Prepublication Release

PEDIATRICS

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

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Committee on Infectious Diseases

DOI: 10.1542/peds.2026-079049

Journal: *Pediatrics*

Article Type: AAP Technical Report

Citation: American Academy of Pediatrics Committee on Infectious Diseases. Recommendations for the Prevention of Respiratory Syncytial Virus Disease in Infants and Children: Technical Report. *Pediatrics.* 2026; doi: 10.1542/peds.2026-079049

AMERICAN ACADEMY OF PEDIATRICS

TECHNICAL REPORT

Recommendations for the Prevention of Respiratory Syncytial Virus Disease in Infants and Children: Technical Report

Committee on Infectious Diseases

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All authors contributed substantially to the conception and design; review and interpretation of relevant literature; drafting and revisions; and final approval of the published version.

All authors have filed conflict of interest statements with the American Academy of Pediatrics. Any conflicts have been resolved through a process approved by the Board of Directors. Author disclosures are provided at the end of this article. The American Academy of Pediatrics has neither solicited nor accepted any commercial involvement in the development of the content of this publication.

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ABSTRACT. This technical report accompanies the American Academy of Pediatrics (AAP) policy statement (https://doi.org/10.1542/peds.2026-079047) and recommendations for respiratory syncytial virus (RSV) immunization during the 2026–2027 RSV season. The rationale is presented for recommending immunization of all infants younger than 8 months born during or entering their first RSV season, unless the infant has documented protection from vaccination of the pregnant parent; and infants and children 8 through 19 months of age who are at high risk of severe RSV disease and entering their second RSV season. The report synthesizes current evidence on RSV epidemiology, disease burden, immunization effectiveness, safety, and cost-effectiveness in

pediatric populations; including evidence supporting expansion of high-risk groups for second season administration. Additionally, the report provides an overview of available RSV immunization products, formulations, and coadministration with other immunizations.

Key words: infectious diseases, RSV, vaccine/immunization

ABBREVIATIONS: AAP American Academy of Pediatrics; AI/AN, American Indian and Alaska Native; CDC, Centers for Disease Control and Prevention; CF, cystic fibrosis; CI, confidence interval; CHD, congenital heart disease; CLD, chronic lung disease of prematurity; DS, Down syndrome; FDA, US Food and Drug Administration; GA, gestational age; ICU, intensive care unit; LRTI, lower respiratory tract infection; mAb, monoclonal antibodies; MALRI, medically attended lower respiratory infection; QALY, quality-adjusted life year; RSV, respiratory syncytial virus; SAE, serious adverse event.

INTRODUCTION

This technical report accompanies the policy statement and recommendations of the American Academy of Pediatrics (AAP) for the routine use of respiratory syncytial virus (RSV) immunization in the prevention of RSV disease in infants and children during the 2026–2027 season.[1] Of note, the products discussed in the AAP technical report for the prevention of RSV are monoclonal antibodies, and the term is being used interchangeably with RSV immunization and RSV antibody.

METHODOLOGY

This technical report and the accompanying policy statement were developed by the AAP Committee on Infectious Diseases (COID) to inform recommendations for RSV immunization during the 2026–2027 respiratory virus season. The COID convened an RSV subgroup consisting of COID members and external experts with relevant expertise to review evidence and develop proposed recommendations.

Recommendation development was informed, in part, through evidence reviews and scientific updates provided through the Vaccine Integrity Project process, which involved collaboration with medical professional societies and other organizations, including the American Medical Association and the Council on Medical Specialty Societies.

To guide the evidence review process, the subgroup developed priority clinical questions and evaluated available evidence addressing those questions, including evidence related to RSV epidemiology, RSV disease burden, immunization effectiveness, immunization safety, and cost-effectiveness. Priority was given to evidence specific to infants and children and to the most recent available data reflecting the current epidemiologic context whenever possible. Sources reviewed included peer-reviewed literature, public health surveillance data, safety monitoring reports, guidance from professional organizations, and other relevant evidence. Recommendation development was further informed by considerations of domains within the Evidence to Recommendations framework.[2]

All participants submitted conflict of interest disclosures, and individuals with relevant conflicts recused themselves from deliberation and voting in accordance with AAP policies. Recommendations and supporting evidence were reviewed and deliberated by COID, and eligible COID members voted on proposed recommendations. Approved recommendations were incorporated into the accompanying policy statement and technical report. The AAP continues to monitor emerging data related to RSV and may update recommendations as additional evidence becomes available. Additional information about the 2026-2027 AAP immunization recommendation development process can be found at https://www.aap.org/en/patient-care/immunizations/aap-immunization-recommendations-process-2026/.

SUMMARY OF RECENT RSV ACTIVITY IN THE UNITED STATES

RSV is a common respiratory virus that typically spreads seasonally along with other respiratory viruses. In most of the United States, RSV typically circulates from the fall, peaks in December or

January, and continues through the spring. In the United States, the normal seasonal pattern of RSV changed during the COVID-19 pandemic, because nonpharmaceutical measures such as school closures and mask wearing reduced the spread of respiratory viruses, including RSV. As a result, fewer people were exposed to RSV, leaving more individuals vulnerable and contributing to unusually large outbreaks in subsequent years that occurred outside the typical season. After COVID-19 pandemic preventive measures began in March 2020, the 2019–2020 RSV season ended earlier than in previous years, and RSV activity remained extremely low throughout 2020. In 2021, as restrictions were relaxed, RSV began spreading earlier than usual, starting in late spring, and the RSV season lasted longer than it had before the pandemic, although peak infection levels were similar to earlier years. During the 2022–2023 season, RSV activity started later than in 2021–2022 but still earlier than before the pandemic, suggesting that RSV was gradually returning to its normal winter seasonal pattern.[3] During the 2023-2024 and 2024–2025 seasons, RSV activity followed typical seasonal patterns observed before the COVID-19 pandemic (ie, increased activity during October–April) that aligned with the timing of RSV immunization guidance for children for most of the United States.[4,5]

During the 2025-2026 RSV season, rates peaked later than is typical and, as a result, the season lasted longer than usual. In 2026, RSV hospitalization rates in children <18 years of age did not peak until late February at 6.5 per 100,000,[4] and the weekly percentage of tests positive for RSV in all ages peaked in late February at 8.8%.[6] As a result, almost every state extended guidance on providing immunizations until the end of April, 1 month later than the usual March endpoint.[7]

RSV IMMUNIZATION RATES

Infants can be protected against RSV in 2 ways: by receiving antibodies passed from the birthing parent who was vaccinated during pregnancy with RSVpreF vaccine (a recombinant stabilized prefusion F protein vaccine, brand name Abrysvo) or by receiving a long-acting monoclonal antibody (ie,

nirsevimab [brand name Beyfortus] or clesrovimab [brand name Enflonsia]) after birth. The Centers for Disease Control and Prevention (CDC) analyzed state and jurisdiction level immunization information system data from the first season the products were available (ie, 2023-2024) and found that 29% of infants were immunized against RSV either through receipt of nirsevimab or through passively acquired antibodies after RSV vaccination of the birthing parent, with coverage varying widely by state.[8] In a cohort study of 13,195 infants in New York City who received medical care before they were 8 months old, 58% of the 6245 infants during the 2023–2024 RSV season and 75% of the 6950 infants during the 2024–2025 RSV season received protection through either the RSV vaccination of the birthing parent or receipt of nirsevimab. The study also found that infants covered by public insurance were less likely to receive either form of RSV immunization.[9]

The CDC's National Immunization Survey-Fall Respiratory Virus Module (FRVM) provides monthly estimates of maternal RSV vaccination or RSV immunization of infants as well as intent for receiving RSV immunization (https://www.cdc.gov/rsvvaxview/dashboard/). As of February 2026, 65.1% of infants born since April 1, 2025, were reported to have protection against RSV, either because their birthing parent received the RSV vaccine during pregnancy (9.4%) or because the infant received a monoclonal antibody (55.7%). Another 8.4% of parents said they definitely planned for their infant to receive the monoclonal antibody.[10]

RSV MORBIDITY AND MORTALITY IN INFANTS AND CHILDREN

RSV causes acute respiratory tract infections in people of all ages and can cause severe illness in infants and children with certain health conditions. RSV is one of the leading causes of intensive care unit (ICU) admission and acute respiratory failure among infants in the United States.[11] Approximately 58,000 to 80,000 children younger than 5 years and up to 3% of children in their first year after birth are hospitalized because of RSV infection each year in the United States.[12-15] Mortality is rare, however,

when supportive care is available.[12]

RSV is transmitted by direct or close contact with those who are already infected or from touching contaminated surfaces. The highest hospitalization rates occur in the first 6 months after birth, then decline as the infant ages.[16] Most children will experience an RSV infection before age 2 years, and approximately 20% to 30% of children who are infected will develop a lower respiratory tract infection (LRTI)[a] such as bronchiolitis or pneumonia, making RSV one of the most common illnesses of childhood.[12] Reinfection is common and is usually less severe than the primary infection.

Globally, there are around 33 million RSV-related LRTI episodes annually in children younger than 5 years of age, 3.6 million RSV hospital admissions worldwide per year, and approximately 100,000 deaths.[17] Almost all (97%) of RSV-related mortality in children occurs in low- and middle-income countries.[17]

One cross-sectional study analyzed data from the 2024-2025 season sourced from national surveillance systems and reported that RSV-associated hospitalization rates per 100,000 were highest among infants (0 through 11 months of age) (RSV-NET: 1116.7 [95% confidence interval [15,18], 1078.4-1157.9]; National Vital Statistics System [NVSS]: 1053.9 [95% , 949.0-1159.0]), followed by children 12 through 23 months of age (RSV-NET: 770.6 [95% CI, 743.1-800.3]; NVSS: 647.5 [95% CI, 576.7-720.8]).[5] The study also reported that of the 672 RSV-associated deaths recorded by the NVSS, 31 (4.6%) were among children and adolescents (<18 years of age) during the same period. Another cross-sectional study explored the clinical outcomes among children (<5 years of age) who were hospitalized for a primary or secondary RSV diagnosis between September 2022 and August 2024 (n=43,766).[19] Most of those hospitalized were younger than 1 year (n=26,477), followed by children 1 year of age (n=8329) and

[a] Defined as at least 1 documented physical examination finding localized to the lower respiratory tract, clinical signs and symptoms of severe respiratory disease, an inpatient or outpatient encounter, and a positive RSV polymerase chain reaction test result.

2 through 4 years (n=8960). More children were hospitalized for RSV than for COVID-19 (n=6697) or influenza (n=6171) during the same period. RSV-associated hospital stays were estimated as mean 3.6 days (standard deviation [SD], 4.5). Of children hospitalized, 46.1% received treatment with supplemental oxygen (n=20,167) and 12% required invasive mechanical ventilation (n=5251). The study identified 43 deaths in children <5 years of age hospitalized for RSV over a 2-year period; 27 of these occurred in children younger than 1 year.

Certain health conditions increase an infant's risk of severe RSV LRTI, including: preterm birth (especially early preterm birth), severe congenital heart defects, chronic lung disease of prematurity, severe immunocompromise, certain immunodeficiency states, Down syndrome (DS), cystic fibrosis (CF) with either manifestations of severe lung disease (previous hospitalization for pulmonary exacerbation in the first year after birth or abnormalities on chest imaging that persist when stable) or weight-for-length <10th percentile, or anatomic pulmonary abnormalities or neuromuscular disorders that hamper swallowing and clearing mucus.[1,12,20] Other risk factors have a limited correlation with RSV disease severity, including: low birth weight, birthing parent's smoking during pregnancy, exposure to secondhand smoke in the household, family history of atopy, lack of breastfeeding, and high household occupancy.[1,12] Additionally, in the United States, American Indian and Alaska Native (AI/AN) children experience disproportionately high RSV disease and hospitalization rates that are 4 to 10 times the rate of other children.[21] Evidence suggests that socioeconomic drivers of health have a significant impact on this increased risk, including the previously noted limited access to health care and transportation, lack of running water in the home, as well as high household occupancy and indoor air pollution.[21-23]

Nonetheless, three-quarters of hospitalized RSV-positive infants younger than 1 year did not have any history of prematurity or chronic conditions and were considered to be healthy.[13] These findings illustrate that *all* infants younger than 1 year are at risk for severe RSV illness.[16]

HIGH-RISK GROUPS IN PEDIATRICS

Infants During Their First RSV Season

RSV is a leading cause of hospitalization among US infants in their first year after birth. Prior to the August 2023 recommendation for universal RSV immunization for all infants <8 months of age, there were up to 80,000 RSV-associated hospitalizations[15,18] and up to 200 to 300 RSV associated deaths among US infants annually.[15,24] As noted above, most infants who are hospitalized for RSV have no history of prematurity or other high-risk conditions, supporting a universal first-season prevention strategy.

Recent data support this strategy. The New Vaccine Surveillance Network evaluated infants ≤12 months of age who were hospitalized with acute respiratory illness from October 2023 through February 2024. Of 699 infants who were hospitalized, 59 (8%) had received nirsevimab at least 7 days prior to symptom onset. Nirsevimab effectiveness against RSV-associated hospitalization was estimated at 90% (95% CI, 75%–96%). Of the hospitalized infants, 79% were born at >37 weeks' gestation and 94% did not have any high-risk medical conditions. These postintroduction data provide evidence that first season RSV immunization substantially reduces severe RSV outcomes, including hospitalization.[25]

Children With High Risk Conditions During Their Second RSV Season

The risk for RSV-associated hospitalization decreases for most children after 12 months of age.[16] However, some children remain at increased risk as they enter their second RSV season.[26] In 2023, the CDC's Advisory Committee for Immunization Practices (ACIP) made the recommendation that 1 dose of nirsevimab is recommended for some children 8 through 19 months of age in certain high-risk groups entering their second RSV season. The ACIP Pediatric/Maternal Work Group recommended nirsevimab for the same groups eligible for palivizumab (brand name Synagis) when entering second RSV season, per the AAP, and for AI/AN children.[27] Previous AAP recommendations for palivizumab were intentionally restrictive because of the high cost of the product (ie, $1455–$2747 per dose) and high

burden of administration (ie, required monthly intramuscular administration during RSV season, typically for 5 consecutive months to cover the peak season). In 2026, given the availability of nirsevimab, with a lower cost (ie, $400–500 per dose) and easier administration (ie, 1 administration per season) to prevent RSV in children with high-risk conditions during their second season, the goal of the AAP was to review the scientific literature supporting recommendations for nirsevimab use for children who are most likely to derive benefit from RSV prophylaxis with this agent during their second season.

A 2025 population-based surveillance study sought to identify the high-risk factors by examining data from 12 states on laboratory-confirmed RSV hospitalizations among 1083 children aged 12 through 23 months from 2022–2023.[28] Results indicated that 23.4% (95% CI, 18.6%–28.7%) of hospitalized children 12 through 23 months of age had an underlying medical condition[28] (in contrast to the 6% of hospitalized infants ≤12 months of age with an underlying medical condition in the New Vaccine Surveillance Network study discussed earlier[25]). Of these hospitalized children, the percentage of ICU admission rates increased with the number of underlying medical conditions. Hospitalized children with 1 or fewer underlying medical conditions had a 22% ICU admission rate, whereas those with 2 or more underlying chronic health conditions had an ICU admission rate of 30%. Hospitalized children 12 through 23 months of age who experienced more severe outcomes had significantly higher odds of having specific underlying medical conditions including airway abnormalities, cardiovascular disease, DS, or feeding tube dependence (which is an indicator for medical complexity). The authors concluded that severe second-season RSV is concentrated in patients with underlying medical conditions.[28]

Another Canadian retrospective population-based cohort study conducted among children born between 2013 and 2023 found that RSV-related hospitalization rates per 1000 person-years for children with chronic medical conditions (as identified by *International Classification of Diseases*, 9th Edition codes) during their *second* RSV season were similar to children without chronic medical conditions in their *first* season: 7.8 (95% CI, 6.7–8.8) and 8.0 (95% CI, 7.7–8.3) respectively.[29] Children who have multisystem chronic health conditions, particularly those affecting respiratory, cardiovascular, or

gastrointestinal systems, had second-season RSV-related hospitalization rates that were more than twice as high as all children in their first RSV season.[29] The populations at highest risk of RSV-related hospitalization in the second season were children with DS and those born extremely preterm (less than 28 weeks' gestation); these patients had second-season rates 5 times that of the general population's first-season rate.[29]

A retrospective multicenter cohort of 11 medical centers in Israel studied 1023 children 12 through 23 months of age who were hospitalized with RSV between 2017–2021. This study assessed risk factors for severe RSV-related disease among hospitalized 12- through 23-month-old children. The results indicate significantly greater risk of prolonged hospitalization and RSV-related complications in children with prematurity, major congenital heart disease (CHD), chronic lung disease of prematurity (CLD), or DS.[20] Children with more than 1 of these risk factors were at highest risk for experiencing severe RSV-related disease and pediatric ICU admission.[20]

Of note, 92% of children with ICU-level second season RSV-related hospitalizations were ineligible for second-season immunization under the previous guidelines.[28] Specific populations show heightened risk of second-season hospitalization, including patients with DS and major CHD, multisystem chronic medical conditions, and prematurity (birth at <32 weeks, 0 days' gestation). In response, second-season criteria were expanded in the accompanying AAP policy statement.[1] Information is provided below about populations for which the AAP recommends second-season immunization.[1]

Children With Prematurity of Less Than 32 Weeks, Regardless of the Need for Medication

In 2024, 3.63 million births were reported in the United States, 10.4% of which were infants born preterm at less than 37 weeks' gestation.[30] Infants born at less than 28 weeks' gestation accounted for 0.6% of the annual birth cohort,[30] and those born from 32 weeks, 0 days to 36 weeks, 6 days' gestation represented approximately 8.9% of the birth cohort.[30]

Infants who are born preterm are at higher risk of developing RSV disease compared with

children born full-term in both their first and second RSV seasons.[16,29,32,33] The risk appears to be higher for infants born at less than 32 weeks' gestation, compared with those born at 32 to 37 weeks' gestation.[31] [16]RSV-associated hospitalization rates for infants and children <2 years of age vary significantly by birth gestation: infants and young children had a hospitalization rate of 24.9 per 1000 children (95% CI, 19.3–30.6) with birth at <29 weeks' gestation; 19.3 per 1000 (95% CI, 14.7–23.7) with birth at 29 to 31 weeks' gestation; and 17.5 per 1000 (95% CI, 14.8–20.2) with birth at 32 to 34 weeks' gestation, compared with a hospitalization rate of 11.3 per 1000 (95% CI, 10.0–12.8) at 35 to 36 weeks' gestation and 7.5 per 1000 (95% CI, 7.2–7.9) for birth at ≥37 weeks' (term) gestation.[16] Risk remains higher for earlier birth gestations in the second season. At 12 through 23 months of age, the risk of hospitalization for RSV disease is significantly higher among infants born at <32 weeks' gestation compared with all infants at this age, whereas there is no significant difference in RSV-associated hospitalization in infants born at 32 to 36 weeks' gestation compared with all infants.[32] Overall, current data suggest that gestational age (GA) under 32 weeks is the threshold for persistent second-season risk.[29,31,32]

Children With CLD or Other Significant Neonatal Conditions Who Required Ongoing Medical Intervention in the 6 Months Prior to the RSV Season

CLD (formerly called bronchopulmonary dysplasia) includes a variety of respiratory pathologies that result from prematurity and range from minimal respiratory symptoms and some lung function loss to more severe cases.[33] Multiple studies have documented that infants and young children with CLD have increased rates of RSV-associated hospitalization.[34] These elevated rates are sustained through the second year of life compared with healthy term infants at 1 month of age.[35,36] Results from the IMpact-RSV trial evaluating all preterm infants with CLD (n=762 randomly assigned preterm infants) demonstrated that the RSV-associated hospitalization rate among placebo recipients was 12.8% and 7.9% among palivizumab recipients (P = .038).[37] A systematic review of publications from 1995 to 2015 assessed RSV-related hospital visit and admission data for infants with CLD.[38] This study determined CLD to be a significant independent risk factor for RSV-associated hospitalization in the first 2 years of a child's life. Rates

ranged from 12% to 21% across Europe, the United States, and Canada—a rate approximately 20 times higher than that of children who do not have CLD.[38] In addition to higher hospitalization rates, infants with CLD had longer duration of hospitalization, higher risk of a more-severe disease course, greater likelihood of ICU admission, and greater likelihood of requiring oxygen supplementation and assisted ventilation, compared with otherwise healthy or preterm infants without CLD.[38] Children with CLD who required ongoing medical support, including chronic corticosteroid therapy, diuretic therapy, and/or supplemental oxygen at any time during the 6-month period before the start of the second RSV season are considered to be at increased risk for severe RSV disease.[39]

Children With Hemodynamically Significant Congenital Heart Disease

Children with hemodynamically significant CHD (ie, a defect that can result in symptoms and/or cardiac chamber dilation) have an equal risk of experiencing RSV but a much higher rate of mortality.[40] Among hospitalized children 12 through 23 months of age with CHD and RSV, mortality was 1.5%, compared with substantially lower mortality among RSV-hospitalized children without CHD.[41] This risk remains substantial through the infant's second RSV season. The risk varies by type of CHD anomaly. Canadian CARESS data show an equal RSV hospitalization hazard in year 1 compared with year 2 among palivizumab-treated infants with hemodynamically significant CHD.[42] An analysis of risk by diagnosis among infants 12 through 23 months of age, from a national inpatient sample from 1997–2013, found that some diagnoses were much more likely to increase RSV- associated mortality, including Ebstein's anomaly, transposition of great arteries, aortic stenosis, heterotaxia/situs inversus, and aortic arch anomalies.[42] Of note, the overall finding of lower risk in the second season for CHD is driven by the study's inclusion of many low-risk, nonhemodynamically significant diagnoses (eg, small atrial septal defects, small muscular ventral septal defects, trivial/silent patent ductus arteriosus). Another large retrospective study analyzed US National Inpatient Sample data from 1997–2013 to assess the risk of RSV-related associated hospitalization among children 12 through 23 months of age who had CHD.[43] The findings suggest that some forms of CHD are associated with a heightened risk of RSV-associated

mortality. The findings also suggest that children with some hemodynamically significant CHD conditions have a higher risk of second-season RSV-associated hospitalization, compared with children who do not have CHD.[43]

Therefore, children with hemodynamically significant CHD who are most likely to benefit from RSV immunization in the second season include those with acyanotic heart disease who are receiving medication to control congestive heart failure and will require cardiac surgical procedures as well as infants with moderate to severe pulmonary hypertension. Decisions regarding RSV prophylaxis for infants with cyanotic heart defects may be made in consultation with a pediatric cardiologist. The following groups of infants with CHD are not at increased risk of severe RSV disease and generally should not receive RSV immunization in the second season (unless they have other qualifying high-risk comorbidities as described elsewhere):

- Infants and children with hemodynamically insignificant heart disease (eg, secundum atrial septal defect, small ventricular septal defect, pulmonic stenosis, uncomplicated aortic stenosis, mild coarctation of the aorta, and patent ductus arteriosus)
- Infants with lesions adequately corrected by surgery, unless they continue to require medication for congestive heart failure
- Infants with mild cardiomyopathy who are not receiving medical therapy for the condition

There are limited data showing increased risk for hospitalization in the second season for children with acquired cardiomyopathy and/or congestive heart failure. For children with these conditions who require medical therapy, decisions about RSV prophylaxis may be made in consultation with a pediatric cardiologist.

Children With Anatomic Pulmonary Abnormalities or Neuromuscular Disorders

Neuromuscular disorders include any neurologic condition, sequelae of hypoxic-ischemic encephalopathy at birth, traumatic brain injury, chromosomal abnormalities, metabolic disorders with

neuro/muscular involvement, cerebral and other degenerative diseases of the central nervous system, muscular dystrophies, neural tube defects, motor neuron diseases, and epilepsy and recurrent seizures.[44] The risk of RSV-associated hospitalization is not well defined in children with neuromuscular disorders or anatomic pulmonary abnormalities that impair the ability to clear secretions from the upper airway because of ineffective cough, recurrent gastroesophageal tract reflux, pulmonary malformations, tracheoesophageal fistula, upper airway conditions, or conditions requiring tracheostomy.

Studies suggest children and infants with neuromuscular disease who are hospitalized with RSV infection tend to be older compared with other groups of patients hospitalized with RSV infection and are more likely to have preexisting immunity to RSV.[45,46] This may reflect the progressive nature of neuromuscular disease, with susceptibility to respiratory tract disease increasing with age. Children with medically complex conditions or anatomic anomalies, including neuromuscular disorders, congenital diaphragmatic hernia, and those who require tracheotomy or ventilatory support, might experience more frequent and prolonged hospitalizations for respiratory infections, including RSV.[47-52]

An analysis of commercial and Medicaid insurance claims from July 2006 through June 2015 found that children with neurologic disorders (defined as including both neurodevelopmental and neuromuscular disorders) had higher rates of LRTI, compared with the general pediatric population. These children had 6 to 11 times higher rates of RSV-specific hospitalizations and 6 to 10 times higher rates of RSV-associated hospitalizations, compared with children in the general population. Admission to the ICU and mortality risk were also higher among children with neurologic disorders, compared with the general population.[51]

Children with anatomic airway abnormalities have higher rates of RSV-associated hospitalization and respiratory failure.[53] This study found that patients with congenital airway anomaly have a respiratory hospitalization rate of 13.6% compared with 6.0% among patients with standard indications.[53] Concurrent gastroesophageal reflux disease (which frequently occurs with airway

anomalies) increases aspiration risk.[53]

Children With Severe Immunocompromise

Children with severe immunocompromise include those who have received hematopoietic cell or solid organ transplants, have primary immunodeficiency, or are undergoing chemotherapy.[54,55] Progression of RSV infection from upper to lower respiratory tract disease depends on the specific abnormalities in the immunocompromised host's immune response attributable to the underlying disease or to treatment. Lymphopenia has been recognized as a risk factor for disease progression in several studies of immunocompromised patients.

RSV is particularly dangerous for these infants and children, because it can lead to respiratory failure and mortality.[56] A single-center retrospective report from 2006 to 2011 on 117 immunized patients with RSV-associated LRTI identified 5 deaths among this group: 2 patients had severe combined immunodeficiency, 1 had uncharacterized immunodeficiency, 1 had chronic granulomatous disease, and 1 had received a solid organ transplant. Profound lymphopenia (<100 cells/mm^3) was associated with progression to lower respiratory tract disease.[57] Another retrospective review assessed outcomes in the Pediatric Health Information System from 1998 to 2009 among 57 RSV-infected pediatric cancer patients, of whom more than two-thirds (37%) developed LRTI; of these patients, 3 died of respiratory failure within 60 days of RSV diagnosis.[58] A 2004 to 2012 retrospective cohort study of 2554 pediatric liver transplant recipients found that, in the first 2 years after transplant, these patients had a significantly higher RSV-associated hospitalization rate (4.0%), compared with those in the general population.[59] These patients had more complicated hospitalizations, longer and more expensive lengths of stay, and higher transplant rejection rates.[59] Another study that used Pediatric Health Information System data from 2003 through 2018 found RSV to be the most common cause of hospitalization among pediatric heart transplant recipients.[60]

Other risk factors for a poor outcome after RSV infection in an immunosuppressed host include

age younger than 2 years, presence of lower respiratory tract symptoms at presentation (particularly in the absence of symptoms of upper respiratory tract infection), corticosteroid therapy, and lymphopenia. Underlying diagnosis, degree of immune suppression, RSV load in bronchoalveolar lavage, or specific humoral immunity to RSV have not been found to correlate with outcome.[61,62] This inability to correlate degree of immunosuppression with disease severity indicates an incomplete understanding of the immune response to viral respiratory infections in the immunocompromised host.

Children With DS or Other Chromosomal Differences

Several factors appear to place children with DS at increased risk of RSV-associated LRTI compared with children without DS.[63-66] CHD, with or without pulmonary hypertension, occurs in approximately 45% of children with DS, and lesions include atrioventricular canal, ventricular septal defect, patent ductus arteriosus, and tetralogy of Fallot.[61] Anatomic abnormalities of the upper or lower respiratory tract, muscle dystonia, and intrinsic immune dysfunction may contribute to viral respiratory disease in this population.

One population-based cohort study over an 11-year period in Colorado reported a statewide total of 85 RSV-associated hospitalizations among 680 children with DS during their first 2 years of life. Concurrent risk factors were present in 35 of the 85 (41%) hospitalized children. RSV-associated hospitalization rates were 67 per 1000 child years for children with DS and other risk factors, 42 per 1000 child years for children with DS without cardiopulmonary disease, and 12 per 1000 child years for children in a control group.[66] These data suggest an estimated overall 7.7 RSV admissions per year (85 admissions over 11 years) in the state of Colorado for children with DS. Using these figures, 4.6 RSV hospitalizations per year occur among children with DS without concurrent factors (50 admissions in 11 years) in Colorado. No deaths were reported in this study.[66] These data suggest children with DS have a slightly higher hospitalization rate, but the absolute number of RSV-associated hospitalizations is small, and a number of children with DS are at increased risk because of qualifying heart disease or other factors.

A meta-analysis of 5 articles published between 1995 and 2017 suggested DS is an independent risk factor for RSV-associated hospitalization for children <2 years, with a 6.8-fold increased risk (95% CI, 5.4–6.7) when compared with unaffected children, but the meta-analysis was limited by a small number of included studies and potential confounding because of additional comorbidities.[67] Another meta-analysis examining RSV-associated hospitalization in children with DS found that children younger than 2 years of age had a 6.06 times higher relative risk of RSV-associated hospitalization compared with children without DS (95% CI, 4.93%–7.45%).[68] A 2018 review of cohort and case-control studies of pediatric patients (birth to <18 years) with DS that assessed RSV infection and associated morbidity or mortality found DS to be associated with a higher risk of hospitalization (odds ratio [OR], 8.69; 95% CI, 7.33%–10.30%) and mortality (OR, 9.4; 95% CI, 2.26%–39.15%) compared with controls.[69]

A 2017 meta-analysis of articles published from 1995 to 2017 found that children with DS who have CHD experience admission rates that are higher than those with CHD and no DS: 19.1% versus 11%.[67] DS and prematurity also confers risk that, in 1 study, was found to be 5 times higher than the all-infants first season rate.[68]

Analyses revealed that even children without additional risk factors had significantly more risk for severe RSV disease.[69] For example, children with DS who do not have CHD also have an elevated risk of hospitalization (relative risk [RR], 6.31; 95% CI, 4.83%–8.23%).[68-70] Studies have additionally found that hospitalization is more severe for children with DS; they tend to have longer length of stay, higher need for assisted ventilation, more frequent use of supplemental oxygen, higher ICU admission rates, and an older mean age of hospitalization.[68-70]

Taken together, these studies support the administration of RSV immunization to children with DS during their second RSV season. Although the data available are limited to DS, it is likely that children with other trisomies or chromosomal differences that predispose a child to a higher risk of RSV disease (eg, problems with airway clearance, immune dysfunction) would also benefit from second season RSV immunization.

Children With CF Who Have Either: Manifestations of Severe Lung Disease (eg, Previous Hospitalization for Pulmonary Exacerbation in the First Year After Birth or Abnormalities on Chest Imaging That Persist When Stable) or Severe Lung Disease or Weight-for-length <10th Percentile

Available studies indicate RSV-associated hospitalization in children with CF is uncommon and the incidence is unlikely to be different from children without CF.[71-73] Children with CF who do not have severe lung disease are not at high risk for RSV-associated hospitalization. However, children with CF who have severe and rapidly progressing symptoms are eligible for second-season RSV immunization.

AI/AN Children

All AI/AN children are included in the high-risk category because of this population's significantly higher rates of severe RSV disease and RSV-associated hospitalization; children who live in rural and reservation communities are the most impacted.[1,21] Evidence supports that the increased risk in AI/AN children is associated with social drivers of health, specifically a lack of access to transportation, health services, and running water in the home in some communities; high household occupancy; and indoor air pollution.[21,22] In 2022-2023, the year before introduction of RSV-prevention products, rates of RSV-associated hospitalization in AI/AN infants were 59.6 per 1000 in the southwest United States and 52.8 per 1000 in the Yukon-Kuskokwim Delta, more than 2 times higher than the general US infant population (22.3 per 1000).[23]

Although social drivers of health may contribute to RSV-associated hospitalization risk in other groups, there are constraints in translating current evidence to implementable recommendations at a population level on the basis of these social risk factors. Limitations in the evidence include specificity regarding social factors that confer risk for poor outcomes related to RSV. Implementation constraints include the absence of available information regarding specific social risk factors at the point of care.

RSV IMMUNIZATION PRODUCTS FOR INFANTS AND CHILDREN

Two monoclonal antibody (mAb) products, nirsevimab and clesrovimab, are recommended for prevention of RSV LRTI in infants younger than 8 months in the United States. Both products are administered as a single dose to infants entering their first RSV season. Prior to nirsevimab's approval, palivizumab was the only licensed product for prevention of RSV; palivizumab was restricted to infants at highest risk for RSV because of its logistical and cost constraints (eg, monthly dosing was required). Palivizumab has since been discontinued.[74] The AAP recommends any licensed RSV immunization product that is appropriate for the patient's age and health status and does not prefer one RSV product over the other.

Nirsevimab

The US Food and Drug Administration (FDA) approved nirsevimab on July 17, 2023. Nirsevimab is a long-acting mAb targeting the RSV prefusion F protein (site Ø). It has a half-life of approximately 71 days. Dosing is as follows: For children younger than 8 months who are entering their first RSV season, 50 mg (for infants weighing <5 kg) or 100 mg (for infants weighing ≥5 kg), intramuscular injection, ×1 dose; for children 8 through 19 months of age who remain at increased risk of RSV LRTI in their second season, 200 mg, intramuscular (two 100-mg doses administered at the same time).[75] Nirsevimab is currently the only product indicated for prevention of RSV in children who remain vulnerable to RSV in their second RSV season.

Clesrovimab

Clesrovimab, a long-acting RSV monoclonal antibody, was approved by the FDA in June 2025. On August 19, 2025, the AAP recommended clesrovimab as a second product for prevention of RSV-associated LRTI for infants younger than 8 months born during or entering their first RSV season if they did not receive protection through RSV vaccination of their birthing parent. Clesrovimab has a half-life of 44 days. Clesrovimab, like nirsevimab, is recommended by the AAP for all infants younger than 8 months

entering their first RSV season. The recommended dose for all infants born during or entering their first RSV season is 105 mg, administered as a single intramuscular injection. Clesrovimab is not approved for use in the second RSV season.[15]

EFFECTIVENESS OF RSV IMMUNIZATION PRODUCTS

Nirsevimab

The efficacy of nirsevimab was established in phase 3 clinical trials. Since then, numerous studies have examined the effectiveness of nirsevimab. In the first RSV season following the ACIP and AAP recommendation for the use of nirsevimab (eg, 2023–2024), the New Vaccine Surveillance Network evaluated nirsevimab effectiveness against RSV-associated hospitalization among infants in their first RSV season to be 90% (95% CI, 75%–96%).[25] In the first RSV season during which nirsevimab was available (2023–2024), an electronic health record-based analysis assessed data from 6 US health systems on infants younger than 8 months who had RSV-like illness at emergency department (ED) or hospital admission. Of 5039 ED encounters, 41% of patients were RSV-positive and 9% had received nirsevimab; of 1025 hospitalizations, 59% were RSV-positive and 9% had received nirsevimab. Nirsevimab effectiveness was 77% (95% CI, 69–83) against RSV-associated ED visits and 98% (95% CI, 95–99) against RSV-associated hospitalization.[76]

A retrospective cohort study assessed outcomes in the 2024–2025 RSV season using electronic health record data on 409,723 infants younger than 8 months, aggregated from more than 1700 hospitals and 40,000 clinics from the United States, Canada, Lebanon, and Saudi Arabia. RSV-associated hospitalization rate among nirsevimab recipients was 0.4%, compared with 1.2% for nonrecipients (P <.001).[77]

For nirsevimab effectiveness against RSV infection resulting in ICU admission and respiratory failure, data are more limited. A case-control study conducted across 27 hospitals using the Overcoming

RSV Network assessed how nirsevimab prevented severe RSV-related illness in infants between December 1, 2024, and April 15, 2025. The study compared 457 infants admitted to the ICU with RSV infection versus 302 infants admitted to the ICU with similar respiratory symptoms who tested negative for RSV. Fourteen percent of the RSV-positive infants had received nirsevimab at least 7 days before symptoms began, compared with 45% of the RSV-negative infants. Nirsevimab was estimated to be 80% effective (95% CI, 70%–86%) against RSV-associated ICU admissions and 83% effective (95% CI, 74%–90%) against acute respiratory failure.

Among AI/AN children in their first RSV season in the southwest United States and Alaska, nirsevimab was shown to be highly effective against RSV-associated hospitalization from 2023 to 2024. A study in Alaska assessed 292 AI/AN children with medically attended acute respiratory illness in their first RSV season; overall, 55% had received nirsevimab 7 or more days before the onset of their illness. Nirsevimab effectiveness against first-season medically attended acute RSV was 76% (95% CI, 42%–90%); vaccine effectiveness against RSV-associated hospitalization was 89% (95% CI, 32%–98%); the large CI reflects the small sample size.[78] Another study assessed 165 AI/AN children hospitalized with acute respiratory illness in their first RSV season in the southwest United States and Alaska; overall, 31% had received nirsevimab 7 or more days before the onset of their illness. Nirsevimab effectiveness against RSV-associated hospitalization was 86% (95% CI, 56%–96%).[79]

The NIRSE-GAL study is an ongoing, population-based, prospective, longitudinal study of nirsevimab being conducted in Galicia, Spain. Initial results published in 2024 showed an effectiveness of 82.0% (95% CI, 65.6%–90.2%) against RSV-associated LRTI hospitalization, effectiveness of 86.9% (95% CI, 69.1%–94.2%) against severe RSV-associated LRTI requiring oxygen support, and effectiveness of 69.2% (95% CI, 55.9%–78.0%) against all-cause LRTI hospitalizations.[80] A NIRSE-GAL study published in 2026 assessed the impact of universal administration of nirsevimab to infants across inpatient and outpatient settings during their first RSV season (2023–2024) until the end of their second RSV season (2024–2025). Compared with historical infant cohorts, RSV-associated LRTI

hospitalizations were reduced by 85.9% (95% CI, 80.2%–90.0%) in the first season and 55.3% (95% CI, 22.5%–74.3%) in the second season. Admissions for acute bronchitis or bronchiolitis also declined, falling by 59.0% (95% CI, 37.9%–72.9%) in the first season and by 58.7% (95% CI, 40.6%–71.3%) up to 18 months after immunization.[81]

Chile was the first country in the Southern Hemisphere to implement a universal nirsevimab strategy. A study of the effectiveness and impact of nirsevimab during the 2024 RSV season assessed RSV-related LRTI hospitalizations among infants who did or did not receive nirsevimab.[82] Outcomes were assessed for 154,173 infants who received nirsevimab and who were born either between October 1, 2023, and March 31, 2024, or April 1, 2024, and September 30, 2024.[82] The combined effectiveness of nirsevimab against RSV- associated LRTI hospitalizations was 76.41% for both catch-up and seasonal cohorts (95% CI, 72.57%–79.72%), 84% to 94% against RSV-associated ICU admissions (95% CI, 79.47%–88.95%), and 66.50% against all-cause LRTI hospitalizations (95% CI, 61.97%–70.50%). In total, the study found an estimated relative reduction of 77.46% in RSV-associated LRTI hospitalizations and 30.05 averted cases per 1000 infants and a number needed to immunize to prevent 1 RSV-associated LRTI hospitalization of 35.[82]

A 2024 Italian study examined outcomes during the 2023–2024 season from a universal prophylaxis campaign with nirsevimab for healthy newborn infants in their first RSV season. Among the 556 infants born during that period, the risk of hospitalization for RSV bronchiolitis was 3.2%, compared with 7% in the 2022–2023 season (P <.001). After the campaign started, the bronchiolitis-related hospitalization risk was 8.3% among infants who did not adhere to the prophylaxis versus 0 among those in the treated sample (P <.001).[83] Another Italian study performed a retrospective observational monocentric study of 2035 infants hospitalized from November 2024 to April 2025, after the introduction of nirsevimab into clinical practice.[84] RSV infection rate among the study population was 0.52%, lower than rates during the 2023–2024 and 2022–2023 seasons (1.61% and 0.71%, respectively). RSV infection rates were lower in 2024–2025 than in 2023–2024, with an estimated 69% reduction; however, the

difference was borderline/nonstatistically significant (P = .051; RR, 0.31; 95% CI, 0.09–1.13).[84]

The Vaccine Integrity Project published a systematic review of studies published from August 1, 2024, through July 31, 2025, evaluating the administration of nirsevimab against hospitalization in children <12 months of age and reported a pooled effectiveness of 83% (95% CI, 74%–88%; case control) and 79% (95% CI, 70%–85%; cohort).[85] An updated systematic review conducted by the Vaccine Integrity Project of studies published since August 2025 reaffirms that RSV immunization offers protection against RSV hospitalization and emergency department consultation for infants in their first RSV season.[86]

Second Season Administration

Data on nirsevimab efficacy for infants at higher risk of severe RSV disease entering their second RSV season came from the MEDLEY trial. The trial included 615 preterm infants born at or before 35 weeks of gestation who were eligible for palivizumab, as well as 310 infants with CLD requiring medical care within 6 months before randomization or with hemodynamically significant CHD.[75,87] Few studies have examined nirsevimab effectiveness among infants with high-risk conditions.

Among AI/AN children in their second RSV season in the southwest United States and Alaska, nirsevimab was shown to be highly effective against medically attended RSV and RSV-associated hospitalization from 2023 to 2024.[78,79] A study in Alaska assessed 180 AI/AN children with medically attended acute respiratory illness in their second RSV season; overall, 37% had received nirsevimab 7 or more days before the onset of their illness. Nirsevimab effectiveness against medically attended second-season acute RSV was 88% (95% CI, 48%–97%).[78] A separate study in Alaska and the southwest United States assessed 126 infants in their second RSV season hospitalized with acute respiratory illness; 10.3% (n=13) had received nirsevimab 7 or more days before presenting for care. Nirsevimab effectiveness was 87.9% (95% CI, 22%–98%).[79] The large CIs reflect the small sample size.

A European multicenter study included Irish, Portuguese, and Spanish children younger than 24

months who were hospitalized for severe acute respiratory infection during the 2024 to 2025 RSV season. The pooled immunization effectiveness was 79% (95% CI, 58%–89%), but the second-season subgroup cannot be fully disaggregated in these data.[88] Carazo et al used population-level data from Quebec, Canada, to estimate the effectiveness of nirsevimab against severe RSV outcomes, including in children younger than 19 months with one of the following chronic conditions: bronchopulmonary dysplasia, CLD, CHD or cardiomyopathy, pulmonary hypertension, DS, CF, or neuromuscular disorder or congenital anomaly that impairs clearance of upper airway secretions in addition to bone marrow, hematopoietic cell, or solid organ transplant recipients. The adjusted immunization effectiveness in this study group against ED consultation and hospitalization was 86.0% (95% CI, 70.0%–93.0%) and 79.0% (95% CI, 60.0%–89.0%), respectively.[89]

Clesrovimab

The efficacy of clesrovimab was established in phase 2b/3 clinical trials. The CLEVER trial was a randomized 2:1 double-blind multicountry study in healthy preterm (>29 weeks' GA) and full-term infants, birth to 1 year of age, entering their first RSV season. In this trial, 2412 infants received clesrovimab and 1202 received placebo. Efficacy against medically attended LRTI was 60.4% (95% CI, 44.1%–71.9%) and efficacy against RSV-associated hospitalization was 84.2% (95% CI, 66.6%–92.6%), showing a robust protection against severe disease as well as increasing efficacy with disease severity.[90]

The SMART trial evaluated clesrovimab in infants and children at increased risk for severe RSV disease in a palivizumab-controlled trial.[91] The study population included infants recommended to receive palivizumab entering their first RSV season: those born early or moderately preterm (≤35 weeks, 0 days' GA), who have CLD, or who have hemodynamically significant CHD at any GA.[91] The incidence of RSV-associated medically attended lower respiratory infection (MALRI) and RSV-associated hospitalization for season 1 was similar in the clesrovimab and palivizumab groups (3.6% and 3.0%, respectively and 1.3% and 1.5%, respectively). At day 150, the geometric mean serum level of

clesrovimab (11.4 μg/mL) was similar in all risk groups and consistent with that observed in healthy infants in the CLEVER study (10.2 μg/mL).[91]

Recent data from the SMART trial show that through 180 days after a 210-mg dose in season 2, RSV-associated MALRI occurred in 7.3% of participants (95% CI, 4.4%–11.4%), and RSV-associated hospitalization occurred in 3.0% (95% CI, 1.3%–5.9%). These rates were similar to those seen among participants who received 105 mg of clesrovimab in season 1 (MALRI: 8.6% [95% CI, 4.3%–15.4%]; hospitalization: 3.8% [95% CI, 1.2%–8.8%]) and those who received palivizumab in season 1 (MALRI: 6.0% [95% CI, 2.6%–11.9%]; hospitalization: 2.2% [95% CI, 0.5%–6.5%]).[92] A supplemental Biologics License Application has been submitted to the FDA and other regulatory authorities for evaluation for an expanded indication in children at increased risk for severe RSV disease through their second season, perhaps for the 2027–2028 season. At the time of publication, there is no FDA-approved second-season indication for clesrovimab.

SAFETY OF RSV IMMUNIZATION PRODUCTS

Nirsevimab

Safety data from phase 2b and phase 3 clinical trials demonstrate that nirsevimab is well tolerated in healthy late-preterm and term infants, with no significant safety signals, anaphylaxis, or serious hypersensitivity reactions reported.[75] Across trials, the incidence of serious adverse events (SAEs), defined as life-threatening events, hospitalization or prolonged stay, persistent disability, or death, was comparable between treatment arms (6.8% vs 7.3% for placebo). Over a 361-day follow-up period in the MELODY trial, 3 deaths occurred in the nirsevimab cohort, all at or after day 140. Causes included untreated gastroenteritis in 2 infants (days 143 and 338) and an unexplained death on day 140 in an infant with failure to thrive and evidence of a previously undiagnosed underlying chronic condition. Independent investigator assessment concluded that no SAEs or deaths were related to nirsevimab or

placebo.[95]

In the phase 2/3 MEDLEY trial of infants at risk for severe RSV who were eligible for palivizumab, nirsevimab demonstrated a safety profile similar to palivizumab across all groups and cohorts. Six deaths occurred during the study; 5 in the nirsevimab group (2 preterm infants, 3 infants with CHD/CLD) and 1 in the palivizumab group (CHD/CLD). Investigators confirmed that none of the deaths were related to either treatment.[87]

The phase 3b HARMONIE study of infants 12 months or younger with GA of at least 29 weeks found no substantial safety concerns, with follow-up data suggesting safety up to 12 months after receipt of nirsevimab.[96]

International peer-reviewed postmarketing and cohort studies also confirm the product's safety. A 2025 Australian study assessed adverse events among 1195 children who had received nirsevimab either alone or coadministered. Approximately one-quarter (277 or 23.2%) of the children were reported to have had 1 or more adverse events in the 3 days after receiving nirsevimab (either alone or with 1 or more vaccinations). Most commonly reported symptoms were: fatigue (14.4%), local reaction (11.7%), fever (10.6%), and gastrointestinal issues (including vomiting/diarrhea) (9.4%). These symptoms were more often reported when nirsevimab was coadministered with 1 or more vaccines than when it was administered alone (P <.001). There were no reports of adverse events requiring inpatient care or that had ongoing sequelae.[97]

In a prospective observational cohort study in the Valle d'Aosta region of Italy from 2023–2024, 360 neonates received nirsevimab. The majority (89.2%) of parents reported no side effects, 6.5% reported fever, 4.0% reported a local reaction at injection site, and 0.4% reported inconsolable crying. None of the reported cases required additional medical visits, and no major adverse effects were reported.[83] In the 2025 Constantino et al retrospective study of 491 term and preterm neonates who received nirsevimab, there were no adverse events following immunization over a 30-day follow-up (95%

upper bound, 0.73%).[84]

Spain added nirsevimab to its national immunization program during the 2023–2024 RSV season, achieving a 91.9% coverage rate.[98] An analysis of this universal program using postmarketing surveillance of the 2023–2024 season found that 67 cases reported 141 suspected adverse events; the overall adverse event notification rate was 23.1 cases per 100,000 doses. Rash (8.51%), drug ineffectiveness (7.09%), and pyrexia (7.09%) were the most commonly reported adverse events. Two fatalities (3.0%) were reported and determined not related to nirsevimab administration. The absence of reported cases of thrombocytopenia or severe hypersensitivity reactions reinforced the results of previous clinical trials.[98]

Canada has also studied health events that occurred after nirsevimab administration (either alone or coadministered) during the 2024–2025 season via questionnaires completed by caregivers of 1559 children.[99] The most frequently reported symptoms were cough (1.8%); changes in feeding or eating (1.6%); fever (1.6%); and diarrhea or other change in bowel habits (1.5%). Local injection-site reactions were reported in 140 children (9.0%), including 79 children who received nirsevimab with another vaccine and 61 who received nirsevimab alone. Health events that interfered with daily activities or required a health care visit were reported in 38 of 1105 infants (3.4%) who received nirsevimab alone and 19 of 454 infants (4.2%) who received coadministered nirsevimab. Rash was reported in 10 children (0.6%), and no cases of anaphylaxis were reported.[99]

Nirsevimab is contraindicated in individuals who have experienced anaphylaxis after a prior dose or in reaction to an ingredient of the product.[75] Components can be found in the package insert for nirsevimab.

Clesrovimab

The safety of clesrovimab was established in phase 3 clinical trials. In the phase 2b–3 CLEVER trial, a single 105-mg dose of clesrovimab was evaluated for safety in healthy preterm and full-term

infants entering their first RSV season. The trial found that clesrovimab had a safety profile comparable to placebo. Rates of all-cause SAEs after administration were similar between infants who received clesrovimab and those who received placebo: 11.5% versus 12.4%, respectively (estimated difference, -0.9%, 95% CI, -3.2 to 1.3).[90] Fewer than 0.5% of infants in either group experienced adverse events of special interest. Most of these events were mild to moderate (grade 1 or 2). One infant who received clesrovimab developed urticaria 9 days after the injection, but the condition resolved within 4 days. The same infant had a respiratory infection 2 days earlier, and investigators concluded that neither event was related to clesrovimab. Another infant in the clesrovimab group experienced a grade 2 bronchospasm, classified as an anaphylactic or hypersensitivity reaction, 3 days after treatment; however, investigators did not consider it to be caused by clesrovimab.[90]

There was 1 treatment-related SAE reported in each study group. In the clesrovimab group, 1 infant was hospitalized after developing a mild fever (100.4°F) on the fourth day after receiving the injection; the fever lasted less than 11 hours. In the placebo group, 1 infant was diagnosed with B-cell precursor acute lymphoblastic leukemia 3 days after receiving the injection. The death rate was nearly the same in both groups. Seven of the 2409 infants (0.3%) who received clesrovimab died, compared with 3 of the 1202 infants (0.2%) (RR, 0.0; 95% CI, -0.4–0.2) who received the placebo. Investigators determined that none of the deaths were related to either clesrovimab or the placebo, and none were caused by RSV.[90]

The phase 3 SMART trial is a randomized, partially blinded, palivizumab-controlled study that enrolled infants entering their first RSV season who were at increased risk for severe RSV disease because of prematurity (<29 through ≤35 weeks' GA), CLD, or hemodynamically significant CHD. During the first RSV season, the overall rate of adverse events was similar between infants who received clesrovimab and those who received palivizumab. Most of the reported adverse events were mild or moderate in severity. No cases of anaphylaxis or hypersensitivity, which were monitored as adverse events of special interest, were observed in either group. Rash was reported infrequently in both groups,

and all cases were mild (grade 1). Eight infants in the clesrovimab group and 4 in the palivizumab group died during season 1 of the study. Investigators determined that none of the deaths were related to either treatment, and most were attributed to preexisting medical conditions or other identifiable causes.[91]

Second-season RSV data from the SMART trial show a safety profile that is generally consistent with first season observations, with no new safety signals indicated and adverse events well-balanced between groups.[92,93]

Clesrovimab should not be given to anyone who has had a severe allergic reaction—for example, anaphylaxis—to any of its components. A complete list of the product's components is available in the clesrovimab package insert.[15]

SPECIAL SITUATIONS

Administration to Infants With Prolonged Birth Hospitalization

Eligible infants with prolonged birth hospitalizations because of prematurity or other causes who are discharged during RSV season should receive RSV immunization ideally shortly before, or promptly after, discharge from the hospital.[22] There is a risk of RSV transmission within the hospital setting. A systematic review of studies reporting health care-associated RSV cases during an outbreak in a hospital setting found a transmission risk of 6% to 56% (median, 28.5%) in neonatal and pediatric units. Patients, visitors, and health care staff are all potential sources for RSV transmission. Infection control practices can help prevent health care-associated RSV disease in uninfected hospitalized infants.[15,100] To prevent health care-associated RSV disease, clinicians may consider administering an RSV immunization to eligible infants who are hospitalized; this decision should be based on clinical judgment, an assessment of potential risks and benefits to the infant, and local RSV activity.[15] Safety data for use of RSV antibody in

infants with a postmenstrual age (GA at birth plus chronologic age) of <32 weeks are limited.[101,102]

RSVpreF Vaccine for Pregnant Individuals for Infant Protection

In addition to products intended for infants, RSV-associated LRTI and severe lower respiratory tract disease can also be prevented by vaccinating pregnant individuals prior to childbirth. In 2023, the FDA approved the RSVpreF vaccine, which contains stabilized prefusion F glycoproteins from RSV A and RSV B and is indicated to prevent disease in infants younger than 6 months of age. RSVpreF vaccine is also indicated to prevent RSV in adults 60 years of age and older and individuals 18 through 59 years of age at increased risk for RSV-associated lower respiratory tract disease.[103] RSVpreF vaccine is not licensed or recommended in children younger than 18 years. It is given as a 1-time 0.5-mL intramuscular dose that is administered between 32 and 36 weeks' gestation.[100,104] As of January 31, 2026, approximately 42% of pregnant individuals in the United States between 18 and 49 years of age were vaccinated with the RSV vaccine overall. Vaccination rates range from a high of 55% among non-Hispanic Asian individuals to a low of 29% among non-Hispanic Black individuals.[105] Recent systematic reviews conducted by the Vaccine Integrity Project affirm the safety of RSVpreF vaccine for both the pregnant and infant populations and the effectiveness of the RSVpreF vaccine against infant RSV-associated hospitalization.[85,86] For more information, see the American College of Obstetricians and Gynecologists' guidance[106] and maternal immunization schedule.[107]

Repeat Dose

A mean decrease in palivizumab serum concentration of 58% was observed after surgical procedures that use cardiopulmonary bypass.[108] Similarly, a reduction in vaccine-elicited maternally derived RSV-specific antibodies would also be expected following cardiopulmonary bypass. A repeat dose of nirsevimab or clesrovimab is recommended for children who have previously received the immunization or whose mother received RSVpreF vaccine during the current pregnancy and subsequently

undergo antibody-depleting treatments or procedures such as plasmapheresis, cardiopulmonary bypass, or extracorporeal membrane oxygenation (ECMO) that may result in the loss of RSV-specific antibodies. See the package inserts for dosing guidance (www.fda.gov/drugsatfda).

COST-EFFECTIVENESS

A cost-effectiveness assessment examines outcomes for patient populations (vs individual patients) and compares health benefits and economic costs. Many such assessments use the quality-adjusted life year (QALY), which is a standard method for qualifying how well a medical treatment extends and/or improves patients' lives. When evidence indicates that a treatment extends survival or improves quality of life, these benefits are combined to estimate the number of additional QALYs the treatment provides. This overall health benefit is then compared with the benefits offered by other treatments available for the same patient population.

No government or officially mandated cost-effectiveness threshold exists for the United States. An analysis by the Institute for Clinical and Economic Review and a study of cost-effective thresholds in publications from 1990 to 2021 suggest that a cost per QALY of between $100,000 to $150,000 is an acceptable threshold for assessing cost-effectiveness.[109] Specifically, when a health product or treatment has an incremental cost-effectiveness ratio of less than this amount, it indicates that the intervention is cost-effective for the benefits gained.[110] It is important to note that cost-effectiveness is never the sole determining factor for whether to recommend a particular product or treatment.

The CDC has estimated the cost-effectiveness of nirsevimab to be $102,811 per QALY for infants younger than 8 months who were born during, or entering, their first RSV season (estimated cost of $445 per dose).[111] RSV risk is lower during the second season compared with the first; cost effectiveness was estimated to be $1,557,544 per QALY if all infants and children were given nirsevimab entering their second season (estimated cost of $890 per dose).[75,111] An economic analysis of clesrovimab

was presented to the ACIP Maternal/Pediatric RSV Work Group in 2025 by researchers from the University of Michigan and CDC staff. The analysis compared the use of clesrovimab in eligible infants with the use of palivizumab in infants who qualify for that therapy, while assuming no RSV immunization for all other infants. From a societal perspective, the model estimated an incremental cost-effectiveness ratio of approximately $105,000 per QALY gained. Sensitivity analyses produced estimates ranging from cost-saving to about $213,000 per QALY gained. The base-case analysis assumed a clesrovimab cost of $457 per dose, with inpatient hospitalization costs, the price per dose of clesrovimab, and RSV-related QALYs lost identified as the primary factors influencing the results.[15]

COADMINISTRATION OF RSV IMMUNIZATION WITH OTHER IMMUNIZATIONS

RSV immunization products may be simultaneously coadministered with other age-appropriate vaccines. In a clinical trial involving late preterm and term infants, 8% of participants who received nirsevimab and 10% of those who received placebo were given a routine childhood vaccine within 7 days after receiving the study treatment. Within 14 days, 31% of infants in the nirsevimab group and 34% in the placebo group had received a childhood vaccine. The most frequently administered vaccine was the diphtheria and tetanus toxoids and acellular pertussis (DTaP) vaccine, which was given to 21% of infants in the nirsevimab group and 20% of those in the placebo group within 14 days. A small increase in reported fever was observed among infants who received both nirsevimab and a childhood vaccine within 14 days (1.5%) compared with those who did not receive a vaccine during that period (0.7%). No significant safety concerns were identified regarding the coadministration of nirsevimab and routine childhood vaccines.[101]

Palivizumab was used for over 20 years in infants who also received routine vaccinations without any alerts concerning safety and efficacy of coadministration. Neither nirsevimab nor clesrovimab are expected to interfere with the immune response to other childhood vaccinations given the general

mechanism of action of antiviral mAbs, which is highly specific targeting viral antigenic sites.[112]

CONCLUSION

This report summarizes the current evidence regarding the use of RSV immunization for the prevention of LRTI caused by RSV in infants and children. The recommendations in the accompanying AAP policy statement reflect the current evidence on RSV disease burden; conditions that confer heightened risk in the second RSV season; and immunization products' efficacy, effectiveness, and safety.[1]

ADDITIONAL RESOURCES

Current guidance, clinical resources, and updates related to RSV immunization are available through the AAP RSV page (https://www.aap.org/RSV) and the AAP *Red Book Online* (https://www.AAPredbook.org).

The guidance in this report does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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FINANCIAL/CONFLICT OF INTEREST DISCLOSURES: *Authors disclosed relevant relationships in accordance with American Academy of Pediatrics (AAP) policy to promote transparency and allow readers to assess relevance. The AAP reviews disclosures through its conflict-of-interest process and implements management strategies when appropriate. The presence of a disclosed relationship does not necessarily indicate a conflict of interest. Dr O'Leary had no relevant disclosures. Disclosures of all committee members were reviewed, and it was determined if disclosures were related to the work of the statement. If a member had disclosures determined to be relevant to the work related to the statement, they did not participate in making recommendations or developing the statement.*

FUNDING: *No external funding.*

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ACKNOWLEDGMENT

The Committee on Infectious Diseases gratefully acknowledges Sean T. O'Leary, MD, MPH, FAAP, for his leadership in drafting the technical report.

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