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SHORT COMMUNICATION

The burden and surveillance of RSV disease in young children in Belgium—expert opinion

Marc Raes[1] · Siel Daelemans[2] · Luc Cornette[3] · Stéphane Moniotte[4] · Marijke Proesmans[5] · Heidi Schaballie[6] · Julie Frère[7] · Koen Vanden Driessche[8] · Daan Van Brusselen[9]

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Abstract

Infections with respiratory syncytial virus (RSV) can cause severe disease. In young children, RSV is the most common cause of lower respiratory tract illness and life-threatening infections most commonly occur in the first years of life. In adults, elderly and immunocompromised people are most vulnerable. Recently there has been an acceleration in the development of candidate RSV vaccines, monoclonal antibodies and therapeutics which are expected to become available in Europe within the next 2–10 years. Understanding the true burden of childhood RSV disease will become very important to support public health authorities and policy makers in the assessment of new therapeutic opportunities against RSV disease. A systematic literature search was performed to map local data on the burden of RSV disease and to evaluate available RSV surveillance systems. A group of 9 paediatric infectious diseases specialists participated in an expert panel. The purpose of this meeting was to evaluate and map the burden associated with RSV infection in children, including patient pathways and the epidemiological patterns of virus circulation in Belgium. Sources of information on the burden of RSV disease in Belgium are very limited. For the outpatient setting, it is estimated that 5–10% of young patients seen in primary care are referred to the hospital. Around 3500 children between 0 and 12 months of age are hospitalized for RSV-bronchiolitis every year and represent the majority of all hospitalizations. The current Belgian RSV surveillance system was evaluated and found to be insufficient. Knowledge gaps are highlighted and future perspectives and priorities offered.

Conclusion: The Belgian population-based RSV surveillance should be improved, and a hospital-led reporting system should be put in place to enable the evaluation of the true burden of RSV disease in Belgium and to improve disease management in the future.

What is Known:
- *RSV bronchiolitis is a very important cause of infant hospitalization.*
- *The burden of disease in the community is poorly studied and underestimated.*

What is New:
- *This expert opinion summarizes knowledge gaps and offers insights that allow improvement of local surveillance systems in order to establish a future-proof RSV surveillance system.*

Keywords RSV · Seasonality · Surveillance · Belgium

Abbreviations

ALRI	Acute lower respiratory infections
CI	Confidence interval
ER	Emergency department
ECMO	Extra-corporal membrane oxygenation
GP	General practitioner
ICU	Intensive care unit
ILI	Influenza-like-illness
LMIC	Low- and middle-income countries
LRTI	Lower respiratory tract infection
NICU	Neonatal intensive care unit
NIRV	Non-influenza respiratory viruses
NO_2	Nitrogen dioxide
NRC	National Reference Centre

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✉ Marc Raes
marc.raes@jessazh.be

Extended author information available on the last page of the article

PICU	Paediatric intensive care unit
RSV	Respiratory syncytial virus
SARI	Severe acute respiratory infection
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
WHO	World Health Organization

Introduction

Respiratory syncytial virus (RSV) is a pathogen causing a wide spectrum of respiratory illness [1]. Globally, it is estimated that approximately 67% of infants aged < 1 year are infected with RSV and 90 to 95% of infants are infected within the first 2 years of life [2–4]. RSV disease ranges from a clinically insignificant picture to severe respiratory distress [5]. RSV-associated lower respiratory tract infections (LRTIs) commonly present in young children as 'bronchiolitis' and can progress to potentially life-threatening respiratory failure, apnoea and possibly death [6–9].

Development of new therapeutics and preventive measures against RSV urge countries to be prepared to evaluate these different candidates. Public health authorities and decision makers will need to know the true burden of childhood RSV disease in their respective country before being able to assess the true value of new approaches.

This study aims to describe the burden of disease and management for in- and out-patients and also the epidemiology and surveillance of RSV infections in children in Belgium.

Methods

Evidence evaluation for Belgium: literature search, surveillance analysis and expert meeting

In preparation of an expert panel discussion, a systematic literature search in Embase was performed by Prof Raes M, to map Belgian information on RSV disease from 2000 to 2021. Search terms used for disease, population and outcome were 'Respiratory Syncytial Virus' OR 'RSV' OR 'bronchiolitis' (title or abstract) AND 'Children' OR 'Child' OR 'Infants' OR 'Infant' OR 'pediatric' OR 'paediatric' OR 'newborn' OR 'preterm' OR 'toddler' OR 'preschool' AND 'disease burden' OR 'clinical burden' OR 'economic burden' OR 'epidemiology' OR 'surveillance' OR 'mortality' OR 'morbidity' OR 'incidence' OR 'infection' OR 'consultation' OR 'hospital admission' OR 'hospitalization' OR 'intensive care unit' OR 'death' OR 'cases' OR 'attack rate' OR 'direct costs' OR 'indirect costs' OR 'absenteeism' OR 'psychological impact' or 'hospital saturation' or 'antimicrobial resistance' OR 'ari' OR 'sari' OR 'ili' OR 'risk factor' OR 'sequalae' OR 'asthma' OR 'wheezing' OR 'allergies' OR 'seasonality'. Excluded were animal, in vitro, cell culture and non-human studies. Of a total of 162 publications, only 4 publications discussed the burden of RSV disease in Belgium [10–13]. The analysis was completed with publications and publicly available information on RSV surveillance in Belgium. To evaluate the value of these local data, a group of 9 paediatric infectious diseases specialists, including 1 neonatologist and 1 paediatric cardiologist, was requested to participate in an expert panel. The expert selection was based on an analysis by the Belgian Society of Paediatrics, taking into account expertise in paediatric pulmonology, infectious diseases or neonatology and work in one of the Belgian university hospitals or renowned paediatric hospitals. The meeting resulted in an evaluation of the burden associated with RSV infection in children, including a discussion on the Belgian patient pathways and the surveillance and epidemiological patterns of virus circulation in Belgium. This publication reflects the discussion of the panel.

Results

The burden of RSV disease in Belgium

RSV case definition and diagnosis

In Belgium, the terms 'bronchiolitis' and 'viral pneumonia' are often used interchangeably [14, 15]. 'Bronchiolitis' is the most common clinical description of LRTI in infants and young children in Belgium: coryza and sometimes (low-grade) fever progresses over a few days to a rather specific cough, tachypnoea, respiratory distress, and widespread (high-pitched) crackles, or wheezes (or both). Bronchiolitis is a descriptive clinical entity and does not need confirmatory viral testing or imaging. Pneumonia following RSV infection can be defined by the presence of localized crackles or reduced breath sounds and consolidation on chest X-ray [14, 15]. The expert panel underlines the need for a standard case definition and uniformity of diagnosis for RSV-bronchiolitis to optimize the accuracy of mapping the RSV disease burden and to be able to compare disease severity in different age groups and regions.

RSV-related hospitalizations

Globally, the burden of severe RSV-LRTI in children < 5 years of age is well known, and there are reasonable estimates for RSV-associated hospitalizations [8]. Detailed data on RSV-related hospitalizations are currently very limited in Belgium due to the lack of a complete national registration system. It is estimated that 5–10% of young patients seen in primary

care are referred to the hospital, often through the emergency department (ER). Additionally, walk-in presentation at the ER is common. In Belgium, around 3500 children between 0 and 12 months of age are hospitalized for RSV-bronchiolitis every year, representing the majority of all hospitalizations [12, 16]. This confirms the calculated estimation shown in the study of Li et al. [17]. The point estimates for RSV-associated ALRI hospitalizations for children were for Belgium 2.65 (0.75–6.18) < 1 year (thousands, 95% CI); 2.41 (0.63–5.88) for 1–5 years and 5.16 (1.52–11.29) for < 5 years total [17]. The high burden of hospitalization for bronchiolitis in Belgium is not so surprising, because it is becoming increasingly clear that there is an association between exposure to different ambient air pollutants—like $PM_{2.5}$ and nitrogen dioxide (NO_2)—and the risk of a 'severe bronchiolitis' [18]. Flanders, and specifically Antwerp, is one of the regions in the world with the highest disease burden because of NO_2 [19]. The Department of Paediatrics at the Jessa Hospital in Hasselt, a large regional hospital, has since 2002 built a database of RSV-related hospitalizations (Fig. 1).

In this population, 70–75% of children hospitalized for RSV disease were below 1 year of age and 40–50% below 6 months of age. Information on underlying diseases was not systematically registered (Raes M, unpublished data—hospital database Jessa Hospital).

Infants with known risk factors, such as prematurity and underlying medical conditions (e.g. cyanotic congenital heart disease, chronic pulmonary disease, immunodeficiency), have an increased individual risk of severe RSV-LRTI; however, in absolute numbers most hospitalizations due to RSV (67% to 80%) occur in previously healthy infants, born at term [20–22].

The Belgian expert panel confirmed the above-mentioned risk factors of RSV-associated LRTI. An underlying disease predisposing to severe RSV disease might however not be known yet at the time of presentation. Due to the complex interactions of multiple risk factors, experts acknowledged that the risk of severe RSV disease is often difficult to predict as all (also term) infants can possibly develop severe RSV infection, with young age being the most common determinant [20–24].

The high risk at a very young age (< 6 months old) highlights the importance of the age of the child in relation to the seasonality of RSV infections. Infants born just before or during the RSV season are at increased risk of severe RSV infection and RSV-associated hospitalization compared with those born at the end of the season [23–26]. A detailed analysis on Belgian hospitalizations, length of stay and prevalence of comorbidities in case of RSV disease is not possible as these data are not captured systematically in a national hospital database. Mean length of hospital stay in Jessa hospital varied between 3 and 5 days (Raes M, unpublished data—hospital database Jessa Hospital). This is in line with a study in 7 European countries that reported median length of stay ranging from 2 days (0.5–4 days) to 4 days (2–6 days) for children under 5 years of age [24].

Global estimates from 2015 indicate that in-hospital case fatality rates in young children aged < 5 years old with acute RSV-LRTI range between 0 and 9.3% across different geographical regions [8]. In Belgium, although no full country

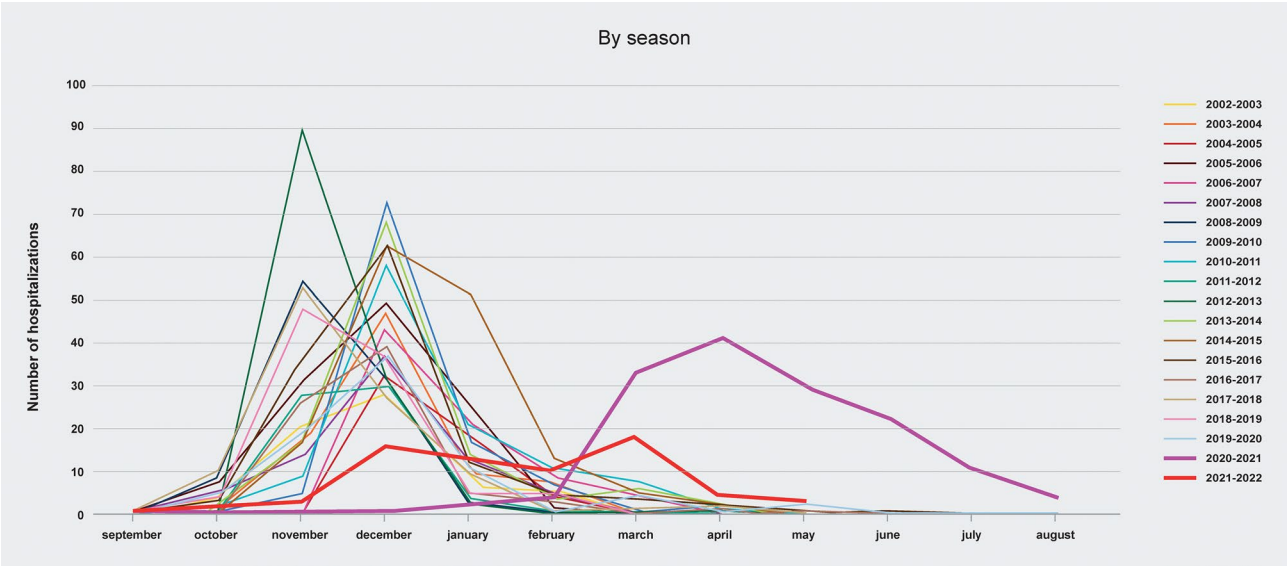

Fig. 1 Overview of hospitalizations due to RSV in the period 2002 -May 2022 in Jessa Hospital, Belgium. Normal RSV seasonality starting in October. The delayed peak in Belgium seen in the spring of 2021 and low number of positive lab tests for RSV near end year of 2021 are exceptional and can be explained by the influence of the COVID-19 measures on the RSV incidence. (Raes M, unpublished data—hospital database Jessa Hospital)

data are available, it is known that the case fatality rate is very low, thanks to efficient support in the regional hospitals and early referral to performant paediatric intensive care (PICU) facilities [27].

Outpatient burden of RSV disease

The burden of outpatient visits due to RSV in younger and older children remains relatively poorly studied. Nevertheless, it is generally accepted that during the epidemic months, RSV puts stress on the outpatient care systems [28]. In low- and middle-income countries (LMIC), it is well known that an important part of the RSV burden lies in the community and not only in the hospital. A large post-mortem surveillance study in Zambia recently showed that RSV caused at least 2.8% of all infant deaths, and 4.7% of infant out-of-hospital deaths, demonstrating that the burden of infant RSV mortality in LMIC is underestimated, especially at community level [29].

In 2017, a European multi-stakeholder community launched the project 'RESCEU'—short for 'REspiratory Syncytial virus Consortium in EUrope'. This consortium aimed to develop robust evidence on the RSV disease burden. In the meantime a new project, called 'PROMISE', 'Preparing for RSV Immunisation and Surveillance in Europe' has started trying to ensure continued data generation to allow informed introduction of novel RSV prevention. RESCEU has published a meta-analysis on the risk of severe RSV-LRTI in children with congenital heart disease [30] and in children with bronchopulmonary dysplasia [31]. In addition to acute disease, RSV bronchiolitis is associated with long-term respiratory problems; it is increasingly recognized as predisposing to severe pneumonia in the short term [32, 33] and as a risk factor for the development of recurrent wheeze and asthma later in life [34–36]. Belgian information is lacking. Nevertheless, published data are likely also applicable to Belgium. Also, complications might emerge after RSV-associated hospitalization in early life and lead to increased healthcare resource utilization among these patients later in life.

The Belgian patient pathway

We identified 3 layers for the evaluation, management and treatment of RSV infections in the Belgian patient pathway (Fig. 2): the primary care setting, the hospitalized child and the follow-up after discharge.

Although only limited data are available for Belgium and the precise impact is unknown, both the primary care setting (with a peak in RSV-related consultations) and the hospital

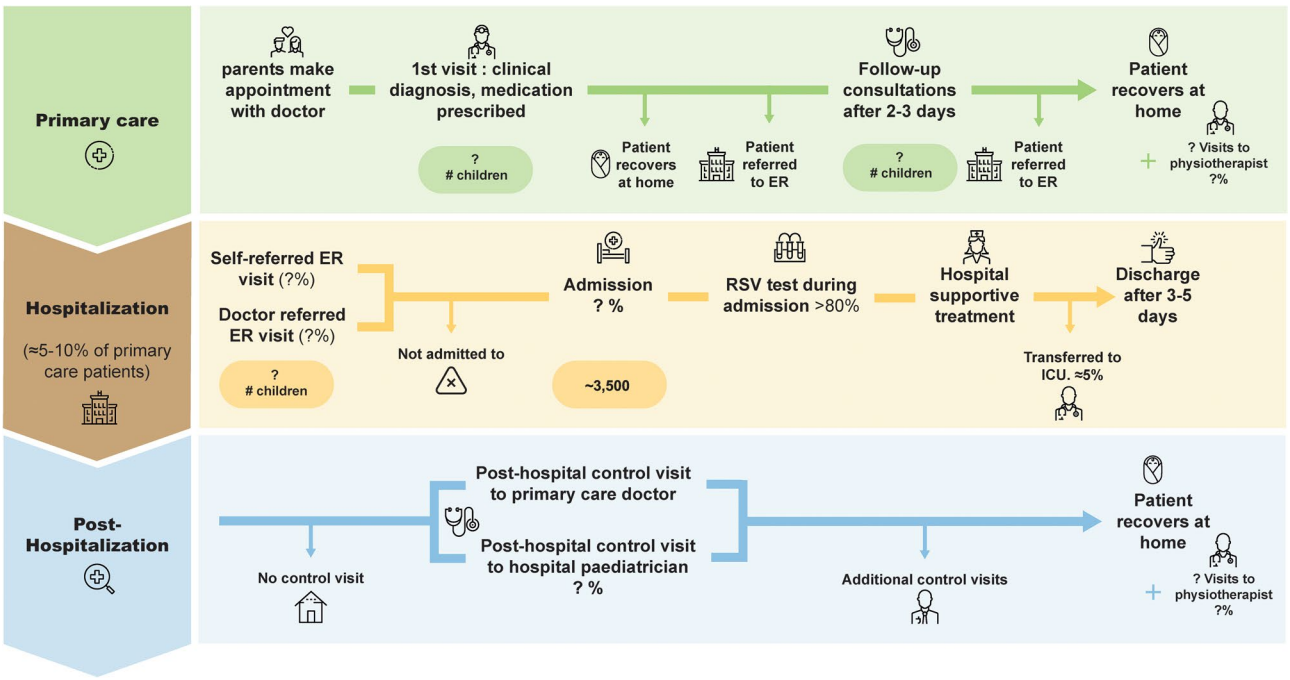

Fig. 2 Belgian patient pathway for (RSV)-bronchiolitis based on a questionnaire among Belgian generalists and specialists in the domain of RSV (CVA, 2021). There are 3 layers to consider in the management and treatment of RSV infections in Belgium: the primary care setting, the hospitalized child and the follow-up phase. Parents first seek advice in primary care setting, severe RSV infections are referred to the ER and can lead to hospitalization or admission to PICU. Post-hospitalization visits are common. It is estimated that around 3500 Belgian children between 0 and 12 months are hospitalized for bronchiolitis on a yearly basis, 5% of those would be transferred to ICU. (Data on file, Sanofi, Questionnaire on burden of RSV disease in Belgium, conducted by CVA, 2021)

setting (with ER visits, possibly leading to hospitalizations and referral towards PICU) are affected. As not all hospitals in Belgium have a PICU facility, it is common practice to transfer patients with severe disease towards a nearby PICU or exceptionally to a neonatal intensive care unit (NICU). In addition, some regions collaborate with nearby intensive care units in neighbouring countries. Due to its seasonality, RSV puts pressure on the Belgian healthcare system every year.

As for the socioeconomic burden of RSV, the expert panel stressed that the parental (emotional) distress during hospitalization and in the ambulatory care setting should not be underestimated. Higher healthcare resource utilization, lost productivity of parents, child-care arrangements, parental stress and anxiety are additional factors to consider when mapping the burden of RSV disease [37–39].

Management of RSV disease

The recommended management of RSV-related illness is currently only supportive. No specific medication is available [4]. In the outpatient setting, infants often present with clear rhinorrhoea, cough, sneezing, fever and shortness of breath; symptomatic care mainly consists of nasal care (normal saline, local decongestives), antipyretics and analgesics. A trial of bronchodilators or hypertonic solutions is sometimes attempted (the latter without much evidence). Common more severe symptoms are poor feeding and respiratory distress, which trigger referral and admission to the hospital. Most hospitals follow evidence-based management protocols which focus on supportive care: a 'minimal touch' approach, nasogastric tube feeding and/or respiratory support [40]. ECMO (extra-corporal membrane oxygenation) is very rarely needed [27].

Treatment and prevention

There is currently no approved antiviral treatment for RSV in Belgium. An effective passive immune prophylaxis exists in the form of palivizumab, a monoclonal antibody against the F glycoprotein of RSV. In Belgium, 3 different risk groups are eligible to receive reimbursement for palivizumab [41].

The eligible groups are:

1. children born at 28 weeks of gestation or less who are less than 1 year old at the beginning of the season
2. children born between 28 and 35 weeks of gestational age who needed more than 48 h of ventilation, stayed in a NIC centre and are less than 6 months of age at the onset of the RSV season
3. children less than 2 years of age with haemodynamically significant congenital heart disease or needing chronic oxygen/ventilation [41]

Palivizumab is administered monthly (five injections per RSV season) [42]. Currently several RSV antivirals, various types of vaccines (live-attenuated, vector-based, particle-based and subunit vaccines) and monoclonal antibodies with prolonged half-life (single injection per season) are being studied [43, 44].

Epidemiology and surveillance of RSV in Belgium

Seasonality of RSV disease

A retrospective study of the seasonal RSV pattern in 9 Belgian hospitals over a 13-year period (2004–2017) was conducted in 2018. The start of the RSV season was relatively consistent, beginning in October (week 41/42), with a median peak in December (week 49) [45]. This was confirmed by an analysis of 24 winter seasons (1999 until 2020), where all—except one—of the peaks fell between weeks 47 and 52. March is often considered the usual end of the season. The 2020 winter peak was clearly non-existent [12].

In the absence of a usual autumn/winter peak during the SARS-CoV-2 outbreak, some countries in both hemispheres unexpectedly experienced subsequent delayed RSV epidemic peaks [46, 47].

Delayed RSV peaks were also observed in Belgium, namely, in the 2021 spring season the epidemic threshold was exceeded twice, first between weeks 11 and 13, and again between weeks 16 and 19, as shown in Fig. 3 [48]. We did not see a peak higher than the regular winter peaks, but an 'ongoing plateau' from early spring to mid-summer. Also 2022 showed an untypical seasonality with the lack of a high winter peak but continued reporting of RSV positive cases beyond normal end of the season in March (week 13).

The shift and occurrence of inter-seasonal RSV peaks raises questions concerning the patterns of annual re-emergence of viruses. In addition, the delayed peaks have created uncertainties regarding predictions, testing capacity and management of Belgian resources. This also asks for a better and continuous surveillance of RSV cases.

RSV surveillance

The Belgian Scientific Directorate of Epidemiology and Public Health (Sciensano) organizes disease surveillance. They use multiple data sources for the epidemiological follow-up of influenza virus and other non-influenza respiratory viruses (NIRV), among which RSV. Therefore, Sciensano works in close collaboration with Belgian monitoring laboratories, the National Reference Centre (NRC) for Respiratory Pathogens, the sentinel network of GPs (general practitioners) and the sentinel network of hospitals [11, 49]. Today, half of the Belgian microbiology laboratories belong

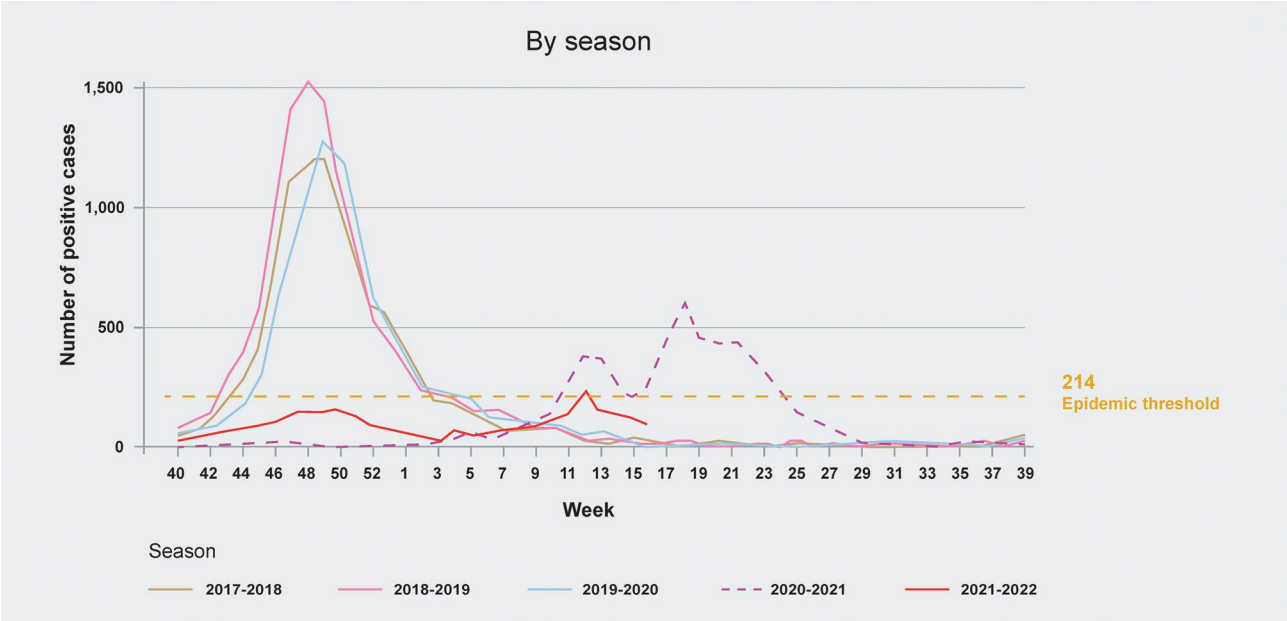

Fig. 3 Weekly number of RSV positive cases in Belgium, reported to Sciensano by the sentinel network of laboratories, seasons 2017–2018 to 2021–2022. Normal RSV seasonality starts around week 41/42; in the dotted line the delayed peaks in Belgium for the spring of 2021, and in the red line the low number of positive lab tests for RSV near end year of 2021, and delayed peak in early 2022 are shown. Adapted from Sciensano, week 16, 2022 [48]

to the network of monitoring laboratories. They report the number of diagnosed cases.

Since 2007, the sentinel network of GPs has continuously registered consultations for acute respiratory infections and influenza syndromes in close collaboration with the NRC for influenza, which carries out microbiological testing of a representative sample. Since the 2011–2012 respiratory season, a sentinel network of 6 hospitals with high ICU activity registers all hospitalizations of severe acute respiratory infections (SARI) that occur during the period of increased flu activity (SARI-surveillance). The registration starts when the first influenza cases are detected by the NRC for influenza. The end of the period is 3 weeks after the moment when the incidence of influenza syndrome (registered by the network of GPs) drops below the epidemic threshold. The registration period normally lasts from the last week of December or first/second week of January to the third/last week of April. But, in Belgium RSV circulation generally occurs between October and January–March, and usually precedes the circulation of influenza. Furthermore, the objective of the SARI surveillance is primarily to evaluate the severity of influenza viruses and the WHO SARI case definition contains criteria like 'fever' and 'cough', which are not really adapted to RSV.

In the season 2018/19, Sciensano decided to test the capability of the existing SARI network to contribute to RSV surveillance in Belgium [11]. SARI surveillance was started earlier than before, being in week 40. Also, the case definition was broadened and the 'fever criterion' was not necessary anymore. Between week 40 (of 2018) and week 2 (of 2019), Sciensano received 508 samples from the SARI network. They found an overall RSV positivity rate of 62.4% (317/508), with rates varying depending on the age group: 77.6% in children aged < 5 years (253/326) and 34.4% in adults aged ≥ 65 years (44/128). Over 90% of the RSV-positive samples that were also positive for another respiratory virus (80/85) came from children aged < 5 years. Differences were noted between age groups for symptoms, comorbidities and complications. It was concluded that with only marginal modifications in the case definition and the period of surveillance, the Belgian SARI network would be able to substantially contribute to RSV surveillance and burden in both children and older adults [11]. Another recent analysis showed that RSV detection rates were systematically higher in SARI than in influenza-like-illness (ILI) samples. The SARI samples positive for RSV came from children (44.1%), mostly younger than 1 year old, and from older adults (42.0%) [50].

Since 2021, the influenza season surveillance period starts at week 40 and goes on to week 20 of the next year [49]. Among the gathered GP surveillance data are age group, vaccination status, patient outcome and hospitalization. In the SARI surveillance, various parameters are recorded during the hospital stay including demographic characteristics of the patient, symptoms, risk factors and comorbidity, vaccination, treatment, severity and outcome. In addition to this registration of clinical data, a nasopharyngeal sample from

Table 1 Main recommendations for improvement of RSV diagnosis, surveillance and management in Belgium

1) Formulate a national standard case definition to allow uniform diagnosis of RSV bronchiolitis
2) Roll out a clear testing policy for laboratory confirmation of RSV cases
3) Improve the registration of RSV disease in the community (based on data from GPs and paediatricians)
4) Improve the registration of RSV disease at hospital level, including patient characteristics (age, comorbidities, length of hospital stay, outcome, transfer to PICU, death)
5) Improve RSV surveillance: increase of the number of sentinel laboratories and sentinel SARI hospitals in Belgium, ensure GPs and paediatricians are represented, ensure RSV specific data collection (not only ILI/SARI), improve specific paediatric data collection, ensure year-round surveillance and limit delays in reporting
6) Implement a clinician-led reporting system to capture RSV infections in hospitals to allow fast reaction in anticipation of inter-seasonal RSV epidemics

a (random) subset of the GP-surveillance patients and each hospitalized patient is tested for influenza, RSV, SARS-CoV-2 and a set of about 15 other respiratory viruses, defined by the NRC for influenza.

Although efforts are done to improve, the current surveillance system still has limitations. The Belgian national RSV case definition consists of a laboratory confirmation of RSV and a clinical definition of bronchiolitis. The sentinel network of GPs collects samples of ILIs, but ILI is not an ideal case definition for RSV. Also, paediatric samples are underrepresented in the ILI registration, likely leading to sampling bias as GPs in Belgium are less likely to see very young children. Also, the SARI case definition is not optimal for RSV, even when flexibility on the 'fever criterion' (see above) is allowed. Furthermore, the SARI-surveillance network consists of only 6 hospitals, most of them tertiary centres. A larger network, also including general hospitals from different geographical areas could reduce the risk for selection bias. Moreover, data collection is mainly focused on adults and extrapolated to children. Specific data on children are lacking.

The clinical utility of surveillance data is limited because currently it informs only retrospectively whether there was RSV circulation [48]. Also, uncertainties exist on testing policies (they differ per centre), data input (not all labs in the sentinel network report on time) and calculation of the RSV epidemic threshold (> '214' cases per week in the Belgian hospital sentinel labs is now used as the 'epidemic threshold'; this is based on the 'Moving Epidemic method') [48, 51].

Improvements that could increase the value of surveillance would be uniform testing policies, reducing the delay in reporting and adding 'reference laboratories' allowing a better representation of all geographical regions. A last point for improvement would be the surveillance period. Today, the sentinel surveillance networks collect data only during the winter season in Belgium. The above-mentioned delayed peaks and the current uncertainty around RSV circulation urge for a broadening of the surveillance timelines to enable early detection of the start of an RSV season. In anticipation of an inter-seasonal RSV epidemic, a clinician-led reporting system to capture RSV infections in hospitals was rapidly and successfully established in Switzerland recently. These data allowed real-time adjustment of RSV prophylaxis guidelines and underscored the need for systematic nationwide RSV surveillance [6]. Main recommendations are listed in Table 1.

Conclusions

Assuming that RSV vaccines and monoclonal antibodies with prolonged half-life would ultimately become licenced, introducing them at a global scale would be challenging and should be justified by a significant burden of disease [29].

In Belgium, the patient pathway for evaluation and management of RSV disease in children is currently not well described. Only rough estimates of the burden of RSV disease in both the community and hospital setting are available. Even though the proportion of paediatric hospital admissions is estimated to be only 5% of all RSV cases, the fact they are concentrated in the autumn/winter period underscores the need for better health service planning, to avoid critical pressure on the system.

Improvement of population-based surveillance suggested by our panel includes proper RSV incidence registration across different age groups, both in the community and in hospitals. Today, the seasonality of RSV is detected through the ILI surveillance system, which is inaccurate to predict the ideal timing of preventive passive immunization. Also, in relation to possible future shifts in the RSV peaks (as we have witnessed recently due to COVID-19 non-pharmaceutical interventions), the establishment of a broader, 'all year round' RSV surveillance system is important. ILI surveillance systems can be used as a starting point for population-based RSV surveillance, but the case definition should be modified to capture the RSV burden in young children.

Furthermore, a hospital surveillance system should be put in place to improve understanding of the true burden of RSV disease. Additional sentinel hospitals are needed,

not only reporting the positivity ratio of samples taken but also clinical data like age, risk factors, oxygen/respiratory care need, need of NG feeding/IV fluids, possible secondary infections and information on PICU transfer.

Both surveillance systems could be instrumental for communication with authorities, may prove useful in raising awareness of RSV infection and provide early information to guide the national policy on RSV prevention, reimbursement of preventive strategies and distribution of healthcare resources between hospitals. Cost-effectiveness calculations of new interventions based on true burden of RSV disease will allow informed decisions. A long-term sustainable clinician-led initiative (as in Switzerland) will require additional (organizational and financial) support, and possibly mandatory reporting of RSV infections by all laboratories involved in RSV detection.

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Declarations

Ethics approval This article does not contain any studies with human participants or animals performed by any of the authors.

Consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests Financial interests: The authors have no relevant financial interests to disclose. Non-financial interest: The panel session was supported by Sanofi. All authors have served on this advisory board for Sanofi.

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Authors and Affiliations

Marc Raes[1] · Siel Daelemans[2] · Luc Cornette[3] · Stéphane Moniotte[4] · Marijke Proesmans[5] · Heidi Schaballie[6] · Julie Frère[7] · Koen Vanden Driessche[8] · Daan Van Brusselen[9]

1 Department of Paediatrics, Jessa Hospital, Hasselt, Belgium
2 Paediatric Pulmonary and Infectious Diseases, University Hospital Brussel, Brussels, Belgium
3 Department of Neonatology, AZ Sint-Jan Hospital, Brugge, Belgium
4 Department of Paediatric Cardiology, University Hospital Saint-Luc, UCLouvain, Brussels, Belgium
5 Paediatric Department, University Hospital Gasthuisberg, Leuven, Belgium
6 Department of Paediatric Pulmonology, Infectious Diseases and Immune Disorders, University Hospital, Ghent, Belgium
7 Department of Paediatrics and Infectious Diseases, University Hospital, Liège, Belgium
8 Department of Paediatric Infectious Diseases, University Hospital, Antwerp, Belgium
9 Department of Paediatric Infectious Diseases, GZA Hospitals, Antwerp, Belgium