RSV: Ready for Some Vaccines?

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Disclosures
Objectives

• Describe the epidemiology of RSV infection.
• Define the characteristics of RSV respiratory tract infection in children and adults.
• Explore efforts to prevent RSV infection – past, present and future.
“Triple-demic”

Weekly counts based on the CDC Surveillance national sample of emergency departments
“RSV Immunity Debt”

• COVID-19 mitigation efforts resulted in fewer RSV exposures of young children
  • School and childcare closures / at home learning
  • Masking, hand hygiene, other non-pharmacologic interventions
• Reduced natural infections through winter of 2020-21
• Reduced immunity of children < 2 years
• In summer of 2021, with *relaxation of COVID measures* an “out of season” RSV epidemic occurred
• In fall of 2022 – “triple-demic”
  • RSV, influenza and COVID-19
Recovered = \( R \) (i.e., temporary immunity)

Infected = \( I \)

Susceptible = \( S \)

"19-20: Restrictions start"

"20-21: Overwhelmed hospitals"

"21-22: Restrictions gone"

"22-23: Still higher than normal"

"23-24"

"24-25: Back to normal?"
RSV – History

- 1956 – identified in secretions of chimps with bronchiolitis
- 1957 – found in children with bronchiolitis
- 1957 – noted to form multinucleated giant cells in tissue culture

**Materials and Methods**

Subjects

Three observations were made as part of a continuing study of acute respiratory illness being made at this hospital. Physicians working in the Pediatric Out-Patient Clinic referred the study patients with acute respiratory illness of uncertain etiology, children with illness of known etiology and children who were considered to be well. During the same interval most of the children admitted to the hospital were included in the study if appropriate specimens were obtained during the first three days in the hospital.

Definition of Clinical Status

Patients were considered to have acute respiratory illness if they had experienced an abrupt change in state of health that was associated with symptoms or signs of inflammation of the respiratory tract. If clinical findings included signs of bronchiolar inflammation such as expiratory dyspnea, emphysema and musical respiratory rates, the child was considered to have bronchiolitis, provided this was the first such episode that he had experienced. If there were signs of consolidation, with or without the findings enumerated above, a diagnosis of bronchopneumonia was made. Patients were considered to be free of respiratory infection if there was no history of adenoidal respiratory symptoms within the two weeks before or the two days after sampling.

Characterization of Study Group

A total of 291 patients were studied. The sex, race and age characteristics of the clinic and hospital patients studied are presented in Table I. The subjects are divided into four groups: the hospital group with acute respiratory illness, which includes approximately 90 per cent of the patients admitted to Bobs Roberts Hospital with acute respiratory illness from late December, 1958, through June, 1959; the hospital control group, which is a sampling of children hospitalized during the same period who had no evidence of respiratory illness (in comparison to the hospital group with acute respiratory illness, this control group contained a higher percentage of white children and the average age was greater); the clinic group with acute respiratory illness, which is a sampling of the outpatients with acute respiratory...
Respiratory Syncytial Virus

• Mainly a pathogen for humans
• Negative strand RNA genome
• 2 major subtypes (A and B)
• 2 surface glycoproteins
  • G – attaches to host cells and determines subtype
  • F – fusion protein facilitates entry into host cell
    • Better conserved than G
    • Target for vaccines and mono-clonal antibodies
Immunity to RSV

- Cellular and humoral immune response
- Young infants have ~ 20% antibody response compared with older children
  - One reason for recurrences
  - Challenge for vaccine development
- Cell-mediated immunity vitally important
  - RSV causes severe disease in SCID and transplant patients
- Secretory and serum antibodies
  - Secretory Ab (IgA) protects upper respiratory tract
  - Serum neutralizing Ab protects lower respiratory tract
  - Maternal IgG provides some protection in young infants
RSV – Epidemiology

• Transmission is via large particle droplets
  • Travel a distance up to 6 feet
  • Viral shedding after infection lasts 3-8 days
• Can persist on surfaces, objects (fomites), and hands
• Once infection acquired, typical incubation period before symptom onset is 4-6 days
• Spread within households and child care facilities
  • Also within hospitals / healthcare settings
  • OFID paper April 19, 2023 – more likely to be transmitted in hospitals than influenza
RSV Disease Across the Age Range
Burden of RSV Lower Respiratory Tract Infection in Children

• United States
  • The leading cause of hospitalizations in all infants
    • 6 per 1000 children < 2 years
    • 15 per 1000 children < 6 months
  • 58,000 - 80,000 hospitalizations and 200 deaths each year
U.S. RSV Hospitalizations

• Previously healthy infants - 72%

• Preterm infants - 16%

• Infants with chronic medical conditions - 12%
Burden of RSV Lower Respiratory Tract Infection in Children

• Most children have acquired RSV by age 2 years
  • 70% upper respiratory
  • 30% lower respiratory

• Most common cause of LRTI in infants
  • Bronchiolitis
  • Pneumonia

• Hospitalized children generally improve with supportive care / brief hospitalization

• 1-3% of all infants develop severe RSV LRTI
  • Especially in first 6 months
What is Bronchiolitis?

• Clinical syndrome usually seen in children < 2 years
• Usually caused by viruses
  • RSV – 67%
• Initial upper respiratory symptoms and signs, followed by lower respiratory findings
• Associated with recurrent wheezing / asthma
Bronchiolitis – Pathophysiology

- Viruses infect respiratory epithelium in small bronchi and bronchioles
- Inflammation ensues
  - Ciliary dysfunction
  - Edema
  - Mucous
  - Sloughing of epithelium
  - Airway obstruction
- Atelectasis
- Impaired gas exchange

Clinical Manifestations

• Fever, usually low grade
• Cough
• Signs of respiratory distress
  • Retractions
  • Grunting
  • Nasal flaring
• Physical findings
  • Wheezing
  • Rales
• Sometimes signs of dehydration
• Apnea
Risk Factors for Severe Disease

• Prematurity
• Age less than 12 weeks
• Chronic lung disease
  • BPD
  • Asthma
• Airway anomalies
• Congenital heart disease
• Immunodeficiency
• Neurologic disease
• Down syndrome
Burden of RSV Lower Respiratory Tract Infection in Adults

- RSV infections kill between 6,000 and 10,000 older U.S. adults every year and results in 60,000 to 120,000 hospitalizations
- Risk factors include lung and heart disease and immunocompromising conditions
- U.S. had an unusually severe RSV season in 2022-2023 affecting older adults as well as children
  - Public largely stopped practicing public health measures implemented in response to the COVID-19 pandemic
  - High community level of RSV disease
FIGURE 1. Underlying medical conditions* † among patients hospitalized with laboratory-confirmed respiratory syncytial virus infection§ — Respiratory Syncytial Virus–Associated Hospitalization Surveillance Network, 12 states, ‡ October 2022–April 2023

%/of/all/hospitalizations

% of all hospitalizations

≥60 yrs (total) 60–69 yrs 70–79 yrs ≥80 yrs

Underlying medical conditions

Obesity COPD Other chronic lung diseases (including asthma) Congestive heart failure Coronary artery disease Other cardiovascular diseases (including cerebrovascular accident) Diabetes mellitus Kidney disorders Immuno-compromising conditions Neurologic conditions (including dementia)

MMWR Oct. 6 2023
“During February 2022–May 2023, hospitalizations for RSV were less frequent but were associated with more severe disease than were hospitalizations for COVID-19 or influenza, including receipt of standard flow oxygen therapy, high-flow nasal cannula or noninvasive ventilation, and intensive care unit admission.” -- MMWR Oct. 6, 2023
Treatment of RSV Infection

• Ribavirin
  • Active in vitro against RSV
  • Numerous studies in infants
  • Improvement in oxygenation
  • No clear benefit in LOS and requirement for ventilation
  • Expensive
  • Concern for HCW exposure
  • Infrequently used
  • May be lifesaving in severely immunocompromised infants, children and adults
Novel Antivirals

- GS-5806 (presatovir)
- Novel, small molecule, oral antiviral agent
- Studied in adult volunteers
  - Lower viral load
  - Decreased mucous
  - Improved symptom scores
- Most research has focused on BMT patients
First RSV Vaccine

- 1960s vaccine (FI-RSV Lot 100)
  - Formalin inactivated RSV particles
  - Studied in children 2 mo – 7 yr, 2 or 3 doses
- Disastrous results in the winter of 1966-67
  - More hospitalizations than placebo recipients and 2 deaths
  - “FI-RSV vaccine enhanced disease”
Photomicrograph of lung section from BALB/c mouse with enhanced RSV disease. Hematoxylin and periodic acid-Schiff stain shows peribronchiolar, perialveolar, and perivascular inflammation with abundant mucus production.
First RSV Vaccine

• 1960s vaccine (FI-RSV Lot 100)
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• Disastrous results in the winter of 1966-67
  • More hospitalizations than placebo recipients and 2 deaths
  • “FI-RSV vaccine enhanced disease”

• Serum from vaccinees showed aberrant response
  • Formalin selectively altered the protective epitopes in the F and G surface glycoproteins
  • Likely immune complex deposition / complement activation
Reduction of Respiratory Syncytial Virus Hospitalization Among Premature Infants and Infants With Bronchopulmonary Dysplasia Using Respiratory Syncytial Virus Immune Globulin Prophylaxis

The PREVENT Study Group*  

ABSTRACT. Objective: To determine the safety and efficacy of monthly prophylaxis with respiratory syncytial virus immune globulin intramuscularly (RSV-IGIV) for the reduction of the incidence of RSV-associated hospitalization in newborns and young children. Methods: A randomized, double-blind, placebo-controlled clinical trial was conducted at 34 centers in the United States during the 1996 to 1997 RSV season. A total of 1,020 preterm infants less than 32 weeks gestation, 86 low birth weight infants with bronchopulmonary dysplasia, 114 infants with severe prematurity and who had a history of prematurity were randomized to receive either placebo or 0.25 g/kg of IV RSV-IGIV at days 0, 7, 14, 21, and 28. Results: 153 infants (15%) were hospitalized with RSV during the study period; 105 (68%) of 157 placebo recipients compared with 48 (31%) of 153 RSV-IGIV recipients (P = 0.0002). Conclusions: Children receiving RSV-IGIV prophylaxis had a significant reduction in the number of days of hospitalization per infant compared to placebo recipients. This finding supports the use of RSV-IGIV prophylaxis to reduce the number of hospital days required for RSV-related illness in high-risk infants. (J Pediatr 1997;131:615-22)

PREVENT: RSV, respiratory syncytial virus; IGIV, intravenous immune globulin; RSV-IGIV, respiratory syncytial virus immune globulin; RSV-IGIV, respiratory syncytial virus immune globulin; RSV-IGIV, respiratory syncytial virus immune globulin; RSV-IGIV, respiratory syncytial virus immune globulin.
Palivizumab, a Humanized Respiratory Syncytial Virus Monoclonal Antibody, Reduces Hospitalization From Respiratory Syncytial Virus Infection in High-risk Infants

The IMpact-RSV Study Group

ABSTRACT. Objective. To determine the safety and efficacy of prophylaxis with palivizumab in reducing the incidence of hospitalization because of respiratory syncytial virus (RSV) infection compared with placebo by a randomized, double-blind, placebo-controlled trial that was conducted at 53 centers in the United States, the United Kingdom, and Canada during the 1996 to 1997 RSV season. 530 children with prematurity (<35 weeks) or bronchopulmonary dysplasia (BPD) were randomized to receive 5 intramuscular doses of either palivizumab (15 mg/kg) or an equivalent volume of placebo by intramuscular injection every 30 days. The primary endpoint was hospitalization with confirmed RSV infection. Children were followed for 100 days (60 days from the last injection). Those with hospitalization as a result of RSV infection were evaluated for total number of days in the hospital, total days with increased supplemental oxygen, total days with stability or descent in oxygen saturation, days with hospitalization, and total days of intensive care and mechanical ventilation. The incidence of hospitalization for respiratory illness not caused by RSV and the incidence of adverse events were also evaluated. The placebo and palivizumab groups were balanced with respect to demographic and RSV risk factors. Ninety-nine percent of children in both groups completed the protocol and 98% received all five scheduled injections.

Results. Palivizumab prophylaxis resulted in a 38% reduction in hospitalization as a result of RSV (6.0% placebo vs 4.8% palivizumab). Children with prematurity but without BPD had a 78% reduction in RSV hospitalization (0.6% vs 1.4%); children with BPD had a 39% reduction (2.9% vs 7.5%). When gender, entry age, entry weight, BPD, and gestational age were included in a logistic regression model, the effect of prophylaxis on palivizumab remained statistically significant. The palivizumab group had proportionally fewer total RSV hospital days, fewer RSV hospital days with increased oxygen, fewer RSV hospital days with a moderate/severe lower respiratory tract illness, and a lower incidence of intensive care unit admissions. Palivizumab was safe and well tolerated. No significant differences were observed in reported adverse events between the two groups. Few children discontinued injections for related adverse events. Adverse events were rare, and the most frequent included mild and transient erythema. Mild or moderate elevations in aspartate aminotransferase occurred in 17% of placebo recipients and 19% of palivizumab recipients for alanine aminotransferase these persisted for 2% and 2%, respectively. Importantly, no serious adverse events related to the study drug were similar in the two groups.

Conclusions. Monthly intramuscular administration of palivizumab is safe and effective for prevention of serious RSV illness in premature children and those with bronchopulmonary dysplasia. Palivizumab, Synagis, pneumospray, bronchopulmonary dysplasia.

RESPIRATORY SYNPTOMATIC VIRUS (RSV) is the leading cause of lower respiratory illness in children and is increasingly recognized as an important pathogen in the elderly and immunocompromised patients of all ages. In children, the risk of serious RSV illness is highest among those with prematurity, chronic lung disease, congenital heart disease, multiple congenital anomalies, and certain immunodeficiencies. In the United States, RSV infection accounts for more than 90,000 pediatric hospitalizations and 4300 deaths annually. Monthly infusions of respiratory syncytial virus vaccine, palivizumab, Synagis, pneumospray, bronchopulmonary dysplasia.
Synagis for Prevention of RSV Disease

• Recommendations have changed multiple times
  • Data driven and cost driven
  • Payers pay close attention

• Infants < 29 weeks gestation at beginning of RSV season may be considered for palivizumab

• CLD in 2\textsuperscript{nd} year requiring medical therapy should receive prophylaxis for next RSV season

• CHD: Discuss with cardiologist

• < 2% of infants eligible based on current criteria
RSV: The Future

• RSV vaccines
  • Adults
  • Children

• Alternative monoclonal antibodies for passive immunization of infants
RSV F Glycoprotein Vaccine

- Prefusion conformation
- Appears safe
  - Mice and macaques
- High levels of RSV neutralizing antibody (subtypes A and B)
- This study set the stage for multiple clinical trials
Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults


ABSTRACT

BACKGROUND
Respiratory syncytial virus (RSV) is an important cause of acute respiratory infection, lower respiratory tract disease, clinical complications, and death in older adults. There is currently no licensed vaccine against RSV infection.

METHODS
In an ongoing, international, placebo-controlled, phase 3 trial, we randomly assigned, in a 1:3 ratio, adults 60 years of age or older to receive a single dose of an ASO1-adjuvanted RSV prefusion F protein-based candidate vaccine (RSVPrefF OA) or placebo before the RSV season. The primary objective was to show vaccine efficacy of one dose of the RSVPrefF OA vaccine against RSV-related lower respiratory tract disease, confirmed by reverse-transcriptase polymerase chain reaction (RT-PCR), during one RSV season. The criteria for meeting the primary objective was a lower limit of the confidence interval around the efficacy estimate of more than 20%. Efficacy against severe RSV-related lower respiratory tract disease and RSV-related acute respiratory infection was assessed, and analyses according to RSV subtype (A and B) were performed. Safety was evaluated.

RESULTS
A total of 24,966 participants received one dose of the RSVPrefF OA vaccine (12,467 participants) or placebo (12,499). Over a median follow-up of 6.7 months, vaccine efficacy against RT-PCR-confirmed RSV-related lower respiratory tract disease was 82.6% (95% confidence interval CI), 57.9 to 94.1, with 7 cases (1.0 per 1000 participant-years) in the vaccine group and 40 cases (5.8 per 1000 participant-years) in the placebo group. Vaccine efficacy was 94.7% (95% CI, 62.4 to 99.9) against severe RSV-related lower respiratory tract disease (assessed on the basis of clinical signs or by the investigator) and 71.7% (95% CI, 56.2 to 82.3) against RSV-related acute respiratory infection. Vaccine efficacy was similar against the RSV A and B subtypes (for RSV-related lower respiratory tract disease: 84.6% and 80.9%, respectively, for RSV-related acute respiratory infection: 71.9% and 70.6%, respectively). High vaccine efficacy was observed in various age groups and in participants with coexisting conditions. The RSVPrefF OA vaccine was more effective than placebo, but most adverse events for which reporting was solicited were transient, with mild-to-moderate severity. The incidences of serious adverse events and potential immune-mediated diseases were similar in the two groups.

CONCLUSIONS
A single dose of the RSVPrefF OA vaccine had an acceptable safety profile and prevented RSV-related acute respiratory infection and lower respiratory tract disease and severe RSV-related lower respiratory tract disease in adults 60 years of age or older, regardless of RSV subtype and the presence of underlying conditions. (Funded by GlaxoSmithKline Biologicals; AlteSvi-006 ClinicalTrials.gov number, NCT0488696.)

The authors’ full names, academic degrees, and affiliations are listed in the Appendix. Dr. Hultstrom can be contacted at vladimir.hultstrom@gsk.com or at GSK, Ave. Fleming 20, 1300 Water, Belgium.

CME at NEJM.org

Dr. Papi and Isom contributed equally to the article.
Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults


BACKGROUND
Respiratory syncytial virus (RSV) infection causes considerable illness in older adults. The efficacy and safety of an investigational bivalent RSV prefusion F protein-based (RSVpreF) vaccine in this population are unknown.

METHODS
In this ongoing, phase 3 trial, we randomly assigned, in a 1:1 ratio, adults (60 years of age) to receive a single intramuscular injection of RSVpreF vaccine at a dose of 1.25 μg (RSV subgroups A and B, 60 μg each) or placebo. The two primary end points were vaccine efficacy against seasonal RSV-associated lower respiratory tract illness with at least two or at least three signs or symptoms. The secondary end point was vaccine efficacy against RSV-associated acute respiratory illness.

RESULTS
At the interim analysis (data cutoff date, July 31, 2022), 34,284 participants had received RSVpreF vaccine (17,215 participants) or placebo (17,069 participants). RSV-associated lower respiratory tract illness with at least two signs or symptoms occurred in 11 participants in the vaccine group (4.19 cases per 1000 person-years of observation) and 33 participants in the placebo group (5.58 cases per 1000 person-years of observation) (vaccine efficacy, 66.7%; 95% confidence interval [CI], 28.8 to 85.8); 2 cases (0.22 cases per 1000 person-years of observation) and 14 cases (1.52 cases per 1000 person-years of observation), respectively, occurred with at least three signs or symptoms (vaccine efficacy, 85.7%; 96.6% CI, 32.0 to 98.7). RSV-associated acute respiratory illness occurred in 22 participants in the vaccine group (2.38 cases per 1000 person-years of observation) and 58 participants in the placebo group (6.30 cases per 1000 person-years of observation) (vaccine efficacy, 62.4%; 95% CI, 37.1 to 77.5). The incidence of local reactions was higher with vaccine (12%) than with placebo (7%); the incidences of systemic events were similar (27% and 26%, respectively). Similar rates of adverse events through 1 month after injection were reported (vaccine, 9.0%; placebo, 8.5%), with 1.4% and 1.0%, respectively, considered by the investigators to be injection-related. Severe or life-threatening adverse events were reported in 0.5% of vaccine recipients and 0.4% of placebo recipients. Serious adverse events were reported in 2.3% of participants in each group through the data cutoff date.

CONCLUSIONS
RSVpreF vaccine prevented RSV-associated lower respiratory tract illness and RSV-associated acute respiratory illness in adults (60 years of age) without evident safety concerns. (Funded by Pfizer; REONIR Clinical Trials.gov number, NCT0963521.)

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Efficacy of Adult RSV Vaccines for LRT Disease

**Arexvy (GSK)**
- Overall
  - 82.6% in first RSV season
  - 56.1% for second RSV season
- For severe disease
  - 94.1% in first RSV season
  - 78.8% over two seasons

**Abrysvo**
- For LRTD with at least three symptoms (cough, wheezing, sputum, SOB, tachypnea)
  - 88.9% in first season
  - 78.6% midway through second season
# RSV Infections Prevented Over Two Seasons

<table>
<thead>
<tr>
<th></th>
<th>Number prevented per 1 million vaccinations among:</th>
<th>Number prevented per 1 million vaccinations among:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults aged ≥65 years</td>
<td>Adults aged 60–64 years</td>
</tr>
<tr>
<td>Outpatient visits&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25,000</td>
<td>19,000</td>
</tr>
<tr>
<td>Hospitalizations&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2,500</td>
<td>960</td>
</tr>
<tr>
<td>Deaths&lt;sup&gt;c&lt;/sup&gt;</td>
<td>130</td>
<td>37</td>
</tr>
</tbody>
</table>
Cost-Effectiveness – ACIP

• Multiple assumptions
  • Two seasons of effectiveness
  • Vaccine cost $200
  • RSV epidemiology and severity

• $94,673 / QALY for > 65 years
• $218,350 / QALY for 60-64 years
### TABLE 2. Safety* of 1 dose of GSK respiratory syncytial virus RSVPreF3 vaccine in adults aged ≥60 years — multiple countries, 2021–2023

<table>
<thead>
<tr>
<th>Safety event</th>
<th>RSVPreF3 recipients no./No. (%)</th>
<th>Placebo recipients no./No. (%)</th>
<th>Relative risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious AE**</td>
<td>549/12,570 (4.4)</td>
<td>540/12,604 (4.3)</td>
<td>1.02 (0.91–1.15)</td>
</tr>
<tr>
<td>Severe reactogenicity events†‡</td>
<td>37/9,797 (3.8)</td>
<td>9/9,767 (0.9)</td>
<td>4.10 (1.99–8.45)</td>
</tr>
<tr>
<td>Inflammatory neurologic events§§</td>
<td>3 events in trials without placebo recipients ‡‡</td>
<td>——</td>
<td>——</td>
</tr>
</tbody>
</table>

3 / 17,922 subjects
One case of GBS
Two cases of ADEM

### TABLE 4. Safety* of 1 dose of Pfizer respiratory syncytial virus RSVpreF2 vaccine in adults aged ≥60 years — multiple countries, 2021–2023

<table>
<thead>
<tr>
<th>Safety event</th>
<th>RSVpreF2 recipients no./No. (%)</th>
<th>Placebo recipients no./No. (%)</th>
<th>Relative risk (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serious AE**</td>
<td>792/18,619 (4.3%)</td>
<td>749/18,334 (4.1%)</td>
<td>1.04 (0.94–1.15)</td>
</tr>
<tr>
<td>Severe reactogenicity events†‡</td>
<td>36/3,673 (1.0%)</td>
<td>24/3,491 (0.7%)</td>
<td>1.43 (0.85–2.39)</td>
</tr>
<tr>
<td>Inflammatory neurologic events§§</td>
<td>3/18,622 (—)§§</td>
<td>0/18,335 (—)</td>
<td>——</td>
</tr>
</tbody>
</table>

3 / 20,255 subjects
Two cases of GBS
One case of polyneuropathy
Both RSV Vaccines Recommended by CDC

• Shared clinical decision-making for adults ≥ 60 years
  • Patient’s risk for acquiring RSV
  • Patient’s risk for severe RSV disease
BOX. Underlying medical conditions and other factors associated with increased risk for severe RSV disease

Chronic underlying medical conditions associated with increased risk

- Lung disease (such as chronic obstructive pulmonary disease and asthma)
- Cardiovascular diseases (such as congestive heart failure and coronary artery disease)
- Moderate or severe immune compromise*
- Diabetes mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders
- Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease

Other factors associated with increased risk

- Frailty†
- Advanced age§
- Residence in a nursing home or other long-term care facility
- Other underlying factors that a health care provider determines might increase the risk for severe respiratory disease
Both RSV Vaccines Recommended by CDC

• Shared clinical decision-making for adults > 60 years
  • Patient’s risk for acquiring RSV
  • Patient’s risk for severe RSV disease
  • Patient’s characteristics, values and preferences

• Single dose
  • Insufficient data for re-vaccination

• Offer before and during RSV season

• Coadministration with other adult vaccines acceptable

• Only contraindication is previous severe allergic reaction to any vaccine component

• So far, 15% of eligible adults have received one of the RSV vaccines
Why Not a Universal Recommendation?

- Highest risk adults not included in trials
- Cost-effectiveness concerns
- Uncertainty about relationship of vaccine to neuro-inflammatory events
  - “Whether these events occurred due to chance, or whether RSV vaccination increases the risk for inflammatory neurologic events is currently unknown. Until additional evidence becomes available from postmarketing surveillance clarifying the existence of any potential risk, RSV vaccination in older adults should be targeted to those who are at highest risk for severe RSV disease and therefore most likely to benefit from vaccination.” MMWR, July 21, 2023
### RSV Immunization of Infants: Potential Approaches

| PROS | CONS |

<table>
<thead>
<tr>
<th>Maternal Immunization</th>
<th>Infant Vaccines</th>
<th>Long-acting monoclonal Ab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trans-placental transfer of IgG</td>
<td>Replicating vaccines (live attenuated or vectored)</td>
<td>Prolonged half life</td>
</tr>
<tr>
<td>Independent of infant immune function</td>
<td>Potential for multi-season protection</td>
<td>Single dose at birth or at start of RSV season</td>
</tr>
<tr>
<td>Works for influenza and pertussis</td>
<td>T-cell as well as antibody response</td>
<td>Independent of infant immune function</td>
</tr>
<tr>
<td>May not work for preterm infants</td>
<td>May require multiple doses</td>
<td>Potential cost</td>
</tr>
<tr>
<td>Protection may not last for entire season ($T_{1/2} = 23$ days)</td>
<td>Youngest infants may not be eligible</td>
<td>Potential for anti-drug antibodies</td>
</tr>
<tr>
<td>Suboptimal uptake</td>
<td>Preterm infants may not respond well</td>
<td>Potential for viral escape by loss of epitope</td>
</tr>
</tbody>
</table>
Nirsevimab (Sanofi and AstraZeneca)

- Recombinant neutralizing human IgG1κ long-acting monoclonal antibody
- Binds to prefusion conformation of the RSV F protein
- Modified with a triple amino acid substitution in Fc region to extend serum half-life
  - $T_{1/2} = 69 \pm 11$ days
  - Compare to palivizumab – 23 days
Phase 3 Pivotal Study in Healthy Infants

- 1490 infants randomized 2:1 to receive either mAb or placebo
- Single IM injection prior to RSV season
- Safety
  - SAEs similar between groups
  - 6.1% antidrug antibodies
- Efficacy
  - 74.5% for MALRTI due to RSV
    - \( P < 0.001 \)
  - 62.1% for RSV hospitalization
    - \( P = 0.07 \)
Nirsevimab: Efficacy and Safety from Pooled Results of Phase 2b and Phase 3 Trials of Infants

- At 150 days, compared with placebo, nirsevimab:
  - Reduced medically attended RSV lower respiratory tract infection by 79.0%
  - Reduced RSV-associated hospitalizations by 80.6%
  - Reduced RSV-associated ICU admission by 90.0%

- Serious adverse events were similar in nirsevimab and placebo recipients

- Minor side effects uncommon
  - Rash
  - Injection site reactions
Nirsevimab: Results for High-Risk Infants Entering Their 2nd RSV Season

• Study enrolled 615 former preterm infants (< 35 weeks) and 310 toddlers with either chronic lung disease or hemodynamically significant congenital heart disease
• Subjects received 200 mg dose of nirsevimab or palivizumab
• Efficacy against LRTI were extrapolated from pharmacologic data
• Nirsevimab levels comparable to those of younger babies entering first RSV season
• Rates of severe adverse events not different between the groups
Nirsevimab: Cost Effectiveness

• Cost per dose:
  • 50 and 100 mg $495
  • 200 mg $890

• First RSV season
  • $102,811 per quality adjusted life year

• High risk toddlers entering second RSV season
  • Much less expensive than 5 doses of palivizumab

<table>
<thead>
<tr>
<th>RSV Season</th>
<th>Patient Characteristic</th>
<th>Additional Dose &amp; Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st RSV Season</td>
<td>Weight &lt; 5 kg regardless of time elapsed since initial dose</td>
<td>50 mg IM once</td>
</tr>
<tr>
<td></td>
<td>Weight ≥ 5 kg and ≤ 90 days since initial dose</td>
<td>100 mg IM once</td>
</tr>
<tr>
<td></td>
<td>Weight ≥ 5 kg and &gt; 90 days since initial dose</td>
<td>50 mg IM once</td>
</tr>
<tr>
<td>2nd RSV Season</td>
<td>≤ 90 days since initial dose</td>
<td>200 mg IM once</td>
</tr>
<tr>
<td></td>
<td>&gt; 90 days since initial dose</td>
<td>100 mg IM once</td>
</tr>
</tbody>
</table>
Nirsevimab: Recommendations for Use

• All infants < 8 months shortly before start of RSV season
• Infants born shortly before or during RSV season within 1 week of birth
  • Prior to discharge from birth hospitalization
  • Outpatient setting
• High risk toddlers shortly before start of second RSV season
  • Chronic lung disease of prematurity requiring medical intervention
  • Severely immunocompromised
  • Cystic fibrosis with significant lung disease
  • American Indians and Alaskan Natives
Nirsevimab Administration Visual Guide

Is it October 1 through March 31, or have health authorities recommended nirsevimab administration currently?

- Yes: Is the patient < 8 months of age today?
  - Yes: Did the mother of this patient receive the RSV vaccine while pregnant?
    - Yes: Was the infant born within 14 days of maternal RSV vaccine administration?
      - Yes: Has the patient received a previous dose of nirsevimab in the current RSV season (e.g., in the newborn nursery)?
        - Yes: Recommended
        - No: Generally Not Recommended
      - No: Not Recommended
    - No or Unknown: Not Recommended
  - No: Not Recommended

- No: Is the patient 8–19 months old today and meet the high risk criteria?
  - Yes: Recommended
  - No: Not Recommended

If not recommended, do not give nirsevimab.

If recommended, continue.

Has the patient received 1 or more doses of palivizumab in the current RSV season?

- Yes: Has 30 days elapsed since the last dose?
  - Yes: Wait until 30 days elapse.
  - No: What is the patient’s current weight (today)?
    - ≤ 5 kg: Nirsevimab 50 mg/mL
    - > 5 kg: Nirsevimab 100 mg/mL
- No: What is the patient’s current weight (today)?
  - ≤ 5 kg: Nirsevimab 50 mg/mL
  - > 5 kg: Nirsevimab 100 mg/mL
Respiratory Syncytial Virus (RSV) Preventive Antibody: What You Need to Know

Why get immunized with a RSV preventive antibody?
A respiratory syncytial virus (RSV) preventive antibody can prevent severe lung disease caused by RSV.

RSV is a common respiratory virus that usually causes mild, cold-like symptoms but can also affect the lungs. Symptoms of RSV infection may include runny nose, decrease in appetite, coughing, sneezing, fever, or wheezing.

Anyone can become infected by RSV, and almost all children get an RSV infection by the time they are 2 years old. While most children recover from an RSV infection in a week or two, RSV infection can be dangerous for infants and some young children, causing difficulty breathing, low oxygen levels, and dehydration. In the United States, RSV is the most common cause of bronchiolitis (inflammation of the small airways in the lungs) and pneumonia (infection of the lungs) in children younger than 1 year of age. Children who get sick from RSV may need to be hospitalized, and some might even die.

RSV Preventive Antibodies
The RSV preventive antibody (generic name nirsevimab, trade name Beyfortis) is a shot that prevents severe RSV disease in infants and young children. Antibodies are proteins that the body's immune system uses to fight off harmful germs. Like traditional vaccines, preventive antibodies are immunizations that provide protection against a specific pathogen. While both are immunizations, the way they provide immunity is different. Nirsevimab is an immunization that provides antibodies directly to the recipient. Traditional vaccines are immunizations that stimulate the recipient's immune system to produce antibodies.

Infants born during the RSV season (typically fall through spring) should receive a single dose of the RSV Immunization within 1 week after birth. Most infants whose mothers got the RSV vaccine don't need to get nirsevimab, too. Both protect infants from severe RSV by providing antibodies, either from the mother to the infant or directly to the infant. Most infants will likely only need protection from either the maternal RSV vaccine or nirsevimab (not both). However, there may be some situations in which nirsevimab would be recommended for an infant after the mother received an RSV vaccine.

Infants born outside of the RSV season who are younger than 8 months should receive a single dose of the RSV Immunization shortly before their first RSV season (typically the fall), but infants who are younger than 8 months who have not yet received a dose may receive a dose at any time during the season.

Some infants and young children who are at increased risk for severe RSV disease may need a single dose of the RSV antibody before or during their second RSV season.

RSV preventive antibodies can be given at the same time as vaccines routinely recommended for infants and young children.

Talk with your health care provider
Tell your health care provider if the person getting the preventive antibody has:
- History of serious allergic reactions to an RSV preventive antibody (nirsevimab) or any of its components,
- Bleeding disorder, or
- Moderate or severe acute illness.

In some cases, your child's health care provider may decide to postpone giving RSV preventive antibodies until a future visit.

People who have a minor illness, such as a cold, can safely receive an RSV preventive antibody. People who are moderately or severely ill should usually wait until they recover.

Your health care provider can give you more information.

Risks of a reaction to RSV preventive antibodies
After getting an RSV preventive antibody, your child might have temporary pain, redness, swelling where the injection was given, or a rash.

As with any medicine, there is a very remote chance that RSV Immunization could cause a severe allergic reaction, other serious injury, or death.

An allergic reaction could occur after your child leaves the hospital or clinic. If you see signs of a severe allergic reaction for example, hives, swelling of the face and throat, difficulty breathing, a fast heartbeat, dizziness, or weakness, call 9-1-1 and get your child to the nearest hospital.

Call your health care provider if you see any other symptoms that concern you.

What if there is a serious problem?
If your child got an RSV preventive antibody without getting a vaccine at the same time, and you suspect an adverse reaction, you or your health care provider can submit a report through https://www.fda.gov/webwatch or by phone at 1-800-FDA-1088.

If your child got an RSV preventive antibody and a vaccine at the same time and you suspect an adverse reaction, you or your health care provider should report it to the Vaccine Adverse Event Reporting System (VAERS) https://vaers.hhs.gov/ or call 1-800-822-7967.

In your report, note that your child got an RSV Immunization along with a vaccine.

Note: MedWatch and VAERS are only for reporting reactions. MedWatch and VAERS staff members do not give medical advice.

How can I learn more?
- Ask your health care provider.
- Call your local or state health department.
- Visit U.S. Food and Drug Administration website at Drugs@FDA, FDA-Approved Drugs.
- Contact the Centers for Disease Control and Prevention (CDC):
  - Call 1-800-332-4556 (1-800-232-2797 in California), or
  - Visit the CDC website https://www.cdc.gov/rrs/about/prevention.html

Immunization Information Statement
Respiratory Syncytial Virus (RSV) Preventive Antibody:
9/26/2022
Limited Availability of Nirsevimab in the United States—Interim CDC Recommendations to Protect Infants from Respiratory Syncytial Virus (RSV) during the 2023–2024 Respiratory Virus Season

Summary
The Centers for Disease Control and Prevention (CDC) is issuing this Health Alert Network (HAN) Health Advisory to provide options for clinicians to protect infants from respiratory syncytial virus (RSV) in the context of a limited supply of nirsevimab, a long-acting monoclonal antibody immunization product recommended for preventing RSV-associated lower respiratory tract disease in infants.

In the context of limited supply during the 2023–2024 RSV season, CDC recommends prioritizing available nirsevimab 100mg doses for infants at the highest risk for severe RSV disease: young infants (age <6 months) and infants with underlying conditions that place them at highest risk for severe RSV disease. Recommendations for using 50mg doses remain unchanged at this time. Avoid using two 50mg doses for infants weighing ≥5 kilograms (≥11 pounds) to preserve supply of 50mg doses for infants weighing <5 kilograms (<11 pounds). Providers should be aware that some insurers may not cover the cost of two 50mg doses for an individual infant.

CDC further recommends that providers suspend using nirsevimab in palivizumab-eligible children aged 8–19 months for the 2023–2024 RSV season. These children should receive palivizumab per American Academy of Pediatrics (AAP) recommendations. Nirsevimab should continue to be offered to American Indian and Alaska Native children aged 3–19 months who are not palivizumab-eligible and who live in remote regions, where transporting children with severe RSV for escalation of medical care is more challenging or in communities with known high rates of RSV among older infants and toddlers. Prenatal care providers should discuss potential nirsevimab supply concerns when counseling pregnant people about RSVpreF vaccine (Abyuvo, Pfizer) as maternal vaccination is effective and will reduce the number of infants requiring nirsevimab during the RSV season.

Background
RSV is a common cause of respiratory infection in U.S. infants, most of whom are infected with RSV during their first year of life (1, 2). RSV is the leading cause of hospitalization among U.S. infants (3). The highest incidence of RSV-associated hospitalization occurs in infants aged <3 months and then decreases with increasing age (4). Because of the high incidence of severe RSV disease in the first months of life, RSV prevention products focus on passive immunization of young infants through maternal immunization or immunoprophylaxis with monoclonal antibodies.

In July 2023, the Food and Drug Administration (FDA) approved nirsevimab (Beyfortis™, Sanofi and Astrazeneca), a long-acting monoclonal antibody, for passive immunization to prevent RSV-associated lower respiratory tract disease among infants and young children. On August 3, 2023, CDC’s Advisory Committee on Immunization Practices (ACIP) recommended nirsevimab for all infants aged ≥6 months who are born during or entering their first RSV season and for infants and children aged 8–19 months who are at increased risk for severe RSV disease and are entering their second RSV season (5). The recommended dosage of nirsevimab for infants weighing <5 kilograms (kg) (<11 pounds (lb)) is 50mg. For infants aged >6 months weighing ≥5 kg (≥11 lb), the recommended dose is 100mg. For infants aged 8–19 months at increased risk of severe RSV disease entering their second season, the recommended dose is
CDC: During nirsevimab shortage, prioritize infants at risk, encourage maternal vaccination
Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants


ABSTRACT

BACKGROUND

Whether vaccination during pregnancy could reduce the burden of respiratory syncytial virus (RSV)-associated lower respiratory tract illness in newborns and infants is uncertain.

METHODS

In this phase 3, double-blind trial conducted in 18 countries, we randomly assigned, in a 1:1 ratio, pregnant women at 24 through 36 weeks' gestation to receive a single intramuscular injection of 120 μg of a bivalent RSV prefusion F protein-based (RSVpreF) vaccine or placebo. The two primary efficacy end points were medically attended severe RSV-associated lower respiratory tract illness and medically attended RSV-associated lower respiratory tract illness in infants within 90, 120, 150, and 180 days after birth. A lower boundary of the confidence interval for vaccine efficacy (95.5% confidence interval [CI] at 90 days; 97.58% CI at later intervals) greater than 20% was considered to meet the success criterion for vaccine efficacy with respect to the primary end points.

RESULTS

At this prespecified interim analysis, the success criterion for vaccine efficacy was met with respect to one primary end point. Overall, 3682 maternal participants received vaccine and 3687 received placebo; 3578 and 3556 infants, respectively, were evaluated. Medically attended severe lower respiratory tract illness occurred within 90 days after birth in 6 infants of women in the vaccine group and 31 infants of women in the placebo group (vaccine efficacy, 81.8%; 95.5% CI, 49.0% to 96.3); 19 cases and 62 cases, respectively, occurred within 180 days after birth (vaccine efficacy, 60.4%; 97.58% CI, 44.3 to 84.1). Medically attended RSV-associated lower respiratory tract illness occurred within 90 days after birth in 24 infants of women in the vaccine group and 56 infants of women in the placebo group (vaccine efficacy, 57.3%; 95.5% CI, 14.7 to 79.8); these results did not meet the statistical success criterion. No safety signals were detected in maternal participants or in infants and toddlers up to 24 months of age. The incidences of adverse events reported within 1 month after injection or within 1 month after birth were similar in the vaccine group (13.8% of women and 37.1% of infants) and the placebo group (13.1% and 34.5%, respectively).

CONCLUSIONS

RSVpreF vaccine administration during pregnancy was effective against medically attended severe RSV-associated lower respiratory tract illness in infants, and no safety concerns were identified. (Funded by Pfizer; MATISSE ClinicalTrials.gov number, NCT04424316.)
Burden of RSV in Pregnancy
J Infect Dis, 2023

- Among 8126 pregnant women, the proportion with respiratory infections that tested (+) for RSV was 3.4%
- Incidence $\rightarrow$ 26 per 1000 person years
- Hospitalization $\rightarrow$ 2.7 per 1000 person years
- No deaths
- Comparing RSV (+) to RSV (-) women, no differences in miscarriage, stillbirth, LBW or SGA
Maternal RSV Vaccination

• Prefusion F vaccines developed by both Pfizer and GSK
• Trials enrolled women from 24 to 36 weeks gestation
• Both GSK and Pfizer vaccine trials showed non-significant increases in preterm deliveries in vaccinees vs placebo recipients
  • Low to middle income countries
  • Uncertain mechanism
  • GSK abandoned research program
• Only Pfizer’s vaccine FDA approved and recommended by CDC
Abrysvo for Pregnant Women

- Placebo-controlled trial involving 7392 pregnant women
- Efficacy against infant RSV hospitalization:
  - 68% at 90 days
  - 57% at 180 days
- Minimal maternal side effects
- No infant adverse effects
  - Other than possible preterm birth
Use of the Pfizer Respiratory Syncytial Virus Vaccine During Pregnancy for the Prevention of Respiratory Syncytial Virus–Associated Lower Respiratory Tract Disease in Infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

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On October 6, 2023, this report was posted as an MMWR Early Release on the MMWR website (https://www.cdc.gov/mmwr).

Abstract

Respiratory syncytial virus (RSV) is the leading cause of hospitalization among U.S. infants. Niruexam (Beyfortis, Sanofi and AstraZeneca) is recommended to prevent RSV-associated lower respiratory tract infection (LRTI) in infants. In August 2023, the Food and Drug Administration (FDA) approved RSVpreF vaccine (Abyzivo, Pfizer Inc.) for pregnant persons as a single dose during 32–36 completed gestational weeks (i.e., 32 weeks and zero days through 36 weeks and 6 days gestation) to prevent RSV-associated lower respiratory tract disease in infants aged <6 months. Since October 2023, CDC’s Advisory Committee, on Immunization Practices (ACIP) RSV Vaccines Pediatric/Maternal Work Group has reviewed RSV epidemiology and evidence regarding safety, efficacy, and potential economic impact of pediatric and maternal RSV prevention products, including RSVpreF vaccine. On September 22, 2023, ACIP and CDC recommended RSVpreF vaccine using seasonal administration (i.e., during September through end of January in most of the continental United States) for pregnant persons as a one-time dose at 32–36 weeks’ gestation for prevention of RSV-associated LRTI in infants aged <6 months. Either maternal RSVpreF vaccination during pregnancy or niruexam administration to the infant is recommended to prevent RSV-associated LRTI among infants, but both are not needed for most infants. All infants should be protected against RSV-associated LRTI through use of one of these products.

Introduction

In August 2023, the Food and Drug Administration (FDA) approved RSVpreF vaccine (Abyzivo, Pfizer Inc.) for pregnant persons to prevent RSV-associated lower respiratory tract disease and severe lower respiratory tract disease in infants aged <6 months (1,2). The Pfizer brentux RSVpreF vaccine, which is the same formulation and dose approved for use in adults aged 18–60 years, contains stabilized fusion F glycoproteins from RSV A and RSV B and is approved as a single 0.5 mL intramuscular dose administered during 32 through 36 weeks’ gestation.

In clinical trials among pregnant persons at 24–36 weeks’ gestation, more preterm births (>37 weeks’ gestation) were observed among RSVpreF vaccine recipients than placebo recipients, although the differences were not statistically significant (1,2). Available data were insufficient to establish or exclude a causal relationship between preterm birth and RSVpreF vaccine. FDA labeled the potential risk for preterm birth as a warning and approved RSVpreF vaccine for use in pregnant persons at 32–36 weeks’ gestation to avoid the potential risk for preterm birth at <32 weeks’ gestation, which is associated with increased risk for morbidity and mortality (1,3). More hypertensive disorders of pregnancy were observed among RSVpreF vaccine recipients compared with placebo recipients, although the differences were not statistically significant. FDA determined that, when RSVpreF is administered during 32–36 weeks’ gestation, the benefit of vaccination in preventing RSV-associated LRTI in infants outweighed risks, including the potential risk for preterm birth and hypertensive disorders of pregnancy (1,2).

On August 3, 2023, CDC’s Advisory Committee on Immunization Practices (ACIP) and CDC recommended niruexam (Beyfortis, Sanofi, and AstraZeneca), a long-acting monoclonal antibody for prevention of severe RSV disease, for infants aged >8 months who are born during or entering their first RSV season and for children aged 8–19 months at increased risk for severe RSV disease entering their second RSV season (3). On September 22, 2023, ACIP and CDC recommended RSVpreF vaccine for pregnant persons as a one-time dose during 32–36 completed weeks’ gestation using seasonal administration (September-January in most of the continental United States) to prevent RSV-associated lower respiratory tract infection (LRTI) in infants. Either maternal RSVpreF vaccination during pregnancy or niruexam administration to the infant is recommended to prevent RSV-associated LRTI in infants, but both are not needed for most infants. This report describes new recommendations for the use of maternal RSVpreF during pregnancy.
<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Do you need it during your pregnancy?</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19</td>
<td>Yes! All adults, including those who are pregnant and people who have had COVID-19 illness, are recommended to be up to date with COVID-19 vaccinations. It’s safe to get the vaccine at any time during your pregnancy.</td>
</tr>
<tr>
<td>Influenza (flu)</td>
<td>Yes! You need a flu shot every fall or winter for your protection and for the protection of your baby. It’s safe to get the vaccine at any time during your pregnancy.</td>
</tr>
<tr>
<td>Tetanus, diphtheria, and whooping cough (TdTw)</td>
<td>Yes! Everyone who is pregnant is recommended to get a dose of Tdap vaccine (the adult whooping cough vaccine) during each pregnancy. Preferably in the early part of the third trimester. Tdap vaccine during pregnancy will help protect your baby from whooping cough in the first few months after birth. Consult your healthcare professional if you haven’t had at least 2 tetanus- and diphtheria-toxoid containing shots sometime in your life or if you have a deep or dirty wound.</td>
</tr>
<tr>
<td>Hepatitis B (HepB)</td>
<td>Yes! All adults younger than 60 years, including those who are pregnant, should get HepB vaccine if they are not already immune. If vaccination is needed during pregnancy, Engerix-B, Recombivax HB, or Tева (combination with hepatitis A vaccine) may be used. Any HepB vaccine may be used while breastfeeding. A screening blood test for hepatitis B infection is recommended during every pregnancy, regardless of vaccination status.</td>
</tr>
<tr>
<td>Respiratory Syncytial Virus (RSV)</td>
<td>Yes! To prevent serious RSV illness in infants, either the Palazyme RSV vaccine (Abraxis) should be given between 32 weeks, 0 days and 36 weeks and 6 days of pregnancy OR a dose of inactivated RSV (pre ventive antibody) should be given to the infant after birth. RSV vaccination during pregnancy is generally offered only between September and the end of January.</td>
</tr>
<tr>
<td>Pneumococcal PCV23, PCV15, PCV22</td>
<td>May be. If you are at increased risk of severe illness from pneumococcal disease, your healthcare professional might recommend pneumococcal vaccination during pregnancy or recommend waiting until after pregnancy. If you inadvertently get pneumococcal vaccine during your pregnancy, this is not a cause for concern.</td>
</tr>
<tr>
<td>Hepatitis A (HepA)</td>
<td>May be. You need this vaccine if you have a specific risk factor for hepatitis A. The vaccine is usually given in 2 doses, 6–18 months apart. If you need to get or continue the HepB vaccine series, it’s safe to do so during pregnancy.</td>
</tr>
<tr>
<td>Haemophilus influenzae type b (Hib)</td>
<td>Maybe. Some adults with certain high-risk conditions* for example, lack of a functioning spleen, need vaccination with Hib. If you need to get Hib vaccine, it’s safe to receive it any time during your pregnancy.</td>
</tr>
<tr>
<td>Measles, mumps, and rubella (MMR)</td>
<td>Maybe. You may also need MMR vaccine if you have one of several health conditions, for example, if you don’t have a spleen. During pregnancy, if you need MMR, it’s safe to get it.</td>
</tr>
<tr>
<td>Human papillomavirus (HPV)</td>
<td>May be. This vaccine is not recommended to be given during pregnancy, but if you inadvertently receive it, this is not a cause for concern. HPV vaccine is recommended for all people age 26 or younger, so if you are in this age group, make sure you are vaccinated before or after your pregnancy. People age 27 through 45 may also be vaccinated against HPV after a discussion with their healthcare professional. The vaccine is given in 2 or 3 doses (depending on the age at which the first dose is given) over a 6–month period.</td>
</tr>
<tr>
<td>Measles, mumps, and rubella (MMR)</td>
<td>May be. This vaccine is not recommended during pregnancy, but if you inadvertently receive it, this is not a cause for concern. At least 1 dose of MMR is recommended for you if you were born in 1957 or later. (And you may need 2nd dose! ) During your prenatal care, your healthcare professional will test your blood to assess your need for MMR following your delivery. It’s best for you (and any future babies) to get the protection vaccination provides before trying to become pregnant.</td>
</tr>
<tr>
<td>Chickenpox (Varicella)</td>
<td>May be. This vaccine is not recommended during pregnancy, but if you inadvertently receive it, this is not a cause for concern. If you’ve never had chickenpox, you were vaccinated, or were vaccinated but got only 1 dose, it’s best for you (and any future babies) to be protected with the vaccine before trying to become pregnant, or after you’ve completed your pregnancy. The vaccine is given in 2 doses 4–8 weeks apart.</td>
</tr>
<tr>
<td>Zoster (Shingles)</td>
<td>May be. If you are age 50 or older and immunocompromised, you are recommended to get the 2-dose series of the Shingrix brand of shingles vaccine. But, since the safety of Shingrix vaccine during pregnancy is unknown, talk with your healthcare professional to determine if the benefits of Shingrix vaccination during pregnancy outweigh the potential risks.</td>
</tr>
</tbody>
</table>

*Consult your healthcare professional to determine your level of risk for infection and your need for this vaccine.
RSV – Yes!

To prevent serious RSV illness in infants, either the Pfizer RSV vaccine (Abrysvo) should be given between 32 weeks, 0 days and 36 weeks and 6 days of pregnancy **OR** a dose of nirsevimab (RSV preventive antibody) should be given to the infant after birth. RSV vaccination during pregnancy is generally offered only between September and the end of January.

NB: GSK vaccine should not be used
RSV – Yes!

To prevent serious RSV illness in infants, either the Pfizer RSV vaccine (Abrysvo) should be given between 32 weeks, 0 days and 36 weeks and 6 days of pregnancy OR a dose of nirsevimab (RSV preventive antibody) should be given to the infant after birth. RSV vaccination during pregnancy is generally offered only between September and the end of January.

Given in this time window, cost will be $167,280 per QALY saved.
Vaccines and Preventable Diseases

RSV Vaccination for Pregnant People

CDC recommends ways to protect babies from getting very sick with Respiratory Syncytial Virus (RSV):

- An RSV vaccine is given during pregnancy.
- A new maternal RSV vaccine is recommended for use during pregnancy (maternal RSV vaccine) in women who are 18 through 36 weeks pregnant, OK.
- An RSV vaccine given during pregnancy can prevent infection in infants and some other babies.

Babies born to mothers who get RSV vaccine at least 2 weeks before delivery will have protection and, in most cases, should not need an RSV intramuscular later.

When is RSV season?

In most regions of the United States, RSV season starts in the fall and peaks in the winter, but the timing and severity of RSV season can vary from place to place and year to year. RSV season is likely to be different for people living in the north, parts of Florida, Hawaii, Denver, Anchorage, and other U.S. islands and Pacific Areas.

The peak of maternal RSV vaccination is in the fall babies get their doses from getting sick with RSV during their first RSV season. In some of the continental United States, this means maternal RSV vaccine will be given in September through January.

Who should get the maternal RSV vaccine?

People who are 22 through 36 weeks pregnant during September through January should get a dose of maternal RSV vaccine to protect their babies. RSV season can vary around the country, so if you live in Alaska, Florida, or outside the continental U.S. talk to your healthcare provider about when RSV season is expected where you live, so that your infant can be protected against RSV disease.

How is the maternal RSV vaccine administered?

Maternal RSV vaccine is given as a shot into the mother’s upper arm. Only a single dose (one shot) of maternal RSV vaccine is recommended. It is not yet known whether another dose might be needed in later pregnancies.

How well does the maternal RSV vaccine work?

When someone gets RSV vaccine, their body responds by making an antibody that protects against the virus that causes RSV. The process takes about 2 weeks.

How to use the maternal RSV vaccine:

- All women who are pregnant should get the maternal RSV vaccine. It is not yet known whether another dose might be needed in later pregnancies.

What are the possible side effects of the maternal RSV vaccine?

There may be a very low risk of harm from RSV. Some vaccine-related side effects are:

- Pain, redness, or swelling at the injection site.
- Localized reactions such as pain, redness, or swelling at the injection site.
- Systemic reactions such as cough, fever, nausea, headache, muscle pain, and rash.

Adverse events following vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS), even if it is not clear that the vaccine caused the adverse event. Your or your doctor can report an adverse event by calling 1-800-822-7967. If you have any questions about adverse effects from the maternal RSV vaccine, talk with your healthcare provider.

Do I need a prescription for a maternal RSV vaccine?

Depending on where you live and whether you are pregnant and get this vaccine, you might need a prescription. See CDC’s Vaccine Finder Services for information on prescriptions for vaccines.
Important Details Regarding Maternal RSV Vaccine

- Recommended to prevent RSV disease in infant, not necessarily mother
- Approved by ChristianaCare P&T and available for distribution to practices
- IM injection for mom vs IM injection for baby
- Cost of Abrysvo $250 vs $495 for nirsevimab
- Counseling about both options (maternal vaccine and mAb) should be provided during pregnancy
- Important to document maternal vaccination for the purposes of management of infant (shot of nirsevimab or not)
Active RSV Vaccines for Infants

• Many challenges to overcome
  • Hauntings from the 1960s FI-RSV vaccine – must not result in enhanced RSV disease
  • Possible suppression of immune response by maternal antibody
  • Must protect against antigenically distinct strains

• Live attenuated RSV vaccines currently being developed and tested
  • Some insufficiently attenuated for use in young infants
Pursuing Infant RSV Vaccine

- Phase 1/2 study
- 82 toddlers
- GSK chimpanzee-derived adenovirus vector expressing 3 RSV proteins
- Well tolerated
- Immunogenic
- Infant study underway
## Table 1
Recommended Child and Adolescent Immunization Schedule for Ages 18 Years or Younger, United States, 2024

These recommendations must be read with the notes that follow. For those who fall behind or start late, provide catch-up vaccination at the earliest opportunity as indicated by the green bars. To determine minimum intervals between doses, see the catch-up schedule (Table 2).

<table>
<thead>
<tr>
<th>Vaccine and other immunizing agents</th>
<th>1st dose</th>
<th>2nd dose</th>
<th>3rd dose</th>
<th>4th dose</th>
<th>5th dose</th>
<th>6th dose</th>
<th>7th dose</th>
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<th>13th dose</th>
<th>14th dose</th>
<th>15th dose</th>
<th>16th dose</th>
<th>17th-18th dose</th>
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<tbody>
<tr>
<td>Respiratory syncytial virus (RSV)</td>
<td>1 dose</td>
<td>1 dose</td>
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<td>Hepatitis B (HepB)</td>
<td>1st dose</td>
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<td>Rotavirus (RV) (rV1, rV2 series), RV5 (3-dose series)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>See Notes</td>
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<tr>
<td>Diphtheria, tetanus, acellular pertussis (DTaP)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<tr>
<td>Hemophilus influenza type b (Hib)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>See Notes</td>
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<tr>
<td>Pneumococcal conjugate (PCV15, PCV20)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<tr>
<td>Inactivated poliovirus (IPV)</td>
<td>1st dose</td>
<td>2nd dose</td>
<td>3rd dose</td>
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<tr>
<td>COVID-19 (1,250-225,1,175, 1,175-2,575)</td>
<td>1 dose</td>
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<tr>
<td>Influenza (IV4)</td>
<td>Annual vaccination 1 or 2 doses</td>
<td>Annual vaccination 1 or 2 doses</td>
<td>Annual vaccination 1 or 2 doses</td>
<td>Annual vaccination 1 dose only</td>
<td>Annual vaccination 1 dose only</td>
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<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>See Notes</td>
<td>1st dose</td>
<td>2nd dose</td>
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<tr>
<td>Varicella (VAR)</td>
<td>1st dose</td>
<td>See Notes</td>
<td>2nd dose</td>
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<tr>
<td>Hepatitis A (HepA)</td>
<td>See Notes</td>
<td>2-dose series, See Notes</td>
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<tr>
<td>Tetanus, diphtheria, acellular pertussis (Tdap)</td>
<td>1 dose</td>
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<td>Human papillomavirus (HPV)</td>
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<td>See Notes</td>
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<td>Meningococcal (MenC)</td>
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<td>See Notes</td>
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<td>Meningococcal B (MenB)</td>
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<td>See Notes</td>
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<td>Respiratory syncytial virus vaccine (RSV) (Abzyme)</td>
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<td>Dengue (DENACD)</td>
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<td>Mumps</td>
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<table>
<thead>
<tr>
<th>Range of recommended ages for all children</th>
<th>Range of recommended ages for catch-up vaccination</th>
<th>Range of recommended ages for certain high-risk groups</th>
<th>Recommended vaccination can begin in this age group</th>
<th>Recommended vaccination based on shared clinical decision-making</th>
<th>No recommendation/not applicable</th>
</tr>
</thead>
</table>

**Notes:**
- Doses are given as needed or at the earliest opportunity, as indicated by the green bars.
- For vaccines requiring a second dose, the second dose is administered either at an earlier age or at the age specified for the second dose.
- For vaccines requiring a third dose, the third dose is administered either at an earlier age or at the age specified for the third dose.
- For vaccines requiring a fourth dose, the fourth dose is administered either at an earlier age or at the age specified for the fourth dose.
- For vaccines requiring a fifth dose, the fifth dose is administered either at an earlier age or at the age specified for the fifth dose.
- For vaccines requiring a sixth dose, the sixth dose is administered either at an earlier age or at the age specified for the sixth dose.
- For vaccines requiring a seventh dose, the seventh dose is administered either at an earlier age or at the age specified for the seventh dose.
- For vaccines requiring an eighth dose, the eighth dose is administered either at an earlier age or at the age specified for the eighth dose.
- For vaccines requiring a ninth dose, the ninth dose is administered either at an earlier age or at the age specified for the ninth dose.
- For vaccines requiring a tenth dose, the tenth dose is administered either at an earlier age or at the age specified for the tenth dose.
- For vaccines requiring an eleventh dose, the eleventh dose is administered either at an earlier age or at the age specified for the eleventh dose.
- For vaccines requiring a twelfth dose, the twelfth dose is administered either at an earlier age or at the age specified for the twelfth dose.
- For vaccines requiring a thirteenth dose, the thirteenth dose is administered either at an earlier age or at the age specified for the thirteenth dose.
- For vaccines requiring a fourteenth dose, the fourteenth dose is administered either at an earlier age or at the age specified for the fourteenth dose.
- For vaccines requiring a fifteenth dose, the fifteenth dose is administered either at an earlier age or at the age specified for the fifteenth dose.
- For vaccines requiring a sixteenth dose, the sixteenth dose is administered either at an earlier age or at the age specified for the sixteenth dose.
- For vaccines requiring a seventeenth dose, the seventeenth dose is administered either at an earlier age or at the age specified for the seventeenth dose.
- For vaccines requiring an eighteenth dose, the eighteenth dose is administered either at an earlier age or at the age specified for the eighteenth dose.
GET THE FACTS
COVID-19, Flu and RSV in Children

In the US, more than 15 million children have tested positive for COVID-19 since the start of the pandemic. But COVID-19 isn’t the only infection we need to look out for.

COVID-19
Caused 22,000 hospitalizations and 800 deaths in children since 2020

FLU
Caused 20,000 hospitalizations and 100 deaths in children last year

RSV
Causes 58,000-80,000 hospitalizations and 100-300 deaths in children each year

FACT:
Vaccines can protect children and their families against all of these severe infections.

Protect your home against unwanted ‘intruders’ this season by getting vaccinated.

Go to vaccines.gov to check your eligibility for vaccines and to find vaccine appointments near you.

For more information on vaccines, visit: COVID19LearningNetwork.org

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