2024 RSV Updates

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Learning objectives

1. Describe emerging evidence on the efficacy and safety of RSV vaccines

2. Compare the 3 approved RSV vaccines for older adults

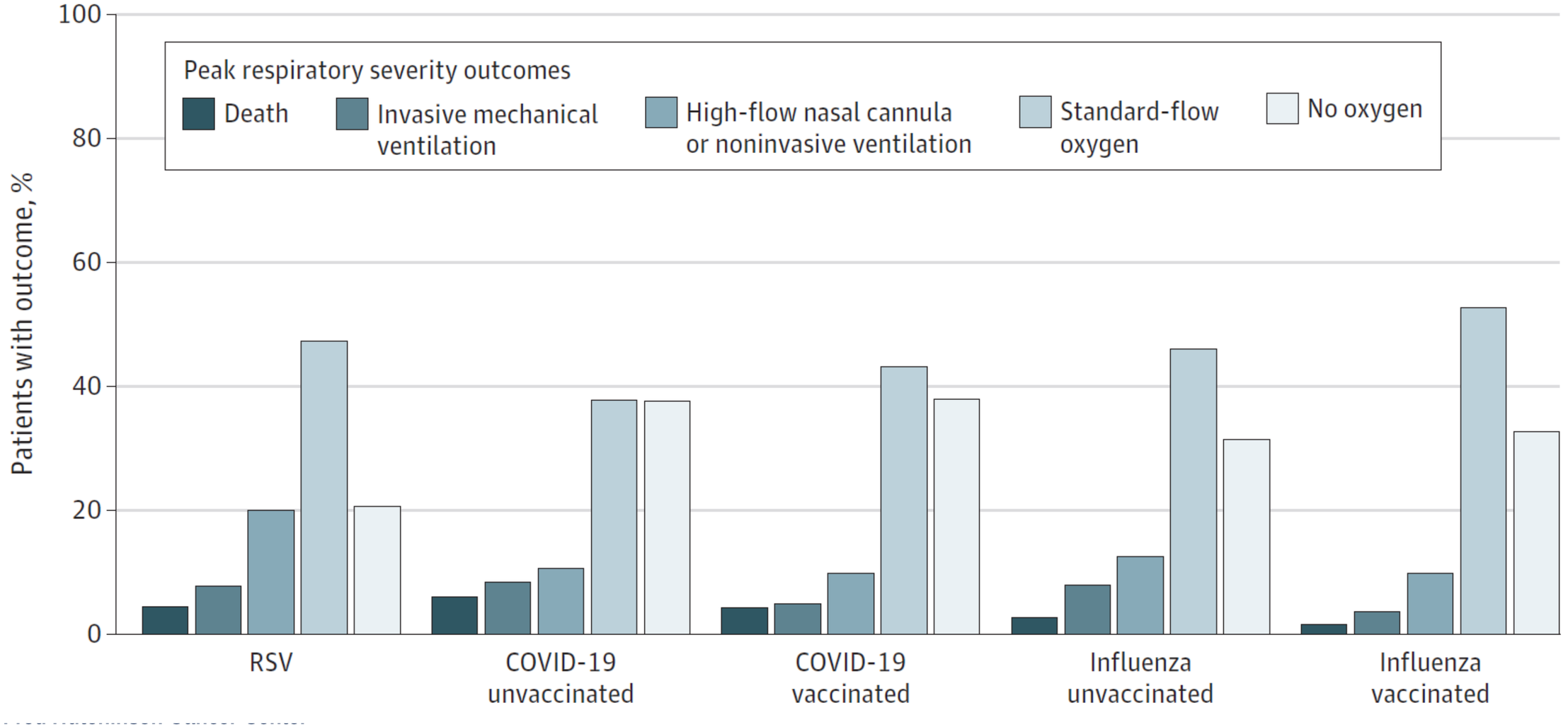
3. Describe the roles of maternal immunization and nirsevimab in pediatric RSV prevention

Background

Background: What is RSV?

- Respiratory virus
- Seasonal outbreaks
- Infects all kids
- Reinfects throughout life
- Substantial M&M – similar to flu

Peak Illness Severity among adults hospitalized with RSV, Covid-19 & Influenza

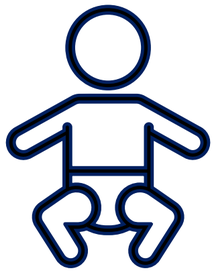


Surie D. JAMA Net Open 2024

RSV: clinical picture

- Infants often present with lower respiratory tract infection
  - Bronchiolitis or pneumonia
- Older children & adults – upper respiratory symptoms
  - Higher risk groups may develop lower respiratory infection, severe disease
- Treatment: supportive care

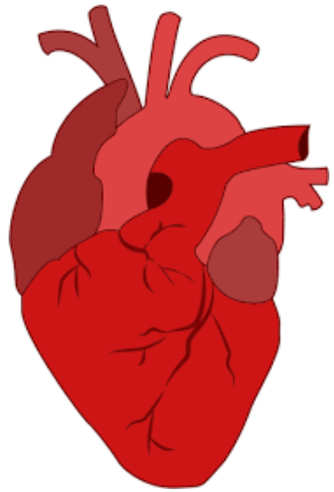
Risk factors for severe RSV disease



Infants

Elderly

Asthma &
COPD



Heart failure
& coronary heart disease

Immunocompromised

Prasad, 2020

RSV vaccines for older adults


CNN Health
Life, But Better
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FDA approves first vaccine for RSV, a moment six decades in the making
By Brenda Goodman, CNN
8 minute read · Updated 3:56 PM EDT, Wed May


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US drug regulator approves world's first RSV vaccine
3 May 2023


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Should You Get the New RSV Vaccine?
BY KATHY KATELLA SEPTEMBER 25, 2023
Effective vaccines for older people and new immunizations for babies could reduce hospitalizations during the RSV season.

2024: Moderna mRNA RSV vaccine

BIOTECH

STAT+

FDA approves Moderna's RSV vaccine, its second licensed product

By Helen Branswell May 31, 2024 Reprints

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

E. Wilson, J. Goswami, A.H. Baqui, P.A. Doreski, G. Perez-Marc, K. Zaman, J. Monroy, C.J.A. Duncan, M. Ujiie, M. Rämet, L. Pérez-Breva, A.R. Falsey, E.E. Walsh, R. Dhar, L. Wilson, J. Du, P. Ghaswalla, A. Kapoor, L. Lan, S. Mehta, R. Mithani, C.A. Panozzo, A.K. Simorellis, B.J. Kuter, F. Schödel, W. Huang, C. Reuter, K. Slobod, S.K. Stoszek, C.A. Shaw, J.M. Miller, R. Das, and G.L. Chen, for the ConquerRSV Study Group*

- Same mRNA vaccine platform as Moderna SARS-CoV-2 vaccine
- mRNA encodes RSV-F protein *(stabilized in pre-fusion conformation – same as other RSV vaccines)*
- 84% efficacy against RSV lower tract disease with ≥2 signs/symptoms

Wilson E. et al. NEJM, December 2023

3 FDA-approved RSV vaccines

	GSK - Arexvy	Pfizer - ABRYSVO	Moderna - mResvia
Age			
Doses			
Vaccine type *All target RSV prefusion F*			
Vaccine efficacy *vs. symptomatic, lab-confirmed lower respiratory disease*			

1. Papi A, et al. N Engl J Med. 2023;388:595-608.

2. Britton A. et al, MMWR. Aug 6 2024

Safety profile

	GSK - Arexvy	Pfizer - ABRYSVO	Moderna - mResvia
Serious adverse events (SAE)			
Unsolicited adverse events			
Inflammatory neurologic events			

VAERS: Vaccine Adverse Event Reporting System. Passive, voluntary surveillance system.

* Comparison: GBS after COVID vaccines was 0.43 and 0.54 for Pfizer and Moderna respectively.

1.Papi A. NEJM, 2023. 2. Walsh, NEJM, 2023. 3. MMWR July 2023 4. Wilson, NEJM, 2023.

Old ACIP recommendation

Adults ≥ 60 may receive a single dose of RSV vaccine, using shared clinical decision making

<u>Challenges:</u>

- Implementation of shared decision-making
- Doesn’t focus on highest risk groups

MMWR, July 21, 2023

ACIP recommendations:

- Adults ≥ 75 years of age: receive a single dose of RSV vaccine

- Adults 60–74 years of age who are at increased risk of severe RSV disease: receive a single dose of RSV vaccine

MMWR, August 6 2024

Co-administration of RSV + influenza vaccines

- ACIP: “Coadministration of RSV vaccines with other adult vaccines is acceptable”[1]
- Immunogenicity: **comparable neutralization titers** for Influenza A/B, RSV A/B, when co-administered[2,3,4]
- Reactogenicity: well-tolerated, acceptable safety profile[2,3,4]

1. MMWR, July 21, 2023
2. Clark, CID, Aug 5 2024
3. Chandler, CID, 2024.
4. Athan, CID, 2023

Real world vaccine effectiveness

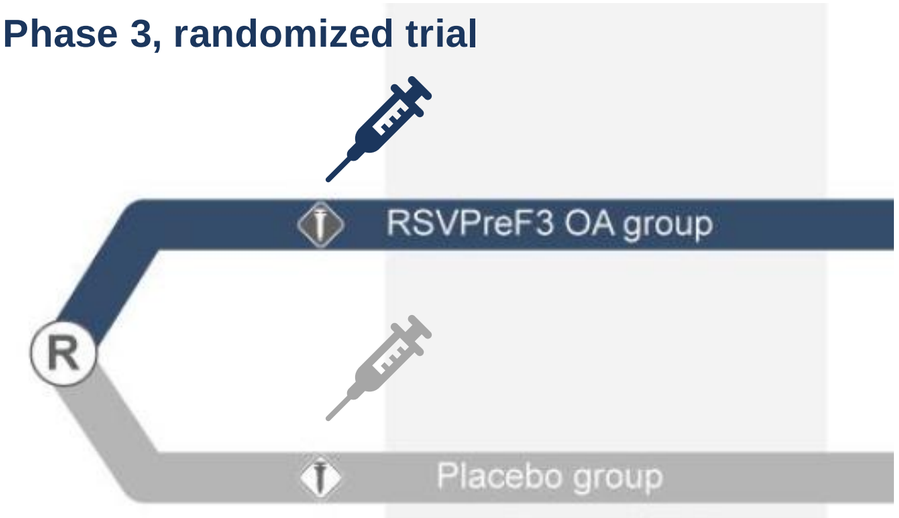
Post-licensure data

- 4 observational studies of vaccine effectiveness against RSV-associated hospitalization among adults aged ≥60 years during the first RSV season after vaccination
- Estimates from the general population or among immunocompetent adults only ranged from 75% (95% CI = 50%–87%) to 82% (95% CI = 69%–89%)
- VE was similar across vaccine products (GSK Arexvy and Pfizer Abrysvo) and patient age groups (60–74 years and ≥75 years
- Effectiveness was demonstrated among adults aged ≥60 years with certain immunocompromising conditions and those with end-stage renal disease.

Britton A. MMWR, August 6, 2024

Vaccine durability

Phase 3, randomized trial



Season 1

Efficacy over 2 seasons:

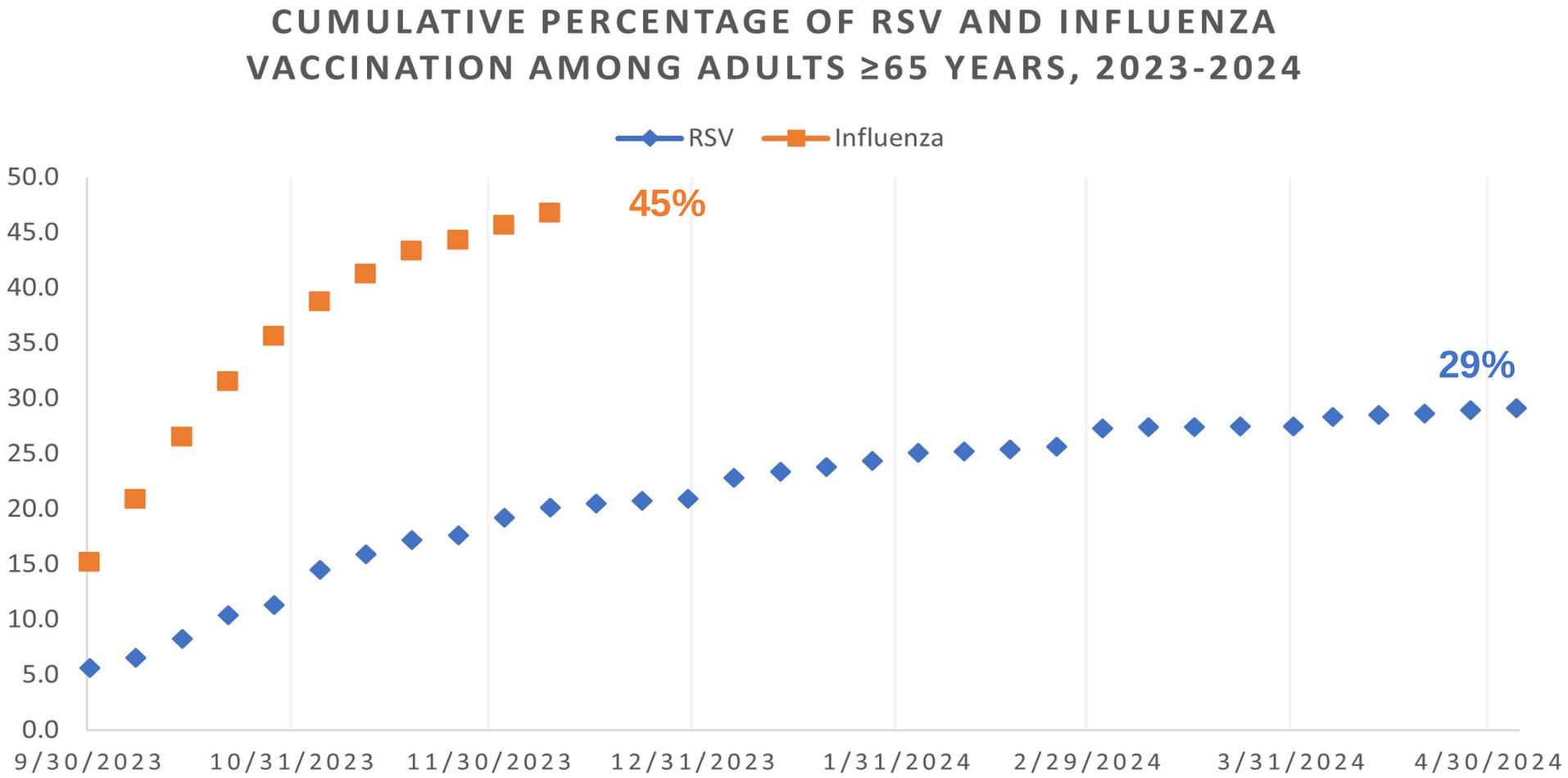
1 dose: 79% efficacy against severe lower tract disease; 67% against RSV lower tract disease

2 doses, 1 year apart: 79% against severe lower tract disease; 67% against RSV lower tract disease

Annual boosters not needed – single dose for now

1. Ison M. CID 2024.

Vaccine uptake



- Awareness
- Convenience
- Insurance coverage
- Vaccine fatigue

1. Branche A. *Clin Infect Dis*, ciae362, https://doi.org/10.1093/cid/ciae362 2. Wang, JAMA Internal Medicine, 2024.

RSV vaccines in older adults – key points

- All 3 vaccines have moderate to high efficacy in preventing severe RSV lower respiratory tract disease [1]

- Overall safe and well tolerated
  - Severe neuro events (GBS) occurred in 0.014% - 0.0005% of participants – very rare[2]

- Unknowns:
  - Vaccine efficacy against hospitalization & death
  - Vaccine efficacy in the highest-risk patients: immunocompromised, very elderly, many comorbidities
  - Durability of protection, if/when boosters will be needed

1. Britton, MMWR, 2024

2. Hause, MMWR, 2024.

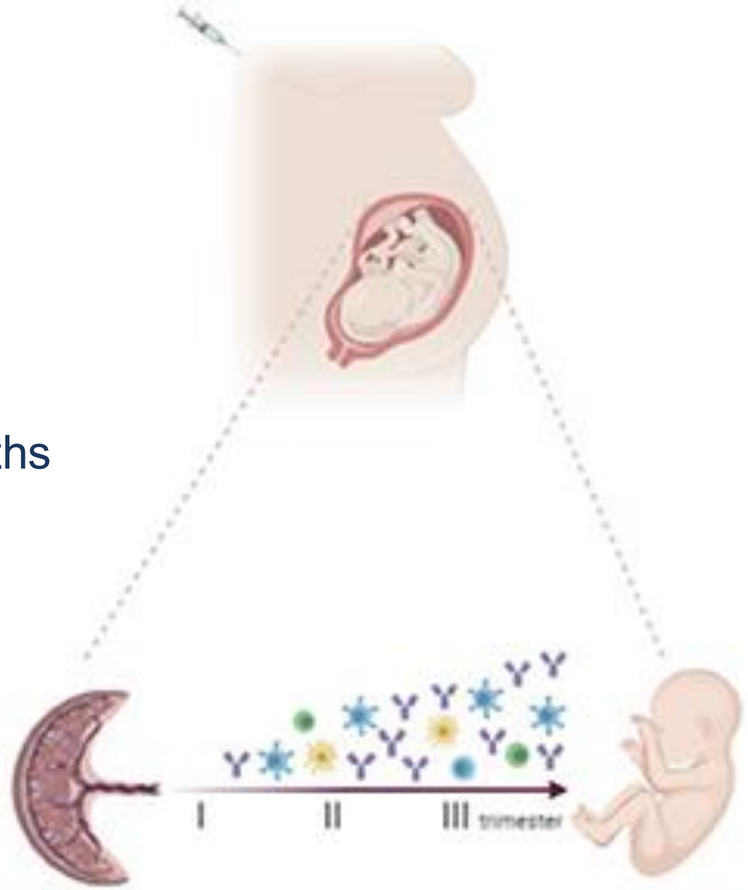
Pediatrics

Maternal immunization

- Transplacental antibody transfer
- Protects infants in first few months of life
- Same strategy used for tetanus, pertussis (Tdap)
- Bivalent vaccine – RSV A and B – Abrysvo (Pfizer)

- Approved for use at **32 - 36 weeks** of pregnancy
- **Vaccine efficacy** among pregnant individuals 32 - 36 weeks
  - ↓ risk of severe lower respiratory disease by 91.1% within first 3 months
  - ↓ risk of severe lower respiratory disease by 76.5% within 6 months
  - ↓ risk of lower respiratory disease by 57.3% within 6 months

- **Safety**:
  - Most common: injection-site pain, headache, muscle aches, nausea
  - **Pre-eclampsia**: **1.8%** of vaccine recipients vs. **1.4%** placebo
  - **Preterm birth**: **5.7%** of vaccine recipients, **4.7%** placebo
  - FDA requiring post-marketing studies of preterm birth and preeclampsia



Kampmann, NEJM 2023 and FDA press release

Image: Cinicola, Front. Pediatr., 28 April 2021

Maternal immunization: post-market surveillance

Limited data; conflicting evidence on perinatal outcomes

Observational study of 2,900 pregnancies in NYC - preterm birth occurred in:

- 5.9% of RSV-vaccinated
- 6.7% of non-vaccinated

- Adjusted analysis:
  - no association between vaccine and preterm birth
  - ↑ risk hypertensive disorders of pregnancy

- Preprint (no peer review)
  - Observational study using VAERS data
  - Signal for increased preterm birth

1. Son M. JAMA Net Open, 2024.

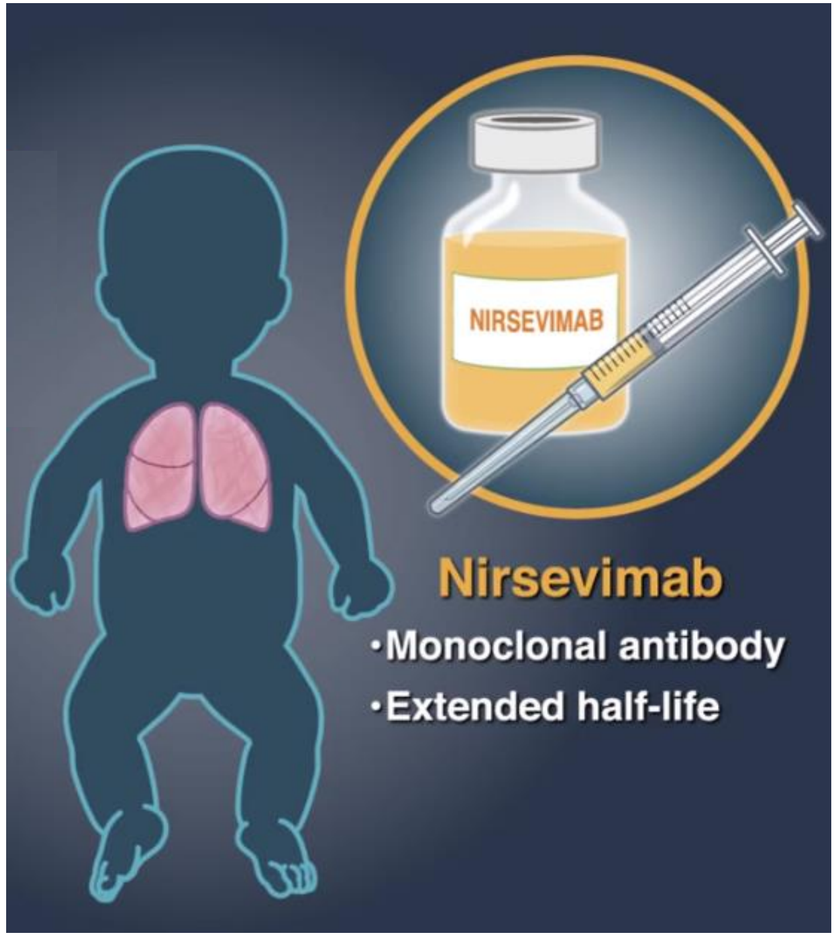
2. Alami A. MedRxiv, 2024.

Nirsevimab (Beyfortus)

- Long-acting monoclonal antibody
- Intramuscular injection
- Single dose (unlike palivizumab) → cheaper
- 79% efficacy in preventing medically attended RSV LRTI

- **Infants <8 months** born during or entering their 1st RSV season
  - Within 1 week of birth
  - During birth hospitalization or outpatient

- **Infants & children 8–19 months** at increased risk for severe RSV disease, entering their 2nd RSV season
  - Chronic lung disease of prematurity requiring medical support
  - Severe immunocompromise
  - Cystic fibrosis with severe lung disease or <10th %ile wt/length
  - American Indian or Alaska Native children



MMWR, August 25, 2023; Hammitt, NEJM, 2022

Pediatric RSV prevention

- **Vaccine advantages**
  - Cheaper
    - More accessible in low-resource settings
    - Area of greatest need: >97% of RSV-attributable deaths are in low-income and middle-income countries
  - Immune response to multiple epitopes
    - Reduce risk of immune escape
    - Anti-drug antibodies in 6% of nirsevimab group vs 1% of placebo group
- **Monoclonal advantages**
  - No concerning safety signals
  - Ideal for preterm infants (mother not yet vaccinated) and infants with impaired transplacental antibody transfer

Real-world vaccine and mAb effectiveness

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

Heidi L. Moline, MD[1]; Ayzsa Tannis, MPH[1]; Ariana P. Toepfer, MPH[1]; John V. Williams, MD[2,3]; Julie A. Boom, MD[4,5]; Janet A. Englund, MD[6]; Natasha B. Halasa, MD[7]; Mary Allen Staat, MD[8,9]; Geoffrey A. Weinberg, MD[10]; Rangaraj Selvarangan, PhD[11]; Marian G. Michaels, MD[2,3]; Leila C. Sahni, PhD[4,5]; Eileen J. Klein, MD[6]; Laura S. Stewart, PhD[7]; Elizabeth P. Schlaudecker, MD[8,9]; Peter G. Szilagyi, MD[10]; Jennifer E. Schuster, MD[12]; Leah Goldstein, MPH[1]; Samar Musa, MPH[2,3]; Pedro A. Piedra, MD[4,5]; Danielle M. Zerr, MD[6]; Kristina A. Betters, MD[7]; Chelsea Rohlfs, MBA[9]; Christina Albertin, MPH[10]; Dithi Banerjee, PhD[12]; Erin R. McKeever, MPH[1]; Casey Kalman, MPH[1]; Benjamin R. Clopper, MPH[1]; New Vaccine Surveillance Network Product Effectiveness Collaborators; Meredith L. McMorrow, MD[1,*]; Fatimah S. Dawood, MD[1,*]

Moline H. MMWR, March 7 2024

What’s next

What's next for RSV prevention and treatment

Products in development:

Combination Vaccines

- RSV + HMPV combo vaccine
- Moderna, AstraZenica

EDP-938[1]

- Phase 2a (human challenge) trials
- **Adults**
- Replication inhibitor

↓ Viral load

↓ Symptom scores

↓ Mucus

Ark Biopharma: Ziresovir[2]

- Phase 3 trials
- Hospitalized **infants**
- Small molecule fusion protein inhibitor
- ↓ symptoms
- ↓ length of ICU stay
- ↓ viral load

1. Ahmad NEJM 2022
2. Oral abstracts, RSV 2022

Take home points

Conclusions

- New RSV vaccines provide ≥2 years of effective protection against severe disease with a single dose
- Overall safe and well-tolerated
- Key populations:
  - Adults >75 or 60-74 + comorbidities
  - Mothers/Birth parents
  - Infants (monoclonal Ab)
- Cost-effective and decrease the burden of illness

Thank you

Teaching Peer Evaluation
for Dr. Denise McCulloch