2024 New Hampshire Immunization Conference

New RSV Immunizations for Respiratory Virus Season

April 18, 2024

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Objectives

- Review the new respiratory syncytial virus (RSV) immunization recommendations for infants, young children, and adults
- Discuss immunization safety and efficacy/effectiveness

Financial Disclosures

- I have no relevant conflicts of interest related to this presentation

RSV Background

RSV Symptoms and Complications

- Common symptoms of RSV infection:
  - Runny nose
  - Decreased appetite
  - Cough
  - Fever
  - Wheezing
- Serious illness can occur, particularly in children younger than 1 year of age, those with risk factors and chronic medical conditions (prematurity, weakened immune systems, etc.), and older adults:
  - Bronchiolitis (inflammation of small airways in lung)
  - Pneumonia
  - Exacerbation of chronic medical conditions (COPD, CHF, etc.)

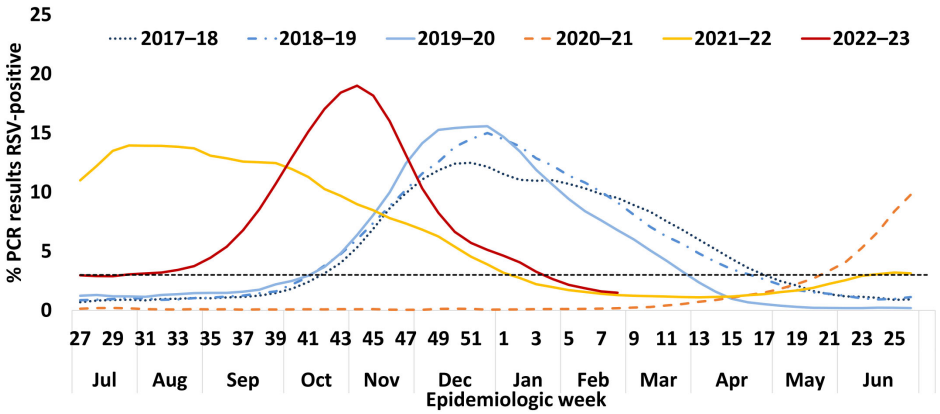
https://www.cdc.gov/rsv/index.html

RSV Burden Estimates

- Nearly all children get RSV by the time they are 2 years old
- RSV is the leading cause of infant hospitalization in the U.S., and risk is highest in the first months of life
- Each year in the U.S., RSV leads to:
  - 58,000 – 80,000 hospitalizations in children younger than 5 years old
  - 100 – 300 deaths in children younger than 5 years old
  - 60,000 – 160,000 hospitalizations in adults 65+ years old
  - 6,000 – 10,000 deaths in adults 65+ years old

https://www.cdc.gov/rsv/research/index.html

Seasonal RSV Activity in the U.S., 2017-2023



https://www.cdc.gov/mmwr/volumes/72/wr/mm7214a1.htm

RSV Treatment and Prevention

- RSV infections in most persons are mild and symptoms resolve in 1-2 weeks
- People with severe disease may need to be hospitalized for supportive care (oxygen, IV fluids, etc.) until symptoms improve
- Monoclonal antibody products are available for prevention in infants and young children
  - Nirsevimab (discuss today)
  - Palivizumab: for infants at highest risk of serious RSV disease, but is administered as **monthly injections** (up to 5 doses) during RSV season
- RSV vaccines for older adults 60+ years of age, and pregnant women (to protect the infant)

https://www.cdc.gov/rsv/index.html

Nirsevimab & RSV Vaccines

- Nirsevimab is a long-acting recombinant human monoclonal antibody that targets and binds the RSV F-protein inhibiting viral fusion and host cell entry
  - Administered directly to infants and young children
  - Prevents RSV through passive immunization
- Two RSV vaccine products currently available:
  - Pfizer: Non-adjuvanted recombinant prefusion F-protein vaccine
  - GSK: Adjuvanted recombinant prefusion F-protein vaccine
- The Pfizer & GSK vaccines can be given to adults 60+ years of age
- Only the Pfizer vaccine (Abrysvo™) can be used during pregnancy

Audience Response Question

True or False: All adults 60 years of age or older are recommended to get a one-time dose of an RSV vaccine.

a. True

b. False

ACIP Recommendations: RSV Vaccines for Adults 60+ Years of Age

- Adults aged 60+ years of age MAY receive a single dose of an RSV vaccine using shared clinical decision-making (based on a discussion between the healthcare provider and patient), taking into account a patient's risk for severe RSV disease
- ACIP decided NOT to initially specify seasonal administration:
  - RSV vaccines are expected to offer protection for at least two RSV seasons
  - Limited data to know if re-vaccination would be beneficial
  - Not having a seasonal recommendation increases flexibility for vaccination
- "Benefits will be highest when RSV vaccination is given in the late summer or early fall, just before the onset of RSV season" (ACIP Work Group, February 2024)

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/08-RSV-Adults-Britton-508.pdf

ACIP Recommendations: Nirsevimab

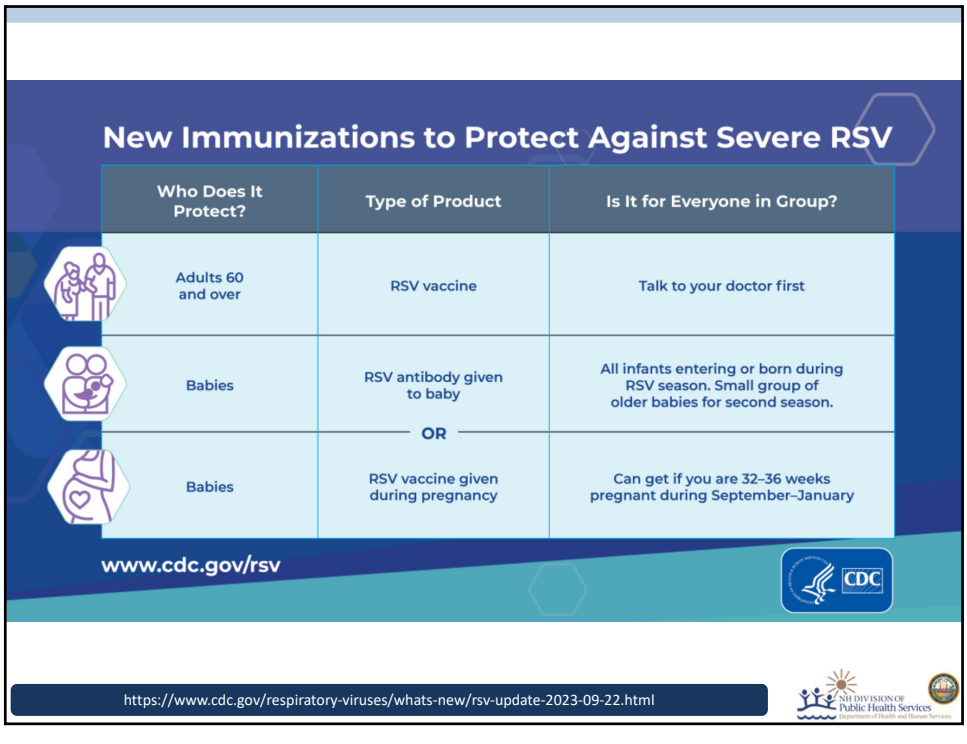
- ALL Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab
- Children aged 8-19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab
- Children at increased risk for severe RSV include children who:
  - Have chronic lung disease of prematurity who required medical support any time in the 6-month period before the start of the RSV season
  - Are severely immunocompromised
  - Have cystic fibrosis with either severe lung disease or weight-for-length measure below the 10th percentile
  - Are American Indian or Alaska Native
- Nirsevimab should be administered shortly before or during RSV season from October through March

https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm
https://www.cdc.gov/vaccines/vpd/rsv/hcp/child-faqs.html

ACIP Recommendations: RSV Vaccination During Pregnancy

- Pregnant persons are recommended to receive a one-time dose of Pfizer's RSV vaccine (Abrysvo™) during 32-36 weeks gestation seasonally during RSV season (September through January) to prevent RSV-associated LRTI in infants
- Either maternal RSV vaccination during pregnancy OR nirsevimab administration to the infant is recommended, but both are NOT needed/recommended for most infants

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm



https://www.cdc.gov/respiratory-viruses/whats-new/rsv-update-2023-09-22.html

ACIP Recommendation Links

- **Monoclonal antibody (nirsevimab)**:
  - https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm
- **RSV vaccines**:
  - Pregnancy (only Pfizer's RSV vaccine, called Abrysvo™): https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm
  - Adults 60 years of age and older (either Pfizer or GSK product): https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm

NH DIVISION OF Public Health Services Department of Health and Human Services

RSV Vaccine for Adults 60+ Years Old

NH DIVISION OF Public Health Services Department of Health and Human Services

ACIP Recommendations: RSV Vaccines

- ACIP recommends that adults aged 60+ years of age MAY receive a single dose of an RSV vaccine using shared clinical decision-making (based on a discussion between the healthcare provider and patient), taking into account a patient's risk for severe RSV disease

https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7229a4-H.pdf

Medical Conditions and Factors Associated with Increased Risk for Severe RSV Disease

Underlying medical conditions associated with increased risk for severe RSV disease include:

- Chronic lung disease (e.g., COPD and asthma)
- Chronic kidney disease
- Moderate or severe immunocompromise
- Chronic cardiovascular disease (e.g., CHF and CAD)
- Chronic liver disease
- Chronic hematologic disorders
- Chronic or progressive neurologic or neuromuscular conditions
- Diabetes Mellitus
- Any underlying *condition* that a provider determines might increase the risk of severe RSV disease

Other factors associated with **increased** risk for severe RSV disease include:

- Frailty or advanced age, as determined by the healthcare provider
- Residence in a nursing home or other long-term care facility
- Any underlying *factor* a provider determines might increase the risk of severe RSV disease

https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
https://www.cdc.gov/vaccines/vpd/rsv/downloads/provider-job-aid-for-older-adults-508.pdf

Morbidity and Mortality Weekly Report

Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

- GSK: 1-dose, adjuvanted recombinant prefusion F-protein vaccine
- Pfizer: 1-dose, (non-adjuvanted) recombinant prefusion F-protein vaccine
- GSK and Pfizer studies were not powered to estimate efficacy against hospitalization, severe RSV illness requiring respiratory support, or death

TABLE 1. Efficacy of 1 dose of GSK respiratory syncytial virus RSVpreF3 vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Efficacy evaluation period	Vaccine efficacy against outcome*	
	RSV-associated LRTD†	RSV-associated medically attended LRTD§
Season 1¶	82.6 (57.9–94.1)**	87.5 (58.9–97.6)††
Season 2§§	56.1 (28.2–74.4)††	—¶¶
Combined seasons 1 and 2 (interim)***	74.5 (60.0–84.5)†††	77.5 (57.9–89.0)††

Abbreviations: LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus.

TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Efficacy evaluation period	Vaccine efficacy against outcome, % (95% CI)*	
	RSV-associated LRTD†	RSV-associated medically attended LRTD§
Season 1¶	88.9 (53.6–98.7)	84.6 (32.0–98.3)
Season 2 (interim)**	78.6 (23.2–96.1)	—††
Combined seasons 1 and 2 (interim)§§	84.4 (59.6–95.2)	81.0 (43.5–95.2)

Abbreviations: LRTD = lower respiratory tract disease; LRTI = lower respiratory tract illness; RSV = respiratory syncytial virus.

https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7229a4-H.pdf

Rare Adverse Events Requiring Further Study

- Inflammatory neurological events:
  - GSK clinical trial – 3 episodes in vaccine group (without a control/placebo comparator group), including 1 case of GBS and 2 cases of ADEM
  - Pfizer clinical trial – 3 events in vaccine group, including 1 case of GBS, 1 case of Miller Fisher syndrome (GBS variant), and 1 case of a worsening undifferentiated motor-sensory axonal polyneuropathy
- Atrial fibrillation (within 30 days):
  - GSK clinical trial – 10 events (0.1%) in vaccine group vs. 4 events (<0.1%) in control group (not all events were new-onset A-fib)
  - Pfizer clinical trial – 10 events (<0.1%) in vaccine group vs. 4 events (<0.1%) in control group (not all events were new-onset A-fib)
- Undergoing further post-marketing evaluation

https://www.cdc.gov/mmwr/volumes/72/wr/pdfs/mm7229a4-H.pdf

ACIP Re-Evaluated Risks/Benefits in Adults Aged 60+ Years (Feb 2024)

	# of Disease-Associated Hospitalizations per 1 Million Adults Aged 65+ Years Each Year in the U.S.	Estimated # of Hospitalizations Averted per 1 Million Older Adults Vaccinated	Estimated Number of Vaccine-Associated GBS Cases per 1 Million Persons Vaccinated
RSV	**1,700 – 2,800**	**2,400 – 2,700** (over **two** RSV seasons, among adults aged 60+ years)	**10 – 25** (**NOT adjusted for background rate** of GBS, which is ~5 cases per million doses given)
Influenza	**3,200 – 9,200**	**2,000** (over **one** influenza season, among adults aged 65+ years)	**1-2** (**additional** cases per million doses given)

GBS: Guillain-Barré Syndrome

Note: Table was modified from an ACIP presentation on February 29, 2024; see Slide #10 for more complete information and data references

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/08-RSV-Adults-Britton-508.pdf

ACIP Discussion on RSV Vaccination for Older Adults (Feb 2024)

"The data support a potential increased risk for GBS after RSV vaccination among adults aged ≥60 years… the Work Group continues to believe that the estimated benefits of RSV vaccination outweigh potential risks when vaccination is implemented using the current recommendation [for adults aged ≥60 years]"

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/08-RSV-Adults-Britton-508.pdf

Audience Response Question

It's October and a 70 year old male is coming to your office for a routine visit. He got vaccinated against influenza, COVID-19, and RSV last fall, and he is wondering if he should get re-vaccinated against all three viruses again this coming fall. How do you counsel him?

a. Recommend only an updated influenza vaccine
b. Recommend an updated influenza and COVID-19 vaccine
c. Recommend an updated influenza and COVID-19 vaccine, AND another dose of an RSV vaccine

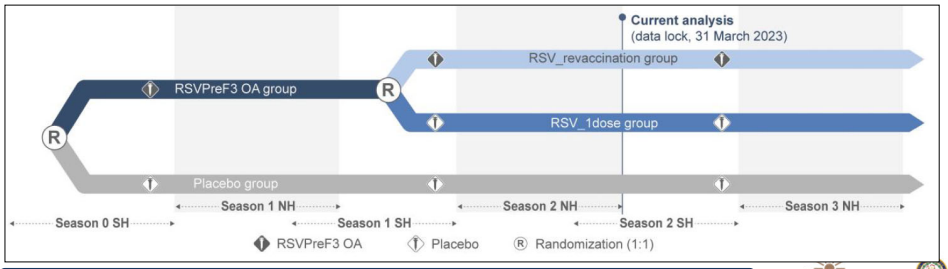
Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America

Efficacy and Safety of Respiratory Syncytial Virus (RSV) Prefusion F Protein Vaccine (RSVPreF3 OA) in Older Adults Over 2 RSV Seasons

- GSK Phase 3 RCT studying their (adjuvanted) RSV vaccine over 2 seasons in adults aged 60+ years
  - RSV vaccine recipients from season 1 were re-randomized (1:1) to receive either a 2nd RSV dose (revaccination group) vs. placebo (1-dose group)



https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae010/7585312

GSK RSV Vaccine Efficacy (VE) Over 2 Seasons

Measured Outcome	1-dose	2-dose (Revaccination)
RSV-LRTD	**67%**	**67%**
Medically attended RSV-LRTD	73%	Not Reported
"Severe" RSV-LRTD	**79%**	**79%**
RSV-associated Hospitalizations	Could not be evaluated due to limited numbers	

LRTD: Lower Respiratory Tract Disease
RSV: Respiratory Syncytial Virus

- No improvement in VE with re-vaccination before 2nd season
- VE estimates tended to decline with increasing follow-up time, hence these 1-dose VE estimates (over 2 seasons) are lower than previously reported

https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciae010/7585312

Pfizer

Pfizer Announces Positive Top-Line Data for Full Season Two Efficacy of ABRYSVO® for RSV in Older Adults

Thursday, February 29, 2024 - 08:00am

- *ABRYSVO, a bivalent vaccine, maintained consistently high protective efficacy for both RSV A and RSV B disease through two seasons after a single dose.*
- *ABRYSVO efficacy was 77.8% against RSV lower respiratory tract disease with three or more symptoms in a second full RSV season in adults 60 years of age or older.*

- VE against RSV-associated lower respiratory tract disease (LRTD) with 3 or more symptoms over 2 seasons combined: **82%**
  - VE against RSV-LRTD with 3 or more symptoms over season 1 vs. season 2: 89% >> 78%

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-data-full-season-two

Future ACIP Considerations

Additional policy issues Adult RSV Work Group plans to address in June 2024

1. Potential FDA approval of Moderna mRNA-1345 vaccine for use in adults aged ≥60 years
2. Potential FDA approval of GSK RSV vaccine for use in adults aged 50–59 years "at increased risk for RSV disease" (*regulatory decision expected June 2024*)
3. Consideration of whether shared clinical decision-making remains the preferred policy option.

35

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2024-02-28-29/08-RSV-Adults-Britton-508.pdf

Pfizer

Pfizer Announces Positive Top-Line Results from Phase 3 Study of ABRYSVO® in Adults Aged 18 to 59 at Increased Risk for RSV Disease

Tuesday, April 09, 2024 - 06:45am

- *ABRYSVO met its trial primary endpoints in adults aged 18 to 59 with an increased respiratory syncytial virus (RSV) disease risk. The vaccine was well-tolerated and demonstrated an immune response non-inferior to adults aged 60 years and older*
- *Pfizer intends to submit these findings to regulatory agencies to seek approval of ABRYSVO in adults 18 to 59 years of age*

https://www.pfizer.com/news/press-release/press-release-detail/pfizer-announces-positive-top-line-results-phase-3-study-1

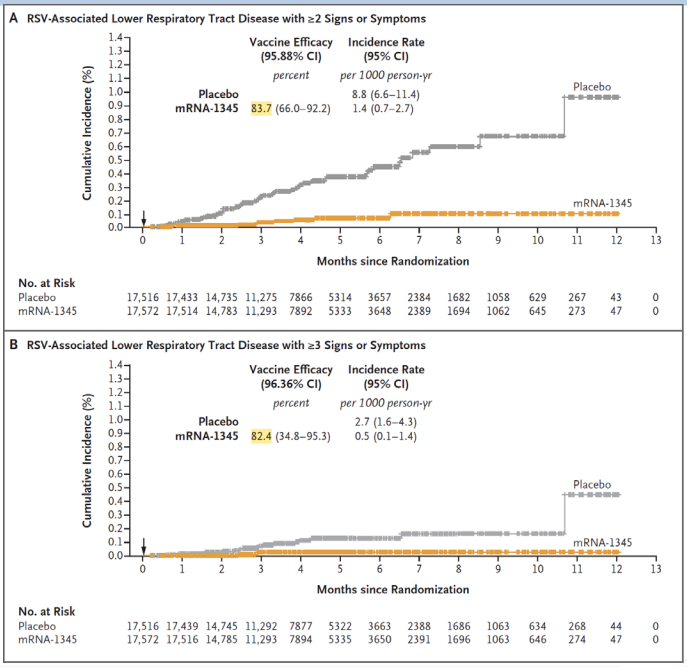
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

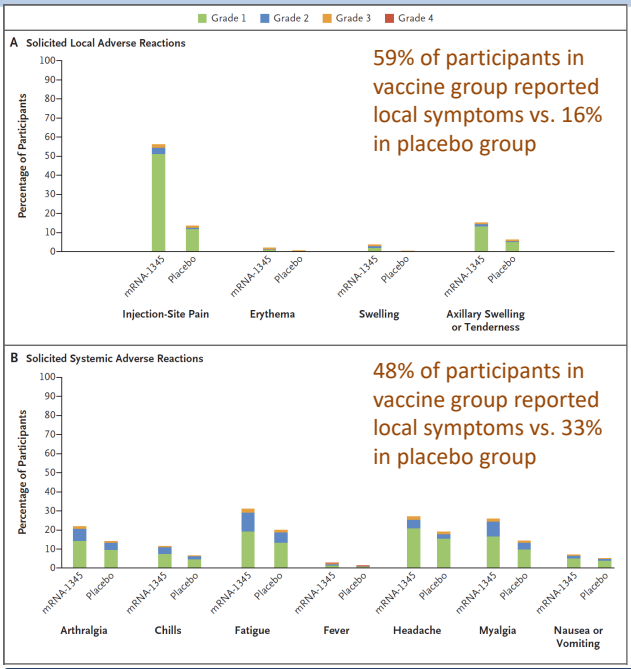
Efficacy and Safety of an mRNA-Based RSV PreF Vaccine in Older Adults

- Randomized, double-blinded, placebo-controlled clinical trial evaluating vaccine safety and efficacy of Moderna's mRNA RSV vaccine (mRNA-1345) in adults aged 60+ years
  - Comparing saline placebo vs. 50 mcg of mRNA-1345 vaccine (more than 17,000 participants in each group)
- Two primary vaccine efficacy (VE) endpoints:
  - 84% VE at preventing RSV-associated LRTD with at least 2 lower respiratory signs or symptoms
  - 83% VE at preventing RSV-associated LRTD with at least 3 lower respiratory signs or symptoms

https://www.nejm.org/doi/pdf/10.1056/nejmoa2307079



https://www.nejm.org/doi/pdf/10.1056/nejmoa2307079



- No cases of acute myocarditis
- 2 cases of acute pericarditis, which occurred more than 42 days after injection and were considered unrelated
- No cases of Guillain-Barré syndrome
- No deaths related to vaccine

https://www.nejm.org/doi/pdf/10.1056/nejmoa2307079

Summary

- Currently RSV vaccines are recommended for adults 60+ years of age under a shared clinical decision-making recommendation, taking into account a person's risk for severe RSV disease
- RSV vaccines appear to be effective over at least 2 seasons
- There does appear to be an rare/uncommon association between RSV vaccine in older adults and Guillain-Barré Syndrome (GBS), but overall benefits of vaccination outweigh risks
- In the future ACIP may move towards more of a risk-based recommendation or even a universal recommendation
- New RSV vaccines for older adults (e.g., Moderna's mRNA RSV vaccine), and expansion of vaccine recommendations to other younger and/or at-risk populations is likely

Monoclonal Antibody (Nirsevimab)

Audience Response Question

It's November and a 6 month old healthy infant is coming to your healthcare provider office for a well child visit. There were no pregnancy or delivery complications, and the infant was born at 39 weeks gestation. It is unknown if the mother received the RSV vaccine during pregnancy. Should you give the infant a dose of nirsevimab?

a. Yes
b. No
c. It Depends

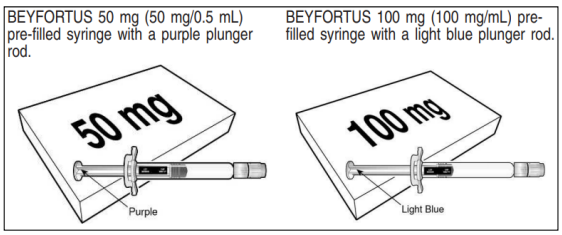
ACIP Recommendations: Nirsevimab

- ALL Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab
- Children aged 8-19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab

https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm

Background on Nirsevimab

- Nirsevimab is a long-acting (half-life is ~71 days) recombinant human monoclonal antibody (immunoglobulin) that targets and binds the RSV F-protein inhibiting viral fusion and host cell entry
- Prevents RSV lower respiratory tract infection/disease (LRTI/LRTD) through passive immunity
- Supplied as 50 mg (purple plunger rod) and 100 mg (light blue plunger rod) pre-filled syringes (50 mg and 100 mg syringes are the same cost)



https://products.sanofi.us/beyfortus/beyfortus.pdf

Dosing and Administration

- Intramuscular (IM) administration
- Neonates and infants born during or entering their 1st RSV season:
  - If body weight <5 kg: 50 mg IM in a single dose
  - If body weight ≥5 kg: 100 mg IM in a single dose
- High-risk children entering their 2nd RSV season:
  - 200 mg IM once (Two, 100 mg injections)

https://products.sanofi.us/beyfortus/beyfortus.pdf

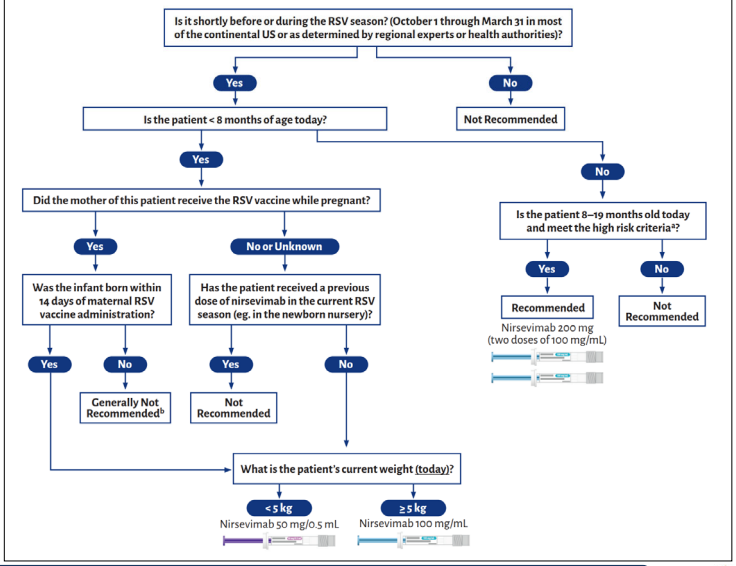
Most Common Side Effects

- Rash (0.9%)
- Injection site reactions (0.3%)

https://products.sanofi.us/beyfortus/beyfortus.pdf

Nirsevimab Administration Visual Guide

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN®



https://downloads.aap.org/AAP/PDF/Nirsevemab-Visual-Guide.pdf?_ga=2.192543721.2133283187.1713294121-356509719.1709066734

NH DIVISION OF Public Health Services

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 30, 2020 VOL. 383 NO. 5

Single-Dose Nirsevimab for Prevention of RSV in Preterm Infants

- Randomized placebo-controlled clinical trial with 150 days of follow-up
- Included **preterm** healthy infants born at 29–34 weeks gestational age entering their first RSV season (N=1,453)
- Participants given a single 50 mg IM injection of nirsevimab or normal saline
- No serious adverse events occurred that were related to nirsevimab
- Efficacy at preventing medically-attended RSV-associated LRTI: **70% lower in nirsevimab group**
- Efficacy at preventing hospitalization due to RSV-associated LRTI: **78% lower in nirsevimab group**

https://www.nejm.org/doi/full/10.1056/nejmoa1913556

NH DIVISION OF Public Health Services

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nirsevimab for Prevention of RSV in Healthy Late-Preterm and Term Infants

- Randomized placebo controlled clinical trial with 150 days of follow-up
- Included healthy infants **born at 35+ weeks gestational age** entering their first RSV season (N=1,490)
- Participants given a single 50 mg or 100 mg IM injection of nirsevimab (based on weight) or normal saline
- No serious adverse events occurred that were related to nirsevimab

https://www.nejm.org/doi/full/10.1056/NEJMoa2110275

Nirsevimab Efficacy Analysis

End Point	Placebo (N=1003)	Nirsevimab (N=2009)	Efficacy (95% CI)
	no. of participants with event (%)		
Medically attended RSV-associated LRTI	54 (5.4)	24 (1.2)	76.4 (62.3–85.2)
Hospitalization for RSV-associated LRTI	20 (2.0)	9 (0.4)	76.8 (49.4–89.4)
Very severe medically attended RSV-associated LRTI	17 (1.7)	7 (0.3)	78.6 (48.8–91.0)

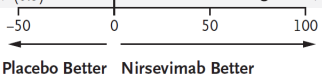


Figure 1. Incidence of Medically Attended Respiratory Syncytial Virus (RSV)–Associated Lower Respiratory Tract Infection (LRTI) through 150 Days after Injection and Efficacy of Nirsevimab as Compared with Placebo.

https://www.nejm.org/doi/10.1056/NEJMc2214773

Morbidity and Mortality Weekly Report

Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

- ACIP pooled data from phase 2b and phase 3 clinical trials (previously shown):
  - **79%** efficacy at preventing medically attended RSV-associated LRTI
  - **81%** efficacy at preventing RSV-associated LRTI with hospitalization
  - **90%** efficacy at preventing RSV-associated LRTI with ICU admission

https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Nirsevimab for Prevention of Hospitalizations Due to RSV in Infants

RAPID COMMUNICATION

Early estimates of nirsevimab immunoprophylaxis effectiveness against hospital admission for respiratory syncytial virus lower respiratory tract infections in infants, Spain, October 2023 to January 2024

Morbidity and Mortality Weekly Report

Early Estimate of Nirsevimab Effectiveness for Prevention of Respiratory Syncytial Virus–Associated Hospitalization Among Infants Entering Their First Respiratory Syncytial Virus Season — New Vaccine Surveillance Network, October 2023–February 2024

Summary of Nirsevimab Efficacy/Effectiveness at Preventing RSV-Associated Hospitalization

Study	Efficacy/Effectiveness
Phase 2b/3 pooled clinical trial data[1]	81%
France, Germany, and UK[2]	83%
Spain (two different analyses)[3]	70% - 84%
U.S. (NVSN)[4]	90%

- Differences in efficacy/effectiveness estimates may partly be due to difference in duration of follow-up (e.g., 150 days vs. 45 days)

[1] https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm
[2] https://www.nejm.org/doi/full/10.1056/NEJMoa2309189
[3] https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2024.29.6.2400046
[4] https://www.cdc.gov/mmwr/volumes/73/wr/mm7309a4.htm

Summary

- Nirsevimab is recommended for ALL infants <8 months of age entering their 1st RSV season (unless mother was appropriately vaccinated with RSV vaccine during pregnancy)
  - Nirsevimab is also recommended for children 8-19 months of age who are at increased risk of severe RSV disease and entering their 2nd RSV season
- Studies show that nirsevimab is 70-90% effective at preventing RSV-associated LRTIs and RSV-associated hospitalizations (higher efficacy for more severe disease outcomes)
- Nirsevimab is safe and very well tolerated with minimal side effects

Audience Response Question

It's November and a healthy 6 month old infant is coming to your healthcare provider office for a well child visit. There were no pregnancy or delivery complications, and the infant was born at 39 weeks gestation. The infant's mother reports receiving an RSV vaccine at 35 weeks gestation. Should you give the infant a dose of nirsevimab?

a. Yes
b. No
c. It Depends

RSV Vaccine During Pregnancy (To Protect the Infant)

ACIP Recommendations: RSV Vaccination During Pregnancy

- Pregnant persons are recommended to receive a one-time dose of Pfizer's RSV vaccine (Abrysvo™) during 32-36 weeks gestation seasonally during RSV season to prevent RSV-associated LRTI in infants
- Either maternal RSV vaccination during pregnancy OR nirsevimab administration to the infant is recommended, but both are NOT needed/recommended for most infants

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Background: RSV Vaccine During Pregnancy

- Pfizer's clinical trial studied vaccination of pregnant persons at **24-36 weeks** gestation
- Observed more preterm births (<37 weeks gestation) in vaccine vs. placebo group; differences were not statistically significant
  - Unclear if a causal relationship between preterm births and RSV vaccination in pregnant persons
- FDA labeled the RSV vaccine with a potential risk for preterm birth, and approved the vaccine for use at **32-36 weeks** gestation to avoid/minimize potential risk of preterm birth
- Also more hypertensive disorders during pregnancy observed in vaccine vs. placebo group; differences were not statistically significant

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Vaccine Efficacy for Selected **Infant** Clinical Endpoints Between 0 – 180 Days of Life

	Clinical Trial Dosing Interval (24-36 weeks gestation)
Medically attended RSV-associated LRTI	**51%** (95% CI: 29.4% – 66.8%)
Severe medically attended RSV-associated LRTI	**69%** (95% CI: 44.3% – 84.1%)
Hospitalization for RSV-associated LRTI	**57%** (95% CI: 10.1% – 80.7%)

LRTI: Lower Respiratory Tract Infection

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Vaccine Efficacy for Selected **Infant** Clinical Endpoints Between 0 – 180 Days of Life

	Clinical Trial Dosing Interval (24-36 weeks gestation)	FDA Approved Dosing Interval (32-36 weeks gestation)
Medically attended RSV-associated LRTI	**51%** (95% CI: 29.4% – 66.8%)	**57%** (95% CI: 29.8% – 74.7%)
Severe medically attended RSV-associated LRTI	**69%** (95% CI: 44.3% – 84.1%)	**77%** (95% CI: 41.3% – 92.1%)
Hospitalization for RSV-associated LRTI	**57%** (95% CI: 10.1% – 80.7%)	**48%** (95% CI: -22.9% – 79.6%)

LRTI: Lower Respiratory Tract Infection

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Relative Risk (95% CIs) for Select Adverse Outcomes (Vaccine vs. Placebo Groups)

	Clinical Trial Dosing Interval (24-36 weeks gestation)
Serious adverse events in pregnant persons	**1.06** (95% CI: 0.95 – 1.17)
Reactogenicity (Grade 3+) in pregnant persons	**0.97** (95% CI: 0.72 – 1.31)
Serious adverse events in infants	**1.01** (95% CI: 0.91 – 1.11)
Preterm birth (<37 weeks gestation)*	**1.20** (95% CI: 0.99 – 1.46)

* Note: Pregnant persons at increased risk for preterm delivery were excluded from clinical trials

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
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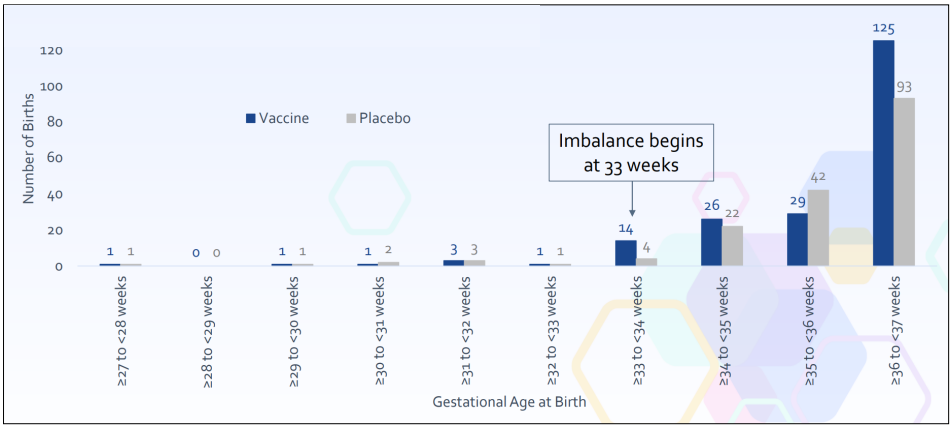
Relative Risk (95% CIs) for Select Adverse Outcomes (Vaccine vs. Placebo Groups)

	Clinical Trial Dosing Interval (24-36 weeks gestation)	FDA Approved Dosing Interval (32-36 weeks gestation)
Serious adverse events in pregnant persons	**1.06** (95% CI: 0.95 – 1.17)	**1.02** (95% CI: 0.87 – 1.20)
Reactogenicity (Grade 3+) in pregnant persons	**0.97** (95% CI: 0.72 – 1.31)	**0.98** (95% CI: 0.62 – 1.54)
Serious adverse events in infants	**1.01** (95% CI: 0.91 – 1.11)	**1.04** (95% CI: 0.90 – 1.20)
Preterm birth (<37 weeks gestation)*	**1.20** (95% CI: 0.99 – 1.46)	**1.15** (95% CI: 0.82 – 1.61)

* Note: Pregnant persons at increased risk for preterm delivery were excluded from clinical trials

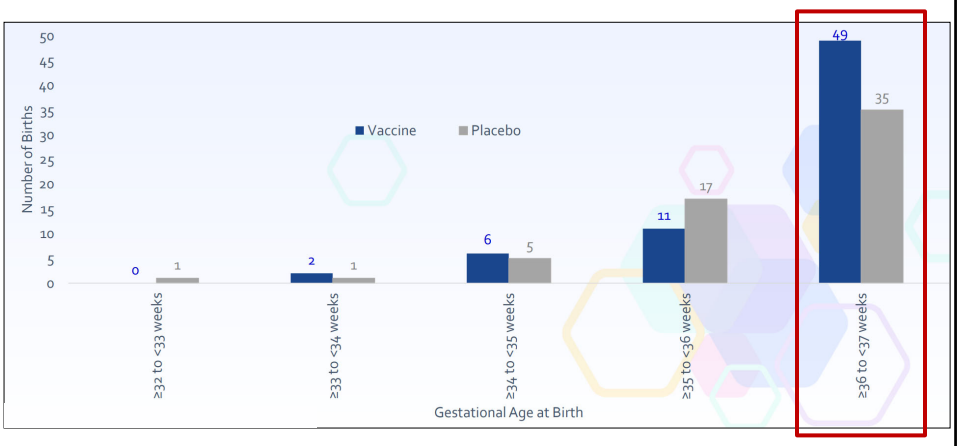
https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

With Clinical Trial Dosing Interval (24 – 36 Weeks Gestation), Preterm Birth Imbalance Began at 33 Weeks



https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-09-22/06-Mat-Peds-Fleming-Dutra-508.pdf

With FDA Approved Dosing Interval (32 – 36 Weeks Gestation), Preterm Birth Imbalance Less Prominent and Later in Pregnancy



https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-09-22/06-Mat-Peds-Fleming-Dutra-508.pdf

A Different GSK RSV Vaccine Studied During Pregnancy Was Associated with Preterm Birth

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

RSV Prefusion F Protein–Based Maternal Vaccine — Preterm Birth and Other Outcomes

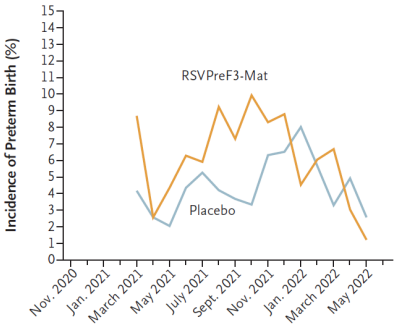
- GSK studied a maternal non-adjuvanted RSV vaccine in pregnant women between 24-34 weeks gestation in a phase 3 RCT
- Enrollment was stopped early due to higher preterm births in the vaccine group and an imbalance of neonatal deaths (probably due to the more preterm births)
- The GSK maternal non-adjuvanted RSV vaccine was never approved/recommended for use in pregnant persons

https://www.nejm.org/doi/full/10.1056/NEJMoa2305478

Preterm Birth Imbalance

Outcome	Vaccine group (N=3494)	Placebo group (N=1739)	Relative Risk
Preterm birth <37 weeks	6.8% (237 births)	4.9% (86 births)	**1.37** (P=0.01)
Neonatal death	0.4% (13 deaths)	0.2% (3 deaths)	**2.16** (P=0.23)

- Unclear cause for the imbalance in preterm births
- Predominantly observed in low- and middle-income countries (RR: 1.56) and not high-income countries (RR: 1.04)
- Preterm imbalance was temporally distributed and primarily occurred between Aug-Dec 2021, but not afterwards (doesn't appear to be COVID-19 related on analyses)



https://www.nejm.org/doi/full/10.1056/NEJMoa2305478

Additional Maternal Adverse Events
(Clinical Trial Dosing Interval Results)

	Vaccine Group	Placebo Group
Maternal Serious Adverse Events	**16.2%** (95% CI: 15.1% – 17.5%)	**15.2%** (95% CI: 14.0% – 16.4%)
Pre-Eclampsia	**1.8%** (95% CI: 1.4% – 2.3%)	**1.4%** (95% CI: 1.1% – 1.9%)
Gestational Hypertension	**1.1%** (95% CI: 0.8% – 1.5%)	**1.0%** (95% CI: 0.7% – 1.4%)
Hypertension	**0.4%** (95% CI: 0.2% – 0.6%)	**0.2%** (95% CI: 0.1% – 0.4%)

- FDA is requiring postmarketing studies to assess hypertensive disorders of pregnancy

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-09-22/06-Mat-Peds-Fleming-Dutra-508.pdf

Additional ACIP Clinical Recommendations

- Nirsevimab is recommended for infants born <14 days after maternal RSV vaccination because ~14 days are needed after maternal vaccination for antibody development and transplacental transfer (i.e., nirsevimab is recommended for all infants born at <34 weeks gestation)
- Nirsevimab "may be considered" for infants born to vaccinated mothers in rare circumstances when the potential incremental benefit of administration is warranted (based on clinical judgement)
- "Providers who care for pregnant persons should discuss the relative advantages and disadvantages of both maternal RSV vaccination and nirsevimab and consider patient preferences when determining whether to vaccinate the pregnant person or to rely on administration of nirsevimab to the infant…"

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Audience Response Question

It's October and a 38 year old pregnant female is at your healthcare provider office for a prenatal visit. She is at 32 weeks gestation and has had NO pregnancy complications. She has a history of diabetes and currently smokes. She has one other 4 year old child who was born at 35 weeks gestation. She is asking you about receiving the Abrysvo RSV vaccine. How do you counsel her?

a. Give Abrysvo now
b. Wait and give Abrysvo when she is at 35-36 weeks gestation
c. Do NOT give Abrysvo and recommend infant nirsevimab
d. Shared clinical decision making

Advantages and Disadvantages of Maternal Vaccination vs. Nirsevimab

Maternal RSV Vaccine	Infant Nirsevimab
Advantages • Provides protection immediately after birth • Might be more resistant to potential viral mutations Disadvantages • Protection is potentially reduced if fewer antibodies are produced or transferred from pregnant person to baby • Potential risk for preterm birth and/or hypertensive disorders of pregnancy	Advantages • Protection may wane slower than protection from maternal RSV vaccine • Direct receipt of antibodies rather than relying on transplacental transfer • No risk for adverse pregnancy outcomes Disadvantages • Potentially limited availability during RSV season • Requires infant injection

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm

Summary

- Pregnant persons are recommended to receive a one-time dose of Pfizer's RSV vaccine (Abrysvo™) during 32-36 weeks gestation during RSV season to prevent RSV-associated LRTI in infants
- The recommended gestational dosing interval reduces the potential risk of preterm birth and associated complications
- Administration of both maternal RSV vaccine during pregnancy and infant nirsevimab is NOT needed for most infants
- Providers should discuss options and advantages/disadvantages of maternal RSV vaccination vs. infant nirsevimab with pregnant persons

Q&A