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REVIEW

Preventing Respiratory Syncytial Virus in Children in France: A Narrative Review of the Importance of a Reinforced Partnership Between Parents, Healthcare Professionals, and Public Health Authorities

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ABSTRACT

The highly contagious respiratory syncytial virus (RSV) is responsible for up to approximately 50,000 hospitalisations during each RSV season in children aged under 5 years in France, with the burden greatest in infants younger than 1 year who were born at term. There is a need for a strategy to universally protect young children from RSV infection, and thereby reduce the pressure that RSV places every year on RSV-infected children, their parents, and French healthcare systems. Potential strategies currently undergoing clinical investigation include passive immunisation via maternal

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vaccination or administration of long-acting monoclonal antibodies at or soon after birth, followed by vaccination later in infancy or childhood. An ongoing partnership and collaboration between parents, public health authorities, and frontline primary healthcare will need to be reinforced once these new RSV prevention strategies are available, to facilitate their use and ensure that all children receive adequate protection from the start of their first RSV season.

Keywords: Children; France; Immunisation; Infants; Nirsevimab; Palivizumab; Pharmacoeconomics; Primary healthcare; Public health; Respiratory syncytial virus

Key Summary Points

Respiratory syncytial virus (RSV) is the most common cause of acute lower respiratory tract infection and hospitalisation for respiratory illness in children under 5 years of age worldwide.

Seasonal RSV infection and its consequences (such as bronchiolitis) place considerable burden on healthcare systems, including in France, emphasising the importance of strategies to reduce RSV transmission, such as efficient epidemiology tracking to anticipate and plan healthcare resources.

Non-pharmaceutical interventions have been shown to reduce transmission and associated hospitalisations and intensive care admissions.

Pharmaceutical approaches to prevent RSV infection include passive immunisation via maternal vaccination or administration of long-acting monoclonal antibodies at birth (or soon after), and active immunisation of infants.

The implementation of national RSV surveillance programs combined with parent education regarding the importance of reducing RSV transmission, and a routine RSV primary prevention program (incorporating immunisation strategies) will assist in reducing the impact of RSV infection on the French healthcare system.

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INTRODUCTION

Respiratory syncytial virus (RSV) is a highly contagious single-stranded, negative-sense RNA virus that infects most children at least once by the age of 2 years [1, 2]. RSV is the most common cause of acute lower respiratory tract infection (LRTI) and hospitalisation for respiratory illness in children under 5 years of age worldwide [3, 4]. Infections usually follow a seasonal pattern, the timing of which varies by year and geographical location [5]. In temperate Northern Hemisphere countries, including France, increased RSV burden generally coincides with colder temperatures in the period from October/November to March/April, with peak infection rates in France in November/December [5, 6]. This causes additional strain on hospitals already facing overlapping seasonal epidemics of other respiratory viruses such as influenza [7].

Infection with RSV does not provide durable immunity and, therefore, reinfections frequently occur, although these are generally milder than primary infections [2, 8]. Primary and recurrent RSV generally starts as an upper respiratory tract infection that tends to be more severe and prolonged than a common cold [2]. Most children have a self-limiting course of disease that responds to supportive home care [2, 9]. However, during the first year of life,

otherwise healthy infants with a primary RSV infection are at increased risk of progressing to severe LRTI, with the highest risk during the first 3 months of life [10]. Although the risk of severe disease and hospitalisation is highest in children with known risk factors (prematurity or comorbidities) [11], up to 90% of children hospitalised with RSV-related LRTI are born at term and have no underlying medical conditions [10, 12, 13].

Bronchiolitis is an inflammation of the small airways of the lungs that typically presents in children in the first 2 years of life and is commonly associated with RSV infection [9, 14–16]. Acute viral bronchiolitis may vary from mild respiratory symptoms, such as cough, tachypnoea, and increased respiratory effort [2, 9, 16], to severe respiratory insufficiency, requiring ventilator support and necessitating or prolonging stays in high dependency units, such as paediatric intensive care units (PICUs) [16, 17].

In most cases, treatment of RSV LRTI is limited to supportive care, including hydration, supplemental oxygen, and respiratory support (mechanical ventilation or more cost-effective continuous positive airway pressure and high-flow nasal cannula) in severe cases of respiratory distress [17–19]. No medications have been validated as safe and effective for the treatment of severe RSV disease and, thus, primary prevention strategies should play an essential role in reducing the burden of RSV illness in young children [20, 21].

In 2020/2021, an increased incidence of late-season RSV LRTIs was observed in France after the relaxation of stringent non-pharmaceutical COVID-19 public health measures while a curfew, social distancing, and respiratory hygiene practices (masks) in adults were maintained (Fig. 1). When the COVID-19-associated public health measures were further relaxed, the subsequent RSV season (2021/2022) started earlier than usual but was of a similar size to that of previous seasons; however, the 2022/2023 season has also started early and has been associated with a particularly large number of infections and hospitalisations [22, 23]. This suggests that asymptomatic or mildly symptomatic adults play a major role in the chain of RSV transmission [24–26]. The impact on RSV of these non-pharmaceutical COVID-19 health measures, and its resurgence after their relaxation [26–32], emphasises both the importance of such measures in preventing RSV infection and illness in children, and the fact that these measures were insufficient to suppress a low, nearly undetectable, circulation and transmission of RSV. Thus, there is a need to evaluate public health measures targeting RSV transmission in the general population [26].

In this review, we explore the importance of reinforcing the working partnership between parents, healthcare professionals, and public health authorities for the implementation of appropriate RSV prevention strategies in France, beginning with an overview of the epidemiology of paediatric RSV and associated costs.

Search Strategy and Selection Criteria

Using the general search terms “respiratory syncytial virus”, “bronchiolitis”, “Europe”, and “France”, we searched PubMed for recently published articles (January 2018 onwards) potentially relevant to this review. Articles that focused on the epidemiology, healthcare resource use, costs, and public health management of RSV in France and other European countries were selected for inclusion.

Compliance with Ethics Guidelines

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

EPIDEMIOLOGY AND THE IMPACT OF NON-PHARMACEUTICAL INTERVENTIONS

Although most RSV-associated deaths occur in resource-limited countries, RSV is associated with substantial morbidity and healthcare resource utilisation worldwide, including in high-income European countries [3, 4, 13, 14, 33, 34]. A retrospective analysis (funded by Sanofi Pasteur and AstraZeneca) of

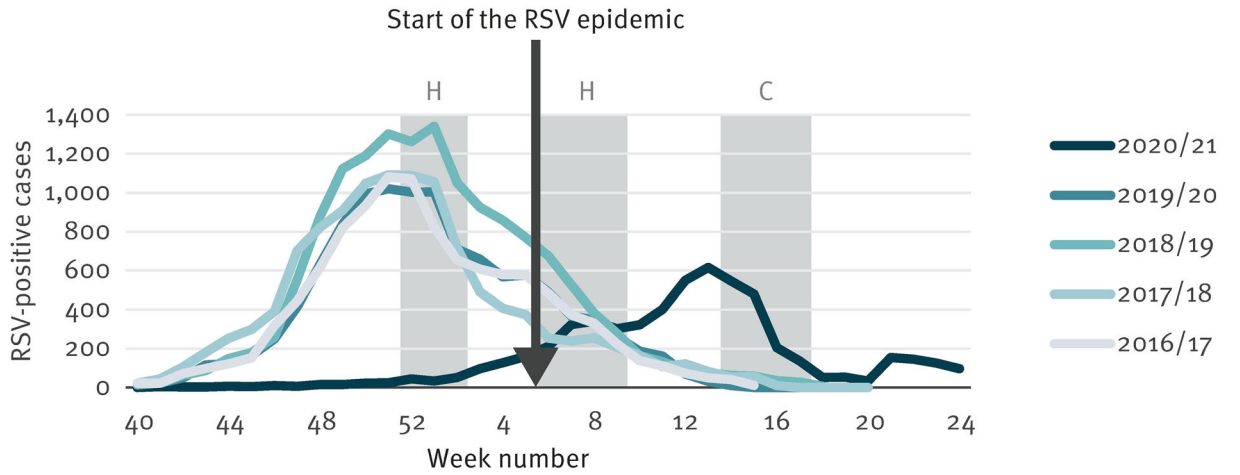

Fig. 1 Weekly number of respiratory syncytial virus (RSV) reported cases in France during the epidemiologic seasons 2016/17 to 2020/21*. Figure from van Summeren et al. 2020 [29], licensed under CC BY 4.0/portion shown with arrow label modified to indicate season date. *Data source: European Influenza Surveillance Network. C, COVID-19 restrictions re-implemented 2021; H, winter school holidays

data on RSV-associated hospitalisations in France covering an 8-year period from 2010 to 2018 found that the number of such hospitalisations in children aged under 5 years ranged from 43,715 to 54,616 per season (Table 1) [13]. Of these hospitalisations, 3% overall (N = 12,496 stays) required PICU admission. Most of the burden was observed in children younger than 1 year, in whom RSV was a leading cause of hospitalisation, responsible for up to 28% of all-cause hospitalisations versus 6% of all-cause hospitalisations in older children during the RSV season. Children younger than 1 year of age represented 69% of RSV-associated hospitalisations and approximately 95% of PICU stays. Among infants younger than 3 months old who were hospitalised as a result of RSV, 7% were admitted to a PICU versus 4% of all children under 1 year of age and 0.5% of children aged 1 year or older. The total number of RSV-associated hospitalisations over the 8-year period was similar for children born outside the RSV season (April to September) and for those born during each RSV season. In total, 87% of children hospitalised for RSV were otherwise healthy, and of the children whose gestational age was known (N = 270,048), 89% were born at term, as were more than half of those admitted to a PICU [13].

After the introduction of strict non-pharmaceutical public health measures in France during the first COVID-19 pandemic wave in February to March 2020, widespread circulation of RSV ceased and PICU admissions for bronchiolitis decreased significantly [26–32]. One study found an 85.3% reduction in PICU admissions for bronchiolitis between September and December 2020 versus predicted admissions [32], while another study found a 36% decrease in admissions for respiratory viral infections from March to May 2020 compared with admissions in March to May 2019 [31]. However, a delayed RSV epidemic, relatively small and short, occurred in France in early 2021 after the relaxation of the measures (Fig. 1) [28, 29]. This delayed 2020/21 RSV season had some atypical features, including an increased proportion of hospitalisations in infants older than 3 months [24, 26–29, 35]. It is unclear whether children with a first RSV infection at an older age are less prone to severe infection [29], but the older median age of children with RSV-associated LRTI in 2020/21 may have been responsible for the shorter median length of hospital stay and less frequent admission to PICUs during this season [26]. As a result of the lack of RSV in the environment during 2020/2021, the corresponding birth cohorts are

Table 1 Number of RSV hospital stays and total hospitalisation cost by age group during RSV seasons from 2010 through 2018 in children aged under 5 years in France

RSV season	Age group (months)													
	< 3		3–5		6–11		12–23		24–35		36–59		All	
	HS, *N*	Cost, € million	HS, *N*	Cost, € million	HS, *N*	Cost, € million	HS, *N*	Cost, € million	HS, *N*	Cost, € million	HS, *N*	Cost, € million	HS, *N*	Cost, € million
2010/2011	13,691	37.0	8146	18.4	8098	16.3	7026	12.1	3105	4.6	3649	4.8	43,715	93.2
2011/2012	15,351	41.2	8665	20.1	8888	18.3	7730	13.4	3482	5.0	3857	5.0	47,973	103.0
2012/2013	17,515	49.9	9191	21.4	8562	17.3	7576	13.2	3658	5.4	4447	5.8	50,949	113.0
2013/2014	17,280	47.8	9476	22.2	8551	17.4	7418	12.6	3471	5.2	4177	5.6	50,373	111.0
2014/2015	16,572	44.4	8735	19.4	8604	16.8	7472	12.5	4071	5.9	5274	7.0	50,728	106.0
2015/2016	18,873	62.9	10,071	27.3	9236	20.8	7918	14.5	3837	5.8	4650	6.1	54,585	137.4
2016/2017	18,102	64.3	10,127	29.3	9397	22.8	8109	15.6	3877	6.1	4474	6.0	54,086	144.2
2017/2018	18,734	54.6	10,458	29.9	9492	19.9	7752	13.2	3703	5.5	4477	6.0	54,616	124.1
Mean	17,015	50.2	9359	22.9	8854	18.7	7625	13.4	3651	5.4	4376	5.8	50,878	116.4

Table from Demont et al. 2021 [13], licensed under a Creative Commons Attribution 4.0 International License
HS hospital stays, *RSV* respiratory syncytial virus

immunologically naïve to RSV. This explains the subsequent observation that very severe RSV-associated LRTI (RSV infection leading to hospitalisation, $SpO_2 < 90\%$, and inability to feed) developed in children of an older age when RSV reappeared [27]. The 2021/2022 RSV season started earlier than usual and was of a similar size to pre-COVID seasons, despite some residual hygiene measures being in place (particularly mask wearing among commuters and during indoor meetings) [27, 28]. In contrast, the 2022/2023 season has been characterised by an early start and a high number of emergency room visits and hospitalisations for bronchiolitis among children under 2 years [22, 23].

It should be noted that even stringent non-pharmaceutical interventions (NPI) do not completely prevent RSV from circulating, especially in households and semi-closed communities such as daycare centres. NPI cannot reasonably be applied throughout childhood and throughout the period of intense RSV circulation; however, behavioural changes among household contacts of newborns and young infants (i.e. increased hand washing, covering the mouth when coughing, and avoidance of large gatherings and close contact with sick people) are likely to assist in decreasing the incidence of infection in infants aged 3 months or younger [25, 27] and, therefore, ongoing promotion of these measures is recommended [25, 36].

HEALTHCARE RESOURCE UTILISATION AND DISTRIBUTION

The morbidity associated with near-universal RSV infection in young children is the source of substantial healthcare and economic burden, including visits to general practitioners (GPs), paediatricians, and emergency departments, as well as inpatient, PICU, and prescription drug costs [12, 33, 37–39]. Direct nonmedical costs (i.e. transportation and food) and indirect costs (i.e. productivity loss) incurred by caregivers and families of children with RSV infection further add to the financial and societal burden of RSV illness [33]. Studies in both high- and low-income countries have demonstrated the impact on families of having a child hospitalised as a result of RSV, in terms of time burden associated with hospital visits, and out-of-pocket expenses (such as travel, parking, meals in the hospital, and added costs of childcare for siblings) that can lead to financial hardship [40, 41]. Also, given the prolonged morbidity associated with RSV LRTI sequelae, long-term costs are likely to be substantial when monitored beyond the acute period [33].

From 2010 to 2018 in France, children born at term generated 66% of the total cost of RSV-associated hospitalisation (89% when considering term and unknown gestational age children). Irrespective of the season, risk factors, and gestational age, children under the age of 1 year represented almost 80% of the cost of hospitalisation, of which half was generated by infants younger than 3 months, likely the result of a higher rate of PICU admission in this youngest age group. The median length of hospital stay was three nights for children under 1 year of age and two nights for children aged 1 year or older [13]. The costs of RSV-associated hospitalisations in all children younger than 5 years old ranged from €93.2 million to €144.2 million per season (Table 1) [13]. During this period, the mean total cost of RSV hospitalisation was €116.4 million, with a mean cost per stay of €2289. The estimated mean cost of RSV-associated hospitalisation of a child with at least one risk factor (congenital heart defects or bronchopulmonary dysplasia, Down syndrome, or cystic fibrosis with pulmonary manifestations) was higher than that for a child without risk factors (€2947 vs €2208, respectively) [13]. The mean estimated cost per hospitalisation in children younger than 1 year old was €2607. As observed in others counties, ICU use and cost has increased substantially in recent years in France [42]. Data from the University Hospital of Lyon show that the cost of hospitalisation per child over four successive RSV seasons (2014–2016) was higher in children younger than 1 month (€4892 for a 5.0-day median stay) than in those aged 1–3 months (€3958 for a 4.0-day median stay) and in those aged 3 months to 1 year (€3234 for a 4.0-day median stay) [43]. When considering these reported RSV-associated hospitalisation cost and burden estimates,

one should note that these may be under-estimates, as the virus involved in hospitalisations is not always determined or accurately recorded [13]. Further, the immediate and longer-term (post-discharge) economic and humanistic impact of RSV-associated hospitalisations were not determined in these studies [13, 43]. These burdens may be particularly important for families considered to be living with precariousness (a multifaceted concept that describes a set of undesirable circumstances related to employment [including low wages], economic insecurity, inadequate housing, health problems, and a lack of social networks) [44].

The high annual cost of RSV-associated hospitalisations in young children in France in the pre-COVID-19 pandemic era reflected the considerable pressure placed on the French hospital system and health resources every winter by RSV infection in infants born inside or outside their first RSV season, as well as the impact on hospital resources and healthcare workers, including potential saturation of PICUs, particularly at the peak of the season. The associated severe disruption to patient flow and the impact on bed capacity resulted in delays for the treatment of non-RSV diseases (e.g. elective surgeries or other specialist-led hospitalisations) and frequent reprioritisation/reallocation of resources was needed [13]. Now that most COVID-19 pandemic-related public health measures have been relaxed in France, significant paediatric hospital resources could be freed up and allocated elsewhere if a successful RSV primary prevention program could be implemented in all young children [13, 33].

In addition to hospital admissions for acute RSV infection, long-term consequences of RSV LRTI (recurrent wheezing, reduced lung function, and asthma), ongoing GP and outpatient visits, and subsequent hospitalisations should also be considered when evaluating the societal and financial burden of RSV infection, and the cost-effectiveness of primary prevention programs [2, 14, 15]. A considerable proportion of children are re-hospitalised following an initial hospitalisation for RSV. In France, from 2010 to 2018, 21% of children were hospitalised for any cause in the 3 months following an initial RSV-associated hospitalisation, of whom almost two-thirds (64%) were less than 1 year of age [13]. However, the rates of re-hospitalisation due to other diseases following initial admission were not known. Another hospitalisation due to RSV occurred during this time frame in 12% of children, with a higher incidence in preterm (21.6%) than term (11.2%) children [13]. Although it is not known whether the association of RSV with recurrent wheeze/asthma is causal, avoidance of chronic respiratory morbidity and associated resource use is a potential secondary advantage of successful strategies to prevent RSV infection in all young children [2, 14, 15, 45, 46]. Additionally, prevention of chronic respiratory morbidity limits the negative impact on a child's quality of life (e.g. family disorganisation, traumatic stress, impact on daily activities, and emotional burden in the child, parents, and siblings).

MANAGEMENT OPTIONS FOR PREVENTION: A PUBLIC HEALTH PERSPECTIVE

During the first 2 years of the COVID-19 pandemic, the benefits of non-pharmaceutical measures on RSV infection in infants have been obvious, although temporary, since the benefits were suspended when the restrictions were lifted [25]. Now, the impetus should be to prevent the onset of pandemic restriction "fatigue" and encourage people to maintain certain long-term non-pharmaceutical hygiene measures. In particular, appropriate use of masks, physical distancing, avoiding close contact with sick people, covering the mouth when coughing, and hand and surface hygiene measures should remain a major public health priority to prevent RSV infection and illness. These measures should be actively promoted in the families of all children up to 1 year of age (but particularly in those who have children younger than 3 months) in France, and other countries, for the foreseeable future, at least during the classical period of RSV seasonal epidemics [25, 27, 47]. Healthcare systems need to be prepared for future annual outbreaks of RSV infections as public health interventions and

international travel restrictions are inevitably relaxed [29, 48–50].

The development of effective surveillance systems that collect information about RSV epidemics, including seasonality, strain characteristics, disease burden/severity, and risk groups, is key to inform decision-making around treatment and prevention strategies for RSV. Such systems could be used to assess the effectiveness and impact of diverse immunisation strategies. Sentinel surveillance systems are those created with surveillance as the primary goal and consist of high-quality networks that systematically sample patients; France has two such systems specifically for RSV surveillance, which are GP- and hospital-based, respectively [51]. Non-sentinel systems, of which France has one, are passive and collect notifications of cases or laboratory results [51]. While sentinel surveillance systems may be considered the preferred option, they have the disadvantage of covering only a small proportion of the population and, therefore, they may not capture information from paediatric populations, unless specifically focused on infants [51]. Genomic surveillance should be used to establish the strains of RSV that are circulating, the severity of disease caused by each strain, and any genetic evolution of the virus. This will provide important information on the impact of immunisation on disease caused by different virus subtypes, and conversely the impact of viral changes on vaccine/antiviral efficacy and antigen detection. All RSV-positive samples received in central laboratories in France are typed [51]. The development of cohesive, region-wide RSV surveillance in the European Union (EU) has been suggested, in which national systems conform to specific recommendations [52]. The aim is to ensure consistency of data collection across member states, which will allow harmonisation of data reporting and comparison at the European level [52].

To date, the only pharmaceutical agent available to prevent severe RSV infection in children is the RSV-specific monoclonal antibody palivizumab [20, 53–55]. Compared with placebo or no intervention, palivizumab has been shown to reduce RSV hospitalisation in high-risk infants in randomised trials, with a review of five trials reporting a risk ratio (RR) of 0.44 (95% confidence interval [CI] 0.30–0.64) for such hospitalisations at 2-years' follow up, although with little to no impact on mortality (RR 0.69, 95% CI 0.42–1.15) [56, 57]. However, palivizumab has not been studied in healthy children and it may be cost-effective only for some subgroups of high-risk children [53]. Passive immunisation with palivizumab is therefore only reimbursed by the French public welfare system for the following subgroups of high-risk infants, as outlined by French Transparency Committee guidelines: birth at no more than 32 weeks' gestation with respiratory disease attested by O_2 requirement at 28 days and (1) age less than 6 months at RSV epidemic onset or (2) age less than 24 months at RSV epidemic onset and moderate or severe bronchopulmonary dysplasia requiring treatment in the previous 6 months; and (3) age less than 24 months at RSV epidemic onset and haemodynamically significant congenital heart disease [53, 58].

Otherwise healthy infants born at term account for up to 90% of RSV-associated hospitalisations in France [13]. Therefore, unless palivizumab is used off-label and not in accordance with Transparency Committee guidance, only a small, very high-risk proportion of the French infant population stands to benefit from RSV immunoprophylaxis [53, 58, 59]. In one study, off-label use of palivizumab was observed in relatively high proportions of the overall (term + preterm) infant population (40% of infants aged less than 6 months and 59% of infants aged less than 24 months) [58]. However, widespread use of palivizumab is restricted by its high acquisition cost, its short half-life (requiring up to five monthly intramuscular injections during the RSV season [20, 60]), and poor compliance (which often leads to incomplete prophylaxis) [53]. There is a clear need for a long-acting, cost-effective alternative to palivizumab to protect all infants, regardless of gestational age at birth or comorbidities, throughout their first RSV season [20, 21, 61].

Potential future universal approaches to RSV prevention combine different passive and active immunisation strategies and include (1) maternal vaccination during pregnancy, (2) infant

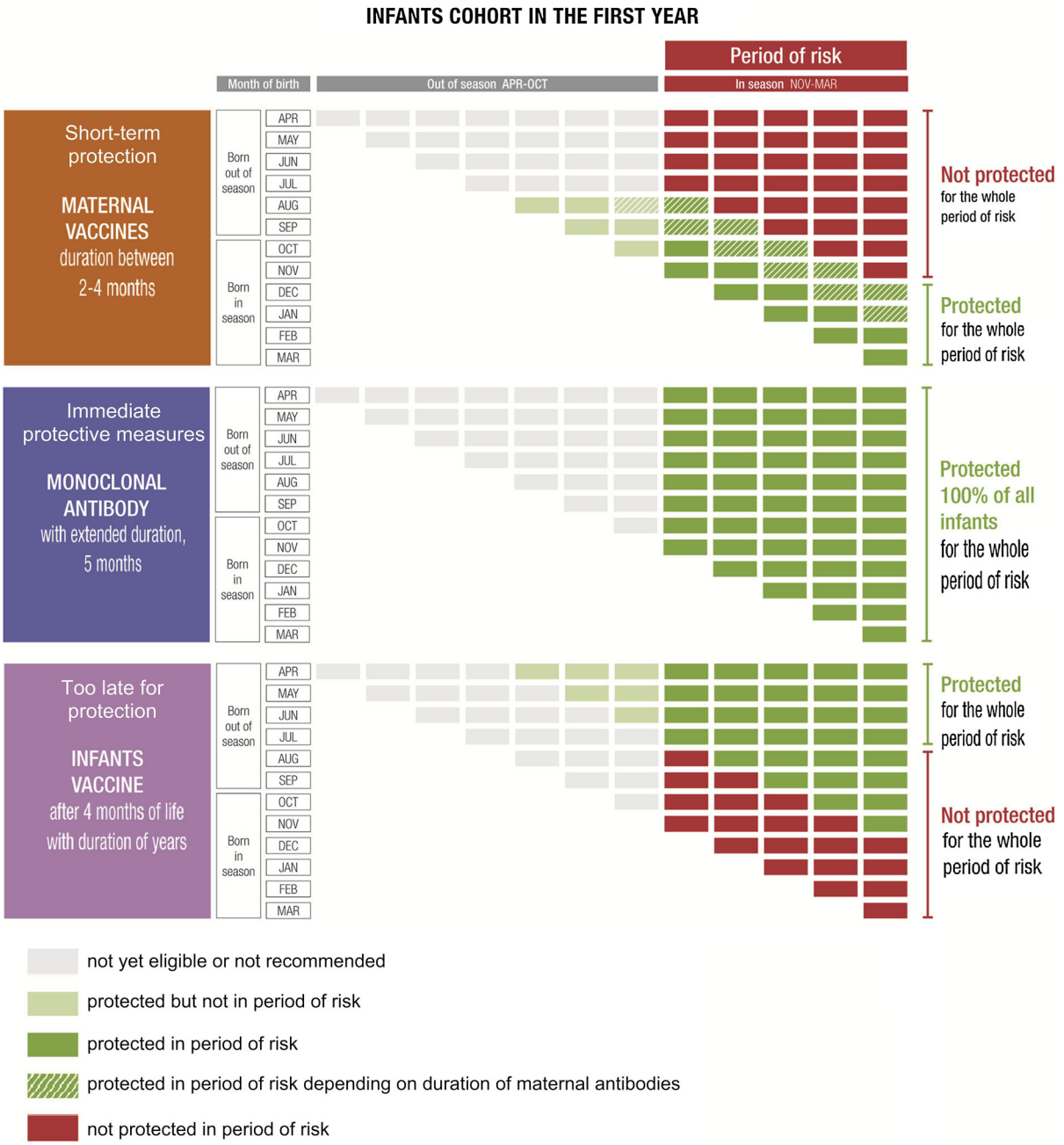

Fig. 2 Potential future options for prevention of respiratory syncytial virus in the first year of life. Figure from Azzari et al. 2021 [14], licensed under a Creative Commons Attribution 4.0 International License, and Janet et al. [62]: Respiratory syncytial virus seasonality and its implications on prevention strategies. Human Vaccines and Immunotherapeutics 2018, 14(1):234–44, reprinted by permission from Taylor & Francis Ltd. http://www.tandfonline.com

vaccination, and (3) administration of long-acting monoclonal antibodies to infants at birth/soon thereafter, possibly followed by infant vaccination to protect them during their second RSV season (Fig. 2) [62].

Maternal vaccination would result in the passive immunisation of infants before delivery by transfer of protective antibodies. As a result of waning acquired antibodies over time, protection from maternal vaccination would likely range from 2 to 4 months, so this would be a valid option to bridge the gap between birth and active vaccination only for children whose birth is expected to occur during or just before the RSV season [14, 62, 63]. If, for example, RSV vaccination of mothers provided infants with 4 months' protection, then only those born in France between September and February would receive protection throughout the peak of their first RSV season, with the greatest reduction of disease occurring in those born in October or November. Although efficient transfer of maternal RSV antibodies to infants has been shown to occur after maternal RSV vaccination [64], this approach failed to confer protection from medically significant RSV-associated LRTI in infants during up to 90 days of life (the primary outcome) in the only completed phase 3 clinical trial of maternal RSV vaccination to date [63]. However, there was evidence of vaccine efficacy against the secondary endpoints of RSV-associated LRTI with severe hypoxaemia and RSV LRTI hospitalisation, suggesting potential benefits of a maternal RSV vaccination strategy [63, 65, 66]. Nevertheless, it should be noted that effective vaccination during pregnancy relies on the transport of antibodies across the placenta. This is an active process, which is saturable and competitive, and may therefore be negatively affected by maternal levels of various factors including immunoglobulins [67] (as has been shown for the transfer of specific antibodies against measles and tetanus from mother to newborn [67, 68]) and antibodies induced by other vaccines administered during pregnancy, such as those for influenza and pertussis. Further, the best time-window for vaccination to induce the most antibody transfer has yet to be defined.

A number of RSV vaccines for delivery to infants are in late-stage clinical development, but it will likely be several years until any vaccine is approved for routine clinical use [20, 69, 70]. Moreover, these vaccines will not be administered at birth, so not all children would be protected for the entirety of their first RSV season if prevention were to rely on vaccination alone [14, 62]. For example, a child born in France in October and immunised in a 2-, 3-, 4-month infant schedule (i.e. December, January, February) would remain susceptible during a large part of their first RSV season.

Nirsevimab, acting as a passive immunisation, is a unique long-acting monoclonal antibody that may lead to almost immediate protection of infants for an entire RSV season after a single intramuscular injection and has demonstrated promising clinical trial results in healthy term and preterm infants [20, 21, 63, 71–73]. Modelling studies have shown that a significantly extended half-life monoclonal antibody, such as nirsevimab, could have high public health benefits, reducing the burden of RSV-related medically attended LRTI by at least 50% through to 6–12 months of age [74, 75], with the estimated annual number needed to be passively immunised to prevent RSV comparing favourably with other childhood vaccines [76]. Depending on cost-effectiveness, administration could routinely take place pre-discharge from maternity units or during the first post-discharge paediatric follow-up visit in all neonates (routinely post-natal administration done 2 weeks after birth, between days 6 and 10; additional follow-up visits may occur between days 11 and 28 of life depending on the initial assessment), or during one of the recommended and reimbursed regular health visits closest to the pre-winter onset of the RSV season [77]. Either possibility could eventually be followed by infant vaccination to achieve more durable protection and eventually limit RSV circulation [14, 62]. The timing of the administration of nirsevimab could also be based on the infant's month of birth relative to the RSV season, i.e. a child born between March and May could receive the monoclonal antibody using a pre-winter administration strategy, while a child born between October and February could receive it at birth. It should be kept in mind that the former strategy may require precise characterisation of the RSV season and evidence-based planning to succeed [61, 78], while a routine post-natal administration strategy would be

relatively easy for physicians and parents to understand and adhere to. Healthcare professionals and medical societies will therefore need to work closely with public health authorities to ensure that appropriate, easily administrable strategies are in place to accommodate the routine use of new technologies, such as long-acting monoclonal antibodies, to prevent severe RSV infection in all infants [78].

CONCLUSIONS

National hospitalisation and cost data underline the importance of RSV epidemics in paediatric hospital capacity planning, as well as the urgent need for effective measures to prevent RSV disease in France. Epidemiological data on RSV in France is in line with international evidence, with most of the burden observed in children under 1 year of age born at term. Ongoing national surveillance of RSV (and possible incorporation of this into an EU-wide system) to allow the collection of data on seasonality, strain characteristics, community incidence, disease severity (including associated hospitalisation rates), and the onset of wheezing and asthma after RSV infection is important for informing prevention policies, and in monitoring their success in reducing the burden of RSV illness.

Reduction of the burden of RSV-associated LRTI will rely on education of parents about the importance of reducing exposure to and transmission of RSV. As part of this educational approach, non-pharmaceutical preventive practices, such as regular hand-washing and social distancing/avoiding close contact with sick people, should be strongly promoted to new parents to reduce RSV burden in RSV-naïve infants. Palivizumab should also continue to be used to reduce RSV disease burden in high-risk infants. Resource and cost savings could be realised and allocated to other healthcare services by an effective, routine RSV primary prevention program encompassing all infants when active and passive immunisation programs become available. Data on RSV vaccines and cost-effective, long-acting RSV monoclonal antibodies should inform policy for future public health decisions. In close collaboration with stakeholders responsible for prescribing and administering the new agents (i.e. obstetricians, paediatricians, GPs, nurses, pharmacists, and midwives), public health authorities should design prevention strategies and establish logistical pathways to ensure that all children are protected throughout their first RSV season, regardless of gestational age at birth or comorbidities. Reinforcement of an ongoing partnership and collaboration between the parents of newborn infants, public health authorities, and frontline primary healthcare professionals will be required for the smooth rollout of new RSV pharmaceutical preventive strategies to reduce the pressure that RSV places on healthcare systems each year.

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REFERENCES

1. Collins PL, Fearns R, Graham BS. Respiratory syncytial virus: virology, reverse genetics, and pathogenesis of disease. Curr Top Microbiol Immunol. 2013;372:3–38. https://doi.org/10.1007/978-3-642-38919-1_1.

2. Hall CB, Simoes EA, Anderson LJ. Clinical and epidemiologic features of respiratory syncytial virus. Curr Top Microbiol Immunol. 2013;372:39–57. https://doi.org/10.1007/978-3-642-38919-1_2.

3. Li Y, Johnson EK, Shi T, et al. National burden estimates of hospitalisations for acute lower respiratory infections due to respiratory syncytial virus in young children in 2019 among 58 countries: a modelling study. Lancet Respir Med. 2021;9(2):175–85. https://doi.org/10.1016/S2213-2600(20)30322-2.

4. Shi T, McAllister DA, O'Brien KL, et al. 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;390(10098):946–58. https://doi.org/10.1016/S0140-6736(17)30938-8.

5. Obando-Pacheco P, Justicia-Grande AJ, Rivero-Calle I, et al. Respiratory syncytial virus seasonality: a global overview. J Infect Dis. 2018;217(9):1356–64. https://doi.org/10.1093/infdis/jiy056.

6. Broberg EK, Waris M, Johansen K, Snacken R, Penttinen P. Seasonality and geographical spread of respiratory syncytial virus epidemics in 15 European countries, 2010 to 2016. Euro Surveill. 2018;23(5):17–00284. https://doi.org/10.2807/1560-7917.ES.2018.23.5.17-00284.

7. Lemaitre M, Fouad F, Carrat F, et al. Estimating the burden of influenza-related and associated hospitalizations and deaths in France: an eight-season data study, 2010–2018. Influenza Other Respir Viruses. 2022;16(4):717–25. https://doi.org/10.1111/irv.12962.

8. Openshaw PJM, Chiu C, Culley FJ, Johansson C. Protective and harmful immunity to RSV infection. Annu Rev Immunol. 2017;35:501–32. https://doi.org/10.1146/annurev-immunol-051116-052206.

9. Smith DK, Seales S, Budzik C. Respiratory syncytial virus bronchiolitis in children. Am Fam Physician. 2017;95(2):94–9.

10. Hall CB, Weinberg GA, Blumkin AK, et al. Respiratory syncytial virus-associated hospitalizations among children less than 24 months of age. Pediatrics. 2013;132(2):e341–8. https://doi.org/10.1542/peds.2013-0303.

11. Fauroux B, Gouyon JB, Roze JC, et al. Respiratory morbidity of preterm infants of less than 33 weeks gestation without bronchopulmonary dysplasia: a 12-month follow-up of the CASTOR study cohort. Epidemiol Infect. 2014;142(7):1362–74. https://doi.org/10.1017/S0950268813001738.

12. Bont L, Checchia PA, Fauroux B, et al. Defining the epidemiology and burden of severe respiratory syncytial virus infection among infants and children in western countries. Infect Dis Ther. 2016;5(3):271–98. https://doi.org/10.1007/s40121-016-0123-0.

13. Demont C, Petrica N, Bardoulat I, et al. Economic and disease burden of RSV-associated hospitalizations in young children in France, from 2010 through 2018. BMC Infect Dis. 2021;21(1):730. https://doi.org/10.1186/s12879-021-06399-8.

14. Azzari C, Baraldi E, Bonanni P, et al. Epidemiology and prevention of respiratory syncytial virus infections in children in Italy. Ital J Pediatr. 2021;47(1):198. https://doi.org/10.1186/s13052-021-01148-8.

15. Barr R, Green CA, Sande CJ, Drysdale SB. Respiratory syncytial virus: diagnosis, prevention and management. Ther Adv Infect Dis. 2019;6:2049936119865798. https://doi.org/10.1177/2049936119865798.

16. Meissner HC. Viral bronchiolitis in children. N Engl J Med. 2016;374(1):62–72. https://doi.org/10.1056/NEJMra1413456.

17. Essouri S, Laurent M, Chevret L, et al. Improved clinical and economic outcomes in severe bronchiolitis with pre-emptive nCPAP ventilatory strategy. Intensive Care Med. 2014;40(1):84–91. https://doi.org/10.1007/s00134-013-3129-z.

18. Simoes EAF, Bont L, Manzoni P, et al. Past, present and future approaches to the prevention and treatment of respiratory syncytial virus infection in children. Infect Dis Ther. 2018;7(1):87–120. https://doi.org/10.1007/s40121-018-0188-z.

19. Coon ER, Stoddard G, Brady PW. Intensive care unit utilization after adoption of a ward-based high-flow nasal cannula protocol. J Hosp Med. 2020;15(6):325–30. https://doi.org/10.12788/jhm.3417.

20. Domachowske JB, Anderson EJ, Goldstein M. The future of respiratory syncytial virus disease prevention and treatment. Infect Dis Ther. 2021;10(Suppl 1):47–60. https://doi.org/10.1007/s40121-020-00383-6.

21. Rocca A, Biagi C, Scarpini S, et al. Passive immunoprophylaxis against respiratory syncytial virus in children: where are we now? Int J Mol Sci. 2021;22(7):3703. https://doi.org/10.3390/ijms22073703.

22. Sante Publique France. Bronchiolitis-weekly newsletter. Week 44; 9 November 2022. https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/bronchiolite/documents/bulletin-national/bulletin-epidemiologique-bronchiolite-semaine-44.-saison-2022-2023. Accessed 15 Nov 2022.

23. European Centre for Disease Prevention and Control. Communicable Disease Threats Report-Weekly Bulletin. Week 43, 23–29 October 2022. https://www.ecdc.europa.eu/sites/default/files/documents/Communicable-disease-threats-report-29-oct-2022.pdf. Accessed 15 Nov 2022.

24. Delestrain C, Danis K, Hau I, et al. Impact of COVID-19 social distancing on viral infection in France: a delayed outbreak of RSV. Pediatr Pulmonol. 2021;56(12):3669–73. https://doi.org/10.1002/ppul.25644.

25. Gastaldi A, Donà D, Barbieri E, Giaquinto C, Bont LJ, Baraldi E. COVID-19 lesson for respiratory syncytial virus (RSV): hygiene works. Children (Basel). 2021;8(12):1144. https://doi.org/10.3390/children8121144.

26. Fourgeaud J, Toubiana J, Chappuy H, et al. Impact of public health measures on the post-COVID-19

respiratory syncytial virus epidemics in France. Eur J Clin Microbiol Infect Dis. 2021;40(11):2389–95. https://doi.org/10.1007/s10096-021-04323-1.

27. Casalegno JS, Ploin D, Cantais A, et al. Characteristics of the delayed respiratory syncytial virus epidemic, 2020/2021, Rhone Loire, France. Euro Surveill. 2021;26(29):2100630. https://doi.org/10.2807/1560-7917.ES.2021.26.29.2100630.

28. Santé Publique France. Bulletin épidémiologique bronchiolite, Saison 2020–2021. 2021. https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/bronchiolite/donnees/#tabs. Accessed 14 Nov 2021.

29. van Summeren J, Meijer A, Aspelund G, et al. Low levels of respiratory syncytial virus activity in Europe during the 2020/21 season: what can we expect in the coming summer and autumn/winter? Euro Surveill. 2021;26(29):2100639. https://doi.org/10.2807/1560-7917.ES.2021.26.29.2100639.

30. Angoulvant F, Ouldali N, Yang DD, et al. Coronavirus disease 2019 pandemic: impact caused by school closure and national lockdown on pediatric visits and admissions for viral and nonviral infections—a time series analysis. Clin Infect Dis. 2021;72(2):319–22. https://doi.org/10.1093/cid/ciaa710.

31. Breinig S, Mortamet G, Brossier D, et al. Impact of the French national lockdown on admissions to 14 pediatric intensive care units during the 2020 COVID-19 pandemic-a retrospective multicenter study. Front Pediatr. 2021;9: 764583. https://doi.org/10.3389/fped.2021.764583.

32. Rambaud J, Dauger S, Morin L, et al. Bronchiolitis admissions to intensive care during COVID. Pediatrics. 2021;147(4):e2021050103. https://doi.org/10.1542/peds.2021-050103.

33. Zhang S, Akmar LZ, Bailey F, et al. Cost of respiratory syncytial virus-associated acute lower respiratory infection management in young children at the regional and global level: a systematic review and meta-analysis. J Infect Dis. 2020;222(Suppl 7):S680–7. https://doi.org/10.1093/infdis/jiz683.

34. Wildenbeest JG, Billard M-N, Zuurbier RP, et al. The burden of respiratory syncytial virus in healthy term-born infants in Europe: a prospective birth cohort study. Lancet Respir Med. 2022. https://doi.org/10.1016/S2213-2600(22)00414-3.

35. Rybak A, Levy C, Jung C, et al. Delayed bronchiolitis epidemic in French primary care setting driven by respiratory syncytial virus: preliminary data from the Oursyn study, March 2021. Pediatr Infect Dis J. 2021;40(12):e511–4. https://doi.org/10.1097/INF.0000000000032702021.

36. Cohen R, Ashman M, Taha MK, et al. Pediatric infectious disease group (GPIP) position paper on the immune debt of the COVID-19 pandemic in childhood, how can we fill the immunity gap? Infect Dis Now. 2021;51(5):418–23. https://doi.org/10.1016/j.idnow.2021.05.004.

37. Hall CB, Weinberg GA, Iwane MK, et al. The burden of respiratory syncytial virus infection in young children. N Engl J Med. 2009;360(6):588–98. https://doi.org/10.1056/NEJMoa0804877.

38. Simoes EA. The outpatient burden of respiratory syncytial virus infections in older children. J Infect Dis. 2017;215(1):1–3. https://doi.org/10.1093/infdis/jiw483.

39. Simoes EAF, Chirikov V, Botteman M, Kwon Y, Kuznik A. Long-term assessment of healthcare utilization 5 years after respiratory syncytial virus infection in US infants. J Infect Dis. 2020;221(8):1256–70. https://doi.org/10.1093/infdis/jiz278.

40. Leader S, Yang H, DeVincenzo J, Jacobson P, Marcin JP, Murray DL. Time and out-of-pocket costs associated with respiratory syncytial virus hospitalization of infants. Value Health. 2003;6(2):100–6. https://doi.org/10.1046/j.1524-4733.2003.00220.x.

41. Bhuiyan MU, Luby SP, Alamgir NI, et al. Costs of hospitalization with respiratory syncytial virus illness among children aged <5 years and the financial impact on households in Bangladesh, 2010. J Glob Health. 2017;7(1): 010412. https://doi.org/10.7189/jogh.07.010412.

42. Mahant S, Parkin PC, Thavam T, et al. Rates in bronchiolitis hospitalization, intensive care unit use, mortality, and costs from 2004 to 2018. JAMA Pediatr. 2022;176(3):270–9. https://doi.org/10.1001/jamapediatrics.2021.5177.

43. Kramer R, Duclos A, Lyon VRS, Lina B, Casalegno JS. Cost and burden of RSV related hospitalisation from 2012 to 2017 in the first year of life in Lyon, France. Vaccine. 2018;36(45):6591–3. https://doi.org/10.1016/j.vaccine.2018.09.029.

44. McKee M, Reeves A, Clair A, Stuckler D. Living on the edge: precariousness and why it matters for health. Arch Public Health. 2017;75:13. https://doi.org/10.1186/s13690-017-0183-y.

45. Abreo A, Wu P, Donovan BM, et al. Infant respiratory syncytial virus bronchiolitis and subsequent risk of pneumonia, otitis media, and antibiotic utilization. Clin Infect Dis. 2020;71(1):211–4. https://doi.org/10.1093/cid/ciz1033.

46. Driscoll AJ, Arshad SH, Bont L, et al. Does respiratory syncytial virus lower respiratory illness in early life cause recurrent wheeze of early childhood and

asthma? Critical review of the evidence and guidance for future studies from a World Health Organization-sponsored meeting. Vaccine. 2020;38(11):2435–48. https://doi.org/10.1016/j.vaccine.2020.01.020.

47. Guedj R, Lorrot M, Lecarpentier T, Leger P-L, Corvol H, Carbajal R. Infant bronchiolitis dramatically reduced during the second French COVID-19 outbreak. Acta Paediatr. 2021;110(4):1297–9. https://doi.org/10.1111/apa.15780.

48. Baker RE, Park SW, Yang W, Vecchi GA, Metcalf CJE, Grenfell BT. The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. Proc Natl Acad Sci USA. 2020;117(48):30547–53. https://doi.org/10.1073/pnas.2013182117.

49. Tang JW, Bialasiewicz S, Dwyer DE, et al. Where have all the viruses gone? Disappearance of seasonal respiratory viruses during the COVID-19 pandemic. J Med Virol. 2021;93(7):4099–101. https://doi.org/10.1002/jmv.26964.

50. Williams TC, Sinha I, Barr IG, Zambon M. Transmission of paediatric respiratory syncytial virus and influenza in the wake of the COVID-19 pandemic. Euro Surveill. 2021;26(29):2100186. https://doi.org/10.2807/1560-7917.ES.2021.26.29.2100186.

51. Mollers M, Barnadas C, Broberg EK, et al. Current practices for respiratory syncytial virus surveillance across the EU/EEA Member States, 2017. Euro Surveill. 2019;24(40):1900157. https://doi.org/10.2807/1560-7917.ES.2019.24.40.1900157.

52. Teirlinck AC, Broberg EK, Stuwitz Berg A, et al. Recommendations for respiratory syncytial virus surveillance at the national level. Eur Respir J. 2021;58(3):2003766. https://doi.org/10.1183/13993003.03766-2020.

53. Torchin H, Rousseau J, Marchand-Martin L, Truffert P, Jarreau PH, Ancel PY. Palivizumab administration in preterm infants in France: EPIPAGE-2 cohort study. Arch Pediatr. 2018;25(2):89–94. https://doi.org/10.1016/j.arcped.2017.12.009.

54. Reeves RM, van Wijhe M, Lehtonen T, et al. A systematic review of European clinical practice guidelines for respiratory syncytial virus prophylaxis. J Infect Dis. 2022;226(Suppl 1):S110–6. https://doi.org/10.1093/infdis/jiac059.

55. Haute Autorité de Santé, Commission de la Transparence, Avis. Synagis. 2017. https://www.has-sante.fr/upload/docs/application/pdf/ct-5014_synagis.pdf. Accessed 25 May 2022.

56. Garegnani L, Styrmisdottir L, Roson-Rodriguez P, Escobar-Liquitay CM, Esteban I, Franco JV. Palivizumab for preventing severe respiratory syncytial virus (RSV) infection in children. Cochrane Database Syst Rev. 2021;11:CD013757. https://doi.org/10.1002/14651858.CD013757.pub2.

57. Impact-RSV Study Group. Palivizumab, a humanized respiratory syncytial virus monoclonal antibody, reduces hospitalization from respiratory syncytial virus infection in high-risk infants. The Impact-RSV Study Group. Pediatrics. 1998;102(3 Pt 1):531–7.

58. Pinquier D, Gouyon JB, Fauroux B, et al. Palivizumab immunoprophylaxis: use in clinical practice, safety and beneficial effects in France. Arch Pediatr. 2009;16(11):1443–52. https://doi.org/10.1016/j.arcped.2009.08.008.

59. Lacaze-Masmonteil T, Truffert P, Pinquier D, et al. Lower respiratory tract illness and RSV prophylaxis in very premature infants. Arch Dis Child. 2004;89(6):562. https://doi.org/10.1136/adc.2003.028282.

60. Staebler S, Blake S. Respiratory syncytial virus disease: immunoprophylaxis policy review and public health concerns in preterm and young infants. Policy Polit Nurs Pract. 2021;22(1):41–50. https://doi.org/10.1177/1527154420965543.

61. Aranda SS, Polack FP. Prevention of pediatric respiratory syncytial virus lower respiratory tract illness: perspectives for the next decade. Front Immunol. 2019;10:1006. https://doi.org/10.3389/fimmu.2019.01006.

62. Janet S, Broad J, Snape MD. Respiratory syncytial virus seasonality and its implications on prevention strategies. Hum Vaccin Immunother. 2018;14(1):234–44. https://doi.org/10.1080/21645515.2017.1403707.

63. Madhi SA, Polack FP, Piedra PA, et al. Respiratory syncytial virus vaccination during pregnancy and effects in infants. N Engl J Med. 2020;383(5):426–39. https://doi.org/10.1056/NEJMoa1908380.

64. Munoz FM, Swamy GK, Hickman SP, et al. Safety and immunogenicity of a respiratory syncytial virus fusion (F) protein nanoparticle vaccine in healthy third-trimester pregnant women and their infants. J Infect Dis. 2019;220(11):1802–15. https://doi.org/10.1093/infdis/jiz390.

65. Meissner HC. Disarming the respiratory syncytial virus. N Engl J Med. 2020;383(5):487–8. https://doi.org/10.1056/NEJMe2021648.

66. Pollard AJ, Bijker EM. A guide to vaccinology: from basic principles to new developments. Nat Rev Immunol. 2021;21(2):83–100. https://doi.org/10.1038/s41577-020-00479-7.

67. Gendrel D, Richard-Lenoble D, Massamba MB, et al. Placental transfer of tetanus antibodies and protection of newborn infants. Arch Fr Pediatr. 1990;47(10):725–9.

68. Gendrel D, Richard-Lenoble D, Blot P, Fribourg-Blanc A. Transfer of measles immunoglobulins and antibodies from mother to child in Africa and Europe. Presse Med. 1988;17(32):1633–6.

69. Billard MN, Bont LJ. Live-attenuated respiratory syncytial virus vaccines: time for the next step. Am J Respir Crit Care Med. 2021;203(5):538–9. https://doi.org/10.1164/rccm.202009-3431ED.

70. Karron RA, Atwell JE, McFarland EJ, et al. Live-attenuated vaccines prevent respiratory syncytial virus-associated illness in young children. Am J Respir Crit Care Med. 2021;203(5):594–603. https://doi.org/10.1164/rccm.202005-1660OC.

71. Griffin MP, Yuan Y, Takas T, et al. Single-dose nirsevimab for prevention of RSV in preterm infants. N Engl J Med. 2020;383(5):415–25. https://doi.org/10.1056/NEJMoa1913556.

72. Domachowske J, Madhi SA, Simões EAF, et al. Safety of nirsevimab for RSV in infants with heart or lung disease or prematurity. N Engl J Med. 2022;386(9):892–4. https://doi.org/10.1056/NEJMc2112186.

73. Hammitt LL, Dagan R, Yuan Y, et al. Nirsevimab for prevention of RSV in healthy late-preterm and term infants. N Engl J Med. 2022;386(9):837–46. https://doi.org/10.1056/NEJMoa2110275.

74. Voirin N, Virlogeux V, Demont C, Kieffer A. Potential impact of nirsevimab on RSV transmission and medically attended lower respiratory tract illness caused by RSV: a disease transmission model. Infect Dis Ther. 2021;11:277–92. https://doi.org/10.1007/s40121-021-00566-9.

75. Rainisch G, Adhikari B, Meltzer MI, Langley G. Estimating the impact of multiple immunization products on medically-attended respiratory syncytial virus (RSV) infections in infants. Vaccine. 2020;38(2):251–7. https://doi.org/10.1016/j.vaccine.2019.10.023.

76. Finelli L, Choi Y, Goldstein E. Number needed to immunize to prevent RSV with extended half-life monoclonal antibody. Vaccine. 2020;38(34):5474–9. https://doi.org/10.1016/j.vaccine.2020.06.034.

77. Haute Autorité de Santé. Maternity discharge after childbirth: conditions and organization of the return home of mothers and their newborns. 2014. https://www.has-sante.fr/jcms/c_1290110/fr/sortie-de-maternite-apres-accouchement-conditions-et-organisation-du-retour-a-domicile-des-meres-et-de-leurs-nouveau-nes. Accessed 29 July 2022.

78. Navarro Alonso JA, Bont LJ, Bozzola E, et al. RSV: perspectives to strengthen the need for protection in all infants. Emerg Themes Epidemiol. 2021;18(1):15. https://doi.org/10.1186/s12982-021-00104-5.

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