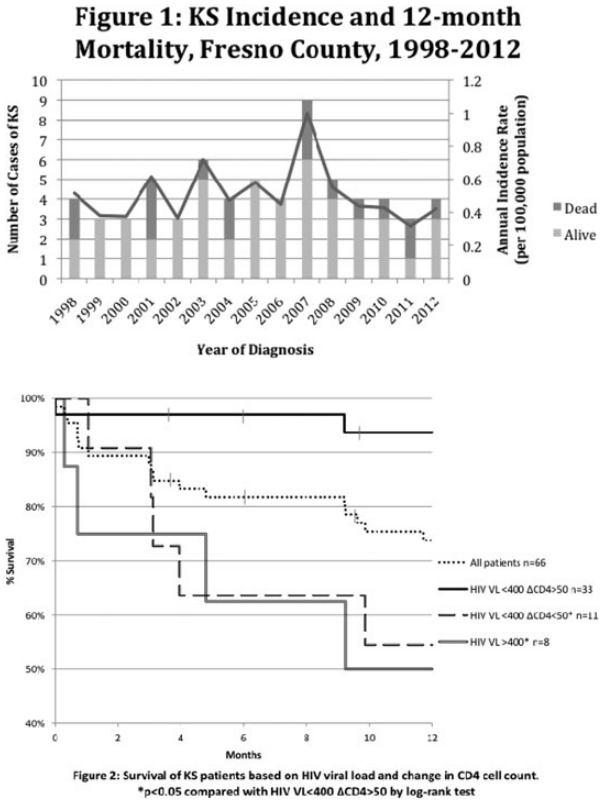
Background. The incidence of Kaposi sarcoma (KS) decreased dramatically after the introduction of highly active antiretroviral therapy (HAART) in 1996. This study determined the ongoing incidence of and mortality from KS in HIV-infected adults between 1998-2012 in Fresno County, California. The role of virologic control and immune reconstitution in patient outcome was also investigated.



Methods. Incident cases of KS were identified from the state Electronic HIV/AIDS Reporting System (EHARS), the California Cancer Registry, and the hospital records of the main HIV treatment center in Fresno.

Results. From 1998–2012, the average incidence rate of KS was 0.51 cases per 100,000 person-years. Of the 66 cases of KS there were 20 deaths, with 85% of the mortality occurring in the first 12 months post KS diagnosis. In patients achieving HIV RNA <400 copies/mL on HAART, but with a <50 cells/mm^3 increase in CD4 count there was no improvement in mortality compared with patients who did not achieve virologic control. For KS patients on successful HAART with virologic control (HIV VL <400 copies/mL) with a >50 cells/mm^3 increase in CD4 count, the 12-month mortality was 6%; for those with a <50 cells/mm^3 increase in CD4, the 12-month mortality was 50%.

Conclusion. The incidence of KS has remained stable since 1998 with an overall 12-month mortality of 30%. Immunologic reconstitution appears to be required for an improvement in outcome.

Disclosures. **All authors:** No reported disclosures.

1596. Spectrum of Kaposi's sarcoma encountered among HIV-infected patients in an inner-city hospital in the established antiretroviral era

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Background. Epidemic Kaposi's sarcoma (KS) is a multicentric angioproliferative cancer of endothelial origin typically occurring in the context of immunodeficiency such as coinfection with Human Immonodeficiency Virus (HIV) or transplantation. The incidence of KS has dramatically decreased in both US in the combined antiretroviral therapy (cART) era. We present our experience with KS encountered among admitted patients in an inner–city hospitalover a 3 year period.

Methods. Hospitalization records were queried for discharge diagnosis that included KS as diagnosis among admission to Grady Memorial Hospital from October 2010 to October 2013. Demographic data as well HIV markers were collected. Excluded are patients with a history of KS, non-active KS or unconfirmed KS.

Results. There were 43 patients admitted with active KS during the 3-year period, with the majority being male (97%) and African (81%). The median age at KS diagnosis was 37 (range: 19-62). The median CD4 count at KS diagnosis was 11(range: 1-462). The most common involved organs are skin, gastrointestinal tract, pulmonary and lymph nodes (table). The median time of HIV diagnosis to KS diagnosis was 2 years (range: 0-26 years). Half of the patients had a concomitant or recent (within past 6 months) opportunistic infection (Pneumocystis pneumonia (n = 14), toxoplasma encephalitis (n = 4), CMV retinitis or colitis (n = 2), or cryptosporidiosis (n = 2)). Of note, a third had coinfection with a viral hepatitis: 11(26%)had chronic active hepatitis B and 3 (7%)had active hepatitis C. A third of the patients had a poor KS prognostic index. A third was on cART at KS diagnosis and 26 patients received chemotherapy for KS. The median follow up from KS diagnosis was 343 days (14-2234). 14(33%)died within one year of KS diagnosis.

Sites of Kaposi's sarcoma involvement

	1 site	2 sites	3 sites	4 or more sites
Skin	7	GI:8,P:3,LN:2, OTHER:1	GI_P:3,GI_LN:1, P_LN:2	GI_P_LN:3, P_LN_OTHER:2
GI	4	P:2, OTHER:1	P_LN:1	
Pulmonary	1		LN_OTHER:2	
Lymph node				

Conclusion. In our hospital, people presenting with KS still had poor outcome despite wide availability of cART and chemotherapy. Vigilance to get patients into care earlier, start arv earlier will help decrease KS severity of disease.

Disclosures. **M. L. Nguyen**, Tibotec: Investigator, Research grant

1597. Treatment of Oropharyngeal Cancer in Patients with Human Immunodeficiency Virus

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Background. The incidence of oropharyngeal squamous cell carcinoma (OPC) is on the rise. This is now known to be largely due to infection with human papillomavirus (HPV), the most common sexually transmitted disease in the world. Patients with human immunodeficiency virus (HIV) are particularly susceptible to all HPV-associated malignancies including OPC, but very little is known to guide their treatment. Studies of other malignancies suggest that patients with HIV experience significant delays in therapy compared to HIV-negative patients. We wished to determine whether this was the case in OPC.

Methods. We obtained treatment data for all HIV-positive subjects diagnosed with OPC at the Hospital of the University of Pennsylvania from January 1, 1996 through April 11, 2013 and compared it to a subset of HIV-negative subjects with OPC diagnosed during the same time period. This information is part of a larger, ongoing multicenter retrospective cohort to evaluate the treatment and survival outcomes of OPC in HIV-positive patients. The primary endpoint was time from diagnosis until start of therapy; a difference of 10 days was deemed clinically important based on studies that showed increased mortality in patients with delays longer than this.

Results. 19 HIV-positive subjects and 86 HIV-negative subjects with treatment data were identified. The unadjusted hazards ratio for starting therapy in HIV-negative patients was 2.71 (95% confidence interval 1.54-4.76) compared to HIV-positive patients. This hazards ratio was 2.31 (95% confidence interval 1.22 – 4.37) after adjustment for age, sex, insurance type, race, and comorbidities including psychiatric disease and substance abuse. The median number of days from diagnosis to start to therapy

was 27 in HIV-negative patients (interquartile range 14-39) and 51 in HIV-positive patients (interquartile range 31-85).

Conclusion. HIV-positive subjects with OPC experience clinically important delays from diagnosis until start of therapy compared to HIV-negative patients. A larger study is underway to explore potential mechanisms for these delays and to determine how this impacts survival.

Disclosures. **All authors:** No reported disclosures.

1598. Risk Factors for Recurrent Skin and Soft Tissue Infections in HIV-Infected Patients Over a 5-Year Period

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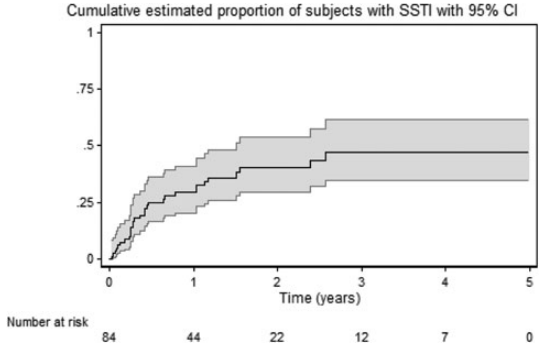
Background. Skin and soft tissue infections (SSTIs) due to Staphylococcus aureus and other pathogens are common in human immunodeficiency virus (HIV) infected individuals, who are at high risk of recurrent SSTIs. We assessed risk factors for recurrent SSTI in a cohort of HIV-infected patients in an urban, largely African American population.

Methods. Retrospective cohort study of 511 HIV-infected patients at an academic medical center between January 1, 2005 and December 31, 2009, with medical record review of physician-diagnosed SSTIs, demographics, comorbidities, antibiotic exposure, and sexually transmitted infections (STIs). Patients with one or more SSTI during this period were analyzed. Time-varying variables were coded appropriately, including CD4+ count, HIV viral load (VL) and HAART use. Patients with and without SSTI recurrence were compared using a multivariate Cox regression analysis to assess associations of variables found to be univariate predictors of recurrent SSTI.

Results. 133 SSTIs occurred in 87 individuals, of whom 30 (34.5%) had a recurrent SSTI. 1 individual had 5 SSTIs, 4 had 4 SSTIs, 5 had 3 SSTIs, 20 had 2 SSTIs, and 57 had 1 SSTI. There were 118.3 person-years of follow-up for people at risk of recurrence. The incidence of second SSTI was 253.6 SSTIs/1,000 person-years (95% CI 166.8-385.7). The 1-year risk of a second SSTI was 29.2% (95% CI 0.2027-0.4102), while the 5-year risk was 47.0% (95% CI 0.3439-0.6155). Risk factors for recurrent SSTI in the multivariate analysis included lymphedema (HR 6.4, p = 0.018, CI 1.369-29.902) and non-viral hepatitis liver disease (HR 6.3, p = 0.006, CI 1.709-22.989). The presence of an indwelling catheter (HR 6.2, p = 0.055, CI 0.96-39.62) trended towards significance. Hemodialysis, currently taking HAART, CD4+ count, HIV VL, trimethoprim-sulfamethoxazole or azithromycin use, STI history, initial SSTI type, DM, or self-report of being a man who has sex with men were not associated with recurrence.



Conclusion. Of HIV-infected patients with an SSTI, nearly 1/3 had a recurrence within 1 year. Risk factors for recurrent SSTI were chronic lymphedema and non-hepatitis liver disease. CD4 count and HIV VL were not found to be significant risk factors for recurrence in contrast to findings of previous studies.

Disclosures. **All authors:** No reported disclosures.

1599. HIV and Progression of Atherosclerosis in Chinese

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Background. We aim to study factors associated with progression of atherosclerosis in HIV infected Chinese. Such knowledge may help to target intervention of high risk patients.

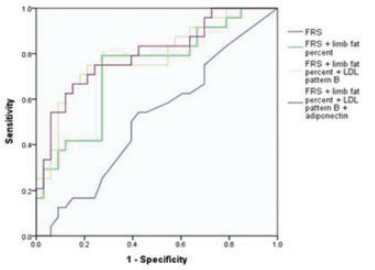
Methods: A prospective case-control study was performed. HIV infected individuals managed in a metabolic clinic in Hong Kong were recruited as cases, and age- and gender-matched HIV uninfected individuals as controls. All subjects were followed up for 24 months. Ultrasonography was performed at baseline and 24 month to measure carotid intima media thickness (cIMT). Body composition (DEXA scan), metabolic and inflammatory biomarkers were measured (including insulin, LDL particle size, hsCRP, adiponectin). Multivariate linear regression was used to identify variables associated with changes in cIMT. ROC analysis was used to evaluate predictive performance for change in cIMT (≥ upper tertile) in HIV infected patients.

Results : Sixty one cases and 30 controls were recruited (mean°"SD age 50.2°"11.6 years, 88% male, 98% Chinese, 54% non-smoker). For HIV infected patients, 30% had hypertension, 39% had diabetes, and 85% had dyslipidemia. At baseline, cIMTs were 0.790 (IQR 0.705-0.890)mm and 0.710 (IQR 0.650-0.833)mm in cases and controls respectively ($p = 0.013$).

Annual rates of change in cIMT were +0.0075 (IQR 0.0000-0.0163) mm/year and 0.0000 (-0.0022-0.0000) mm/year in cases and controls respectively ($p < 0.001$). After adjustment for traditional cardiovascular risk factors (age, gender, smoking, hypertension, diabetes, and LDL cholesterol), HIV infection is an independent risk factor for cIMT progression (beta coefficient 0.012, 95% CI 0.005-0.018, $p = 0.001$)

Among HIV infected patients, baseline limb fat percentage, LDL cholesterol subclass pattern (type B), and adiponectin were associated with greater cIMT progression on univariate analysis. ROC analysis showed combination of Framingham risk score, limb fat percentage, LDL cholesterol pattern B and adiponectin best predict cIMT progression, with AUC of 0.799 (95% CI 0.680-0.918, $p < 0.001$).

Figure. ROC curves of various combinations of variables in predicting progression of cIMT (highest tertile) in HIV-infected patients



Variables	Area under the curves (AUC)	95% confidence interval	p
FRS (10-year cardiovascular disease risk prediction using Framingham risk score)	0.516	0.364-.669	0.834
FRS + limb fat percent	0.731	0.597-0.865	0.003
FRS + limb fat percent + LDL pattern B	0.788	0.665-0.911	<0.001
FRS + limb fat percent + LDL pattern B + adiponectin	0.799	0.680-0.918	<0.001

Conclusion. In Chinese, HIV is an independent predictor of atherosclerosis progression. Limb fat percentage, LDL particle size and adiponectin may help to identify HIV infected patients with the highest risk of progression.

Disclosures. **All authors:** No reported disclosures.

1600. Lower lipid screening rates among HIV positive outpatients in an urban clinic

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Background. As a result of advances in antiretroviral therapy, non-HIV related conditions including cardiovascular diseases are becoming the leading causes of morbidity and mortality in patients with HIV. Thus, appropriate lipid screening is increasingly important in the outpatient care of HIV patients. We compared rates of lipid screening of HIV patients compared with non-HIV controls in an urban tertiary care center.

Methods. We performed a case-control study of all HIV-positive patients > 20 years (cases) who had at least 2 visits between January 1-December 31, 2011 with Infectious Diseases (ID) physicians. Controls were age-and gender-matched patients seen by Internal Medicine (IM) physicians at least twice during the same period. We collected the following information: demographics, underlying conditions (including hypertension, diabetes mellitus, tobacco use and family history of cardiovascular disease), whether screening was performed and if it was compliant with USPSTF lipid profile screening guidelines. For the cases, we also collected data on whether they had a primary care provider (PCP). Statistical analysis was done by chi-squared analysis using SPSS vs 21.0. A $p < 0.05$ is considered significant.

Results. A total of 153 cases and 152 controls were included in the study. The groups were evenly matched in terms of age (46.6 years in both groups) and gender (69.9% male in cases, 71.1% in controls). Cases had a higher frequency of tobacco use (50.9% vs 25.6%, $p < 0.0001$), hypertension defined by increased blood pressure (31.4% vs 19.1%, $p < 0.013$) and non-coronary atherosclerosis (7.2% vs 2%, $p < 0.03$). There was an overall lower rate of compliance with lipid screening among cases (60.1% vs 78.9%, $p < 0.0001$). There was no difference in compliance with lipid screening based on whether or not cases had a PCP (61.9% PCP vs 57.1% no PCP, $p = 0.586$).

Conclusion. In our institution, HIV-positive patients had lower rates of compliance with standard lipid screening guidelines compared with age- and gender-matched controls. The level of compliance was not affected by the presence of a PCP. Further education to all providers is needed to ensure appropriate lipid screening in this population.

Disclosures. **All authors:** No reported disclosures.

1601. Screening for chronic obstructive pulmonary disease (COPD) in an urban HIV clinic

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Background. COPD prevalence in People Living with HIV/AIDS (PLWHA) is higher than in the general population and likely underreported. While smoking rates are higher, there is also evidence of an increased detrimental response to tobacco smoke in the lungs of PLWHA. We aimed to determine the predictive value of a COPD screening strategy validated in the general population and to identify HIV-related factors associated with decreased lung function.

Methods. A convenience sample of subjects at least 35 years of age at an HIV primary care clinic in New York City were enrolled and completed a COPD screening questionnaire and peak flow measurement. Those with abnormal results and a randomly selected 1/3 of normal screens went on to have spirometry testing.

Results. In total, 235 individuals were included in the study and 94 qualified for spirometry (89 produced interpretable results). The majority of patients were male, men who have sex with men, low income earners, had a smoking history and carried an AIDS diagnosis. Eleven subjects (12%) were found to have undiagnosed obstructive lung disease and 5 of these had COPD by GOLD criteria. The combination of positive screening questionnaire and abnormal peak flow yielded a sensitivity of 20% and specificity of 93% for COPD. Peak flow alone had a sensitivity of 80% and a specificity of 80%. Abnormal peak flow (<70% of predicted) was associated with an AIDS diagnosis ($p = 0.04$), lower nadir ($p = 0.001$) and current CD4 counts ($p = 0.001$), but only nadir CD4 remained associated in multivariate analysis ($p = 0.05$). In multivariate analysis, decreased FEV1 (<80% predicted) was associated with lower CD4 count nadir ($p = 0.04$) and having a detectable current HIV viral load ($p = 0.01$). Decreased FVC was associated with having a detectable current viral load ($p = 0.01$).

Conclusion. In summary, the combination of a screening questionnaire and peak flow had low sensitivity, but abnormal peak flow alone showed potential as a simple office-based screening tool for the diagnosis of COPD in PLWHA. In addition, measures of lung function, including peak flow, may be influenced by HIV-related factors.

Disclosures. **All authors:** No reported disclosures.

1602. Impact of IGF-1 and Sex Steroids on Bone Health in HIV- and HCV-Infected US Male Veterans

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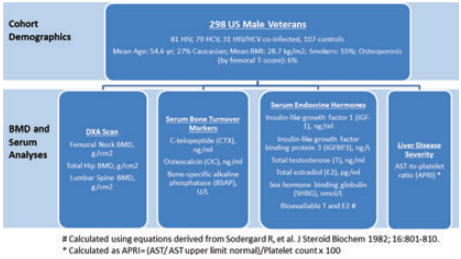
Background. The mechanisms of decreased bone mineral density (BMD) in HIV or HCV infections remain poorly understood. While HIV increases bone turnover markers (BTM), HCV does not. Insulin-like growth factor-1 (IGF-1), testosterone (T) and estradiol (E2) also play key roles in osteogenesis. In this analysis, we explored if their levels are associated with BMD in HIV or HCV.

Multivariate models examining the impact of HIV and HCV on femoral neck BMD

	Model 1 (HIV, HCV, BMI, Race, Age, Smoking)	Model 2 (Model 1 + IGF-1)	Model 3 (Model 1 + Bioavailable T)	Model 4 (Model 1 + Bioavailable E2)
HIV	-0.041 (p=0.02)	-0.044 (p=0.01)	-0.041 (p=0.02)	-0.042 (p=0.02)
HCV	-0.041 (p=0.01)	-0.044 (p=0.01)	-0.042 (p=0.01)	-0.039 (p=0.01)
IGF-1		-0.000 (p=0.80)		
Bioavailable T			-0.000 (p=0.45)	
Bioavailable E2				-0.000 (p=0.27)



Methods. This cross-sectional study recruited 298 US male veterans with HIV, HCV, HIV/HCV and non-infected controls. All HIV patients were virally suppressed on HAART. Subjects underwent BMD testing and analysis of serum biomarkers (Figure 1). The association of HIV or HCV with BMD and BTMs was evaluated in multivariable models adjusting for IGF-1, T and E2 in addition to age, race, BMI, smoking status. Correlations between IGF-1, T or E2 with BMD and BTMs were also calculated.

Results. HCV was associated with decreased levels of IGF-1 ($p < 0.01$), but HIV was associated with increased levels ($p = 0.03$). In all groups, IGF-1 levels were negatively correlated with severity of liver disease ($r = -0.214$; $p < 0.01$). However, in multivariate modeling including IGF-1, bioavailable T (or E2), neither hormone was associated with BMD, nor did they attenuate the effect of HIV or HCV on lower femoral neck BMD (model 2-4, table). IGF-1 was associated with higher bone specific alkaline phosphatase (BSAP; $p = 0.04$) and a trend toward higher osteocalcin (OC; $p = 0.09$), but not with C-telopeptide (CTX; $p = 0.13$). T and E2 were associated with lower BSAP ($p < 0.01$ and $p = 0.02$), but not with OC or CTX.

Conclusion. IGF-1 was lower in patients with HCV or greater severity of liver disease, likely representing decreased hepatic production. However, levels of IGF-1, T or E2 do not appear to explain bone loss in in HIV or HCV.

Disclosures. **R. Bedimo**, Merck and Co.: Grant Investigator and Scientific Advisor, Consulting fee, Grant recipient and Research grant; Bristol Myers Squibb: Grant Investigator and Scientific Advisor, Consulting fee, Grant recipient and Research grant; ViiV Healthcare: Scientific Advisor, Consulting fee

1603. Increased Risk of Hip Fracture Associated with Dually-Treated HIV/Hepatitis B Virus Coinfection

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Background. HIV and hepatitis B virus (HBV) infection are each associated with reduced bone mineral density, but it is unclear whether HIV/HBV coinfection is associated with an increased risk of fracture. We determined whether dually-treated HIV/HBV patients have a higher incidence of hip fracture compared to treated HBV-monoinfected, antiretroviral therapy (ART)-treated HIV-monoinfected, and HIV/HBV-uninfected patients.

Methods. We condicted a population-based cohort study among 4,156 dually-treated HIV/HBV-coinfected, 2,053 treated HBV-monoinfected, 96,253 ART-treated HIV-monoinfected, and 746,794 randomly sampled uninfected persons within the U.S. Medicaid populations of California, Florida, New York, Ohio, and Pennsylvania (1999-2007). Coinfected patients were matched on propensity score to persons in each comparator cohort. Weighted survival models accounting for competing risks were used to estimate cumulative incidences and hazard ratios (HRs) with 95% confidence intervals (CIs) of incident hip fracture for dually-treated coinfected patients compared to: 1) HBV-monoinfected receiving nucleos(t)ide analogue or interferon alfa therapy, 2) HIV-monoinfected on ART, and 3) randomly selected uninfected persons.

Results. Dually-treated coinfected patients had a higher cumulative incidence of hip fracture compared to ART-treated HIV-monoinfected (at 5 years: 1.49% vs 1.07%; adjusted HR, 1.40 [95% CI, 1.05-1.87]) and uninfected (at 5 years: 1.48% vs 0.83%; adjusted HR, 1.83 [95% CI, 1.33-2.51]) persons. The cumulative incidence of hip fracture was higher among coinfected than treated HBV-monoinfected patients (at 5 years: 0.70% vs 0.27%), but this difference was not statistically significant in competing risk analysis (adjusted HR, 2.62 [95% CI, 0.92-7.51]). At five years, dually-treated HIV/HBV coinfection was associated with 4.3 additional hip fractures per 1,000 compared to both treated HBV-monoinfected and ART-treated HIV-monoinfected persons, and 6.6 additional hip fractures per 1,000 compared to uninfected persons.

Conclusion. Among U.S. Medicaid enrollees, the risk of hip fracture was significantly higher among dually-treated HIV/HBV-coinfected patients compared to ART-treated HIV-monoinfected and uninfected persons.

Disclosures. **V. Lo Re III**, Gilead Sciences: Grant Investigator, Research grant

1604. Chronic Kidney Disease Is Associated with Bone Mineral Density Loss among Elderly HIV-infected Individuals in Japan

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Background. Reduced bone mineral density (BMD) is common in adults infected with HIV. HIV-infected individuals have more risk factors for low BMD than general population. Our aim is to evaluate BMD and risk factors for BMD loss in HIV-infected individuals in Japan.

Methods. We analyzed BMD in 178 elderly HIV-infected individuals (defined as greater than 40 years of age) who were consulting us in our outpatient clinic. Dual-energy X-ray absorptiometry scan of lumbar spine and femoral neck was obtained at the clinical visit. Low BMD was defined as T-score less than -1. HIV-related factors (CD4 cell count, HIV viral load, ART duration, tenofovir exposure years, and ritonavir-boosted protease inhibitor exposure years), and comorbidities [hypertension, diabetes mellitus (DM), dyslipidemia, chronic kidney disease (CKD), and HBV/HCV coinfection] were evaluated by reviewing medical charts. The definition of CKD was based on the 2012 KDIGO CKD classification, determined using combinations of 5 stages of eGFR and 3 grades of albuminuria. Risk factors for low BMD were determined using multivariate logistic regression analysis.

Results. The mean age was 54.1 years, 97% were Japanese, 94% were male. ART was performed in 96% of cases and 52% of them have been treated by regimens that contained tenofovir. The mean CD4 cell count was 504.2/μL and 88% had undetectable HIV-RNA level. Osteopenia and osteoporosis were diagnosed in 38% and 8% of the patients at lumbar spine, and 51% and 7% at femoral neck, respectively. The prevalence of CKD was 23%. In multivariate analysis, factors associated with low BMD at femoral neck were age [hazard ratio (HR) 1.059 per 1 year increase; 95% confidence interval (CI) 1.006-1.114; P = 0.028], body mass index (HR 0.892, 95%CI 0.805-0.989; P = 0.030), DM (HR 0.189, 95%CI 0.049-0.733; P = 0.016), and CKD (HR 2.990, 95% CI 1.138-7.854; P = 0.026).

Conclusion. In elderly Japanese HIV-infected individuals, age and CKD were correlated with femoral neck BMD loss. BMI and DM were inversely correlated with BMD loss. The influences of HIV-related factors for BMD loss were not identified in this study.

Disclosures. **All authors:** No reported disclosures.

1605. Active Marijuana Use Was Not Associated with Changes in Body Mass Index or CD4 T-Cell Countsi n HIV-Infected Patients

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Background. Marijuana (MJ) use is prevalent among HIV-infected persons. Cellular and animal models suggest that cannabinoids may affect immune modulation and HIV disease processes, but evidence on the effects of MJ use in HIV-infected persons is limited.

Methods. We conducted an observational cohort study of HIV-infected adults initiating their first antiretroviral therapy (ART) at the Vanderbilt Comprehensive Care Clinic. Self-reported MJ use in the last 7 days was assessed by a dedicated intake form at each visit. Associations between MJ use and body mass index (BMI), CD4 T cell count, and HIV RNA levels at each visit were determined. Nine random effects models adjusted for age, sex, and race were used to isolate the impact of changing MJ use on outcomes.

Table 1: Descriptive statistics for patients reporting MJ use at ≥1 visit vs never reporting MJ use

	No MJ use	MJ use ≥1 visit
Total	811	199
Gender		
Male	584 (72%)	164 (82%)
Race		
African American	293 (36%)	88 (44%)
Caucasian	404 (50%)	104 (52%)
Age at ART Initiation	36	34
Mean (SE) BMI across visits (kg/m^2)	27.19 (0.23)	25.76 (0.42)
Mean (SE) CD4 count across visits (cells/μl)	487 (10)	477 (23)

Table 2: Estimated coefficients (95% CI) by different specifications of self-reported MJ use

	Ever MJ use (Yes/No)	MJ use in last 7 days (Yes/No)	Times MJ used in last 7 days
CD4 count	0.13 (-.42–1.88)	-0.005 (-0.28–0.15)	-0.001 (-0.008–0.001)
BMI	-0.80 (-1.73–0.13)	-0.11 (-0.35–0.13)	-0.02 (-0.05–0.01)
Odds of detectable viral load (>400 copies/mL)	2.0* (1.1–3.5)	1.2 (0.7–2.2)	0.99 (0.91–1.07)

*p<0.05; all others non-significant.

Results. 4290 patient-visits from 2008 to 2011 were available from 1010 patients (Table 1). Overall, there were no statistically significant differences in CD4 count and BMI across multiple models with various measures of MJ use (Table 2). Persons who reported MJ use at any time during follow up were more likely to have at least one HIV-1 RNA >400 copies/mL.

Conclusion. Self-reported MJ use in the prior 7 days was not associated with changes in BMI, CD4 count, or detectable HIV RNA in HIV-infected persons starting ART. This suggests that active MJ use did not significantly impact these measures. Associations between MJ use and HIV RNA suppression on ART require further study.

Disclosures. **All authors:** No reported disclosures.

1606. Obesity and Weight Misperception are Common in HIV Positive Patients

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Background. Recent studies have noted an increasing prevalence of obesity in HIV+ individuals. HIV+ individuals may be concerned about being "underweight" due to HIV/AIDS related stigma. We hypothesized that HIV+ individuals would exhibit a high degree of weight misperception, defined as discordance between perceived and actual body mass index (BMI). The objectives of our study were to determine the prevalence and factors associated with weight misperception in HIV+ individuals.

Methods. We surveyed 100 HIV+ patients, aged 21 to 60 for weight perception using a self-administered questionnaire with the Stunkard Figure rating scale. BMI categories were: underweight (BMI<18.5), normal (18.5 - 24.9), overweight (25- 29.9), obese (30 - 34.9) and morbidly obese (> = 35). Patients were classified as underestimating weight if their BMI weight class was higher and overestimating weight if their BMI weight class was lower than Stunkard weight class. Concordance between actual and perceived weight class was quantified using weighted Kappa. The association between demographic characteristics and perception class was explored using the Cohen's w (nominal) or Cohen's f (continuous) effect size.

Results. The median age was 48; 56% were male, 63% were Hispanic, 23% were African-American and 69% identified themselves as heterosexual. Median year since HIV diagnosis was 12. Median CD4 count was 539; 61% had viral load < 20 copies/ml. 83% were on HAART and 22% had history of lipodystrophy. Median BMI was 27; BMI was normal (33%), overweight (30%), obese (16%) and morbidly obese (20%). Agreement between actual and perceived weight class was poor (weighted Kappa 0.39). 48% underestimated their weight class; 47% correctly identified and 5% overestimated their weight class. Among patient classified as obese/morbidly obese, 34/36 (94%) underestimated their weight class. Bisexual patients also tended to underestimate their weight. There was no association between correct weight perception and age, gender, race, CD4 count or HIV viral load.

Conclusion. Obesity was common in our cohort and was higher than recent national estimates (Medical Monitoring Project, 26.5%). Obese HIV+ patients tended to underestimate their weight class, potentially complicating providers' efforts to encourage weight loss and to reduce cardiovascular risk.

Disclosures. **All authors:** No reported disclosures.

1607. Veterans Aging Cohort Study (VACS) Index, Functional Status, and Other Patient Reported Outcomes in Older HIV-positive (HIV+) Adults

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Background. Aging HIV+ patients present challenges to overburdened health systems. To better understand this, we assessed results of comprehensive geriatric screenings in this population. We also hypothesized that age and the Veterans Aging Cohort Study (VACS) index, a validated measure of organ system dysfunction predictive of mortality, would be associated with patient-reported outcomes in older HIV+ patients

Methods. Cross-sectional survey-based study performed December 2012 – January 2014 of >50 year old HIV+ patients at two UCSF affiliated San Francisco clinics. We evaluated multiple aspects of four basic functional domains using validated measures: physical function (Activity of Daily Living/ADL, Instrumental ADL/IADL, Falls, Short Physical Performance Battery/SPPB), social support (perceived support, loneliness), mental health (depression, anxiety, post-traumatic stress/PTSD), cognitive function (Montreal Cognitive Assessment/MOCA) as well as adherence. Descriptive statistics and ANOVA analyses assessed associations between these domains with age and VACS Index scores.

Results. 359 patients were screened (median age 57; 85% males; 57% Caucasian, 30% African-American, 11% Latino; 72% >high school education). Mean CD4 count was 507 cells/mm^3, 83% had undetectable viral load, and 85% were HIV-positive > 10 years. On functional screening, 26% (91) reported difficulty with ≥1 ADL, 39% (136) reported difficulty with ≥1 IADL, and 40% reported falls in the previous year. On cognitive screening, 40% had MOCA scores < 26. In addition, 58% had findings of loneliness, 60% the lowest levels of perceived social support, 55% depression, 50% anxiety,

and 12% PTSD. Older age was associated with lower CD4 counts, increased difficulty with IADLs, and chair stand component of SPBB. VACS Index score was associated with IADL and medication adherence.

Conclusion. We are the first to report an association between VACS index and functional status in older HIV+ patients. Our surveys also revealed a high prevalence of functional, social and cognitive deficits in this population. More comprehensive assessment tools, incorporating the VACS index, are likely to improve predictive models and management paradigms for older HIV-infected individuals.

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1608. Low rates of advance directive completion among HIV-infected patients: a retrospective analysis

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Background. While HIV has become a largely chronic disease, people living with HIV (PLWH) are at increased risk for comorbid disease and premature death. As a result, this aging population is appropriate to target for advance care planning (ACP) discussions and completion of advance directives (AD). We sought to examine current ACP completion rates and factors influencing completion among PLWH.

Methods. We conducted a retrospective chart review of PLWH who receive their routine care in an HIV clinic at the University of Wisconsin Hospital and Clinics. Patients were included if they were over 18, not imprisoned or institutionalized, and were active patients within 12 months prior to November 2013. Data were extracted from the electronic health record. Demographic and clinical characteristics were reported as n (%) by AD status while univariate associations were assessed by calculating odds ratios (OR). All variables were entered into a stepwise multivariate logistic regression model to assess which factors were independently associated with AD after adjusting for important predictors. OR and 95% confidence intervals were calculated on the final model.

Results. We reviewed 588 electronic health records of PLWH. 81% of patients were male and 72% were white; mean age was 46.8 years. ADs were completed by 134 patients (23%). Of completed ADs, only 6.7% were completed at the HIV clinic, while the majority were completed in the inpatient or pre-surgical setting (44%), another outpatient or community clinic (34%), or with an attorney/notary (13%). In the final multivariate model, those who had completed an AD were more likely to be older than age 45 (OR 3.4; CI 2.0-5.8; $p < 0.001$); ever been diagnosed with AIDS (OR 1.7; CI 1.1-2.7; $p = 0.02$); have cardiovascular disease (OR 2.4; CI 1.2-4.7; $p = 0.01$), neurologic disorder excluding cerebrovascular disease (OR 5.3; CI 2.2-12.7; $p < 0.001$), chronic kidney disease (OR 3.4; CI 1.3-8.5; $p = 0.01$), or malignancy (OR 3.0; CI 1.5-6.2; $p = 0.002$).

Conclusion. In this study, a small percentage of patients in HIV care had documented AD, with only a small proportion completed in the HIV clinic. As the primary providers for many of the patients, the HIV clinic should ensure that patients are engaged in ACP. Interventions are needed to identify patients without AD and provide the necessary ACP resources in order improve AD completion rates.

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1609. Plasma markers of immune activation likely reflect related but distinct processes of cellular immune activation in HIV-infected persons before and after suppression of viremia by antiretroviral therapy: ACTG 5260

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Background. Cellular markers of immune activation are strong predictors of disease progression and comorbidities in HIV infection. It is unclear whether soluble biomarkers of T cell (sIL-2r) and monocyte (MNC) activation (sCD14, sCD163) represent robust surrogate markers of cellular immune activation during the course of antiretroviral therapy (ART).

Methods. In the ACTG A5260s study, Spearman correlations between biomarkers of T-cell and MNC activation and proinflammatory MNC (pMNCs) subsets were estimated at entry and 96 weeks in 328 HIV-infected treatment-naive subjects randomized equally to tenofovir/emtricitabine plus raltegravir or ritonavir-boosted atazanavir or darunavir. Analyses were restricted to 234 (71%) subjects who had HIV-1 RNA <50 copies/ml by week 24 and thereafter. Plasma and cellular immune markers were determined by ELISA and flow cytometry, respectively.

Results. sIL-2r and sCD163 were significantly associated with T cell activation (% CD38 + DR+ CD8 T cells) at entry and 96 weeks. sCD163 was also associated with both T cell activation and pMNCs (% CD14 + CD16+ MNCs) after successful ART. sCD14 was significantly associated with T cell activation and pMNCs only at entry. After 96 weeks of ART, sIL-2r and sCD14 were not associated with cellular markers of pMNCs (table).

	Plasma Markers					
		Week 0			Week 96	
Cellular Markers	sIL-2r	sCD14	sCD163	sIL-2r	sCD14	sCD163
% CD38+DR+ of CD8+ T cells (T cell activation)	*0.36 (<0.001)*	*0.25 (<0.001)*	*0.38 (<0.001)*	*0.18 (0.011)*	0.11 (0.11)	*0.40 (<0.001)*
% CD14+CD16+ of MNCs (pMNCs)	0.07 (0.30)	*0.27 (<0.001)*	0.06 (0.38)	-0.06 (0.40)	0.07 (0.32)	*0.16 (0.022)*
% CD163+ of MNCs (pMNCs)	-0.01 (0.90)	0.03 (0.65)	-0.02 (0.78)	-0.07 (0.29)	-0.02 (0.81)	-0.05 (0.52)

[1]Similar correlations on CD4+; [2]associations with CD16 (h) CD14 (l) not apparent.

Conclusion. There were modest associations between all plasma markers of immune activation and cellular markers of T activation in viremic subjects. However, after successful ART, only sCD163 had a modest association with cellular markers of T cell activation. Plasma markers of immune activation may reflect different immune activation pathways with differential dependence on viral replication vs immune dysregulation that is not reversed with viral suppression by ART.

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1610. Pervasive B cell Activation during Viremic HIV-1 Infection but Effective Responses with Appropriate Stimulation *in vitro*

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Background. HIV-1 infection is associated with increased rates of secondary infections and decreased antibody responses to protective vaccines. Identifying specific HIV-1-associated B cell defects may direct interventions to circumvent them.

Methods. We studied 34 viremic HIV-1-infected adults (HIV-1 + ; median CD4+ T cells 276/μL; HIV-1 RNA 320,289 copies/mL) and 20 HIV-1-seronegative age-matched control subjects. We measured frequencies and activation of circulating B cell subsets and T follicular helper cells (T_{FH}) by flow cytometry, expression of activation-induced cytidine deaminase (AID) and IL-21 by RT-qPCR, and B cell activating factor (BAFF) and IL-21 by ELISA. Cells were stimulated with surrogates for antigen (anti-IgM), cognate (anti-CD40), and soluble (IL-4) T cell factors. Values were compared by unpaired t, paired t, and Mann Whitney tests.

Results. At baseline, B cells from HIV-1+ adults showed perturbations in B cell subsets (increased immature transitional and IgM memory cells and decreased anergic cells) vs controls. Activation (CD21-) was increased across all 8 B cell subsets as were levels of B cell-activating constituents (BAFF and activated T_{FH} cells, but not IL-21) in HIV-1+ vs controls. However, upon stimulation *in vitro*, transitions from naïve to class-switch memory cells and activation of B cells from HIV-1+ increased significantly to levels comparable to those of controls, as did levels of AID, the protein that mediates antibody class switch.

Conclusion. Viremic HIV-1 infection perturbs circulating B cell subsets and activation from the earliest developmental stages of circulating B cells. However, with appropriate stimulation (cross-linking antigen and T cell factors), B cells can effectively activate and mature. These data provide impetus for novel and effective vaccine development to prevent secondary infections by circumventing these early B cell defects that may limit primary protective antibody responses.

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1611. Antibodies to conformational epitopes interfere with T20 fusion inhibition

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Background. The Human Immunodeficiency Virus (HIV) is an RNA-enveloped virus that fuses with human CD4+ cells during infection. Fusion occurs when the viral envelope glycoprotein binds with the CD4 cell receptor and two co-receptors on the T-cell. The functional viral envelope glycoprotein spike is a trimeric structure composed of three heterodimers of gp120 and gp41 proteins. When the receptor-binding domain of gp120 interacts with the CD4 receptor, it induces a conformational change in the heterotrimer that fuses the viral envelope membrane to the target cell, thus forming syncitia. Antibodies that form against structural epitopes on the surface of this heterotrimeric envelope spike are hypothesized to be more efficient at blocking this fusion. Other antibodies have been shown to interfere with the fusion inhibitor T20, an analog of the gp41 heptad repeat 2 region.

Methods. Our lab has previously isolated the antibody gene sequences of a number of trimer-specific antibodies. These bind to four seemingly conformational epitopes. We established an assay to assess functional interference with T20 fusion inhibition. We then screened a panel of control antibodies and trimer-specific and neutralizing antibodies in this assay.

Results. Two of our trimer specific antibodies that were epitope mapped to gp41 inhibit fusion of t20 in this assay. We established a production and functional screening method for antibodies that target structural epitopes to HIV and report novel findings that our trimer-specific gp41 targeting Abs interfere with T20 fusion inhibition.

Conclusion. Antibodies targeting these epitopes have implications in both potential therapy strategies and vaccine development.

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1612. Intrarenal and Systemic Inflammation and HIV-related Renal Disease

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Background. HIV-associated nephropathy is an intrarenal inflammatory disease. Proteinuria in ART-naïve patients is associated with greater systemic immune activation and independently predicts HIV disease progression, thereby suggesting nephropathy in HIV is associated with systemic immunology. However, the contributions of intrarenal and systemic inflammation to renal disease in HIV are not well understood.

Methods. Using ELISA assays, we measured paired serum and urinary levels (normalized to urine creatinine) of MCP-1, RANTES, IP-10, IL-8, and B2M in two groups of HIV-infected subjects not receiving ART [A: not initiating ART (N = 26); B: about to initiate ART (N = 19)], C: HIV-infected subjects receiving FTC/TDF/EFV (N = 30), and D: HIV-uninfected, healthy volunteers (N = 45). The Kruskal-Wallis rank sum tests were used to compare levels across groups. Spearman rank correlations were used to examine associations between biomarker levels and urine protein/creatinine ratio (uPCR), urine albumin/creatinine ratio (uACR), and estimated glomerular filtration rate (eGFR). P-values were adjusted for multiple testing with <0.05 considered significant.

Results. The median (Q1, Q3) age (y), CD4 count/μL, HIV-1 RNA $\log_{10}$c/mL, and %Black, respectively, were [A: 37 (29, 43), 585 (433, 639), 4.2 (3.7, 4.6), 62], [B: 34 (29, 42), 187 (52, 375), 5.0 (4.5, 5.6), 63], [C: 38 (30, 44), 541 (423, 960), all <1.7, 60], and [D: 34 (26, 45), 880 (724, 1164), N/A, 31]. Statistically significant differences were found across groups in all markers except for urine IL-8 and urine MCP-1, with the highest levels most often found in Group B. When combining all 4 study groups, uPCR was positively correlated with urine IL-8, urine MCP-1, urine IP-10, and serum IP-10; uACR was positively correlated with urine IL-8, urine B2M, serum IP-10, and serum B2M; and eGFR was negatively correlated with serum MCP-1 and serum B2M.

Conclusion. The levels of urine inflammatory markers tested differed by HIV status and use of virologically suppressive ART. These urine and serum inflammatory markers were differentially correlated with uPCR, uACR, and eGFR, suggesting different intrarenal and systemic inflammatory pathways may contribute to different measures of nephropathy in HIV.

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1613. Dysfunctional HDL in HIV-infected adults with suppressed viremia on antiretroviral therapy may directly increase dendritic cell maturation and contribute to immune activation

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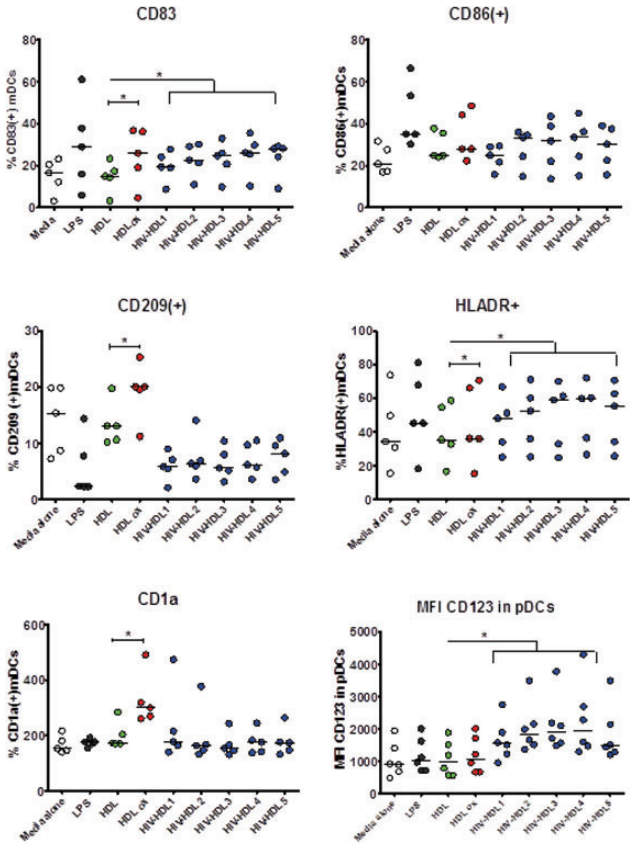
Background. While normal HDL is protective, during systemic inflammation it can be oxidized (ox-HDL) and become dysfunctional (dys-HDL). We recently showed that HIV-1-infected persons have dys-HDL that is associated with biomarkers of T cell activation, and dys-HDL upregulates T cell activation *in vitro*. Oxidized lipids regulate both innate and adaptive immunity, and may interfere with maturation of both myeloid and plasmacytoid dendritic cells (mDCs and pDCs). Given the pivotal role of DCs in T cell activation, a driver of HIV-1 immunopathogenesis, we investigated whether dys-HDL affects DC maturation *in vitro*.

Methods. Native HDL dys-HDL (by a functional assay) was isolated from 5 HIV-1 infected subjects (all males aged 21-56, median 44) with viremia <50 RNA/ml on antiretroviral therapy and normal lipid profiles (HIV-HDL). Normal HDL from healthy donors was also oxidized (ox-HDL) *in vitro*. Endotoxin (LPS; positive control), HDL, ox-HDL and HIV-HDL were added (6.25 ug/ml) in serum free media to monocyte-derived (IL-4/GM-CSF) DC (MDDC) and peripheral blood mononuclear cells (PBMCs) from healthy subjects (n = 6). Flow cytometry was utilized for expression of CD123 in pDCs (relatively specific marker for pDCs) and mDC markers CD83, CD86, HLA-DR, CD209 (DC-SIGN) and CD1a. Data were analyzed using paired t-tests.

Results. Compared to normal HDL, HIV-HDL and ox-HDL resulted in increased expression of co-stimulatory molecules HLA-DR and CD83 on mDCs (critical molecules for their interaction with T cells); CD209 (an ICAM adhesion molecule) was increased by ox-HDL but decreased by HIV-HDL. On pDCs, CD123 (α chain of IL-3 receptor) was upregulated by HIV-HDL but not ox-HDL (figure).



In vitro effects of oxidized lipids on DC markers.

Conclusion. Dysfunctional HDL in HIV-1-infected persons may upregulate differentiation of DCs and thereby contribute to immune activation despite successful virologic therapy.

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1614. High Rates of Preterm Birth and Small for Gestational Age in a Cohort of HIV Infected Women in Canada: Role of Ritonavir Boosted Regimens?

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Background. The rate of preterm delivery (PTD) among HIV positive women and the possible association with the use of Antiretroviral therapy (ART) during pregnancy remains a subject of debate. The primary objective of this study is to determine risk factors for PTD and Small for Gestational Age (SGA) among HIV infected pregnant women in Canada.

Methods. Mother-infant pairs were identified from the Canadian Perinatal HIV Surveillance Program, an active surveillance system that captures data on perinatal HIV exposure annually from 22 sites in Canada. PTD was defined as delivery at less than 37 weeks gestational age (GA), and SGA as weight less than 10th percentile for age. Multivariable logistic regression was used to adjust for available known risk factors for PTD, and accounted for the dependence between multiple pregnancies of the same woman.

Results. Between 1987 and 2013, the overall incidence of PTD was 16.26% (427 out of 2626 births), compared to a PTD rate in Canada of 8% over this time period. The majority (13.52%) were late pre-term infants (32-36 weeks GA), The overall incidence of SGA was 20.48%. Significant risk factors for PTD on univariate analysis included detectable vs undetectable viral load (VL) (OR: 1.62, p = 0.008), aboriginal vs white race (OR 1.65, p = 0.002), HIV acquisition risk factor (intravenous drug use vs heterosexual transmission, OR 2.17, p < 0.001), and no ART vs any ART (OR 1.58, p = 0.004). Among ART treated women, there was an increased risk of PTD among those treated with boosted vs unboosted PIs (OR 1.58, p = 0.004), and more specifically, among women starting boosted PIs at 21-27 weeks as compared to 13-20 weeks (OR 3.17 p = 0.01). In the multivariable analysis adjusting for maternal race, HIV acquisition risk factor and ART start time, the risk of PTD associated with the use of boosted PIs remained statistically significant (aOR 1.48, p = 0.01). There was no association between SGA and ART exposure.

Conclusion. Our results show that HIV positive pregnant women have high rates of PTD and SGA. A modifiable risk factor may be the type of ART regimen used, as an increased risk of PTD was seen in association with the use of ritonavir boosted regimens. Further study is needed to identify the safest ART regimens to be used in pregnancy.

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1615. Pregnancy-Related Outcomes and Mortality in the Years Following Pregnancy among Women Perinatally Infected with HIV — New York City, 2005–2011

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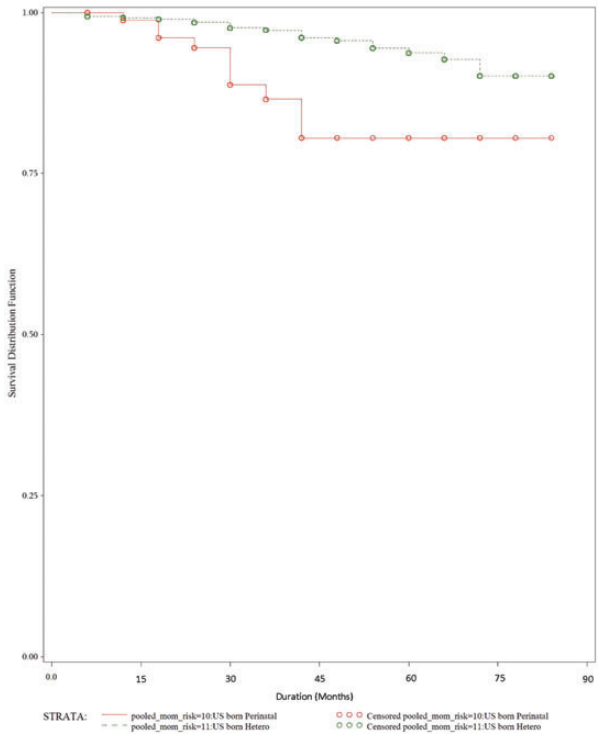
Background. Survival among individuals with perinatally-acquired HIV has improved in the United States due to the availability of effective antiretroviral therapy (ART). In New York City (NYC), an epicenter for the early HIV epidemic, there is an aging cohort of perinatally infected individuals who have reached their reproductive years. The aim of our study was to describe pregnancy outcomes and mortality in the years immediately following pregnancy among perinatally infected women who delivered in NYC during 2005–2011.

Figure 1. Survival Analysis of U.S.-born HIV-Infected Pregnant Women by Mode of Acquisition — New York City, 2005–2011



Methods. We utilized data from the NYC HIV Surveillance Registry and the Enhanced Perinatal Surveillance system, an active surveillance system targeting 16 hospitals which account for approximately two-thirds of deliveries among HIV positive mothers in NYC. We compared pregnancy and subsequent mortality outcomes among U.S.-born perinatally infected mothers to U.S.-born heterosexually infected mothers and conducted survival analyses.

Results. During 2005–2011, there were a total of 123 deliveries among 95 U.S.-born perinatally-infected mothers and 612 deliveries among 503 U.S.-born heterosexually infected mothers. Perinatal mothers were younger at the time of delivery (median: 21 vs 29 years), more likely to be aware of their HIV status and to use ART during their pregnancy but less likely to use substances during their pregnancy. At the time of delivery, perinatal mothers were more likely to have viral loads >1,000 copies/ml (35.8% vs 20.1%) and severe immunosuppression (15.4% vs 6.7%), and to deliver by elective C-sections (66.7% vs 51.5%). There were no differences in receipt of prenatal care, use of intrapartum and neonatal ART, mother-to-child transmission (MTCT) rate (1.6% vs 1.3%), gestational age and birth weight of the delivered infants, and infant mortality. Perinatal mothers, while no more likely to die in the year following delivery, were more likely to die in the ensuing four years (figure) (p = 0.0029).

Conclusion. There were no differences between perinatally- and heterosexually-infected mothers in pregnancy-related outcomes and maternal death. However, perinatally-infected mothers were more likely to die during the next four years, likely related to their more advanced HIV disease.

Disclosures. **All authors:** No reported disclosures.

1616. Long Term Outcomes of a Cohort of HIV-Infected Children in Mexico City, 1998-2013

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Background. Worldwide, morbidity and mortality associated with HIV in children has decreased. In Mexico the information available is limited. We describe the sociodemographic features, clinical manifestations, laboratory parameters, antiretroviral history and the follow up of a cohort of HIV infected children during 1998-2013.

Methods. We reviewed medical records and database of a cohort of children with diagnosis or suspected HIV infection, which were in follow up at Pediatric HIV Clinic, National Autonomous University of Mexico/General Hospital of Mexico.

It was obtained sociodemographic, clinical and laboratory features at baseline and last visit data.

Results. A total of 669 children and adolescents with diagnosis or suspected HIV infection attended the study period; 445 children was non-infected at follow up (217 children <2 years and 228 children > 2 years). In 224 children HIV/AIDS diagnosis was established, 54% were male. HIV transmission was perinatal in 95% of the cases. 52% were residents of Mexico City.

During admission to the Clinic, median age was four years (0-16.8 years). 139 (62%) patients were in advanced diseases. Median viral load was 689 439 cop/mL (300 - > 10,000,000). Median CD4+ count was 666 del/uL (3-3254).

At the time of this study, 62% were orphans. Median CD4+ count was 754/uL (12-2867) and we observed undetectable viral load (<40 copias) in 78.8% of the children. They had received antiretroviral treatment on average during 89 months.

During the study period there was a loss of follow-up of 42 (19%) children, 15 patients died and 11 were transferred to adult service. Twenty five patients were hospitalized, the most, with pneumonia (36%).

Conclusion. Diagnosis of pediatric HIV cases in Mexico continue to occur despite interventions to eliminate the number of cases. The diagnosis of HIV in the population studied was performed in most cases when they had advanced stages of the disease. Although morbidity and mortality has decreased mainly secondary to HAART, efforts in this age group should be directed to the elimination and early diagnosis of new cases.

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1617. Safety, Tolerability, and Antiretroviral Activity of Raltegravir in HIV-1 Infected Russian Children and Adolescents – a 24 Week Study

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Background. Raltegravir (RAL) is indicated in combination with other antiretroviral therapies (ARTs) for the treatment of HIV-1 infection in pediatric patients (pts) 2-18 years old (yo) in the US and elsewhere.

Methods. This was a multicenter, open-label, noncomparative, 24-week study of 2 oral formulations of RAL in Russian children and adolescents with HIV-1 infection. Pts 12 to <18 yo received the film-coated tablet (400 mg bid). Pts 2 to <12 yo (weight [wt] ≥7 to <25 kg) received the chewable tablet (wt-based dose of ~6 mg/kg, maximum 300 mg bid). Pts 6 to <12 yo (wt ≥25 kg) could receive either formulation. Safety was the primary endpoint and included all enrolled pts who received at least one dose of RAL. For efficacy, missing HIV RNA (vRNA) values were handled with the Observed Failure approach.

Results. Thirty-two pts were enrolled; 4 received the film-coated tablet (median age 10.5 y) and 28 received the chewable tablet (median age 7 y), in addition to background ART chosen by the investigator. The majority were white (97%) and treatment naïve (81%). At baseline, median vRNA was 4.6 (range 3-6) $\log_{10}$ copies(c)/mL, and median CD4 count was 518 (range 22-1295) cells/mm^3. Twenty-nine pts (91%) completed the study. Clinical adverse events (AEs) were reported by 12 pts (37.5%), all on the chewable tablet; 4 (12.5%) had AEs that were considered drug-related: diarrhea, vomiting, abdominal pain/nausea, and somnambulism; all resolved and none led to discontinuation. One patient (3%), who received the chewable tablet, had a laboratory AE (decreased platelet count), which was considered drug-related and resolved after 84 days. No serious AEs were reported. At week 24, 86.2% of pts achieved ≥1 $\log_{10}$ decline from baseline vRNA or vRNA <200 c/mL, and 44.8% and 72.4% had vRNA <40 and <200 c/mL, respectively. The mean increase from baseline in CD4 count was 267 cells/mm^3. Virologic failure occurred in 4 pts; post-baseline RAL resistance mutations were identified in 2 of the 3 pts with genotype data available: L74I + N155H, and L74I alone.

Conclusion. In HIV-infected Russian children and adolescents 2 to <18 yo, RAL given as the 400-mg film-coated tablet or the pediatric chewable tablet, in combination with other ARTs for up to 24 weeks, was generally safe and well tolerated, had a favorable antiretroviral effect, and demonstrated immunological benefit.

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1618. Elevated IP10 Associates with CD8 Cell Activation and Low CD4 in Perinatally Acquired HIV Infection

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Background. High levels of interferon gamma-induced protein (IP10) associate with rapid disease progression, chronic immune activation and HIV-1 replication in adults; however, the association of this cytokine with HIV disease in perinatally HIV infected children and adolescents, is not established.

Methods. We measure plasma IP10 levels by Luminex and CD8+ T cell activation (HLA-DR+ and CD38+) by flow cytometry. HIV+ patients are parsed into viremic (n = 28) and aviremic (n = 11) (HIV RNA < 400 or ≥ 400 copies/ml). Wilcoxon rank-sum is used to compare groups and Spearman's coefficient is used for correlation analysis.

Table 1: Immunologic parameters

Outcome	HIV- ‡	Aviremic ‡	Viremic ‡	*p*
IP10 *	182.1(118.2-227.6)	485.9 (289.7-976.1)	1086.9 (425.8-2408.6)	<0.001 †
CD4+ %		30.9 (23.2-39.2)	28.0 (19.0-39.0)	-
CD8+ %		35.2 (30-47)	47.2 (32.4-54.1)	-
CD8+CD38+ %		12.0 (8.0-14)	20.5 (16.0-34.0)	0.001
CD8+HLA-DR+ %		10.0 (4.0-21)	23.0 (14.0-33.0)	0.01

Table 2: Correlation analysis

	IP10		Early cARV therapy	
Outcome	r	*p*	r	*p*
CD4 %	-0.57	**<0.001**	-0.50	**0.001**
CD8 %	0.43	**0.01**	0.47	**0.002**
CD8+CD38+ %	0.37	**0.04**	0.13	0.43
CD8+ HLA+DR+ %	0.53	**0.002**	0.32	**0.04**
IP10			0.37	**0.03**

*pg/ml; ‡ median (IQR), † Viremic vs HIV-.

Results. 39 HIV+ on cARV [median CD4 % 30.2 IQR (23.2-39.4) and HIV RNA1.8 $\log_{10}$(1.6-3.0) copies/ml] and 14 HIV- are studied. HIV+ have significant higher concentrations of IP10 compared with HIV- ($P < 0.0001$); especially viremic individuals (Table 1). We observe significantly higher % of T cell activation markers in viremic compared with aviremic (Table 1). Higher levels of IP10 correlate with higher CD38 % and HLA-DR and lower CD4 % (Table 2). Lastly, early cARV therapy correlates with lower levels of IP10, CD8 %, CD8+ HLA-DR %, and higher CD4 % (Table 2).

Conclusion. Perinatally HIV infected children and adolescents have a pattern of IP10 elevation comparable to HIV infected adults. Notably, IP10, a product of monocytes and dendritic cells, is significantly elevated-especially in viremic children- and associates with T cell activation and low CD4 %. The results support the view that IP10 is secreted in part as a direct effect of viral replication. Furthermore, our data suggest that early initiation of cARV might help to prevent immune system activation and disease progression in this population.

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1619. Western Blot Seroreversion Pattern among Uninfected Children Perinatally Exposed to Human Immunodeficiency Virus

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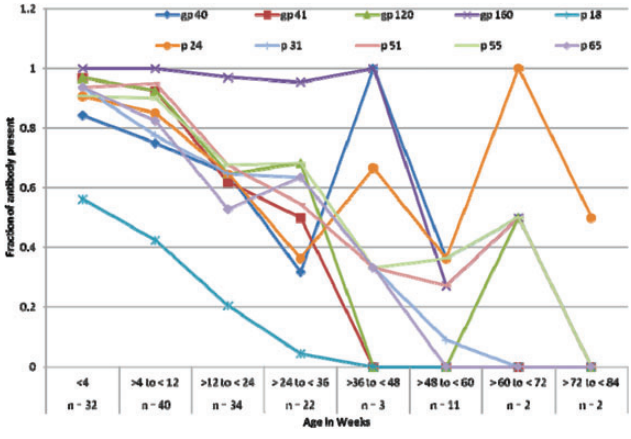
Background. Over the years, the seroreversion time among uninfected children perinatally exposed to Human Immunodeficiency Virus (HIV) has increased. The mechanisms for this phenomenon are not well understood. In addition, little is known regarding seroreversion pattern of antibodies to HIV among exposed but uninfected children born to HIV-1 infected women in the era of highly active antiretroviral therapy. The objective of our study was to determine the HIV antibody seroreversion patterns in this unique population.

Methods. A retrospective review of infants born to HIV-1-infected mothers from January 1, 2009 to December 31, 2013 evaluated at the University of South Alabama Family Specialty Clinic was performed. Infants were included in the study if HIV infection was ruled out by HIV polymerase chain reaction assays, documentation of seroreversion *and* if they have had at least one HIV western blot test result during the same period. Demographic, clinical and laboratory information on the infant and mother were collected from the medical records. Uninfected infants who had not seroreverted yet, even if they have had a western blot test at some point, were excluded.



Results. Fifty-two infants were included in the study and all of them seroreverted by a mean age 466 days (range 278-980, median 422). Out of the 52, 31 (60%) were males and 41 (79%) were African-American. Mean gestational age was 36.5 weeks (range 27-40, median 38). Mean maternal age and duration of maternal infection at the time of delivery was 28.5 years and 59.3 months, respectively. Latest viral load before delivery was <100 copies/ml for 52% of the mothers, while 25% had >1,000 copies/ml.

Aggregate of the infants' specific HIV antibody by western blot were plotted over time to determine the pattern of antibody decay from 0 to 84 weeks of life at 12 week intervals (figure). Antibody decay occurred more rapidly for the p18 antibody while p24 antibody was detected the longest.

Conclusion. p18 antibody decay occurs first and may be an early predictor of full seroreversion among HIV exposed but uninfected infants. Knowing the pattern of antibody loss may have implications in clarifying the status of an infant in a more expedited fashion.

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1620. Extraintestinal *Clostridium difficile* infections: A Single Center Experience

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Background. *Clostridium difficile* is the most common cause of infectious diarrhea in hospitalized patients, but is rarely isolated from sites outside the gastrointestinal tract. Considering the increasing burden of infection due to this organism in both the community and health care settings, the increased virulence of some strains, and the expansion of "at risk" patient populations, an increasing number of extraintestinal *C. difficile* infections (CDI) might be anticipated.

Methods. A retrospective chart review was conducted to identify patients with extraintestinal *C. difficile* culture isolates from January 1, 2004 to December 31, 2013. Medical records were reviewed and data, including demographics, microbiology, risk factors, management and infection outcomes, were abstracted.

Results. Overall, 40 patients with extraintestinal CDI were identified; 25 had abdominopelvic infections; 11 had bloodstream infections; three had wound infections and one had pulmonary infection. *C. difficile* was isolated with other organisms in 63% of cases. A majority (85%) of infections were nosocomial. Risk factors associated with extra-intestinal CDI included surgical manipulation of the gastrointestinal (GI) tract (88%), recent antibiotic exposure (88%), malignancy (50%) and proton pump inhibitor (PPI) use (50%). Diarrhea was present in 18 patients (45%), 12 of whom had *C. difficile* PCR positive stool samples. All isolates were susceptible to metronidazole and piperacillin-tazobactam. Management included both antimicrobial therapy and guided drainage or surgical intervention in all but one patient. The infection-associated mortality rate was 25%, with death occurring a median of 16 days (range 1-61 days) after isolation of *C. difficile*.

Conclusion. Extraintestinal CDI is uncommon, and often occurs in patients with surgical manipulation of the GI tract and well-recognized risk factors for intestinal CDI. Management of extraintestinal CDI includes both antimicrobial and surgical therapies. Extraintestinal CDI is characterized by poor outcome with high mortality.

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1621. US Costs and Outcomes Associated with *Clostridium difficile* Infections: a Systematic Literature Review, Meta-analysis, and Mathematical Model

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Background. Information about the health and economic impact of *C. difficile* infections (CDI) in the US can inform investments in prevention and treatment interventions. The objective was to estimate the morbidity, mortality, and cost burden of CDI in the US using a systematic literature review, meta-analysis and economic model.

Methods. We searched MEDLINE, CINAHL, Cochrane Library, NHS Economic Evaluation Database, Web of Science and Scopus for multicenter studies published in the US from 2000-2014 that evaluated CDI outcomes or costs. Studies were included in the economic analysis if they either measured post-infection costs, post-infection length of stay (LOS), or propensity score-matched CDI patients to non-CDI controls. We also included studies that evaluated CDI-associated mortality with a control group. We created an economic model using TreeAgePro 2014. We used gamma distributions for cost estimates, beta distributions for probabilities, and lognormal distributions for relative risks. The analysis consisted of 1,000 first order simulations and 10,000 second order simulations.

Results. 22 studies that evaluated mortality due to CDI were pooled, and CDI was associated with a 2.5-fold increase in mortality compared with other patients (pooled RR = 2.54; 95% CI: 1.89, 3.40). Only 4 low to moderate quality studies evaluated costs of CDI. The mean CDI-attributable cost of the index hospitalization ranged from $8,426 to $48,500. The mean costs per CDI after discharge were $1,592 for outpatient visits and $14,847 for readmissions. When these were adjusted to 2013 US dollars and included in the economic model, the mean total cost of a CDI was $32,198 (SD = $9,798). Of the 3 studies that evaluated LOS using propensity matching, the mean CDI-attributable LOS was 12.3 days. When this excess LOS was multiplied by an average cost per day from a private 3rd party payer perspective, CDI cost an average of $56,663 (SD =$19,804).

Conclusion. Pooled estimates from the current literature suggest that CDI is associated with large health and economic burdens. Yet, most of the studies were of mid-to-low quality and may overestimate the outcomes, as they did not exclude pre-infection LOS and costs. These estimates should be used with caution and high quality studies should be done.

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1622. Statin Use and Hospital-onset *Clostridium difficile* Infection; A Case Control Study

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Background. Hospital-onset *Clostridium difficile* infection (CDI) is the leading infectious cause of healthcare acquired infectious diarrhea. In addition to adding to morbidity and mortality in hospitalized patients, it is adding significant financial burden with estimated attributable costs of $436–$580 million in 2003. In this study we aim to evaluate association between statin use and risk of hospital-onset C. *diffcile* infection

Methods. This matched case-control study was conducted in a 310-bed community hospital catering suburban population. Hospital-onset CDI cases were identified as patients developing diarrheal illness beyond 48 hours of hospital admission and tested positive for C. *difficile* on stool assay (enzymeimmune assay for toxin A and B or polymerase chain reaction for toxin producing gene) from October 2005 through September 2012. Controls (matched for age, gender, proton pump inhibitor (PPI) use, length of hospital stay and Elixhauser co-morbidity index, 2:1) were obtained from cohort of patients admitted to medical service during same period. Use of statin was reviewed during hospital stay and/or prior to admission. Two-tailed p-value of <0.05 was considered significant.

Results. Total of 269 cases and 538 controls were included in study. Mean age, gender, PPI use, length of hospital stay and Elixhauser co-morbidity index were comparable amongst cases and controls. Statin use was not associated with hospital-onset CDI, chi-square 0.024, p = 0.8762, p = 3694. Relative risk was 0.91 (95% CI 0.73 to 1.22).

Conclusion. Our study suggests that use of Statins doesn't alter the risk of hospital-onset CDI infection.

Disclosures. **All authors:** No reported disclosures.

1623. Ertapenem is Associated with an Increased Risk of *Clostridium difficile* Infections Among Surgical Patients

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Background. We observed high rates of *Clostridium difficile* infections (CDI) among 2 surgical units at UCSF despite improvements in hand hygiene, adherence to contact precautions, and environmental cleaning. Our objective was to identify risk factors for CDI among surgical patients at our institution.

Methods. We designed a case-control study that included 46 patients with hospital-onset CDI who were directly admitted to 2 surgical units between July 2012 and September 2013. Each case was matched to 2 controls without CDI selected from the same unit and calendar quarter by incidence density sampling. We used conditional logistical regression for bivariate analysis and included risk factors with a p-value less than 0.2 into a final multivariate model to identify independent risk factors for CDI (p-value < 0.05).

Results. Cases and controls were similar in demographics, underlying comorbidities, need for emergency surgery, total parenteral nutrition, enteral feeding, use of bowel prep and gastric acid suppressants. Multivariate analysis revealed that receipt of ertapenem (OR = 4.41, p = 0.003; 95% CI 1.7-11.7), cystectomy (OR 5.29, p = .03; 95% CI 1.1-24.5) and Whipple procedure (OR 5.58, p = .048, OR 1.02-30.6) were associated with a significantly increased risk of CDI. The median ertapenem duration among the cases and controls was 1 day of therapy (DOT), interquartile range 0.5 DOT to 1 DOT. We noted that ertapenem prophylaxis was highly associated with CDI risk on bivariate analysis (OR 4.2, p = .003, 95% CI 1.64-10.8) and this also held true when included in multivariate analysis (OR = 3.89, p = .009, 95% CI 1.41-10.8).

Conclusion. Surgical procedures with prolonged operative time such as cystectomies and Whipple procedures may be independent risk factors for CDI, although numbers were small in our study. Ertapenem, particularly its use as prophylaxis, was associated with an increased risk of CDI among surgical patients, which may offer an appropriate target to improve antibiotic stewardship among the surgical patient population.

Disclosures. **All authors:** No reported disclosures.

1624. Risk Factors for Hospital-Acquired *Clostridium difficile*

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Background. Hospital-acquired *Clostridium difficile* infection (HA-CDI) increases morbidity, length of stay, and hospitalization costs. Environmental contamination is suspected of increasing risk for HA-CDI, but the effect size has not been characterized. We created a risk-factor model for HA-CDI, including an indicator of whether the patient inhabited a hospital room recently occupied by a CDI case.

Methods. All cases of HA-CDI from January 2012 through December 2013 were identified. Three inpatient controls for each case were randomly selected from the same time period. Gender, age, recent exposure to 3rd-generation cephalosporins or fluoroquinolones, recent proton pump inhibitor (PPI) exposure, and length of stay (LOS) were collected. For cases, LOS was limited to the number of days from admission to onset. After sensitivity analysis indicated likely confounding, patients with LOS greater than two standard deviations from the mean were excluded from the analysis. The room location history of each case and control was then compared with those of all cases to determine whether a patient subsequently inhabited the same hospital room as a previous case within 5 months of the previous case's onset ('CDI room'). Univariate analysis using the Chi-square or Wilcoxon rank-sum test assessed the association between each risk factor and HA-CDI. Logistic regression was performed for variables with univariate p-value < 0.3.

Results. 96 cases and 288 controls were identified; 90 cases and 281 controls were included in the analysis. Univariate analysis indicated that gender, LOS, and CDI room were significantly associated with HA-CDI. In multivariate logistic regression, staying in the same room as a previous CDI case was the only significant predictor of HA-CDI.

		Univariate		Multivariate	
Risk Factor	No CDI (n=281)	CDI (n=90)	P-value	OR	95% CI
CDI Room	57 (20)	38 (42)	<0.001	2.6	1.5-4.4
Recent Antibiotics	18 (6)	11 (12)	0.07	1.6	0.7-3.8
Recent PPI	25 (9)	12 (13)	0.22	1.5	0.7-3.3
Age, mean (standard deviation)	49 (18)	52 (17)	0.13	1.0	0.9-1.0
Male	132 (47)	56 (62)	0.01	1.6	0.9-2.7
LOS, mean (standard deviation)	8 (7)	10 (8)	0.001	1.1	0.9-1.3

Conclusion. Environmental contamination may be a more important factor in HA-CDI than previously thought. Effective cleaning procedures for rooms occupied by patients with CDI should be emphasized.

Disclosures. **All authors:** No reported disclosures.

1625. Evaluation of the Diagnosis and Management of Hospital-Onset Healthcare Facility Associated (HO-HCFA) *Clostridium difficile* Infection at a Veterans Affairs (VA) Hospital

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Background. *Clostridium difficile* infection (CDI) is a growing problem. Deciding which patients will benefit from CDI testing remains a challenge as only 10-20% of nosocomial diarrhea is due to *C. difficile*. Testing for CDI without evaluation for common causes of nosocomial diarrhea and testing asymptomatic patients may lead to detection and unnecessary treatment of asymptomatic *C. difficile* carriage. Our objective was to define the characteristics and appropriateness of CDI testing as well as management of confirmed cases, and identify opportunities for quality improvement.

Methods. We conducted a retrospective chart review of patients undergoing testing for HO-HCFA CDI from July 1, 2012 to July 31, 2013. Each CDI testing episode was evaluated for documentation of a clinical syndrome consistent with CDI (> 3 unformed stools in 24 hour period), laxative use within 72 hours prior to testing and receipt of concurrent enteral nutrition. Each CDI case was classified by severity and treatment assessed for agreement with guidelines.

Results. 117 CDI testing episodes occurred in 92 patients, of which 79% (93/117) were negative. 21% of patients lacked documentation of > 3 unformed stools in 24h. 42% (49/117) of patients received at least one dose of laxative prior to CDI testing. Of those who tested negative, 39% (36/93) were receiving laxatives prior to testing, and 33% (31/93) were receiving enteral feeds at the time of testing. Of those with confirmed CDI, 100% (9/9) with mild-moderate infection were treated appropriately, 0% (0/5) with severe infection, and 0% (0/2) with severe-complicated infection. Asymptomatically-colonized patients were treated 88% (7/8) of the time.

Conclusion. A significant proportion of CDI tests at our facility are avoidable due to testing of asymptomatic patients and those with alternative explanations for nosocomial diarrhea. Excessive CDI testing may lead to detection and inappropriate treatment of asymptomatically colonized patients. A significant number of patients are not treated according to recommended guidelines. We identified significant variations from best practices in diagnosis and management of CDI among our Veteran population, which will serve as opportunities for future antimicrobial stewardship intervention.

Disclosures. **All authors:** No reported disclosures.

1626. The relationship of Bristol Stool Scale to Clostridium difficile infection

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Background. The Bristol Stool scale is a graded visual scale that classifies stool density, with scores of 1 (most dense stool) through 7 (liquid stool). At our institution, we require a Bristol score of ≥5 for stool specimens to reduce inappropriate *C. difficile* testing. We determined the relationship between the Bristol scale and the rates, complications, severity of inpatient *C. difficile* infection (CDI), and whether Bristol score 5 stools should be excluded from testing due to a lower rate of toxin detection.

Methods. We recorded the Bristol score on all stool specimens from adult inpatients tested for *C. difficile* over a 10-month period. Two inter-rater reliability studies were performed. We tested using an algorithm of enzyme immunoassay (EIA) for glutamate dehydrogenase and toxins A/B followed by molecular amplification and detection (MAD) for indeterminate EIA results. Hospital-onset CDI was defined by National Healthcare Safety Network criteria for assays sent 48 hours after hospitalization. Severe hospital-onset CDI was defined using the criteria of Zar et al (Clin Infect Dis 2007; 45:302-7). Positive *C. difficile* assays, severe CDI, and complications of hospital-onset CDI (colectomy, ICU transfer, death) were compared between Bristol scores using the χ^2.

Results. There were 3005 specimens tested for *C. difficile*. The Fleiss Kappa score for inter-rater reliability was 0.675. *C. difficile* assays were positive in 43 (15.0%), 144 (13.6%), and 177 (10.7%) specimens of Bristol scores 5, 6, and 7, respectively (p = 0.031). Semi-formed stools (Bristol score 5 or 6) were more likely to be positive by MAD compared to liquid stool (Bristol score 7) (RR = 1.50, 95% CI 1.11-2.04). Rates of hospital-onset CDI, severe CDI, and complications of CDI did not differ by Bristol score.

Conclusion. *C. difficile* toxin was more likely to be found in semi-formed stool. Bristol 7 stools had the lowest rate of detection, suggesting a lower clinical threshold to test liquid stools. The rate of toxin detection by MAD was 50% higher for semi-formed vs liquid stools, indicating a lower concentration of *C. difficile* toxin in semi-formed stool. In conclusion, when MAD testing is used, semi-formed stools account for a meaningful proportion of *C. difficile*-positive specimens.

Disclosures. **All authors:** No reported disclosures.

1627. Diagnostic Accuracy of Loop-Mediated Isothermal DNA Amplification (LAMP) Assay for Detection of *Clostridium difficile* Infection (CDI): a Meta-Analysis

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Background. Nucleic acid amplification tests including real-time polymerase chain reaction and loop-mediated isothermal DNA amplification (LAMP) are

currently used as standalone diagnostic tests of *C. difficile*infection (CDI) in the United States. These assays are reported to have similar sensitivity and specificity to toxigenic culture. The aim of this meta-analysis study is to evaluate the diagnostic accuracy of LAMP in detecting CDI.

Methods. We searched MEDLINE and 4 other databases to identify diagnostic accuracy studies that compared LAMP with cell culture cytotoxicity neutralization assay (CCCNA) or anaerobic toxigenic culture (TC) of *C. difficile*from database inception to 2013. Screening for inclusion, data extraction, and quality assessment were carried out independently by 2 investigators and disagreements resolved. Data in the tables, figures, or text were independently extracted by 2 authors. We used the Mantel-Haenszel (MH) random effects model to calculate summary receiver operating characteristic curves, diagnostic odds ratios and their 95% CIs.

Results. A search of the databases yielded 16 studies (6,798 samples) that met the inclusion criteria. When TC was used as the gold standard (n= 14), the pooled sensitivity was 0.95 (95% CI, 0.93-0.96; $I^2 = 37.7$); specificity, 0.98 (95% CI, 0.97-0.98; $I^2 = 94$); and diagnostic odds ratio, 1180 (95% CI, 537-2592; $I^2 = 62.2$). With CCCNA as a gold standard (n = 3), the pooled sensitivity was 0.90 (95% CI, 0.82-0.95; $I^2 = 64.8$); specificity, 0.95 (95% CI, 0.92-0.97; $I^2 = 94.8$); and diagnostic odds ratio, 346 (95% CI, 95-1255; $I^2 = 0$).

Conclusion. LAMP appears to have high diagnostic accuracy for identifying CDI. Although there was high heterogeneity among the studies, this meta-analysis suggests that LAMP is a useful diagnostic tool with high sensitivity and specificity for detecting CDI.

Disclosures. **All authors:** No reported disclosures.

1628. Accuracy of Healthcare Facility-Onset *Clostridium difficile* Classification

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Concise Statement. We compared the day of diagnosis of healthcare facility-onset *Clostridium difficile* with the day of symptom onset to determine the accuracy of our classification.

Background. *Clostridium difficile* (*C. difficile*) is a publically reportable infection which contributes to 14,000 deaths yearly in the United States. The National Healthcare Safety Network defines healthcare facility-onset (HO) *C. difficile* as laboratory-confirmed cases identified on day 4 or greater of admission to a facility. However, HO cases may be misclassified if patients are symptomatic prior to day 4 without laboratory confirmation. Our objective is to determine if community-onset (CO) cases are being misclassified as HO cases.

Methods. We reviewed 121 HO cases of *C. difficile* from January 2013 to December 2013. We compared the day of laboratory diagnosis of *C. difficile* by PCR with the day of the first documented occurrence of diarrhea, including loose and liquid stools.

Results. Thirty-seven of the 121 HO cases of *C. difficile* had diarrhea documented prior to day 4, representing 30.58% of our HO cases.

Timing of *C. difficile* Detection Compared to Onset of Symptoms

Quarter	C. difficile detected ≥ day 4 (No. of cases)	Onset of diarrhea ≤ 3 days (No. of cases)	Opportunity for early detection (% of cases)
Q1	27	7	25.93
Q2	29	9	31.03
Q3	30	6	20
Q4	35	15	42.86
Total	121	37	30.58

Conclusion. Approximately 31% of HO cases of *C. difficile* had the onset of diarrhea prior to day 4 of hospitalization. The potential exists that these cases could have been classified as CO if specimen collection occurred closer to symptom onset. Timely diagnosis of *C. difficile* may have implications for reporting accuracy, early intervention, and improved patient outcomes. Future education initiatives for medical and nursing staff should focus on early disease recognition.

Disclosures. **All authors:** No reported disclosures.

1629. The Incidence of *Clostridium difficile* Infection in Hospitalized Patients with Cystic Fibrosis in the United States

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Background. Patients with cystic fibrosis (CF) are reported to have a high asymptomatic carriage rate of *Clostridium difficile* (*C. difficile*). However, most reports are limited to case reports and case series. The objective of this study was to investigate the incidence of *C. difficile* infection (CDI) in hospitalized patients with CF in the United States.

Methods. Data were obtained from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality for the years 2002 to 2010. Data were weighted to generate national-level estimates.

Results. For the year 2010, there were a total of 9,706,097 weighted hospital discharges in the 18 – 44 year age group. In this age cohort, 32,541 patients had a diagnosis of CDI and 19,278 patients had a diagnosis of CF. The incidence of CDI in the hospitalized CF population was 1.6% compared to an incidence of 0.3% in the non-CF hospitalized population ($P < 0.05$). After matching to control for demographic factors and comorbidities; patients with CF continued to have a higher risk for CDI than their matched counterparts (OR 3.0 95% CI 2.6-3.5). Patients with CF + CDI had an overall worse outcome than patients with CDI only ($P < 0.05$). Utilizing a multiple variable regression model, patients in the CF + CDI group continued to demonstrate poor outcomes compared to patients in the CDI only group. This was evident as a higher risk of death (adjusted odds ratio (aOR) 3.1 95% CI 1.9-5.1), colectomy (aOR 2.6 95% CI 1.3-5.3) and higher hospital charges (adjusted regression coefficient $42,000 95% CI $22,000- $62,000). The difference in LOS between the two groups was not significant (adjusted regression coefficient 3.3 days 95% CI 0.81-5.8 days). Between the years 2002 – 2010, the incidence of CDI in the hospitalized CF population (ages 18 – 44 years) increased from 0.9% to 1.6% whereas the incidence of CDI in the corresponding non-CF population increased from 0.2% to 0.3%. For both these groups, this represented a significant increasing trend in the incidence of CDI ($P < 0.05$).

Conclusion. There was an increasing trend in the incidence of CDI complicating CF in the years 2002 - 2010. CDI had worse outcomes (higher risk of death, colectomy and hospital charges) in the setting of CF.

Disclosures. **All authors:** No reported disclosures.

1630. Excess Length of Stay Attributable to *Clostridium difficile* Infection (CDI) in the Acute Care Setting: A Multi-State Model

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Background. Evaluation of the economic impact of interventions designed to reduce the incidence of *Clostridium difficile* infection (CDI) depends on accurate estimates of healthcare resource use attributable to infection. Studies that do not account for the timing of infection overestimate attributable length of stay (LOS). The purpose of this study was to evaluate the excess LOS due to CDI using a multi-state model

Methods. We conducted a retrospective cohort study of all patients hospitalized on a general medical, surgical, or intensive care unit within the US Department of Veterans Affairs (VA) health care system between January 1, 2005 and December 31, 2012. A diagnosis of CDI was based on a positive laboratory result by enzyme immunoassay or cytotoxin test. A multi-state approach, implemented through the *etm*package in R, was used to estimate the excess LOS attributable to CDI while accounting for the timing of infection. Confidence intervals were estimated using bootstrapping techniques. A composite outcome of discharge or death was used. Estimates from the multistate model were compared to traditional estimates, including crude comparisons, ordinary least squares (OLS), and a generalized linear model (GLM) with a log link and gamma distribution

Results. During the study period, 4.2 million Veterans were followed up for nearly 22 million patient-days of observation. CDIs were observed in 43,661 (1%) of hospitalizations. The median LOS among patients with and without CDI was 10 (IQR: 17) and 3 (IQR: 4) days, respectively, for a crude difference of 7 days ($p < .0001$). OLS regression returned an estimated excess LOS of 14.3 (95%CI: 14.0 – 14.6) days. The estimated increase in LOS from the GLM model was 7.0 (95% CI: 6.9 – 7.1) days. When accounting for the timing of infection in a multi-state model, the attributable LOS was estimated to be 2.28 (95% CI: 2.14 – 2.41) days

Conclusion. CDI significantly contributes to LOS in the acute care setting but the magnitude of its estimated impact is substantially smaller with methods that account for the time-varying nature of infection. Further efforts to control for time-varying confounding will refine these estimates. Estimates of CDI costs should be based on more accurate measures of attributable LOS to avoid overstating the benefit of interventions to reduce CDI

Disclosures. **R. E. Nelson**, Roche: Consultant and Grant Investigator, Consulting fee, Research grant and Research support

1631. The Impact of Obesity of *Clostidium difficile* Recurrence

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Background. *Clostridium difficile* infections (CDIs) related discharge diagnoses have doubled from approximately 139,000 to 336,600 during this decade. Recent studies suggest that obesity may increase the risk of CDI acquisition due to dysbiosis of commensal gut flora seen in obese patients. No prior studies have examined whether obesity impacts the rate of CDI recurrence.

Methods. We conducted a retrospective review of patients with laboratory confirmed CDI at the VA Boston Healthcare System between March 1, 2010 and February 28, 2013. Identified cases were patients who were treated for the first episode of CDI. A chart review was conducted to gather baseline characteristics such as body mass index (BMI), comorbidities (Charlson Index), age, use of proton pump inhibitors or H2-blockers, and initial treatment antibiotics. Patients with Charlson Index score of >3 were considered high risk. Each of the cases were followed forward for 6 months after initial diagnosis to identify recurrence (positive CD diagnostics within 60 days following complete resolution of first episode.) Patients who died within 60 days of primary CDI and those who received fidaxomicin as first line therapy were excluded. Univariate analysis as well as logistic regression was performed evaluating known risk factors for recurrence and obesity (defined as BMI $\geq$ 30).

Results. Among 257 patients meeting inclusion criteria, 41 (16%) developed a recurrent CDI. Thirty-one/184 (16.8%) patients with normal BMI had a recurrence, compared to 10/73 (13.7%) of obese patients ($p = 0.53$). In a logistic regression adjusting for known risk factors, age was found to be the only variable predicting recurrence ($p = 0.09$).

Conclusion. Our data suggests that obesity was not associated with an increased risk of CDI recurrence within the first 6 months after initial CDI diagnosis. The influence of other covariables in this high-risk nosocomial population may outweigh that of obesity and it would be interesting to explore this analysis in low risk, community dwelling patients with CDI. Like prior studies, we found age to be a strong predictor of recurrence in this population.

Disclosures. **K. Gupta**, Paratek: Consultant, Consulting fee

1632. Preventon of Clostridium Difficile Infection: A Human Factors and Systems Engineering Approach

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Background. C. difficile infection prevention centers around optimal deployment of infection control practices. However, there is significant variability across institutions regarding adherence to and implementation of optimal C. difficile infection prevention practices.

Methods. Using a human factors approach – the Systems Engineering Initiative for Patient Safety (SEIPS) – we performed a work system analysis to guide direct observation data collection with the goal of systematically identifying work system barriers and facilitators of adherence to hospital-mandated contact isolation protocols for patients with suspected or confirmed CDI at two hospitals.

Results. A total of 288 observations were undertaken at the two sites. 175 observations were of nurses, 59 observations were of physicians, 17 observations were of visitors, remainder were of ancillary staff. Full compliance with contact isolation precautions was low at both hospitals, the main SEIPS *process*measure. At hospital A, 17 persons (7%) fully complied with contact isolation precautions. Full compliance in hospital B was significantly higher and observed for 11 persons (22%) (P = .004). Rates of gown and glove use were similar between hospitals A and B (63% vs 71%; P = .337; 52% vs 61%; P = .283). The rate of hand hygiene use before room entry was low at both hospital A and B (18% vs 29%; P = .079). After room exit, use of soap and water for hand hygiene was significantly higher at hospital B (23% vs 55%; P = <.001). Full compliance with contact isolation precautions as compared to noncompliance required a significantly greater amount of time before room entry, inside room, and after room exit (59.9 seconds vs 3.2 seconds; P < .001; 507.3 seconds vs 149.7 seconds; P = .006; 15.2 seconds vs 1.3 seconds; P < .001). Significantly less time was required before room entry and inside room in non-isolation rooms as compared to full compliance (59.9 seconds vs 0 seconds; P < .001, 507.3 seconds vs 28.4 seconds; P = .027). Physicians had a significantly higher rate of full compliance compared to nursing staff (17% vs 7%; P = .043).

Conclusion. Infection control interventions for CDI prevention are complex, time consuming tasks. An analysis of the work system using a human factors approach can guide understanding of CDI prevention practices.

Disclosures. **All authors:** No reported disclosures.

1633. The Importance of Considering Different Healthcare Settings When Estimating the Incidence of *Clostridium difficile*

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Background. Traditional surveillance systems for *Clostridium difficile* infection (CDI) fail to capture cases identified in outpatient settings or during non-face-to-face patient-provider interactions, such as telephone or email encounters. We examined the potential degree to which the burden of CDI is underestimated.

Methods. We identified CDIs among Kaiser Permanente Northwest (KPNW) patients between June 1, 2005 and December 30, 2012. CDIs were categorized by whether they were diagnosed during an inpatient or outpatient encounter and also by whether they were diagnosed during a face-to-face (e.g., hospitalization, outpatient visit) or non-face-to-face encounter (e.g., phone, email). Our baseline surveillance estimate included only CDIs identified during hospitalization, to represent CDI burden captured through traditional surveillance approaches. We then constructed two additional estimates: one that includes CDIs identified during outpatient face-to-face encounters and one that further includes CDIs identified during non-face-to-face encounters.

Results. During the study time period, we identified 8,024 CDIs. Twenty-four percent of all CDIs (1,944 of 8,024) occurred during a hospitalization, while 6,080 CDIs (76%) were recognized in the outpatient setting. Seventy-nine percent (6,322 of 8,024 CDIs) were identified during face-to-face healthcare encounters; an additional 1,702 CDIs (21% of the total) were identified during a non-face-to-face encounter. Surveillance focused on hospitalized patients would capture less than 25% of the CDI burden among KPNW patients. The addition of cases from outpatient care settings, when added to hospitalizations, would account for 80% of all CDIs. An additional 1,702 CDIs would not be accounted for without the inclusion of non-face-to-face encounters; thus, surveillance approaches that do not include telephone or email encounters would miss 21% of CDIs.

Conclusion. Surveillance approaches that do not include outpatient or non-traditional encounters miss a substantial proportion of CDIs. Failure to capture these cases not only leads to underestimation of disease burden, but also makes it difficult to measure the impact of interventions to control CDI.

Disclosures. **All authors:** No reported disclosures.

1634. Clinical Characteristics of Relapses AND Reinfections in Clostridium difficile Infection

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Background. The purpose of this study was to identify factors associated with relapses or reinfections in patients with recurring *Clostridium difficile* infections (CDIs).

Methods. From September 2008 to January 2012, cases with two or more isolates from consecutive CDI episodes were included. PCR-ribotyping and multilocus variable-number tandem-repeat analysis (MLVA) were performed using paired isolates.

Results. Among 473 patients, 68 (14.4%) experienced 1–5 recurrences. Fifty-one of these with two or more isolates from consecutive CDI episodes were included in the study; 25 (49 %) were classified as relapses and 26 (51%) as reinfections. Recurrence interval was shorter in relapse group (26.0 vs 67.5 $p = 0.001$), but more patients in reinfection group were hospitalized during recurrence interval (53.8% vs 8.0%, $p < 0.001$). Relapse rates in infections by ribotype 017, ribotype 018 and other ribotypes were 63.6%, 63.6% and 22.2%, respectively ($p = 0.274$, $p = 0.069$, and $p = 0.005$). In multivariate logistic regression, infections by ribotype 017 and 018 were associated with CDI relapse (OR 4.77, 95% CI 1.02-22.31, $p = 0.047$; OR 11.49, 95% CI 2.07-63.72, $p = 0.005$). Conversely, admission during recurrence interval lowered relapse (OR 0.044, 95% CI 0.006-0.344, $p = 0.003$).

Conclusion. In conclusion, relapse was more likely when infection was caused by PCR ribotype 017 and 018.

Disclosures. **All authors:** No reported disclosures.

1635. A Retrospective Study Comparing Outcomes of Present on Admission *Clostridium difficile* Infection (CDI) vs Non-present on Admission CDI at a Tertiary-care Hospital in Detroit

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Background. The aim of this study was to compare hospital-onset (Non-POA) CDI discharges to community-onset (POA) CDI discharges in order to assess the healthcare burden of hospital acquired CDI.

Methods. A retrospective chart review of patients diagnosed with CDI was conducted at a tertiary-care hospital in Detroit between January 2011 and December 2012. CDI Patients were classified as present-on-admission (POA) if they were primarily admitted with CDI or tested positive for CDI 48 hours prior and/or 48 hours after admission. Non-present-on-admission (Non-POA) patients were defined as being tested positive for CDI 48 hours after admission. Collected data included demographics, admission source, comorbidities, and length-of-stay (LOS). Thirty-day readmissions due to all causes including recurrent CDI as well as 30-day mortality rates were calculated and compared between POA and Non-POA CDI discharges.

Results. The cohort included 710 patients with POA CDI and 602 patients with Non-POA CDI. Although the mean age of POA group was not significantly different from the mean age of Non-POA group (61 ± 19 vs 61 ± 18, p = .95), Non-POA patients were more likely to be admitted with a rapidly fatal condition compared to POA patients (49 % vs 42%, p = .022). On the other hand, POA patients were more likely to be admitted from home compared to Non-POA patients (76% vs 70%, p= .015). The median LOS for Non-POA patients was significantly higher than that for POA patients (16 days, interquartile range {IQR} [10 – 27] vs 5 days, IQR [3 – 10], p < .001). Although not statistically significant, 30-day readmissions due to CDI recurrence in the POA group were higher than that in the Non-POA group (5% vs 3%, p = .09). The median time to readmission for POA patients was significantly higher than that for Non-POA patients (53 days, IQR [17 – 199] vs 34 days, IQR [11 – 137], p = .003). Thirty-day mortality rate of Non-POA CDI patients was higher than that of POA CDI patients (11.5 % vs 6%, p < .001).

Conclusion. Given the high morbidity and mortality rates among patients with hospital-onset CDI (Non-POA), efforts should focus on prevention strategies including regular surveillance, antimicrobial stewardship and quality improvement programs.

Disclosures. **K. Kaye**, Cubist Pharmaceuticals: Consultant, Grant Investigator and Speaker's Bureau, Consulting fee, Grant recipient and Speaker honorarium

1636. Low Incidence Of *Clostridium Difficile* Infection (CDI) in Patients Treated with Community Outpatient Parenteral Antimicrobial Therapy (CoPAT)

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Background. Hospital stay and antimicrobial therapy are the major risk factors for developing *Clostridium difficile*infection (CDI). Community outpatient parenteral antimicrobial therapy (CoPAT) allows patients to reside in the community while being treated with parenteral antimicrobials. The purpose of this study was to evaluate the incidence and clinical outcomes of community onset CDI (CO-CDI) in patients treated with CoPAT.

Methods. All patients ≥ 18 years, discharged home with CoPAT from January-December 2013 were retrospectively reviewed. Patient who developed symptomatic diarrhea with positive stool toxin PCR assay within 4 weeks of CoPAT initiation in the community were identified as CO-CDI. A review of the electronic medical records was done to identify known CDI related risk factors, severity, treatment, recurrence, readmission and attributable mortality.

Results. During the study period, 2401 patients were discharged on CoPAT with 680 patients through the Cleveland Clinic Home Care agency. Five patients (0.74%) developed CO-CDI with an estimated incidence of 5 cases per 1,000 CoPAT courses. The mean age of CO-CDI patients was 61.2 (SD ± 16) years and 4/5 patients (80%) were men. In patients with CO-CDI, the most frequently administered antimicrobials (2/5) were pipercillin/tazobactam and amikacin with a median duration of 12 days (IQR: 6.5-28). Four of 5 patients completed CoPAT prior to developing CO-CDI. The median duration from CoPAT completion to developing CDI was 9.5 days (IQR: 3-13). All five patients had a recent exposure to a healthcare facility excluding follow-up office visits. The median duration from exposure to development of CO-CDI was 8 days (IQR: 2-11.5). Of the 5 patients, 2 had hospital re-admissions and 3 had outpatient procedures. Four of 5 (80%) patients were on concomitant acid suppressive therapy. All patients had mild-moderate CDI and responded to medical therapy. Two patients had a hospital readmission but none were CDI related. There was no history of CDI recurrence or attributable mortality.

Conclusion. Patients receiving CoPAT had a low incidence of CO-CDI with no major complications. Most patients who developed CO-CDI had a recent healthcare exposure and were on concomitant acid suppressive therapy

Disclosures. **N. Shrestha**, Forest: Speaker's Bureau, Speaker honorarium; Merck: Speaker's Bureau, Speaker honorarium; The Medicines Company: Scientific Advisor, Consulting fee

1637. Epidemiology of *Clostridium difficile* Infection in an Integrated Healthcare System Over a 10-year Period

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Background. The epidemiology of *Clostridium difficile* (*C. diff*) infection (CDI) has changed with increased incidence and mortality in many settings. Recent population based surveys indicate an increasing burden of community acquired (CA) CDI. The purpose of our study was to assess the epidemiology of CDI in an integrated healthcare system.

Methods. We queried Intermountain Healthcare's electronic data warehouse for *C. diff* tests collected from >185 clinics and 22 hospitals between 2003 and 2012. Lab defined cases of CDI were categorized as healthcare associated (HA) (positive test >48 hours after admission or ≤30 days after hospital discharge), CA (no hospitalization ≥90 days prior to a positive test) or recurrent (positive test 14-90 days after a prior positive test). Positive tests ≤14 days of an index positive were excluded. Enzyme immunoassay (EIA) for Toxins A/B was used from 2003–2010 and nucleic acid amplification testing (NAAT) replaced EIA in October 2010. Incidence rates for HA and CA CDI were calculated as episode/10,000 hospital discharges and episode/10,000 patient encounters, respectively.

Results. The number of *C. diff* tests ordered increased 81% from 2003 (9,613 tests) to 2012 (17,385 tests). During the EIA period, 7–10% of samples tested each year were positive compared to 15% with NAAT. During the entire study period 10,689 CDI episodes were identified in 8,993 patients. HA accounted for 35% (n = 3,757) of the episodes, CA 48% (n = 5,108), recurrent 11% (n = 1,197) and 6% (n = 627) were indeterminate. From 2003 to 2012, there was a decline in proportion of HA CDI (46% vs 26%, p < 0.05) with an increase in CA (41% vs 53%, p < 0.05) and recurrent (9% vs 15%, p < 0.05) CDI (Figure A). The incidence of HA CDI increased between 2003 and 2006 (22.8 vs 28.6/10,000 hospital discharges) and subsequently decreased through 2010. By contrast, incidence of CA CDI increased 53% from 2003-2010 (Figure B). When NAAT tests were implemented, both HA and CA rates increased but this may in part be related to increased test sensitivity. The proportion of recurrent CDI (10% vs 14%) also increased with NAAT use.

FIGURE A. Proportion of positive *C. difficile* tests classified as healthcare associated, community associated and recurrent

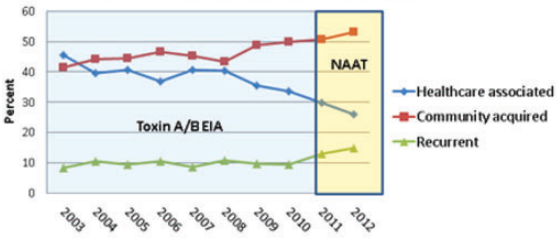
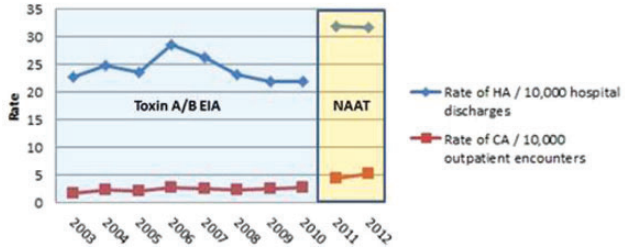


FIGURE B. Incidence of *C. difficile* Infection by Lab Diagnosis



Conclusion. We detected an increase in rates of CA CDI throughout the study period. HA CDI rates declined between 2006 and 2010. With use of NAAT CDI rates increased however trends are not yet clear.

Disclosures. **All authors:** No reported disclosures.

1638. *Clostridium difficile* Strains Colonizing Long-Term Care Facility (LTCF) Residents are Similar to Strains Causing Infection in both LTCF and Hospital Patients Suggesting a Shared Continuum of Transmission

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Background. *Clostridium difficile* infection (CDI) is endemic in long-term care facilities (LTCFs). Asymptomatic residents colonized with toxigenic strains are a potential reservoir for transmission both in LTCFs and affiliated hospitals. We used

restriction endonuclease analysis (REA) to type and compare *C. difficile* isolates colonizing LTCF residents and infecting both LTCF and hospital patients.

Methods. Asymptomatic residents were enrolled from the LTCF associated with either Cleveland VA Hospital (n = 200) or Hines VA Hospital (n = 200) from February 2012 through August 2012. Cultures for asymptomatic colonization with *C. difficile* were obtained from the perirectal area on admission and at 2-week intervals during LTCF stay. All colonizing isolates underwent REA typing. In addition, available isolates causing CDI with onset in either the LTCF or affiliated VA hospital were typed for comparison.

Results. Four percent of enrolled Hines LTCF residents were colonized with a toxigenic *C. difficile* strain during the study, most commonly BI 6/8/17, L group, or BM group (Table). For hospital- and LTCF-onset Hines CDI isolates, BI 6/8/17 was also the most common group isolated accounting for 33% of cases. Group AL was found only at Hines. In comparison, 19% of Cleveland LTCF residents were colonized; the predominant groups were BI 6/8/17, BI non-6/8/17, and DQ, a binary toxin positive group not found at Hines (Table). In Cleveland, the three most common REA groups isolated from both hospital- and LTCF-onset CDI were also the same as those found in colonized LTCF patients (table).

	Hines		Cleveland	
REA Group	Colonizing, N=10 No.	Infecting, N=30 No.	Colonizing, N=41 No.	Infecting, N=42 No.
BI 6/8/17	2	10	8	9
BI non-6/8/17	1	3	8	8
BM	2	1	2	0
L	2	0	1	0
DH	1	1	3	1
AL	1	4	0	0
DQ	0	0	7	9
G	0	3	1	2
Y	0	1	3	2
Other groups	0	5	5	4
Non-specific	1	2	3	7

Conclusion. The BI group and specifically BI 6/8/17 remains endemic at both sites. Although the prevalence of toxigenic *C. difficile* colonization varied significantly between the two LTCFs, in both sites the predominant colonizing strain(s) were the most common infecting strains in both the LTCF and hospital. This suggests a shared continuum of transmission between asymptomatic, colonized LTCF residents and both affiliated hospital and LTCF CDI cases.

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1639. A Tale of Two States: An Exploration of Disparities in the Proportion of Long-term Care Facility–onset *Clostridium difficile* Infections in Minnesota and New Mexico

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Background. Long-term care facility (LTCF) residents are at higher risk for developing *Clostridium difficile*infections (CDI). Both Minnesota (MN) and New Mexico (NM) perform active population-based surveillance for CDI in select counties. While both states have historically similar overall CDI incidence rates, the proportion of LTCF-onset CDI is much higher in NM. We compared surveillance data from the two states to identify differences.

Methods. We analyzed population-based CDI data from January 1, 2011– September 30, 2013. A CDI case was defined as a stool specimen positive for *C. difficile* obtained from a patient without a *C. difficile*-positive specimen in the previous 8 weeks. A CDI case was classified as LTCF-onset if positive stool specimen was collected in a LTCF or within 3 days after hospital admission from a LTCF. A medical record review was performed on all LTCF-onset CDI cases in MN and a 10% random sample in NM. LTCF utilization data was obtained from the 2012 Area Resource File. Chi-square test was used for comparisons across the two states.

Results. A total of 1597 and 3289 CDI cases were identified in MN and NM, respectively. Among all CDI cases, MN cases were less likely to be LTCF-onset (6% vs 26%; $p < 0.0001$). Among cases with full review, no differences were detected between MN and NM in mean age (80 vs 77 years; $p = 0.1$), recent H2 receptor antagonist (18% vs 22%; $p = 0.6$), proton pump inhibiter (53% vs 48%; $p = 0.6$), or antibiotic usage (71% vs 77%; $p = 0.4$) in the 12 weeks prior to stool collection. MN LTCF-onset cases were more likely to have a positive test as a hospital inpatient (34% vs 18%; $p = 0.02$). Among persons greater than 65 years, LTCF utilization was higher in MN than NM (5.7% vs 2.9%, $p < 0.0001$) and MN had significantly higher population rate of LTCFs (47 vs 25 per 100,000 persons; $p < 0.0001$) and LTCF beds (2235 vs 2832 per 100,000 persons; $p < 0.0001$).

Conclusion. Despite LTCF utilization being higher in MN, this state had a lower proportion of LTCF-onset CDI cases compared to NM. No differences in age or prior use of antibiotics or acid reducing medications were detected between LTCF-onset cases in the two states. Further exploration of the variability in testing and infection control practices in LTCFs is warranted to identify prevention strategies directed to this patient population.

Disclosures. **All authors:** No reported disclosures.

1640. Antibiotic Use Patterns in a Population with Long Term Care-Onset *C. difficile* Infection Developing after Recent Hospitalization

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Background. *Clostridium difficile* infection (CDI) is common in the elderly due to decreased immunity and frequent antibiotic and healthcare exposure. We investigated antibiotic use in hospitalized long term care facility (LTCF) residents that developed CDI to identify potential stewardship targets.

Methods. CDI cases were identified by the CDC's Emerging Infections Program active population surveillance. Incident cases were LTCF residents with a positive stool test within 30 days post-hospitalization and more than 8 weeks from a previous positive. Antibiotic use and readmission data were abstracted from hospital medical records.

Results. Records of 130 Monroe County, NY residents discharged from 4 acute care hospitals to 33 LTCFs were reviewed. Thirty-one (24%) patients were readmitted to the hospital within 2 days before or 7 days after CDI. Thirty-two (25%), 104 (80%), and 51 (39%) patients received antibiotics pre- and during hospitalization and at hospital discharge, respectively (table). Fluoroquinolones, first and third generation cephalosporins and extended-spectrum penicillin combinations were the most common. Common indications included lower respiratory tract infections (LRTI) and urinary tract infections (UTI); however review of the UTI cases showed that 60% of 25 non-catheterized patients did not meet the McGeer UTI criteria.

Antibiotic Use Characteristics

		Hospitalization	
	Pre N=32 N (%)	During N=104 n (%)	At Discharge N=51 n (%)
No. of antibiotics			
1	21 (66)	18 (17)	49 (96)
2	9 (28)	19 (18)	2 (4)
≥3	2 (6)	67 (64)	0
Common classes*			
Extended-spectrum penicillin combo	1 (2)	68 (20)	8 (15)
Fluoroquinolones	10 (20)	35 (11)	12 (24)
1st gen. cephalosporins	6 (12)	9 (3)	13 (25)
3rd gen. cephalosporins	6 (12)	15 (5)	6 (12)
Common indications*			
UTI	11 (22)	67 (18)	16 (25)
LRTI	3 (6)	72 (19)	14 (22)
Skin/Soft Tissue Infection	8 (16)	55 (14)	6 (10)
Bloodstream Infection	4 (8)	23 (6)	7 (11)

*Can be >1/resident

Conclusion. LTCF residents developing CDI after acute care hospitalization had frequent antibiotic exposure prior to CDI diagnosis to treat presumed UTI and LRTI. These antibiotics were administered before, during and at discharge from hospitalization. This highlights the need for stewardship activities that target antibiotic usage across the continuum of care, particularly at care transition.

Disclosures. **E. Dodds-Ashley**, Cubist Pharmaceuticals: Scientific Advisor, travel reimbursement

1641. Evaluation of Co-Infections among Patients with Community-Associated *Clostridium difficile* Infection

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Background. Though not considered common features of *Clostridium difficile* infection (CDI), patients with community-associated CDI (CA-CDI) often report nausea or vomiting. We evaluated the prevalence of co-infection with other gastrointestinal (GI) pathogens that cause nausea or vomiting and diarrhea among patients with CA-CDI to ascertain how frequently co-infection may contribute to CA-CDI illness.

Methods. We enrolled CA-CDI cases (*C. difficile*-positive stool specimen collected as an outpatient or within 3 days after admission from a person aged ≥1 year who did not have a positive assay ≤8 weeks and an overnight stay in a healthcare facility ≤ 12 weeks prior to stool collection) from December 1, 2012 – February 28, 2013 in 5 Emerging Infections Program sites participating in CDI surveillance. Demographic data, clinical data and GI bacterial pathogen testing were abstracted from medical records. *C. difficile*-positive stool specimens associated with case data were submitted for *C. difficile* culturing and RT-PCR for norovirus, rotavirus, sapovirus, astrovirus and adenovirus. Chi-square or Wilcoxon rank-sum tests were used to evaluate differences between co-infected and non-co-infected cases.

Results. Of 187 CA-CDI cases enrolled, 14 (7.5%) tested positive for norovirus, 4 (2.1%) for enteric adenovirus, 3 (1.6%) for rotavirus, and 2 (1.1%) for sapovirus; one had a positive *Campylobacter* test. There were no significant differences between co-infected (n = 24) and non-co-infected cases (n = 163) with regards to age (median = 58 vs 55, $p = 0.6$), documentation of diarrhea (41% vs 45%, $p = 0.7$), nausea or vomiting (45% vs 30%, $p = 0.1$), antimicrobial exposure in the 12 weeks prior to specimen collection (41% vs 57%, $p = 0.1$), or detection of *C. difficile* by molecular assay (66% vs 61%, $p = 0.6$). Co-infected cases were less likely to be *C. difficile*-culture positive (66% vs 88%, $p = 0.01$) and to be North American Pulsed-Field type 1 (NAP1) (4% vs 20%, $p = 0.03$).

Conclusion. Although lower rates of *C. difficile* isolation and the NAP1 strain suggest co-infection could be a cause of *C. difficile* pseudoinfection in the community, this appears uncommon. Based on our data, clinical characteristics alone cannot differentiate these cases.

Disclosures. **All authors:** No reported disclosures.

1642. Identifying Targets for Prevention Through *Clostridium difficile* Population Surveillance

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Background. Antibiotics and *Clostridium difficile* spores exposures are both important factors for the development of *C. difficile* infection (CDI). Patient movements across healthcare facilities help with *C. difficile* spread. Designing CDI prevention strategies requires an understanding of these transmission dynamics as well as predisposing factors.

Methods. Population-based surveillance for CDI started in 2010 in Monroe County, NY as part of the CDC's Emerging Infections Program. Medical chart reviews were performed on all county residents with positive *C. difficile* tests reported by the laboratories. Incident CDI cases had no history of a *C. difficile* positive test in the prior 8 weeks. We divided CDI cases into 4 epidemiologic classifications depending on location of patient at the time of testing: community-associated (CA: no overnight stay at hospital or long-term facility (LTCF) in the previous 12 weeks), community onset healthcare facility-associated (COHCFA: positive test within 12 weeks of discharge from healthcare), hospital onset (HO) and long-term care facility onset (LTCFO).

Results. Over 4 years, 6642 incident CDI cases were identified across the county which includes 4 hospitals and 33 LTCFs, for an average annual incidence of 225 per 100,000 population. Thirty-five percent of CDI cases were CA, 20% COHCFA, 23% HO and 22% LTCFO. Exposure to the hospital prior to CDI was common, as 55% COHCFA and 47% LTCFO cases were discharged from the hospital in the 30 days prior to CDI. In addition, hospitalization within 7 days of CDI occurred in 29% of CA cases. Twenty-eight percent of LTCFO and 58% of COHCFA cases were re-hospitalized. Forty percent of HO cases were discharged to LTCF. The majority of CDI cases received antibiotics 12 weeks prior to their illness; 89% of COHCFA, 97% of HO, 86% of LTCO and 60% of CA CDI cases.

Conclusion. CDI patients frequently moved across the continuum of care and the community, facilitating *C. difficile* spread. Antibiotic use prior to infection was common. Reducing the local burden of CDI therefore requires a community-wide approach harmonizing both infection control and antimicrobial stewardship efforts in the hospital, LTCF and outpatient settings.

Disclosures. **All authors:** No reported disclosures.

1643. *Clostridium difficile* Infection Related Emergency Department Visits in the United States 2006-2009

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Background. There has been an alarming uptrend in the number of cases of *C. difficile* infection (CDI) after the introduction of real-time PCR based diagnostic testing. The objective of this study was to interrogate a nationwide emergency department (ED) database to determine the trend of ED visits related to CDI for the years 2006-2010.

Methods. Data were obtained from the Nationwide Emergency Department Sample (NEDS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality for the years 2006-2010. Data were weighted to generate national-level estimates.

Results. For years 2006–2010, a weighted total of 462,160 patients were discharged from the ED with a primary diagnosis of CDI. The rate (cases/100,000 population) of ED visits with CDI as a primary diagnosis increased from 34.08 in 2006 to 42.37 in 2010; this represented an increase of 24.32% ($P < 0.01$). There was an increased trend in the number of ED visits with CDI as a primary diagnosis from 2006–2010 ($P < 0.01$). The highest incidence rate of CDI related ED visits was observed patients ≥ 65 years, while the lowest incidence was in patients 18–24 years. Of the 462,160 patient cohort, 92.48% of cases were admitted as inpatients to the hospital. 17,638 of these patients (4.1%) died during the hospital admit. Inpatient and ED charges increased during the period of the study, from a median of $20,000 (interquartile range [IQR] $25,000) to $24,000 (IQR $27,000) ($P < 0.01$). LOS remained constant at a median of 5 days (IQR 5 days) for this period. Factors associated with an increased risk of hospital admission included female sex, a comorbid burden of ≥3 (aOR 8.25 95% CI 7.89 – 8.62), age ≥65 years (aOR 3.13 95% CI 2.95 – 3.32) and presentation to a metropolitan facility (aOR 2.77 95% CI 2.69 – 2.85). Much smaller risks were associated with female gender (aOR 1.12 95%CI 1.09 – 1.15), Medicaid or Medicare insurance (aOR 1.21 95% CI 1.18 – 1.25), and presentation to a facility in the Southern region of the United States (aOR 1.06 95% CI 1.02 – 1.09).

Conclusion. CDI related ED visits represent a considerable burden on the healthcare system in the United States. Additionally, an increasing trend in the incidence of these cases was observed for the years 2006–2010.

Disclosures. **All authors:** No reported disclosures.

1644. Risk Factors for Community-Associated *Clostridium difficile* Infection in Children

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Background. A substantial proportion of *Clostridium difficile*infection (CDI) in children occurs in community settings. The aim of this study was to characterize and identify the risk factors for community-associated (CA-) CDI in children.

Methods. Children with CA-CDI evaluated at Texas Children's Hospital from January 1, 2012 through June 30, 2013 were identified. Two control subjects, frequency matched by age group, were randomly selected among children with community-associated diarrhea (symptom onset > 12 weeks after last hospitalization) who tested negative for *C. difficile*. Data on demographics, medication use, and outpatient healthcare encounters were collected from medical records. Multivariate logistic regression was performed to identify predictors of pediatric CA-CDI.

Results. A total of 69 CA-CDI pediatric cases were identified and compared with 138 control subjects. The majority (62.3%) of CA-CDI cases had an underlying chronic medical condition. CA-CDI cases had exposures to antibiotics (40.6%), gastric acid suppressants (21.7%), and outpatient healthcare settings (66.7%) within 30 days of illness. However, exposure to an antibiotic, gastric acid suppressant, or outpatient healthcare setting was not identified within 30 and 90 days of illness in 23.2% and 15.9% of CA-CDI cases, respectively. On univariate analysis, CA-CDI cases were more likely to have a gastrointestinal feeding device (20.3% vs 8.0%; $P = 0.01$) than control subjects. Additionally, exposure to cephalosporins (13.0% vs 4.4%; $P = 0.02$), clindamycin (5.8% vs 0.7%; $P = 0.04$), and outpatient healthcare settings (66.7% vs 48.6%; $P = 0.01$) within 30 days of illness were more common in CA-CDI cases than control subjects. On multivariate analysis, CA-CDI was associated with cephalosporin use within 30 days (OR 3.32; 95% CI 1.10-10.01) and the presence of a gastrointestinal feeding device (OR 2.59; 95% CI 1.07-6.30).

Conclusion. A substantial proportion of children with CA-CDI did not have a "traditional" risk factor for CDI. Antibiotics are an important risk factor for CA-CDI in children with risk varying by antibiotic class. Outpatient healthcare settings may be a source of *C. difficile* acquisition among children in community settings.

Disclosures. **All authors:** No reported disclosures.

1645. Do asymptomatic carriers of toxigenic *Clostridium difficile* identified through inappropriate testing represent a significant risk for transmission?

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Background. Inappropriate testing may result in false-positive diagnoses of *Clostridium difficile* infection (CDI) due to detection of asymptomatic carriers of toxigenic *C. difficile*. It has been proposed that carriers identified through inappropriate testing may contribute to transmission. However, the risk for transmission by carriers identified through inappropriate testing is unclear.

Methods. During a 1-year period, we determined the proportion of CDI cases in our facility attributable to inappropriate testing and tested the hypothesis that inappropriately tested patients present a significant risk for shedding of spores. For inpatients with PCR assays from unformed stools, chart review and interviews were conducted to assess symptoms of CDI. CDI testing was deemed inappropriate if the patient did not have diarrhea (>3 unformed stools/24 hours) or if diarrhea was present but with an alternative cause (e.g., laxatives) in the absence of prior antibiotics. For inappropriately tested patients, we compared the frequency of shedding in those with or without prior antibiotic exposure.

Results. Of 134 CDI patients, 30 (22%) were deemed to have inappropriate testing. Skin and/or environmental shedding occurred in 33/58 (57%) CDI cases with appropriate testing vs 5/30 (17%) with inappropriate testing ($P = 0.003$); for inappropriately tested patients with positive CDI test results, skin and/or environmental shedding was significantly more common for patients who had received prior antibiotics vs those not receiving prior antibiotics (5/11, 45% vs 0/19, 0%; $P = 0.003$). Of the 30 inappropriately tested cases, 20 (67%) had received prior laxatives.

Conclusion. Nearly one-fourth of CDI cases were diagnosed through inappropriate testing. These cases may represent asymptomatic carriers of toxigenic *C. difficile* with unformed stools or diarrhea for other reasons. Shedding of spores was relatively infrequent among cases diagnosed through inappropriate testing, particularly those who had not received prior antibiotics.

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1646. Evidence of hospital-associated *Clostridium difficile* transmission between patients with asymptomatic carriage and patients with *Clostridium difficile* infection

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Background. Despite strategies to reduce transmission, *Clostridium difficile* (CD) remains a leading cause of morbidity in health care settings. The aims of our study were (1) to determine if asymptomatic inpatient CD carriers can be liked by molecular epidemiology to other inpatients with CD infection (CDI) and (2) to determine if active surveillance testing (AST) criteria to identify inpatients at risk for vancomycin-resistant *Enterococcus* (VRE) colonization are sufficiently sensitive to capture asymptomatic CD carriage.

Methods. Over a 5 day period, all inpatients at University of Pittsburgh Medical Center – Presbyterian Hospital (UPMC) were targeted for one-time AST for CD via perirectal sampling. Archived stool specimens were obtained from (1) clinical CDI cases 7 weeks prior to AST for CD, (2) clinical CDI cases during AST for CD, and (3) clinical hospital-associated CDI (HA-CDI) cases 12 weeks after AST for CD. CD carriage was defined as AST positivity in the absence of clinical CDI during or +/- 3 months from AST; clinical CDI was defined as clinician-requested, nucleic stool test positivity for toxigenic CD. Specimens were cultured for CD using broth enrichment. CD isolates were typed using *tcdC* and multilocus variable number tandem repeat (MLVA) genotyping. Isolates whose MLVA genotypes had a summed tandem-repeat difference of ≤ 2 were considered highly related. "Probable" transmission events were inferred when patients exhibited simultaneous occupancy of the same inpatient ward and their isolates were highly related. "Possible" transmission events were inferred when patients exhibited simultaneous occupancy of the hospital, but not the same inpatient ward, and their isolates were highly related. AST for VRE was performed according to UPMC policy throughout.

Results. 53 (10%) inpatients were identified as CD carriers. 123 clinical CDI cases were identified; isolates from 101 (83%) of these episodes were obtained. 6 (5.9%) clinical CDI isolates were highly related to CD carrier isolates, 4 of which were HA and could be linked epidemiologically to CD carriers – 2 by probable and 2 by possible transmission events. None of the CD carriers implicated in transmission events underwent VRE AST.

Conclusion. Hospital-wide AST for CD carriage may identify a reservoir of CD involved in CDI.

Disclosures. **All authors:** No reported disclosures.

1647. Are Hospital Floors an Underappreciated Reservoir for Transmission of *Clostridium difficile* and Methicillin-Resistant *Staphylococcus aureus*?

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Background. Limited attention has been paid to disinfection of floors in healthcare facilities because they are not frequently touched by hands. However, it is plausible that floors could be an underappreciated reservoir for pathogen transmission because they are frequently contacted by surfaces that are subsequently touched by hands (e.g., shoes, wheelchair wheels).

Methods. In 4 Cleveland area hospitals, we cultured 2 standardized 1 foot^2 areas of the floor in *Clostridium difficile* infection (CDI) isolation rooms and in non-CDI rooms for *C. difficile*, methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococci (VRE). Occupied hospital rooms were surveyed to determine the frequency and identification of high-touch objects on floors. Cultures were collected from surfaces or objects that come in direct contact with floors (e.g., shoes, socks, wheelchair wheels) and the potential for transfer from these surfaces to hands was assessed.

Results. Of 120 floor sites, 86 (72%) were positive for *C. difficile*, 26 (22%) were positive for MRSA, and 32 (33%) were positive for VRE, with similar results for each of the hospitals. *C. difficile* was recovered more frequently from non-CDI than from CDI rooms (64% vs 43%; $P = .003$). Occupied rooms had an average of 1.4 high-touch objects in contact with the floor. Of 24 sampled objects in contact with floors, 14 (24%) were contaminated with one or more of the pathogens. Of the 14 contaminated objects on floors, 8 (57%) transferred pathogens to hands.

Conclusion. Our results demonstrate that hospital floors are frequently contaminated with pathogens and often contacted by high-touch objects. Hospital floors could be an underappreciated reservoir for transmission of healthcare-associated pathogens.

Disclosures. **All authors:** No reported disclosures.

1648. Sixty Percent (60%) reduction in *Clostridium difficile* infection (CDI) associated with the introduction of hydrogen peroxide vapor (HPV) automated room disinfection

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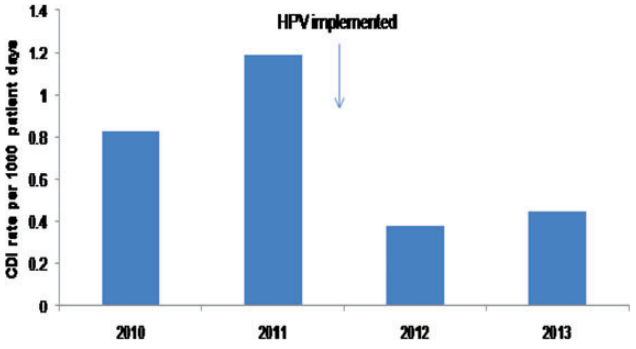
Background. *Clostridium difficile* is shed into the hospital environment, and contaminated surfaces are considered to be important in the transmission of *C. difficile* spores and the acquisition of *C. difficile* infection (CDI). A number of studies have shown that hydrogen peroxide vapor (HPV), an automated room disinfection (ARD) system, may prevent the transmission of CDI in hospitals. We implemented HPV for the terminal disinfection of CDI patient's rooms in 2012 and performed a retrospective study to evaluate whether HPV was associated with a reduction in CDI.



CDI rate, 24 months prior HPV and first 24 months of HPV (2012 and 2013).

Methods. All cases of CDI are reported to infection control who attribute them as healthcare-associated (HAI) or non-HAI using the Centers for Disease Control and Prevention's criteria for national reporting purposes. HPV was implemented in early 2012 for the terminal disinfection of rooms vacated by patients with CDI. Rooms vacated by patients with CDI were disinfected using HPV

immediately, or held for HPV disinfection prior to the admission of the next patient when HPV equipment was not available immediately. We evaluated the rate of HAI CDI in the 2010 and 2011 (pre-HPV) vs the 2012 and 2013 (during HPV usage). A database recording the details of HPV usage in the hospital was collected prospectively.

Results. The rate of CDI fell from 1.0 to 0.4 cases per 1,000 patient days in the 24 months before HPV was implemented vs the first 24 months of HPV usage (figure; 258 vs 123 cases, 60% reduction, $p < 0.001$ using Fisher's exact test). A total of 3060 rooms were disinfected using HPV in 2012 and 2013; the average HPV cycle time was 1 hr 48 mins.

Conclusion. Our study suggests that improved disinfection at the time of patient discharge reduces transmission of CDI in hospitals. Our findings are consistent with other studies, which have reported a similar magnitude of reduction in CDI associated with the implementation of HPV (30-50%). Our study was before-after in design, so we cannot rule out the possibility that other factors explain, at least in part, the difference in rate of CDI that we observed. However, no formal infection control initiatives were implemented during this period. HPV should be considered for the terminal disinfection of rooms vacated by patients with CDI.

Disclosures. **All authors:** No reported disclosures.

1649. Acquisition of *Clostridium difficile* Associated with Potentially Contaminated Inpatient Rooms

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Background. Hospital rooms of inpatients with *Clostridium difficile* infection (CDI) can become contaminated with this major pathogen; unless adequately disinfected, rooms can serve as a reservoir where subsequent patients hospitalized in the same room can also become infected with *C. difficile* (CD). It was incidentally noted that a patient acquired severe CDI while in a room in our hospital that had recently been occupied by another patient with CDI. As a pilot for a new surveillance measure, we sought to estimate the frequency that patients acquire CDI after exposure to a room recently occupied by a patient with CDI.

Methods. CD test results and room location data were obtained from our 500-bed tertiary care center's MedMined database. For the purposes of this surveillance pilot, hospital-acquired CDI was defined as positive CD PCR test ≥3 days after admission. A room was defined as "*potentially contaminated*" when occupied by a patient who had a positive CD test within the prior 14 days. A patient was defined as exposed if he/she occupied a *"potentially contaminated"* room within 14 days prior to testing positive for CD. The Emergency Department and operating rooms were excluded from the study.

Results. During the period July-September 2013, 93 patients had a positive CD PCR. Of the 47 hospital-acquired cases, 5 (11%) had developed CDI after exposure to a *"potentially contaminated"* room (occupied 0-2 days prior by a person with CDI).

Geographically associated cases	Room	Dates same room was occupied	Date 1st *C. difficile* positive
Index	A	Jul 23-28	Jul 22
HAI	A	Jul 28-Aug 18	Jul 31
Index	B	Aug 1–Aug 7	Aug 1
HAI	B	Aug 7-Sep 5	Aug 15
Index	C	Aug 3-6	Aug 4
HAI	C	Aug 6-7	Aug 15
Index	D	Jul 22-Aug 23	Aug 20
HAI	D	Aug 25-Sep 10	Sep 8
Index	E	Sep 9-12	Sep 11
HAI	E	Sep 12-17	Sep 16

Conclusion. In a 3-month period, this specialized surveillance measure uncovered a small but important percentage of inpatients who had acquired CDI potentially from a contaminated room. Our hospital subsequently instituted sporicidal (bleach-based) disinfectants for terminal cleaning of all inpatient rooms. It is relevant to develop computerized algorithms in surveillance systems that can recognize these geographical associations for hospital-acquired infections; this data can then be used to guide environmental health interventions.

Disclosures. **All authors:** No reported disclosures.

1651. Role of Metronidazole vs Vancomycin as Initial Therapy in Hospitalized Patients with Mild to Moderate *Clostridium difficile* Infection (CDI) with NAP1 vs non-NAP1 Disease

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Background. Oral metronidazole (Mtz) is regarded as standard therapy for mild to moderate (mm) CDI. As hypervirulent BI/NAP1/027 strain may result in serious disease, oral vancomycin (Vm) is increasingly being used as initial therapy for such infections. However, favorable impact of this shift in treatment strategy is not certain. To this effect, we reviewed treatment outcomes in patients with mmCDI at our University hospital.

Methods. Standard IDSA guidelines were used to define mmCDI. Response to treatment and rate of recurrence within 12 weeks after successful initial therapy were assessed retrospectively. Clinical failure was defined as persistence of diarrhea or progression to severe disease. Treatment responses to Mtz (500 mg PO 3x daily) vs Vm (125 mg PO 4x daily) were assessed in patients with NAP1 and nonNAP1 CDI, respectively.

Results. From 513 hospitalized patients with positive *C. difficile* stool PCR (June 2011 – July 2013), 168 with mmCDI (NAP1 n = 85, non-NAP1 n = 83) were included. Age, gender, comorbidities, serum creatinine, albumin and white blood cell count were comparable among these patients. Fever at initial presentation was common in patients treated with Vm vs Mtz (34% vs 12%; $p = 0.01$ and 31% vs 12%; $p = 0.04$, NAP1 and non-NAP1 CDI, respectively). Also, proton pump inhibitors were frequently given in patients treated with Vm vs Mtz (74% vs 50%; $p = 0.02$ and 43% vs 22%; $p = 0.04$, NAP1 and non-NAP1 CDI, respectively). In patients with non-NAP1 CDI treated with Vm vs Mtz, prior antibiotic exposure (<30 days) (86% vs 66%; $p = 0.03$) and concurrent antibiotic use were common (86% vs 59%; $p = 0.006$). For NAP1 CDI, clinical response to Mtz was 86% vs 97% to Vm ($p = 0.1$); CDI recurrences were 12% vs 15% in Mtz and Vm treated patients, respectively ($p = 0.7$). For non-NAP1 CDI, clinical response to Mtz was 78% vs 97% to Vm ($p = 0.007$); recurrences were 6% after Mtz and 12% after Vm therapy ($p = 0.5$). In logistic regression after adjusting for community-acquired CDI and NAP1 strain chronic liver disease was identified as a predictor of Mtz treatment failure (OR 4.4, 95% CI 1.19-16.4, $p = 0.03$).

Conclusion. In this cohort of hospitalized patients Mtz and Vm had similar efficacy in the treatment of NAP1 mmCDI. Clinical response to Vm was higher in patients with non-NAP1 mmCDI. Reduced Mtz efficacy was observed in patients with chronic liver disease.

Disclosures. **All authors:** No reported disclosures.

1652. Retrospective Comparision of Oral Vancomycin Capsules vs Oral Vancomycin Solution for the Treatment of Severe Clostridium Defficile Infection

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Background. Oral vancomycin was the first agent approved for the treatment of *Clostridium difficile* infection (CDI). Vancomycin achieves high concentrations in the feces following oral administration and is typically formulated as a capsule. Because vancomycin capsules are significantly expensive, hospital pharmacies extemporaneously compound an oral solution using the generic intravenous formulation of vancomycin. Oral vancomycin solution has been shown to display comparable dose-dependent fecal concentrations with therapeutic levels over 100 times the minimum inhibitory concentration for *C. difficile*. The purpose of this study is to evaluate clinical outcomes between oral vancomycin capsules and oral vancomycin compounded solution for the treatment of CDI.

Methods. A retrospective review was conducted on adult inpatients who received oral vancomycin capsules or solution for ≥ 48 hours for the treatment of severe or severe complicated CDI from 2008 to 2013. Data was collected and analyzed to compare clinical cure and failure rates, CDI recurrence rates, length of hospital stay, and incidence of complications related to CDI between oral vancomycin capsules and solution.

Results. One hundred two patients received oral vancomycin for the treatment of CDI, but 34 patients were evaluated for CDI clinical outcomes. Fifty percent of the patients were male with a median age of 62 years (range 25 – 97). CDI severity was similar between the oral capsule and solution groups with 47% of patients with severe CDI and 35% of patients with severe complicated CDI ($p = 0.7908$). Overall, patients treated with oral vancomycin capsules and solution were found to have clinical cure rates of 74% (14/19) and 67% (10/15), respectively (OR 1.40 (0.32-6.16), $p = 0.7176$). Three patients treated with oral vancomycin solution had CDI recurrences compared to zero patients in the oral capsule group (OR 0.08 (0-1.78), $p = 0.0667$).

Conclusion. Severe CDI treated with oral vancomycin solution appears to be associated with similar clinical outcomes when treated with oral vancomycin capsules. However, larger, prospective studies are warranted to further characterize this relationship.

Disclosures. **All authors:** No reported disclosures.

1653. Results of a Treatment Protocol Encouraging First-Line Use of Fidaxomicin for Select Patients with *Clostridium difficile* Infection (CDI)

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Background. Large comparative trials found fidaxomicin to decrease recurrence rates relative to vancomycin for CDI. The price of fidaxomicin makes universal use cost-prohibitive. This study evaluates outcomes of patients who received fidaxomicin or vancomycin after a pathway encouraging fidaxomicin use for recurrent or serious CDI.

Methods. This was a single-center retrospective study of patients who received vancomycin or fidaxomicin for CDI during January 2012-January 2014. By protocol patients were eligible for fidaxomicin if they experienced a recurrent CDI or had 2 of 4 of: immunocompromising conditions; concomitant antibiotics; age > 65 years; lab values of WBC >15K, SCr rise 1.5x baseline, or albumin <3 gm/dL. Included patients were adults with *C. difficile* positive assays and acute diarrhea. All included patients were fidaxomicin-eligible per the institution protocol. Patients who failed initial therapy for the CDI episode were excluded. Baseline and clinical characteristics were collected. The primary outcome was readmissions due to recurrence of CDI within 90 days. Data were analyzed by Chi-square and t-test as appropriate and logistic regression with readmission as a binary variable was performed to determine characteristics associated with recurrence.

Results. On multivariate analysis that included treatment, severity of initial CDI, creatinine increase, and concomitant antibiotics, treatment with fidaxomicin was associated with lower risk of readmission with CDI (OR 0.33, 95% CI 0.12-0.93).

Variable	Vancomycin (n=46)	Fidaxomicin (n=49)	P-value
Age (mean±SD)	72.1±10.1	73.2±11.8	0.64
Length of stay (mean±SD)	10.6±7.42	8.96±725	0.26
ICU (n, %)	9 (19.6%)	13 (26.5%)	0.42
Current CDI episode was recurrence of earlier infection (n, %)	22 (47.8%)	38 (77.6%)	0.008
Concomitant antibiotics (n, %)	14 (30.4%)	24 (49.0%)	0.065
Creatinine >1.5x baseline (n, %)	9 (19.6%)	18 (36.7%)	0.064
Moderate or severe CDI (n, %)	23 (50%)	34 (69.4%)	0.154
Readmission with CDI within 90 days (n, %)	19 (41.3%)	10 (20.4%)	0.027

Conclusion. Treatment with fidaxomicin according to institutional protocol in our population was associated with less 90-day readmission due to CDI and may be cost-effective when readmission is taken into consideration.

Disclosures. **J. Gallagher**, Cubist: Consultant, Consulting fee; Optimer: Scientific Advisor and Speaker's Bureau, Consulting fee and Speaker honorarium; Astellas: Speaker's Bureau, Speaker honorarium **J. Reilly**, Optimer: Speaker's Bureau, Speaker honorarium; Cubist: Speaker's Bureau, Speaker honorarium **M. Trivedi**, Optimer: Speaker's Bureau, Speaker honorarium.

1654. Fecal Microbiota Transplant for the Treatment of Recurrent *Clostridium difficile* Infection via Encapsulated Cryopreserved Concentrated Fecally Derived Bacteria: A Cohort Review

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Background. *Clostridium difficile* infection (CDI) is a common and dangerous illness with a profound medical and economic impact. With the evolution of hypervirulent strains, standard antibiotic approaches are ineffective for increasing numbers of patients with recurrent CDI. Fecal microbiota transplant (FMT) is an effective strategy which utilizes the complex fecal microbiota of a healthy donor, providing exogenous bacterial flora as a therapeutic agent. Although FMT is already being more widely utilized, there is limited data assessing the effectiveness of an orally administered encapsulated modality. We reviewed the response of a cohort of patients that received cryopreserved concentrated fecally derived bacteria by capsules to evaluate the efficacy of this novel therapeutic approach.

Methods. A total of 19 patients with recurrent CDI were identified from April 2013 to February 2014 as candidates for FMT. Patients' ages ranged from 27-92 years. In an outpatient setting, under direct supervision, the patients were asked to swallow approximately 10 capsules. Post transplant, they were monitored for any adverse events and followed to assess clinical status. They were monitored for any post transplant symptoms with primary end point being resolution of CDI without relapse within 90 days.

Results. The overall cure rate was 90%. 13 patients (68%) had resolution after the first transplant; of the 6 patients that did not respond to the initial treatment, 4 went on to have resolution after subsequent transplantation. Abdominal pain was the only side effect reported post procedure by 5 subjects, or 26%. Of note, one of the 2 patients that did not achieve remission later died from complications of health-care acquired pneumonia which was not considered to be related to the study procedure.

Conclusion. In this retrospective study we found that FMT with oral capsules is highly effective against recurrent CDI. Although one third of the cases required repeat transplant, the procedure was well tolerated with an overall cure rate of 90%; with transient epigastric discomfort noted in 5 instances. This procedure offers an aesthetic, non-invasive, effective and cost efficient option for treatment of recurrent and persistent CDI.

Disclosures. **B. Hirsch**, Symbiotic Health: Shareholder, none received

1655. Lack of Adherence to SHEA-IDSA Treatment Guidelines for Severe *Clostridium difficile* Infection is Associated with Increased Mortality

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Background. *Clostridium difficile* infection (CDI) is associated with 14,000 deaths every year in the US according to the Centers for Disease Control and Prevention. In 2010, the Society for Healthcare Epidemiology of America and the Infectious Diseases Society of America (SHEA-IDSA) published guidelines stratifying the severity of CDI in patients based on their clinical presentation and laboratory values. They recommend specific initial treatment of CDI based on this severity stratification. The aims are to determine our institution's compliance with the *Clostridium difficile treatment* guidelines and to determine whether noncompliance with the *Clostridium difficile treatment* guidelines was associated with adverse outcomes.

Methods. Patients presenting to our institution from December 2012 to November 2013 with a diagnosis of CDI were identified. Clinical parameters, Laboratory values and Clinical course were obtained from electronic medical records. An adverse outcome of 90 day mortality with CDI as a primary or contributing factor was used.

Results. 230 patients met our inclusion criteria with a mean age of 63 ± 17. 143 (62%) patients from our study population were male. Adherence to the treatment guidelines recommended by SHEA-IDSA revealed that 124 (54%) were appropriately treated, 45 (19.5%) were under-treated and 61 (26.5%) were over-treated. Adherence to SHEA-IDSA treatment guidelines in different CDI groups was as follows: mild-moderate (61%), severe (57%), severe-complicated (33%), first recurrence (33%) and second recurrence (100%). 90 day CDI related mortality occurred in 22 patients. 10 of 45 under-treated patients (22%), 10 of 124 appropriately treated patients (8%) and two of 61 over-treated patients (3%) had 90 day CDI related mortality.

Conclusion. 46% patients did not receive treatment in accordance to SHEA-IDSA guidelines. More than half of these were over-treated while under-treatment occurred in 19.5% of cases. Under-treatment was associated with a high mortality (22% vs 8% in those appropriately treated; p = 0.027). These data suggest that adherence to CDI guidelines is associated with improved outcomes and emphasis on provision of appropriate guideline-based treatment appears warranted.

Disclosures. **All authors:** No reported disclosures.

1656. One Case of Pediatric Severepdeudomembranous Enteritis Treated with Fecal Microbiota Transplantation and Literature Review

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Background. Pseudomembranous enteritis (PME) is an acute inflammatory bowel disease affecting pediatric population. The aim of this study was to discuss the characteristics, diagnosis, and management of pediatric PME, and the potential possibility of fecal microbiota transplantation (FMT) application in pediatric PME.

Methods. The clinical manifestations, laboratory testing, diagnosis, and treatment of one case with severe pediatric PME were reviewed, analyzed, and summarized. Meanwhile, associated literatures of FMT were reviewed in this article.

Results. 1.A 13-month-old boy admitted with 2-month diarrhea, half-month edema, hypoalbuminemia, and malnutrition. At the beginning, exploratory laparotomy and high ligation of inguinal hernia was performed. Multiple broad-spectrum antibiotics

were daily introduced to this patient during 2 months. Protein-losing gastroenteropathy, severe PME, electrolyte disturbance, and malnutrition were diagnosed and treated accordingly. For PME, the patient was treated with 10-day oral metronidazole plus vancomycin for twice, then FMT was performed via nasal jejunal feeding tube. The patient completely recovered and released.2.In total 143 published articles were reviewed, 217 cases of recurrent Clostridium difficile infection, PME, and antibiotic associated diarrhae using FMT were included. 191 (88.0%) patients recovered at the first time treated with FMT. 8 of 9 (88.9%) recurrent patients who received the second FMT recovered. There was only one report of one pediatric PME case treated with FMT.

Conclusion. It needs to pay more attention to pediatric PME during clinical practice. Although, FMT might be another practicable option for severe or recurrent PME cases that was failed with empirical therapy, it is recommend that this strategy should be taken cautiously to the complicated cases of PME until more data generated from randomized studies can confirm the safety and effectiveness of FMT.

Disclosures. **All authors:** No reported disclosures.

1657. Who Seeks a Fecal Microbiota Transplant for Recurrent *C. difficile* Infection?: Patient Profile of the PUNCH CD Study

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Background. Managing recurrent *C. difficile* infection (CDI) is challenging due to the limited effectiveness of current treatment options. Fecal transplant (FT) appears to be an effective mechanism for managing multiply recurrent CDI. Studies have looked at the acceptability of FT. However, little is known about the patients who seek FT for recurrent CDI. We report the demographics of subjects enrolled in an ongoing Phase 2 study (PUNCH CD) of RBX2660 (microbiota suspension), a next generation standardized and commercially prepared version of FT for the treatment of recurrent CDI.

Methods. The PUNCH CD study enrolled a range of patients with recurrent CDI who were: ≥ 18 years with recurrent CDI who had at least two recurrences after a primary episode and completed at least two rounds of standard-of-care oral antibiotic therapy or had at least two episodes of severe CDI resulting in hospitalization.

Results. A total of 40 subjects were enrolled at 11 US centers with 34 subjects receiving treatment with RBX2660. Study centers were geographically and functionally diversified to include academic health centers located in major metro areas, community-based specialty clinics, and an integrated health system serving a sparsely populated largely rural state. Baseline characteristics of the 34 treated subjects were: mean age: 66.8 years (range 26.7 to 89.6 years); female (67.6%, n = 23); Caucasian (94.2%, n = 32) with a mean BMI 24.4 (range: 15.0 to 37.0). Comorbid illnesses included: gastrointestinal (61.8%, n = 21), cardiovascular (55.9%, n = 19), genitourinary (69.2%, n = 18), and psychiatric (28.1%, n = 9). A total of 76% (n = 26) of subjects were not working (mostly retired) while 24% (n = 8) reported working full- or part-time with no restrictions.

Conclusion. The population of patients seeking treatment in this study of next-generation FT drug was primarily Caucasian, elderly and female with multiple comorbidities. These demographics highlight populations with recurrent CDI and increase the awareness of opportunities to diversify enrollment in trials for recurrent CDI.

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1658. *C. difficile* Recurrence is a Strong Predictor of 30-day Rehospitalization Among ICU Patients

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Background. *C. difficile* infection (CDI) is as a deadly and costly problem. As a healthcare-associated complication, CDI has been immune to clinical and policy efforts to reduce its impact. While its incidence, mortality, morbidity and recurrence rates among critically ill have been investigated, the impact of recurrence on 30-day readmission, another important policy focus, has not been reported.

Methods. We conducted a secondary analysis of a multi-center retrospective cohort study of critically ill patients who survived their index hospitalization complicated by CDI. CDI was defined by the presence of diarrhea or pseudomembranous colitis and a positive assay for *C. difficile* toxins A and/or B. Recurrence of CDI (rCDI) was defined as diarrhea and positive *C. difficile* toxin after cessation of therapy and need for retreatment. We used descriptive statistics and a logistic regression to examine the rates and characteristics of 30-day readmission and the factors that impact it, with a specific attention to rCDI.

Results. Among 287 hospital survivors, 76 (26.5%) required a readmission within 30 days after discharge. At baseline, the group requiring a readmission did not differ significantly from the group that did not based on demographics, comorbidities, APACHE II scores or ICU type. Those with a readmission, however, were more likely to have hypotension at CDI onset (48.7% vs 34.1%, p = 0.025) and require vasopressors (40.0% vs 27.1%, p = 0.038), had a lower median BMI (24.7 vs 27.8, p < 0.001), and were less likely to require mechanical ventilation (56.0% vs 77.3%, p < 0.001). A far greater proportion of those requiring a readmission than those who did not had developed a recurrence either during the index hospitalization or within 30 days after discharge (28.95% vs 2.84%, p < 0.001). In a logistic regression, rCDI was a strong predictor of the need for 30-day rehospitalization (OR 15.33, 95% CI 5.68-41.40).

Conclusion. Over ¼ of all survivors of critical illness complicated by CDI require readmission within 30 days of discharge. CDI recurrence is a strong driver of such readmissions.

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1659. Relapse vs Reinfection. Evaluation of *Clostridium difficile* Isolates from Incident and Recurrent Infections, Minnesota 2009-2011

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Background. Recurrent *Clostridium difficile* infections (CDI) can be challenging. Recent studies suggest patients with recurrent infections are more likely to have a relapse of their previous strain type than be infected with a new strain of *C. difficile*, particularly those patients infected with the NAP1 strain. We used PFGE to type and compare 2009-2011 incident and recurrent isolates collected in Minnesota.

Methods. We analyzed data from clinical laboratories in 4 Minnesota counties participating in active population-based CDI surveillance as part of the CDC Emerging Infections Program. An incident case was defined as a *C. difficile* positive stool by either toxin or molecular assay in a surveillance area resident at least 1 year of age without a positive test in the prior 8 weeks. A recurrent case was defined as an additional positive stool collected >2 weeks but <6 months following an incident infection. Pairs of incident and recurrent isolates underwent PFGE and assigned a NAP type based on the PFGE pattern. Isolates were classified as indistinguishable if 0 PFGE bands different, related if = 6 bands and unrelated if > 6 bands.

Results. Of 581 patients with *C. difficile* isolates, 118 (20%) patients had incident and recurrent infections and isolates available for analysis. Fifty-four percent of patients had 1 recurrence (range: 1-5). Among first recurrent isolates, 72% were indistinguishable, 14% were related, and 15% were unrelated when compared to the incident isolate. The median time between the two episodes was 41 days (range: 15-170 days). Increases in time to recurrence were correlated with increases in PFGE pattern band differences (r = 0.39, n = 116, p < 0.0001). Most recurrences (82%) occurred within 8 weeks of the incident specimen. Patients with incident NAP1 infections were not more likely to have recurrences (15% vs 12%; p = 0.5), nor more likely to relapse on first recurrence (94% vs 82%; p = 0.1) than patients with non-NAP1 infections.

Conclusion. The majority of patients with recurrent CDI had a relapse of their initial strain type. Patients with NAP1 infections were not at higher risk for recurrence or relapse. Evaluation of CDI treatment and minimizing risk factors for recurrence are warranted to ensure patients are able to control the initial infection.

Disclosures. **All authors:** No reported disclosures.

1660. Risk of Recurrent *Clostridium difficile* Infection: Impact of Diagnostics and Treatment

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Background. In the setting of expanded use of molecular diagnostics and availability of fecal microbiota transplant (FMT) for treatment, understanding the epidemiology of recurrent *C. difficile* infections (CDI) is important.

Methods. We used active laboratory- and population-based surveillance data in metro Atlanta to identify a cohort of patients aged ≥ 18 years who developed an initial CDI (iCDI) from January 2010-September 2013. iCDI was defined as the first *C. difficile*-positive specimen by either molecular or toxin assay during study period. Patients were excluded from cohort if a prior CDI was identified from September-December 2009. Each iCDI patient was followed up for at least 3 months for recurrent CDI (rCDI), defined as a *C. difficile*-positive specimen >14 days from a previous positive test. A descriptive analysis of patients with rCDI was performed. Cox regression model was used on a random sample of iCDI patients stratified by age and

gender to determine adjusted hazard ratios (HR) for recurrence based on iCDI treatment.

Results. Of 11,945 iCDI cases identified, 22.0% developed a first recurrence, 7.0% developed a second recurrence, and 2.8% developed three or more recurrences. The median time to first recurrence was 39 days (IQR: 24-85 days), and 63% occurred within 2 months of iCDI and 94% within a year. Diagnosis was made using a molecular assay in 49% of iCDI, 54% first, 57% second and 61% of third recurrences. The risk for a subsequent CDI was higher in those with one recurrence compared to those without any recurrences (HR 1.56, $p < 0.01$). For every 10-year increase in age the HR was 1.12 ($p < 0.01$) for first recurrence and 1.05 ($p = 0.01$) for second recurrence. Of the 1,814 sampled cases, controlling for age, gender and diagnostic method, rCDI rates were similar in those treated with either metronidazole or vancomycin alone ($p = 0.13$).

Conclusion. Almost a quarter of iCDI cases developed recurrent disease. However, only a small proportion of cases had multiple recurrences and may benefit from FMT. The uptake of molecular diagnostics by clinical laboratories may increase detection of real or perceived recurrences. Additional studies are needed to further evaluate the link between more sensitive diagnostics and initial therapeutic choices with risk of CDI recurrence.

Disclosures. **All authors:** No reported disclosures.

1661. Travel-Associated Infectious Disease Surveillance Using the Pediatric Health Information System (PHIS) Database

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Background. International travel is increasing among US children and adolescents, potentially leading to increased rates of travel-associated infectious diseases (TAIDs). Surveillance networks for TAIDs in the United States are limited. The Pediatric Health Information System (PHIS) database now collects detailed data on all pediatric admissions to 44 children's hospitals in the United States.

Methods. We identified all discharges with an ICD-9 diagnosis for malaria, typhoid, and dengue from 1999 to 2012 from 16 participating hospitals with complete data. Readmissions were excluded. Incidence rates were determined by cases divided by total hospital discharges per year. Individual disease and pooled incidence rates were compared between 1999-2005 and 2006-2012 as well as before (1999-2006), during (2007-2009), and after (2010-2012) the US economic recession.

Results. Pooled incidence of TAIDs (malaria, typhoid, and dengue) increased significantly between 1999-2006 and 2007-2012, from 12.0 to 15.2 cases per 100,000 person-years ($p = 0.048$). Incidence rates of each individual disease also increased but did not achieve statistical significance. Four of 16 hospitals (25%) had a statistically significant increase in pooled TAID incidence and none saw a significant decrease. When comparing before, during, and after the 2007-2009 economic recession, there was a significant change in incidence rates for dengue ($p = 0.016$) and pooled TAID ($0 = 0.009$), though all diseases studied showed a similar trend (table).

Hospital incidence rates (cases per 100,000 person-years) of TAIDs in time periods spanning the US economic recession

	1999-2006	2007-2009	2010-2012
Malaria	6.7	6.4	8.4
Typhoid	5.0	4.4	7.0
Dengue†	1.1	0.6	2.5
Pooled†*	12.9	11.3	18.0

†$p<0.05$ (2007-2009 vs 2010-2012)
*$p<0.05$ (1999-2006 vs 2010-2012)

Conclusion. Hospital admissions for pediatric TAIDs, including malaria, typhoid, and dengue, are increasing among a large group of pediatric hospitals in the United States. Incidence rates decreased in 2007-2009 perhaps related to the economic recession and reduced travel. The PHIS database may provide a useful surveillance tool to measure incidence of travel-associated diseases among children in the United States.

Disclosures. **All authors:** No reported disclosures.

1662. Rates and Risk Factors for Multidrug-resistant Bacterial Colonization Before and After International Travel

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Background. Multidrug-resistant (MDR) *E. coli* (MDREC) colonization increases from 2% in US-based to 11% in deployed, healthy military personnel. It is unclear if colonization with MDR organisms occurs through deployment exposures or risks related to routine overseas travel. This study evaluates rates and risk factors associated with MDR gram-negative bacterial and MRSA colonization after international travel.

Methods. Participants traveled internationally ≥5 days. Pre- and post-travel, colonizing bacteria from oropharyngeal, nares, groin, and peri-rectal (PR) areas were collected using BD CultureSwab™ MaxV(+). Identification and susceptibilities were done by the BD Phoenix system. Non-MDR pre- and post-travel MDR within a subject were compared by pulsed-field gel electrophoresis (PFGE). A questionnaire solicited demographics and potential risk factors for MDR acquisition (purpose, itinerary, accommodations, water exposure, antimalarials, antibiotics, hospitalizations, and illness).

Results. Of 58 participants, 41% were male and median age was 64. Pre- and post-travel swabs were obtained a median of 10 and 7 days before and after travel, respectively. Itineraries included 18 to the Caribbean and Central America, 17 to Asia, 16 to Africa, 5 to Europe, 4 to South and North America. 17 of 22 taking malaria prophylaxis used atovaquone/proguanil. Additional systemic antimicrobials included 2 ciprofloxacin, 1 erythromycin, 1 azithromycin, 1 cephalexin, and 1 unknown antibiotic. The only MDR organism isolated was MDREC in 5 (9%) participants post-travel (all PR and unrelated by PFGE). There were no statistically significant associations between exposure risks and new MDREC colonization. Of 36 participants colonized with *E. coli* pre- and post-travel, new resistance was detected: 15 (42%) trim/sulfa ($p < 0.01$) and 16 (44%) tetracycline ($p < 0.01$). Risks associated with new resistance only occurred with tetracycline; notably local water ingestion ($p < 0.05$). No participants were colonized with MRSA pre- or post-travel.

Conclusion. Consistent with prior studies, new antibiotic resistance was noted in colonizing *E. coli* after international travel. 9% of participants acquired new strains of MDREC without identified risks.

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1663. Imported Exotic Infectious Diseases in Columbia, Missouri

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Background. The variety and number of imported exotic infections acquired by Midwest travelers and immigrants is not well known. Midwest physicians, particularly in rural settings, may not consider a foreign exotic infection as the cause of illness among patients who were also travelers or immigrants. We reviewed our past experience in patients diagnosed with a foreign exotic infection at the University of Missouri, in Columbia, Missouri.

Methods. From the Geo-sentinel master list, we created a sublist of exotic infections acquired outside of the United States of America and performed a retrospective chart review for patients with one or more of these diagnoses. Inclusion criteria: Patients seen by the Division of Infectious Diseases from January 2001 to January 2014, who had a diagnosis of an imported exotic infection and 18 years or older. We abstracted demographic data, travel history, clinical findings, and laboratory results.

Results. We recorded 38 cases of exotic infections. Tuberculosis (TB) was seen in 17 patients with one or more of the following: 4 lymphadenopathy, 4 gastrointestinal, 7 pulmonary, 2 each disseminated and latent TB, and 1 each of genitourinary and spine TB. There was no specific geographical trend: 3 Central America (CA), 4 Asia, 4 Africa, 2 Oceania and 1 Europe; 3 TB cases also had HIV and 1 had Echinococcosis. The remaining cases were diverse in diagnoses and origins: Africa: 4 cases of malaria (3 Africa, 1 Sri Lanka) and 1 each of typhoid (Ghana), paratyphoid (Sierra Leone), giardiasis (Sudan), loa loa (Gabon) and schistosomiasis (West Africa); Asia: 1 each of typhoid (Nepal), Leprosy (Sri Lanka), viral hepatitis A (Bangladesh), Japanese encephalitis (Thailand) and chronic Q fever (Iraq); CA: 2 cases each of neuro-cysticercosis (Mexico) and HTLV-1 (Mexico); 1 each of giardiasis (Ecuador), Chagas disease (El Salvador) and brucellosis (Mexico).

Conclusion. Like travelers and immigrants from coastal and urban USA settings, rural Midwest travelers and immigrants can present with a wide variety of foreign exotic infections. Knowledge of the variety and types of such infections is important for the education and training of health care providers; evaluation of ill patients; and preventive medicine for travelers.

Disclosures. **All authors:** No reported disclosures.

1664. Case Series of Imported Enteric Fever in Japan: Clinical Characteristics, Antibiotics Susceptibility, and Relapse Risk Factors

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Background. To the best of our knowledge, there are limited reports of enteric fever cases in returning travelers. Following the revision of levofloxacin and ciprofloxacin breakpoints by the Clinical Laboratory Standard Institute (CLSI) in 2012, we determined clinical characteristics, antibiotics susceptibility, and relapse risk factors for enteric fever in Japan.

Methods. The retrospective cross-sectional study was conducted in a single institute in Tokyo, Japan between January 2006 and December 2013. Enteric fever was defined as isolation of *Salmonella* Typhi or *S.* Paratyphi from blood and/or stool in a patient with fever.

Relationship between isolate source and fluoroquinolone sensitivity (n=29)

Antibiotics susceptibility	Isolate source: South Asia (n=24),n (%)	Isolate source: Southeast Asia (n=5), n (%)
Susceptible	0 (0)	4 (80)
Intermediate	18 (75)	1 (20)
Resistant	6 (25)	0 (0)

Results. Of the 35 cases of enteric fever that were diagnosed during the study period, 28 (80%) patients had returned from South Asia and 6 (17%), from Southeast Asia. Only 8 (23%) patients had a pre-travel consultation, including 4 (11%) with a typhoid vaccination in previous 2 years. Only 16 (47%) of 34 fulfilled the criteria for sepsis, while 19 (90%) of 21 cases experienced relative bradycardia. Of 35 cases, rose spots were observed in only 2 (6%) cases and eosinopenia (0-1%) was present in 34 (97%). Of 32 cases with image findings observations include splenomegaly (n = 17, 52%), paraileocecal lymph node swelling (n = 8, 24%), and ileocecal thickening (n = 4, 11%). All cases were sensitive to ceftriaxione except for 1 case of ESBL producing *Enterobacteriaceae*. None of the detected bacteria from South Asia were susceptible to fluoroquinolone according to the CLSI 2012 breakpoint (table). The relapse rate was 8.6% with no significant risk for relapse related to days from onset to treatment ($P = 0.28$) or sepsis ($P = 0.71$). However, >7 days to reach defervescence was a significantly relapse risk factor ($P = 0.035$).

Conclusion. Fluoroquinolones are not recommended as empiric treatment for enteric fever in travelers returning from South Asia. While there are no concerns for relapse based on the time to start treatment and the severity at the initial presentation, there are for prolonged duration (>7 days) to reach defervescence.

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1665. Health Information Given by Travel Agencies in Pereira, Colombia

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Background. There are no previous studies in Latin America regard health information provided by travel agencies. For that reason this study was conducted to assess health-related information provided by agencies of Pereira, Colombia.

Methods. Five covert investigators visited 36 agencies and requested information on a package holiday for 1 of 5 destinations randomly assigned to the assessed agency (Mexico, Panama, Cuzco, Manaus, Rio de Janeiro). Following an in-person interview, the investigator recorded any health-related information provided on a pretested form. If none was mentioned, the agent was prompted using a standardized procedure. Assessed information included vaccinations, destinations diseases and recommendation to consult a health professional, among others.

Results. About 11% of the travel agents gave health-related advice spontaneously and all of those recommended yellow fever (YF) vaccination, while 25% of them gave information about destination diseases. After being partially prompted by the investigator, 44% provided health advice, 63% mentioned the need for vaccinations, 31% the recommendation to consult a health professional. After being fully prompted by the investigator, 33% provided health advice, 77% on vaccinations, 23% about consult a health professional. However, 11% gave none health-related information. After asked by Manaus, Brazil (risky for YF), only 1 agency (3%) advice spontaneously about YF vaccination.

Conclusion. Health-related information provided by travel agencies in Pereira is low. When given, is superficial and mainly recommending YF vaccination, without considering destination. Even more, not providing advice in risky destinations (e.g., Manaus). Up-to-date and readily available information on health risks should be provided to travel agencies and structured training given in collaboration with health professionals.

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1666. Transmission potential and operational costs for possible mumps virus exposure among immigration detainees

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Background. On January 13, 2014 a previously healthy 43 year old male detainee who had been in custody for 323 days was evaluated for fever, unilateral parotid gland swelling and pain; he was referred to a local hospital given hemodynamic instability. In the hospital he was treated empirically for bacterial parotitis with intravenous vancomycin and was serologically evaluated for possible mumps virus infection.

Methods. A commercial mumps virus IgM assay was positive for the case-patient which initiated clinical examination, cohorting and mumps serology testing of 105 individuals who were in the same detention dormitory or worked with the ill detainee during kitchen duty.

Results. Among the 105 cohorted detainees, 12.4% (n = 13) were found to be susceptible to mumps; none were found to have clinical evidence of mumps. Medical staff spent an estimated 35 hours evaluating the cohort with an estimated laboratory cost of $2,400. Subsequent confirmatory testing by the Washington State Public Health Laboratory on the same initial serum specimen of the suspected index case was negative for mumps IgM while positive for mumps IgG, indicating that preliminary testing was a false positive.

Conclusion. Our study indicates that immigration detention populations are vulnerable to mumps virus outbreaks given immunity levels below the threshold necessary to prevent transmission in a closed population. Initial submission of a salivary specimen for detection of mumps virus RNA as well as serum for mumps IgG could have excluded the diagnosis of mumps expeditiously, preventing the direct and opportunity costs noted above as well as unmeasured cost related to delays in custody operations and patient anxiety.

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1667. Typhoid fever among immigration detainees: infection control challenges and potential for intra-and inter-facility spread

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Background. In 2013, five patients with confirmed typhoid fever were diagnosed while in U.S. Immigration and Customs Enforcement (ICE) or U.S. Customs and Border Protection (CBP) custody. Four patients required hospitalization; two of the patients, both from a South Asian country, were infected with drug resistant isolates. All hospitalized patients survived without sequelae and were returned to the respective law enforcement agency in stable clinical condition.

Methods. Confirmed cases had fever as well as a stool and/or blood culture positive for *Salmonella typhi*. Potential contacts were calculated for each typhoid fever case based on facility layout and dormitory census. Each patient was housed in at least two distinct facilities during their period of ICE custody; some patients transferred multiple times. The census of ICE detainees housed in these facilities ranged from approximately 180 to 1800 detainees.

Results. These cases had close contact with an estimated 1300 other detainees in a total of nine facilities. All of cases were barred from kitchen duties. Challenges were encountered during the education of infected patients and other detainees due to low English proficiency and cultural diversity requiring the use of multilingual, low literacy posters and the use of telephonic translators.

Conclusion. Although the average time in custody prior to diagnosis and treatment was less than one week, asymptomatic carriers pose a unique risk given the potential for direct contact for extended periods of time and contamination of food as kitchen workers. Providers seeing patients in the immigration detention setting who present with febrile illness, even after extended custody stays, should consider typhoid fever in the differential diagnosis given the potential of intra- and inter-facility transmission. Hand hygiene, sanitary toileting practices and food handling training are cornerstones in prevention of spread within the detention setting.

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1668. Prevalence of Eosinophilia and Parasites in a Newly Arrived Refugee Population

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Background. Eosinophilia is a major health issue concerning immigrant populations from parasite endemic regions such as Sub-Saharan Africa, the Middle East and Asia. The presence of eosinophilia is most commonly due to parasite infections in this group. This study was undertaken to assess the prevalence of eosinophilia and the prevalence of parasitic infections in refugees being resettled in Dayton, Ohio.

Methods. This was a retrospective chart review of all refugees who were evaluated at Public Health – Dayton and Montgomery County (Ohio) from 2009-2013. Inclusion criteria was country of origin in Africa, Asia or Middle East. Evaluation included a single stool examination for O&P as well as a CBC with automated differential. Refugees were excluded from the study if there was no country of origin listed, or for missing lab values. Eosinophilia was defined as absolute eosinophil count > 500 cells/μL or eosinophil percentage ≥ 7.0.

Results. A total of 637 charts of individuals were reviewed; 39 were excluded from analysis. Of the remaining 598 refugees, 364 were male and 234 female. A total of 300 were from countries in Africa, 211 from the Middle East and 87 from Asia. The mean age was 29.1; 450 (75.3%) of refugees were adults (age ≥ 18 years). Overall, 197 (32.9%) of the refugees had a positive screen for O&P. The most common parasite found was *Giardia* (29), followed by *E. histolytica/dispar* (17), *Schistosoma* (4), Hookworm (4), *Strongyloides* (3), *Trichuris* (3), and *Ascaris* (1). Non-pathogens were found in a total of 165 refugees. Eosinophilia was noted in 95 (15.9%) of the refugees and was associated with the finding of a tissue parasite in the stool O&P screen.

Conclusion. The percentage of refugees arriving with intestinal helminth infection was fairly low in this study, as compared to studies prior to the recommendation for refugees from sub-Saharan Africa and Asia to receive empiric therapy with albendazole prior to departure. Despite the recommendations for pre-departure treatment, many refugees arrive in the United States with parasitic infection, and many more have significant eosinophilia, emphasizing the need for prompt and thorough screening after arrival in the US.

Disclosures. **All authors:** No reported disclosures.

1669. Genetic Diversity of Pneumolysin and Pneumococcal Histidine Triad Protein D of *Streptococcus pneumoniae* Isolated from Invasive Infections in Children

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Background. The currently available vaccines for *Streptococcus pneumoniae* have limited serotype coverage. A protein-based universal vaccine could be a feasible and preferable alternative to broaden the protection provided by the vaccine. Pneumolysin (Ply) and pneumococcal histidine triad protein D (PhtD) are considered to be next-generation protein vaccine candidates. We aimed to analyze the genetic diversity of Ply and PhtD, and to evaluate their antigenic homogeneity.

Methods. A total of 173 pneumococcal invasive isolates were obtained during the period between 1991 and 2011. Serotypes were determined using the Quellung reaction, along with additional sequencing for capsular genes. Sequencing and allele typing for *ply* and *phtD* genes were performed using known or newly designed primers. Phylogenetic analysis was performed and antigenicity was compared for each allele type of the *ply* and *phtD* genes.

Results. A total of 27 serotypes were identified, with 19A (n = 30, 17.3%) and 23F (n = 24, 13.9%), being most common. In the *ply* gene, allele 1 (n = 64, 37.0%), 2 (n = 87, 50.3%), 3 (n = 4, 2.3%), 9 (n = 14, 8.1%), 10 (n = 1, 0.6%), and the newly assigned alleles 19 (n = 2, 1.2%) and 20 (n = 1, 0.6%) were identified. Analysis of the *phtD* gene with respect to nucleotide size revealed 13 allele types. Allele 5 (n = 127, 73.4%) was most common, followed by allele 9 (n = 14, 8.1%), 2 (n = 8, 4.6%), and 3 (n = 5, 2.9%). The sequence and antigenicity of the *ply* and *phtD* alleles displayed extensive homogeneity.

Conclusion. The genetic and antigenic diversity of Ply and PhtD was very limited. As candidates for the universal protein vaccine, the Ply and PhtD may have potential to broaden the coverage provided by the vaccine.

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1670. Comparative Metagenomics of Polymicrobial Surface Organisms and Their Invasive Monomicrobial Analogs Indicates the Rate of Genetic Alterations in the Infectious Organisms not Influenced by the Local Microbiome

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Background. Why only some bacteria isolated from mixed populations predominate or become infectious is incompletely understood, although ecological interactions of communities of bacteria referred to as the microbiome is gaining popularity as one explanation. We hypothesized that whole genome mapping (WGM) and sequencing (WGS) could reveal metagenomic differences pertinent to this phenomenon.

Methods. From a collection of >20,000 isolates and clinical data, we identified patients who had the same species isolated from both a sterile site such as blood (monoculture), and a non-sterile (polymicrobial) site such as a wound or surveillance culture. These 'paired isolates' then underwent WGM and WGS to determine if genomic rearrangements and/or single nucleotide changes occur more frequently in pathogens isolates from mixed vs pure infection habitats.

Results. WGM of 18 paired isolates did not reveal larger genomic rearrangements more frequently in polymicrobial than monomicrobial cultures. Further supporting these data at higher resolution, WGS did not reveal more subtle (i.e., single nucleotide variations (SNV) or point mutations) that were intrinsic to the pathogen or influenced by the ecology of the surrounding bacterial community. On rare cases, a stretch of DNA was found unique to an individual isolate within a pair, but this finding is not enough to substantiate a claim that presence of a pathogen in a microbiome environment is correlated with heritable genetic alterations relative to monoculture sites. There were no significant genomic differences between polymicrobial surface organisms and their invasive monomicrobial analogs.

Conclusion. Interactions between the pathogen and the greater bacterial population did not influence the frequency in which large scale genomic rearrangements, SNVs, or point mutations accumulated. Rather, our data suggests that the influence of other nearby organisms on the pathogen was minor, if any, and supports the notion that pathogenicity is inborn to the organism itself regardless of the surrounding community.

Disclosures. **All authors:** No reported disclosures.

1671. A Fatal Outbreak of a Rare but Emerging Clone of Extensively Drug-resistant *Acinetobacter baumannii* with Enhanced Virulence

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Background. The virulence mechanisms of *Acinetobacter baumannii*(AB) are not completely understood. Also, a high degree of virulence in immunocompetent hosts is unusual for AB. A cluster of six fatal AB infections in mostly immune-competent patients who received early infectious diseases consultation and appropriate antimicrobial therapy led us to hypothesize that isolates from these patients could possess unique traits that enhance virulence.

Methods. To test our hypothesis, we determined the health status of patients using three different co-morbidity and illness severity scoring systems, characterized isolates using comparative genomics, and evaluated the virulence of each isolate in a validated animal model.

Results. No patient had scores that indicated excessive co-morbidities or critical physiologic dysfunction. Two patients had bacteremia scores that indicated severe illness. Genomic analysis showed that two unrelated AB clones were associated with the infections. The clone associated with the majority (5 of 6) of patient deaths, clade B, is evolutionarily distinct from the three main international clonal complexes and is most closely related to strains isolated in the Czech Republic in 1994 and in a U.S. military hospital in Germany in 2003. One clade B isolate, MRSN16897, is hyper-virulent in a murine pulmonary model of infection when compared to other well-known and previously tested AB isolates. Of note, MRSN16987 establishes disseminating, fatal infections, even in healthy mice when other strains of AB cannot. Clade B strains contain virulence genes whose products differ from those in the majority of AB strains, including loci involved in iron metabolism, protein secretion, and glycosylation. Using genome sequences of the fatal strains and related isolates from our repository, we developed a PCR-based assay to rapidly and specifically detect clade B isolates. (This clade is not distinguishable by multi-locus sequence typing.)

Conclusion. We identified genomic correlates of virulence (a unique gene set in the progenitor, and 4 single nucleotide changes a hypervirulent derivitave) in the emerging AB clone. This clone is notable for a combination of resistance and higher virulence. Our findings highlight the value of combining surveillance, biobanking, and basic research.

Disclosures. **All authors:** No reported disclosures.

1672. *Streptococcus pneumoniae* Evades the Acute Inflammatory Response to Mucosal Colonization through Regulation of the Paracrine Lipid Mediator Platelet-Activating Factor

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Background. *Streptococcus pneumoniae* (the pneumococcus) remains a leading cause of infectious mortality worldwide. Acquisition of the pneumococcus occurs at the nasopharyngeal mucosa and elicits a rapid influx of neutrophils (PMNs) to the nasal lumen. However, the pneumococcus efficiently eludes clearance by PMNs and persists in the nasopharynx weeks after the acute inflammatory response recedes, amplifying the risk of invasive disease. A growing number of studies implicate the secreted phospholipid platelet-activating factor (PAF) as an important local mediator of PMN recruitment and activation in response to mucosal infections. While the pneumococcus has been shown to secrete a cell wall-bound esterase, Pce, which efficiently hydrolyzes PAF *in vitro*, it remains unknown whether regulation of local PAF concentration influences pneumococcal survival during colonization.

Methods. We make use of atraumatic colonization of the murine nasopharynx to model carriage in the human upper respiratory tract.

Results. We demonstrate that pneumococci lacking Pce (Pce^-) elicit greater numbers of luminal PMNs with elevated expression of the phagocytic receptor CD11b compared to wild type (WT) bacteria. Despite unaltered sensitivity to PMN phagocytosis *in vitro*, Pce^- bacteria exhibit a significant competitive survival defect during colonization which is completely abrogated upon systemic PMN depletion. Intranasal treatment with PAF receptor antagonists also abrogates the Pce^- survival defect, indicating that local PAF signaling may mediate this PMN-dependent effect. *In vitro,* pre-

incubation of PAF with WT (and not Pce$^-$) pneumococcal lysates prior to PMN stimulation inhibits CD11b surface expression, suggesting Pce inhibits PAF-mediated PMN activation directly. Accordingly, restoration of neutrophil activation *in vivo* through intranasal administration of PAF or pro-inflammatory bacterial by-products suppresses the competitive advantage of wild type pneumococci over the Pce$^-$ mutant.

Conclusion. Taken together, our findings suggest that pneumococcal Pce esterase contributes to innate immune evasion through hydrolysis of PAF, thereby actively inhibiting PMN phagocytic capacity *in trans* and promoting pneumococcal persistence during colonization.

Disclosures. **All authors:** No reported disclosures.

1673. Microbial and Inflammatory Markers for Fatal *Clostridium difficile* Associated Diarrhea

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Background. With its rising mortality rate in *C. difficile* infection (CDI), understanding the microbial factors and host inflammatory response associated with fatal infection is of public health importance. We hypothesize that subjects with fatal compared with treatment-responsive CDI are different in terms of host fecal inflammatory markers and toxin type of infecting *C. difficile* strain.

Methods. Between June 2011 and March 2013 in a teaching hospital in Texas Medical Center, a prospective study of all consenting CDI subjects identified 34 fatal cases. Patients in a comparison group consisted of the next subjects enrolled in the study without fatality (N = 34). All participates submitted a diarrheal stool that was *C. difficile* cytotoxin B positive. Aliquots of the original stool sample were tested for interleukin (IL)-8.

Results. Twenty-four of 34 (71%) fatal cases died within 10 weeks of onset of CDI. The number of patients with detectable fecal IL-8 concentration for the fatal cases was 12/34 (35%) compared with the non-fatal controls that were positive for IL-8 in 8/34 (24%). The mean value of fecal IL-8 in the fatal group was 940.62 ± 1001.66pg/mL compared with 185.24 ± 592.39pg/Ml for the non-fatal subjects ($p = 0.094$). Eleven of 21 patients with fatal outcome within 10 weeks of CDI had detectable fecal IL-8 with a mean concentration of 511.17 ± 1168.38pg/mL; statistically higher than in the controls ($p = 0.04$).

Presence of *tcdC* deletion in *C. difficile* isolates from patients with fatal CDI (13/34 = 38%) was statistically higher than found with controls (5/34 = 15%, $p = 0.02$). Patients who died within 10 weeks of onset CDI had higher prevalence of *tcdC* deletion (13/24 = 54%) than patients who survived more than 10 weeks ($p = 0.007$).

Conclusion. Host and microbial factors are important in the fatal outcome in CDI. Patients who had a fatal outcome more often had stools positive for IL-8 and had increased concentrations of fecal IL-8 compared with non-fatal CDAD. Fatal cases of CDAD more often were infected by a potentially hypervirulent strain of *C. difficile* positive for *tcdC* deletion. The differences seemed particularly striking when looking at the group who expired within 10 weeks of a CDI diagnosis, probably more indicative of CDAD-associated mortality than the patients showing more remote fatality.

Disclosures. **All authors:** No reported disclosures.

1674. Genomic Variation in Human Herpesvirus-8 and Implications for Pathogenesis of Kaposi Sarcoma: an analysis of GenBank sequences

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Background. Human herpesvirus 8 (HHV-8) is the etiologic agent for Kaposi sarcoma, Primary Effusion Lymphoma and Multicentric Castleman's Disease, conditions with heterogenous clinical manifestations. Little information exists on diversity in the genomic sequences of HHV-8 which codes for proteins that modulate cell cycle regulation, immune function and angiogenesis and the impact of this diversity on HHV-8-associated disease.

Methods. All HHV-8 sequences from GenBank were aligned in MOSAIK with refinement in Geneious (Biomatters, Ltd.). Perl scripts were used to calculate genome sequence coverage, regional variation by Hamming distance and nucleotide positional variation by Shannon entropy score. Hamming distance for each 50 nucleotide window is the pairwise distance between 2 sequences averaged over all sequences. Shannon Entropy score is given by $H_n =$, where is the probability of each of 4 possible nucleotides at position n, based on the distribution in all sequences.

Results. Six whole genome sequences of HHV-8 (half derived from cultured virus) were available in GenBank, along with 2558 subgenomic fragments, 93% of which were <1kb. Only 6 regions of the HHV-8 genome had >25 sequences available with K1, ORF26/27 and ORF75/K15 accounting for 2140 (83%) of the total available sequences. Across the HHV-8 genome, mean Hamming distance was 0.3. In K1 and K15, mean (range) Hamming distance was 3.7 (0-15.8), and 2.0 (0-6.6), respectively. Hn = 0 for 97.0% of the genome with a maximum of 1.27. For the 4206 positions with Hn > 0, mean (SD) Hn = 0.31 (0.18) and only 17.6% of these fell into non-coding regions. Of the 10% most variable positions (n = 469, Hn > 0.562), 322 (68.7%) of these single nucleotide polymorphisms (SNPs) fell within 11 of 24 pre-identified viral oncogenes.

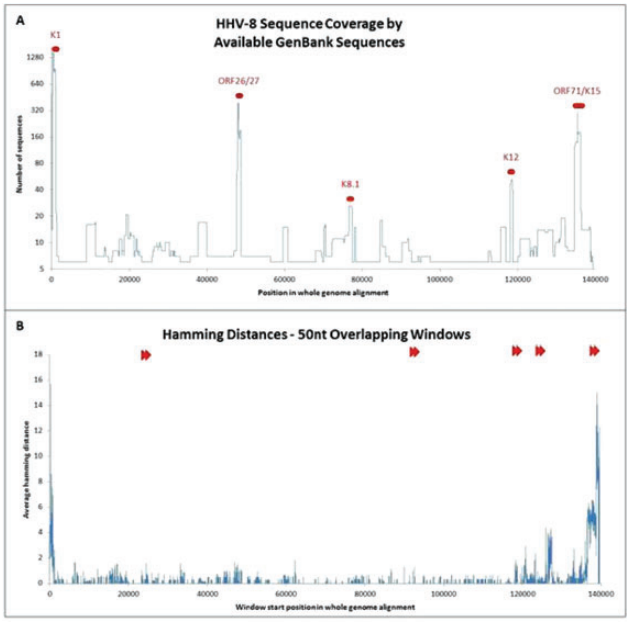

Figure: Available sequence data and viral genetic variation across the HHV-8 genome. (A) The number of bases at each position of the alignment of all 2564 HHV-8 sequences. (B) Hamming distance, describing the genetic variation in 50 nucleotide overlapping windows. Alignments were expanded in regions of multiple short direct repeats (shown by multiple arrow heads).

Conclusion. There are scant sequences available for most of the HHV-8 genome. Hamming distance analysis revealed low regional diversity except in the known highly divergent genes of K1 and K15/ORF75. Remaining positional genomic heterogeneity were SNPs in coding regions, including many in genes with putative oncogenic activity. Newer sequencing technologies have great potential to explain the relationship between HHV-8 genomic diversity and disease phenotypes.

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1675. A Novel Murine Pneumonia and Bacteremia Model for Carbapenem-Resistant *Klebsiella pneumoniae* Infection

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Background. The incidence of carbapenem-resistant *Klebsiella pneumoniae* (CRKP) infections has increased significantly in recent years, posing a major public health threat. Invasive CRKP infections may retain *in vitro* susceptibility only to second-line agents such as tigecycline and polymyxins, with mortality as high as 58% in some series. Present clinical data has relied principally on retrospective studies. Developing effective animal models is critical in evaluating future treatment combinations.

Methods. Animal use committee approval was obtained. Following 7 days of acclimation, outbred female Swiss-Webster mice were administered cyclophosphamide 150 mcg/kg four days and 100 mcg/kg one day prior to inoculation to induce neutropenia with hematologic verification. Under isoflurane anesthesia, mice received 50 µL of a 10^8 colony forming units per milliliter (CFU/mL) aerosolized suspension of American Type Culture Collection (ATCC) strain 1705, *K. pneumoniae* via tracheal intubation. Mouse wellness was evaluated using a standardized scoring system to establish a humane marker for euthanasia and was also used as a surrogate of mortality prior to the pre-defined 96-hour end-point. At necropsy, quantitative blood cultures were obtained via terminal cardiac puncture, and lung samples were taken for histologic evaluation and quantitative tissue culture. Specimens were plated on CHROMagar KPC® plates (CHROMagar, Paris, France) to confirm CRKP.

Results. Initially, a lethal dose (LD) study was performed utilizing doses from 10^6-10^9 CFU/mL. A total of 79 mice were inoculated with the 10^8 CFU/mL dose establishing a 75% pre-endpoint mortality (LD 75) with lung bacterial counts averaging 7.46 x 10^{10} CFU/mL and average time to mortality of 69.3 hours. CRKP bacteremia was detected in 79% of infected mice. Lung weights averaged 0.523 grams (normal 0.280 grams/ 21 gram mouse). Gross lung pathology routinely demonstrated moderate to severe consolidative pneumonia often with alveolar hemorrhage.

Conclusion. Findings suggest that sepsis and bacteremia can be reliably produced in neutropenic Swiss-Webster mice via the tracheal inoculation of *K. pneumoniae* (ATCC 1705). This model has promise for future *in vivo* testing of antimicrobial regimens for highly drug-resistant Gram-negative bacilli.

Disclosures. **All authors:** No reported disclosures.

1676. Salivary Levels of *Streptococcus mutans* in Individuals with Temporomandibular Disorders

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Background. Individuals with temporomandibular disorders (TMD) may experience higher levels of psychological stress and chronic pain, as well as some biochemical and immunological salivary changes; however, microbiological parameters related to dental caries have not yet been investigated in this population. The aim was to evaluate whether TMD patients present higher levels of *Streptococcus mutans* in saliva.

Methods. Cross-sectional study which included 39 patients with TMD, selected according to the Fonseca's questionnaire and the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD), and other 33 individuals with no TMD symptoms (control group). The volunteers were classified according to their caries risk in low, intermediate or high risk. Unstimulated saliva samples were collected from both TMD and the control group on the morning shift from 9 to 11am, at least one hour after the last meal. Aliquots of 100mL of each saliva sample were diluted, plated on Mitis Salivarius Agar containing Bacitracin, and then they were incubated (5% CO_2, 37°C, 48 hours) in order to quantify *S. mutans* levels (CFU/mL); the colonies growth was confirmed by polymerase chain reaction (PCR).

Results. When the Student's t-test was applied, there was no statistically significant difference between the TMD and the control group ($p > 0.05$).

Conclusion. Individuals with TMD did not show higher levels of *S. mutans* in saliva than the control group. Further studies investigating such a relationship should be carried out.

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1677. Macrophage migration inhibitory factor (MIF) promotes clearance of pneumococcal colonization

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Background. Human genetic polymorphisms associated with decreased expression of macrophage migration inhibitory factor (MIF) have been linked to the risk of community-acquired pneumonia (CAP).

Methods. Since *Streptococcus pneumoniae* is the leading cause of CAP and nasal carriage a precursor to invasive disease, we explored the role of MIF in the clearance of pneumococcal colonization in a mouse model.

Results. MIF-deficient mice (*Mif* $^{-/-}$) showed prolonged colonization with both avirulent (23F) and virulent (6A) pneumococcal serotypes compared, to wild-type animals. Pneumococcal carriage led to both local upregulation of MIF expression and systemic increase of the cytokine. Delayed clearance in the *Mif* $^{-/-}$ mice was correlated with reduced numbers of macrophages in upper respiratory tract lavages as well as impaired upregulation of monocyte chemotactic protein-1 (MCP-1/CCL2). We found that primary human monocyte derived macrophages as well as THP-1 macrophages produced MIF upon pneumococcal infection in a pneumolysin-dependent manner. Pneumolysin-induced MIF production required its pore-forming activity and phosphorylation of p38-MAPK in macrophages, with sustained p38-MAPK phosphorylation abrogated in the setting of MIF-deficiency. Challenge with pneumolysin-deficient bacteria demonstrated reduced MIF upregulation, decreased numbers of macrophages in the nasopharynx, and less effective clearance. *Mif* $^{-/-}$ mice also showed reduced antibody response to pneumococcal colonization and impaired ability to clear secondary carriage. Finally, local administration of MIF was able to restore bacterial clearance and macrophage accumulation in *Mif* $^{-/-}$ mice.

Conclusion. Our work suggests that MIF is important for innate and adaptive immunity to pneumococcal colonization and could be a contributing factor in genetic differences in pneumococcal disease susceptibility.

Disclosures. **All authors:** No reported disclosures.

1678. Triclosan, triclocarban, metabolism and microbiome: a randomized, cross-over study

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Background. The human microbiome has been implicated in the development and maintenance of obesity. We hypothesized that triclosan and triclocarban(TCS), microbicides found in many household and personal care products (HPCP) and present in 75% of US human urine samples, play a role in altering microbiota, metabolic function and weight.

Methods. In a double-blind, randomized, cross-over study participants were given TCS or non-TCS containing toothpaste, dish and hand soap for 4 months then switched arms. Of 16 subjects enrolled, 13 completed the trial. Blood, stool, skin swabs, gingival plaque, saliva, urine samples and weights were obtained at baselineand at regular intervals throughout each period. Bloods were analyzed for metabolic and endocrine markers and urines for TCS. Illumina sequencing of stool skin, skin, saliva and gingival plaque is underway. All statistics were performed in R.

Results. In the TCS arm, TC levels where higher (median 25,555 pg/ul) than in the non-TCS arm (median 218 pg/ul) ($p < 0.001$). No significant differences were found in testosterone, T4 or TSH levels or in 17 adipocytokines on the obesity panel. Six subjects gained more than 0.6% of body weight (the highest quartile) in the TCS arm but lost or stayed at the same weight in the non-TCS arm; the reverse (weight gain in non-TCS but not in TCS arm) was seen in only one person (OR = 6, p = 0.13, McNemar test). Microbiota analysis of saliva, skin and stool samples is pending.

Conclusion. In this pilot study we found that individuals were somewhat more likely to gain weight while using TCS-HPCP than when not using TCS-HPCP; this was not explained by hormonal or adipocytokine changes. Sequencing studies will examine whether TCS affects microbial communities.

Disclosures. **All authors:** No reported disclosures.

1679. Interactions of the *Herpes Simplex Virus* γ34.5 Protein With Host Signaling Pathways Influence Central Nervous System Disease in Newborn Mice

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Background. Central nervous system (CNS) disease from HSV is a feared outcome of infection, and survivors often suffer lifelong neurologic sequelae. The HSV-1 protein γ34.5 is important for neurovirulence, counteracting the host type I interferon (IFN) response. Three distinct functions of γ34.5 have been reported, but their contributions to CNS disease have not been individually elucidated in different age groups.

Methods. We used mutant viruses and their corresponding revertants in models of HSV encephalitis to study the contribution of different functions of HSV γ34.5 to CNS disease in newborn and adult mice. Groups of mice, some with targeted mutations, were inoculated intracranially and followed over time for mortality. Viral replication in the CNS was assessed by plaque assay.

Results. Genetic deletion of the type I IFN receptor increases CNS virulence of wild-type (WT) HSV-1 in adult mice, leading to higher overall mortality, shorter time to mortality, and increased viral replication compared with WT hosts. In contrast, newborn mice had 100% mortality within four days of inoculation independent of the expression of the type I IFN receptor, with equivalent viral titers in the brains of both genotypes. Based on these results, we hypothesized that mutations of HSV-1 γ34.5 would retain virulence in this age group. Complete deletion of γ34.5 attenuated virulence in both adult and newborn WT mice, but virulence of this mutant remained distinct from its revertant virus in IFN receptor knockout mice, suggesting functions of γ34.5 other than affecting type I IFN are important. We have shown that the autophagy-inhibiting function of γ34.5 is dispensable for pathogenesis in newborn but not adult mice. In contrast, we show here that mutations in γ34.5 which disrupt the ability of HSV to counteract host translational shutoff via host PP1α, and mutations abrogating interaction with the host signaling protein TBK1, individually attenuate virulence in WT newborns.

Conclusion. The host translational shutoff and TBK1 functions of γ34.5 are important for HSV virulence in the CNS in newborn mice. Identification of factors important for HSV virulence in the CNS can identify therapeutic targets that may attenuate disease and serve as potential adjuvants to acyclovir.

Disclosures. **All authors:** No reported disclosures.

1680. Lung Cellular Bioenergetics in Galectin-3 Deficient Mice Infected with Respiratory Syncytial Virus

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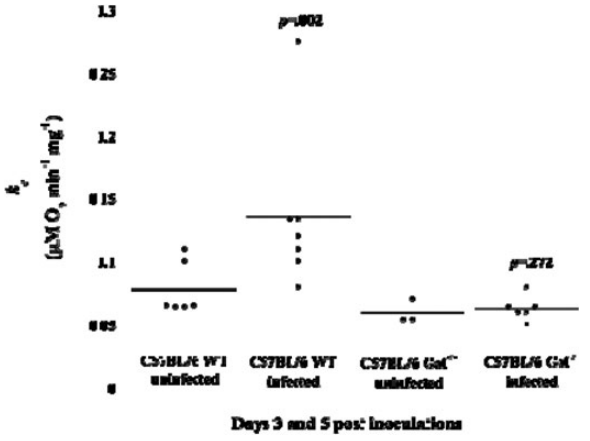
Background. Cellular bioenergetics includes all metabolic processes involved in energy conversion. Cellular respiration implies delivery of O_2 and metabolic fuels to the mitochondria, oxidation of reduced metabolic fuels and passage of electrons to O_2. Lung cellular bioenergetics (mitochondrial O_2 consumption and ATP synthesis) are increased in C57BL/6 mice infected with respiratory syncytial virus (RSV). This study investigated these biomarkers in galectin-3 deficient (Gal-$3^{-/-}$) C57BL/6 mice infected with RSV. Gal-3 (b-galactoside-binding lectin) is an immune modulator with pro-inflammatory activity. Its absence is expected to ameliorate the disease.

Methods. RSV A2 infection was induced by intranasal inoculation of wild-type and Gal-$3^{-/-}$ mice. Lung fragments were then collected on days 3 and 5 after inoculation and analyzed for cellular bioenergetics (mitochondrial O_2 consumption and ATP content). Cellular respiration was measured using phosphorescence O_2 analyzer. Cellular ATP was measured using the luciferin/ luciferase system.

Results. In wild-type mice, the rate of respiration (mean ± SD, in μM O_2 mg^{-1} min^{-1}) in uninfected lungs was 0.08 ± 0.02 (n = 6) and in RSV-infected lungs was 0.14 ± 0.06 (n = 7, $p = 0.002$). In Gal-$3^{-/-}$ mice, the rate of respiration in uninfected lungs was 0.06 ± 0.01 (n = 3) and in RSV-infected lungs was 0.06 ± 0.01 (n = 6, $p = 0.272$) (figure). Lung cellular ATP increased by 18% in wild-type mice infected with RSV and decreased by 16% in Gal-$3^{-/-}$ mice infected with RSV.



Conclusion. The increase in lung cellular bioenergetics is not observed in Gal-3 deficient mice. Thus, Gal-3 plays a role in RSV-induced modulation of cellular metabolism. The impact of Gal-3 on RSV infection requires further investigation.

Disclosures. **All authors:** No reported disclosures.

1681. Randomized Clinical Trial of the Recovery of Probiotics *Lactobacillus rhamnosus* GG (LGG) and *Bifidobacterium animalis* subspecies *lactis* (BB-12) from the Gastrointestinal (GI) Tract of Healthy Volunteers

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Background. Probiotics are live microorganisms that confer a health benefit when ingested. The dietary supplement ProNutrients® Probiotic contains the probiotics LGG and BB-12 in a powder sachet. The objectives of this study were to confirm the survival and recovery of the organisms from the GI tract of healthy volunteers after ingestion of the supplement and to assess safety.

Methods. This was a 2 arm, parallel group, open label randomized prospective study of healthy volunteers. All subjects underwent a run-in period (> 14 days). Thereafter, the subjects were randomized to a non-supplemented control group (C) or the probiotic (P) group, which consumed 1 sachet of supplement (S) containing > $1x10^9$ colony forming units (CFU) of each organism/day for 21 days. There was a 28 days post-S period. Fecal samples were collected at baseline (the end of the run-in period), and after 14, 21, and 28 days. LGG and BB-12 were quantified by (1) quantitative culture (qCX) with colony ID confirmed by polymerase chain reaction (PCR) and (2) qPCR. The primary endpoint was the recovery of LGG and BB-12 (CFU/g) from the fecal samples of all subjects at 21 days. CFU were log_{10} transformed. Paired t-tests were used to compare within subjects change from baseline. ANOVA models with a treatment term were used to compare groups.

Results. 27 subjects (13 males and 14 females) were randomized and included in the analysis. The Table shows results for recovery of LGG and BB-12 by qCX at 21 days Similar results were obtained at 14 days and for recovery by qPCR at 14 and 21 days.

	LGG		BB-12	
	P N=19	C N=8	P N=19	C N=8
Baseline				
Mean (SD) log_{10} CFU/g sample	3.5 (0.6)	3.4* (0.0)	5.4 (0.0)	5.4* (0.0)
21 days after baseline				
Mean (SD)	5.5 (1.7)	3.4* (0.0)	7.2 (1.1)	5.4* (0.0)
p-value 21 d vs baseline	< 0.001	-	< 0.001	-
p-value P vs C	0.006		<0.001	

*Lower limit of detection.

6 subjects (31.6%), all in the P group, reported 14 mild and 7 moderate severity adverse events (AE). The 2 treatment-related AEs were mild: diarrhea and abdominal distension, each in 1 subject.

Conclusion. Few studies have examined the recovery of viable organisms after ingestion of probiotic combinations. Here we demonstrate the recovery of viable LGG and BB-12 from the GI tract of healthy volunteers who consumed this probiotic product matrix. The supplement was well tolerated.

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1682. Clinical Outcomes Associated with Biofilm-Related Bacterial Infections

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Background. Biofilms are associated with persistent infection. Reports characterizing clinical outcomes and patient risk factors for colonization or infection with biofilm forming isolates (BFI) are scarce. This exploratory study aims to identify potential risk factors associated with BFI and assess clinical outcomes.

Methods. A convenience sample of 187 unique clinical isolates from 144 patients collected from 2005 to 2012 was studied. 48h static biofilms were assessed by the microtiter plate method with crystal violet staining. Clinical information including demographics, comorbidities, antibiotic usage and clinical outcomes was determined retrospectively, and associations with BFI were determined by univariate analysis (SPSS v19.0).

Results. Patients were primarily male (82%) military members (65%) with combat trauma (56%). Of the 113 (60%) BFI, 5 were MSSA, 14 MRSA, 32 *Klebsiella pneumoniae* (KP), 5 *Escherichia coli* (EC), 29 *Acinetobacter baumannii* complex (ABC), and 28 *Pseudomonas aeruginosa* (PA). There were 1 MSSA, 2 MRSA, 12 KP, 29 EC, 24 ABC, and 6 PA among 74 non-BFI. BFI were more frequent among MRSA ($p = 0.021$) and PA ($p = 0.004$), and less common among EC ($p < 0.001$). 80 BFI and 34 non-BFI were recovered from wounds (71% vs 46%, $p < 0.01$), 10 BFI and 1 non-BFI were recovered from respiratory cultures (9% vs 1%, $p = 0.03$), 3 BFI and 18 non-BFI were recovered from urine (3% vs 24%, $p < 0.01$), 20 BFI and 21 non-BFI were recovered from blood (18% vs 28%, $p = 0.08$). BFI were not associated with Foley, orthopedic devices or venous catheters. Diabetes was more common in the non-BFI group ($p = 0.026$). Non-significant variables included CAD, CKD/ESRD, burn/%TBSA, infection vs colonization, polymicrobial infection, antibiotic exposure, number of surgeries, proportion cured, persistent infection and mortality. 30 of 131 infecting isolates, (19 BFI), were associated with persistent infection, and compared to cured infections, had more MSSA (17% vs 1%, $p = 0.002$) and PA (23% vs 9%, $p = 0.034$), and higher median % TBSA burned (77% vs 53.5%, $p < 0.01$). Wound isolates were more often cured than became persistent (68% vs 27%, $p < 0.01$).

Conclusion. BFI were more commonly MRSA and PA, and observed in wound and respiratory cultures. BFI and non-BFI had similar infectious outcomes.

Disclosures. **All authors:** No reported disclosures.

1683. Is Neuritis the cause of gastrointestinal hemorrhage in patients with scrub typhus?

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Session: 205. Microbial and Host Factors
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Background. Scrub typhus results in vasculitis due to *Orientia tsutsugamushi* infection. The present study investigated whether *O. tsutsugamushi* infection is associated with gastric ulcer etiology and whether immunohistochemical staining of stomach tissue is useful to diagnose scrub typhus.

Methods. A 78-year-old woman was hospitalized owing to general weakness that begun 4 days prior. As scrub typhus was suspected, doxycycline was administered. On 2nd day of hospital admission, the patient had melena and thus underwent an endoscopic examination. Endoscopic findings revealed oozing at the ulcer near the cardia. Endoscopic hemostasis was performed to arrest the bleeding from the ulcer. Five days after admission, the patient exhibited gastric hemorrhage that required emergency total gastrectomy. The stomach tissue subjected to surgery for the scrub typhus gastrointestinal bleeding was immunohistochemically stained with polyclonal antibodies for *O. tsutsugamushi*.

Results. Immunohistochemical staining using the surgical biopsy samples after 5 days of antibiotic administration confirmed the presence of *O. tsutsugamushi* within the macrophage. The stomach biopsy verified the presence of vasculitis and simultaneously confirmed the neuritis finding. The present study is clinically significant in two aspects. First, the presence of *O. tsutsugamushi* was confirmed by performing immunohistochemical staining using polyclonal antibodies against *O. tsutsugamushi* from the stomach tissue of a scrub typhus patient with gastric ulcer bleeding. Patients with unknown causes of gastric bleeding can benefit from the proposed method of immunohistochemical staining to diagnose scrub typhus. Second, the present study is the first to report a neuritis finding in a scrub typhus patient, suggesting the necessity of additional studies to investigate the association between neuritis and gastric ulcer or bleeding.

Conclusion. Immunohistochemical staining of stomach tissue is useful to diagnose scrub typhus that causes gastric ulcer. Furthermore, it is the first to confirm the presence not only of vasculitis but also of neuritis during a stomach biopsy of a scrub typhus patient. Further research is needed to confirm neuritis as the causal agent of gastric ulcer and bleeding in scrub typhus.

Disclosures. **All authors:** No reported disclosures.

1684. Diagnostic usefulness of IFN-gamma releasing assays in patients with disseminated tuberculosis compared with conventional tests

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Session: 206. Mycobacterial Infection: Screening and Diagnosis
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Background. Rapid diagnosis and treatment for disseminated tuberculosis (TB) are important prognostic factors for patients with disseminated TB. Recently, IFN-gamma releasing assay (IGRA) shows promising results for diagnosis of TB. However, little is known about the usefulness of these assays for diagnosing disseminated TB. We therefore evaluated their usefulness compared with traditional tests in patients with disseminated TB.

Methods. All adult patients with suspected disseminated TB were prospectively enrolled at a tertiary hospital in an intermediate TB-burden country during a 6-year period. Disseminated TB was defined as the involvement of bone marrow, ≥ 2 noncontiguous organs, or the presence of miliary lung lesions.

Results. A total of 101 patients with confirmed and probable disseminated TB were finally analyzed. Of these 101 patients, 52 (52%) were miliary TB and the remaining 49 (48%) were non-miliary disseminated TB. The 29 (29%) patients including 6 HIV patients had immunosuppressive conditions. T-SPOT.TB assay was positive in 90% (91/101). The sensitivity of T-SPOT.TB assay in patients with miliary TB (90%) was similar to that in those with non-miliary TB (90%)($p > 0.99$). In the subgroup analysis including the 58 patients in whom both QFT-GIT and T-SPOT.TB were available, the sensitivity of QFT-GIT (67%) showed a trend of being lower than that of T-SPOT.TB (90%).

Result of diagnostic test for disseminated TB

Diagnostic tool	Total (n=101)	miliary TB (n=52)	non-miliary TB (n=49)	P
Granulomatous inflammation with/ without necrosis seen in biopsy specimen	47/58 (81)	20/24 (83)	27/34 (79)	>0.99
Positive MTB AFB of specimen[1]	54/229 (24)	31/114 (27)	23/115 (20)	0.54
Positive MTB PCR of specimen[1]	83/164 (51)	41/85 (48)	42/79 (53)	0.68
Positive MTB culture of specimen[1]	110/208 (53)	60/100 (60)	50/108 (46)	0.11
Positive MTB AFB in sputum	21/94 (22)	17/51 (33)	4/43 (9)	0.006
Positive MTB PCR in sputum	25/46 (54)	17/31 (55)	8/15 (53)	0.92
Positive MTB culture in sputum	56/94 (60)	37/51 (73)	19/43 (44)	0.005
Positive tuberculin skin test	28/64 (44)	8/32 (25)	20/32 (63)	0.002
Positive QFT-GIT	39/58 (67)[2]	18/27 (67)[3]	21/31 (68)[4]	0.48
Positive T-SPOT.*TB*	91/101 (90)[2]	47/52 (90)[3]	44/49 (90)[4]	0.99

1) including sputum. 2) p = 0.25. 3) p = 0.33. 4) p => 0.99.

Conclusion. T-SPOT.TB assay may be a helpful adjunct test for disseminated TB.
Disclosures. **All authors:** No reported disclosures.

1685. Screening for TB in Health Care Workers – QFT may not be the answer!

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Background. Tuberculosis (TB) screening of healthcare workers (HCWs) is an important component of hospital infection control programs. Many institutions have replaced tuberculin skin tests (TSTs) with interferon-release gamma assays (IGRAs). Challenges of IGRA tests include daily fluctuations of IGRA values, serial testing variability, higher conversion rates of IGRAs than TSTs, and indeterminate IGRA results. In addition, reversions of positive QuantiFERON® TB test (QFT) with low cut-off values (0.35 IU/mL to 1 IU/mL) to negative have also raised concerns. Additional data is needed for IGRA use in HCWs. An Employee Health algorithm was created prior to implementation of QFT testing at our institution.

Methods. Retrospective review of all HCWs undergoing screening from January 2011 through December 2013 with QFTs was conducted. Employee health records including pre-employment TB screening questionnaire, and specific TB risk factors such as country of birth, history of BCG vaccination, prior TST and QFT results, chest radiograph, and occupational and social TB exposures were collected.

Results. A total of 1267 employees were tested with QFT during the study period: 1154 (91%) were negative, 109 (8.6%) were positives and 4 (0.3%) were indeterminates. None of the HCWs with positive QFTs had chest radiograph findings consistent with active TB disease. The positive QFT values ranged from 0.35 to 15.29 IU/mL. Out of 109 positive QFT test results, 36 (33%) were within the low-positive QFT range and of those who had a repeat QFT within three months, all were negative. TB risk factors associated with a true-positive QFT were foreign born, travel to TB endemic country, direct patient care and known TB exposure.

Conclusion. The risk of TB infection or conversion of QFT is low in persons without direct patient care. Low positive QFT cut-off values may indicate false positivity and the test should be repeated in 1 to 3 months especially in HCWs with no TB risk factors. Current healthcare employee TB testing program should be reviewed. Consideration for possible revision of policy for serial testing of only high risk HCWs with direct patient care will reduce health care expenses and unnecessary testing and treatment for low-risk HCWs.

Disclosures. **All authors:** No reported disclosures.

1686. A Rapid and Non-Invasive 2-Step Algorithm for Diagnosing Tuberculous Peritonitis Using T Cell-Based Assays on Peripheral Blood and Peritoneal Fluid Mononuclear Cells and Peritoneal Fluid Adenosine Deaminase

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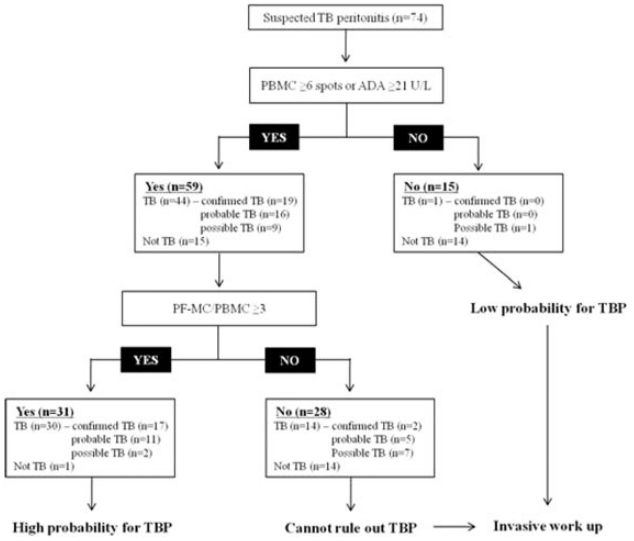
Background. The diagnosis of tuberculous peritonitis (TBP) is still challenging, largely dependent on invasive procedures such as laparoscopic biopsy. A recently developed *RD-1* (region of difference 1) gene-based assay for diagnosing TBP shows

promising results. We thus created a clinical algorithm to enable clinicians to differentiate patients with TBP from those with other diagnoses by using peripheral blood mononuclear cells (PBMC) and peritoneal fluid mononuclear cells (PF-MC) with conventional tests.



A proposed 2-step algorithm using PBMC/PF-MC ELISPOT and PF-ADA for diagnosing TBP.

Methods. All adult patients with suspected TBP in whom enzyme-linked immunosorbent spot (ELISPOT) assays were performed both on PBMC and PF-MC were prospectively enrolled over a 6-year period. In addition to the conventional tests for diagnosing TBP, the IFN-gamma-producing T cell response to early secretory antigenic target-6 (ESAT-6) and culture filtration protein-10 (CFP-10) by ELISPOT assays using PBMC and PF-MC were performed.

Results. The total 74 patients with suspected TBP were enrolled. Of these, 45 (61%) patients with 19 confirmed, 16 probable, and 10 possible TBP were classified as TBP, and 29 (39%) patients were classified as not-TB. Of the 74 patient, 5 (7%) patients in the PBMC ELISPOT assays and 15 (20%) patients in the PF-MC ELISPOT assays gave indeterminate results, respectively. The sensitivity and specificity, respectively, of the tested methods for diagnosing TBP were as follows: PBMC ELISPOT (=> 6 spots), 84% and 59%; PF-MC ELISPOT (=> 6 spots), 87% and 86%; PF-MC/PBMC ratio (=> 3), 69% and 97%; and PF-ADA level (=> 21 IU/L), 82% and 79%. The areas under the receiver operating characteristics curves were as follows: PF-MC ELISPOT, 0.90; PF-MC/PBMC ratio, 0.82; PBMC ELISPOT, 0.80; and PF-ADA, 0.80, respectively. If a 2-step algorithm (first step, PBMC ELISPOT => 6 spots or PF-ADA => 21 IU/L as a rule-out test; second step, PF-MC/PBMC ratio => 3 as a rule-in test) was applied, 67% (30/45) of patients with TBP were exactly classified without undergoing invasive procedures.

Conclusion. A 2-step algorithm using PBMC/PF-MC ELISPOT and PF-ADA appears to be a promising rapid and non-invasive approach for diagnosing TBP.

Disclosures. **All authors:** No reported disclosures.

1687. Comparision of Xpert MTB/RIF assay and the conventional sputum analysis in detecting *M. tuberculosis* at Maharaj Nakorn Chiang Mai hospital

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Background. Thailand is a country with high incidence of tuberculosis. Despite low sensitivity in detection of *M.tuberculosis*, sputum smear remains the main diagnostic method. Recently, WHO endorsed Xpert MTB/RIF (Xpert) assay, real-time polymerase chain reaction technique to detect *M. tuberculosis*and rifampin resistance mutation. This study aimed to evaluate the diagnostic performance of Xpert assay among patients with clinically suspected pulmonary tuberculosis.

Methods. A cross-sectional study was conducted at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University between September 2012 and November 2013. We included patients who were aged ≥ 15 years and had clinically suspected pulmonary tuberculosis.

Results. 99 specimens from 56 patients were included in the analysis; 29, 11, and 16 patients provided 1, 2, and 3 specimens, respectively. *M. tuberculosis*were detected from both Xpertassay and culture in 41 specimens, detected from Xpert assay but not culture in 5 specimens, detected from culture but not Xpert assay in 2 specimens, and neither detected from both methods in 51 specimens. Forty-three of 99 specimens (43.4%) had culture confirmed tuberculosis. Using sputum culture as a reference standard, the overall sensitivity (SEN), specificity (SPEC), positive predictive value (PPV), and negative predictive value (NPV) for Xpert assay were 95.4% (95% confidence interval [CI], 84.2%, 99.4%), 91.1% (95% CI, 80.4%,97.0%), 89.1% (95% CI, 76.4%, 96.4%), and 96.2% (95% CI, 87.0%, 99.5%), respectively. The overall SEN, SPEC, PPV, and NPV for sputum smear were 60.5% (95% CI, 44.4%, 75.0%), 98.2%, (95% CI, 90.4%, 100%), 96.3% (95% CI, 81.0%, 99.9%), and 76.4% (95% CI, 64.9%, 85.6%), respectively. Sensitivity of Xpert assay was 100% (95% CI, 86.7%, 100%) among smear positive specimens (n = 26) and 93.3% (95% CI, 68.0%, 99.8%) among smear negative specimens (n = 15). Subgroup analysis in HIV-infected patients (26 specimens) showed similar results. There were 3 specimens from 1 patient showed both INH and rifampin resistance, which Xpert failed to detect rifampin resistance in these specimens.

Conclusion. This study demonstrated good sensitivity and specificity of Xpert assay in detecting *M. tuberculosis* from pulmonary specimens. This may help in diagnosis of patients who had smear-negative pulmonary TB, resulting in early detection and treatment initiation.

Disclosures. **All authors:** No reported disclosures.

1688. Diagnosis of Pulmonary Tuberculosis among Admitted Patients at a Large, Urban Safety-net Facility — Los Angeles, 2010–2013

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Background. Health care facilities face substantial challenges in diagnosis and infection prevention for patients suspected to have infectious tuberculosis (TB). LAC + USC Medical Center is a large, urban safety-net facility with 105 confirmed TB cases reported in 2013, >1% of all reported cases in the United States.

Methods. We reviewed all inpatient admissions from January 2010 to September 2013 with at least one sputum specimen collected for acid fast bacilli (AFB) smear and culture (nucleic acid amplification tests (NAATs) were not routinely performed). Using AFB culture for *Mycobacterium tuberculosis* as the gold standard, we evaluated the sensitivity and specificity of the first 3 AFB sputum smears and the incremental yield of consecutive sputa. We examined demographic differences among patients by AFB culture result; the chi-square test was used to detect differences in proportions. We calculated inpatient length of stay stratified by AFB smear results.

Results. Among 2,775 inpatient admissions (2,572 unique patients), median age was 51 (IQR 42–59), 2,023 (72.9%) were male, and 1,568 (56.5%) were foreign-born. At least one sputum culture grew *M. tuberculosis* for 219 (7.9%); a positive culture was more frequent among foreign-born (10.4%) compared to U.S.-born patients (4.6%) ($P < .001$). The sensitivity and specificity of the first 3 sputum smears were 58.9% (CI 52.1–65.5) and 99.5% (CI 99.2–99.8), respectively. The incremental yields for each of the first 3 sputa were 86.8%, 6.2%, and 7.0% (for smear) and 91.8%, 4.1%, and 4.1% (for culture). Median length of stay was greater for admissions where at least one of the first 3 smears was positive (14.7 days (IQR 8.1–23.5)) compared to admissions where the first 3 smears were all negative (4.9 days (IQR 2.7–9.8)). Among 12 admissions with a positive sputum smear but no positive culture for *M. tuberculosis*, the median length of stay was 9.7 days (IQR 6.1–21.8).

Conclusion. One culture-confirmed pulmonary TB case was diagnosed for every 13 inpatient evaluations. The sensitivity of the first 3 sputum smears was low; although specificity was high, false-positive smears represent a burden on hospital resources. The improved sensitivity and specificity of NAATs might have substantial impact at this institution.

Disclosures. **All authors:** No reported disclosures.

1689. Performance Comparison of Two Commercial Tests for Rapid Molecular Diagnosis of Exprapulmonary Tuberculosis in a Low TB Incidence Country

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Background. Extrapulmonary tuberculosis (EPTB) accounts for >20% of tuberculosis (TB) cases in low TB incidence countries. Unlike pulmonary TB, diagnosis of EPTB is difficult due to atypical presentation and low culture positivity due to lower bacterial load. This study evaluated the performance of Xpert MTB/RIF (Xpert) and ProbeTec ET (PTec-ET) assays in diagnosing EPTB.

Methods. A total of 1660 consecutive extrapulmonary clinical specimens from suspected patients during October 2011 to August 2013 were investigated. The specimens included cavitary fluids (n = 890), fine needle aspirate (FNA), pus (n = 482), tissue biopsy (n = 102), cerebrospinal fluid (CSF) (n = 85), urine (n = 67), and others (n = 36). All specimens were processed for acid-fast bacilli (AFB) smear microscopy by Ziehl-Neelsen staining, liquid culture in MGIT 960 system and nucleic acid

detection by Xpert and PTec-ET. All procedures were performed according to manufacturer's instructions and sensitivity and specificity of Xpert and PTec-ET was calculated in comparison with a reference standard comprising a combination of culture and clinical diagnosis of TB.

Results. Of 1660 specimens, 34 were AFB-SM positive, 157 were culture positive and 197 yielded a positive culture and/or a clinical diagnosis of TB. The overall sensitivity and specificity values for Xpert were 93% and 100%, respectively and for PTec-ET were 82% and 100%, respectively, while the sensitivity values for microscopy and culture alone were 17% and 80%, respectively. The sensitivity of Xpert was higher for biopsies, FNA and pus, urine and CSF than in cavitary fluids. Xpert was more sensitive than PTec-ET as it detected EPTB in 15 more AFB-SM-negative, culture-positive and 6 more AFB-SM-negative, culture-negative specimens. More importantly, Xpert detected EPTB in 40 samples with clear histological evidence of infection of which only 7 samples were AFB-SM-positive but none of these 40 samples yielded a positive culture.

Conclusion. Molecular methods can help in rapid diagnosis of extrapulmonary tuberculosis. The higher sensitivity of Xpert offers a better choice compared to PTec-ET or smear microscopy in rapidly diagnosing the disease. However the negative predictive value of Xpert in EPTB specimens remains suboptimal.

Disclosures. **All authors:** No reported disclosures.

1690. Opportunities for Improved Detection and Treatment of Latent Tuberculosis Infection Among Veterans — Western United States, January 2010–July 2013

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Background. The Veterans Health Administration (VHA) previously estimated that tuberculosis (TB) incidence among Veterans was over twice that for the U.S. population overall. Treatment of latent tuberculosis infection (LTBI) decreases progression to TB by approximately 90% among adherent persons. We describe characteristics of Veterans with TB and their previous screening and treatment for LTBI.

Methods. We queried VHA infection control practitioners and QC PathFinder, VHA's infection surveillance application, to identify Veterans with TB (confirmed by laboratory, clinical, or provider diagnosis criteria), diagnosed or treated during January 1, 2010–July 31, 2013 and evaluated for symptoms or signs of TB at 31 VHA facilities in the western United States. We reviewed VHA electronic medical records for TB risk factors and prior LTBI screening by tuberculin skin test or interferon-gamma release assay.

Results. We identified 113 Veterans with TB in the western United States; 110 (97%) of whom were men. The median age was 61 years (range: 30–91 years). Among 109 with known race or ethnicity and national origin, 31 (28%) were foreign-born, including 21 (68%) from the Philippines and 5 (16%) from Guam. Fifty-four (50%) were non-Hispanic white; 24 (22%) were Asian; 16 (15%) were black; 7 (6%) were Hispanic; 5 (5%) were Native Hawaiian or Other Pacific Islander, and 3 (3%) were American Indian or Alaska Native. Among 107 not previously treated for TB, 90 (84%) had risk factors, 61 (68%) of whom reported or had VHA-documented screening. Of 42 diagnosed with LTBI, only 18 (43%) had initiated and 13 (31%) completed LTBI treatment.

Conclusion. TB could have been prevented in some Veterans by targeted testing and treatment of LTBI per current guidelines. Investigating reasons certain Veterans with TB risk factors are not screened and others with LTBI are not treated may help tailor prevention efforts.

Disclosures. **All authors:** No reported disclosures.

1691. The Relevance of Biopsy in Tuberculosis Patients without Human Immunodeficiency Virus Infection

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Background. Although chronic granulomatous inflammation(CGI) with concomitant caseous necrosis(CN) is a typical histological feature of tuberculosis(TB), few studies have investigated its frequency or various pathologic findings in the setting of a TB-positive sampleidentified other possible TB pathological findings in patients without CN or CGI.

Methods. The medical records of 231 HIV-negative, culture-positive TB patients who presented at Chosun University Hospital and underwent biopsy from January 2002 to December 2011 were studied retrospectively. After the frequency of TB-specific pathological findings was determined, a pathologist reanalyzed the findings and reclassified suspected TB into 'possible TB pathologic findings.'

Results. The initial biopsy interpretation revealed that 63 (34.8%) of 181 patients with pulmonary TB had caseating granulomas, 36 (19.9%) had only CGI, and six (3.3%) had only CN. Among the 46 patients with extrapulmonary TB, 16 (34.8%) had only caseating granulomas and 14 (30.4%) had only CGI. Of the patients with pulmonary and extrapulmonary TB, 58% and 65.2% had either CN or CGI, respectively. More patients who underwent percutaneous lung biopsy had CGI or CN (76.3%) than did the patients who underwent transbronchial lung biopsy (53.6%). The reanalysis confirmed all CN cases of the first interpretation, and 20 (95.2%) of 21 non-CN cases were reclassified as possible CN. Eleven cases (four pulmonary, seven extrapulmonary) were reclassified as 'possible TB pathologic findings' from just necrosis.

Conclusion. Biopsy results in TB-diagnosed patients revealed that caseating granuloma was present in only one-third of pulmonary and extrapulmonary TB cases. Even in cases where only necrosis is identified, CN may be present. Thus, clinicians should recognize that some cases reported as other types of necrosis may in fact be CN

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1692. Do Resident Physicians Agree with LTBI Treatment Guidelines?

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Background. Previous studies have demonstrated that foreign-born physicians in the U.S. are less accepting of latent tuberculosis infection (LTBI) treatment among themselves and their patients. It is uncertain whether these differences are motivated by differences in medical education or by cultural beliefs regarding BCG vaccination. Our objective was to determine whether a resident physician's decision to treat LTBI under various scenarios was associated with their personal history of BCG vaccination.

Methods. We surveyed internal medicine residents from an single academic medical center regarding their personal history of LTBI, as well as their attitudes towards LTBI diagnosis and treatment in their patients. We queried country of birth, year of birth, and country of medical school training. The BCG World Atlas (www.bcgatlas.org) was used to ascertain the personal history of BCG vaccination for all respondents, based on country and year of birth.

Results. 37 of 60 residents (62%) responded to the survey. Among 23 respondents born outside the U.S., 18 (78%) were assigned a history of BCG vaccination. There were 6 respondents with a personal history of LTBI, and 2 of 6 (33%) reported completing treatment. One respondent had a personal history of pulmonary TB. Among 30 respondents without a history of LTBI, 22 (73%) would accept LTBI treatment based on a positive TST, while 26 (87%) would accept treatment based on a positive IGRA ($p = 0.2$). Overall, 17 of 37 respondents (46%) would recommend LTBI treatment for a BCG-vaccinated individual with a first-ever positive TST, increasing to 86% (32/37) for a first-ever positive IGRA in a BCG-vaccinated individual ($p < 0.01$). In contrast, there was no difference in attitudes towards treating a converted TST (32/37, 86%) or IGRA (33/37, 89%) in BCG-vaccinated individuals. Contrary to our hypothesis, we did not find a significant relationship between a resident physician's personal history of BCG vaccination and LTBI treatment attitudes.

Conclusion. A resident's personal history of BCG vaccination was not associated with acceptance of LTBI treatment in their patients. Further work is needed to define both the cultural and educational factors that motivate attitudes towards LTBI treatment among resident physicians.

Disclosures. **All authors:** No reported disclosures.

1693. Do We Need Public Health Providers and Programs to Provide Tuberculosis Care and Management?

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Session: 206. Mycobacterial Infection: Screening and Diagnosis
Saturday, October 11, 2014: 12:30 PM

Background. Historically, declines in TB incidence have resulted in decreased funding for TB control. Currently TB incidence is at a historic low and many TB control programs have experienced reduction in resources. In 2012, Chicago closed all public health TB clinics shifting care to the private sector. How this shift affects the quality of TB care is unknown. We compared TB care by provider type in Chicago, Illinois.

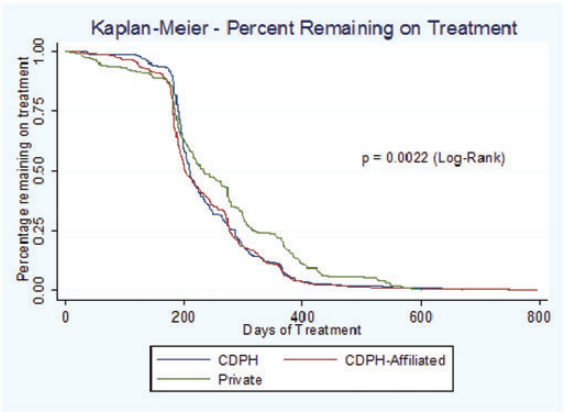
Methods. We retrospectively reviewed TB cases reported to the Chicago Department of Public Health (CDPH) between January 2008 and December 2011. Cases were excluded if they were dead at the time of TB diagnosis, died during initial hospitalization, failed to initiate treatment, or were diagnosed with multi-drug resistant TB.

Primary provider type was stratified into three groups: public health clinic, public health-affiliated clinic contracted by CDPH to provide TB services, and private physician. Multivariate regression and Kaplan Meier were used to evaluate treatment duration.

Results. Of 703 cases, 203, 314, and 186 were treated primarily by public health clinics, public health-affiliated clinics and private providers, respectively. Significant differences were found between groups (table).

In adjusted regression, private provider patients had a 48-day (95% CI 21.98-74.30) increase in treatment duration. Kaplan-Meier analysis showed significant differences in

treatment duration by provider type (figure). There were no differences between public and public-affiliated providers.



Clinical Characteristics by Provider Type, Chicago Illinois 2008 - 2011

	% Public (n=203)	% Public-Affiliated (n=314)	% Private (n=186)
Age (mean)	42.9	44.4	51.1
Male	59.6	66.6	49.5
African American	40.9	38.7	36.2
Substance Abuse	26.2	30.8	11.2
Received DOT	96.1	89.2	38.8
Completed Treatment	95.1	93.0	87.6

All associations were significant p-value <0.05

Conclusion. Our data showed private provider patients were more likely to be on treatment longer, increasing exposure time to toxic medications and potential for side effects. We found no difference in treatment duration between public and public-affiliated providers. As funding for TB control shifts, public-private collaboration may serve as a model to provide optimal care for patients in the face of limited resources.

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1694. Risk factors and outcomes of isoniazid hepatotoxicity in children with latent tuberculosis

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Session: 206. Mycobacterial Infection: Screening and Diagnosis
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Background. To determine the overall incidence of hepatotoxicity in children and risk factors such as age, gender, and their outcomes.

Methods. Patients who were admitted to the Pediatric Infectious Disease Clinic during the period from December 2009 through August 2013 with the diagnosis of latent TB infection were included in this study. Isoniazid hepatotoxicity was classified according to the of WHO Toxicity Classification Standards.

Results. Among 1038 patients, Overall hepatotoxicity was observed in 23 patients (2,2 %), while 5 patients (0,48 %) had moderate-severe hepatotoxicity; while other 18 patients had grade I-II hepatoxicity (1,73%). Age and gender were found to be not risk factors for hepatotoxicity. The median time for therapy rechallenge in patients with grade III-IV hepatotoxicity was 21 days (ranging from 14 to 25 days) and 7 days (ranging from 5 to 21 days) in grade I-II hepatotoxicity and significantly longer 18 in grade III-IV hepatotoxicity (p= 0,02) recovery of hepatotoxicity and restarting of INH therapy and at least 14 days were required for complete recovery of INH hepatotoxicity in children with severe hepatotoxicity.

Conclusion. In conclusion, in children, INH hepatotoxicity is lower and generally reversible after ceasation of INH. The grade of hepatotoxicity affects the duration for

Disclosures. **All authors:** No reported disclosures.

1695. Implementation of Tuberculosis Infection Control Guidelines in South India

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Session: 206. Mycobacterial Infection: Screening and Diagnosis
Saturday, October 11, 2014: 12:30 PM

Background. India has more Tuberculosis (TB) patients than any other country, which can partly be attributed to poor Tuberculosis infection control (TBIC) in healthcare facilities (HCFs). The evidence form high income countries demonstrate that an implementation TBIC reduces TB transmission in HCFs. India adapted TBIC guidelines in the year 2010, however the implementation of guidelines in HCFs has not been studied. The aim of the study was to assess the implementation of TBIC in 5 districts in South India.

Methods. We conducted a cross-sectional study in 25 HCFs in 5 districts of South India. The study included: facility survey and observations of practices regarding three main parts of TBIC guidelines (administrative and environmental control and personal protective measures).

Results. Only 16% of HCFs (4/25) had all components of TBIC in South India. The other parameters studied were shown in the table.

Implementation of National TBIC guidelines by HCFs in South India

TBIC Guidelines	Number of HCFs following guidelines	Percentage
Availability of TBIC guidelines	10	40%
Screening for cough on arrival to HCF	7	28%
Fast tract the appointments of coughing patients	5	20%
Avoiding admission of stable TB patients	5	20%
Isolation rooms (natural or mechanical ventilation)	10	40%
Personal protective measures (N 95 masks)	8	32%

Conclusion. TBIC guidelines were not implemented in most of the HCFs in South India. There is an urgent need to scale up and standardize TBIC policies in Indian HCFs to decrease nosocomial TB transmission.

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1696. Total-deletion mutation of *pncA* as a new mechanism of pyrazinamide resistance in *Mycobacterium tuberculosis* - The first report from Japan

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Session: 207. Mycobacterial Infections: Drug-Resistance
Saturday, October 11, 2014: 12:30 PM

Background. Pyrazinamide (PZA) is an indispensable first-line anti-tuberculosis drug that is part of the currently used short-course, combination chemotherapy against tuberculosis (TB). PZA is a prodrug that has to be converted to the active form, pyrazinoic acid, by pyrazinamidase (PZase) activity, encoded by the *pncA* gene of *Mycobacterium tuberculosis*, and loss of PZase activity is associated with PZA resistance. Thus most of PZA-resistant strains are due to mutations of the *pncA* gene. Though many *pncA* mutations are known, total-deletion of the gene has never been reported in clinical case yet. We report the first case of PZA-monoresistant TB by total-deletion of the *pncA* gene.

Methods. A 73-year-old man had no history of TB treatment. His chest CT demonstrated multiple discrete nodules in the bilateral upper lung fields and cavitary lesions in right upper lobe.

Results. Sputum examination showed positivity of smear-microscopy, culture and TB-PCR. Together with chronic occupational exposure to silica dust, he was diagnosed of silicotuberculosis. In vitro anti-tuberculosis drug susceptibility testing by standardized proportion method revealed that the isolate was susceptible to isoniazid (INH), rifampin (RIF), rifabutin (RBT), ethambutol (EMB), streptomycin (STR) and levofloxacin (LVFX), whereas it was resistant to PZA. PZA susceptibility testing was carried out in liquid media (Kyokuto Pharmaceutical Industrial Co., Ltd.). Further investigation by the Research Institute of Tuberculosis revealed that the species was identified as *Mycobacterium tuberculosis* sensu stricto and kept no pyrazinamidase activity. Further sequencing analysis revealed the large deletion (22,934bp) including the total *pncA* gene.

Conclusion. Yee DP et al. reported that patients with PZA-monoresistant TB had significantly worse clinical outcomes than patients with fully susceptible strains. PZA resistances were almost due to point mutations in *pncA*. The total-deletion mutation of *pncA* shown in the present case was also highly resistant to PZA. To the best of our knowledge, this is the first reported case of total *pncA* deletion with PZA resistance. Not only *pncA* mutation but also *pncA* deletion will cause PZA resistance.

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1697. Prevalence and associated factors of infection with drug-resistant *Mycobacterium tuberculosis* in Thailand

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Session: 207. Mycobacterial Infections: Drug-Resistance
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Background. Drug-resistant *Mycobacterium tuberculosis* is one of the most serious forms of tuberculosis (TB). We sought to estimate the prevalence of resistance to anti-tuberculosis drugs and to identify associated factors.

Methods. Culture positive *M. tuberculosis* cases were identified from microbiological database. Clinical and laboratory data were retrieved retrospectively from January 1, 2010 to December 31, 2012. Logistic regression was performed to determine associated factors of infection with drug-resistant *M. tuberculosis*.

Results. A total of 758 patients were identified with median (interquartile range) age was 47 (32-64) years and 55% were males. Of all, 71.8% had pulmonary involvement. Extrapulmonary involvement was lymph node (14.9%), bone and joint (4.2%), pleura (3%), blood (2.4%) and central nervous system (1.6%). HIV infection was identified in 10.6%. Patients with HIV infection were younger (36 vs 49 years, p <0.001), had higher proportion of males (76.2% vs 53.1%, p <0.001) and smoking (60% vs 33.4%, p <0.001), lower proportion of positive sputum culture (53.8% vs 73.9%, p <0.001), and having favorable outcomes (cure or complete treatment) (33.8% vs 61.7%, p <0.001). Resistance to any first-line drugs were 18.2%; isoniazid 12.7%, rifampicin 2.1%, ethambutal 2.5%, and streptomycin 8.2%. Prevalence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) were 1.3% and 0.4%, respectively. By multivariate logistic regression, chronic cough [odds ratio (OR) 1.71; 95% confidence interval (CI) 1.17-2.49, p = 0.005] and had a history of contact person with TB (OR 2.38; 95% CI 1.32-4.28, p = 0.004) were associated with any first-line drug resistance. Of all, 58.7% patients had favorable outcomes. Female (OR 1.59; 95% CI 1.16-2.18, p = 0.004), weight at TB diagnosis (OR 1.02; 95% CI 1.00-1.03, p = 0.025), and HIV infection (OR 0.36, 95% CI 0.22-0.60, p <0.001) were associated with favorable outcome.

Conclusion. We demonstrate high prevalence of any first-line drug resistance, but low prevalence of both MDR-TB and XDR-TB in Thailand. Only approximately 60% patients had favorable outcomes. HIV screening in patients with TB was important for identifying patients with unfavorable outcome.

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1698. Characteristics and Outcomes Among Patients with MDR-TB Treated in a Decentralized Community-based Treatment Program in Rural KZN, South Africa

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Session: 207. Mycobacterial Infections: Drug-Resistance
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Background. In 2006, an epidemic of multidrug resistant tuberculosis (MDRTB), with extremely high mortality rates, was uncovered in rural KwaZulu-Natal, South Africa. To address treatment delays and high rates of mortality and default at the single centralized provincial treatment facility, a decentralized MDRTB treatment program was established in 2008 in a rural district with high MDRTB prevalence. Program components include an inpatient facility, outpatient clinic and community-based treatment provided by mobile teams. We evaluated treatment outcomes at this program.

Methods. We reviewed the standardized Department of Health MDRTB treatment register to abstract data on demographics, diagnostics, and treatment outcomes among patients initiating MDRTB treatment between February 8, 2008 and December 18, 2013.

Results. Of 718 registered MDRTB patients, median age was 35 years (IQR 29-43), 382 (53.2%) were female, and 596 (83.0%) were HIV positive. MDRTB was the first TB diagnosis for 159 patients (22.1%). Of 573 with available treatment outcomes, 294 (51.3%) completed treatment or were cured, 131 (22.9%) died, 33 (5.8%) failed treatment, and 82 (14.3%) had extensively-drug resistant TB (XDRTB) and were transferred to the provincial XDR-TB treatment facility. Overall, only 33 (5.8%) defaulted. Mortality rates fluctuated over time with lowest rate of 10.9 deaths /100 person-years of treatment in 2008, rising to 50.7 in 2011, and declining to 38.2 in 2013. HIV+ patients had a non-significant trend towards higher mortality; however mortality was significantly lower among those on ART ($p < 0.001$).

Conclusion. Low overall default rates support program effectiveness. Results in HIV+ patients support HIV/TB integration. The substantial proportion of MDRTB as initial TB diagnosis highlights the need for improved infection control in health care and community settings. Though low overall, fluctuations in mortality need further evaluation and may reflect changes in patient and TB program characteristics over time, including disease severity, improved case finding, earlier diagnosis, and increasing MDRTB program maturity. This review supports benefit of decentralization and community-based MDRTB treatment programs in high prevalence areas.

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1699. Characteristics and Post-Treatment Outcomes of Pediatric Central Nervous System (CNS) Tuberculosis (TB); California 2001-2011

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Session: 208. Mycobacterial Infections: Extrapulmonary
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Background. Central nervous system (CNS) tuberculosis (TB) can result in severe disability in children. We aimed to describe the clinical characteristics and post-treatment outcomes of pediatric CNS TB cases in California.

Methods. All pediatric (aged ≤ 18 years) patients with CNS TB reported to the TB registry during 2001-2011 were included. We systematically abstracted information about clinical characteristics and outcomes within 1 year after treatment completion from local public health records, hospital admission records and outpatient follow-up records. Outcomes were categorized into good or poor on the basis of disability in hearing, vision, language, ambulation, development or focal neurologic deficits. Modified Medical Research Council (MRC) Score was used to classify severity of disease at presentation. We report preliminary findings from records abstracted to date.

Results. Of 94 pediatric CNS TB cases reported, 45 cases were abstracted to date. Of those, 86.7% were 0-4 years old, 97.8% were U.S.-born and 73.3% were Hispanic. Fever (91.1%), vomiting (73.3%) and altered mental status (60%) were the most common symptoms at presentation. Tuberculin skin test was positive in 51.1% of cases tested. MRC score classified cases into Stage I (18.6%), Stage II (53.5%) and Stage III (27.9%). A positive *M. tuberculosis* culture was identified in 75.6% of the patients. Mono pyrazinamide resistance was seen in 17.6% of culture positive cases. Patients had poor post-treatment outcomes (62.2%) including moderate clinical sequelae (28.6%), severe clinical sequelae (60.7%) and death (10.7%). In unadjusted analysis, children aged 0-4 years and those with Stage III MRC Score were more likely to have poor outcomes.

Conclusion. The majority of pediatric CNS TB cases reviewed have poor post-treatment outcomes, with younger age and advanced disease at presentation associated with poor outcomes. Interventions to improve outcomes and prevent CNS TB in young children are needed.

Disclosures. **All authors:** No reported disclosures.

1700. Tuberculous Lymphadenitis in Children in a Tertiary Care Center of Mexico City: Review of 85 Cases

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Session: 208. Mycobacterial Infections: Extrapulmonary
Saturday, October 11, 2014: 12:30 PM

Background. One third of the world's population is infected with the tubercle bacillus, of which 1% are children. The aim is to describe the clinical features and evolution of mexican children with tuberculous lymphadenitis (TL).

Methods. An observational, retrospective and descriptive cohort study. We reviewed 85 clinical files of children with diagnosis of TL from 2003 to 2013 at the National Pediatrics Institute in México City. Patients were included if they had a clinical picture suggestive of TL plus one or more of the criteria, referred as positive AFB smear, positive culture, biopsy compatible with TB and response to therapy.

Results. The mean age was 86 months (2-195 months), 41% were malnourished, 14% had an underlying disease (most commonly chronic granulomatous disease followed by defect in the IL-12/IFN-gamma axis). 92% had received TB vaccine, 17% had TB contact. The mean time of disease before diagnosis was 237 days. Cervical TL was the most common localization in 90%; unilateral lymph nodes were found in 75%. Mean lymph node size was 3 cm, the average number of lymph nodes affected was 2 (1-10 lymph nodes). 25% presented suppuration with scarring as the most important sequelae. Positive PPD was found in 72%, abnormal chest X ray in 22%, positive AFB smear in 21%, and positive culture in 14/80 (18%), with *M. tuberculosis* complex in 6/14 (43%). All patients underwent biopsy. For the intensive phase, treatment included the combination of isoniazid, rifampin, pyrazinamide and ethambutol with a mean duration of 2 months. For the maintenance phase, treatment included the combination of isoniazid and rifampin in 78% of cases, with a mean duration of 7 months. Relapses or failure to therapy occurred in 23/85 (27%). In 7/23 patients (30%), the combined secondary therapy consisted in isoniazid, rifampin, ciprofloxacin and clarithromycin. This was the scheme mostly used as secondary treatment, with a mean duration of 12 months if adequate response. No deaths were reported.

Conclusion. TL still represents an important public health problem in developing countries. It is one of the most common extrapulmonary forms of TB, and also a diagnostic challenge. There is an important delay in the diagnosis, that is why we must be alert to identify TL early and avoid the sequelae.

Disclosures. **All authors:** No reported disclosures.

1701. Breast Tuberculosis: A Rare Cause of Breast Masses

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Session: 208. Mycobacterial Infections: Extrapulmonary
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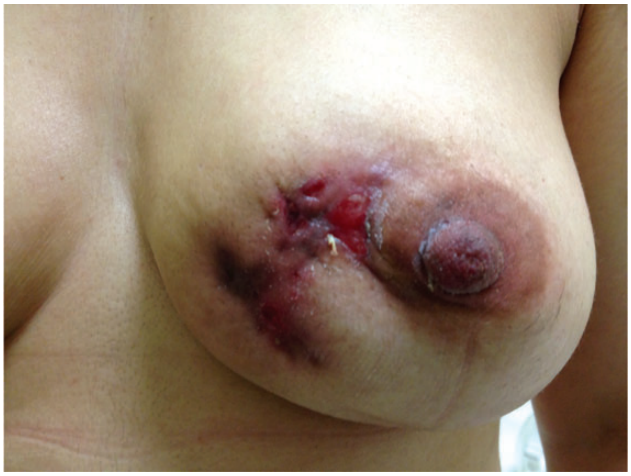
Background. Breast tuberculosis (TB) is a rare form of tuberculosis. Incidence of the disease is less than 0.1% of all breast lesions in western countries and 4% in TB endemic countries. In Turkey, TB is an endemic disease but breast tuberculosis is very rarely reported. With this report, we aimed to review 11 cases of breast TB retrospectively.

Methods. The records of 11 patients were evaluated retrospectively. Histopathological examination, Erlich-Ziehl-Nielsen stain, tuberculosis culture and PCR were performed to confirm the diagnosis.

Results. The mean age of the patients was 37.8. The mean symptom duration was 15.5 months. All of the patients had received non-specific antibiotic regimens during this prolonged symptom period. The most common signs were painful breast mass with discharge through the fistula, palpable lymph nodes in the ipsilateral axilla and skin retraction (Figure 1). The diagnosis was confirmed by histopathological examination in all the patients. Acid-fast bacilli was achieved in 1/10 and culture positivity in 3/10 and PCR positivity in 2/10 of cases. The most common radiological findings were breast abscesses and axillary lymph nodes. All of the patients were treated with antituberculous therapy with or without surgical drainage.



Breast mass with discharge through the fistula and and skin retraction of a patient.

Conclusion. Mycobacteria should be kept in mind for differential diagnosis in patients who have no response to standard antibiotic therapy with chronic breast or soft tissue infections including recurrent breast abscess. The main striking symptoms of breast tuberculosis are painful breast mass, discharge through the fistula, and prolonged symptom duration over one year.

Disclosures. **All authors:** No reported disclosures.

1702. A Comparative Analysis of Tuberculous and Brucellar Spondylodiscitis

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Session: 208. Mycobacterial Infections: Extrapulmonary
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Background. Our aim was to compare clinical, laboratory and radiological features of spontaneous spondylodiscitis secondary to tuberculosis and brucellosis.

Methods. A retrospective study which included 86 patients diagnosed as spondylodiscitis with confirmed aetiology between 1995 and 2012. Of these patients, 56 (65.1%) had tuberculous spondylodiscitis (TS) and 30 (34.9%) had brucellar spondylodiscitis (BS).

Results. The clinical, laboratory and radiological features of TS and BS were summarized in the table.

Summary of clinical, laboratory and radiological features of spondylodiscitis secondary to tuberculosis and brucellosis

		TS	BS	p
Gender (Male/Female)		24/32	22/8	**0.007**
Age (mean years)		46.7	50.5	0.3
Temperature > 38.5°C		24 (43%)	20 cases (66.7%)	**0.03**
Sweating		25 (44.6%)	20 (66.7%)	**0.05**
Chills		3 (5.4%)	7 (23.3%)	**0.01**
Motor neurological deficit		12 (21.4)	3 (10%)	0.1
Sensory neurological deficit		11 (19.6%)	1 (3.3%)	**0.03**
ESR (mean)		85 mm	54 mm	**0.04**
Leucocytes (mean)		8200 cells/mm^3	6140 cells/mm^3	**0.001**
Vertebral level affected	Cervical	7 (12.5%)	1 (3.3%)	**0.01**
	Dorsal	11 (55.4%)	8 (26.7%)	**<0.0001**
	Lumbar	25 (44.6%)	25 (83.3%)	**0.001**
Psoas abscess		10 (41.7%)	8 (28.6%)	**0.05**
Posterior vertebral lesions		14 (14%)	4 (17.4%)	**0.04**
Duration of treatment (mean months)		13	7	**< 0.0001**
Sequelae		28 (62.2%)	11 (45.8%)	0.1

TS = Tuberculous spondylodiscitis; BS = Brucellar spondylodiscitis; ESR = Erythrocyte sedimentation rate

Conclusion. There are significant clinical, biological and radiological differences between TS and BS. These differences allow a presumptive aetiological diagnosis while awaiting a definite microbiological confirmation.

Disclosures. **All authors:** No reported disclosures.

1703. Delta-like 1 ligand (DLL) measurement in cerebrospinal fluid for detection of *Mycobacterium tuberculosis* meningitis

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Session: 208. Mycobacterial Infections: Extrapulmonary
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Background. Tuberculosis meningitis (TBM) diagnosis is notoriously difficult, new biomarkers are needed to allow for improved diagnostic accuracy. We evaluated the diagnostic utility of a novel biomarker, delta-like ligand 1 (DLL1), a Notch ligand, which selectively drives antigen-specific CD4 T helper1 cell responses. DLL1 polymorphisms increase susceptibility to other intraceullar (Th1) organisms (e.g., leishmaniasis).

Methods. CSF DLL1 concentrations were measured by ELISA in 116 patients with suspected meningitis, of which 18 patients had TBM, 65 patients cryptococcal meningitis (CM), and 33 patients tested negative for both CM and TBM (termed "other"). TBM was diagnosed either by GeneXpert MTB/Rif assay (Cepheid, Sunnyvale, CA) or Bactec MGIT culture. We evaluated the diagnostic performance of DLL1 for TBM.

Results. Patient characteristics were similar at diagnosis except for CSF protein and CSF WBC count. Protein was higher in TBM patients than 'other' meningitis, and CSF WBC count, was higher in TBM than in non-TBM meningitis. Mean DLL1 CSF concentrations were significantly higher in patients with TBM (1293 pg/mL; 95%CI, 602-1985 pg/mL) than CM (447 pg/mL; 95%CI, 398-495pg/mL) or other meningitis (534 pg/mL; 95%CI, 290-669pg/mL). A cutoff of >600pg/mL in CSF for TBM had 72% sensitivity, 77% specificity, 36% positive predictive value (PPV), and 94% negative predictive value (NPV) 94% (AUC = 0.794). As the DLL1 level increased, the likelihood of TBM increased with specificity of 92% and PPV of 56% above >800pg/mL.

Conclusion. CSF DLL1 exhibited good diagnostic performance, and may have a role as a low cost adjunctive diagnostic tool for TBM. Misclassification bias (of non-detection of TBM classified as 'other') hampers diagnostic studies, and larger studies are required in the future.

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1704. Optimal treatment of BCG Osteomyelitis: A Review

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Session: 208. Mycobacterial Infections: Extrapulmonary
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Background. There are few data about the optimal drug regimen and duration of therapy for Bacillus Calmette-Guerein (BCG) osteitis.

Methods. We searched Medline using terms: Mycobacterium bovis, immunization, BCG vaccine, osteitis, and bone diseases; infectious. Exclusion criteria were; non-English, single case report, intravesicular BCG, non-human subjects, and insufficient description of treatment and complications.

Results. Our search yielded 66 studies, with 6 case series (n = 2-222), the cumulative total was 261 patients.

Median onset of BCG osteitis was 1 year post-vaccination (3-26 months). The lower extremity was the most common site. Most cases were immune-competent, however variations in the interferon-gamma receptor (n = 6), and mannose-binding lectin (n = 56) genotypes were found.

Surgical biopsy was performed in 255 cases, diagnosis was via culture in 135 cases, pathology in 227 and exclusively clinical/radiologic in 6. TB skin tests were positive in 95 cases.

The number of patients who underwent surgical debridement is unclear. Drug therapy usually included an early intensive phase of 2 months, followed by consolidation therapy for a total duration of 6-24 months. Drug combinations included INH, Rifampin, and a third drug, 13 cases received <3 effective drugs. No definite

association between duration, drug regimen, and complication rate could be discerned (table).

Complications occurred in 5%, including fistulae, abscess formation, and further surgical intervention, relapses occurred in 2%. The largest series reported complications in 3%.

Treatment modalities

Case Series	n	Regimen (n) Intensive (1-2m)	Regimen (n) Consolidation (4-6m)	Duration median (m)	Surgery (n) B = biopsy D = debridement
Kroger	222	S + (EA or I) or S + I + R	I + (EA OR R) Followed by I	12	B or D (217)
Castro-Rodriguez	10	I, R, P	I, R	6.5	B or D
Bergdahl	18	S, I, R	I, R	7	D
Karnak	2	I, R I		6	D
Al Jassir	3	I, R, PAS		12	D
Sasaki	6	I (1) I, R, S (3) I, R, E (2)		N/a	D (2) B (3)

m = month, S-Streptomycin, EA-Ethionamide, I-Isoniazid, R-Rifampin, P-Pyrazinamide, E-Ethambutol, PAS-Para-amino salicylic acid

Conclusion. BCG osteitis is a rare complication with limited literature. Most patients respond well but the optimal therapy to prevent relapse and complications requires further study.

Disclosures. **All authors:** No reported disclosures.

1705. Non-Tuberculous Mycobacterial Bloodstream Infections in Patients with In-Dwelling Vascular Access Catheters- Role of Sickle Cell Disease

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Background. Risk factors for non-tuberculous mycobacteria (NTM) lung infections have been well investigated. However, few studies have examined risk factors for NTM in-dwelling vascular catheter (IDVC) infections. Sickle cell anemia is known to affect several aspects of the immune system leading to relative immune deficiency. The purpose of this retrospective nested case-control study is to determine if sickle cell anemia (HbSS/SC) is a risk factor for NTM bloodstream infections among individuals with IDVCs.

Methods. All NTM IDVC infections (cases) at Palmetto Health Richland Hospital from 2008-2014 were reviewed. Cases were matched 2:1 with controls who had IDVC infections due to organisms other than NTM. Infections due to *Mycobacterium avium complex* and coagulase-negative *Staphylococcus* were excluded. Matching criteria included age within 10 years and IDVC infection within 3 months. Logistic regression was used to identify risk factors for IDVC infection due to NTM.

Results. The 16 cases of NTM IDVC infection were matched to 32 controls with IDVC infections due to other organisms. Overall, the mean age of patients with IDVC infections was 48.5 years and 28 (58%) were male. Compared to the control group those with NTM infections were more likely to have sickle cell anemia 38% vs 6% ($p = 0.006$). Time from catheter placement to infection was similar for both groups; 199 vs 197 days for NTM and control groups respectively ($p = 0.98$). Most patients (68%) with NTM IDVC infections underwent catheter removal followed by antibiotics.

Conclusion. IDVCs are a risk factor for NTM bloodstream infections. Sickle cell anemia appears to be a risk factor for IDVC infections due to NTM. This study is limited by the small sample size. A larger study is needed to further investigate the association between HbSS/SC and NTM IDVC infections.

Disclosures. **All authors:** No reported disclosures.

1706. Characteristics of Nontuberculous Mycobacterial Infections in Thai Population

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Background. Diseases caused by nontuberculous mycobacteria (NTM) have varied manifestations in different groups of patients. NTM infection has been an important cause of morbidity and mortality. We aimed to describe the clinical and microbiological characteristics, including outcomes of NTM infection in Thai population.

Methods. A retrospective study was conducted among patients who were infected with NTM between January 1, 2008 and December 31, 2012. Criteria of NTM infection diagnosis was used by the American Thoracic Society (ATS) and the Infectious Disease Society of America (IDSA) jointly published guidelines in 2007.

Results. A total of 225 patients with NTM infection were identified. Median (interquartile range) age was 55 (46-67) years old and 66.2% was female. Most of the patients had underlying conditions such as hypertension (20%), malignancy (14.2%), diabetes mellitus (10.2%), dyslipidemia (7.1%), and HIV infection (7.1%). Cough (62.2%) was the most common presentation, followed by skin lesion(s) (25.3%) and fever (17.3%). The common sites of infection were lungs (62.2%), skin and soft tissue (20.4%) and lymph node (11.6%). Disseminated infection was found in 10.7%. The common species isolated were *M. abscessus* (56.4%), *M. avium* complex (19.6%) and *M. fortuitum* (11.6%). By multivariate logistic regression, predicting factors for rapid growing NTM infection were presentation with skin lesion(s) [odds ratio (OR) 5.46; 95% confidence interval (CI) 1.77-16.89, $p = 0.037$), positive bronchoalveolar lavage fluid culture (OR 0.47; 95% CI 0.23-0.95, $p = 0.020$) and HIV infection (OR 0.01; 95% CI 0.00-0.12, $p < 0.001$). Of all, 24.9% patients did not receive any treatment, 17% patients were treated with antituberculosis regimen and 41.3% patients received treatment for NTM. For treatment outcomes, 53.8% patients had clinical improvement, 18.2% patients had stable clinical disease and 6.7% patients died.

Conclusion. NTM infection was uncommon among Thai population. A significant number of rapid growing NTM infections were determined. Identify predicting factors associated with rapid growing NTM infection may be helpful for a physician in choosing appropriate treatment while waiting for the culture results or enable to perform culture.

Disclosures. **All authors:** No reported disclosures.

1707. Investigation of a Cluster of Mycobacterium interjectum Cases at a Tertiary Care Cancer Center

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Background. *Mycobacterium interjectum* is a rare NTM infection that was first described in 1993 in a patient with submandibular lymphadenitis, since then 15 additional cases have been reported. The diagnosis of infection is often delayed as identification of the organism is based on 16S rRNA sequencing. No outbreaks due to *M. interjectum*have been reported in the literature.

Methods. Retrospective review of medical records.

Results. The five cases occurred between July 23 and November 5, 2013. The mean age was 60.6 years (range 54-71 years); 4 were females. The underlying cancers were ovary, prostate, colon, CLL and Hodgkin's lymphoma. 3 patients had pre-existing lung conditions, 2 had history of smoking. 4/5 patients had respiratory symptoms at clinical presentation. *M. interjectum* was isolated from sputum (4) and bronchoalveolar lavage (1); time to culture positivity was 6-8 weeks. CT findings were present in all cases- bronchiectasis (3), nodules (4) and ground glass infiltrates were most common (2); cavitary changes were noted in one case. Co-pathogens included *M. avium-intracellulare* (MAI) (2) and ***Pseudomonas aeruginosa***(1). Two patients received treatment for MAI with symptomatic improvement and recurrence of symptoms after discontinuation. Two patients that were untreated had symptomatic and radiographic progression of lung infection. None of the patients overlapped in time or space during their hospitalization, ambulatory visits or procedures; 4/5 isolates were genetically characterized by rep-PCR and were found to be distinct from each other. Laboratory review did not identify any contamination during processing of samples.

Conclusion. *M. interjectum* is an emerging pathogen among persons undergoing treatment for cancer. The clinical and radiographic presentation is indistinguishable from other nontuberculous mycobacteria (NTM) infections, especially MAI. Our cluster of five cases of *M. interjectum*was attributed to increasing use of sequence-based technologies for difficult to identify NTM. No evidence of common source, patient –to- patient transmission or laboratory contamination was found.

Disclosures. **All authors:** No reported disclosures.

1708. Clinical Outcomes of *Mycobacterium abscessus* Infections in Miami, Florida

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Background. Infections caused by *Mycobacterium abscessus* (*MA*) are usually resistant to multiple antimicrobials and challenging to treat worldwide. The prevalence

of *MA* infections in Florida is unknown. We describe the risk factors, treatment and clinical outcomes of patients in 2 large academic hospitals.

Methods. Retrospective cohort study of hospitalized adults with a positive culture for *MA* at Jackson Memorial Hospital (1,550-beds) and the University of Miami Hospital (550-beds) Miami, FL (January 1, 2011 to January 31, 2014). Demographics, comorbidities, source of infection, antimicrobial susceptibilities and clinical outcomes were analyzed. Treatment failure was defined as death and/or infection relapse within 4 weeks of treatment. Mortality was defined as death related to *MA* during hospital stay. Data were analyzed using SPSS version 16.

Results. 68 patients were analyzed. Mean age 51.16 ± 19.46 years, 35 (51.5%) males, 28 (41.2%) Hispanics, 7 (10.3%) end-stage renal disease, 16(21.9%) were on immunosuppressive therapy (IT). Organisms were isolated: 40 (58.8%) respiratory sources, 14 (20.6%) blood, 11 (16.2%) skin and wound cultures, 5 (7.4%) peritoneal catheter associated infections, 2 (2.9%) bone. Antimicrobial susceptibility reports were available for 26 (35.4%) of the patients. Of those: 26 (100%) were susceptible (S) to amikacin, 19 (73.1%) clarithromycin, 10 (38.5%) tigecycline, 8 (30.7%) linezolid, 4(15.4%) cefoxitin. Only 2 (7.7%) were S to imipenem, fluoroquinolones (FQs) and tobramycin, 14 (53.8%) were intermediate to imipenem and 17 (65.4%) to cefoxitin. Few organisms were tested for susceptibilities to clofazimine 5 (100%) and azithromycin 4 (80%). 24 (35.3%) patients failed treatment; of those, 12 (14.7%) died. Risk factors significantly associated with treatment failure were acute kidney injury (p =0.001), dialysis (p = 0.002), solid organ transplant (p = 0.03), second site of infection (p = 0.04), IT (p = 0.02) and presence of prosthetic device (p = 0.04).

Conclusion. There is a high prevalence of *MA* in Miami with an in-hospital mortality rate of 14.7%. The most frequent source of infections was respiratory (57.4%). We found a high proportion of FQs resistance. Clarithromycin and amikacin were the most likely to be susceptible in-vitro. Immunosuppression and renal disease were significantly associated with treatment failure.

Disclosures. **All authors:** No reported disclosures.

1709. *Mycobacterium Arupense* in Cancer Patients: A Commensal Organism or a Pathogen?

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Background. *Mycobacterium arupense* is a non-chromogenic acid-fast bacillus. The clinical spectrum, epidemiology, and frequency of colonization vs true infection of *Mycobacterium arupense* remain unknown. We evaluated the clinical significance of *M. arupense*and assessed its role as a commensal organism or a pathogen requiring treatment in cancer patients.

Methods. We retrospectively identified all cancer patients treated at our institution between January 1, 2007, and June 30, 2012, who had at least one positive sputum sample, bronchoalveolar lavage (BAL), or sterile body fluid culture for *M. arupense. M. arupense* was identified by sequencing the 16S rRNA and hsp65 genes. Definite cases of *M. arupense* were defined according to nontuberculous mycobacterial disease (NTM) clinical and microbiologic criteria from the American Thoracic Society (ATS) / (IDSA). Other cases were classified as probable, possible and colonizer. We compared the outcomes of patients who did or did not receive treatment for *M. arupense* infection.

Results. We identified 36 patients with positive cultures for *M. arupense*; of these patients, 7 received treatment for *M. arupense* infection and 29 did not. Six patients met the ATS/IDSA criteria for the definitive diagnosis of nontuberculous mycobacterial disease. The two groups' baseline clinical characteristics did not differ significantly. *M. arupense* was isolated from sputum (18 patients [50%]), BAL samples (17 [47%]), and pelvic fluid (1 [3%]). The outcomes of the treated and the untreated patients did not differ significantly; clinical symptoms improved in 86% of treated patients and 67% of untreated patients (P = 0.76). Similarly, radiological findings showed improvement in 67% and 57% of the patients in each group, respectively (P = 0.99). There were no relapses of *M. arupense* infection. In addition, there were no *M. arupense*related mortalities in either group.

Conclusion. In cancer patients, *M. Arupense* seems to be mostly a commensal organism rather than a pathogen. Patients who did or did not receive treatment had similar outcomes. Further assessments to validate these findings in a larger trial are warranted.

Disclosures. **All authors:** No reported disclosures.

1710. Using Information Technology (IT) to Facilitate Infection Prevention and Control (IP&C) and Communication during a Measles Outbreak

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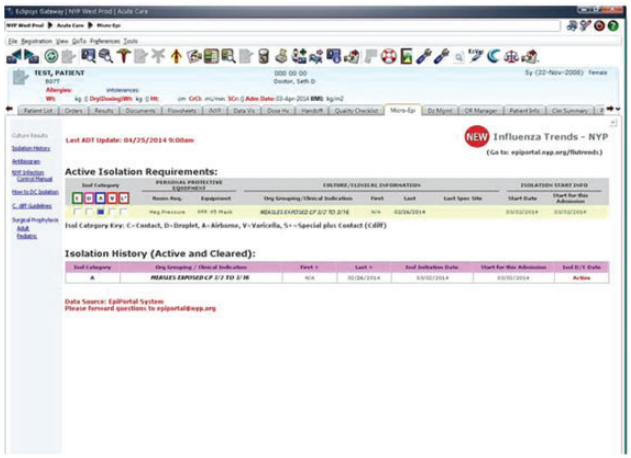
Background. Our multi-campus medical center responded to a rapidly evolving measles outbreak in New York City (NYC). We have >25,000 healthcare providers (HCPs) at 5 acute care facilities, 5 Emergency Departments (EDs) with >275,000 annual visits and >1.8 million ambulatory visits. We describe innovative uses of IT to facilitate communication for: 1) measles exposures 2) managing suspected measles and 3) increasing vaccination.

Methods. From February 5, 2014 – April 29, 2014, there were 26 cases of measles in NYC; we saw 13 (10 children, 3 adults; 4 months – 35 years). IT resources mobilized for our medical center response were: intranet website for HCPs, IP&C's electronic surveillance system (EpiPortal), patient and HCP electronic health records (EHR), linked immunization registries, and text messaging.

Figure: Screen shot of patient EHR indicating need for isolation for exposed patients including dates of communicable period (CP)



Results. We disseminated educational materials to HCPs via a measles intranet site. In response to measles exposures, our immunization registry was synchronized with the NYC registry to assess the vaccination status of 537 potentially exposed patients. Knowing that some of the 287 exposed patients with no/unknown immunity might return during their communicable periods (CP), we configured an EpiPortal alert within the EHR for Airborne Isolation if exposed patients returned (Figure). In all, 57 (20%) exposed patients returned during their CP (16 ED, 35 ambulatory, 6 inpatient). The HCP EHR identified 8 non-immune HCPs; all had medical contraindications to vaccination. We created a measles order set in the patient EHR to prompt HCPs to order the correct tests and included hyperlinks to Department of Health specimen forms. This order set was linked to EpiPortal, which can generate a list of tested patients to alert IP&C of suspect cases. The hospital immunization registry identified 266 patients 12-72 months old who had not received measles vaccination. We sent text messages asking these families to return to have their child vaccinated urgently and providing walk-in hours; to date, 127 (48%) have been vaccinated.

Conclusion. Given the complexity of our medical center, IT resources were invaluable in communication and implementing our comprehensive response. No healthcare-associated measles was identified. Processes established during this outbreak can be modified for future outbreaks.

Disclosures. **L. Saiman**, Cystic Fibrosis Foundation: Collaborator, Consultant and Scientific Advisor, Consulting fee and Salary

1711. Acute Respiratory Disease and the Reintroduction of Adenovirus Vaccine in US Army Trainees

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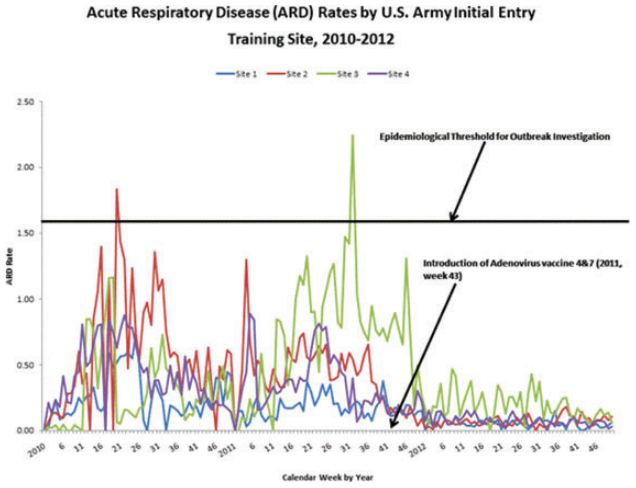
Background. Adenoviruses are a cause of respiratory illness in civilian and military populations. The Army's Acute Respiratory Disease Surveillance Program (ARD-

SP) was implemented in 1966 to monitor the occurrence of respiratory disease in Initial Entry Training (IET or recruit) centers where outbreaks associated with Adenovirus Types 4 (ADV 4) and 7 (ADV 7) were occurring. The ARD-SP later documented the effectiveness of live, oral ADV 4 and ADV 7 vaccine introduced in 1971. Manufacture of ADV 4 and ADV 7 vaccine ended in 1994 and all vaccine stocks were depleted in 1999. Subsequently, ARD rates increased at IET installations. In March 2011, a new ADV 4 and ADV 7 vaccine was licensed by the Food and Drug Administration for use in US Military Members. Administration of the new vaccine began in November 2011.

Methods. Weekly ARD-SP data from four Army IET sites collected by the US Army Public Health Command were evaluated to develop ARD rates per 100 trainee weeks for the total Army IET population and each IET installation for calendar years 2010, 2011 and 2012 using SPSS ver. 21.

Results. ARD rates dropped dramatically at the end of 2011 (figure). The overall mean ARD rate was five times higher in 2010 than in 2012 (0.43/100 trainee weeks vs 0.08/100 trainee weeks). ARD rates varied between sites. Site 2 saw the biggest decrease (88%), with ARD rates decreasing from an average of 0.59/100 trainee weeks in 2010 to 0.07/100 trainee weeks in 2012.



Conclusion. The reintroduction of the two tablet, oral Adenovirus vaccine has been associated with a dramatic and sustained decrease in ARD rates in US Army Initial Entry Training populations. This was expected since during the absence of the vaccine two-thirds of recruits with respiratory disease tested were positive for an adenovirus and 80% of those specimens were positive for ADV 4. Since adenovirus outbreaks have been reported in militaries of other countries and civilian settings such as residential facilities with close personal contact, other populations might benefit from the Adenovirus vaccine.

Disclosures. **All authors:** No reported disclosures.

1712. An Integrated Surveillance for Antimicrobial-Resistance in *Salmonella* from Clinical and Retail Meat Sources — Pennsylvania, 2009-2013

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Background. *Salmonella* is a leading cause of foodborne illness in the United States. Although salmonellosis is often self-limiting, persons with drug-resistant infections are at risk for severe clinical outcomes. Pennsylvania has implemented an integrated system that compares enteric pathogens from ill persons with pathogens recovered from retail meat.

Methods. During August 2009 through June 2013, *Salmonella* isolates from meat (chicken breasts, ground turkey, ground beef, and pork chops, 470 of each) purchased from randomly selected retail outlets in southeastern Pennsylvania were analyzed by pulsed-field gel electrophoresis (PFGE). We compared the PFGE patterns with those of clinical isolates in the Pennsylvania surveillance database. All meat isolates and a subset of matched clinical isolates were tested for susceptibility to antimicrobial agents.

Results. A total of 148 *Salmonella* isolates were recovered from 1880 meat samples: 20% of chicken samples, 9.6% of turkey, 0.64% of beef, and 1.3% of pork were culture-positive. PFGE patterns of 66 (44.6%) retail meat isolates had PFGE matches among 1304 clinical isolates; 28 distinct PFGE patterns were represented. Sixteen (57.1%) of these patterns were associated with multi-drug resistance (resistance to ≥3 antimicrobial agents), and 11 (39.3%) were associated with drug-resistance profiles that were identical to profiles of PFGE-matched retail meat isolates. One Dublin PFGE pattern found in 10 clinical isolates and one beef isolate was associated with resistance to ≥6 antimicrobial agents. All eleven isolates demonstrated resistance to ampicillin and ceftriaxone. Six distinct patterns of clinical Typhimurium isolates shared resistance profiles that were identical to matched retail meat isolates. One isolate from pork was resistant to the same five antimicrobial agents (ACSSuT phenotype) as were 22 clinical Typhimurium isolates.

Conclusion. In this comparison, *Salmonella* isolates known to have caused human illness had PFGE patterns indistinguishable from those found in retail meats. Of these, more than half were multidrug resistant. These data suggest that some antimicrobial resistant Salmonella infections in humans originate from contaminated retail meat.

Disclosures. **All authors:** No reported disclosures.

1713. Interventions to Increase Healthcare Worker Influenza Vaccination: a meta-analysis

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Background. Rates of healthcare worker (HCW) influenza vaccination remain suboptimal, however the most effective way to increase uptake is controversial. We conducted a systematic review of the literature of interventions to increase influenza vaccine coverage in HCWs.

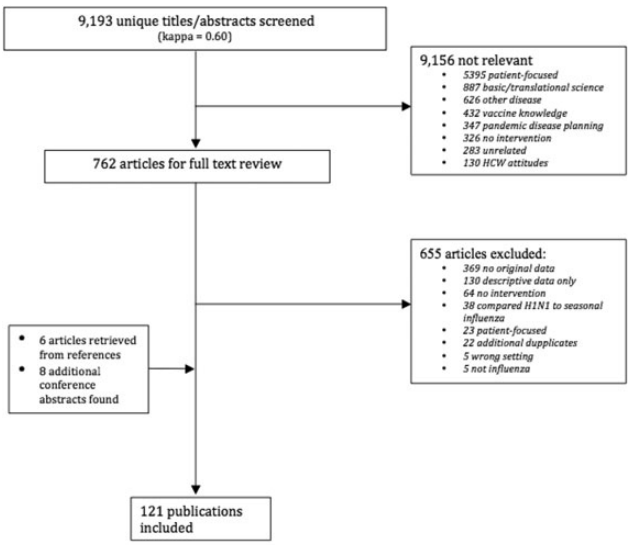
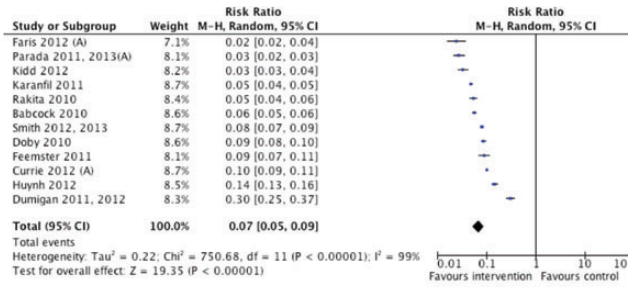


Figure 1. Flow Diagram of Search Results

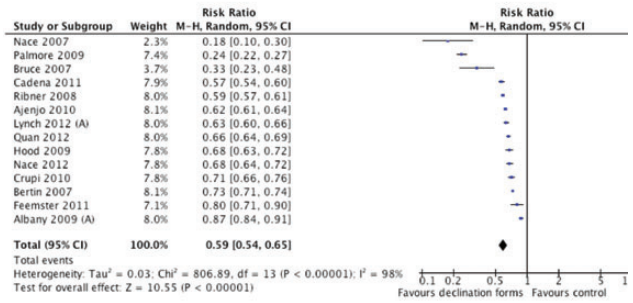
Methods. An expert librarian searched the following databases to July 9, 2013: MEDLINE, EMBASE, CENTRAL, Web of Science, Scopus, and CINAHL. References and conference abstracts were also searched. Interventions were classified into 9 categories (see Results). Two reviewers independently extracted data and classified risk of bias. Primary outcomes were 1) reduction in number of unvaccinated HCWs, and 2) interventions that achieved 95% vaccination rates; each at 1 year (early) and 3 ±1 years (late) after intervention implementation.

Results. 9193 titles/abstracts were reviewed, and 121 were included (Figure 1). Of 174 comparisons, 78 were low risk of bias (RoB), 30 were moderate RoB, and 66 were high RoB. There were 132 before/after studies, 23 randomized trials, 12 surveys, 7 cohort studies, and 1 case-control study. All interventions were significantly associated with a reduction in unvaccinated HCWs (listed from largest to smallest effect size): condition of service [12 studies; 357,560 HCWs; 93% reduction in unvaccinated HCWs, (95%CI 91-95%); $I^2 = 99\%$], vaccine-or-mask [12 studies; 581,926 HCWs; 74% (61-88%); 100%], declination forms [14 studies; 209,290 HCWs; 41% (35–46%); 98%], audit-and-feedback [15 studies; 545,403 HCWs; 35% (29–40%); 99%], increased vaccine access [46 studies; 764,570 HCWs; 32% (27–36%); 100%], role models [18 studies; 204,514 HCWs; 30% (24–36%); 99%], peer-vaccination [7 studies; 120,670 HCWs; 29% (10–45%); 100%], incentives [17 studies; 188,933 HCWs; 28% (21–33%); 99%], and education/promotion only [16 studies; 554,706 HCWs; 11% (7–16%); 99%]. The interventions that achieved 95% HCW vaccination rates were: condition of service

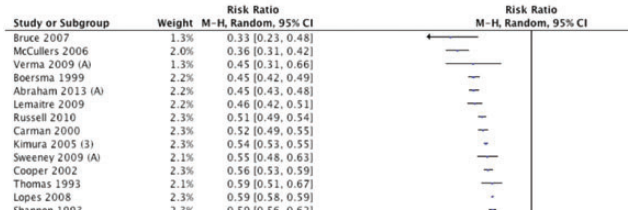
(13/13 early; 4/4 late), vaccine-or-mask (3/15 early; 0/2 late), and role models (1/19 early; 1/10 late).



A. Condition of service



C. Declination forms



Conclusion. All interventions examined increased HCW influenza vaccine uptake to various degrees. However, only condition of service policies appear to result in sustained HCW vaccination rates of >95%.

Disclosures. **B. Coleman**, Sanofi Pasteur: Investigator, Research grant; GSK: Grant Investigator, Research grant; Novartis: Grant Investigator, Research grant **A. Mcgeer**, Sanofi Pasteur: Grant Investigator and Scientific Advisor, Research grant; GSK: Grant Investigator, Research grant; Novartis: Grant Investigator, Research grant

1714. Influenza antiviral agent use among adults hospitalized with community-acquired pneumonia

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Background. Influenza is a common cause of community-acquired pneumonia (CAP). Data on the use of influenza antiviral treatment among patients hospitalized with all-cause CAP are limited.

Methods. Adults ≥18 years old hospitalized with CAP were enrolled year-round at 5 hospitals in Chicago and Nashville. Clinicians ordered influenza tests (rapid test, direct fluorescent antigen, or polymerase chain reaction [PCR]) and prescribed antivirals per clinical judgment. Nasopharyngeal /oropharyngeal specimens for influenza PCR testing were systematically collected for the study but results were unavailable to clinicians. Treatment was defined as influenza antiviral agent receipt during hospitalization for any period of time. We compared factors associated with receipt and non-receipt of treatment during influenza season (October – April in each year).

Results. From January 2010 – June 2012, we enrolled 2323 adults with CAP. Of 1491 (64%) adults enrolled during influenza season, 180 (12%) received treatment. Clinicians ordered influenza tests in 583 (39%) patients (96% were PCR); 37/48 (77%) with a positive result received antivirals. Study testing revealed 100 influenza positive cases, 41 of whom received antivirals. Compared with those who did not receive treatment, adults who received treatment were younger, admitted earlier during illness, less likely to have a comorbidity, and more likely to need intensive care unit (ICU) admission or mechanical ventilation.

Characteristic	Receipt of treatment (n=180) No. (%)	Non-receipt of treatment (n=1311) No. (%)	P value
Median age (interquartile range [IQR]) years	54 (41-66)	58 (47-71)	<0.01
Median days from illness onset to admission (IQR)	3 (2–6)	4 (2–8)	0.03
Any comorbidity	146 (81)	1163 (89)	<0.01
Positive clinician-ordered influenza test/total tested	37/129 (29)	11/454 (2)	<0.01
ICU admission	68 (38)	242 (19)	<0.01
Invasive mechanical ventilation	32/68 (47)	59/242 (24)	<0.01

Conclusion. Among adults hospitalized with all-cause CAP, receipt of influenza antiviral treatment was low and associated with having a positive influenza result available to clinicians, presenting earlier in course of illness, and with severe disease. Reasons for the underutilization of antiviral treatment warrant exploration.

Disclosures. **R. Wunderink**, Genentech: Consultant, Consulting fee; Crucell/Janssen/Johnson and Johnson: Consultant, Consulting fee **K. Edwards**, Novartis: Grant Investigator and Scientific Advisor, Research grant

1715. Oseltamivir use in an Influenza Outbreak: Linking Pharmacology to Pharmacoeconomics

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Background. Recent pharmacokinetic/pharmacodynamic (PK/PD) evaluations find that higher oseltamivir exposures may reduce duration of viral shedding and symptoms. However, the impact of such findings on pandemic planning decisions and use of stockpiles has not been described. This study explored the economic impact of oseltamivir dose optimization in supporting pandemic influenza planning decisions in the US.

Methods. We simulated the infected population across a 1 year seasonal influenza outbreak using a health economic model linked to a PK/PD-epidemiology model (SEIR). Different scenarios were considered to evaluate the cost-effectiveness of high dose (150mg BID) vs standard dose (75mg BID) oseltamivir, low and high virulence, varying transmissibility (low and high attack rates (37% and 67.5% respectively)) and drug uptake (25%, 50%, and 80%). The analysis was conducted from a societal perspective, incorporating both direct and indirect costs. Disease epidemiology and costs were US-specific. Sensitivity analyses were performed to test model robustness.

Results. Results for incremental cost, deaths averted, quality-adjusted life-years (QALY) gained, and incremental cost-effectiveness ratios (ICERs) for high dose compared with standard dose oseltamivir under different scenarios are given in the table.

Comparators (150 mg vs 75 mg)	Incremental cost (USD)[3]	Death averted	QALY gained	ICER(per QALY)
High virulence[1]				
high transmissibility				
25%[2]	-21,935,208	148.4	149.1	-147,108
50%[2]	-31,673,695	227	227.2	-139,384
80%[2]	-21,126,363	190	189.4	-111,573
low transmissibility				
25%[2]	-4,212,570	44.3	44.5	-94,729
50%[2]	4,335,233	13.7	13.7	317,341
80%[2]	9,116,920	9	9	1,015,910
Low virulence				
high transmissibility				
25%[2]	-14,661,284	74.5	77.2	-190,011
50%[2]	-20,562,861	114	117.2	-175,496

continued.

Comparators (150 mg vs 75 mg)	Incremental cost (USD)[3]	Death averted	QALY gained	ICER(per QALY)
80%[2] low transmissibility	-11,842,304	95.4	97.2	-121,822
25%[2]	-2,043,215	22.2	23	-88,790
50%[2]	5,003,199	6.9	7	710,268
80%[2]	9,556,934	4.5	4.6	2,074,257

[1] Proportion of infected cases who visited ED was assumed to be twice as high as in low severity scenario [2] Uptake [3]negative signs mean cost-saving

Conclusion: These results suggest the potential for high dose oseltamivir to provide economic value, and may have a role in pandemic influenza particularly in high transmissability scenarios; the role of high dose oseltamivir should be investigated further.

Disclosures. **N. Chaiyakunapruk**, Roche: Grant Investigator, Consulting fee and Research grant **D. Wu**, Roche: Grant Investigator, Research grant **C. Pratoomsoot**, Roche: Collaborator, Research grant and Research support **K. Lee**, Roche: Consultant, Consulting fee **H. C. Yi**, Roche: Research Contractor, Research grant and Research support **R. E. Nelson**, Roche: Consultant and Grant Investigator, Consulting fee, Research grant and Research support **P. Smith**, Roche: Grant Investigator, Consulting fee **C. Kirkpatrick**, Roche: Consultant, Consulting fee **M. Kamal**, Roche: Employee, Salary **K. Nieforth**, Roche: Consultant, Consulting fee **G. Dall**, Roche: Consultant, Consulting fee **S. Toovey**, Roche: Consultant, Consulting fee **D. Kong**, Roche: Consultant, Consulting fee **A. Kamauu**, Roche: Consultant and Grant Investigator, Consulting fee and Research support **C. Rayner**, Roche: Research Contractor, Consulting fee

1716. Engagement in *OutSmart Flu*, a smartphone-based surveillance system for influenza-like illness among students on a university campus

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Background. Crowd-sourcing methods have been used in surveillance for influenza-like illness (ILI) to detect epidemic influenza earlier than the Centers for Disease Control and Prevention's (CDC) ILINet. Mining of search engine query data (passive surveillance) and email-based approaches (active surveillance) have been used, but both primarily focus on detecting epidemic flu at the national level.

Methods. At University of Wisconsin-Madison (UW), during the 2013-14 academic year, we began passive surveillance for ILI using a smartphone app called OutSmart Flu (OSF). Users reported their ILI symptoms or feeling well. As feedback, users received near-real time, past 7-day rates of ILI among fellow OSF users and one-week lagged ILI rates estimated by UW University Health Services (UHS), a CDC ILINet sentinel site. We promoted OSF using social marketing, social media, student volunteers, email, and raffles. Nine months after deployment of iOS and Android versions of the app, we examined the composition of OSF users, app engagement, and compared ILI trends among OSF users with trends among UHS attendees.

Results. Overall, 776 users (35% men, 65% women) installed OSF, 583 (75.1%) completed a baseline research survey, 557 (71.8%) completed a profile, 556 (71.2%) submitted at least one symptom report during the academic year. The median (IQR) time elapsed between joining OSF and last use of the app (i.e., length of engagement) was 102 (31, 209) days. Although women were more likely to join OSF, their relative hazard (RH) of using the app was greater than men's use for the first month (RH = 1.41; 95% CI: 1.03, 1.95; p = 0.035), but not thereafter (RH = 0.79; 95% CI: 0.64, 0.99; p = 0.038). Individuals who reported not receiving the previous year's seasonal flu vaccine (2012-13) were significantly more likely to use OSF (RH = 1.64; 95% CI: 1.39, 1.95; p < 0.001). ILI rates mostly paralleled UHS ILI rates, but neither detected the ILI peak identified by national surveillance systems as this fell during UW Winter Recess when both OSF app use and UHS clinic attendance was lower.

Conclusion. College campuses are unique environments for influenza transmission. In its first year, uptake and use of a smartphone-based, surveillance system for ILI among UW students was moderately successful and provide us reason to expand OSF to more users and more campuses during the 2014-15 flu season.

Disclosures. **All authors:** No reported disclosures.

1717. Eagle County and Flu Near You: An Innovative Partnership to Implement a Participatory Epidemiology Tool to Enhance Infectious Disease Preparedness Prior to a Mass Gathering Event

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Background. Eagle County, CO will host the World Alpine Ski Championships in 2015 during the height of the respiratory illness season. This international event will quadruple the population of our rural community and increase the risk for importation and dissemination of infectious diseases. Traditional public health (PH) surveillance relies on laboratory and healthcare provider reporting. System limitations include delayed reporting, inconsistent population coverage, and poor sensitivity for emerging diseases. Our goals were to test Flu Near You (FNY), a free, participatory mobile disease tracking system using existing staffing and PH resources to determine if the data enhances our surveillance capabilities prior to the 2015 event.

Methods. The confidential participant data collected on a weekly basis through the FNY website is aggregated on a web-based map to show the spread of influenza-like illness (ILI) across the U.S. and locally. Eagle County Public Health (ECPH) and FNY built community-specific recruitment tools to increase participation for our region. Local and national data was reviewed routinely as part of standard PH surveillance during the 2013-2014 season, alongside traditional ILI data.

Results. The FNY data detected the arrival of ILI in our county a week before the first reported hospitalized case. Spikes in FNY reports coincided with community reports of illnesses in schools and workplaces that were not detected using traditional surveillance. Though the results were anecdotal and limited by a small sample size, the early warning allowed ECPH to rapidly disseminate infection prevention messages to community partners. In addition, the novelty of the FNY program opened doors to community groups that traditionally would not have engaged in influenza prevention and control.

Conclusion. The use of a free, participatory epidemiology tool to enhance disease surveillance in a rural community demonstrated promising results. When communities are presented with high-risk events, such as a mass gathering, PH professionals should look outside of their traditional circles to leverage additional resources. With increased adoption, we expect the program will provide sustainable surveillance data to enhance the preparedness of our community for future disease outbreaks.

Disclosures. **All authors:** No reported disclosures.

1718. Resistance among Invasive Group A Streptococcal Infections, United States, 1999-2012

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Background. Macrolide resistance among group A *Streptococcus* (GAS) is common in many countries. We analyzed prevalence of resistance to erythromycin (EryR) and other antibiotics among GAS isolates obtained from CDC's Active Bacterial Core surveillance (ABCs) over a 14-year period.

Methods. ABCs is active, laboratory- and population-based surveillance for select bacterial infections in 10 geographically diverse U.S. sites. Isolates from invasive GAS infections were collected in participating ABCs sites from 1999-2012. Susceptibility was assessed using broth microdilution and D-zone testing for inducible clindamycin resistance (CliR); *emm* typing was performed using DNA sequencing.

Results. We tested 9175 (85%) isolates from 10,794 invasive GAS cases; 10.5% were EryR. Both EryR and CliR increased over the 14 years (test for trend: $P < 0.001$). Marked yearly shifts in EryR prevalence occurred among several ABCs sites: CA (2001: 8.5%; 2006: 23.6%; 2010: 4.0%), MD (1999: 3.4%; 2008: 34.2%; 2012: 8.0%) and OR (2007: 4.4%; 2012: 28.3%). No penicillin or cephalosporin resistance was found. Among >85 *emm* types, 10 (*emm* 12, 49, 58, 73, 75, 76, 83, 92, 94, 114) accounted for 21% of all isolates but 65% of EryR isolates. Site-specific variability in EryR prevalence was primarily due to fluctuations of these *emm* types. Among 105 EryR isolates from 2012, 62 (59%) were inducibly CliR and 35 (41%) constitutively CliR; 72 of CliR (74.2%) were also tetracycline-resistant. Data from 2001-2010 indicated that a genetic element that contains both *erm*TR and *tet*M accounted for most CliR. The patient case fatality ratio did not differ by EryR (10.7% EryR vs 12.2% erythromycin susceptible; $P = 0.18$). EryR infections were more common ($P < 0.05$) among men than women (11.7% vs 9.3%) and among persons age 18-34 (13.2%) and 50-64 years (13.1%) than other age groups. EryR was lowest among children age <5 years (7.5%).

Conclusion. Macrolide resistance among invasive GAS infections in the U.S. gradually increased over 14 years. However, local frequency of macrolide-resistant GAS infections fluctuated markedly, depending on circulating strains. Community-specific susceptibility testing is important for clinical management. Penicillin remains a good choice for therapy of invasive GAS infections.

Disclosures. **All authors:** No reported disclosures.

1719. Public health response to a school-based norovirus gastroenteritis outbreak: Environmental sampling as a novel investigative tool

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Background. Norovirus outbreaks in schools can amplify rapidly through multiple routes of transmission, and have led to campus closures. Ensuring implementation of transmission-prevention measures is challenging in large secondary schools, where exclusion criteria for ill persons may be limited, and sufficient environmental surface disinfection may be difficult to achieve. During a norovirus outbreak in a Dallas County public high school in 2014, supplemental approaches to outbreak control were assessed, including environmental testing.

Methods. Students and staff with vomiting or diarrheal illness reported to the health department were interviewed with standardized questionnaires. Exposure surveys were also administered to all 2500 students. A case-control analysis included 300 cases and 600 controls randomly selected from respondents and matched on gender. Data were analyzed using multiple logistic regression with SAS 9.4. Stool samples from cases and environmental surface swabs were tested for norovirus by RT-PCR assay.

Results. An overall attack rate of 32% occurred over 4 weeks, with a peak in cases on January 30, the day of initial report to public health. Cases reported vomiting (83%), diarrhea (57.3%), and fever (40.3%). Norovirus genogroups GI (n = 4) and GII (n = 1) were identified in stool samples. Ongoing new cases 5 days following public health notification prompted environmental sampling. Norovirus GI (n = 8) and GII (n = 2) were identified from multiple surfaces, including: door handles, stair rails, computer keyboards, and a water cooler spigot. Numbers of cases declined after enhanced cleaning targeting these fomites. In the case-control analysis, significant predictors included: water fountain use (OR = 1.79, p= 0.004); and participation in the dance team (OR = 1.91, p= 0.03) or theater (OR = 1.78, p= 0.02).

Conclusion. Customary public health interventions to control norovirus outbreaks can be difficult to implement comprehensively in public secondary schools. Environmental surface testing for norovirus during persistent outbreaks may assist with identification of particular surfaces and previously unrecognized transmission vehicles to target limited school resources for enhanced disinfection.

Disclosures. **All authors:** No reported disclosures.

1720. Decreased Survival among AIDS Patients in the United States who Screened Positive for Cryptococcal Infection

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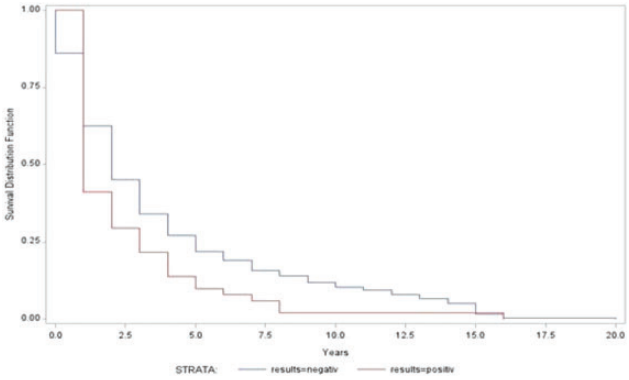
Background. Cryptococcus meningitis (CM) is the most common cause of AIDS-related mortality in the world. In sub-Saharan Africa the WHO recommends routine cryptococcal antigen (CrAg) screening in AIDS patients with a CD4 T-cell count ≤ 100 cells/μl and initiating anticryptococcal therapy among positives to prevent CM. In the United States (US) however, there are no recommendations for routine cryptococcal screening. In a cohort study among 1872 AIDS patients in the US, the prevalence of cryptococcal infection was 2.9% overall; in some sub-groups the prevalence was as high as 6.4%. We aimed to determine if survival among those who screened positive was different from those who screened negative for CrAg.

Methods. Using stored sera from the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS), we screened 1,872 specimens from donors with CD4 T-cell count < 100/μl using the CrAg Lateral Flow Assay (Immy, Norman, OK). Overall survival and survival between multiple sub-groups were compared using adjustment methods.

Results. The number of CrAg positive within this cohort was 55 (2.9%). Survival analysis results (Figure 1) showed a significantly lower survival in those with a positive CrAg result (median = 1 year, P = 0.02) and those with a negative CrAg result (median = 2years, P= 0.02). After controlling for CD4 count, age, and if specimen were collected pre or post ART era, women had a longer survival than men (p-value 0.01), and blacks had a longer survival than both Hispanics and whites (p-value 0.02). The probability of 5 year survival for blacks and Hispanics was 30% compared to 10% for whites. Further, the probability of 5 year survival for women was greater than 30% compared to less than 10% in males.



Survival analysis by CrAg test result

Conclusion. Presently, there are no recommendations for routine cryptococcal screening in AIDS patients in the U.S. The results from this study coupled with the results from an earlier study assessing the prevalence of cryptococcal infection among AIDS patients in the US, suggest not only that cryptococcal screening in those with CD4 ≤ 100 cells/ ul is well above the published cost-effectiveness threshold of 2.0% but that screening could reduce mortality.

Disclosures. **All authors:** No reported disclosures.

1721. Cost-Effectiveness of Meningococcal Quadrivalent Conjugate Vaccination Campaign among Men Who Have Sex With Men in New York City

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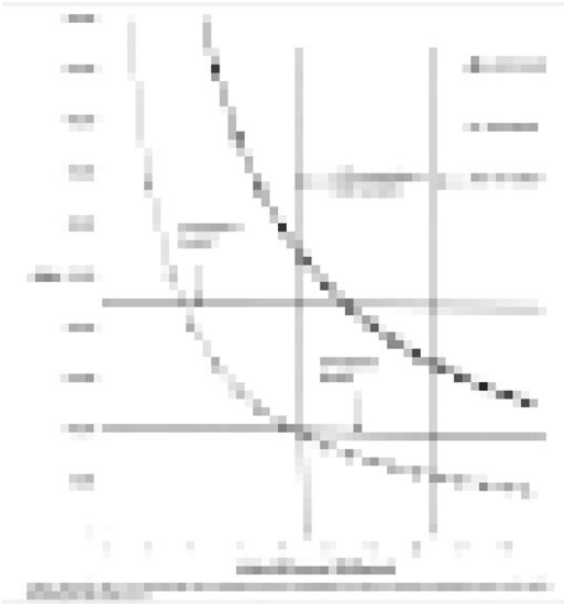
Background. To control an outbreak of invasive meningococcal disease (IMD) among men who have sex with men (MSM) in New York City (NYC), the NYC Department of Health and Mental Hygiene (DOHMH) recommended vaccination of all HIV-positive MSM and HIV-negative MSM with "intimate contact with a man met through an online Web site, digital application or at a bar or party"

Methods. We used a decision analytic model to estimate the effectiveness and cost-effectiveness of the meningococcal quadrivalent conjugate vaccination campaign as compared to no vaccination. We estimated approximately 60,000 NYC MSM to be targeted through DOHMH recommendations based on NYC Community Health Survey and NYC HIV/AIDS surveillance registry data. Model inputs, including IMD incidence of 20.5 per 100,000 HIV-positive MSM (42% fatal) and 7.6 per 100,000 HIV-negative MSM (20% fatal), were from DOHMH data and published sources. Outcome measures included costs (2012 US dollars), IMD cases averted, IMD deaths averted, quality-adjusted life-years (QALYs) and incremental cost-effectiveness ratios ($/QALY). Sensitivity analyses were performed on key inputs including herd immunity (base case 20% protection in all unvaccinated MSM).

Results. Compared to no vaccination, the targeted vaccination campaign averted an estimated 2.7 IMD cases (modeled range 0.9-6.0) and 1.0 IMD deaths (modeled range 0.2-2.5) and had an incremental cost-effectiveness ratio of $60,100/QALY. At a cost-effectiveness threshold of $100,000/QALY, vaccination remained cost-effective at an IMD incidence as low as 10 per 100,000 persons or at a case fatality rate greater than 13% in all MSM. At a societal willingness to pay consistent with adopted meningococcal vaccination guidelines for adolescents ($230,000/QALY), vaccination was cost-effective at an IMD incidence as low as 5

per 100,000 persons. Results were sensitive to assumptions regarding herd immunity (figure).



Conclusion. Vaccination during a community-wide IMD outbreak among MSM in NYC was projected to avert IMD cases and deaths and had an incremental cost-effectiveness ratio less than $100,000/QALY. Cost-effectiveness was highly dependent on herd immunity.

Disclosures. **All authors:** No reported disclosures.

1722. Potential Impact of Vaccination of College-Age Adolescents against *N. meningitidis* Serogroup B: Results of a Transmission Dynamic Model

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Background. Studies in the 1990s establishing an increased risk of invasive meningococcal disease (IMD) in first year college students living in residence halls were the foundation for US ACIP recommendations for routine meningococcal serogroup A, C, W-135 and Y (MenACWY) vaccination in this group. Recent college campus outbreaks of meningococcal serogroup B (MenB), such as that at Princeton University where the attack rate was 134 per 100,000, highlight the unpredictability of IMD and the need in the US for a licensed, broadly protective MenB vaccine. We estimated the potential impact of introducing routine MenB vaccination of students preparing for the first year of college.

Methods. A transmission dynamic model was adapted to simulate MenB carriage prevalence and IMD incidence within the college-attending US young adult population (17-22 year olds). Carriage prevalence and vaccine efficacy against IMD and carriage were obtained from published literature and expert opinion. Incidence of IMD was estimated from the US national surveillance system utilizing the 2008 to 2011 average. College attendance data were obtained from US Bureau of Labor and Statistics. IMD cases and deaths avoided over a 30 year period were calculated for the entire US population, and separately for a closed (i.e., no transmission into or out of the population) college-attending cohort.

Results. In a closed-cohort of college-attending young adults aged 17-22 years, routine vaccination of 90% of 17-year-olds entering college would prevent an estimated 293 cases and 35 deaths. If college attendees had limited interaction with other members of general population, an estimated 2,278 cases and 224 deaths could be prevented in the US. An estimated 2,788 cases and 266 deaths could be prevented with routine vaccination of 11 year olds receiving a booster dose at 16 years of age.

Conclusion. A strategy of vaccinating first year college entrants could have a sizable impact on MenB disease and help control college campus outbreaks. However, the overall cases of disease and deaths prevented utilizing a strategy of vaccinating college entrants are fewer than if an age-based vaccination strategy was pursued. A program addressing disease in college students and adolescents would have the greatest impact.

Disclosures. **S. J. Snedecor**, Pharmerit: Employee, Consulting fee **R. Farkouh**, Pfizer: Employee, Salary **L. York**, Pfizer: Employee, Salary **M. Xue**, Pharmerit: Employee, Consulting fee **D. Strutton**, Pfizer: Employee, Salary

1723. Trends in Tuberculosis Cases in State Prisons and Local Jails, California, 2000–2009

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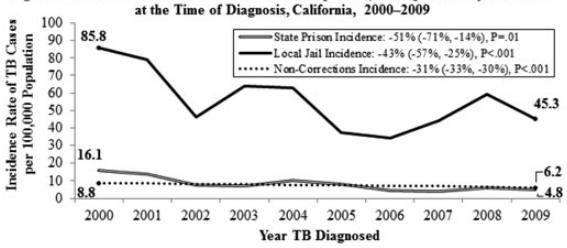
Background. To our knowledge, no studies have evaluated trends in tuberculosis (TB) incidence in the California (CA) correctional system. We assessed trends in TB incidence during 2000–2009 and compared demographic and clinical characteristics among cases in state prisons and local jails.

Methods. TB cases aged ≥15 years reported to the CA TB registry during 2000–2009 were included in the analysis. Population estimates were obtained from CA Department of Corrections and Rehabilitation for state prisons, Board of State and Community Corrections for local jails, and Department of Finance for non-correctional populations. Trends in incidence per 100,000 population were assessed using Poisson regression, and trends in percentages were assessed using weighted linear regression. Because population estimates were not available for other CA correctional facilities, all comparisons of demographic and clinical characteristics were restricted to case-patient's in state prisons and local jails and were conducted using the Chi-square test.

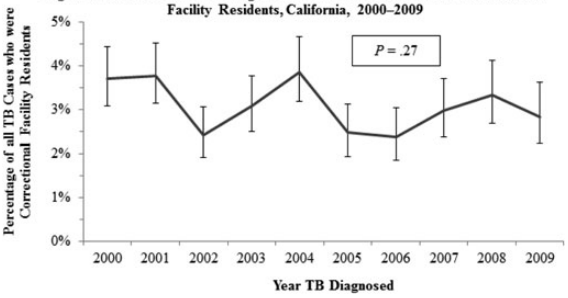
Results. Of 29,564 TB cases reported, 838 (3%) were residents of correctional facilities. Among the 838 correctional TB cases, 433 (52%) occurred in residents of local jails, and 134 (16%) in state prisons. From 2000–2009, TB incidence decreased significantly in local jails (85.8 to 45.3; $P = .01$), state prisons (16.1 to 4.8; $P < .001$), and in non-correctional (8.8 to 6.2; $P < .001$) populations (Figure 1). No significant change in the percentage of TB cases who were correctional facility residents was detected (Figure 2). A higher proportion of case-patients in local jails, compared to state prisons, were foreign-born [223/427 (52%) vs 38/128 (30%); $P < .001$], homeless in the past year [145/433 (33%) vs 14/134 (10%); $P < .001$], and had culture-positive pulmonary TB [340/433 (79%) vs 89/134 (66%); $P < .001$].

Figure 1: Trends in Tuberculosis Incidence Rates per 100,000 Population by Residence at the Time of Diagnosis, California, 2000–2009



Population	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
State Prison	161,480	161,166	157,559	160,120	162,818	162,766	170,926	172,669	170,637	167,949
Local Jail	73,428	72,202	75,433	75,016	77,568	80,761	81,375	84,000	82,970	81,599
Non-Corrections	33,765,927	34,279,374	34,705,298	35,153,792	35,512,379	35,742,055	35,994,521	36,295,860	36,602,615	36,827,656

Figure 2: Trends in the Percentage of Tuberculosis Cases who were Correctional Facility Residents, California, 2000–2009



Conclusion. While TB rates have declined significantly since 2,000, the percentage of TB cases diagnosed in CA correctional facilities has remained constant. TB rates in local jails are seven to nine times higher than in state prisons and non-correctional populations. The risk of TB transmission in correctional facilities, particularly local jails, remains a concern and efforts to rapidly detect TB continue to be important.

Disclosures. **All authors:** No reported disclosures.

1724. Clinical Presentations and Interactions of the Chikungunya Viral Infection in HIV Patients During the Chikungunya Epidemic in Southern Thailand

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Background. Between 2004 and 2010, the chikungunya virus (CHIKV) spread from East Africa, India, Southeast Asia to China, affected millions of people. There exists no previous report on chikungunya in HIV patients. Therefore, we studied the clinical pictures of chikungunya in HIV patients and examined whether HIV infection worsened the clinical course of chikungunya.

Methods. This is a retrospective case review of all laboratory-confirmed cases of chikungunya fever (CHIKF) from August 2008-September 2009 at Songklanagarind Hospital, a teaching hospital in Southern Thailand. We compared the demographic data, clinical course, severity, and complication of CHIKF in HIV and non-HIV patients. CD4 cell count and HIV viral load were also assessed in CHIKV-coinfected HIV patients.

Results. Thirteen HIV patients (CD4 cell count range of 250-873 cells/μL) and 71 non-HIV patients with CHIKF were identified. There were no significant differences in the demographic data and clinical course, except HIV patients were younger (mean age ± SD, 36± 4 years vs 42 ± 14 years, *P= 0.005*). All patients presented with fever and bilateral arthralgia. Eighty-four percent of both groups developed rash. The median duration of arthralgia and rash was 14 days and 3 days, respectively. However, more non-HIV patients needed opioid analgesics (tramadol) (50% vs 9.1%, *P = 0.018*), and were more likely to temporarily stop working (83.6% vs 46.2%, *P = 0.007*). None of the HIV patients were hospitalized, developed complication or had chronic arthritis, compared with 11.2%, 5.6%, and 2.8% of non-HIV patients, respectively. There was no HIV viral load rebound in the previously viral suppressed HIV patients during or after CHIKF. Two HIV patients, in whom pre-CHIKF illness HIV viral load was 3,630 and 30,100 copies/mL, had their HIV viral load decrease to 901 and 17,500 copies/mL after 1 and 21 days of CHIKV infection, respectively. Long term follow-up (16-32 months post chikungunya) did not detect any alarming fall in blood CD4 counts in any of the HIV patients.

Conclusion. HIV infection did not worsen the clinical course of CHIKF. CHIKV also had no adverse effects upon CD4 cell count or HIV viral load.

Disclosures. **All authors:** No reported disclosures.

1725. Surveillance for *Borrelia burgdorferi* in *Ixodes* Ticks and Mice in British Columbia

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Background. Historically, Lyme disease prevalence has been low in the Pacific Northwest of North America. Because there have been many public misconceptions regarding the ability of laboratories to identify Lyme disease, we studied the prevalence of *B. burgdorferi* in the *Ixodes pacificus* tick (vector) and *Peromyscus maniculatus* mouse (host) in British Columbia (BC).

Methods. In this study, mice were trapped from 11 different jurisdictions in BC from May to September. IFA and Western blots were performed on mice serum to determine the presence of *B. burgdorferi* antibodies. Ticks were collected from trapped mice and with the flagging/dragging technique. A maximum of 5 ticks from each mouse were pooled for DNA extraction and subjected to real-time PCR which targeted the 23S rRNA gene of *Borrelia* spp. and *osp*A gene of *B. burgdorferi* at the BC Public Health Microbiology and Reference Laboratory. Two organs from each mouse were also subjected to the same molecular tests. A subset of tick DNA extracts (n = 48) were also sent to CDC Fort Collins where multiplex PCR targeting *fliD* and *gB31genes* for *B. burgdorferi* was performed to check for concordance between the results.

Results. No ticks were found by flagging during this study period; however a total of 467 ticks of different developmental stages were retrieved from 237 mice. For the serology results, 19 mice were confirmed to have antibodies against *B. burgdorferi.* For the molecular results, 3 tick pools were positive for *B. burgdorferi* but all mouse organs tested were negative. Of the positive tick pools, the corresponding mice were serologically positive. The subset of ticks tested by the two laboratories had identical results.

Conclusion. The positivity rate of *B. burgdorferi* in the B.C. *Ixodes* tick population was found to be **>0.71%,** suggesting very low incidence. The exposure rate in the mouse population to *B. burgdorferi* was determined to be **8.18%**, suggesting that the infestation rate is also low in the host population. This observation may explain the continued low incidence of Lyme disease in BC.

Disclosures. **All authors:** No reported disclosures.

1726. What Defines Carbapenem-Resistant Enterobacteriaceae (CRE) in a Low Prevalence State? Oregon, 2010 — 2013

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Background. Preventing the spread of carbapenem-resistant Enterobacteriaceae (CRE) is important to public health because of high infection-related morbidity, mortality, and cost. Carbapenemase producing (CP)-CRE are most concerning because of their rapid global dissemination. In 2013, CRE in Oregon were defined as Enterobacteriaceae with non-susceptibility to ≥1 carbapenem, including ertapenem, and resistance to any 3rd generation cephalosporin. Review of surveillance data raised concerns of poor definition specificity for CP-CRE creating burden for laboratories and public health investigators.

Methods. We analyzed all CRE isolates reported in Oregon December 2010 – October 2013. We reviewed surveillance data from other states and published literature, focusing on CRE minimal inhibitory concentration breakpoints.

Results. Of our 125 unique isolates, 75 (60%) were *Enterobacter cloacae*, 13 (10%) *Enterobacter aerogenes*, 11 (9%) *Escherichia coli*, 11 (9%) *Klebsiella pneumoniae*, and 14 (11%) were other species. Non-susceptibility only to ertapenem was demonstrated by 66 (53%), of which 47 (72%) were *E. cloacae.* Of the 34 isolates non-susceptible to multiple carbapenems, 18 (53%) were *E. cloacae,* 5 (15%) *E. aerogenes,* 4 (12%) *E. coli,* and 6 (18%) *K. pneumoniae*. Ninety-nine (81%) isolates were resistant to all 3rd generation cephalosporins tested. Three were CP-CRE; all were *K. pneumoniae* producing *K. pneumoniae* carbapenemases.

Review of literature and other states' data confirmed carbapenemases were present in *E. cloacae.* Excluding ertapenem from the definition for laboratories using the updated Clinical Laboratory Standard Institute (CLSI) breakpoints did not greatly reduce sensitivity for the most common carbapenemases. Finally, retaining the cephalosporin-resistance requirement enhanced specificity. The new definition decreased the number of cases to investigate by 57%, without missing any CP-CRE.

Conclusion. We modified our case definition to increase CP-CRE specificity, without losing sensitivity, thus decreasing investigation burden. For laboratories using current CLSI breakpoints, the new definition includes all Enterobacteriaceae, removes ertapenem, and requires resistance to all 3rd generation cephalosporins tested.

Disclosures. **All authors:** No reported disclosures.

1727. Prevalence, Genetic Drift of Haemagglutinin, and Antiviral Resistance of *Influenza B Viruses* Circulating in Shanghai During January 2009 – May 2014

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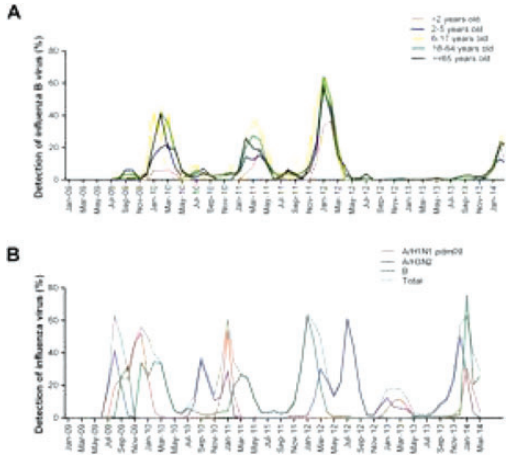
Background. Influenza type B viruses cause epidemics and are responsible for substantial morbidity and mortality in mainland China. A need for quadrivalent vaccines, antiviral resistance and continued antigenic drift are the major concerns regarding prophylaxis and treatment of influenza B. This retrospective study revealed the circulating situation, antiviral drug resistance and the genetic evolution of the hemagglutinin (HA) epitopes of influenza B viruses in Shanghai over a 6-year period.

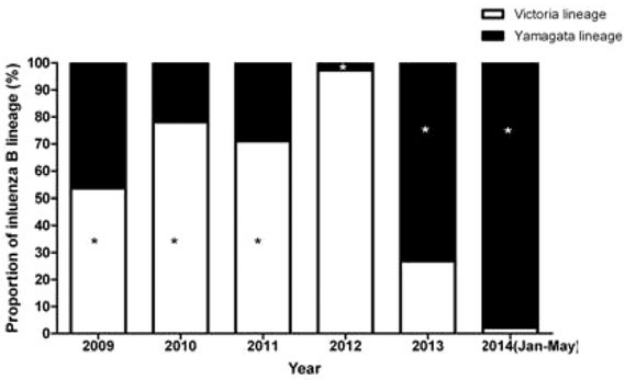
Methods. Records and information from Influenza Surveillance Net were used to estimate the influenza B incidence rate and the vaccine mach ratio. Sequences of 56 influenza B isolates were analyzed to identify HA antigen drift and NA antiviral mutations.



A. The incidence rate of five age group populations of influenza B viruses in Shanghai. B. The incidence rate of influenza viruses in Shanghai.

Results. Four epidemic peaks occur in the studied period and all peaks were correlation with influenza B viruses. The influenza B infection rate in 6-17 years old group is higher than in other studied population. The vaccine match ratio is 83.3% in the six studied years. The 56 influenza B strains, including 27 Victoria and 29 Yamagata, were sequenced to characterize the genotypic antiviral resistance and genetic drift in the HA epitopes. All, except one, were genotypically sensitive to oseltamivir. The HA sequence analysis revealed that the B viruses underwent constant mutations in the HA antigenic sites over the six seasons compared with the corresponding vaccine strains, and amino acid changes of Yamagata lineage in 2013-2014 season play an important role in B virus circulation in the subsequent seasons. Phylogenic analyses indicated

that the B strains circulating in Shanghai fell into two branches and each branch has two clades.



Distribution of influenza B lineages in Shanghai, January 2009 - May 2014.

Conclusion. Quadrivalent vaccine inoculated in 6-17 years old group may improve the effectiveness of vaccine in Shanghai population. The continuous monitoring of genetic drift and antiviral resistance of influenza viruses is important for the management of influenza and for updating the vaccine composition.

Disclosures. **All authors:** No reported disclosures.

1729. Preventing Coccidioidomycosis (Valley Fever) at Highly Endemic Prisons in California: Estimating the Effect of a Screening Skin Test to Identify Immune Inmates

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Background. Valley Fever (VF) is a respiratory disease caused by inhalation of *Coccidioides* spp. spores; prior infection confers lifelong immunity. During 2011, VF incidence at two highly endemic prisons (HEP) was >100 times higher than surrounding areas. Screening inmates with a new delayed-type hypersensitivity skin test (Spherusol®) that identifies persons with prior *Coccidioides* infection could be used to populate HEP with immune inmates. Our objective was to estimate the change in VF incidence following implementation of a skin test screening program.

Methods. We used Microsoft Excel to create a dynamic model of a hypothetical screening program where all California inmates are tested. Skin test-negative (non-immune) inmates are excluded from HEP; prisons are repopulated with skin test-positive inmates. Data from prison clinics on laboratory-confirmed infections were used to calculate predicted incidence rates, using 2011 mid-year population at HEP. We used published data for assumptions of prevalence of skin test positivity in different populations, and for skin test sensitivity and specificity. A sensitivity analysis varied prevalence of prior infection and test sensitivity and specificity.

Results. Without a skin test screening program, we expect an annual incidence of 5.3% at HEP. According to the model, 87% of inmates will test negative and will be excluded from HEP when prevalence of prior infection is 9% among California inmates. Following re-population of HEP with skin test-positive inmates, the expected incidence will be 1.8% (61% decline, 268 cases prevented); inmates with false-positive Spherusol® tests will comprise 99% of subsequent infections. Sensitivity analysis demonstrated an expected incidence of 0.09-4.7% (12-98% decline; 54-432 cases prevented), largely influenced by prior infection prevalence and test specificity.

Conclusion. Implementation of a hypothetical skin test-based screening program could sharply reduce incidence of VF at HEP. If implemented, additional studies to refine assumptions and evaluate the effectiveness of this program should be considered.

Disclosures. **All authors:** No reported disclosures.

1730. Improperly Used Insulin Pen Lookback Investigation in a Veterans Affairs (VA) Medical Center

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Background. Improper use of insulin pens has been reported in multiple hospitals. In 2009, US FDA issued a safety alert indicating that insulin pens are for single patient use only. We performed a lookback investigation to identify possible bloodborne pathogen transmission at one VA facility where insulin pens were not dedicated to individual patients, although staff reported changing needles between patients.

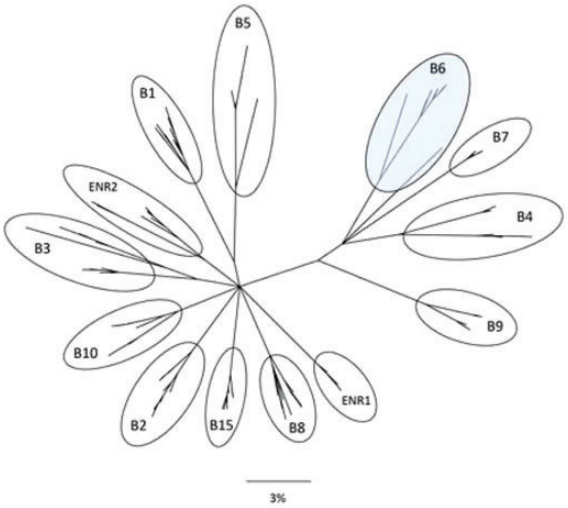

Figure 1. Phylogenetic tree of genotype 1a HCV E1/E2 sequences. Single genome sequences (average of 20 sequences per sample, range 10 – 24 sequences) were aligned with MUSCLE, and a neighbor-joining tree was created using Geneious, employing a Jukes-Cantor distance model with 1000 bootstrap replications. Scale bar represents percent nucleotide variability. Newly-found-to-be-infected patient sequences (B6) are shaded. ENR = epidemiologically non-related patient.

Methods. Inpatients receiving insulin from Lantus® SoloSTAR® pens from October 19, 2010–November 1, 2012 were identified by the facility and VA Corporate Data Warehouse using bar coded medication administration data. Identified patients were offered hepatitis B (HBV), C (HCV) and human immunodeficiency virus (HIV) testing. Previous viral testing history was assessed by chart review. Available patients' HCV viral strains were sequenced and genetically fingerprinted to assess linkage.

Results. The exposure cohort included 718 patients, of whom 197 were deceased. See the table for testing results. No newly identified HIV positive patients were found. 17 were newly identified as serologically HBV positive, but did not have HBV DNA viremia. Two of 5 newly identified HCV infected were compared to 17 known HCV positive patients and 4 epidemiologically non-related patients (Figure 1/2). No linkage was identified.

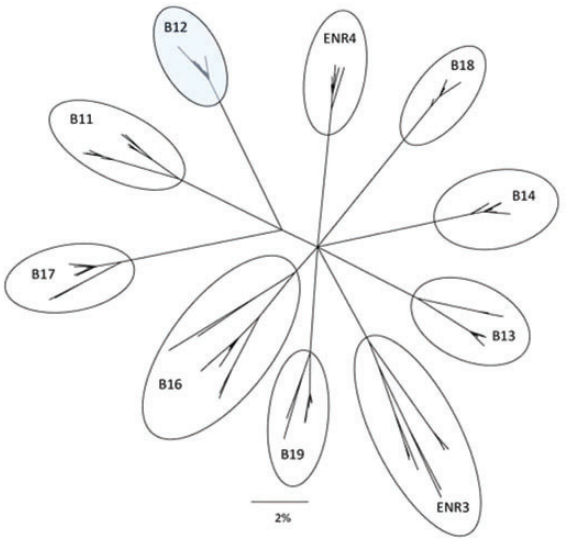

Figure 2. Phylogenetic tree of genotype 1b HCV E1/E2 sequences. Single genome sequences (average of 21 sequences per sample, range 15 – 24 sequences) were aligned with MUSCLE, and a neighbor-joining tree was created using Geneious, employing a Jukes-Cantor distance model with 1000 bootstrap replications. Scale bar represents percent nucleotide variability. Newly-found-to-be-infected patient sequences (B12) are shaded. ENR = epidemiologically non-related patient.

HIV, HBV, HCV Test Results for Exposure Cohort - For each virus, patients may appear in more than one category.

HIV Results	
Newly identified positive	0
Previously positive	5
Testing inadequate or incomplete	0
Viral testing results unknown	216
Negative	497
HCV Results	
Newly identified positive	5
Previously positive	48
Testing inadequate or incomplete	8
Viral testing results unknown	194
Negative	469
HBV Results	
Newly serologically identified positive	17
Previously positive	57
Testing inadequate or incomplete	75
Viral testing results unknown	180
Negative	421

Conclusion. No evidence of HIV, HBV or HCV transmission was identified with reuse of insulin pens at this VA facility. Many newly identified positive patients had no prior viral testing making it impossible to determine if transmission occurred as a result of this breach in infection control practice. Improved HBV, HCV and HIV testing would help in future similar investigations.

Disclosures. **All authors:** No reported disclosures.

1731. Medicalizing Prevention: Divergent Views of HIV+ and HIV- Women on PrEP and TasP

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Background. Pre-Exposure Prophylaxis (PrEP) and Treatment as Prevention (TasP) are biomedical HIV prevention strategies that could have a significant impact on reducing HIV infection rates among U.S. women. This qualitative study examined HIV+ and HIV- women's views of these prevention modalities.

Methods. Five focus groups, stratified by HIV status were conducted in 2014 with 26 women (11 HIV- and 15 HIV+) of the Washington Metropolitan Women's Interagency HIV Study. Topics discussed included PrEP /TasP knowledge; beliefs and acceptance; barriers and facilitators to use.

Results. Participants had no previous knowledge of PrEP and TasP. However, their opinions diverged based on their HIV status. HIV- women expressed a lot of enthusiasm about PrEP. They wanted to use PrEP and recommend it to others despite concerns about side effects and stigma of using HIV medicines. PrEP would provide a preventive method they could control, and the combination of PrEP and condom use was thought to provide the best preventive approach.

In contrast, HIV+ women were less supportive of PrEP based on their knowledge and experience of the side-effects associated with HIV medications, as well as the invasive nature of a comprehensive PrEP package—routine HIV testing, continued condom use, comprehensive HIV prevention and medication adherence counseling. HIV+ women preferred the use of condoms over PrEP given its efficacy, accessibility without prescription, and for preventing other STIs and pregnancy. Both groups agreed that PrEP should be an available intervention for women.

Opinions differed on TasP based on HIV status as well. HIV- women liked the concept of TasP because of the dual benefit for both the HIV+ individual and uninfected partner. In opposition, HIV+ women were concerned with starting medication sooner, potential long-term side effects, and risk of drug resistance with fewer subsequent treatment options.

Conclusion. This study identifies potential challenges and opportunities for advancing PrEP/TasP uptake among U.S. women. The results demonstrate the urgent need for appropriate educational and public health campaigns to maximize the potential benefits of these interventions.

Disclosures. **All authors:** No reported disclosures.

1732. 13-years of Tuberculosis in the St. Bernard Parish, Louisiana

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Background. At the Region 1 TB clinic in New Orleans, LA extensive tuberculosis (TB) contact investigations have occurred over the last 13 years involving the same cluster of individuals. The objectives of this study were to investigate these cases and link them epidemiologically.

Methods. In this IRB-approved study, the subject population consisted of the family members and their contacts between the years 2000 and 2013. Information on demographics, diagnosis, risk factors, and treatment was collected via reviewing medical records and interviewing the involved personnel. A family tree and maps were created based on the zip-codes of their residence.

Results. 69 cases were reviewed (47 adults, 22 children) as of April 2014. All the 37 (17 males, 20 females) individuals were otherwise healthy (HIV negative when tested), of white race, and US. born with no travel history outside of the USA. The family tree and mapping data outlined four families with involvement of four generations, mainly residing in the St. Bernard Parish. Smoking history was reported in 19 and drug use was reported in 3 individuals.

Out of 69 cases, 30 were reported as latent tuberculosis infection (LTBI), 11 as having no infection, and 4 remained unknown. 50% of LTBI patients completed age-appropriate treatment. 24 were active cases of TB, including 6 cases of children. 23 out of 24 individuals completed appropriate treatment for active TB infection with directly observed therapy (DOT). One individual migrated to another region towards the end of the therapy. There were 12 subjects who had a repeat treatment either as a latent TB or an active case. Of those repeat cases, 5 patients had active TB twice and they were treated with appropriate TB therapy with DOT each time. 17 out of 18 (1 diagnosed at death) TB strains isolated from adult active pulmonary cases were all pan-sensitive. The genotypes of the collected strains were identical from the years 2000 (3), 2006 (5), and 2008 (1).

Conclusion. We are reporting the largest outbreak of tuberculosis, spanning over 13 years, in the St. Bernard Parish in the state of Louisiana. The next part of the project would involve searching for etiologies for persistence of TB in this cluster of individuals by tracing their migration, work and social activities more closely.

Disclosures. **All authors:** No reported disclosures.

1733. Incidence of Community-Acquired Pneumonia in the Veterans Health Administration, 2011

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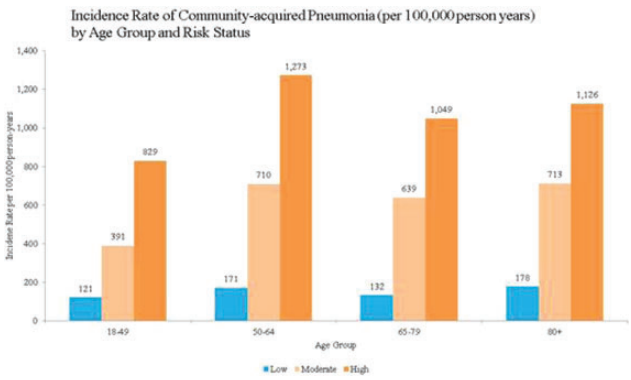
Background. Community-acquired pneumonia (CAP) is a significant cause of morbidity and mortality.

Methods. Incidence rates (IR) of adult CAP in the national Veterans Health Administration (VHA) population in 2011 by age and risk status were determined using data from the VHA corporate data warehouse. Cases were defined as a pneumonia diagnosis (ICD9 480-487) with a procedural claim for chest x-ray. Community-acquired cases were those without prior (90 days) mechanical ventilation, long-term care, hospitalization, pneumoconiosis, or wound care. Low, moderate, and high risk were defined as immunocompetent without chronic medical conditions, immunocompetent with ≥1 chronic medical condition, and immunocompromised, respectively.

Results. Most Veterans aged 50-64 (53%) and aged ≥65 (66%) had ≥1 chronic medical or immunocompromising condition. In 2011, 34,101 Veterans developed CAP (35,380 episodes) over 7,739,757 VHA person-years. Median age of CAP patients was 65 years (95% male). Incidence rates were higher for those aged ≥50 *vs* 18-49. Compared to those at low risk, moderate- and high-risk patients were >3 and >6 times more likely to develop CAP, respectively (Figure). Older CAP patients and those at moderate or high risk were more likely to be hospitalized and die (Table). Percentage of CAP patients who were hospitalized was 45%, ranging from 12% (aged 18-49 at low risk) to 57% (aged ≥65 at high risk). One-year all-cause mortality rates ranged from 1% (aged 18-49 at low risk) to 36% (aged ≥65 at high risk).



	18-49		50-64		≥65	
Risk Status	% hospitalized	% died	% hospitalized	% died	% hospitalized	% died
Low	12	1	26	3	42	10
Moderate	20	4	42	8	55	26
High	34	17	50	21	57	36

Conclusion. In 2011, >35,000 CAP cases occurred in the VHA. More than half of Veterans aged ≥50 and nearly two-thirds of Veterans aged ≥65 had ≥1 chronic medical or immunocompromising condition, and these conditions were associated with several fold higher risk of CAP. Surprisingly, Veterans aged 50-64 had risk status-specific CAP incidence rates similar to those aged ≥65. A focus on CAP prevention and the management of modifiable risk factors among those with comorbid or immunocompromising conditions is important, as patients at moderate or high risk for developing CAP were more likely to be hospitalized and die.

Disclosures. **J. Mclaughlin**, Pfizer Inc.: Employee, Salary **S. Kagan**, Pfizer Inc.: Employee, Salary

1734. Cyclosporiasis 2013: Collaborative Outbreak Investigations

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Background. *Cyclospora cayetanensis* is a parasite that can cause a prolonged or remitting/relapsing diarrheal illness. U.S. outbreaks of cyclosporiasis, since the mid-1990s, have been linked to various types of imported fresh produce. In late June 2013, public health officials in Iowa and Nebraska began receiving reports of laboratory-confirmed cases of cyclosporiasis not associated with international travel. A total of 631 such cases, with onset dates during June–August, were reported by 25 states; 497 (79%) of the cases were from Iowa, Nebraska, and Texas.

Methods. FDA, State and Local officials reviewed distribution records for pertinent food items identified in epidemiologic investigations. An environmental investigation was conducted at the processing facility and farms.

Results: In Iowa and Nebraska, restaurant-associated cases were linked to a bagged salad mix (iceberg and romaine lettuces, carrots, and red cabbage) from Taylor Farms, Guanajuato, Mexico. The environmental investigation conducted by FDA, in conjunction with CDC, industry and Mexican officials, at the processing facility and selected growing areas in Guanajuato found no clear sources of *Cyclospora* or routes of contamination at the locations that were visited; environmental samples collected by FDA, CDC and Taylor Farms tested negative for *Cyclospora*. Epidemiologic and traceback investigations for several case clusters in Texas pointed to cilantro harvested from Puebla, Mexico, although a single processor or farm could not be identified.

Conclusion. In 2013, at least two unrelated outbreaks of cyclosporiasis occurred, which were linked to different types of produce from different regions of Mexico. As with previous outbreaks, the sources and routes of contamination of these food items were not identified. To reduce the risk for future outbreaks of cyclosporiasis, investigations to determine what leads to contamination of produce and novel molecular methods to detect and link cases to each other and to food vehicles/sources are needed. Mexico is working with the firms to identify any areas for concern and take necessary corrective actions.

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1735. Potential Public Health Impact of Having Included *N. meningitidis* Serogroup B in the 2005 Recommendation for Adolescent Meningococcal Serogroup A, C, Y, and W-135 Vaccination

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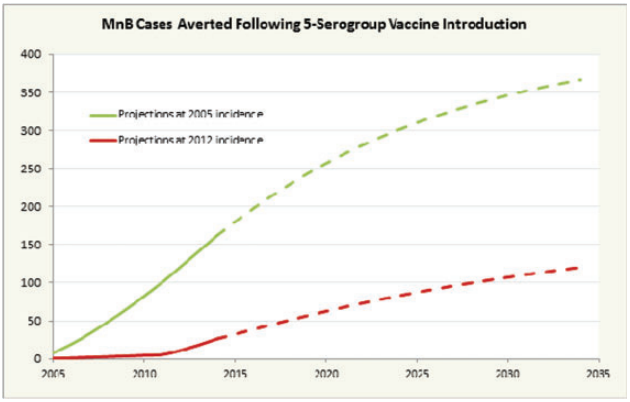
Background. Routine conjugate vaccination against IMD caused by *N meningitidis* serogroups A, C, W-135 and Y (MenACWY) began in the United States in 2005, with a single dose of MnACWY vaccine given at age 11 years, and later augmented to include a booster dose at age 16 years. At that time, there was no licensed, broadly protective vaccine against serogroup B (MenB), which represented half of the IMD cases reported in children aged 5-17 in the US. We estimated the potential historical public health impact, measured in cases of invasive meningococcal disease (IMD) avoided, if an adolescent MenB vaccine had been available and included in the 2005 recommendation.

Methods. A transmission dynamic model was developed to simulate prevalence of meningococcal carriage and incidence of IMD within the US population over the past 10 years following initiation of the five serogroup adolescent vaccination program. Carriage prevalence and vaccine efficacy against IMD and carriage were obtained from the published literature and expert opinion. Sensitivity analyses were performed with recent IMD incidence estimates from the national surveillance system in 2005 and 2012. Cases and deaths averted were calculated.

Results. The model estimated that 784 serogroup B IMD cases and 73 deaths would have been prevented through 2014, if a MnB vaccine had been similarly implemented in 2005 (Figure, top line). At 2012 epidemiology, the cases and deaths avoided would have been 77 and 7, respectively (Figure, bottom line).



Conclusion. IMD incidence, including that of serogroup B, has declined in the US over the past 15 years. IMD is severe and unpredictable, and it is unknown whether incidence will remain low. While the impact of a MnB vaccine at current epidemiology will be limited, had a MenB vaccine been available and recommended alongside MenACWY in the US, substantial disease avoidance could have been realized over the past 10 years.

Disclosures. **S. J. Snedecor**, Pharmerit: Employee, Consulting fee **R. Farkouh**, Pfizer: Employee, Salary **L. York**, Pfizer: Employee, Salary **M. Xue**, Pharmerit: Employee, Consulting fee **D. Strutton**, Pfizer: Employee, Salary

1736. Arsenic enhances immune dysfunction and susceptibility to viral infection during pregnancy

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Background. We aimed to determine whether arsenic exposure during pregnancy is associated with immune dysfunction and susceptibility to viral infection during pregnancy and postpartum in a low resource setting where host exposures to immunotoxic and infectious agents coexist.

Methods. Since 2007, the JiVitA Research Project has prospectively followed the pregnancies of ~60,000 women from Northern Bangladesh. In a sub-study of 1,100 pregnancies, IgG seroconversion to hepatitis E virus (HEV) was assessed between the 3rd trimester (TM) and 3 months postpartum. 40 women seroconverted to HEV (cases) and were matched with 40 non-seroconverting women (controls) by age-, parity-, and sector of residence. For all 80 women, we assessed urinary concentrations of inorganic arsenic plus methylated species (InAs) (μg/L) at first and third TM and plasma concentrations of pro- and anti-inflammatory cytokines (pg/ml) at first TM, third TM and 3 months postpartum.

Results. Among HEV seroconverters, urinary InAs was high throughout pregnancy (first TM median = 66 μg/L; interquartile range (IQR) = 41-132 μg/L; third TM median = 65 μg/L; IQR = 26-106 μg/L; $p = 1.0$), whereas among non-seroconverters urinary InAs declined significantly during pregnancy (first TM median = 62 μg/L; IQR = 37-82 μg/L; third TM median = 36 μg/L; IQR = 26-77 μg/L;

p = 0.002). Among HEV seroconverters, first TM urinary InAs was positively associated with IL-2 in the first TM (beta per IQR-unit change in InAs = 0.29; $p < 0.006$) and subsequent time points (third TM beta = 0.33, $p < 0.004$; 3 months postpartum beta = 0.17; $p < 0.03$). The average of first and third TM urinary InAs was also positively associated with IL-2 among HEV seroconverters at third TM (beta = 0.27; $p = 0.002$) and 3 months postpartum (beta = 0.16; $p = 0.005$). Exposure-response associations between InAs and IL-2 were null among non-seroconverters.

Conclusion. Since HEV seroconversion occurred between third TM and 3 months post-partum, differential arsenic exposure during pregnancy increased susceptibility to subsequent viral infection. Cytokine shifts among HEV seroconverters suggest immune responses biologically consistent with arsenic-induced immune dysfunction and viral infection. Further investigation of arsenic's role in enhancing susceptibility to infection during pregnancy is needed, particularly immunotoxic and infectious synergies.

Disclosures. **All authors:** No reported disclosures.

1737. Managing a Cluster Outbreak of Psittacosis

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Background. Psittacosis is category B bioterrorism disease. Here we present a cluster outbreak in Belgium and the steps taken by the authorities to prevent further spread.

Methods. In July 2013 a husband a wife, both 54 years old, presented at our department with a history of fever and dry cough since five days. Laboratory test showed strongly elevated inflammation parameters. Chest X-ray confirmed a diagnosis of pneumonia in both patients. The patients were specifically asked if they had had contact with birds. It appeared that they had bought a lovebird (*agapornis roseicollis*) 11 days earlier in the Netherlands. The bird became ill the day of the purchase, with a flu-like syndrome and died a few days later. In addition, the couple's daughter who accompanied them at the bird trader, reported similar symptoms, but was at the time on holiday in Brazil. Pharyngeal swabs from the couple were taken and sent to the Belgian reference laboratory for psittacosis in Ghent. The couple was treated with a 14 day course of doxycyclin and the daughter started with quinolone-therapy. They all had an uneventful recovery.

Since *Chlamydia psittaci* is a notifiable disease in Belgium and the local health care authorities (WIV) were informed. They contacted their Dutch counterparts (nVWA). The pet-shop was visited and a sales ban was issued. Seven samples of bird manure were taken and analysed by PCR for presence of *Chlamydia psittaci.*

Results. Cultures from the pharyngeal swabs of the patients on BGM cells became positive and additional genotype-specific real-time PCR indicated a genotype A. Four of the seven manure samples tested positive with PCR-analysis. Genotyping also showed genotype A.

The health authority issued the treatment of all approximately 60 birds in the pet shop with a 6 week course of doxycyclin. Manure cultures after treatment remained negative. No more cases of psittacosis were reported that could be linked to the pet shop.

Conclusion. Asking for bird contact is essential for identification of psittacosis in patients with pneumonia. Furthermore, rapidly informing health authorities is warranted so that appropriate action can be taken to prevent further spread

Disclosures. **All authors:** No reported disclosures.

1738. Estimated Annual Perinatal Hepatitis B Virus Infections, 2000-2009

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Background. Ninety-percent of perinatal hepatitis B virus (HBV) infection results in chronic HBV which usually is asymptomatic, but carries a 25% risk of premature death from progressive liver injury, cirrhosis, and liver cancer. In 1990, the Centers for Disease Control and Prevention (CDC) funded the Perinatal Hepatitis B Prevention Program (PHBPP) to accelerate elimination of perinatal HBV transmission in the United States. The annual rate of perinatal chronic HBV (CHBV) infections reported by PHBPP (0.8%-2.4%) was consistently lower than the annual rate estimated in CDC models employed from 2000-2009, suggesting not all cases in infants were identified. To better understand the factors with greatest impact on the estimated number of cases, we applied updated inputs to the current CDC model and performed sensitivity analyses for best and worst case scenarios.

Methods. Models employed estimates of annual births to hepatitis B surface antigen (HBsAg)-positive women, data from PHBPP, and National Immunization Surveys (NIS) hepatitis B (HepB) vaccine coverage. Prenatal maternal HBsAg screening rates, the efficacy of post-exposure prophylaxis (PEP) consisting of HepB vaccine and hepatitis B immune globulin, and perinatal HBV transmission rates were from published literature.

Results. The modeled estimate of the number of perinatal CHBV infections in 2009 was 952, equivalent to a baseline infection rate of 3.84%. Best and worst case sensitivity analysis yielded perinatal CHBV infection rates of 0.60% and 15.41%. One-way sensitivity analysis identified three major drivers: the proportion of infants receiving timely PEP, efficacy of PEP, and the perinatal HBV transmission rate. Three-way sensitivity analysis yielded perinatal CHBV infection rates of 0.70% and 13.64%.

Conclusion. Modeling suggests a substantial number of perinatal HBV infections that occurred in 2009 in the United States were not identified by PHBPP. Limitations of the data contributed to discrepancies between the estimated and reported number of cases, but remain useful programmatic goals of achieving elimination of perinatal CHBV infection.

Disclosures. **All authors:** No reported disclosures.

1739. Babesiosis in Eastern Pennsylvania: an emerging concern

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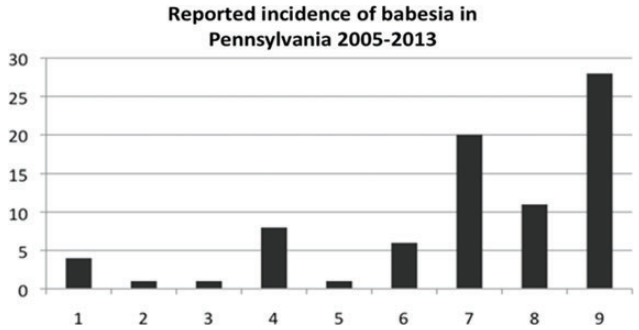
Background. Babesiosis is a human tick-borne parasitic infection affecting erythrocytes with potentially severe and complications and some fatalities. Endemic areas include areas in the northeastern and midwestern United States. The incidence and prevalence of babesiosis has steadily increased over the past decade, and appears to be spreading to areas previously regarded as low endemic regions, including eastern Pennsylvania, where it had not been previously described.

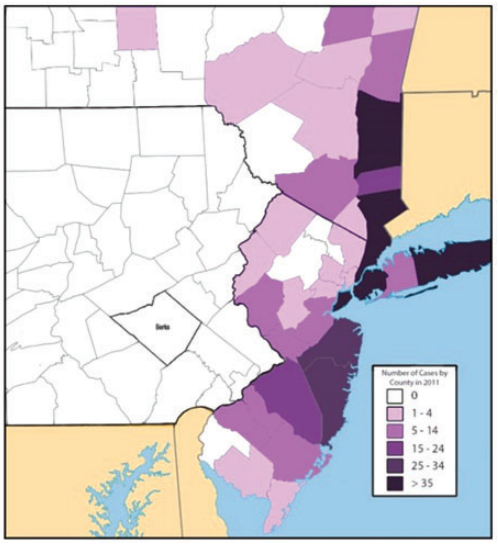


Reported incidence of babesia in Pennsylvania 2005–2013.

Methods. Shown in the table.

Results. We report five cases of babesiosis in eastern Pennsylania in patients with no history of travel outside the region, pointing to the emergence of babesiosis in this region (table and figures).

Figure 2. Number of cases of babesia in the counties of surrounding states that border easte reported by the CDC in 2011 (3)



Conclusion. As the symptoms of babesiosis are non-specific, a thorough history, including travel, woodland exposure and blood transfusions are important in

Summary of patient characteristics presenting with babesiosis

Case	Age (y), sex	LOS (d)	Presentation	Comorbidity	Parasitemia (%)	Nadir hemoglobin level (g/dL)	Nadir platelet count (10^9/L)	Nadir WCC (10^9/L)	Elevated AST/ALT	Exposure	Co-infection	Time of Diagnosis
1	55, male	6	Fever Malaise Rigors	Splenectomy OSA HTN	14%	8.7	86	9.2	Yes	Tick bite Travel to NJ Blood transfusion	E. coli bacteremia	July
2	69, male	7	Fever Malaise Rash	Lung carcinoma	6%	10.1	75	2.8	Yes	None	None	August
3	56, male	7	Fever Malaise Arthralgia	Afib HTN	1%	9.8	82	4	Yes	Travel to Canada	None	July
4	55, male	4	Fever Nausea Abdominal pain	OSA CHF NIDDM	2%	9.4	15	2.8	Yes	Tick bite Travel to NJ, NY, VA	Lyme	July
5	53, male	5	Fever Headache	None	<1%	12.7	162	6	No	Tick bite	Lyme	July

y = years; LOS = length of stay; d = days; OSA = obstructive sleep apnea; HTN = hypertension; Afib = atrial fibrillation; CHF = congestive heart failure; NIDDM = non insulin dependent diabetes mellitus; WCC = white cell count; AST = aspartate aminotransferase; ALT = alanine aminotransferase

identifying high-risk individuals. Increased physician awareness regarding the increasing geographical spread of babesia should further assist in the identification and appropriate treatment of affected individuals. More comprehensive disease reporting and data may enable public health authorities to better determine trends and evaluate geographic patterns as endemic areas evolve.

Disclosures. **All authors:** No reported disclosures.

1740. Assessment of Antimicrobial Efficacy on New Fiber Embedded with Silver

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Background. Silver has been used for years in the medical field due to its antibacterial efficacy. Silver has been applied topically to fabrics as an antimicrobial agent but the process lacks efficacy because the silver percent is too low. A new yarn which can be used to weave or knit fabrics uses novel technology to extrude the silver into the yarn fibers. This process allows the silver to physically disperse and embed, throughout the yarn and subsequently the fabric. Fabrics made with this technology do not "wash off" and is made in different strengths depending on the degree of antimicrobial activity required. The object of this study was to evaluate the antimicrobial efficacy of the innovative fabric. Medium strength antimicrobial activity fabrics were used in this study.

Methods. Swatches of the 1-inch square material were placed into sterile petri dishes, inoculated with 0.1 mL of the bacteria or surrogate virus (bacteriophage MS-2). Spores of the mold *Trichophyton mentagrophytes*were also tested. At the contact time points of 2 and 4 hours, samples were taken and processed according to the appropriate assay for bacteria, virus or mold being tested.

Results. Results are in the following table.

Organism	Percent Reduction	
	2 Hour Contact Time	4 Hour Contact Time
Methicillin-Resistant Staphylococcus aureus (MRSA)	99.7	99.997
Carbapenem-Resistant Enterobacteriaceae (CRE)	99.95	99.999
Vancomycin-Resistant Enterococcus (VRE)	99.90	99.9999
Escherichia coli	99.98	99.998
Staphylococcus aureus	99.96	99.98
Salmonella choleraesuis	99.99	99.99
MS-2	3.9	99.5
Propionibacterium acnes	99.999	>99.999
Trichophyton mentagrophytes	44.9	>99.998

Conclusion. This unique fabric has demonstrated antimicrobial properties against a wide range of bacteria, mold and a surrogate virus within 2 to 4 hours. The fiber or yarn can be knit or woven to make most any fabric used in home, industrial or hospital environments where a reduction of bacteria, mold and virus on garments or linens would be advantageous.

Disclosures. **C. Gerba**, Consumer Specialty Products Association: Consultant, Consulting fee

1741. Emergence of Shigellosis in Males ≥13 Years — Philadelphia, 2008–2013

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Background. In recent years in Philadelphia, shigellosis has shifted from a disease primarily affecting children and women of childbearing age to one that more commonly affects males ≥13 years of age. Studies of similar shifts in other U.S. cities have concluded that increased incidence among adult males may result from outbreaks among men who have sex with men (MSM). Antibiotic resistance among *Shigella* species is an additional emerging health concern.

Methods. Surveillance data from all nontravel-related culture-confirmed cases of shigellosis among Philadelphia residents aged 13 years or older from 2008–2013 were analyzed. Susceptibility data for antibiotics including ampicillin, trimethoprim/sulfamethoxazole (TMP-SMZ), and ciprofloxacin was also collected. Trends in incidence over time and across gender, and patterns of antimicrobial resistance were assessed using chi-square analysis.

Results. From 2008–2013, 317 shigellosis cases were identified. The proportion of cases among males increased from 28.6% in 2008 to 83.8% in 2013 ($p < 0.0001$). The proportion of cases exhibiting resistance to one or more antibiotics increased from 44.4% to 91.2% ($p < 0.0001$). For TMP-SMZ, resistance increased from 44.4% to 65.6% ($p = 0.0046$). Among males, 79.0% of *Shigella* specimens tested for antibiotic susceptibility exhibited intermediate or full resistance to at least one antibiotic, compared to 35.8% of specimens from females ($p < 0.0001$). Among males, 61.1% of

specimens tested for TMP-SMZ susceptibility displayed intermediate or full resistance, compared to 33.9% among females (p =0.0006). A non-significant increase in ampicillin resistance was observed among males (77.4%) relative to females (63.6%). Of the 75 cases reported from males during 2011–2013, 15 (20%) self-identified as MSM.

Conclusion. The proportion of males aged ≥13 years reported with shigellosis increased during 2008–2013 in Philadelphia. This gender disparity could indicate increasing rates of infection among MSM. Cases among males displayed greater antibiotic resistance than those among females. These findings suggest a need to further characterize risk factors associated with these trends and to develop appropriate interventions among males ≥13 years.

Disclosures. **All authors:** No reported disclosures.

1742. Impact of Material and Social Seprivation on Serogroup B Invasive Meningococcal Disease (IMD-B) Incidence and Outcomes in the Province of Quebec, Canada

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Background. The objective of this work was to assess the social pattern of serogroup B invasive meningococcal disease (IMD-B) incidence and outcomes in the province of Quebec, Canada.

Methods. Medical records of laboratory confirmed cases of IMD-B between 1997 and 2010 in the province of Quebec were reviewed through a standardized questionnaire. Social and material deprivation index within the Province of Quebec, by quintile, was assigned to each patient according to postal code of residence. The incidence of IMD-B according to social and material deprivation index was calculated, and the effect of deprivation on the risks of acute complication, major sequelae in survivors and fatal outcome were assessed using logistic regression.

Results. Over the 14 year period, 571 cases were identified. Deprivation index were assigned for 527 cases. Incidence rate, by quintile of material deprivation, ranged from 0.31 to 0.54/100,000 person-years, with the lowest incidence found for the most affluent quintile and the highest for the most deprived quintile (P < 0.0001). Among infants <1 year-old and children 1-14 year-old, incidence rates were respectively 3.5 and 2.5 times higher in the most materially deprived quintile than in the most affluent quintile (P = 0.0002 and P = 0.002 respectively).

The risk of major sequelae rose with level of material deprivation index and the association was statistically significant (OR = 1.20, 95%CI: 1.01 -1.43, P = 0.04). It rose with level of social deprivation index but was not statistically significant (OR = 1.10, 95%CI: 0.93-1.30, P = 0.28). No association with material and social deprivation was found for acute complication and fatal outcome.

Conclusion. In the Province of Quebec, material deprivation is associated with higher incidence rates of IMD-B and higher risk of major sequelae, but not with risk of acute complication or risk of death. Social deprivation does not seem to play a significant role.

Disclosures. **P. De Wals**, GSK: Research Contractor, Research grant; Novartis: Research Contractor, Research grant; Sanofi Pasteur: Research Contractor, Research grant; Pfizer: Research Contractor, Research grant; Health Canada: Research Contractor and Scientific Advisor, Research grant; Quebec Ministry of Health and Social Services: Research Contractor and Scientific Advisor, Research grant

1743. Racial Disparities Among Tuberculosis Deaths in the United States, 1999-2009

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Background. Despite overall declines in tuberculosis (TB) incidence in the U.S., there remain racial disparities in TB incidence rates, with a reported 8-fold increase in the TB rate among non-Hispanic blacks compared with non-Hispanic whites. Our objective was to determine whether racial disparities also exist in TB mortality rates in the U.S..

Methods. The Compressed Mortality File maintained by the National Center for Health Statistics (wonder.cdc.gov) is a county-level national mortality database, and includes race categories (White, Black or African American, Asian or Pacific islander, American Indian or Alaska Native). Cause of death is included an ICD-10 code onwards from 1999. We selected all records with TB as the primary cause of death, and grouped ICD-10 codes according to disease site: pulmonary, central nervous system (CNS), extra-pulmonary (non-CNS), and miliary. We calculated death rates by race per 100,000 population, and performed time-trend analyses to examine TB mortality rates for each racial category.

Results. Over a 10-year period (1999-2009), TB was the primary cause of death among 7590 individuals in the U.S.: 5919 (78%) pulmonary TB, 846 (11%) extra-pulmonary (non-CNS) TB, 205 (3%) CNS TB, and 620 (8%) miliary TB. The death rate overall (per 100,000) was 0.62 for Asians, 0.46 for blacks, and 0.17 for whites, corresponding to a 3.6-fold difference between Asians and whites, and a 2.7 fold difference between blacks and whites. We did not observe significant time trends in these proportional differences during the observation period (p > 0.05). The excess TB mortality burden among non-white individuals can be partly explained by the site of disease, as overall 8.2% of TB deaths among whites were due to CNS or miliary disease, compared with 14.7% of deaths among blacks and 13.9% of deaths among Asians (p < 0.01).

Conclusion. We observed significant racial disparities among TB deaths in the U. S. over a 10-year period, with higher TB mortality rates among Asians and blacks, as compared with whites, that remained stable over this time period. Future analyses that link TB databases with the National Death Index will identify patient-level factors responsible for racial disparities in TB treatment outcomes.

Disclosures. **All authors:** No reported disclosures.

1744. *Staphylococcus aureus* CC398 and pig-specific fecal *Bacteroidales* qPCR concentrations decline with increasing time away from work among industrial hog operation workers

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Background. In the US, knowledge of industrial hog operations (IHOs) as a reservoir of occupational and community exposure to *Staphylococcus aureus*, including drug-resistant and livestock-associated strains, is emerging. But the dynamics and sources of *S. aureus* exposure remain poorly characterized in part because of a lack of quantitative measures of exposure specificity and limited access to IHOs to sample during work. The present study, conducted among IHO workers at non-work locations, aimed to determine the utility of quantitative polymerase chain reaction (qPCR) measures of microbes with livestock and/or swine specificity in nasal swabs as markers of recent IHO work exposure to *S. aureus*. We also examined associations of qPCR estimates with time since last work shift stratified by the antibiogram and livestock-association of culture-based *S. aureus* isolates.

Methods. 22 IHO workers collected 316 nasal swabs before and after an IHO work shift over 7 days and again 14 days after enrollment and recorded time since last IHO shift. Swabs were cultured for *S. aureus* presence and assessed for multidrug-resistance (MDR = resistant >2 antimicrobial drug classes), tetracycline-resistance, clonal complex (CC), and absence of the *scn* gene (marker of livestock association). *femA*, *mecA*, *S. aureus* CC398, and pig-specific fecal *Bacteroidales* (Pig-2-Bac) DNA per nasal swab were estimated by qPCR.

Results. *femA* and *mecA* qPCR estimates remained stable in nose swabs with increasing time since last IHO work shift, whereas *S. aureus* CC398 and Pig-2-Bac qPCR estimates declined significantly. Declines of *S. aureus* CC398 and Pig-2-Bac qPCR estimates were strongest among persistent carriers of *S. aureus* as well as during periods of tetracycline-resistant, MDR, CC398, and *scn*-negative *S. aureus* nasal carriage.

Conclusion. *S. aureus* CC398 and Pig-2-Bac qPCR declined with increasing time since last IHO shift, particularly among persistent *S. aureus* nasal carriers and during periods of drug-resistant, livestock-associated *S. aureus* nasal carriage. qPCR estimates of *S. aureus* CC398 and Pig-2-Bac appear to improve knowledge of IHO work as a source of drug-resistant, livestock-associated *S. aureus* exposure among IHO workers and warrant further consideration in studies of *S. aureus* transmission dynamics between IHO workers and household and community contacts.

Disclosures. **All authors:** No reported disclosures.

1745. Cardiac Abnormalities in Leptospirosis and Prognostic significance of Electro-Cardiographic manifestations – A cross-sectional study from South-India

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Background. Leptospirosis is a zoonotic spirochetal disease caused *Leptospira*. Spectrum of clinical illness varies from mild, anicteric form to severe disease characterized by jaundice, renal dysfunction and hemorrhagic diathesis. The disease is endemic in South India, with clusters occurring during Monsoon season (June – September) with mortality ranging from 3 % to 54%. Cardiac manifestations include myocarditis, pericarditis, arrhythmias, conduction blocks and cardiac failure. But extent of this involvement and its implications on clinical outcome are largely unknown.

Methods. A cross-sectional study done in patients admitted with Leptospirosis at Kottayam Medical College, Kerala, India from January 2008 to December 2008. Patient's satisfying modified Faine's criteria score above 25 and those with IgM serology positive for Leptospira were included and those with other concomitant infections and with

previously diagnosed heart disease with ECG abnormalities were excluded. Data for the association between ECG and prognosis was tested using chi-square test and t-test.

Results. 100 patients were studied during the period. Leptospirosis was most common among males (62%) and in middle-aged group (range: 40-59 years; mean age 46 years).Fever and myalgia were universally present (100%). Muscle tenderness was the commonest sign (88%), followed by conjunctival congestion(82%).The common laboratory abnormalities were albuminuria (100%), renal impairment (88%), and thrombocytopenia (72%). ECG abnormalities were noted in 40 % and atrial fibrillation(12%) was the commonest, followed by T wave inversion(10%), type 1 A-V block (8%), and sinus bradycardia (6%). 20% had clinical evidence of myocarditis and 5/20 were confirmed with echocardiography. 96% were treated with crystalline penicillin. 88% patients recovered whereas 12% died. Of those with abnormal ECG, 7.5% (3/40) died. ECG abnormalities were not related to myocarditis (p= 0.349) and mortality (p= 0.258) but predicted the development of ARDS (p= 0.041), renal failure requiring dialysis (p= 0.002), Multi-Organ Dysfunction Syndrome (p= 0.0001) and morbidity (hospital stay > 10 days) (p= 0.005).

Conclusion. Cardiac manifestation in the form of ECG changes predicts the onset of complications including MODS in patients with Leptospirosis.

Disclosures. **All authors:** No reported disclosures.

1746. Rapid Point-of-Care Testing for Nine Sexually Transmitted Diseases

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Background. Delays in the reporting of STD testing sometimes result in inappropriate patient care where a patient must be called back in for treatment. Some STDs may be missed because not all specimens are tested in a comprehensive manner. A multiplex PCR-based point-of-care test was developed using the FilmArray® system capable of detecting 9 STD pathogens from a single specimen in about an hour. This system is currently in development and is not FDA approved.

Methods. A Sexually Transmitted Disease (STD) Panel was designed for the FilmArray device to detect the following organisms: *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (GC), *Treponema pallidum* (TP), *Trichomonas vaginalis* (TV), *Mycoplasma genitalium* (MG), *Ureaplasma urealyticum* (UU), *Haemophilus ducreyi*, and herpes simplex viruses (HSV1, HSV2). Several sets of PCR primers for the detection of each of these pathogens were multiplexed and validated with laboratory strains or plasmids. Pathogen detections were confirmed by melt curve analysis. The STD panel test results were compared to standard clinical tests including gram stain, CT/GC amplification (Roche Aptima), wet mount examination, HSV PCR, and serum syphilis IgG/TP-PA with RPR staging.

Results. 293 symptomatic subjects were consented and enrolled at the Salt Lake Valley STD clinic, providing 296 directly comparable specimens including urine (N = 183), vaginal (35), rectal (31), ulcer (28), cervical (16), and urethral swabs (3). STD pathogen detections by FilmArray included CT (47), GC (19), TP (10), TV (9), MG (26), UU (56), HSV1 (6), HSV2 (5), and none (178). The concordances between the FilmArray® STD panel and standard PCR testing were CT (kappa = 0.93), NG (0.95), HSV1 (1.00), and HSV-2 (1.00). FilmArray detections of the reportable STD pathogens were immediately referred for contact notification and treatment.

Conclusion. Point-of-care STD testing using the FilmArray was feasible and well accepted in our STD clinic. The test was useful, easy to run, and it provided timely results for the patients and providers. This rapid multiplex PCR detection method offers the prospect of improved clinical care for symptomatic patients presenting to an STD clinic.

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1747. Are Screening Blitzes Contributing to the Observed Trends in Syphilis Outbreaks in Urban Men Who Have Sex with Men?

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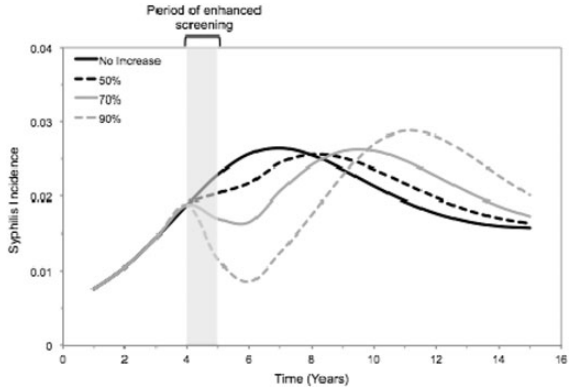
Background. Syphilis has reemerged as a significant public health problem in many urban centers in North America, with outbreaks focused in men who sex with men (MSM). In many jurisdictions, these recent outbreaks have displayed a stereotyped behavior, with initial increases in diagnosed cases followed by a period of plateau or decrease, and a subsequent resurgence in rates. We hypothesized that intensive screen and treat campaigns ('blitzes') may be contributing to observed syphilis trends.

Methods. We developed a dynamic compartmental mathematical model of syphilis transmission in a population of sexually active MSM. Parameters were derived from the biomedical literature and by model calibration. We assumed that base case annual screening coverage was 30%. We modeled a one-year transient increase in syphilis screening, with population coverage of screening during this blitz period ranging from 50-90%, followed by a return to base case screening levels. We evaluated the impact of screening blitzes on model-projected syphilis incidence and incidence of diagnosed early syphilis over a 10-year period following the transient screening increase.

Results. Blitzes were projected to result in transient stabilization (blitz coverage of 50-60%) or decreases (blitz coverage of ≥70%) in diagnosed cases and syphilis incidence. These declines were followed by rebounds in disease occurrence. Diagnoses of early syphilis cases were projected to exceed base case levels by the end of the evaluation period, regardless of blitz intensity. At the end of the evaluation period, syphilis incidence was projected to reach higher levels (4-28% relative to base case) than in the absence of intervention (figure). The overall impact on disease burden was minimal, with no significant change in cumulative syphilis incidence in the post-intervention period.



Conclusion. Sharp increases in syphilis screening as a result of screening blitzes may account for observed trends in syphilis diagnoses in MSM. Such interventions are not projected to reduce disease burden in the long-term, suggesting that efforts to achieve regular, sustained screening of at-risk individuals are likely to be more impactful for outbreak control.

Disclosures. **All authors:** No reported disclosures.

1748. The Persistence of Congenital Syphilis Epidemic in Chicago

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Background. Untreated syphilis during pregnancy can result in wide spectrum of fetal clinical manifestations including death. Peaks in Congenital Syphilis (CS) usually occur one year after peaks in Primary and Secondary (P&S) syphilis in women. Between 2007 and 2011, total number of female P&S syphilis cases in Chicago increased by 195% (from 20 to 59 cases) in parallel with an increase in the total number of CS cases (from 12 cases in 2008 to 22 cases in 2012). At the same time, national rates of CS cases decreased by 27% to 7.8 cases/per 100,000 live births, while during the same period CS rates in Chicago increased by 103% (from 26.5 to 53.7 cases).

Methods. Retrospective analysis of all 2008-2012 surveillance data of CS cases reported to Chicago Department of Public Health (CDPH) was performed.

Results. Out of 73 CS reported cases, 70(96%) were presumptive cases and 3 (4%) were CS stillborns. Mothers who delivered newborns with CS were predominantly single (68%), young (median age 22) and African American (82%). Among the mothers who gave birth to infants with CS: 53% (39/73) were diagnosed with early syphilis (9 P&S syphilis and 30 early latent syphilis). Only one mother was HIV+.

Over 40% (30/73) of infants with CS were born to mothers who did not receive any prenatal care (PNC) and almost 60% (43/73) of the CS cases were among infants whose mothers received PNC and were attributed to inadequate testing and/or treatment. Twenty six cases were not tested or tested within 30 days prior to delivery. Among females who were tested >30 days to delivery, twelve females were not treated, four of them were treated less than 30 days prior to delivery, and eight females had inadequate treatment or seroconverted at the time of delivery.

Conclusion. The increase in the number of CS cases in Chicago is attributed to multiple factors that include the increase in the number of female P&S syphilis cases, lack of early access to prenatal care, and inadequate testing and treatment by clinical providers.

Disclosures. **All authors:** No reported disclosures.

1749. Predictors of serological response after treatment of syphilis in HIV negative persons

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Background. The therapeutic response is monitored serologically after syphilis treatment. However, some patients remain serologically active despite treatment. We tried to identify the clinical characteristics associated with remaining serofast.

Methods. We conducted a retrospective cohort study of patients treated for syphilis in Seoul National University Bundang Hospital. Factors related to the serological response after 1 year of treatment was analyzed. 4 folds decrease in nontreponemal antibody titer was regareded as serological cure and others as serofast.

Factors associated with remaining serofast, 1 year after treatment of the syphilis

	Serofast (n=107)	Serological cure (n=47)	OR(95% CI)
Age Group			
10-29	1(25.0%)	3(75.0%)	1
30-49	17(50.0%)	17(50.0%)	3.00(0.28-31.80)
50-69	50(71.4%)	20(28.6%)	7.50(0.74-76.46)
>= 70	39(84.8%)	7(15.2%)	16.71(1.51-184.60)
Sex			
Male	45(63.4%)	26(36.6%)	1
Female	62(74.7%)	21(25.3%)	1.71(0.85-3.41)
History of syphilis			
No	86(68.8%)	39(31.2%)	1
Yes	21(72.4%)	8(27.6%)	1.19(0.49-2.92)
Stage			
Primary	0(0%)	4(100%)	N/A
Secondary	1(12.5%)	7(87.5%)	1
Early latent	7(87.5%)	7(87.5%)	3.11(0.28-34.42)
Late latent	102(79.7%)	26(20.3%)	27.46(3.23-233.19)
Tertiary	0(0%)	1(100%)	N/A
Initial RPR titer			
1:1	40(81.6%)	9(18.4%)	26.67(2.85-249.76)
1:2	24(92.3%)	2(7.7%)	72.00(5.56-932.99)
1:4	18(94.7%)	1(5.3%)	108.00(5.81-2005.95)
1:8	13(76.5%)	2(23.5%)	19.50(1.78-213.95)
1:16	11(68.8%)	5(31.3%)	13.20(1.24-140.68)
1:32	1(14.3%)	6(85.7%)	1
>=1:64	0(0%)	11(100%)	N/A

Abbreviations: CI, confidence interval; OR, odds ratio; RPR, rapid plasma regain; N/A, not applicable

Results. A total of 154 HIV negative patients with primary, secondary, tertiary and latent syphilis were included in the final analysis. Among them, 107 patients remained serofast and the other 47 patients showed serological cure. Older patients and patients with later disease stage were more likely to remain serofast. Having initial nontreponemal antibody titer of 1:2 and 1:4 was also associated with the serofast.

Conclusion. The disease stage, age and initial nontreponemal antibody titer were important factors related to the serological response.

Disclosures. **All authors:** No reported disclosures.

1750. Prevalence of Non-Genital *Neisseria gonorrhea* (GC) and *Chlamydia trachomatis* (CT) among Men and Women Tested on the Basis of Sexual Exposure at an Urban Sexually Transmitted Diseases Clinic

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Background. Current guidelines recommend screening for rectal GC and CT and pharyngeal GC only in men having sex with men (MSM). We sought to determine the incidence of GC and CT based on anatomic exposure (oral, anal or genital) in all men and women.

Methods. In 2012-13 the Kansas City Health Department STD clinic screened all men and women for GC and CT according to anatomic site of sexual exposure. Pharyngeal and rectal swabs were collected utilizing the Aptima unisex swab specimen collection kit, and performed at the Missouri Department of Health and Senior Services. We report the result of pharyngeal and rectal GC and CT among MSM, bisexual men, men having sex with women (MSW), women having sex with men (WSM), women having sex with women (WSW), and bisexual women.

Results. 3832 men and women engaged in oral or anal sex. The rates of pharyngeal, rectal and urogenital GC and CT among this group are [results expressed as number positive/number exposed (percentage)] :

	GC			CT		
	Pharyngeal	Rectal	Urogenital	Pharyngeal	Rectal	Urogenital
MSW	61/1908 (3.2)		139/1900 (7.3)	12/1908 (0.6)		371/1900 (19.5)
MSM	47/480 (9.8)	53/315 (16.8)	26/480 (5.4)	10/480 (2.1)	63/315 (20.0)	28/480 (5.8)
Bisexual men	9/157 (5.7)	8/55 (14.6)	8/152 (5.3)	6/157 (3.8)	7/55 (12.7)	13/152 (8.2)
WSM	51/1128 (4.5)	3/100 (3.0)	70/1095 (6.4)	23/1128 (2.0)	11/100 (11.0)	139/1095 (12.7)
WSW	1/38 (2.6)		1/32 (3.1)	0/38 (0.0)		1/32 (3.1)
Bisexual women	2/121 (1.7)	1/21 (4.8)	6/114 (5.3)	4/121 (3.4)	4/21 (19.1)	10/114 (9.6)

Among all men, 62%, 80%, 64% and 91% with pharyngeal GC, rectal GC, pharyngeal CT, and rectal CT had negative results at their genital site (urethral or urine). Among MSW, 42% of those with pharyngeal GC tested negative at their urogenital site. Among all women, 35%, 25%, 37% and 33% with pharyngeal GC, rectal GC, pharyngeal CT, and rectal CT had negative results at their genital site (vaginal, cervical or urine).

Conclusion. Although rates of infection were higher in MSM, 3.2% of MSW and 4.5% of WSM had pharyngeal GC. 11.0% and 3.0% of WSM had rectal CT and GC, respectively. Many MSW and women would have been missed if oral and rectal testing had not been performed. We recommend that STD guidelines for screening at non-genital sites include exposed women and MSW.

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1751. High Prevalence of Rectal *Neisseria gonorrhoeae* and *Chlamydia trachomatis* Infection in Women Attending an Urban Sexual Health Clinic

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Background. Screening women for urogenital *Neisseria gonorrhoeae* (GC) and *Chlamydia trachomatis* (CT) infections is common in sexual health clinics (SHC). However, women may not be routinely screened for *rectal* GC/CT. This may lead to missed infections in women who report anal intercourse (AI).

Methods. This was a retrospective review of all women who underwent rectal GC/CT screening from August 2012 to June 2013 at an urban SHC in Columbus, Ohio. All women who reported AI in the last year had a rectal swab collected for GC/CT nucleic acid amplification testing (NAAT) (n = 331). All women were also screened for urogenital GC/CT by urine NAAT. Using log-binomial regression models, we computed unadjusted and adjusted associations for demographic and behavioral predictors of rectal GC/CT infection.

Results: Patients were 47% African-American, 39% White and 5% Hispanic. Median age was 29 years (interquartile range (IQR): 23-35 years) and median number of male sex partners in the last year was 2 (IQR: 1-3). The prevalence of rectal GC was 6%, rectal CT was 13% and either rectal GC or CT was 19%. The prevalence of urogenital GC was 7% and urogenital CT was 13%. Among women with rectal GC, 14% tested negative for urogenital GC. In addition, 13% of women with rectal CT tested negative for urogenital CT. In unadjusted analyses, prevalence of rectal GC was associated with reporting sex in the last year with an injection drug user (prevalence ratio (PR): 6.99, 95% confidence interval (CI): 1.25-38.96), with a person who exchanges sex for drugs or money (PR: 6.81, 95% CI: 1.86-24.97), with an anonymous partner (PR: 3.08, 95% CI: 1.08-8.81), and while using drugs or alcohol (PR: 5.99, 95% CI: 1.34-26.69). For rectal CT, only age <26 years was associated with prevalent infection (PR: 4.94, 95% CI: 2.53-9.62). After multivariable adjustment, no variables remained associated with rectal GC, but a trend of increased prevalence was seen for younger women ($p = 0.06$) and those reporting sex while using drugs or alcohol ($p = 0.05$). Only age <26 years was predictive of rectal CT by multivariable analysis (PR: 6.03, 95% CI: 2.29-15.90).

Conclusion. Nearly 1 in 5 women in this study had rectal GC or CT infection. Urogenital screening alone would have missed 13-14% of rectal infections. Increased rectal GC/CT screening efforts in women reporting AI would detect infections that may currently be missed.

Disclosures. **All authors:** No reported disclosures.

1752. Incident Genitourinary and Extragenital Gonococcal and Chlamydial infections in a Racially Diverse Well Characterized Cohort of HIV-infected Persons with Free Access to Care and Counseling

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Background. Asymptomatic genitourinary (GU) and extragenital chlamydia (CT) and gonococcal (GC) co-infections are a common problem in HIV-infected persons. Studies suggest ethnic minorities are disproportionately affected. We examined incidence, trends and risk factors for GC/CT co-infections in a racially diverse cohort of HIV-infected persons with free access to healthcare and counseling, the US Military HIV Natural History Study (NHS)

Methods. Urine nucleic acid amplification testing (NAAT) was implemented in 2006; whereas willing NHS subjects have undergone extragenital NAATs beginning in 2012. Incident GC/CT was defined as infections acquired ≥ 6 months after HIV diagnosis. A multivariate Cox proportional hazards model was used to evaluate risk factors associated with incident GC/CT infections. Rates and hazard ratios (HR) are reported with 95% confidence intervals.

Results. Between 2006 and 2014, 2082 subjects [94% male, 40% White] contributed 237 cases of GU GC/CT. 108 cases of extragenital GU GC/CT (rectal-73, pharyngeal 35) were observed in 1955 men. The incidence of GU GC/CT per 100 PY of follow-up for the time periods 2006-2009, 2010-2013, were 2.0 and 2.7 respectively. The incidence of extra genital GC/CT was 2.8/100 PY in 2012 and 6/100 PY in 2013. Male gender {HR 2.63 [1.16-5.99]}, and younger age {per 10 year increase; HR 0.26 [0.20-0.33]} were associated with GU GC/CT infections; in turn ART use {HR 0.81 [0.78-0.83]} was associated with reduced risk. Extragenital infections were associated with younger age {ref per 10 year increase; HR 0.17 [0.11-0.25]}, ART use was associated with reduced risk {HR 0.83 [0.78-0.87]}. Race was not associated with either GU {Ref White: non White; HR 1.20 [0.88-1.65]} or extragenital GU GC/CT infections {Ref White: non White; HR 1.05 [0.67-1.65]}.

Conclusion. The burden of asymptomatic GC/CT infections in the NHS is substantial, underscoring the importance of screening programs for asymptomatic individuals. Younger men were disproportionately affected, emphasizing the need for tailored prevention in positive programs targeting these at-risk groups. Ethnicity was not associated with incident GC/CT infections. Free access to healthcare and counseling may help mitigate the observed ethnic disparities in GC/CT infections.

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1753. Adherence to New Treatment Guidelines for Uncomplicated Anogenital and Pharyngeal *Neisseria Gonorrhea* Cases in Adults in Alberta, Canada

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Background. The emergence of reduced susceptibility of *N. gonorrhoeae* (NG) to cephalosporins and azithromycin has required the global revision of treatment guidelines. In Alberta, Canada in December 2011, guidelines for preferred treatment were changed from monotherapy with cefixime 400 mg orally or ceftriaxone 125 mg IM to dual therapy with cephalosporins (cefixime 800 mg orally or ceftriaxone 250 mg IM) plus azithromycin 1g. We examined the adherence to new treatment guidelines introduced in 2012 in Alberta, Canada.

Methods. Treatment data for provincial NG cases diagnosed between 2010 and 2013 were reviewed. Treatment data was coded as adhering to preferred or alternate guidelines if the case received medication meeting guideline recommendations at that time. Three time periods were created: pre-guideline change, guideline change, and one year post-guideline change.

Results. A total of 6,685 NG cases were diagnosed; 4% (n = 267) of cases had no treatment data available. Forty percent (n = 2,653) of cases were treated prior to the guideline change, 31.8% (n = 2,038) during the first year of change, and 26.9% (n = 1,727) cases were treated one year post-change. Overall, 89.3% (n = 2,367) of pre-guideline change cases were treated with a recommended treatment regimen; this dropped to 57.6% (n = 1,174) during the first year of change, with a return to 85.4% (1,474) one year post-change. Cases treated by a provincial STI Clinic were more likely to be treated according to guidelines than cases treated by other healthcare providers throughout all time periods (P < 0.001). Adherence dropped for other healthcare providers from 86.4% pre-guideline change to 41.1% during the first year of guideline change returning to 78.8% one year post-guideline change. During the first year of guideline change, the most common scenarios in which guidelines were not met included the use of cefixime 400 mg orally alone (60.5%; n = 523) or cefixime 800 mg orally/ceftriaxone 250 mg IM monotherapy (20.1%, n = 174). In addition, 5.4% (n = 47) of cases were treated solely for chlamydia and 5.4% (n = 47) of cases received a treatment regime containing ciprofloxacin.

Conclusion. One year post-guideline change, the rate of adherence to provincial guidelines for NG treatment returned to rates similar to those prior to guideline change.

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1754. *Trichomonas vaginalis* prevalence in the United States

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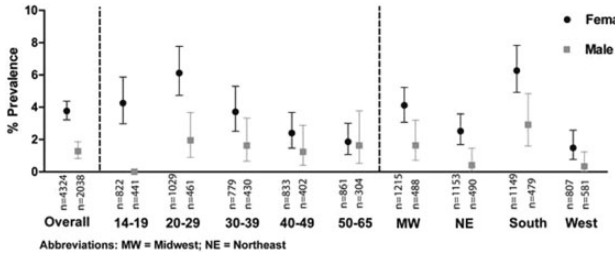
Background. *Trichomonas vaginalis* prevalence is not well characterized and two national studies (NHANES 2001-2004; Ginocchio *et al.* 2012) provided estimates for women between 3.2% and 8.7%. This may be related to differences in study populations, methodologies, and changes over time. In both studies, prevalence was highest in women age 30+ years. The prevalence of *T. vaginalis* in men is much less studied. To assess prevalence in both, men and women, we screened samples from individuals (n = 6362) of all four CDC STD surveillance regions.

Methods. For women (n = 4324), residual vaginal/cervical swab specimens for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhea* (NG) screening (age 14-29 years, n = 1851) and cervical cytology specimens for HPV screening (age 30+ years, n = 2473) were included. Urethral swab and urine specimens from men ages 14-65 years for CT/GC testing (n = 2038) were also included. Overall, samples were enrolled from 38 U.S. states over a 8 month period. Testing was performed with the APTIMA Trichomonas vaginalis Assay on the PANTHER System (Hologic, GenProbe).

Results. Overall positivity rates were 3.8% (95% CI 3.2-4.4) in women and 1.3% (0.8-1.9) in men (Figure). Rates differed by age for women (p < 0.0001) and by geography for women and men (p < 0.0001). Positivity rates were highest in the 20-29 year age group (women: 6.1%, 4.7-7.8; men: 2.0%, 0.9-3.7) and in the South (women: 6.3%, 4.9-7.8; men: 2.9%, 1.6-4.9). Positivity for *T. vaginalis* correlated with CT/NG detection in women ages 14-29 (odds ratio [OR] 2.5; 1.4-4.2; adjusted OR [aOR] for age 2.7; 1.6-4.7) and for HPV in women ages 30-65 (OR 2.2; 1.2-4.2, aOR for age 2.0; 1.0-3.8). No significant association with CT/NG detection was observed in men (OR 0.9; 0.3-3.1; aOR for age 1.0; 0.3-3.4)



Conclusion. For this cross-sectional study we targeted a routine screening population by using samples submitted for STD screening in women age 14-29, cervical cancer screening age 30-65, and STD screening in men age 14-65. Prevalence estimates in women are similar to those from NHANES 2001-2004 (2.3%-4.1%). In contrast to the two previous studies but similar to other STIs, positivity rates were highest in the 20-29 year age group. The overall prevalence of *T. vaginalis* in men was almost 3-times lower than in women.

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