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The impact of an intervention to predict multidrug-resistant infection upon admission to acute-care hospitals: a prospective multi-centre crossover trial

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Background
Delay in initiation of appropriate antimicrobial therapy (DAAT) is the strongest modifiable independent predictor for mortality in severe sepsis. DAAT is common among patients with multidrug-resistant (MDR) organism infections upon admission (UA) to hospitals. Our aim was to analyze the impacts of a bedside calculator that predicts MDR-UA infection, with regards to DAAT reduction and patients' outcomes.

Methods
Prospective multi-center crossover trial was conducted at two large academic acute care facilities, i·e·, Hospital A (900 beds) and Hospital B (700 beds), from 17/07/2023 to 16/09/2024 (15 months, with 3 washout periods). Adults with sepsis UA were enrolled. During the intervention, the MDR-UA score result was provided to prescribers within 48 hours. DAAT and hospitalization's outcomes were compared between the intervention and control periods, using the crossover design to control for confounding.

Results
Overall 1,524 patients were enrolled (1,011 from Hospital A, 513 from Hospital B). Of 514 patients (33%) with microbiologically confirmed infection, 200 (39%) had MDR-UA. The calculator's performances in predicting MDR-UA were low (ROC-AUC 0.68), and DAAT was not impacted by the intervention (p=0.97). However, the intervention was significantly associated with reduced 14-days mortality rate (4.5% vs. 12.2%, p<0.0001), decreased discharge rate to health facilities (6.3% vs. 10.7%, p=0.007), but increased readmission rate among survivors (43% vs. 29%, p<0.001).

Conclusions
While the calculator did not perform well in predicting MDR-UA infections, nor in reducing DAAT, the intervention was significantly associated with improved patients' outcomes. Artificial Intelligence (AI) supporting technologies are expected to display higher MDR-UA predictive performances in the future. The favorable impacts on early outcomes, plausibly result from the early close clinical attention provided by expert prescribers during the intervention periods. (ClinicalTrials.gov number, NCT05304221).

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Evaluation of piperacillin/tazobactam appropriateness and underlying drivers of inappropriate prescribing in a Belgian university hospital: a retrospective study

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Background
An estimated 30-50% of antibiotics prescribed in healthcare settings are either unnecessary or inappropriate. Inappropriate use contributes to antibiotic resistance and associated morbidity and mortality. Conducting prospective audits with feedback and interventions is among the key strategies advocated by the Infectious Diseases Society of America to optimise antimicrobial prescribing. In line with this guidance, this approach was selected to evaluate piperacillin-tazobactam (PTZ) use within our institution.

Methods
A prospective audit of PTZ prescribing was conducted over an 11-week period at the CHU of Liège. Prescriptions were reviewed weekly by an infectious disease specialist and a clinical hospital pharmacist. The primary outcome was to evaluate the appropriateness of PTZ prescriptions across three main evaluation criteria -indication, spectrum and duration- and one minor criterion -notification of the indication in the medical records-. The secondary outcome was to identify potential drivers of inappropriate prescribing. Interventions involved antibiotic discontinuation, de-escalation, oral step-down therapy and optimising the pharmacokinetic and pharmacodynamic (PK/PD) profile.

Results
91,8% of the prescriptions were deemed appropriate for indication, 74.5 % for spectrum, and 50% for duration. Notification was adequate in 65.5% of cases. Broad-spectrum antibiotics were discontinued or de-escalated in 33.6% and 19.1% of cases, respectively. Intravenous-to-oral switch and PK/PD optimisation were suggested in 17.3% and 11.8% of cases. Our study identified several statistically significant determinants of inappropriate antibiotic use, including the type of care unit and the Charlson Comorbidity Index (CCI). Patients managed in surgical units had a 9.8-fold higher risk of inappropriate indication and a 7.8-fold higher risk of inappropriate notification. In contrast, higher CCI scores were associated with a lower risk of spectrum inappropriateness.

Conclusions
Our findings point out the role of an antimicrobial stewardship program in improving antibiotic use, especially in surgical units where inappropriate indication and poor notification were most common. Importantly, antibiotic treatment duration remains problematic across all hospital units. By linking patient characteristics to outcomes, our study identifies key drivers of inappropriate use, which could be further confirmed and refined in future research.

Table 1. Antibiotic therapy evaluation (N =110 stays)

	N no missing	N (%)
Treatment type	109	
Empirical		98 (89.9)
Targeted		11 (10.1)
Appropriate indication	110	101 (91.8)
Appropriate spectrum	110	82 (74.5)
Reason for which it was considered as inappropriate	*28*	
No indication		*6*
Isolates with susceptibility to narrower-spectrum antibiotics		*17*
Source control failure¥		*2*
PTZ-resistant strains		*2*
Isolate with susceptibility to narrower-spectrum antibiotics and PTZ-resistant strain		*1*
Appropriate duration	110	55 (50.0)
Appropriate notification in medical records	110	72 (65.5)

¥Source control failure was defined as the persistence of infection despite appropriate interventions, such as drainage or removal of an infected device

Table 2. Interventions (N=110 stays) - Multiple interventions were possible for the same antibiotic prescription

	N (%)
Discontinuation (effective or proposed end date) of broad-spectrum antibiotics without de-escalation or escalation	37 (33.6)
De-escalation and escalation of antibiotic therapy	23 (20.9)
De-escalation	*21*
Escalation	*2*
PTZ duration reduction	35 (31.8)
PTZ dose reduction	3 (2.7)
Oral step-down therapy	19 (17.3)
PK/PD optimisation	13 (11.8)

Table 3. Determinants of inappropriate antibiotic use (N=110 stays) – Modelling of inappropriateness risks: for each risk modelled, a simple logistic regression model per explanatory factor.

Risk	Explanatory factor	OR (95% CI)	p-value
Indication inappropriateness	Gender (reference = Male)	0.73 (0.17 – 3.1)	0.67
	Age (years)	0.99 (0.95 – 1.04)	0.80
	Charlson Comorbidity Index (0 – 24)	0.94 (0.69 – 1.3)	0.71
	Immunosuppression (reference = No)	0.38 (0.045 – 3.2)	0.37
	Number of days since PTZ initiation	0.88 (0.66 – 1.2)	0.40
	Care units: surgery vs internal medicine	9.8 (1.2 – 81.2)	**0.035**
Spectrum inappropriateness	Gender (reference = Male)	1.2 (0.49 – 2.8)	0.72
	Age (years)	0.98 (0.95 – 1.002)	0.069
	Charlson Comorbidity Index (0 – 24)	0.74 (0.59 – 0.94)	**0.013**
	Immunosuppression (reference = No)	0.63 (0.21 – 1.9)	0.41
	Number of days since PTZ initiation	1.1 (0.97 – 1.3)	0.13
	Care units: surgery vs internal medicine	2.3 (0.89 – 5.8)	0.087
Duration inappropriateness	Gender (reference = Male)	1.0 (0.47 – 2.1)	1.0
	Age (years)	1.0 (0.997 – 1.05)	0.087
	Charlson Comorbidity Index (0 – 24)	0.99 (0.84 – 1.2)	0.90
	Immunosuppression (reference = No)	0.54 (0.22 – 1.3)	0.18
	Number of days since PTZ initiation	0.94 (0.83 – 1.1)	0.29
	Care units: surgery vs internal medicine	1.1 (0.50 – 2.4)	0.83
Notification in medical records inappropriateness	Gender (reference = Male)	0.69 (0.30 – 1.6)	0.37
	Age (years)	0.98 (0.96 – 1.006)	0.12
	Charlson Comorbidity Index (0 – 24)	1.0 (0.85 – 1.2)	0.85
	Immunosuppression (reference = No)	1.2 (0.50 – 3.1)	0.63
	Number of days since PTZ initiation	0.87 (0.74 – 1.03)	0.10
	Care units: surgery vs internal medicine	7.8 (3.0 – 20.1)	**<0.0001**