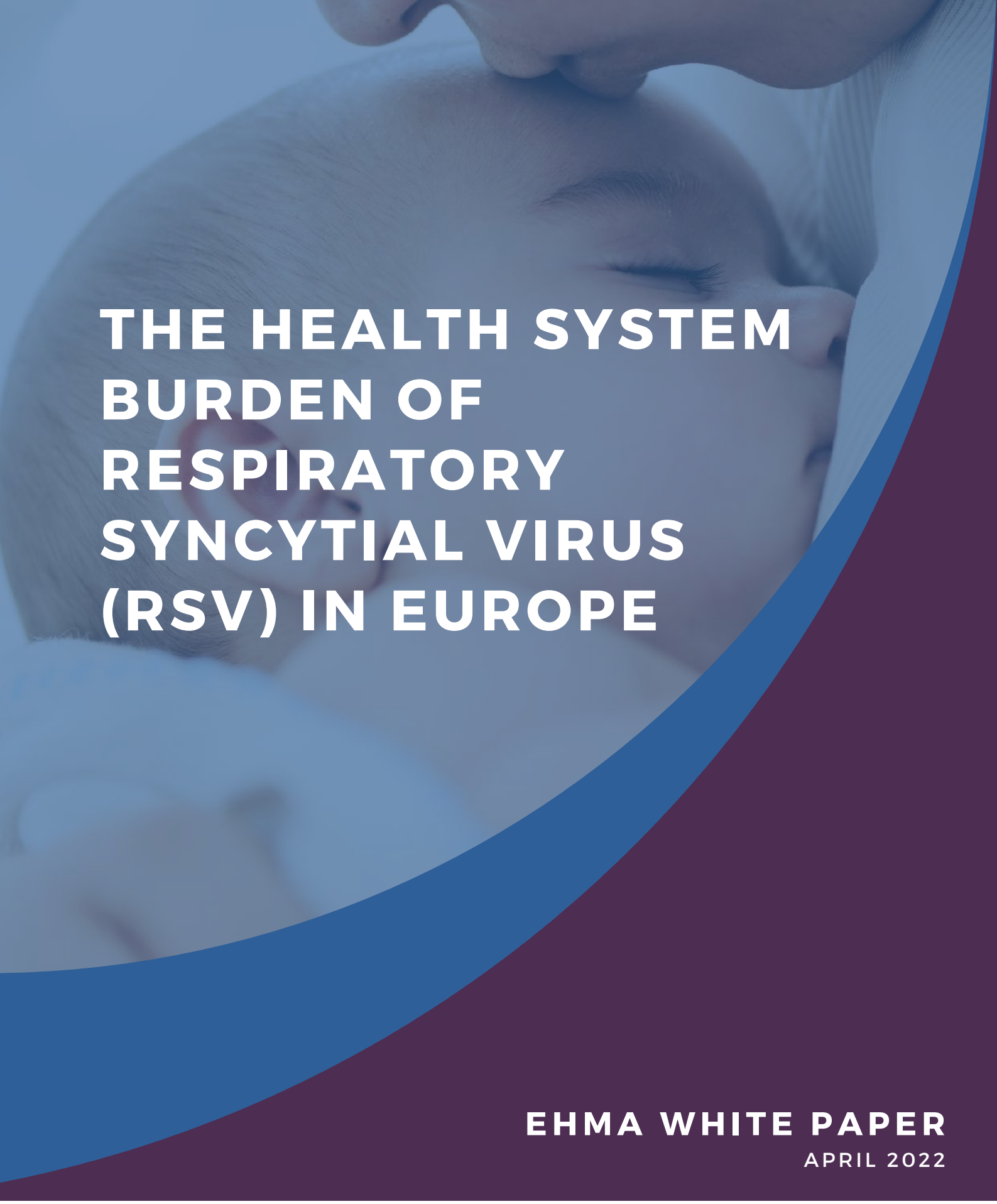


THE HEALTH SYSTEM BURDEN OF RESPIRATORY SYNCYTIAL VIRUS (RSV) IN EUROPE

EHMA WHITE PAPER

APRIL 2022

EHMA
European Health Management Association

TABLE OF CONTENTS

Executive summary 1
1. Introduction: RSV is a major public health issue 4
2. Study description and methodology 6
3. Survey results 9
    3.1 Health system disruption due to RSV 12
    3.2 Healthcare resource use due to RSV 17
4. Recommendations to strengthen the healthcare system's response to RSV 22
5. Conclusions 25
6. Abbreviations 26
7. Acknowledgements 27
8. Bibliography 29

EXECUTIVE SUMMARY

Respiratory syncytial virus (RSV) is an urgent and immediate threat to all infants and leads to significant burden to health systems. Nearly every child is infected by RSV by the age of 2. Globally, RSV is responsible for 33 million cases annually. It accounts for 63% of acute lower respiratory tract infections in infants and is the most common cause of bronchiolitis and pneumonia in infants. RSV is also a leading cause of hospitalisations for infants in their first year of life, and responsible for a significant outpatient burden.

Despite these concerning statistics, RSV is chronically underreported, and its burden widely underappreciated. RSV burden is strongly felt as there is no active treatment for RSV and RSV-related disease management is limited to symptomatic relief. At present, the only approved agent for RSV prophylaxis is the anti-RSV monoclonal antibody, Palivizumab (Synagis®, AstraZeneca), which is utilised for passive immunoprophylaxis of various high-risk infants predisposed to developing severe RSV disease and must be injected monthly throughout the RSV season. No preventive option for all infants is available yet.

The lack of a well-tolerated, clinically efficient, and cost-effective RSV preventive option that protects all infants is a global unmet medical need. New immunisation solutions in the horizon could help address that gap, with several pediatric and maternal vaccines and monoclonal antibodies under clinical development.

Most recently, the monoclonal antibody nirsevimab demonstrated the ability to immunise all infants from medically attended RSV-LRTI (lower respiratory tract infections) across the first RSV season with a single intramuscular (IM) dose for all infants experiencing their first RSV season and infants with specific conditions, such as congenital heart disease or chronic lung disease, entering their first and second RSV season. Nirsevimab is likely to be available prior to RSV maternal or infant vaccines [1].

There are compelling reasons today to prioritise RSV prevention and raise public policy awareness on its public health impact. The ongoing COVID-19 pandemic continues to place unprecedented strain on finite public health capacity. At the same time, COVID has highlighted the value of preventive measures to control infectious disease in an efficient way.

The learnings from our COVID experience and the new approaches to infection control and prevention will be critical to building a RSV-prepared and RSV-resilient health care system.

The European Health Management Association (EHMA) plays a crucial role in engaging with the full health ecosystem and is a recognised and respected amplifier of best practices in health management, with a European and global reach. This white paper presents the study findings on the burden of paediatric RSV in hospitals (paediatric general wards and paediatric

[1] Hammitt LL, Dagan R, Yuan Y, Cots MB, Bosheva M, Madhi SA, Muller WJ, Zar HJ, Brooks D, Grenham A, Hamrén UW, Mankad VS et. al. for the MELODY Study Group. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants. N Engl J Med, 2022; 386: 837-846.

intensive care units) and the community (primary and emergency care), and the impact of RSV-infection on health systems performance and healthcare resource use over the last three RSV season (2018/19, 2019/20, 2020/21).

The study is based on a survey conducted among HCPs (physicians in hospitals and the community, nurses, and health managers) in 20 European countries, from August 2021 to January 2022. The survey results reflect the experience and perception of healthcare professionals.

This study documents the burden and impact of RSV on hospitals and community. Specifically, it characterises the impact of RSV infection on health system performance, on care delivery and the workforce, and increased healthcare consumption due to RSV.

The study finds that the burden of paediatric RSV is significant and system-wide and affects all care settings. The seasonality of RSV is a strong factor impacting on optimal health system performance. The peak rise in RSV infections, occurring between October to March in Europe, results in acute pressure on primary care providers, emergency services and paediatric hospital capacity.

Increased demand for health care services leads to lowered levels of patient safety, deteriorated work conditions for healthcare providers, and significant delays and disruptions to care delivery. The survey results find that HCPs across all care-settings ranked increased workload and high levels of stress and exhaustion, as the foremost impacts of the RSV-associated health system burden. Moreover, the study finds that most infants are not optimally managed and routinely undergo unnecessary investigations and receive treatments (e.g., antibiotics) of doubtful efficacy for RSV infection. This is an avoidable and unnecessary public health burden.

After a careful assessment of the burden and impact of paediatric RSV infections on health systems in Europe, we developed five evidence-supported, actionable recommendations geared towards building an RSV-resilient health system. We believe that collectively acting upon these recommendations, together with policymakers and healthcare managers, has the potential to minimise and contain the disruption of paediatric RSV on our health systems, alleviate the workforce strain, and benefit RSV patients and their caregivers.

KEY RECOMMENDATIONS

1 Broaden the understanding of RSV among caregivers, communities, and clinicians

Caregivers and communities (e.g., schools, nurseries) should be equipped with basic information on the symptoms of RSV, its mode of transmission, the potential severity and best ways to protect all infants from RSV infection. To better manage RSV across care settings, HCPs should be better informed about RSV covert circulation and how to manage it in an efficient way, based on the implementation of clinical practice guidelines and replication of good practices observed in the community and in hospitals.

2 Maintain infection control measures

Behavioural and non-pharmacological interventions (e.g., use of personal protective equipment, hand hygiene) played a significant role in reducing COVID transmission. These can be successfully harnessed to control RSV transmission in the community. It is vital to apply infection prevention measures in a compliant way to protect against nosocomial RSV outbreaks and limit its onward transmission to the community.

3 Improve and expand diagnostic capability

Early diagnosis is critical to efficiently manage RSV symptoms and complications. The use of point-of-care tests (POCT) should be promoted at hospitals and community settings to be able to pose the right diagnostic and overall improve RSV surveillance.

4 Standardise the management of RSV infection

Limit the use of non-evidence-based practices in RSV infection management. At present little consensus exists on the best management strategies for RSV infection, and treatment varies substantially across practice settings. The EHMA survey results detect considerable variability in the management of RSV infection in infants. Specifically, the results indicate that infants with bronchiolitis routinely receive medications (e.g., antibiotics) despite a lack of evidence in their efficacy to treat RSV infection and undergo unnecessary investigations (e.g., chest X-rays, blood gas analysis). The frequent use of corticosteroids, bronchodilators and salbutamol is not evidence-based nor effective [1]. This is an additional cost and burden to the health system and to caregivers.

5 Prepare for access to immunisation

Preparing for the access to new RSV immunisation solutions for all infants currently in development would certainly help. Ensuring that these new solutions can be accessed both in the community and hospital settings will be of crucial importance to reduce the current health system burden, disruption, and healthcare resource use stemming from paediatric RSV. 75% of respondents in hospitals and the community ranked access to immunisation, vaccines, or monoclonal bodies as an “Important” or “Very Important” solution to reduce the burden of RSV on healthcare systems.

1 INTRODUCTION: RSV IS A MAJOR PUBLIC HEALTH ISSUE

KEY TAKE-AWAYS

RSV is a threat to all infants. Exposure to the infection does not confer immunity and reinfections are common. The severity of the infection in infants is unpredictable, and 72% of infants hospitalised for RSV were previously healthy and born at term.

The absence of a preventive option for RSV in all infants is a major unmet medical need and should be a public health priority. RSV burden is strongly felt as there is no effective preventive option available to all infants, and the current management of RSV infection is purely supportive.

1.1 THE RSV BURDEN

Respiratory syncytial virus (RSV) poses an urgent and immediate threat to all infants. RSV affects nearly every child by the age of 2 [2]. It accounts for over 60% of acute respiratory tract infections in infants worldwide and is the most common cause of bronchiolitis and pneumonia in infants [3]. Global estimates from 2015 reported 33.1 million new episodes of RSV-associated acute lower respiratory tract infection, requiring 3.2 million hospitalisations, and 59,600 in-hospital deaths in children under the age of 5 years [4]. In children younger than 6 months, there were 1.4 million hospital admissions, 27,300 in-hospital deaths due to RSV-acute lower respiratory tract infections [5], [6]. But these are still conservative estimates; the actual burden is likely to be higher, due to underreporting of RSV infections including in the EU/EEA, where the data on the RSV disease burden still needs to be improved [7].

Exposure to RSV does not lead to life-long immunity and reinfections are common. Reinfections occur throughout life and can occur more than once in the same season [8], even though subsequent infections are less severe.

The natural course of the infection is highly unpredictable in infants, and there is no way of predicting which patient will require hospitalisation due to severe RSV. In fact, 72% of infants hospitalised for RSV were previously healthy and born at term [9]. Symptoms range from mild flu-like presentations to severe lower respiratory tract infections (LRTI), including

bronchiolitis and pneumonia, that might require acute care admissions and mechanical ventilation [10].

In the short-term, RSV infection is associated with an increased incidence of acute otitis media (inflammation or infection located in the middle ear), pneumonia and excessive antibiotic usage [11]. In the long-term, RSV-LRTI is a significant risk factor for long-term respiratory morbidity, and is characterised by early transient or recurrent wheezing, asthma and impaired lung function [12], [13]. RSV-associated hospitalisation in the first year of life leads to increased healthcare resource utilisation among patients later in life, with increased paediatric office visits and ED attendances [14].

Moreover, RSV infection is associated with long-term healthcare utilisation and attendant costs, some of which may extend onto adolescence [15].

1.2 AN UNMET MEDICAL NEED

RSV burden is strongly felt as there is no preventive solution for RSV infection in all infants, and no active treatment. Pharmacological interventions such as bronchodilators and corticosteroids are found to be of uncertain benefit to RSV-infected infants. As a result of the lack of an evidence-base on the efficacy of these interventions, the current routine management of viral bronchiolitis is purely supportive [16]. The cornerstone of the management of viral bronchiolitis is the administration of oxygen and fluid therapy [17], [18], confirmed by leading international guidelines such as those issued by the National Institute for Health and Care Excellence, UK [19].

Similarly, there are few effective preventive options available. So far, the anti-RSV monoclonal antibody, Palivizumab (Synagis®) is the only licensed prophylaxis for RSV. It has demonstrated efficacy in reducing the risk of hospitalisation in infants born preterm, suffering from heart or lung conditions [20], who represents only a small part of paediatric population. Beyond the restriction in the birth cohort entitled to get access to Palivizumab, its high costs and the fact that it requires monthly injections limit its use even in high-resource settings [21]. Most recently, the monoclonal antibody nirsevimab demonstrated the ability to immunise all infants from medically attended RSV-LRTI (lower respiratory tract infections) across the first RSV season with a single intramuscular (IM) dose for all infants experiencing their first RSV season and infants with specific conditions, such as congenital heart disease or chronic lung disease, entering their first and second RSV season [22]. Nirsevimab is likely to be available prior to RSV maternal or infant vaccines.

2 STUDY DESCRIPTION & METHODOLOGY

KEY TAKE-AWAYS

The study gathered information on the treatment, management, and burden of RSV to hospitals (in general wards and in Paediatric Intensive Care Units) and community settings (in primary care and emergency services) and the actions required to mitigate the impact of RSV-associated health system disruption over the last three RSV seasons (2018/19, 2019/20, 2020/21).

It is based on a cross-sectional survey targeting healthcare professionals (HCPs) in Europe. The survey was conducted between August 2021 and January 2022. It was distributed among a wide cross-section of physicians, nurses, and hospital administrators/ managers – engaged in the treatment and management of paediatric RSV infection in hospitals and the community.

The survey explored to which extent paediatric RSV affects three key dimensions of health system performance – provider-related dimension (workload for health providers, levels of stress and exhaustion, burnout, staff turnover); resource-related dimension (e.g., point of care testing, investigations, bed occupancy, supportive therapies, pharmaceutical intervention, measures to reduce nosocomial infections); health system-related dimension (e.g., disruptions to patient flow, delayed care) – and identified the solutions that can help address the impact that RSV has on health system performance.

This white paper encompasses the results from the survey. It was developed through an iterative process of discussion, review, and content validation with scientific experts, focus group members, and other stakeholders.

2.1 STUDY GOALS

This survey documents the health system burden and impact of RSV infection, and the actions required to mitigate the effects of RSV-associated health system disruptions. The study gathered data on: (1) the treatment, management, and burden of RSV in hospitals and the community, and the disruption to optimal health system performance; (2) testimonies on the optimal approaches and strategies for RSV infection management in the community; and (3) current best practices and organisational adaptations required to minimise system-wide disruptions from RSV, and to contain its impact.

This paper studies the burden and impact of RSV across the care spectrum, with data for paediatric hospitals and the community.

2.2 STUDY DESIGN, SETTING, & POPULATION

We performed a cross-sectional survey targeting HCPs in Europe. We targeted 13 countries in Europe and received responses from 20 countries. The countries specifically targeted for this study were: Belgium, Finland, France, Germany, Ireland, Italy, the Netherlands, Portugal, Romania, Spain, Sweden, Switzerland, and the UK. The survey targeted a wide cross-section of HCPs, including: physicians (general practitioners and family doctors, primary care paediatricians, emergency physicians, paediatric specialists, ICU physicians, respiratory medical specialists, and paediatric intensivists); bedside nurses (registered nurses, nurse practitioners, paediatric nurses); and hospital administrators and hospital managers. The survey was conducted between August 2021 and January 2022.

The survey results are based on HCPs perceptions of the health system burden and impact of RSV in their care setting. The study does not draw on source documents.

2.3 SURVEY DEVELOPMENT

The survey was derived from a literature assessment and in-depth interviews with experts. We conducted a rapid review of peer-reviewed literature, grey literature, and scientific reports to identify the main themes representing the impact of RSV infections on healthcare systems. Emerging themes were discussed, reviewed, and prioritised at a focus group meeting with five European experts taking place on 29 June 2021.

The scientific experts advising this study were: Professor Javier Díez-Domingo of the Centre of Public Health Research of Valencia-FISABIO, Spain; Professor Susanna Esposito of the Università degli Studi di Perugia, Italy; Dr Sarah Marchal of the Hopitaux Pédiatriques Nice CHU-Lenval, France; Dr Simon Nadel of the Imperial College Healthcare NHS Trust, UK; and Professor Dr. med. Arne Simon of the Saarland University Hospital, Germany.

Following literature research and our consultations with experts, we identified several dimensions of health system performance most affected by seasonal RSV epidemic and placed them at the center of the survey.

These were:

- Provider-related dimension concerning the impact of RSV on staff morale and performance (e.g., "large or increased workload for health providers", "increased levels of stress and exhaustion", "burnout in health providers", "high staff turnover").

- Resource-related dimension covering RSV-related bed occupancy, pharmaceutical interventions, diagnostic tests (e.g., "volume of point-of-care tests conducted").

- Health system-related dimension covering health-related stay including protocols for nosocomial infection prevention (e.g., "risk of nosocomial risk for patients", "risk of nosocomial risk for staff", "disruptions to patient flow", "delayed urgent care").

THE QUESTIONNAIRE

The survey was a web-based 56-item questionnaire. It comprised four questionnaires, one for each of the following care setting: (1) primary care; (2) emergency care, including primary care urgent care clinics, emergency services, and hospital EDs; (3) paediatric general wards; and (4) paediatric intensive care units.

The survey integrated questions on: HCP demographics (PART A); HCP perceptions of the causes and impact of health system disruption in the peak RSV season (PART B); information on the current regimes of RSV treatment and management in hospitals and the community (PART C); and the priorities for RSV prevention (PART D).

The survey comprised:

- Part A integrated socio-demographic factors (6 questions) including the seniority and medical specialty of the HCP completing the questionnaire, their location and type of practice setting. (**section 3**)
- Part B measured HCP perceptions of the causes of health system burden and impact of health system disruption in the RSV peak season (12 questions). Survey questions utilised a 5-point Likert scale (1-Strongly Disagree to 5-Strongly Agree) with an additional open-ended question for free text comment. (**section 3.1**)
- Part C gathered data on health care resource utilisation for RSV bronchiolitis patients (33 questions). Questions included information on the respiratory attendances and admissions in the RSV season, viral testing of infants with bronchiolitis, protocols to contain health-stay related/nosocomial infection, and the current regimen of investigations and interventions for infant RSV bronchiolitis. (**section 3.2**)
- Part D gathered data on the mitigation plans and priorities for prevention in hospitals and the community (5 questions). Questions included the safety netting structure required to reduce the burden of RSV bronchiolitis in the community, and the measures in place to shorten the length of stay for RSV infected patients. (**section 4**)

The length of the questionnaire varied by care setting. The average time for completion ranged from 8 mins (questionnaire 1: primary care) to 15 mins (questionnaire 3: paediatric general wards). The survey questions were independently reviewed by the focus group over two meetings taking place on 16 July and 19 July 2021. The survey underwent pre-testing for clarity, comprehension, language consistency, and ease of administration. It was built in the open access QuestionPro survey software and the link was pilot tested to evaluate online functionality and flow.

SEASONAL COVERAGE

The survey questions covered the RSV-related healthcare consumption and HCP experiences of the last three RSV seasons – 2018/19, 2019/20, 2020/21.

DEFINITIONS

We used descriptive categories, characterising RSV patients by disease severity ("infants with RSV bronchiolitis", infants with bronchiolitis brought to the Emergency Department", "infants with bronchiolitis requiring general admission", "infants with severe bronchiolitis requiring PICU admission").

2.4 SURVEY ADMINISTRATION

In August 2021, an electronic, structured English language survey was distributed to HCPs through email, membership newsletters, and e-zines of professional medical associations specifically contacted for this study. The survey was distributed by 40 European professional medical associations and organisations representing medical specialities in primary care, emergency medicine, paediatrics, paediatric infectious disease, respiratory medicine, and specialist nursing (listed in the acknowledgements). In addition, the survey was promoted on the EHMA website the EHMA newsletter, and on relevant social media platforms. The administration of the survey complied with GDPR requirements.

2.5 CONTENT VALIDATION & WHITE PAPER DEVELOPMENT

The white paper was developed through an iterative process of discussion, review, and content validation, with focus group members, scientific experts, and project sponsors. The emerging themes and preliminary survey results were presented and deliberated upon at expert roundtables at the EHMA conference in September 2021 and the Excellence in Paediatrics conference in Amsterdam, in December 2021.

3 SURVEY RESULTS

KEY TAKE-AWAYS

We received 380 completed responses from healthcare professionals.

The survey respondents comprise different grades of healthcare professionals, working within the community (individual practice to hospital EDs) and in different varieties of hospitals (university hospitals and community hospitals), and specialities (general practice and family medicine, inpatient paediatrics, emergency medicine, intensive care medicine), suggesting that the data are applicable to health systems across Europe.

SURVEY RESPONSES

We received responses from 982 HCPs, of whom 380 completed the questionnaire.

BY COUNTRIES

There were 380 completed responses. We received 374 responses from 20 countries in Europe: 79 from Spain, 46 from the UK, 34 from Belgium, 29 from Italy, 25 from Sweden, 24 from Switzerland, 23 from France, 19 in Portugal, 18 from Ireland, 16 from Romania, 15 from Croatia, 14 from Finland, 13 from Germany, 7 from the Netherlands, 5 from Austria, 3 from Slovenia, and 1 from Estonia, Luxemburg, Moldova, Serbia each. We received 4 from Asia/Middle East (2 from Turkey, 1 from Israel, Bahrain); and 2 from Africa (1 each from Algeria and Nigeria).

Spain	79
United Kingdom	46
Belgium	34
Italy	29
Sweden	25
Switzerland	24
France	23
Portugal	19
Ireland	18
Romania	16
Croatia	15
Finland	14
Germany	13
Netherlands	7
Austria	5
Slovenia	3
Estonia	1
Moldova	1
Luxembourg	1
Serbia	1
Others	6

Respondents by country (n=380)

BY CARE SETTINGS

There were 224 (59%) completed responses from the community setting and 156 (41%) completed responses from the inpatient setting.

From the outpatient settings, we received: 55 responses from Spain, 28 from Italy, 26 from the UK, 19 from France, 18 from Switzerland, 11 from Portugal, 10 from Germany, 9 from Romania, 9 from Croatia, 8 from Ireland, 8 from Sweden, 7 from Finland, 4 from Belgium, 3 from the Netherlands, 2 from Austria, 2 from Slovenia, 1 from Estonia, 1 from Moldova. The remainder were from outside Europe.

The inpatient respondent demographics were divided as follows: 30 from Belgium, 24 from Spain, 20 from the UK, 17 from Sweden, 10 from Ireland, 8 from Portugal, 6 from Switzerland, 6 from Croatia, 7 from Finland, 7 from Romania, 4 from France, 4 from Netherlands, 3 from Germany, 3 from Austria, 1 each from Italy, 1 from Luxembourg, 1 from Serbia, 1 from Slovenia. The remainder were from outside Europe.

BY PRACTICE SITES

Outpatient respondents represented a variety of practice sites in the community. Of the 224 respondents from outpatient settings, we received: 25% (55) responses from individual practice, 25% (55) responses from small group practice (5 or fewer physicians), 24% (54) from large group practice of 6 or more physicians, 21% (48) from hospital emergency departments, 3% (7) from pre-hospital settings (e.g., urgent care centre), and 1% (2) were from ambulatory services, 1% (3) from other primary care settings (e.g., paramedics).

Different variety of hospitals are represented in the survey. Of the 156 respondents in hospitals, 36% (56) worked in university hospitals, 30% (47) in secondary hospitals, 14% (22) in tertiary/ referral hospitals, 14% (22) in specialised children's hospitals each, and 6% (9) in community hospitals.

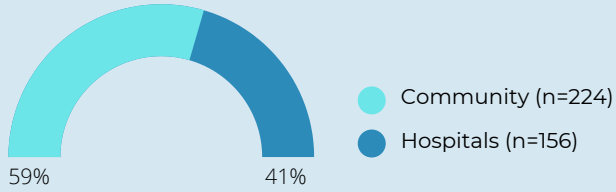
BY MEDICAL SPECIALTY

General paediatricians comprised nearly one-half of the total survey respondents. There were 45% (171) general paediatricians, 19% (72) general practitioners (GPs) and family physicians, 11% (42) hospital paediatricians, 7% (27) ICU physicians, 6% (23) nurses, 4% (15) emergency physicians, 3% (11) infectious disease specialists, 2% (8) neonatologists, 2% (8) respiratory medical specialists, 1% (3) internal medicine.

BY PROFESSIONAL EXPERIENCE

Over half of the responses 55% (209) were received from senior professionals with 20 or more years of clinical experience. 14% (53) respondents had 15-19 years of practice while 18% (68) respondents had 10-14 years. 10% (38) responses came from more junior HCPs with 5-9 years of work experience, and 3% (12) respondents had worked for less than 5 years.

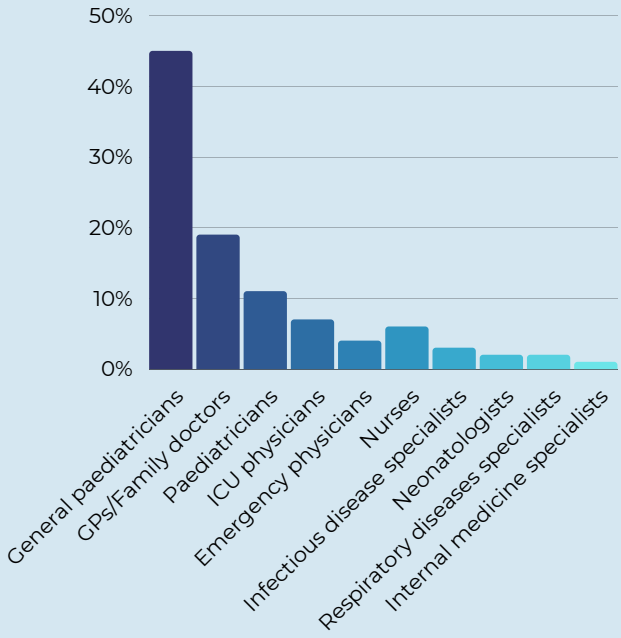
Respondents by care setting (n=380)



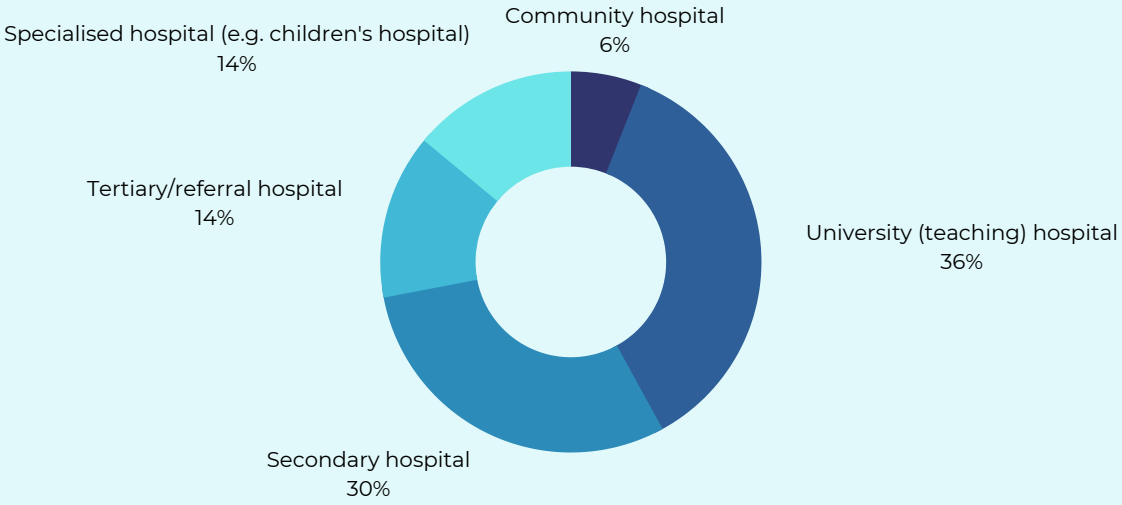
Respondents by years of experience (n=380)

20+ years	55%
15-19 years	14%
10-14 years	18%
5-9 years	10%
Less than 5 years	3%

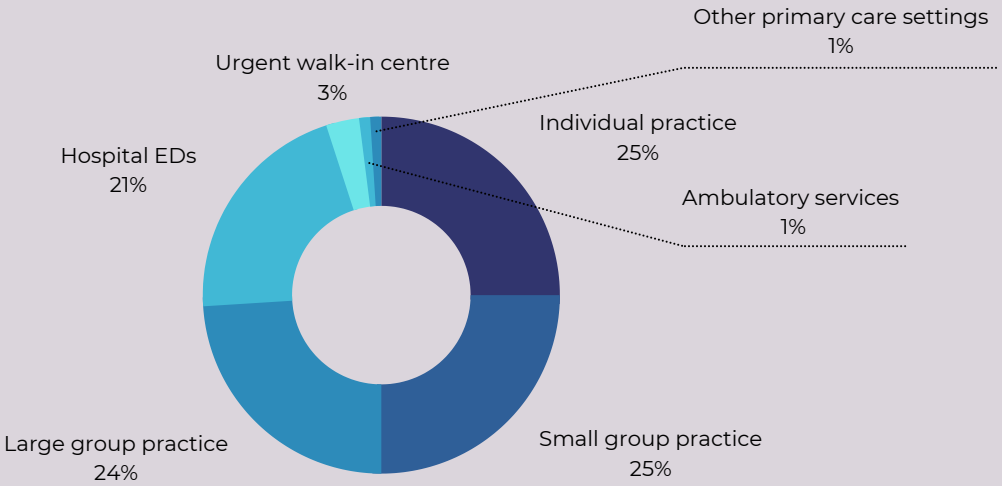
Respondents by medical specialty (n=380)



Inpatient respondents by practice settings (n=156)



Outpatient respondents by practice settings (n=224)



3.1 HEALTH SYSTEM DISRUPTION DUE TO RSV

KEY TAKE-AWAYS

The burden and disruption of RSV to health systems is significant and system-wide and affects all care settings. 89% of respondents consider RSV's disruptive effects is moderate to extreme. But while the increased healthcare demand by RSV patients is a disruptive factor common across all care settings, we find that its manifestation is markedly different across the care spectrum.

Workforce issues are a major contributor to the pressures observed on healthcare systems, affecting health system performance. In our survey results we observed that a majority of respondents believed that the increased workload at the peak RSV season contributed to excess levels of work-related stress and exhaustion and predisposed them to burnout.

Primary care is the first point of contact for paediatric health needs, and how they manage the increased healthcare demand in the RSV season has consequences in other care settings. Our respondents report significant delays to elective care and specialist-led treatment, as the top impacts of the RSV-associated disruptions to health system performance.

Within hospitals, bed capacity is a major contributor to backlog of paediatric patient care with cross-cutting effects across the hospital system. Survey respondents report high bed occupancy to be the major contributor of RSV-associated disruptions to the hospital system.

3.1.1 OVERALL IMPACT OF RSV ON HEALTH SYSTEM PERFORMANCE

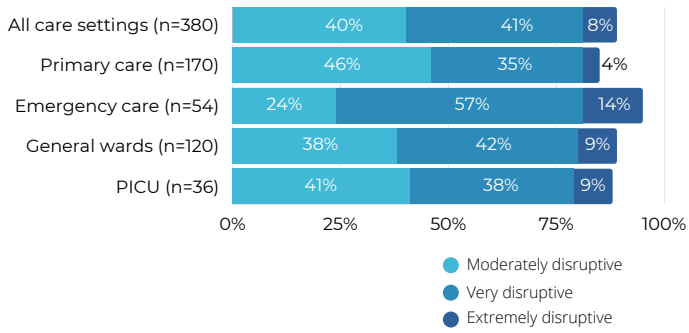
The seasonality of RSV is a strong factor bearing on health system performance. RSV has a well-defined seasonality in temperate countries [23]. In Europe, the RSV season runs from October to March [24], [25]. The peak rise in infections is concentrated to a 4-to-6 week window towards the end of the year, with a peak of hospitalisations, office and emergency visits occurring within a small spate of time [26],[27]. The resultant surge in demand for health and care services (i.e., the winter pressures) results in significant delays for patient care, deteriorated working conditions for healthcare professionals, and other disruptions to optimal healthcare performance.

The survey finds that the burden and disruption of RSV to healthcare systems is significant and system-wide, and affect all care settings. 89% of respondents consider the disruption to health system performance in the peak of the RSV season is moderate to extreme. (**Graph 1**)

The EHMA survey results indicate that the increased incidence of respiratory infection is the common and disruptive factor affecting health systems in the peak RSV season. Overall, the system saturation caused by the rise in respiratory illnesses in the peak RSV season has an adverse impact on the ability to deliver timely and quality care to patients in both primary and secondary care. But while the challenges of increased patient demand affect all care settings, their manifestations vary across the care spectrum.

Graph 1. Health systems under pressure

Average disruption to health system performance in peak RSV season (% of respondents)



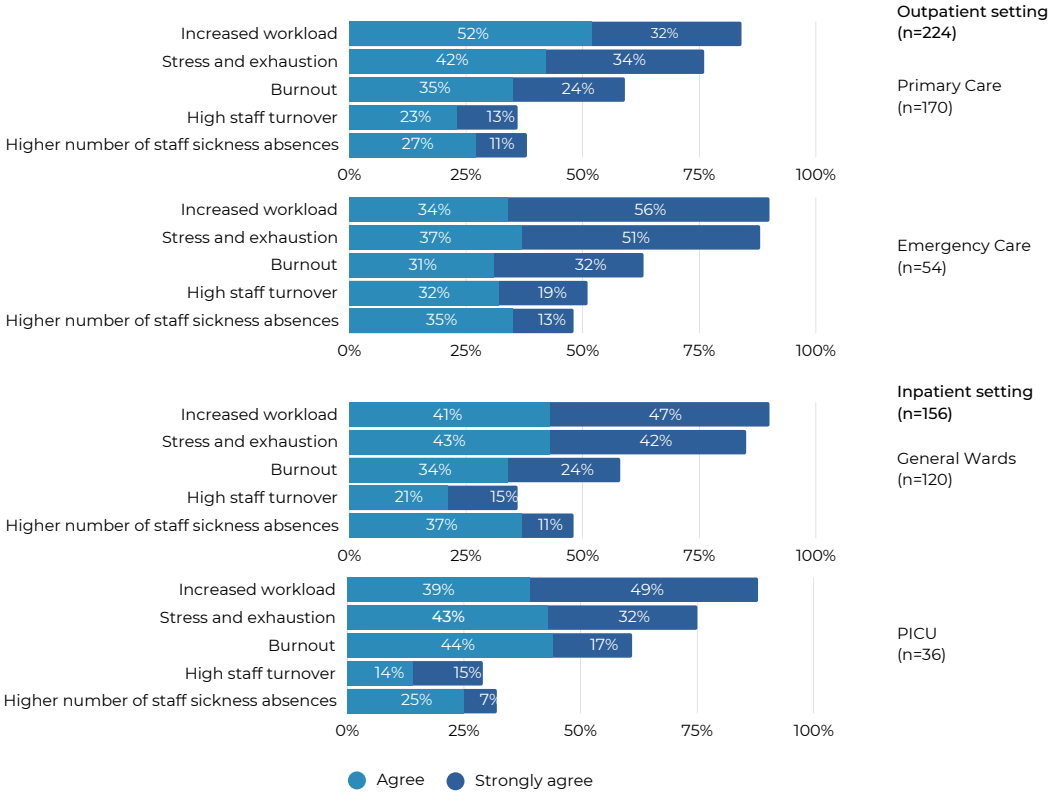
3.1.2 WORKFORCE CHALLENGES RELATED TO RSV

The EHMA survey found that the healthcare workforce is most severely impacted in the peak of the RSV season. Respondents across all care settings reported that increased workloads, high levels of stress and exhaustion contribute to burnout. Within the outpatient setting, 84% of respondents in primary care and 90% of respondents in the ED agree/strongly agree that an increased workload is a leading impact of the RSV season. In hospitals, 88% of respondents in paediatric general wards and 88% of respondents in the paediatric intensive care units (PICU) similarly agree/strongly agree that increased workloads is a leading impact of the RSV season. The impact of these challenges causes excess levels of work-induced stress and exhaustion and contributes to burnout. In the outpatient settings, 76% of respondents in primary care and 88% of respondents in the ED rank stress and exhaustion as a top impact of the RSV season. In hospitals, 85% of respondents in paediatric general wards and 75% of respondents in the PICU consider stress and exhaustion to be a top impact of the RSV peak season. (**Graph 2**)

Similarly, 59% of respondents in primary care and 63% in the ED report the increased work pressures of the RSV season contribute to burnout. Similarly, within the hospital setting 58% for respondents in paediatric general wards and 61% of respondents in the PICU report experiencing burnout (even though multifactorial).

Graph 2. Workforce challenges across care settings

Perceptions of the average health system disruption on staff performance
(% of respondents)



3.1.3 DISRUPTION OF OUTPATIENT CARE DUE TO RSV

PRIMARY CARE

76% of respondents in primary care report an increase in paediatric consultations for respiratory infections, 69% of respondents report increased demand for GP consultations, and 67% of respondents report the increased demand due to RSV-related complications (e.g., "asthma, recurrent wheezing and other breathing difficulties"). (**Graph 3**)

The scale of impacts on primary care may differ by geographical area and the GP practice size, but regardless of these differences, increased work hours to meet patient needs is commonly reported. 79% of respondents in primary care report increased work hours in the peak of the RSV season. (**Graph 4**)

Peaks in healthcare demand on primary care in the RSV season have a knock-on effect throughout the system and considering that the bulk of bronchiolitis cases pass through the primary care agencies, how well the outpatient setting copes with the increased demand has consequences in other care setting. Specifically, 67% of respondents report an increase in urgent GP referrals to the ED and 45% of respondents report delays to elective care. (**Graph 4**)

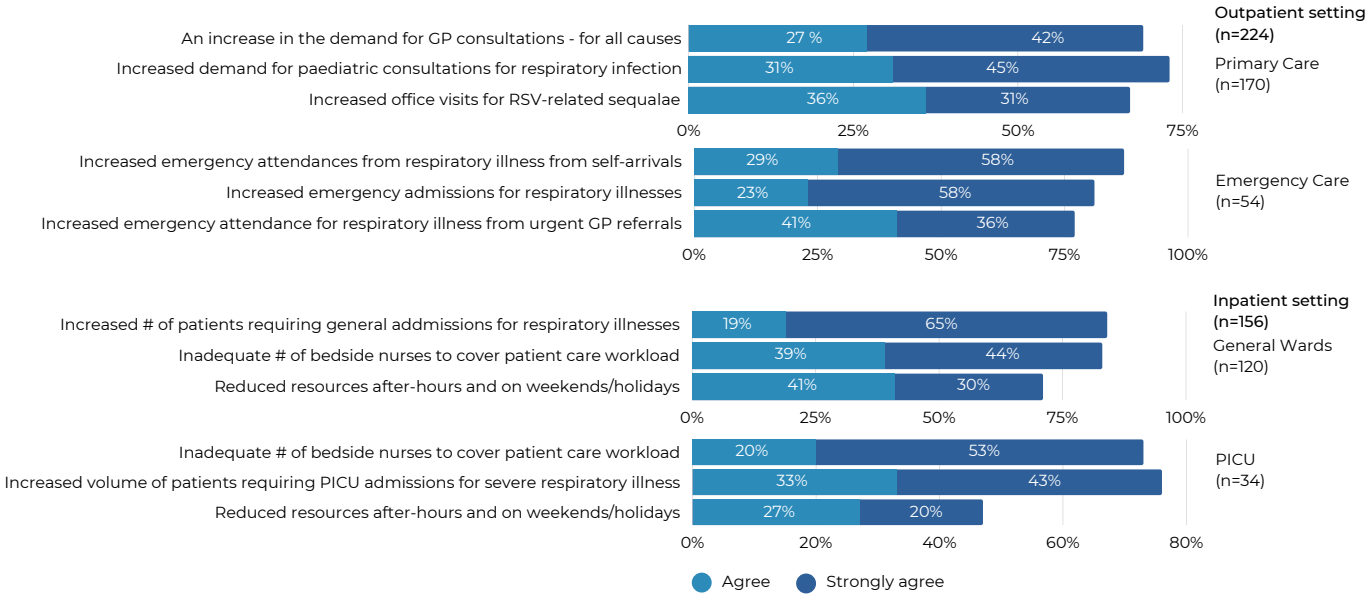
EMERGENCY CARE

In the Emergency Departments (ED), the increase in visits and admissions attributed to respiratory illnesses is the leading cause of health system disruption during the peak of the RSV season. 87% of the survey respondents in the ED report increased paediatric emergency attendances from self-referrals, 81% of respondents report increased emergency admissions for respiratory illnesses, and 77% of respondents report increased emergency attendances for respiratory illnesses from urgent GP referrals, as the leading sources of service saturation in the ED. (**Graph 3**)

Increased patient wait times in the EDs are the most visible indicator of health system performance deterioration during the peak of the RSV season. 81% of respondents in the ED report increased patient waits as the top consequence of RSV-associated health system disruption. Along the same line, respondents list the general deterioration of standards and delays to care as further impacts of RSV. These include: increased nosocomial risk for patients (75%), reduced patient safety (70%), and delayed clinical assessment of patients (64%). (**Graph 4**)

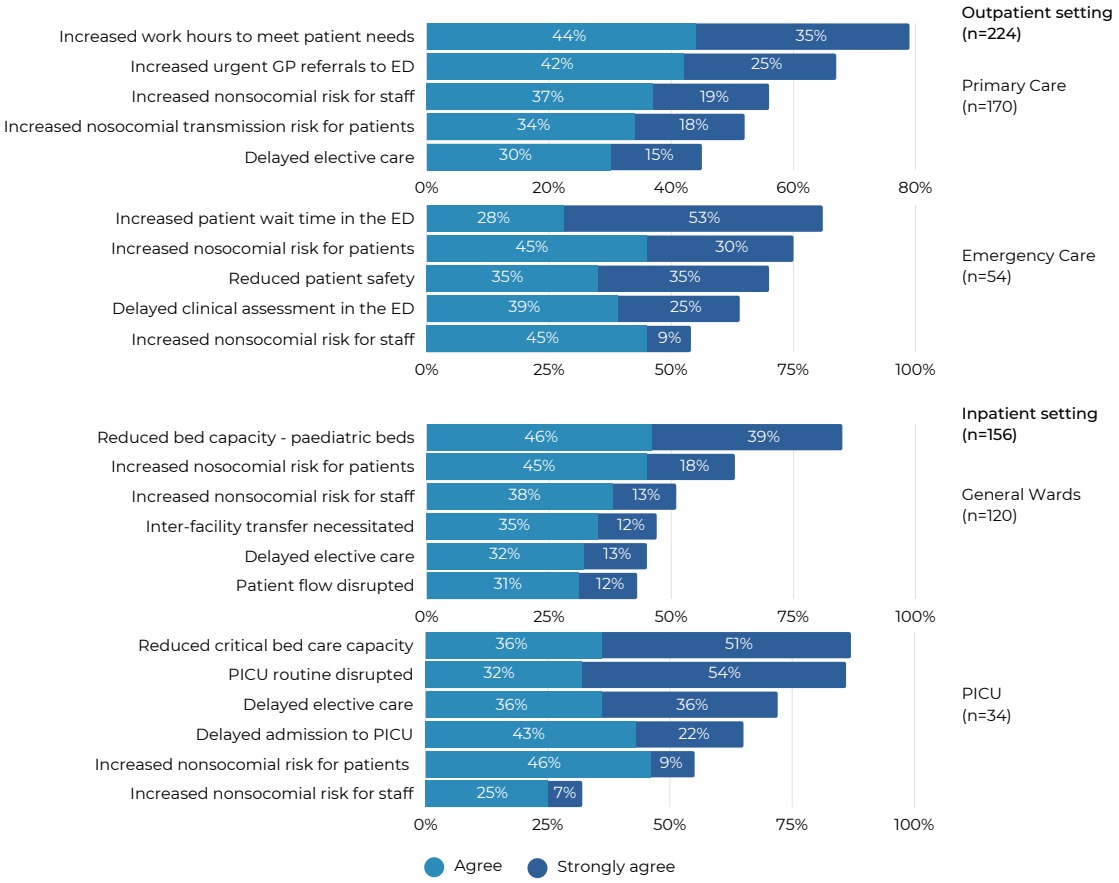
Graph 3. Health system burden across care settings

Perceptions of contributors to RSV-related health system burden
(% of respondents)



Graph 4. Disruption across care settings

Perceptions of the impact of RSV-associated health system disruption (% of respondents)



3.1.4 DISRUPTION TO INPATIENT/HOSPITAL CARE DUE TO RSV

PAEDIATRIC GENERAL WARDS

The leading causes of health system disruption in paediatric general wards due to RSV were as follows: 84% of respondents agreed/strongly agreed the increase in paediatric admission for respiratory illnesses, 83% respondents reported inadequate number of bedside nurses to cover increased patient workload, and 71% respondents reported reduced resources afterhours and on weekend/holidays. (**Graph 3**)

Reduced bed capacity is a major contributor to backlog of patient care in hospitals, with cross-cutting effects on optimal hospital performance. The leading impacts of disruption in paediatric general wards reported by respondents were as follows: 85% of respondents reported reduced paediatric general bed capacity, 63% of respondents reported increased nosocomial risk for patients, and 51% respondents reported increased nosocomial risk for staff. (**Graph 4**)

PAEDIATRIC INTENSIVE CARE UNITS (PICU)

The leading causes of health system disruption in paediatric intensive care units (PICU) due to RSV were as follows: 76% of respondents reported the increased volume of patients requiring PICU admissions for severe respiratory illness, 73% respondents reported inadequate number of bedside nurses to cover increased patient workload, and 47% respondents reported reduced resources afterhours and on weekend/holidays. (**Graph 3**)

Reduced bed capacity and severe disruptions to patient flow in the paediatric intensive care units were the leading impacts of RSV infection. The leading impacts of disruption in the PICU as reported by respondents were as follows: 87% respondents reported reduced paediatric intensive care bed capacity, 86% respondents reported disruptions to PICU routine, 72% reported delayed elective care, 65% reported delayed admissions to the PICU, 55% reported increased nosocomial risk for patients. (**Graph 4**)

3.2 HEALTHCARE RESOURCE USE DUE TO RSV

KEY TAKE-AWAYS

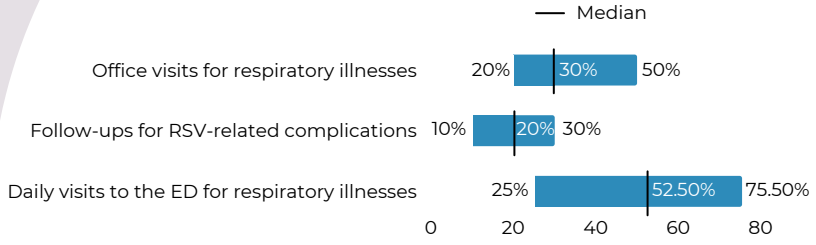
Survey results confirm that RSV-related respiratory illnesses significantly increase outpatient services demand in the peak RSV season. Survey respondents report a median increase of 30% in primary care office visits for respiratory illnesses, and a median increase of 20% in paediatric office visits for follow-up on RSV-related complications. Survey respondents report a median increase of 52.5% in daily attendances to the Emergency Departments (ED) for respiratory illnesses at the peak RSV season.

RSV infection stretches paediatric hospital capacity. Survey respondents report RSV patients occupied 54%, 45%, and 28% of paediatric general beds, and 54%, 36%, and 8% of paediatric intensive care unit (PICU) beds, in the peak RSV season for 2018/19, 2019/20, and 2020/21 respectively.

The EHMA results find that the variability in paediatric RSV infection management is high. Survey respondents report a wide degree of variability in the primary methodologies used for viral testing of bronchiolitic infants, the protocols for inpatient infant isolation, and the management and treatment of RSV infection in the community and hospitals.

Little consensus exists on the best management strategies for RSV infection, and treatment varies substantially across practice settings. The EHMA survey results find that infants with RSV bronchiolitis routinely receive medications (e.g., antibiotics) despite a lack of evidence on their efficacy to treat RSV infection and undergo unnecessary investigations (e.g., chest X-rays, blood gas). The frequent use of corticosteroids, bronchodilators, and salbutamol is not evidence-based nor effective and even sometimes not recommended. This is an additional cost and burden to the health system, and potentially to caregivers.

Graph 5. Increase in outpatient visits attributed to respiratory causes (%) in peak RSV season (n=224)



3.2.1 COMMUNITY/OUTPATIENT HEALTHCARE RESOURCE USE DUE TO RSV

PRIMARY CARE

The EHMA survey confirms that RSV-related respiratory illnesses significantly increase outpatient services demand particularly during the peak of the RSV season. Survey respondents in the primary care setting report a median increase of 30% in paediatric office visits for respiratory illnesses in the peak RSV season (interquartile range [IQR], 20-50%). Respondents report a median increase of 20% in paediatric office visits for follow-up appointments relating to RSV-related complications (IQR, 10-30%). (**Graph 5**)

EMERGENCY CARE

The reported pressures on the Emergency Departments (ED) are considerably higher. Survey respondents report a median increase of 52.5% in daily visits for respiratory illnesses at the peak of the RSV season (IQR, 25-75.5%). (**Graph 5**)

3.2.2 HOSPITAL/INPATIENT HEALTHCARE RESOURCE USE DUE TO RSV

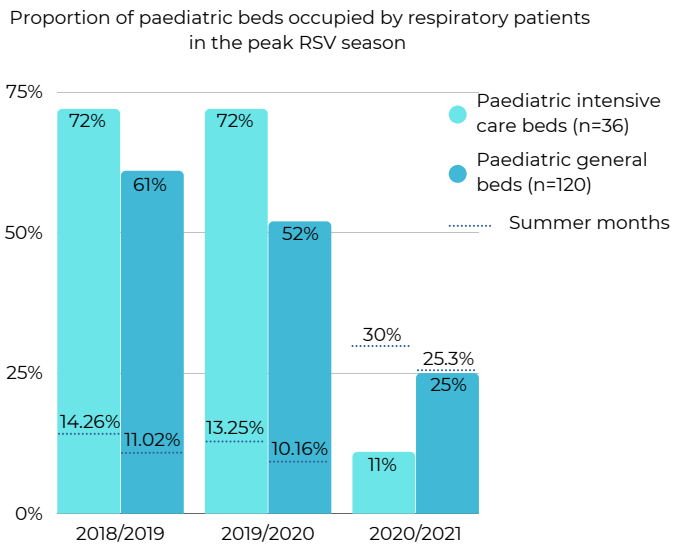
PAEDIATRIC GENERAL WARDS

In the paediatric general wards, survey respondents report that respiratory patients occupied 61%, 52% and 25% of paediatric general beds in the peak RSV season (Oct.-Mar.) for 2018/19, 2019/20 and 2020/21 respectively. In the summer, the paediatric general bed occupancy for respiratory patients were 11%, 10% and 25% for the same period: 2018/19, 2019/20, and 2020/21 respectively. (**Graph 6**)

Survey respondents report that RSV patients occupied 54%, 45%, and 28% of paediatric general beds in the peak RSV season (Oct.-Mar.) for 2018/19, 2019/20 and 2020/21, respectively.

The reported average median length of stay (LOS) for paediatric RSV patients in the paediatric general ward was: 4.18 inpatient days for RSV patients without comorbidities and 8.63 days for high-risk RSV patients with comorbidities (e.g., extreme prematurity, neuromuscular diseases, chronic heart disease or CHD, immunodeficiency, bronchopulmonary dysplasia or BPD).

Graph 6. Bed occupancy for respiratory patients (n=156)



PAEDIATRIC INTENSIVE CARE UNIT (PICU)

In the PICU, survey respondents report that respiratory patients occupied 72%, 72%, and 11% of paediatric intensive care beds in the RSV season (Oct.-Mar.) for 2018/19, 2019/20 and 2020/21 respectively. In the summer, the paediatric intensive care bed occupancy was 14%, 13%, and 30% for the same period: 2018/19, 2019/20, 2020/21 respectively. (**Graph 6**)

Survey respondents report that RSV patients occupied 54%, 36%, and 8% of paediatric intensive care beds in the RSV season (Oct.-Mar) for 2018/19, 2019/20 and 2020/21.

The reported average median LOS for paediatric RSV patients in the paediatric intensive care unit was: 4.5 inpatient days for RSV patients without comorbidities and 8.33 days for high-risk RSV patients with comorbidities (e.g., extreme prematurity, neuromuscular diseases, chronic heart disease, immunodeficiency, broncho-pulmonary dysplasia or BPD).

Survey respondents reported that on average 25% of RSV inpatients in the PICU required mechanical ventilation.

3.2.3 MANAGEMENT OF PAEDIATRIC RSV IN HOSPITALS AND IN THE COMMUNITY

HEALTH-STAY RELATED/ NOSOCOMIAL RSV INFECTIONS

Containment of health-stay related/ nosocomial RSV infection is an urgent, yet unevenly addressed priority. Within hospitals, separate cubicles for each infant were the most commonly reported means of infant isolation protocol for RSV-positive infants. By care settings, these figures are as follows: in the emergency department (ED), 61% of respondents report the use of separate cubicles for infants testing positive for RSV, influenza, and other viruses, 33% of respondents report the 'contact isolation' of infants with bronchiolitis in the same room, and 6% of respondents use other infant isolation policies.

In the paediatric general wards, 80% of respondents report the use of separate cubicles, 15% of respondents report contact isolation, and 6% of respondents report the use of other infant isolation policies. In the paediatric intensive care units (PICU), 58% of respondents report the use of separate cubicles, 30% of respondents report the use of contact isolation of bronchiolitic infants, and 12% of respondents report the use of other infant isolation policies. "Other isolation policies" mentioned include droplet isolation of bronchiolitic infants.

TESTING

Infants suffering from bronchiolitis are routinely tested for the causal agent in the inpatient setting. 72% of survey respondents recommended respiratory virus testing for all infants hospitalised for bronchiolitis, 5% of respondents advised virus testing for infants admitted to the PICU, and 21% of respondents advised virus testing for all infants with bronchiolitis going to the ED. Only 2% of respondents advised against taking respiratory sample from any infant.

RT-PCR (reverse transcription polymerase chain reaction) tests are reported as the primary test methodology for RSV detection

in hospitals. 50% of respondents reported the use of RT-PCR tests to test for RSV infection, 35% of respondents reported the use of antigen test by rapid detection, and 12% of respondents reported the use of antigen test by EIA (enzyme immunoassays).

60% of respondents reported the respiratory sample was collected by nasopharyngeal aspirates or washes and 92% of respondents reported the respiratory sample was sent to the hospital microbiology or virology laboratory for testing. 26% of respondents report that samples were routinely tested for RSV, influenza, and other respiratory viruses, 30% responded the samples were tested for only SARS-CoV-2, and 21% responded the samples were tested only for influenza, and 23% responded the samples were tested for only RSV.

INVESTIGATIONS FOR BRONCHIOLITIS

Infants suffering from bronchiolitis often undergo unnecessary investigations such as blood gas analysis, chest X-rays, despite a lack of evidence for their efficacy. The number of respondents performing blood gas analysis on each patient group are as follows: 60% of respondents responded they performed blood gas analysis on "all infants with severe bronchiolitis requiring PICU admission"; 26% on "most infants suffering from bronchiolitis requiring paediatric general hospital admission"; 12% on "all infants with bronchiolitis going to the emergency department (ED)"; and 2% of respondents responded they do not perform blood gas analysis on "infants hospitalised with bronchiolitis". The number of respondents ordering chest X-rays for each patient group are as follows: 72% of respondents ordered chest X-rays for "all infants with severe bronchiolitis requiring PICU admission"; 16% of respondents ordered chest X-rays for "most infants with bronchiolitis requiring paediatric general hospital admission"; 8% on "all infants with bronchiolitis going to the emergency department (ED)"; and 4% of respondents responded they do not perform chest X-rays on" infants hospitalised with bronchiolitis".

SUPPORTIVE THERAPIES

The survey responses indicate profound differences in European health systems in their inpatient management of RSV bronchiolitis in infants. Survey respondents indicated considerable variability in their internal practice guidelines concerning the regular level of oxygen saturation that requires to administer supplementary oxygen. 70% of respondents administered supplemental oxygen at <90-92% of oxygen saturation. 30% of respondents administered supplemental oxygen at <93-95% of oxygen saturation.

Supportive care is reported as the mainstay of RSV treatment in the inpatient setting, with an emphasis on fluid replacement and oxygen therapy. 78% of respondents reported administering supplemental oxygen to most infants with bronchiolitis in the hospital paediatric general wards, and 63% to infants with severe bronchiolitis admitted to the PICU. 76% of the respondents administered hydration and nutritional support to most infants hospitalised with bronchiolitis in the paediatric general wards, and 63% administered hydration and nutritional support to patients suffering from severe bronchiolitis requiring PICU admission.

In addition, upper airway suctioning via the High Flow Nasal Cannula (HFNC) and continuous positive airway pressure (CPAP) was reported by 56% of respondents for infants hospitalised in the paediatric general wards and by 50% of respondents for infants hospitalised in the PICU.

PHARMACOLOGICAL INTERVENTIONS

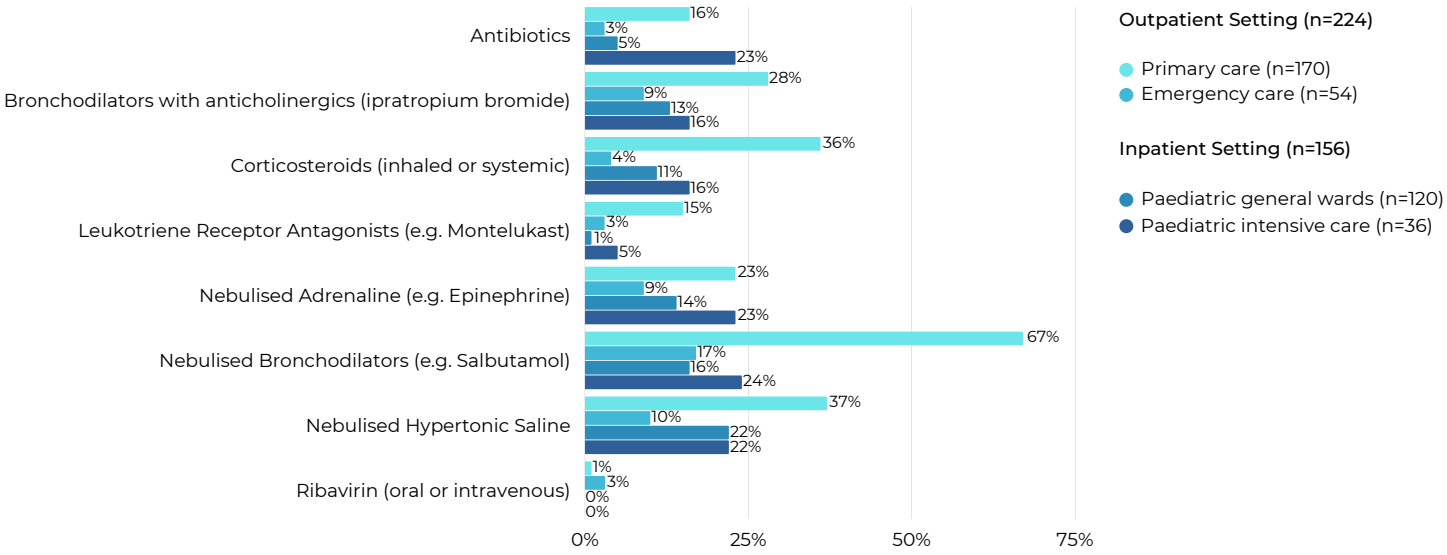
Pharmacological interventions and prescriptions for managing bronchiolitis in infants vary greatly across regions and practice sites.

Within hospitals, bronchodilators with β2-agonist (salbutamol) and anticholinergics (ipratropium bromide), and epinephrine were the most common pharmacological interventions: 14% of respondents in the paediatric general wards and 23% of respondents in the paediatric intensive care units (PICU) prescribed epinephrine to treat RSV bronchiolitic infants; salbutamol was used by 16% of respondents in the paediatric general wards and 24% of respondents in the PICU, and nebulised hypertonic saline by 22% of respondents in both paediatric general wards and the PICU. Comparable figures for ipratropium bromide were 13% in general wards and 16% in the PICU. (**Graph 7**)

Salbutamol is the most common intervention in primary care. 67% of respondents in primary care reported the use of salbutamol to manage RSV bronchiolitis in infants. Corticosteroids (inhaled and systemic) and nebulised hypertonic saline were also commonly prescribed in primary care: 37% of respondents in primary care report the use of nebulised hypertonic saline and 36% for corticosteroids, (**Graph 7**), not always efficacious or even recommended by medical guidelines.

The routine prescription of antibiotics used to treat RSV bronchiolitis in infants is concerning and can contribute to antimicrobial resistance. Antibiotic prescriptions to treat RSV bronchiolitis is reported for all care settings and is significant in primary care and paediatric intensive care units. 16% of respondents in primary care and 23% of respondents in PICU report the administration of antibiotics for treatment of RSV-bronchiolitis in infants, probably to prevent a subsequent bacterial infection. (**Graph 7**)

Graph 7. RSV management across care settings



4 RECOMMENDATIONS TO STRENGTHEN THE HEALTHCARE SYSTEMS' RESPONSE TO RSV

Building a RSV-prepared and RSV-resilient health system will call on a multisectoral approach. Having carefully assessed the health system disruption due to RSV (section 3.1) and the RSV-related healthcare resources use (section 3.2) in Europe, we identified five evidence-supported, actionable recommendations for healthcare systems to pursue in the future.

These are: broaden the understanding of RSV; maintain infection control measures; improve and expand diagnostic capability; standardise RSV infection management; and prepare for access to immunisation.

We believe that collectively acting upon these recommendations, together with policy makers and healthcare managers, has the potential minimise and contain the disruptive force of paediatric RSV on our health systems, alleviate the workforce strain, and benefit RSV patients and their caregivers.

4.1 BROADEN THE UNDERSTANDING OF RSV AMONG CAREGIVERS, COMMUNITIES, AND CLINICIANS

Caregivers and communities (e.g., schools, nurseries) should be equipped with basic information on the symptoms of RSV, its modes of transmission, and how to protect all infants from RSV, to mitigate the impact that RSV has on healthcare systems. To better manage RSV across care settings, healthcare professionals should be better equipped to understand the nature of RSV's circulation and how to manage it in an efficient way, based on the implementation of clinical practice guidelines and replication of good practices observed in the community and in hospitals. Policymakers should be made aware of the tremendous impact that RSV has on healthcare systems, how it disrupts system performance every year, and utilises healthcare resources, to be able to act upon that public health issue.

4.2 MAINTAIN INFECTION CONTROL MEASURES

COVID has highlighted the value of prevention measures such as limiting close contacts, adequate ventilation of community spaces, and consistent hand and respiratory hygiene, to control infectious diseases in an efficient way. The learnings from our COVID experience and the new approaches to infection control and prevention will be vital to building a RSV-prepared and RSV-resilient healthcare system. Such initiatives should be co-produced, promoted and optimised by intersectoral collaboration.

The prevention of nosocomial infection in the workplace was ranked a top priority of RSV infection management by respondents completing the survey. To contain them, it is vital to take and apply in a compliant way measures especially in the hospital setting.

The timely reporting, investigation, and root-cause analysis of hospital-acquired infection will also be key. Adequate provision, guidance, and training in the use of personal protective gear (PPE) is also needed. Such measures will also alleviate staff sick absences during the RSV season and help contain the onward transmission of hospital-acquired infection onto the community.

4.3 IMPROVE AND EXPAND DIAGNOSTIC CAPABILITY

Early diagnosis of RSV symptoms, based on the availability of convenient and affordable diagnostic tests, will be key to managing RSV infections, and overall improve RSV surveillance. The survey respondents identify the use of point-of-care tests (POCT) to inform cohort selection and clinical management as a clear priority of RSV prevention.

Early care is critical to manage properly RSV symptoms and complications. A combination of actions will be needed: creating more convenient and affordable diagnostic tests; and addressing logistical and procedural barriers, including delayed or incomplete reporting of test results.

HCP education will also be important to increase the uptake of available diagnostic tests. Clear guidance on when to test for RSV particularly as diagnosis and management of RSV-related disease varies from institution to institution.

4.4 STANDARDISE RSV INFECTION MANAGEMENT

At present little consensus exists on the best management strategies for RSV infection, and treatment varies substantially across practice settings. The EHMA survey results detect considerable variability in the management of RSV infection in infants. Specifically, the results indicate that bronchiolitic infants routinely receive medications (e.g., antibiotics) and undergo unnecessary investigations (e.g., chest X-rays, blood gas) despite a lack of evidence in their efficacy to treat RSV infection. The frequent use of corticosteroids, bronchodilators, and salbutamol is not evidence-based nor effective. This is an additional cost and burden to the health system, and potentially caregivers.

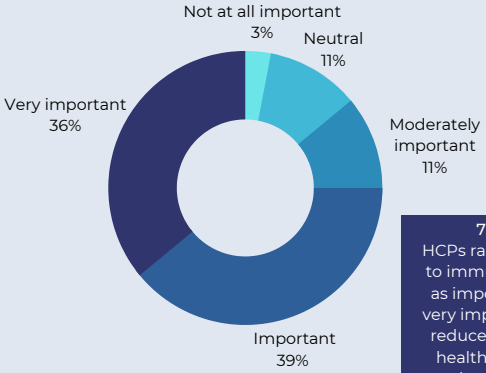
4.5 PREPARE FOR ACCESS TO IMMUNISATION

Access to immunisation for all infants is key to the RSV prevention landscape. There is a widespread agreement among the HCPs surveyed on the crucial importance of providing access to immunisation to reduce the health system burden and disruption due to RSV every year. 75% of respondents in hospitals and the community ranked access to immunisation, vaccines, or monoclonal bodies as an "Important" or "Very Important" solution to reduce the burden of RSV on healthcare systems. (**Graph 8**)

The development of new RSV vaccines, antiviral treatments, and monoclonal antibodies such as nirsevimab promise to improve and revitalise the RSV prevention and treatment landscape. But major changes will be needed in societal attitudes and to health systems, if new technologies are to achieve their full potential. We believe the use of new prevention tools must rest on education.

Since the threat of RSV to infants is still insufficiently understood by parents, and continues to be underreported in the community setting, it is vital to invest in the effort to inform caregivers, clinicians, and policy makers on the burden of RSV infection, and the importance of an effective RSV preventive strategy that extends protective cover to all infants.

Graph 8. Importance of immunisation (n=380)
Importance of access to immunisation to reduce the RSV health system burden (percentage of respondents)



75%
HCPs rank access to immunisation as important or very important to reduce the RSV health system burden.

5 CONCLUSION

Since the threat of RSV to infants is still insufficiently understood by parents, and continues to be underreported in the community setting, it is vital to invest in the effort to inform caregivers, clinicians, and policy makers on the awareness of the burden of RSV infections, and the importance of an effective RSV preventive strategy that extends protective cover to all infants to reduce the impact on the health system. Even as the ongoing COVID-19 continues to place unprecedented strain on finite public health capacity, the pandemic has highlighted the value of preventive measures (such as the use of personal protective equipment, consistent application of respiratory and hand hygiene) to control effectively infectious diseases, in hospitals and the community

EHMA's interest in the present study stemmed from EHMA's long-standing commitment to contribute to promoting resilient healthcare systems and infrastructure, to contribute to the evidence-base and share knowledge in the field of health management, and implement research findings into practice.

The survey finds clear evidence on the health system burden and disruption of paediatric RSV and the widespread agreement in the HCP community that providing access to immunisation is key to reducing the RSV burden. 89% of respondents consider the disruption of RSV to be moderate to extreme and it affects all care settings.

Specifically, the seasonality of RSV is a strong factor impacting on optimal health system performance. The peak rise in RSV infections occur between October to March in Europe. This results in acute pressure on primary care providers, emergency services and paediatric hospital capacity. Within the outpatient setting, in the RSV season survey respondents report median increase of 30% in primary care office visits for respiratory illnesses, a 20% increase for follow-up on RSV-related complications, and a 52.5% increase in daily attendances to the Emergency Departments (ED) for respiratory illnesses. In the inpatient setting, RSV patients occupied 54%, 45%, and 28% of paediatric general beds, and 54%, 36%, and 8% of paediatric intensive care unit (PICU) beds, in the RSV peak season of 2018/19, 2019/20, and 2020/21 respectively.

Increased demand for health care services due to RSV infection impacts on health system performance in both inpatient and outpatient settings. In paediatric hospitals, the increase in RSV inpatients leads to reduced bed capacity, severe disruptions to patient flow, and delays to elective surgery. In primary and emergency care, the health system impact of RSV is evident causing significant delays to care of chronic conditions, increased patient wait time for elective surgeries and other specialist-led treatment.

Moreover, the study finds that most infants are not optimally managed and routinely undergo unnecessary investigations and receive treatments (e.g., antibiotics) of doubtful efficacy, potentially by contributing to antimicrobial resistance. This is an avoidable and additional public health burden.

The learnings from the COVID-19 experience, together with the results of the EHMA survey will be critical to building RSV-resilient healthcare systems. As the survey results highlight, prioritising RSV prevention programmes for all infants with the new immunisation tools in the short-term horizon is key.

This type of prevention programme will help render European health systems more resilient, addressing one of the goals for the European Health Union, for stronger health crises preparedness and response. In addition it will relieve the recurrent seasonal pressure that RSV has on both hospitals and outpatient care.

6 ABBREVIATIONS

AHPs, Allied healthcare professionals;
ALRTI, Acute lower respiratory tract infection;
BPD, Bronchopulmonary dysplasia;
CHD, Chronic heart disease;
CPAP, Continuous positive airway pressure;
ED, Emergency department;
EIA, Enzyme immunoassays;
FDs, Family doctors;
GPs, General practitioners;
HCP, Health care professionals/practitioners;
HFNC, High flow nasal cannula;
ICU, Intensive care unit;
IPC, Infection prevention and control;
IQR, Inter quartile range;
LOS, Length of stay;
LRTI, Lower respiratory tract infection;
mAbs, Monoclonal antibodies;
NICE, National Institute of Health and Care Excellence, UK;
NPI, Non pharmacological interventions;
PCPs, Primary care paediatricians;
PICU, Paediatric intensive care unit;
POCT, Point-of-care-tests;
PPE, Personal protective equipment;
RSV, Respiratory syncytial virus;
RT-PCR, Reverse transcription polymerase chain reaction.

7 ACKNOWLEDGEMENTS

We are grateful for their contribution to EHMA white paper on the burden of RSV to health systems:

Professor Javier Díez-Domingo, MD
Centre of Public Health Research of Valencia-FISABIO, Spain.
Professor Susanna Esposito, MD
University of Parma, Italy.
Dr Sarah Marchal, MD Hopitaux Pédiatriques Nice CHU-Lenval, France.
Dr Simon Nadel, Imperial College Healthcare NHS Trust, UK.
Professor Dr. med. Arne Simon, MD
Saarland University Hospital, Germany.

The survey was distributed through the following European scientific societies, HCP member associations, and RSV research consortia. We are grateful to them for their support of this research, and to their members for participating in the survey.

In Europe, the European Academy of Pediatrics (EAP); European Children's Hospitals Organization (ECHO); European Confederation of Primary Care Pediatricians (ECPCP); European Forum of Primary Care (EFPC); European Junior Doctors (EJD); European Public Health Association (EUPHA); European Specialist Nurses Association (ESNO); European Society of Pediatric Neonatal Intensive Care (ESPNIC); European Union of GPs/Family Physicians (UEMO); Respiratory Syncytial Virus Consortium in Europe (RESCEU); Respiratory Syncytial Virus Network (ReSViNet); World Association for Infectious Diseases and Immunological Disorders (WAIDid).

In Belgium, Association professionnelle belge des Pédiatres- Belgische beroepsvereniging van Kinderartsen (VBS/GBS); Sociéte Belge de Pédiatrie/ Belgische Vereniging voor Kindergeneeskunde (BVK/BSP); Nationaal Verbond van Katholieke Vlaamse Verpleegkundigen en Vroedvrouwen (NVKVV).

In Finland, the Suomen Lastenlääkäriyhdistys.

In France, Association Francaise de Pediatrie Ambulatoire (FPS), Syndicat National des Pédiatres Français (AFPA).

In Germany, the Berufsverband der Kinder- und Jugendärzte (BVKJ); Duetsche Gelleschaft für Pädiatrische Infektiologie (DGPI); Berufsverband der Kinderkrankenpflege Deutschland (BeKD); the Gessellschaft für Pädiatrische Pneumologie (GPP).

In Italy, Associazione Culturale Pediatri (ACP); Societa' Italiana di Pediatria delle Cure Primarie (SICUPP); Federazione Italia Medici Pediatria (FIMP); Società Italiana per le Malattie Respiratorie Infantili (SIMRI).

In Portugal, Associação Portuguesa de Medicina Geral e Familiar (APMGF); Secção de Pediatria Ambulatória da Sociedade Portuguesa de Pediatria (SPA-SPP).

In Romania, Societatea Naţională de Medicina Familiei (SNMF); Societatea Romana de Pediatrie Sociala (SRPC).

In Spain, Asociacion Española de Pediatria de Atencion Primaria (AEPap); Sociedad Española de Pediatría de Atención Primaria (SEPEAP); Consejo General de Colegios Oficiales de Medicos Nacional de Médicos de Atención Primaria Rural (CGCOM); La Asociación Española de Pediatría (AEP-FEP).

In Switzerland, Médecins de Famille et de l'Enfance Suisse (mFE); Pediatric Emergency Medicine Switzerland (PEMS); Pediatric Infectious Disease Group of Switzerland (PIGS).

In the United Kingdom, the Royal College of Pediatrics and Child Health (RCPCH); NRS Primary Care Network, Scotland; Pediatric Critical Care Society, England (PCCS); National Institute for Health Research – NHS England (NIHR).

This white paper was produced with the support of Sanofi.

8 BIBLIOGRAPHY

1] Florin TA, Plint AC, Zorc JJ. Viral Bronchiolitis. Lancet. 2017 Jan. 14; 389 (10065): 211-224. https://doi.org/10.1016/S0140-6736(16)30951-5.

[2] Meissner HC. Viral Bronchiolitis in Children. N Engl J Med. 2016 Jan 7;374(1):62-72. doi: 10.1056/NEJMra1413456.

[3] Karron R. Respiratory Syncytial Virus Vaccines, in Plotkin SA, Orenstein WA, Offitt PA, Edwards KM, eds. Plotkin's Vaccines. 7th ed. Philadelphia, PA: Elsevier; 2018: 943-949.

[4] Mollers M, Barnadas C, Broberg EK, Penttinen P, Teirlinck AC, Fischer TK; European Influenza Surveillance Network. Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017. Euro Surveill. 2019 Oct;24(40):1900157. doi: 10.2807/1560-7917.ES.2019.24.40.1900157.

[5] Shi T, McAllister DA, O'Brien KL, Simoes EAF, Madhi SA, Gessner BD, Polack FP, Balsells E, Acacio S, Aguayo C, Alassani I, Ali A, Antonio M, Awasthi S, Awori JO, Azziz-Baumgartner E, Baggett HC, Baillie VL, Balmaseda A, Barahona A, Basnet S, Bassat Q, Basualdo W, Bigogo G, Bont L, Breiman RF, Brooks WA, Broor S, Bruce N, Bruden D, Buchy P, Campbell S, Carosone-Link P, Chadha M, Chipeta J, Chou M, Clara W, Cohen C, de Cuellar E, Dang DA, Dash-Yandag B, Deloria-Knoll M, Dherani M, Eap T, Ebruke BE, Echavarria M, de Freitas Lázaro Emediato CC, Fasce RA, Feikin DR, Feng L, Gentile A, Gordon A, Goswami D, Goyet S, Groome M, Halasa N, Hirve S, Homaira N, Howie SRC, Jara J, Jroundi I, Kartasasmita CB, Khuri-Bulos N, Kotloff KL, Krishnan A, Libster R, Lopez O, Lucero MG, Lucion F, Lupisan SP, Marcone DN, McCracken JP, Mejia M, Moisi JC, Montgomery JM, Moore DP, Moraleda C, Moyes J, Munywoki P, Mutyara K, Nicol MP, Nokes DJ, Nymadawa P, da Costa Oliveira MT, Oshitani H, Pandey N, Paranhos-Baccalà G, Phillips LN, Picot VS, Rahman M, Rakoto-Andrianarivelo M, Rasmussen ZA, Rath BA, Robinson A, Romero C, Russomando G, Salimi V, Sawatwong P, Scheltema N, Schweiger B, Scott JAG, Seidenberg P, Shen K, Singleton R, Sotomayor V, Strand TA, Sutanto A, Sylla M, Tapia MD, Thamthitiwat S, Thomas ED, Tokarz R, Turner C, Venter M, Waicharoen S, Wang J, Watthanaworawit W, Yoshida LM, Yu H, Zar HJ, Campbell H, Nair H; RSV Global Epidemiology Network. Global, regional, and national disease burden estimates of acute lower respiratory infections due to respiratory syncytial virus in young children in 2015: a systematic review and modelling study. Lancet. 2017 Sep 2;390(10098):946-958. doi: 10.1016/S0140-6736(17)30938-8.

[6] Mollers M, Barnadas C, Broberg EK, Penttinen P, Teirlinck AC, Fischer TK; European Influenza Surveillance Network. Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017. Euro Surveill. 2019 Oct;24(40):1900157. doi: 10.2807/1560-7917.ES.2019.24.40.1900157.

[7] Hall CB, Long CE, Schnabel KC. Respiratory Syncytial Virus Infections in Previously Healthy Working Adults. Clin Infect Dis. 2001;33:792–6. doi:10.1086/322657

[8] Arriola CS, Kim L, Langley G, Anderson EJ, Openo K, Martin AM, Lynfield R, Bye E, Como-Sabetti K, Reingold A, Chai S, Daily P, Thomas A, Crawford C, Reed C, Garg S, Chaves SS. Estimated Burden of Community-Onset Respiratory Syncytial Virus-Associated Hospitalizations Among Children Aged <2 Years in the United States, 2014-15. J Pediatric Infect Dis Soc. 2020 Nov 10;9(5):587-595. doi: 10.1093/jpids/piz087.

[9] Barr R, Green CA, Sande CJ, Drysdale SB. Respiratory syncytial virus: diagnosis, prevention and management. Ther Adv Infect Dis. 2019 Jul 29;6:2049936119865798. doi: 10.1177/2049936119865798.

[10] Heikkinen T, Ojala E, Waris M. Clinical and Socioeconomic Burden of Respiratory Syncytial Virus Infection in Children. J Infect Dis. 2017 Jan 1;215(1):17-23.

[11] Fauroux B, Simões EAF, Checchia PA, et al. The Burden and Long-term Respiratory Morbidity Associated with Respiratory Syncytial Virus Infection in Early Childhood. Infect Dis Ther. 2017;6(2):173-197. doi:10.1007/s40121-017-0151-4

[12] Kneyber MCJ, Steyerberg EW, de Groot R, Moll HA. Long-term effects of respiratory syncytial virus (RSV) bronchiolitis in infants and young children: a quantitative review Acta Paediatr. 2000 Jun;89(6):654-60. doi: 10.1080/080352500750043945.

[13] Bont L, Aalderen WM, Kimpen JL. Long-term consequences of respiratory syncytial virus (RSV) bronchiolitis. Paediatr Respir Rev. 2000 Sep;1(3):221-7. doi: 10.1053/prrv.2000.0052. PMID: 12531083.

[14] Piedimonte G, Perez MK. Respiratory syncytial virus infection and bronchiolitis. Pediatr Rev. 2014;35(12):519-530. doi:10.1542/pir.35-12-519.

[15] Eiland LS. Respiratory syncytial virus: diagnosis, treatment and prevention. J Pediatr Pharmacol Ther. 2009;14(2):75-85. doi:10.5863/1551-6776-14.2.75

[16] Chkhaidze I, Zirakishvili D. Acute viral bronchiolitis in infants (Review). Georgian Med News. 2017 Mar; 264:43-50. PMID: 28480848.

[17] Hashmi NA, Cosgrove JF, MacMahon P. Prophylaxis in RSV infection (Palivizumab)--is it worthwhile? Ir Med J. 2000 Dec;93(9):284. PMID: 11209917.

[18] Ricci V, Nunes VD, Murphy MS, Cunningham S. Bronchiolitis in children: summary of NICE guidelines. BMJ 2015; 350:h2305. doi: https://doi.org/10.1136/bmj.h2305.

[19] Blanken M, Rovers M, Molenaar J, Winkler-Seinstra P, Meijer A, Kimpen J. Respiratory syncytial virus and recurrent wheeze in healthy preterm infants. New Engl J Med 2013; 386: 1791-1799. doi: 10.1056/NEJMoa1211917.

[20] WHO. Sampling strategy for RSV testing. https://www.who.int/teams/global-influenza-programme/global-respiratory-syncytial-virus-surveillance/sampling-strategy-for-rsv-testing (last accessed: 22.2.2022).

[21] Hammitt LL, Dagan R, Yuan Y, Cots MB, Bosheva M, Madhi SA, Muller WJ, Zar HJ, Brooks D, Grenham A, Hamrén UW, Mankad VS et. al. for the MELODY Study Group. Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants. N Engl J Med, 2022; 386: 837-846.

[22] Obando-Pacheco P, José Justicia-Grande A, Rivero-Calle I, Rodríguez-Tenreiro C, Sly P, Ramilo O, Mejías A, Baraldi E, Papadopoulos NG, Nair H, Nunes MC, Kragten-Tabatabaie L, Heikkinen T, Greenough A, Stein RT, Manzoni P, Bont L, Martinón-Torres F, Respiratory Syncytial Virus Seasonality: A Global Overview. J Infect. Dis., 2018 May ; 217(9): 1356–1364, https://doi.org/10.1093/infdis/jiy056

[23] Cattoir L, Vankeerberghen A, Boel A, Van Vaerenbergh K, De Beenhouwer H. Epidemiology of RSV and hMPV in Belgium: a 10-year follow-up. Acta Clin Belg. 2019 Aug;74(4):229-235. doi: 10.1080/17843286.2018.1492509.

[24] Broberg EK, Waris M, Johansen K, Snacken R, Penttinen P; European Influenza Surveillance Network. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. Euro Surveill. 2018 Feb;23(5):17-00284. doi: 10.2807/1560-7917.

[25] White, C. 'Seasonal healthcare Pressures and Patient Safety'. https://www.cnahardy.com/news-and-insight/insights/english/seasonal-healthcare-pressures-and-patient-safety (last accessed: 22.2.2022).

[26] Academy of Medical Sciences, Preparing for a Challenging Winter. 2020/1. https://acmedsci.ac.uk/file-download/51353957 (last accessed: 22.2.2022).