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Pediatric RSV Prevention: Critical Insights for the Nurse Practitioner

Featuring Wheel of KNOWLEDGE Challenge!

The continuing education for this activity is provided by the National Association of Pediatric Nurse Practitioners.

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Agenda

The Burden of Pediatric RSV
Andrea Kline-Tilford, PhD, CPNP-AC/PC

The Latest Guidance on RSV Immunoprophylaxis
Ravi Jhaveri, MD

Panel Discussion: Strategies for Improving Immunization Rates
Patsy Stinchfield, RN, MS, CPNP

Wheel of KNOWLEDGE Challenge!

The Burden of Pediatric RSV

Andrea M. Kline-Tilford PhD, CPNP-AC/PC, FCCM, FAAN

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University of Michigan Health
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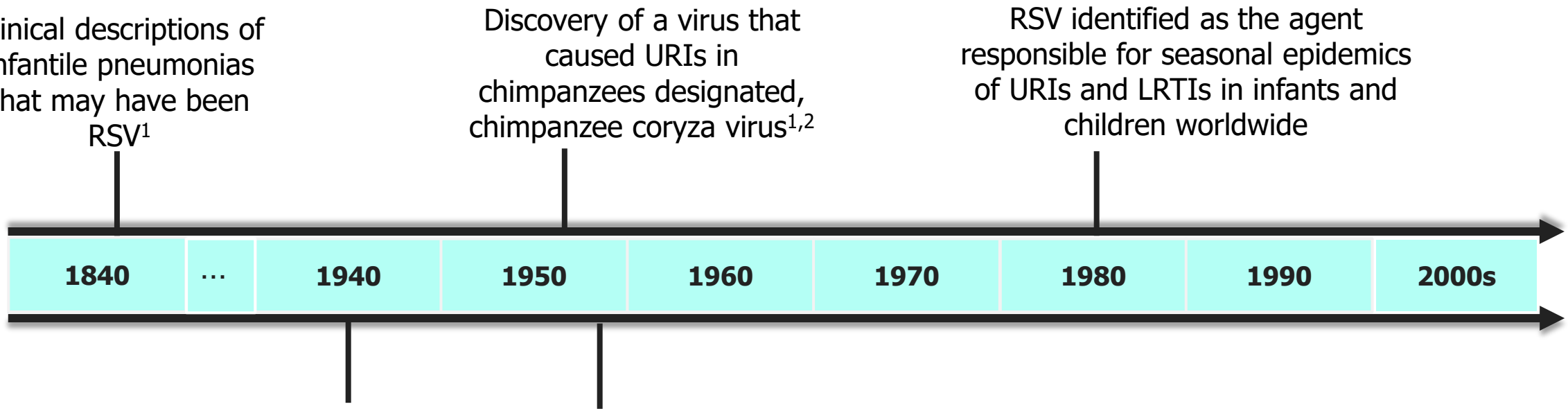
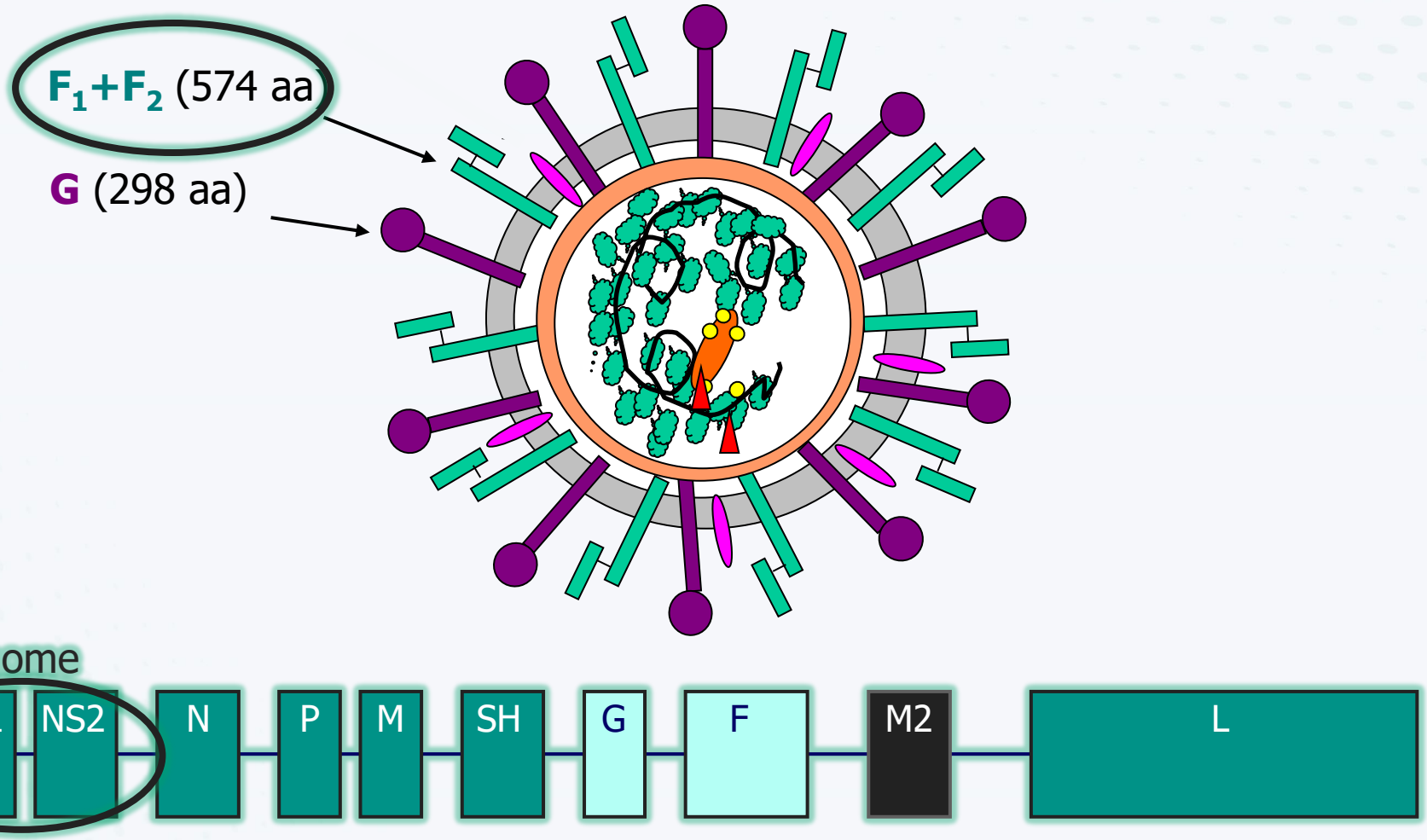
History of RSV



LRTI = lower respiratory tract infection; RSV = respiratory syncytial virus; URI = upper respiratory infection.

1. Oldstone MB. *Viruses, Plagues and History*. Oxford University Press. Oxford, UK. 2000; 2. Morris JA, et al. *Proc Soc Exp Med*. 1956;92(3):544-549;
3. Chanock R, et al. *Am J Hygiene*. 1957;66(3):281-290.

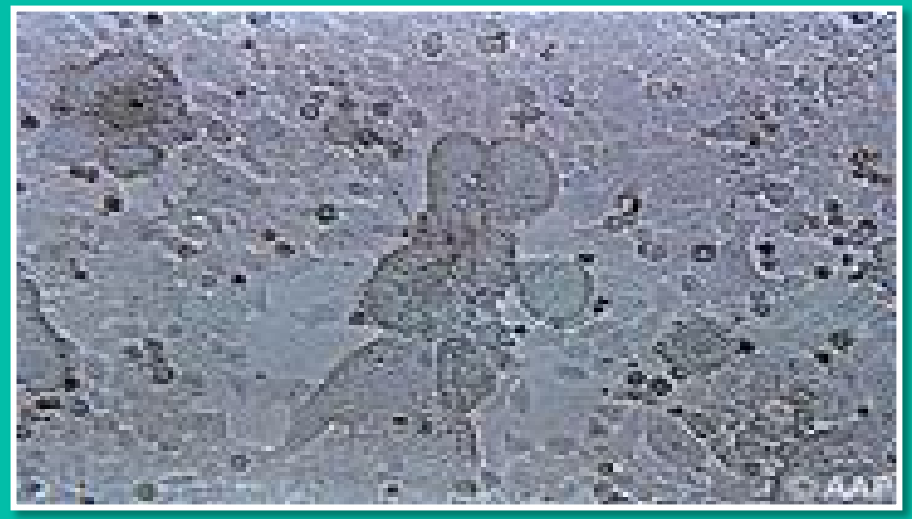
RSV: The Virus

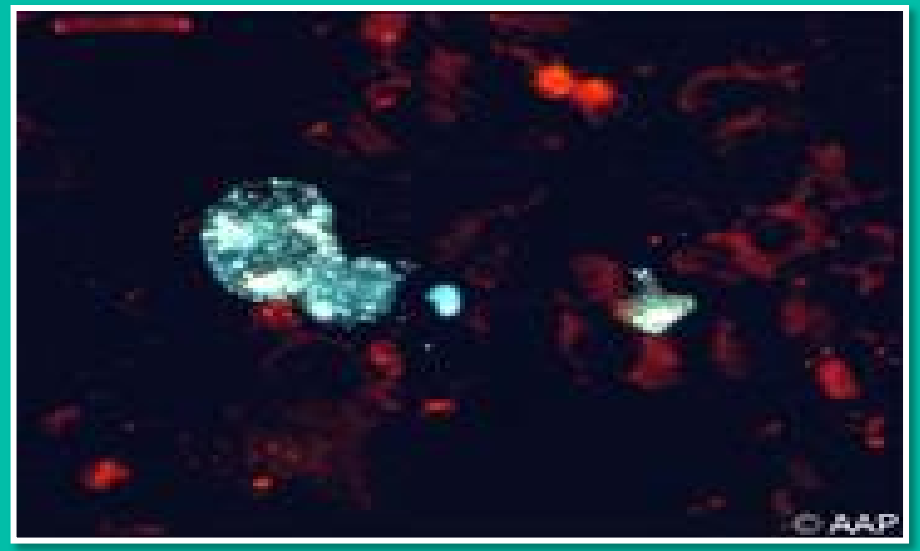


Mejias A, et al. *Vaccine*. 2017;35(3):496-502.

RSV Facts

- Ubiquitous and highly contagious
- Annual US epidemics: winter and early spring, although sporadic infection may occur all year
- **RSV in infants:**
  - **Most important cause of bronchiolitis and pneumonia; leading cause of hospitalization**
  - **~2/3 infected during the 1st year of life; almost 100% infected by age 2**
- Most often, URI and cold-like symptoms beyond infancy
- RSV in adults:
  - Increased recognition: 177,000 hospitalizations; ~14,000 deaths/year in the United States – primarily in individuals >65 years old and/or those with COPD





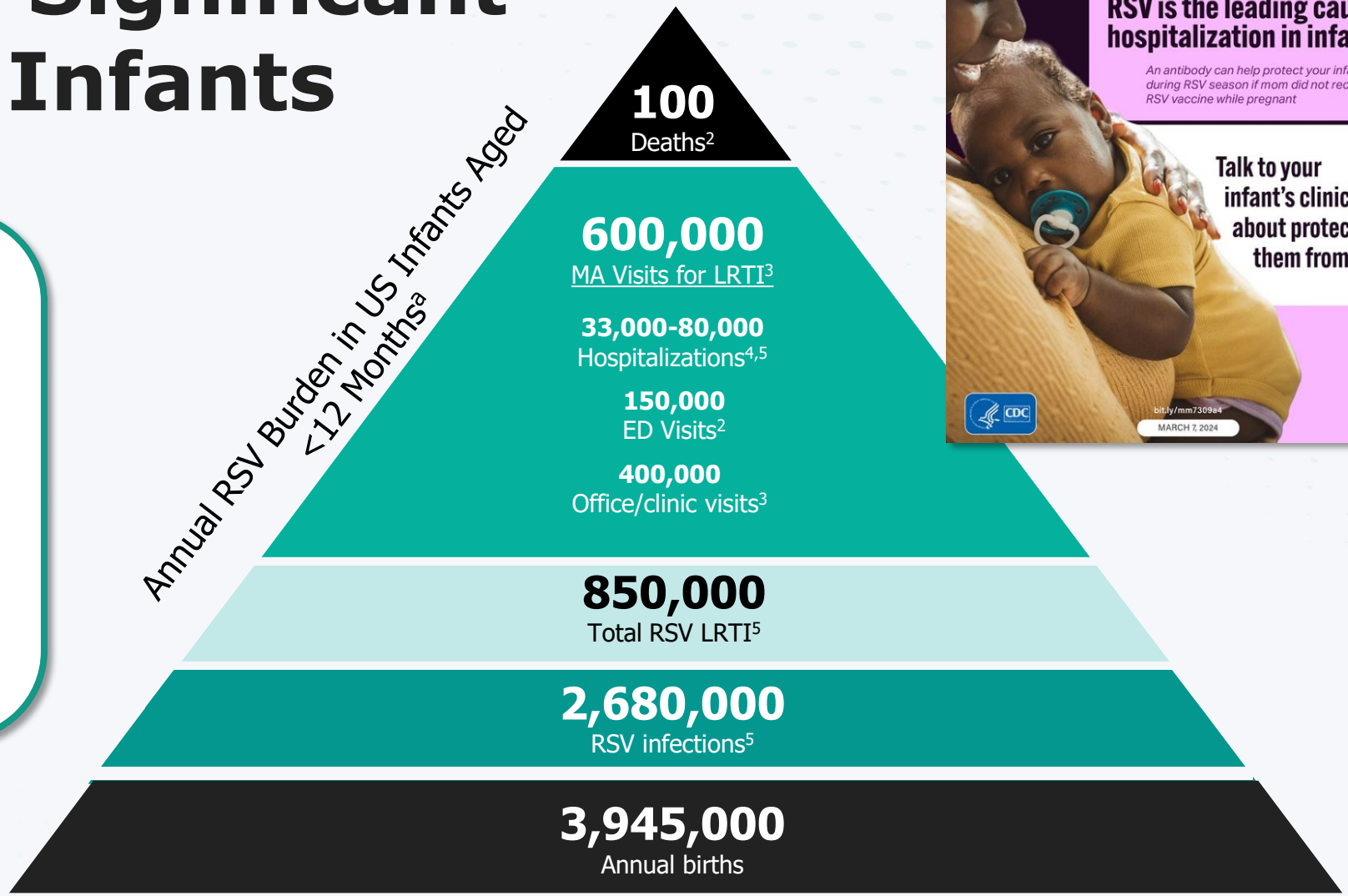
COPD = chronic obstructive pulmonary disease.

Crowe JE Jr, Williams JV. *Viral Infections of Humans*. 2014;27:601–27. Walsh E, et al. *Health Sci Rep*. 2022;5(3):e556.

RSV Causes a Significant Burden in US Infants

From 2009-2019, RSV was the **leading cause of US infant hospitalizations**.

Overall, approximately **9% (1 in 11) of infant hospitalizations are due to RSV infection** (acute bronchiolitis).



[a] Estimated typical RSV season based on references below.
ED = emergency department; MA = medically attended.

1. Suh M, et al. *J Infect Dis*. 2022;226(Suppl 2):S154-S163; 2. Hansen CL, et al. *JAMA Netw Open.* 2022;5(2):e220527; 3. Rainisch G, et al. *Vaccine.* 2020;38(2):251-257; 4. McLaughlin JM, et al. *J Infect Dis.* 2022;225(6):1100-1111; 5. Glezen WP, et al. *Am J Dis Child.* 1986;140(6):543-546.

Annual RSV Burden

Preliminary 2024-2025 US RSV Burden Estimates

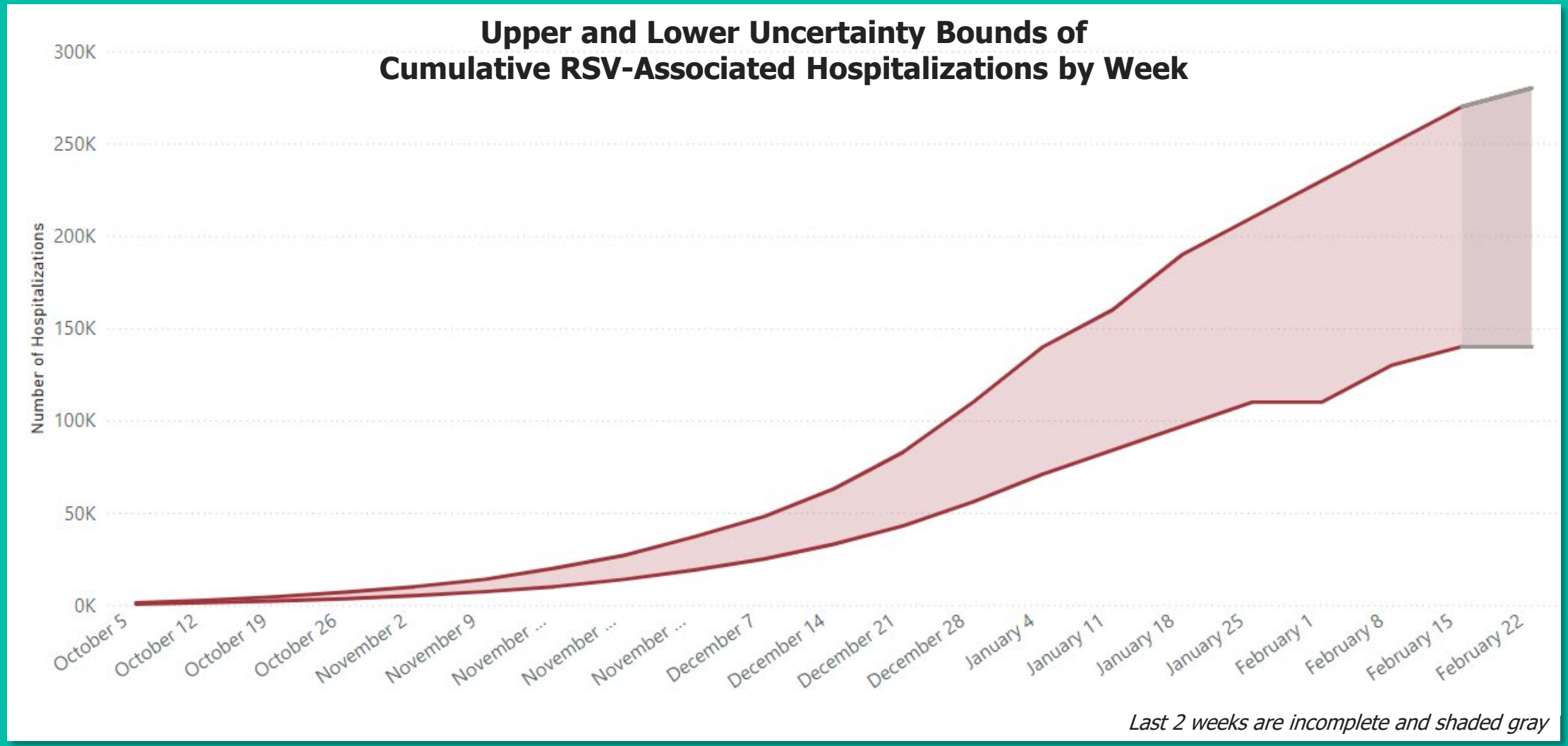
CDC estimates* that, from October 1, 2024 through February 22, 2025, there have been:

RSV Outpatient Visits	RSV Hospitalizations	RSV Deaths
2.8 million–5.4 million	140,000–280,000	7,700–18,000

*Based on data from September 29, 2024 through February 22, 2025.

Centers for Disease Control and Prevention (CDC). Accessed March 4, 2025. https://www.cdc.gov/rsv/php/surveillance/burden-estimates.html

RSV-Associated Hospitalizations



CDC. Accessed March 4, 2025. https://www.cdc.gov/rsv/php/surveillance/burden-estimates.html

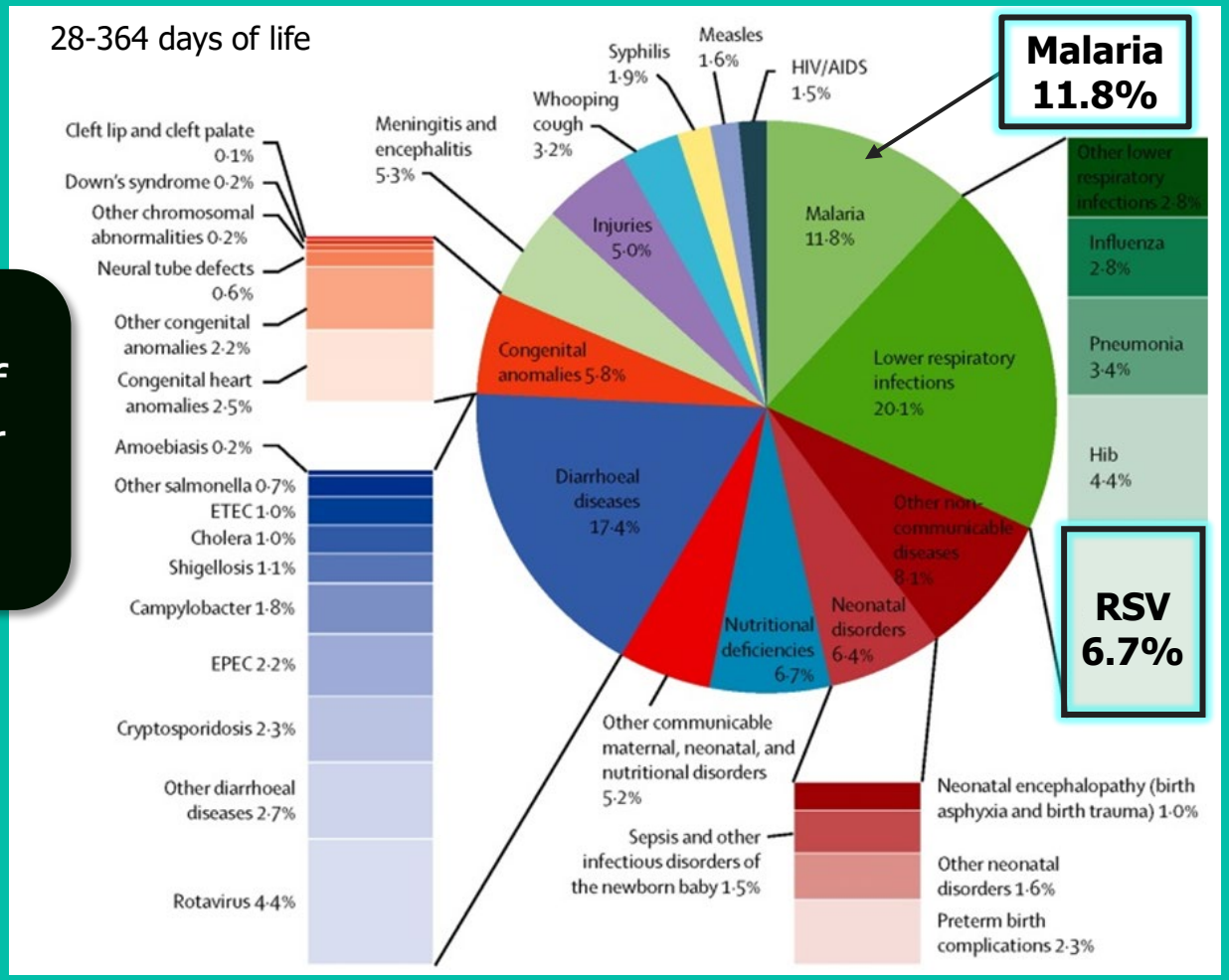
Children Are at Highest Risk for Severe RSV
(~80% RSV Hospitalizations Without Risk Factors)

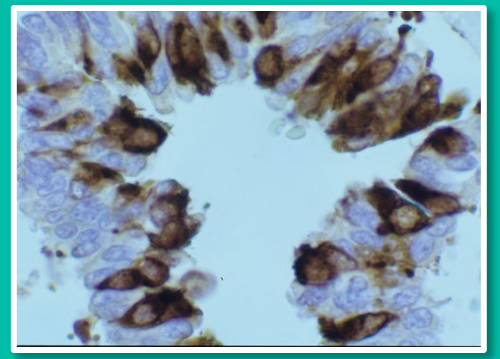
Premature birth[1]	• Altered airway anatomy • Absence of maternal antibodies
Chronic lung disease[1]	• Bronchial hyperresponsiveness • Reduced lung capacity
Congenital heart disease[2]	• Pulmonary vascular hyperresponsiveness • Pulmonary hypertension • Increased pulmonary blood flow
Neuromuscular disease[3,4]	• Decreased respiratory muscle strength and endurance
Immune deficiency[5]	• Decreased host defenses • Impaired capacity to eliminate virus

1. Weisman LE. *Pediatr Infect Dis J.* 2003;22(2 Suppl):S33-37; 2. Macdonald NE, et al. *N Engl J Med*. 1982;307(7):397-400;
3. Panitch H. *Ped Infect Dis J.* 2004;23(11 Suppl):S222-S227; 4. Arnold SR, et al. *Ped Infect Dis*. 1999;18(10):866-869; 5. Navas L, et al. *J Peds.* 1992;121(3):348-354.

Global RSV Disease Burden

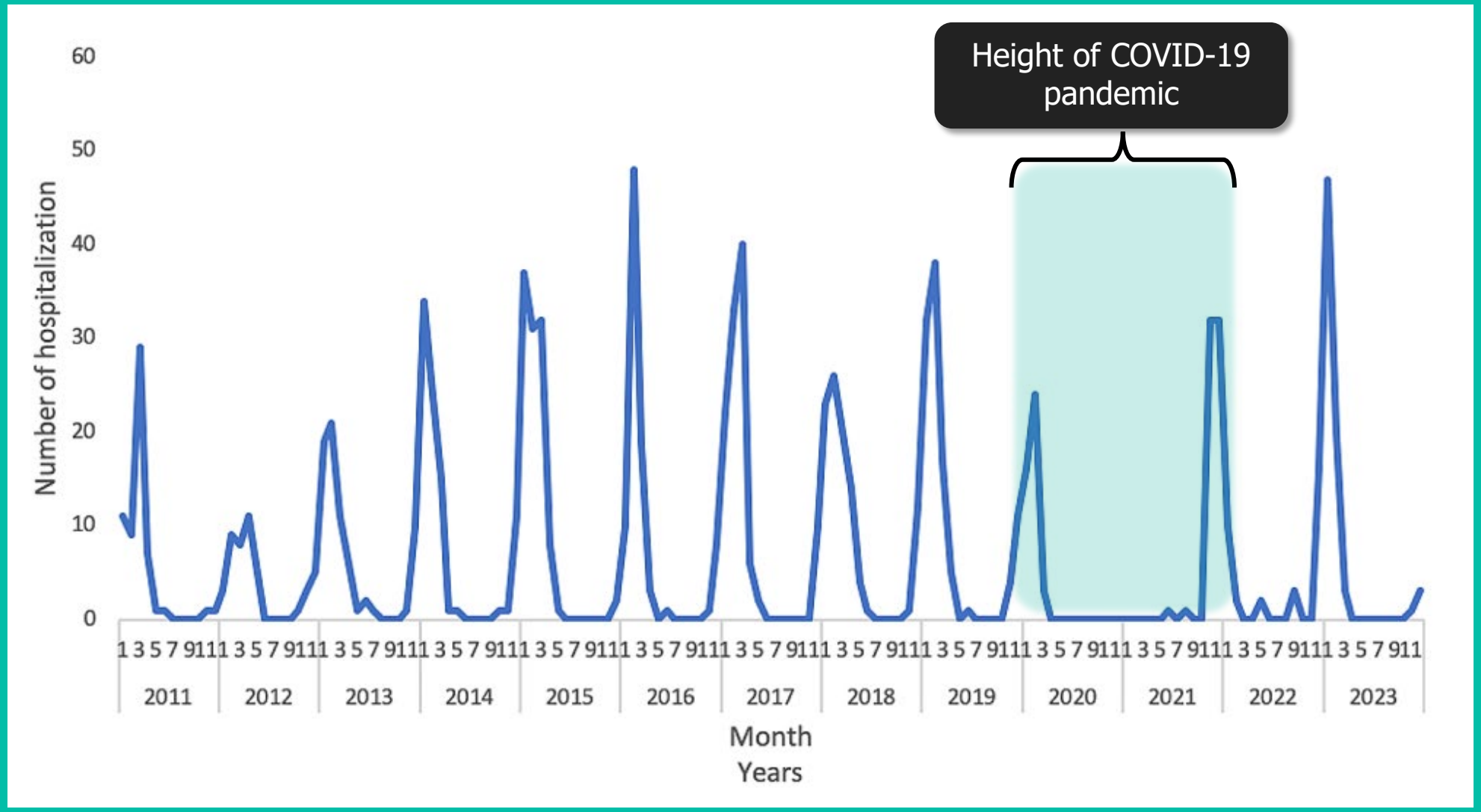
RSV kills more children <1 year of age than any other single pathogen (except malaria)





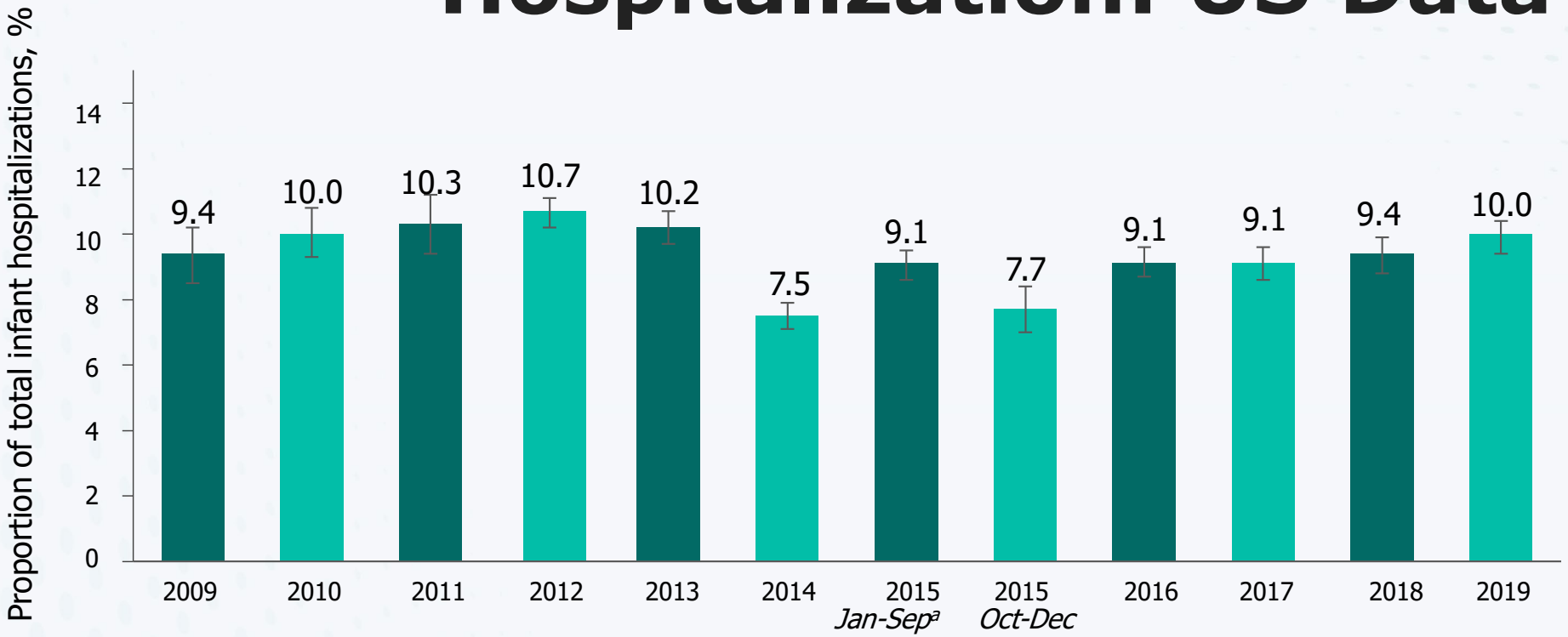
Slide courtesy of Asun Mejias, MD. EPEC = enteropathogenic *Escherichia coli*; ETEC = enterotoxigenic *Escherichia coli*; Hib = *Haemophilus influenzae* type B.
Lozano R, et al. *Lancet*. 2012;380(9859):2095-2128.

RSV Seasonality



Fortunato F, et al. *Ital J Pediatr*. 2024;50(1):45.

RSV Is the Leading Cause of Infant Hospitalization: US Data



A median of 9.4% infant hospitalizations were due to RSV

[a]Transition from ICD-9-CM to ICD-10-CM in October 2015.

Acute bronchiolitis due to **RSV was the leading cause of infant hospitalization** and represented nearly **10% of total infant hospitalizations**

ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification.

Data from Movva N, et al. Medicaid infants have the highest respiratory syncytial virus (RSV) hospitalization burden and rates among United States (US) infants aged <1 year: an analysis of the 2011-2018 National Inpatient Sample (NIS). Presented at: AAP 2021 National Conference & Exhibition; October 8-12, 2021; Virtual.

Suh M, et al. *J Infect Dis*. 2022;226(Suppl 2):S154-S163.

More Than 70% of Hospitalizations Due to RSV Occur in Otherwise Healthy, Full-term Infants

- Study including 600 infants requiring ICU care for RSV across 39 US hospitals during the 2022 RSV outbreak (median age: 2.6 months)
- **Over 80% of infants hospitalized with RSV had no underlying medical conditions and >70% were born full-term**
- Age less than 3 months and prematurity independent risk factors for mechanical ventilation

Table 1. Demographic and Clinical Characteristics of Infants Admitted to the Intensive Care or High Acuity Unit With Respiratory Syncytial Virus Infection

Characteristic	Infants, No. (%) All (N = 600)	Nonintubated (n = 457)	Intubated (n = 143)	*P* value[a]
Age, median (IQR), mo	2.6 (1.4-6.0)	3.1 (1.6-6.4)	1.9 (1.0-3.2)	<.001
Age group				
0-2 mos	323 (53.8)			
3-5 mos	127 (21.2)			
6-11 mos	150 (25.0)			
Prematurity	169 (28.9)			
Gestational age, median (IQR)[d]	34.0 (32.0-35.7)			
Multiple pregnancy	28 (4.7)			
Underlying conditions				
None	487 (81.2)			
At least one	113 (18.8)			
Nonrespiratory, noncardiac	48 (8.0)			
Cardiac, nonrespiratory	20 (3.3)			
Respiratory	45 (7.5)			
Chronic lung disease	22 (3.7)			
Neurologic	13 (2.2)			
Trisomy 21	8 (1.3)			
Reason for admission				
LRTI	594 (99.0)	453 (99.1)	141 (98.6)	.58
Apnea or bradycardia	77 (12.8)	36 (7.9)	41 (28.7)	<.001
Cardiac arrest at home with CPR	3 (0.5)	1 (0.2)	2 (1.4)	.14
CNS infection	2 (0.3)	0	2 (1.4)	.06
Shock requiring vasopressors	5 (0.8)	0	5 (3.5)	.001

Characteristic	Infants, No. (%) All (N = 600)
Prematurity	169 (28.9)
Gestational age, median (IQR)[d]	34.0 (32.0-35.7)
Multiple pregnancy	28 (4.7)
Underlying conditions	
None	487 (81.2)
At least one	113 (18.8)
Nonrespiratory, noncardiac	48 (8.0)
Cardiac, nonrespiratory	20 (3.3)

CNS = central nervous system; CPR = cardiopulmonary resuscitation; ICU = intensive care unit.

Halasa N, et al. *JAMA Netw Open*. 2023;6(8):e2328950.

Most RSV Disease Occurs in Healthy Term Infants

RSV-associated hospitalized children <2 years old by gestational age and age group

Gestational age at birth	0-2 mo	3-5 mo	6-11 mo	12-23 mo	<24 mo
<29 wk, *n* (%)	0 (0)	2 (1)	6 (3)	11 (6)	19 (2)
29-31 wk, *n* (%)	2 (1)	3 (2)	8 (4)	5 (3)	18 (2)
32-34 wk, *n* (%)	14 (4)	16 (9)	11 (6)	9 (5)	50 (6)
35-36 wk, *n* (%)	34 (10)	18 (10)	12 (7)	6 (3)	70 (8)
≥37 wk, *n* (%)	288 (84)	144 (78)	141 (79)	164 (82)	737 (82)
Total,[a] *n*	**342**	184	178	199	903

[a] Includes 4 patients with an unknown history of prematurity and 5 patients with a history of prematurity with unknown gestational age.

mo = months; wk = weeks.

Rha B, et al. *Pediatrics*. 2020;146(1):e20193611.

Infants Hospitalized for RSV: Consequences

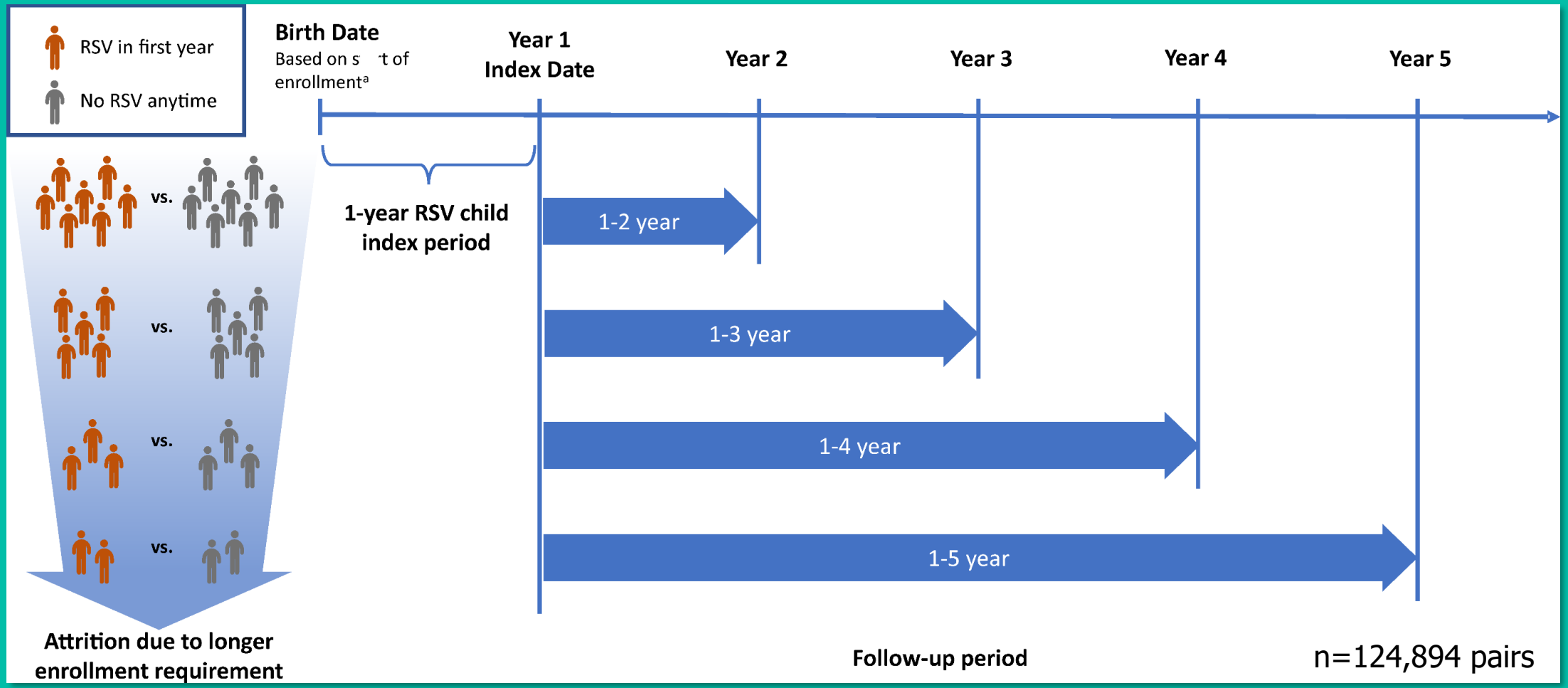
Groups	ICU	Ventilation
High-risk		
Premature (≤36 weeks)[2]	28%-31%	12%-22%
CLD of infancy[3]	32%	17%
CHD[1,3,4]	26%-33%	19%-24%
No risk factors		
Full-term (>36 weeks)[1]	11%	4.6%

- 2- to 3-fold increase in morbidity in high-risk vs no-risk groups[2]
- The mortality rate is 15- to 30-fold higher in high-risk groups[2]

CHD = congenital heart defect; CLD = chronic lung disease.

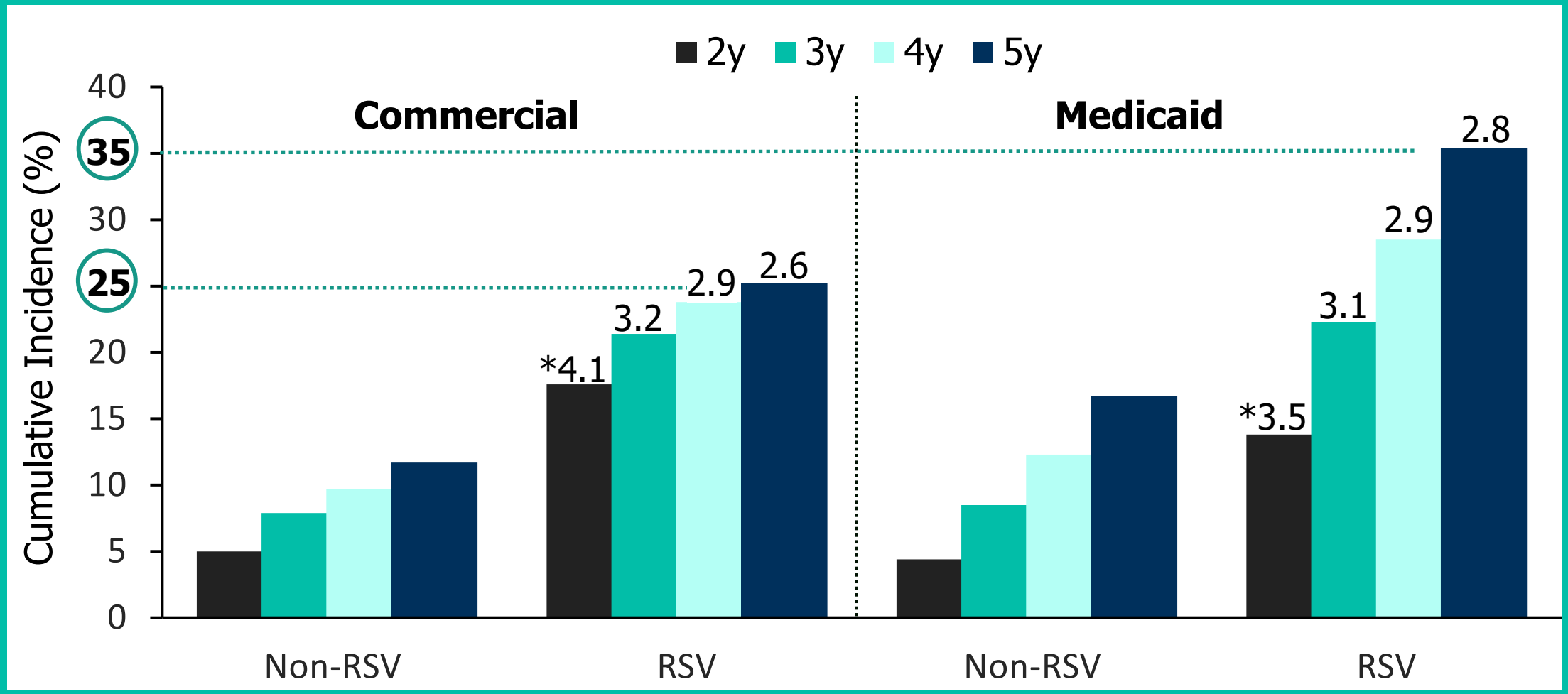
1. Altman CA, et al. *Pediatr Cardiol*. 2000;21(5):433-438; 2. Law BJ, et al. *Paediatr Child Health*. 1998;3(6):402-404; 3. Moler FW, et al. *Crit Care Med*. 1992;20(10):1406-1413; 4. Navas L, et al. *J Pediatr*. 1992;121(3):348-354.

Post-RSV Wheezing/Asthma: United States 2010-2016



Mejias A, et al. *Pediatr Allergy Immunol.* 2020;31(1):47-56.

Cumulative Incidence of Post-RSV Recurrent Wheezing/Asthma



y = years. *Adjusted odds ratio.

Mejias A, et al. *Pediatr Allergy Immunol.* 2020;31(1):47-56.

The Latest Guidance on RSV Immunoprophylaxis

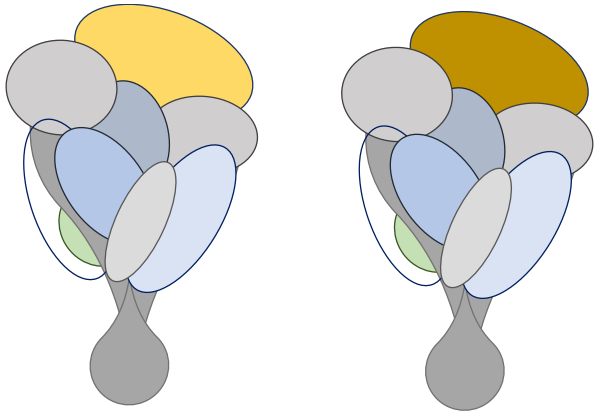
Ravi Jhaveri, MD, FIDSA, FPIDS, FAAP

Division Head
Pediatric Infectious Diseases
Ann & Robert H. Lurie Children's Hospital of Chicago
Professor of Pediatrics
Northwestern University Feinberg School of Medicine
Chicago, IL

RSV Preventive Strategies for Young Infants

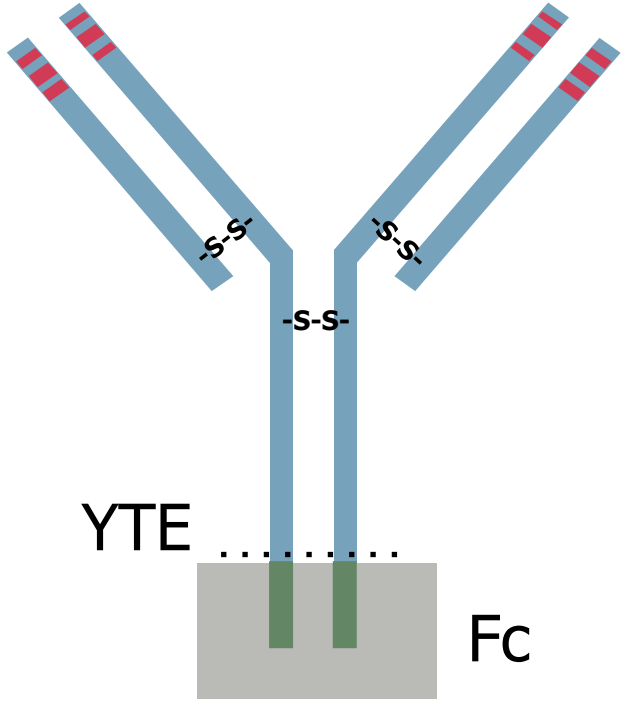
Maternal Immunization

RSV preF



RSV A RSV B

Extended Half-Life mAbs



Fc = fragment crystallizable; mAbs = monoclonal antibodies; RSV = respiratory syncytial virus; YTE = triple amino acid substitution.

Ramilo O, et al. *J Infect Dis*. 2023;228(1):4-7.

Potential Strategies for RSV Prevention in Infants

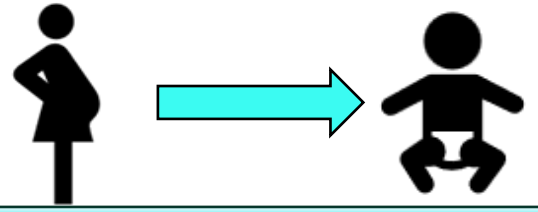
Infant vaccination (active immunization)

- Inactivated vaccines
- Live attenuated vaccines
- F-protein based vaccines
- mRNA vaccines

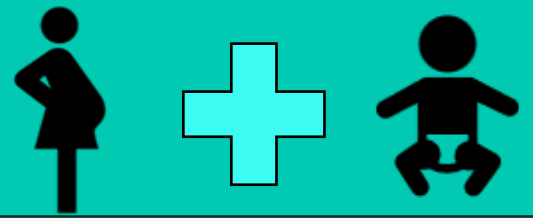
Passive antibodies directly administered to infant

- RSV-Ig
- Humanized monoclonal antibodies – Palivizumab
- Extended half-life monoclonal antibodies – Nirsevimab

Passive antibodies to infant via maternal immunization



Maternal vaccine or monoclonal antibody
AND **Infant *active* immunization**



mRNA = messenger ribonucleic acid; RSV-Ig = respiratory syncytial virus immunoglobulin. Centers for Disease Control and Prevention (CDC). Accessed February 28, 2025. https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/infants-young-children.html

Comparison of Currently Available Interventions (First RSV season)

	Palivizumab	Nirsevimab	Maternal vaccine
Product composition	RSV F inhibitor mAb	RSV F inhibitor mAb	Stabilized RSV F protein (1:1 RSV A and RSV B)
Dose	15 mg/kg body weight	50 mg if <5 kg body weight 100 mg if ≥5 kg body weight	0.5 mL
Administration	IM to baby	IM to baby	IM to mother
Frequency	**Monthly** throughout RSV season	**Single dose** prior to or during RSV season	**Single dose**
Population	Children with BPD, infants with a history of premature birth (≤35 weeks GA), and children with hemodynamically significant cCHD	Neonates and infants born during or entering their first RSV season	Pregnant individuals at 32 through 36 weeks GA
Adverse effects	Fever, rash	Rash, injection site reactions	Pain at injection site, headache, muscle pain, nausea

BPD = bronchopulmonary dysplasia; cCHD = complex congenital heart defects; GA = gestational age; IM = intramuscular. CDC. Accessed September 5, 2024. https://www.cdc.gov/vaccines/vpd/rsv/hcp/child.html#recommendations; https://www.cdc.gov/rsv/immunizations-protect-infants/index.html

Guidance and Recommendations

Summary: ACIP Recommendations for RSV Prevention

To protect infants from severe RSV: CDC recommends an RSV vaccine for pregnant people (RSVPreF [Abrysvo]) or a monoclonal antibody (nirsevimab [Beyfortus]) given to the baby.

To protect older adults from RSV: CDC recommends only a single dose of RSV vaccine for all adults ages 75 and older and for adults ages 60–74 with increased risk of severe RSV disease. No preferential recommendation for any specific vaccine in older adults.

Important note: many GPs are primary caretakers for newborns!

Monoclonal Antibodies:

Nirsevimab (Beyfortus)

Long-acting mAb

- Administered ONCE prior to or during RSV season (Oct-March)
- ALL newborns regardless of GA or underlying conditions at birth
- High risk children aged 8–19 months before or entering their second RSV season

Palivizumab (Synagis)

Existing mAb

- Administered monthly during RSV season (Oct-March)
- Preterm infants <29 weeks gestation at birth and high-risk infants with CLD/CHD

Vaccines:

RSVpreF (Abrysvo)*

- Adults ages 75 and older and for adults ages 60–74 with increased risk of severe RSV disease.
- **Only vaccine indicated for PREGNANT WOMEN;** to be given at 32 to 36 6/7 weeks of gestation

RSVPreF (Arexvy)

- Adults ages 75 and older and for adults ages 60–74 with increased risk of severe RSV disease

NOT for use in pregnant women

mRNA (mResvia)

- Adults ages 75 and older and for adults ages 60–74 with increased risk of severe RSV disease

CHD = chronic heart disease; CLD = chronic lung disease; GP = general practitioner; RSVpreF = RSV prefusion F protein-base.

Fleming-Dutra KE, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(41):1115-1122; Jones JM, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(34):920-925; Melgar M, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(29):793-801.

Recommendations for Pediatric RSV Prevention

All infants should be protected against severe RSV disease with either maternal RSV vaccine or nirsevimab

RSVpreF Maternal Vaccine

- Pregnant persons **32 through 36** weeks' gestation
- Administer **September through January** in most of the continental US

Nirsevimab

- All infants <8 months
- Second season dose for children ages 8-19 months at increased risk of severe RSV disease
- Administer October through March in most of the continental US (the earlier the better)

! *Either* maternal RSV vaccine or nirsevimab is given to protect against severe RSV disease – only 1 is needed in most instances

CDC. Accessed March 3, 2025. https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/01-RSV-Mat-Peds-Chu-508.pdf

Nirsevimab

FDA U.S. FOOD & DRUG ADMINISTRATION

FDA NEWS RELEASE

FDA Approves New Drug to Prevent RSV in Babies and Toddlers

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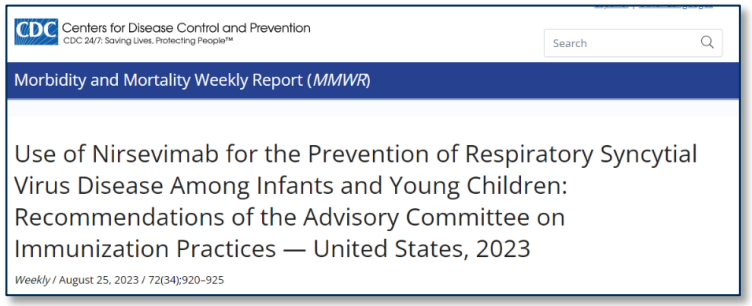
For Immediate Release: July 17, 2023

Español

Today, the U.S. Food and Drug Administration approved Beyfortus (nirsevimab-alip) for the prevention of Respiratory Syncytial Virus (RSV) lower respiratory tract disease in neonates and infants born during or entering their first RSV season, and in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Food & Drug Administration. June 17, 2023.
https://www.fda.gov/news-events/press-announcements/fda-approves-new-drug-prevent-rsv-babies-and-toddlers

ACIP Recommendations: Nirsevimab


CDC Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™
Search
Morbidity and Mortality Weekly Report (*MMWR*)

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

Weekly / August 25, 2023 / 72(34);920-925

A **single dose** of nirsevimab is recommended for:

1. **All infants aged <8 months born during or entering their 1st RSV season**
2. **Children aged 8 to 19 months who are at increased risk of severe RSV disease and entering their 2nd RSV season**
   - Chronic lung disease of prematurity: medical support (chronic corticosteroid therapy, diuretic therapy, or supplemental oxygen) during the 6-month period before the start of the RSV season
   - Severely immunocompromised children
   - Cystic fibrosis with severe lung disease: previous hospitalization for pulmonary exacerbation in 1st year of age, abnormal and persistent chest imaging, or weight-for-length <10%
   - American Indian and Alaska Native children

Jones JM, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:920-925; American Academy of Pediatrics. August 15, 2023. Accessed March 3, 2025. https://publications.aap.org/redbook/resources/25379/ACIP-and-AAP-Recommendations-for-Nirsevimab

Nirsevimab Recommendations

- Infants with prolonged hospitalization: shortly before or promptly after discharge (NOT during NICU stay!)
- Additional dose after surgery/ECMO during RSV season if age-eligible
- Per FDA, children who have received nirsevimab should not receive palivizumab in the same RSV season
- Eligible infants may receive nirsevimab after an RSV infection
- Can be coadministered with routine childhood vaccines

ECMO = extracorporeal membrane oxygenation; FDA = US Food and Drug Administration; NICU = neonatal intensive care unit.

Jones JM, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:920-925; American Academy of Pediatrics. August 15, 2023. Accessed March 3, 2025. https://publications.aap.org/redbook/resources/25379/ACIP-and-AAP-Recommendations-for-Nirsevimab

Considerations for Maternal RSVpreF Vaccine and Nirsevimab

- Nirsevimab is recommended if:
  - Mother did not receive RSV vaccine *or not known*
  - Mother was vaccinated but infant *born <14 days after vaccination*

- Nirsevimab is **not** needed for MOST infants born ≥14 days after maternal vaccination

CDC. Accessed March 3, 2025. https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/infants-young-children.html

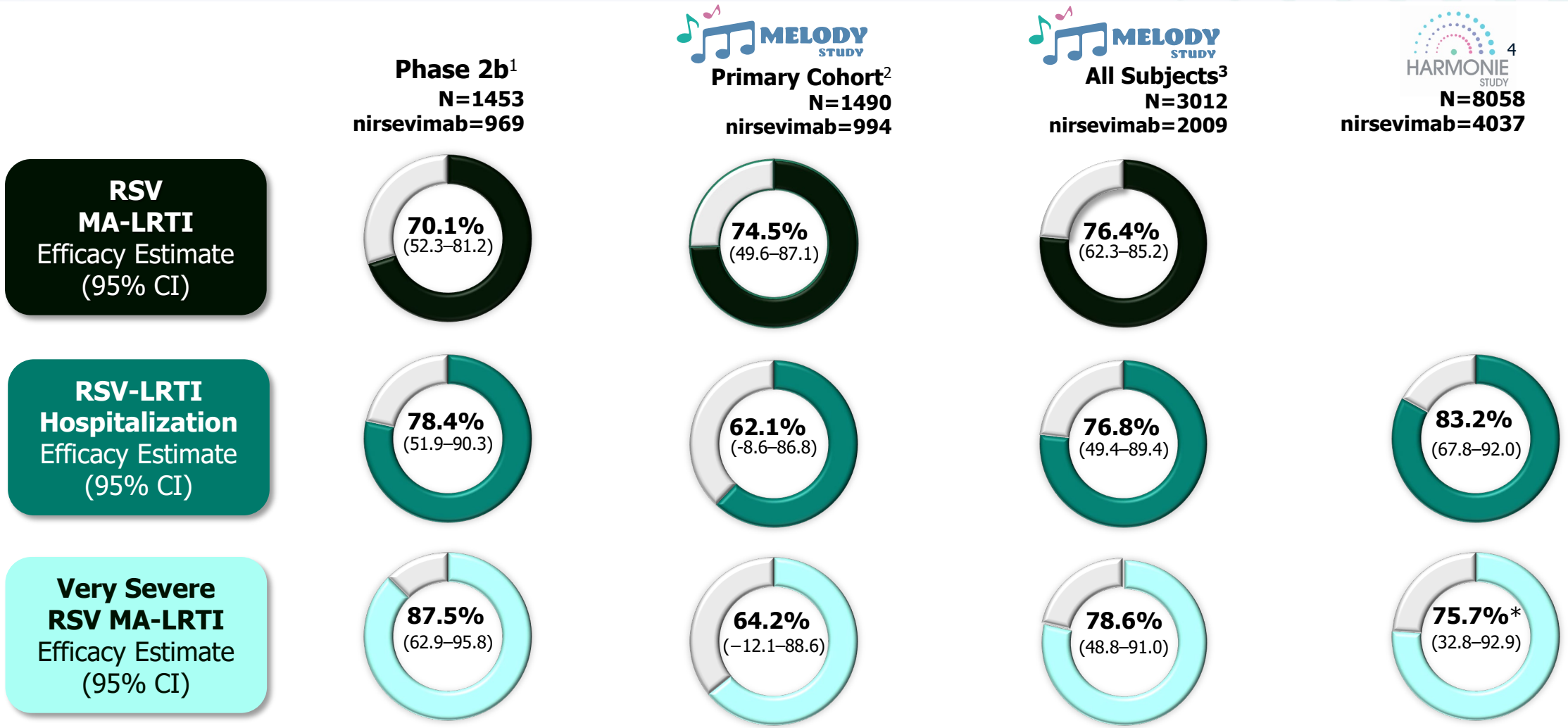
Guidance on Maternal RSVpreF Vaccine + Nirsevimab

- Only select infants should receive nirsevimab after maternal vaccination:
  - Infants of mothers who may not mount an adequate immune response to vaccination (eg, immunocompromised) or have conditions associated with reduced transplacental antibody transfer (HIV-infected)
  - Infants who are post cardiopulmonary bypass, ECMO
  - Infants with substantial risk for severe RSV disease: hemodynamically significant congenital heart disease, intensive care admission requiring oxygen at discharge

HIV = human immunodeficiency virus.

Fleming-Dutra KE, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(41):1115-1122.

Nirsevimab Efficacy Against Medically-Attended RSV LRTI (Licensure Studies)



MA-LRTI = medically-attended lower respiratory tract infection. *Very severe RSV-LRTI hospitalization.

1. Griffin MP, et al. *N Engl J Med*. 2020;383(5):415-425; 2. Hammitt LL, et al. *N Engl J Med.* 2022;386:837-846; 3. Muller WJ, et al. *N Engl J Med.* 2023;388(16):1533-1534; 4. Drysdale SB, et al. *N Engl J Med*. 2023;389:2425-2435.

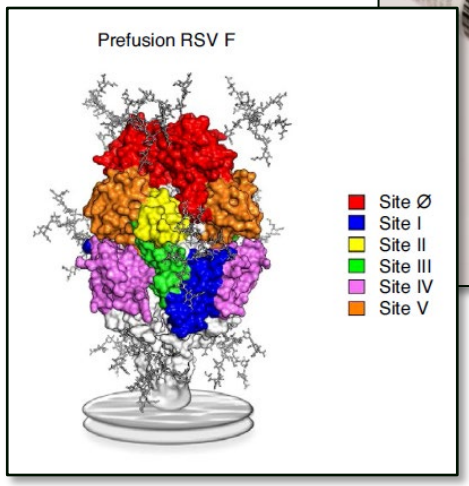
Nirsevimab Efficacy Estimates From Clinical Trials (at 150 Days)

Outcome	Efficacy Estimate
Benefits	
Medically attended RSV LRTI	79.0% (95% CI: 68.5%–86.1%)
RSV LRTI with hospitalization	80.6% (95% CI: 62.3%–90.1%)
RSV LRTI with ICU admission	90.0% (95% CI: 16.4%–98.8%)
Death due to RSV respiratory illness	None recorded
All-cause medically attended-LRTI	34.8% (95% CI: 23.0–44.7%)
All-cause LRTI-associated hospitalization	44.9% (95% CI:24.9%–59.6%)

ICU = intensive care unit.

Muller WJ, et al. *N Engl J Med.* 2023;388(16):1533-1534; Griffin MP, et al. *N Engl J Med.* 2020;383(5):415-425.

Maternal RSV Vaccine



FDA U.S. FOOD & DRUG ADMINISTRATION

FDA NEWS RELEASE

FDA Approves First Vaccine for Pregnant Individuals to Prevent RSV in Infants

Share | Post | Linkedin | Email | Print

For Immediate Release: August 21, 2023

Español

Today, the U.S. Food and Drug Administration approved Abrysvo (Respiratory Syncytial Virus Vaccine), the first vaccine approved for use in pregnant individuals to prevent lower respiratory tract disease (LRTD) and severe LRTD caused by respiratory syncytial virus (RSV) in infants from birth through 6 months of age. Abrysvo is approved for use at 32 through 36 weeks gestational age of pregnancy. Abrysvo is administered as a single dose injection into the muscle. The FDA approved Abrysvo in May for the prevention of LRTD

Food & Drug Administration. August 21, 2023. https://www.fda.gov/news-events/press-announcements/fda-approves-first-vaccine-pregnant-individuals-prevent-rsv-infants
Fleming-Dutra KE, et al. *MMWR Morb Mortal Wkly Rep.* 2023;72(41):1115-1122; Taleb SA, et al. *Eur J Clin Microbiol Infect Dis*. 2018;27(10):1817-1827.

MATISSE: Bivalent Prefusion F Vaccine for Pregnant Women to Prevent Infant RSV Illness

Administered to pregnant women at **24 through 36** weeks EGA

- 3495 received RSVpreF vaccine, 3480 received placebo

RSVpreF efficacy at 90 days:
Severe MA-LRTI: 82%

RSVpreF efficacy at 150 days:
Severe MA-LRTI: 71%

Time since birth	Incidence of MA severe RSV LRTI		Efficacy against MA severe RSV LRTI
	Maternal vaccine group	Placebo group	
90 days	0.2%	0.9%	**82%**
150 days	0.5%	1.6%	**71%**
180 days	0.5%	1.8%	**69%**

EGA = estimation of gestational age.

Kampmann B, et al. *N Engl J Med.* 2023;388(16):1451-1464.

Maternal RSVpreF Vaccine: ACIP Effect Estimates for Administration During the FDA-Approved Dosing Window

Outcome	Vaccine Efficacy (95% CI): 32-36 weeks pregnancy
Medically attended RSV-associated LRTI in infants (0-180 days)	57% (30-75)
RSV hospitalization (LRTI) in infants (0-180 days)	48% (30-80)
RSV ICU admission in infants (0-180 days)	1 event in vaccine 2 events in placebo
Mechanical ventilation	0 event in vaccine 2 events in placebo
All-cause medically attended LRTI in infants (0-180 days)	7% (16-26)
All-cause hospitalization for LRTI in infants (0-180 days)	35% (19-65)

CDC. Accessed March 3, 2025. https://www.cdc.gov/acip/evidence-to-recommendations/pfizer-rsvpref-pregnant-people-etr.html?CDC_AAref_Val=https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-rsvpref-pregnant-people-etr.html

RSVpreF Vaccines: Safety Concerns?

- **Phase 2b/3 trial:** vaccine given at 24-36 weeks gestation
  - Numerical imbalance in preterm births in vaccine group vs placebo (5.4% vs 4.3%)
- **Trial:** 6.8% of births were preterm in the vaccine arm, compared with 4.9% in the saline placebo arm (RR 1.37; 95% CI, 1.08-1.74); 66% and 69% efficacy against medically attended RSV and severe RSV disease, respectively
- **FDA:** licensed (RSVPreF) for 32-36 weeks with postmarketing surveillance to assess preterm birth and hypertensive disorders of pregnancy

Jones JM, et al. *MMWR Morb Mortal Wkly Rep*. 2023;72(34):920-925.
Dieussaert I, et al. *N Engl J Med.* 2024;390:1009-1021.

No Apparent Cause for Concern …

- Initial studies suggested there may be an increased rate of preterm birth in recipients of maternal RSV vaccine
- This data from Vaccine Safety Datalink did not show a difference

Preterm birth[a] risk among pregnant persons receiving RSV vaccine and unvaccinated matches, 30–36 weeks GA

	Matched pairs, N	RSV vaccinated		Unvaccinated match		Risk Ratio (95% CI)
		N events*	Preterm birth %	N events*	Preterm birth %	
Overall[b]	14,099	571	4.0	637	4.5	0.90 (0.80–1.00)
32–36 weeks	13,965	563	4.0	628	4.5	0.90 (0.80–1.00)

GA = gestational age
[a]Preterm birth = birth <37 weeks gestational age
[b]N RSV vaccines administered <32 weeks = 134 (0.95%)
*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

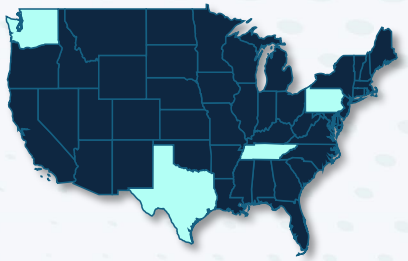
CDC. Accessed March 3, 2025.
https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/03-RSV-Mat-Peds-DeSilva-508.pdf

Nirsevimab and Maternal PreF Vaccine Real-World Data

2023-2024 CDC NVSN Nirsevimab Effectiveness

Trial Design

- Test-negative, case-control design*
- **Outcome**: Effectiveness against RSV-associated hospitalization from October 2023-February 2024
- **Inclusion**: Infants <8 months as of October 1, 2023, or born after, hospitalized with ARI in the US
- Conducted in Houston, TX; Nashville, TN; Pittsburgh, PA; Seattle WA



N=699	Case N=407	Control N=292
	Positive RSV Test Result	Negative RSV Test Result
Infants Received Nirsevimab	6 (1%)	53 (18%)

Endpoint	Effectiveness, % (95% CI)	*P*-value
RSV Associated Hospitalization	90 (75-96)	Not reported

Time since receipt of nirsevimab to ARI symptom onset ranged from 7 to 127 days with a median of 45 days (IQR = 19-76 days)

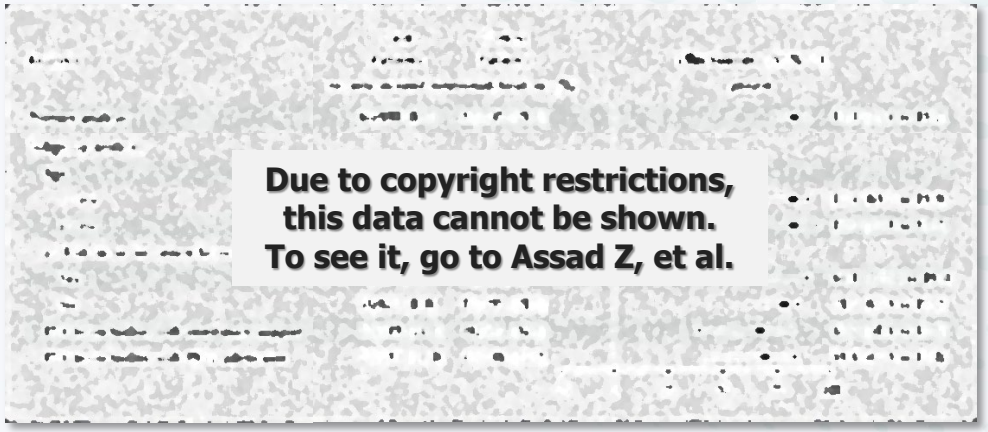
*Case-patients were infants who received a positive RSV test result. Control patients were infants who received a negative RSV test result.
Analysis was adjusted for age at enrollment, month of illness, enrollment site, and high-risk medical conditions. ARI = acute respiratory illness; NVSN = The New Vaccine Surveillance Network, IQR = interquartile range. Moline HL, et al. *MMWR Morb Mortal Wkly Rep 2024* ;73:209-214.

Global "Real-World" Effectiveness of Nirsevimab Against RSV Hospitalization

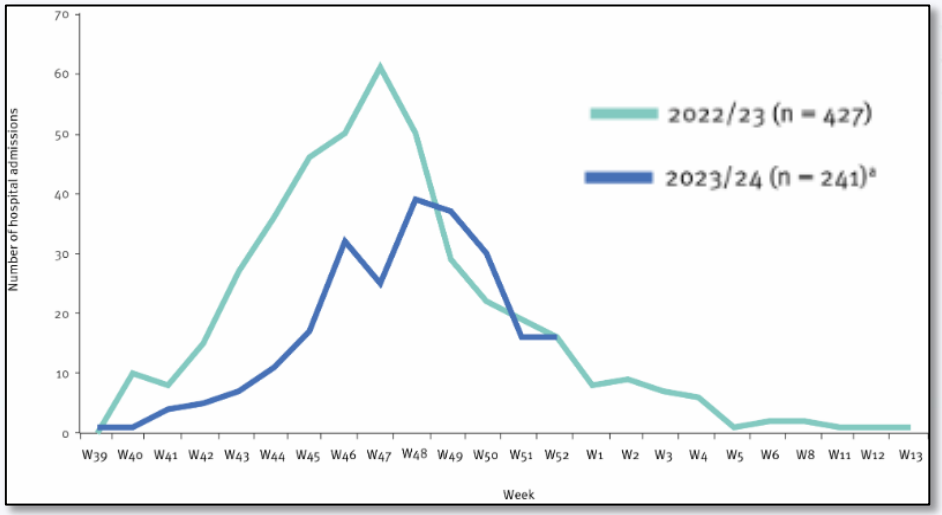
Location/Study Size	Outcomes
Spain (9 hospitals, 15,676 infants) [1]	70%-84% effectiveness
Spain (Navarre, population-based, 1177 infants, 92% coverage)[2]	88% effectiveness
Luxembourg (668 infants, 84% coverage in maternity wards)[3]	69% decrease in RSV hospitalization in infants <6 months old vs 2022-2023
France (ENVIE case control study of 1035 infants)[4]	83% effectiveness
Spain (Galicia, 9408 infants)[5]	82% effectiveness

International real-word data corroborates clinical trial results, with remarkably consistent findings

ENVIE: Nirsevimab and Hospitalization for RSV Bronchiolitis in France



RSV Hospital Admission of Children <5 Years of Age in Luxembourg's National Pediatric Hospitals



PICU = pediatric intensive care unit.

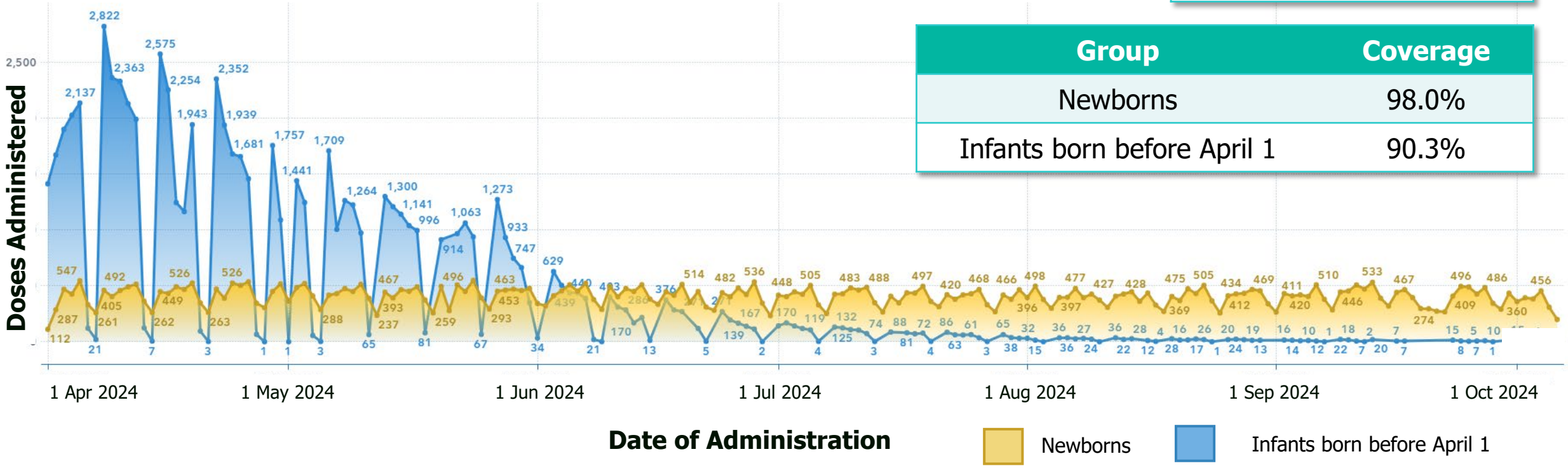
1. López-Lacort M, et al. *Euro Surveill.* 2024;29(8); 2. Ezpeleta G, et al. *Vaccines (Basel).* 2024;12(4):383; 3. Ernst C, et al. *Euro Surveill.* 2024;29(4):2400033; 4. Assad Z, et al. *N Engl J Med.* 2024;391:144-154; 5. Ares-Gomez S, et al. *Lancet Infect Dis.* 2024;24(8):817-828.

Uptake of Nirsevimab in Chile

Target Population and Doses Administered in 2024

Expected Population[1]
172,820

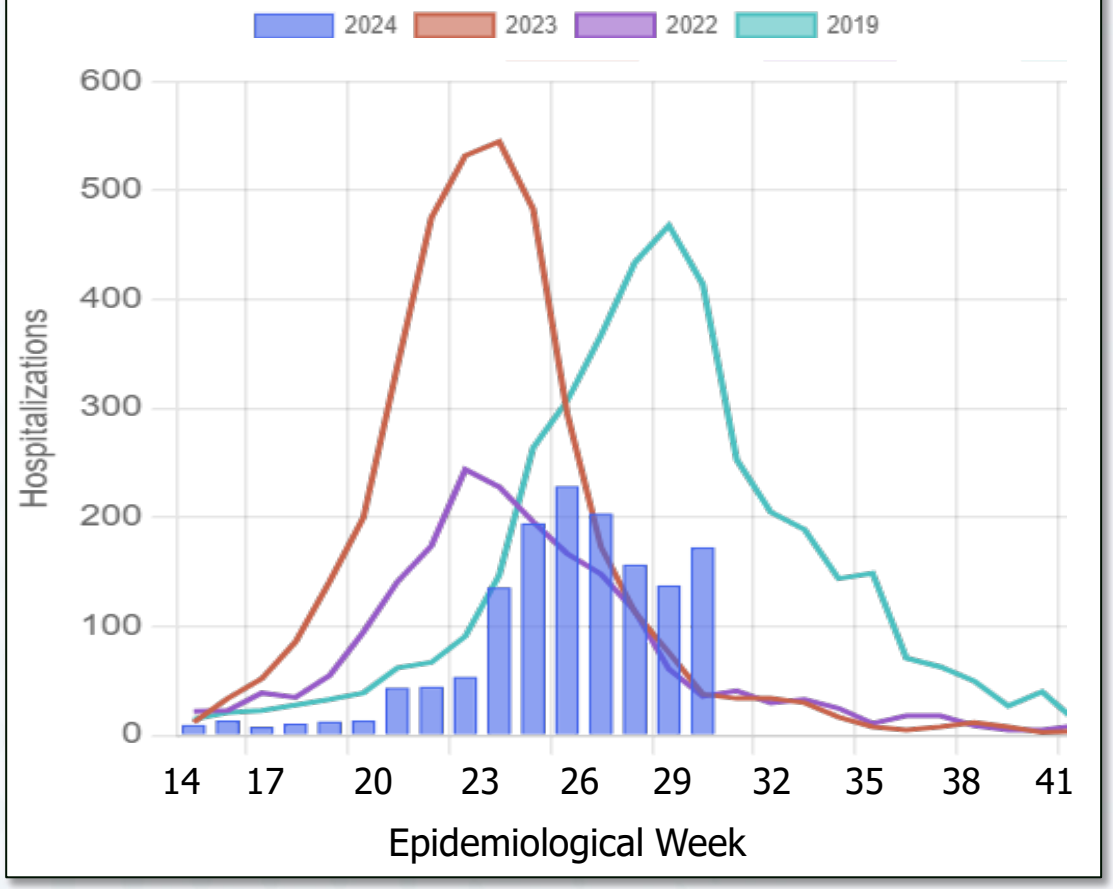
Group	Coverage
Newborns	98.0%
Infants born before April 1	90.3%



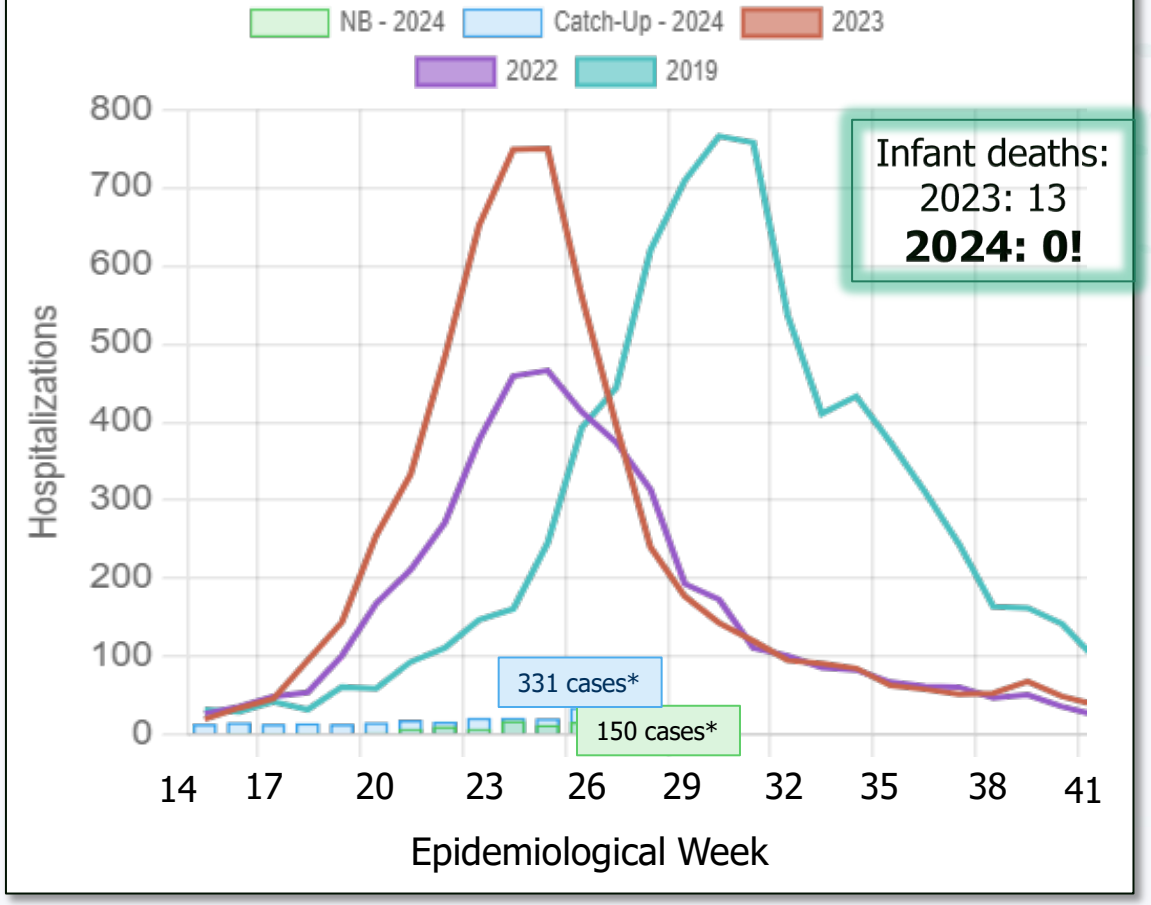
Institute of Engineering Systems Complexity (ISCI). Accessed March 3, 2025. https://nirse.isci.cl/

Public Health Impact: Weekly Hospitalizations

Weekly RSV Hospitalizations (non-eligible population)



Weekly Infant RSV Hospitalization (nirsevimab-eligible population)



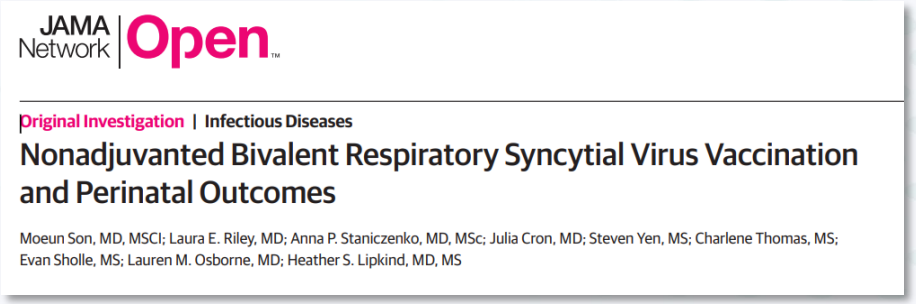
*Total cases reported in the 2024 season through September 30 for each group.

ISCI. Published August 27, 2024. Accessed March 3, 2025. https://nirse.isci.cl/#reporte

https://academic.oup.com/ofid/article/12/Supplement_1/ofae631.006/7986730

Disclaimer: This is preliminary data that has not yet been published in a peer-reviewed journal and may change prior to final publication.

RSVpreF Vaccine: Postmarketing Surveillance


JAMA Network | Open

Original Investigation | Infectious Diseases

Nonadjuvanted Bivalent Respiratory Syncytial Virus Vaccination and Perinatal Outcomes

Moeun Son, MD, MSCI; Laura E. Riley, MD; Anna P. Staniczenko, MD, MSc; Julia Cron, MD; Steven Yen, MS; Charlene Thomas, MS; Evan Sholle, MS; Lauren M. Osborne, MD; Heather S. Lipkind, MD, MS

- Retrospective, observational cohort: 2023-2024 RSV season
- 2 New York City hospitals: women delivered at ≥32 weeks from 9/2023-1/2024
- 2973 women: 35% vaccinated at 32-36 weeks
  - **5.9% preterm birth (vaccine) vs 6.7% (no vaccine)**

Prenatal vaccination not associated with increased risk of preterm birth
(aOR, 0.87; 95% CI, 0.62-1.20),
nor with neonatal outcomes,
but increased risk of hypertensive disorders of pregnancy
(HR, 1.43; 95% CI, 1.16-1.77)

aOR = adjusted odds ratio.
Son M, et al. *JAMA Netw Open.* 2024;7(7):e2419268.

Barriers to Implementation

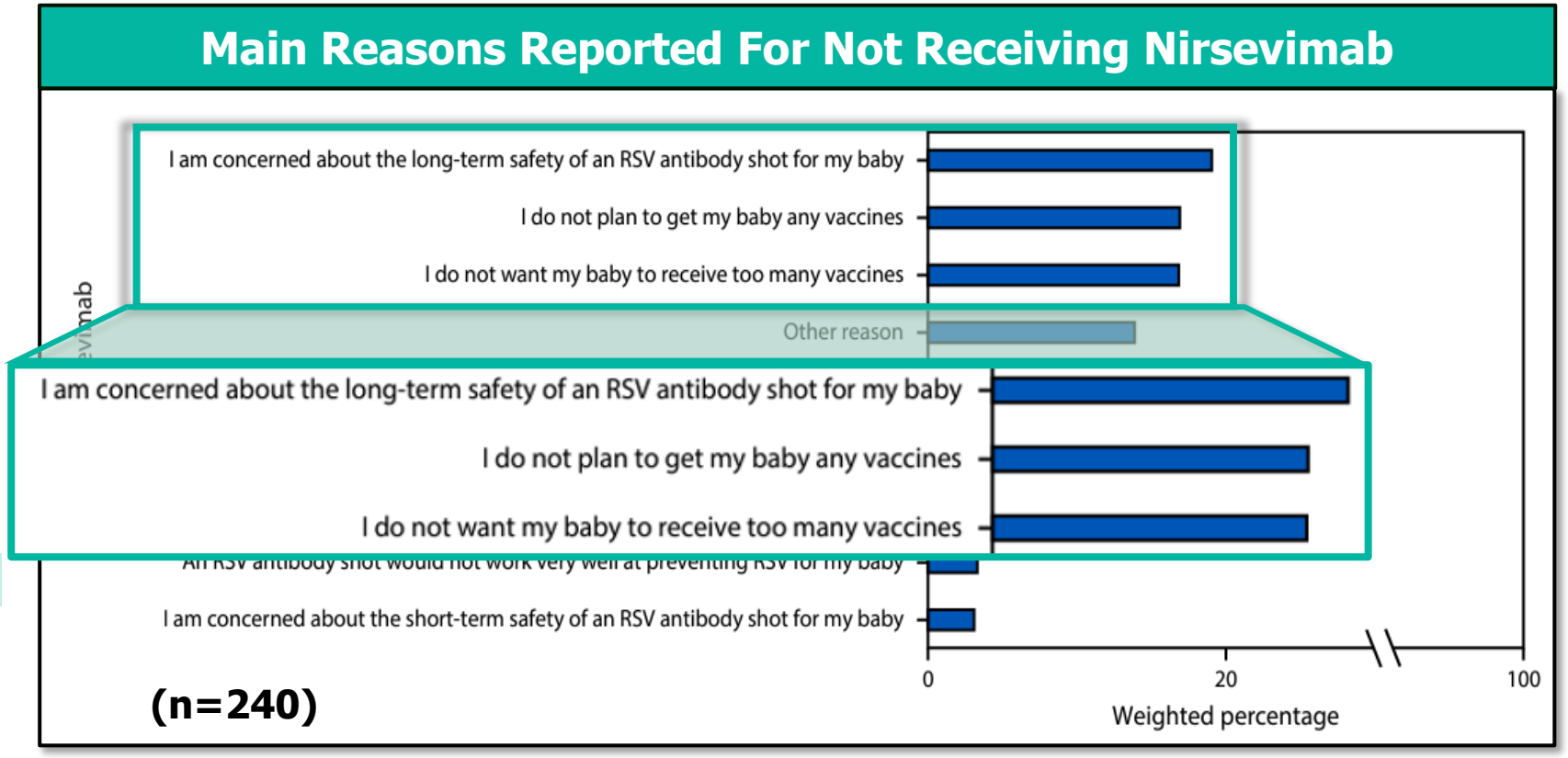
RSV Prevention Implementation and Uptake During Year 1

Morbidity and Mortality Weekly Report (*MMWR*)

Maternal Respiratory Syncytial Virus Vaccination and Receipt of Respiratory Syncytial Virus Antibody (Nirsevimab) by Infants Aged <8 Months — United States, April 2024

Hilda Razzaghi, PhD[1]; Emma Garacci, MS[2]; Katherine E. Kahn, MPH[3]; Megan C. Lindley, MPH[1]; Jefferson M. Jones, MD[4]; Shannon Stokley, DrPH[1]; Kayla Calhoun, MS[1]; Carla L. Black, PhD[1]

- Overall, 56% of infants were protected against severe RSV disease by either product or both
- Provider recommendation for immunization was associated with higher coverage
- **Among women with a live birth, 45% reported that their infant received nirsevimab**



Razzaghi H, et al. *MMWR Morb Mortal Wkly Rep.* 2024;73:837-843.

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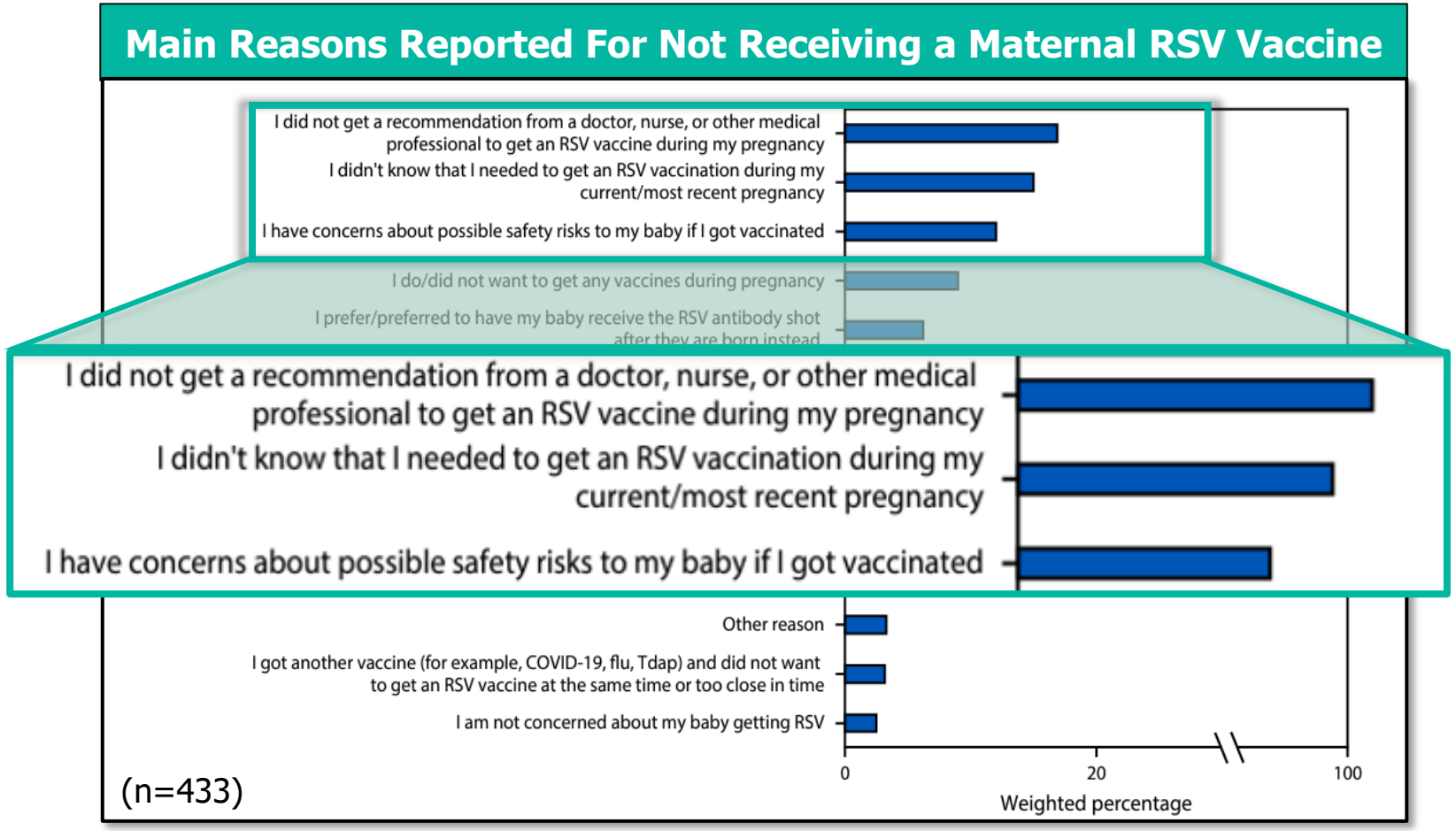
- Overall, 56% of infants were protected against severe RSV disease by either product or both
- Provider recommendation for immunization was associated with higher coverage
- **33% of eligible pregnant women reported receiving an RSV vaccine**



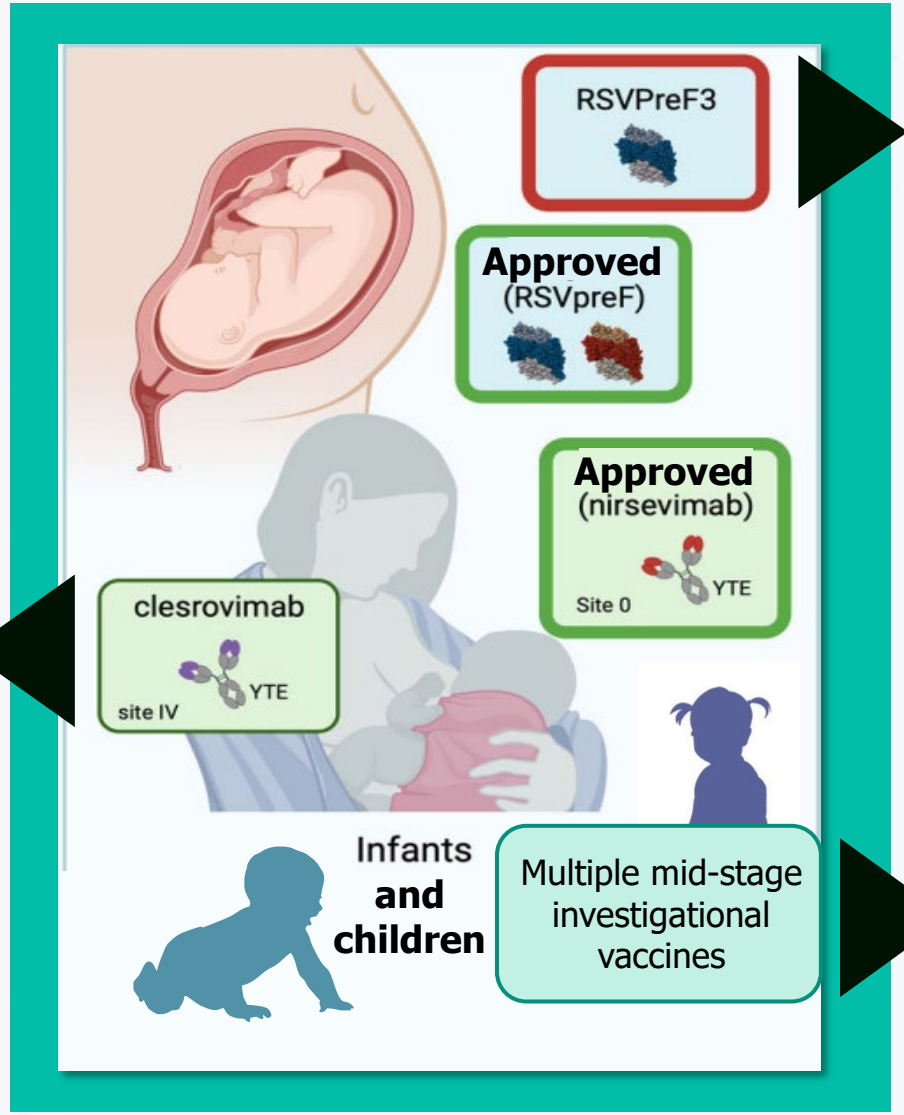
Razzaghi H, et al. *MMWR Morb Mortal Wkly Rep.* 2024;73:837-843.

Emerging Agents

Emerging Options for RSV Prevention in Infants

Clesrovimab:

- Phase 3 RCT enrolling 3300 healthy pre-term and full-term infants (placebo controlled)
- Phase 3 study enrolling 1000 infants at high risk for severe RSV disease (palivizumab controlled)



Development of the A subtype RSVPreF3 was stopped due to a safety signal

Agents in phase 2 development

- SP0125 intranasal (entering Phase 3)
- MV-012-968 intranasal
- mRNA-1345 IM

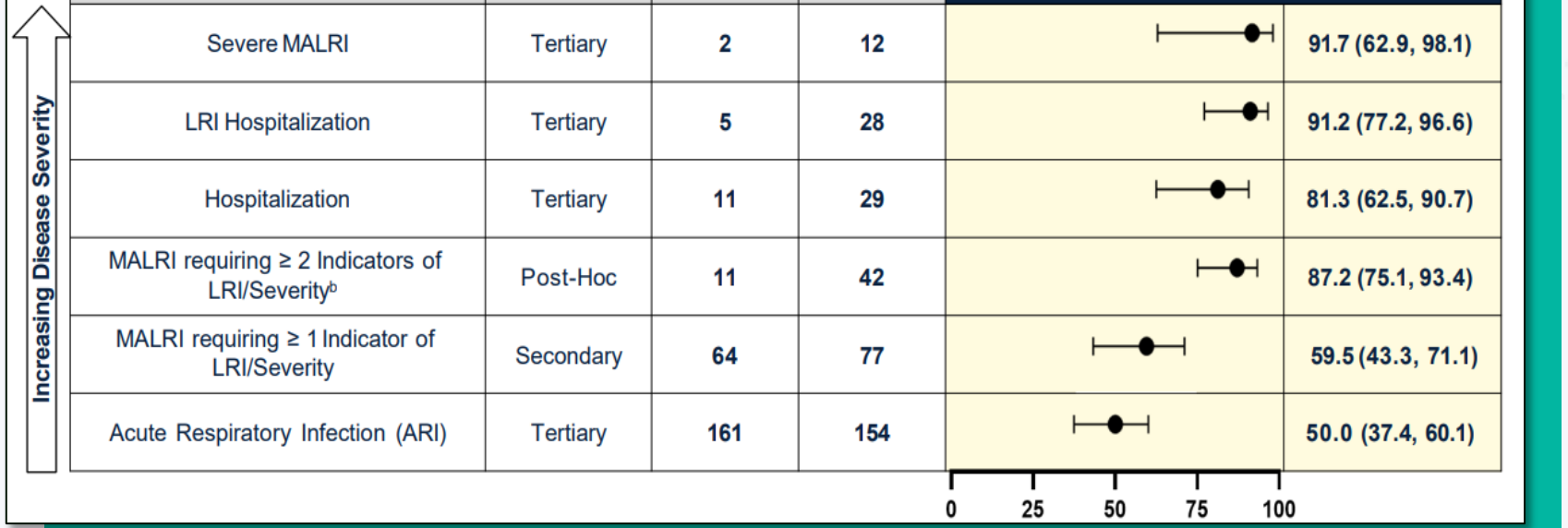
RCT = randomized controlled trial. Adapted from Ruckwardt TJ. *NPJ Vaccines*. 2023;8(1):138; Clinicaltrials.gov. Accessed March 3, 2025. https://www.clinicaltrials.gov/study/NCT04767373; Clinicaltrials.gov. Accessed March 3, 2025; https://www.clinicaltrials.gov/study/NCT04938830; Mass B, et al. Presented at: International Society for Influenza and Other Respiratory Virus Diseases. 12th International RSV Symposium; September 29 to October 2, 2022; Belfast, Ireland. Abstract ARNI0268

Phase 2b/3 Study on the Efficacy and Safety of Clesrovimab in Healthy Preterm and Full-Term Infants

Findings:

- Clesrovimab reduced RSV-associated hospitalizations and RSV-associated LRTI hospitalizations by more than 84% and 90%, respectively, through 5 months
- Clesrovimab reduced the incidence of RSV-associated MALRI requiring ≥1 indicator of LRI/severity and ≥2 indicators of LRI/severity, RSV hospitalization, and severe MALRI through day 150 post-dose compared to placebo
- Efficacy increased with increasing RSV-associated disease severity and was similar from days 1-180 compared to days 1-150 across endpoints

RSV-Associated Endpoint[a] (Through 6 months)	Endpoint Designation	Efficacy through 6 months		
		Clesrovimab (n = 2,398) # of Cases	Placebo (n = 1,201) # of Cases	Observed Efficacy %, (95% CI)
Severe MALRI	Tertiary	2	12	91.7 (62.9, 98.1)
LRI Hospitalization	Tertiary	5	28	91.2 (77.2, 96.6)
Hospitalization	Tertiary	11	29	81.3 (62.5, 90.7)
MALRI requiring ≥ 2 Indicators of LRI/Severity[b]	Post-Hoc	11	42	87.2 (75.1, 93.4)
MALRI requiring ≥ 1 Indicator of LRI/Severity	Secondary	64	77	59.5 (43.3, 71.1)
Acute Respiratory Infection (ARI)	Tertiary	161	154	50.0 (37.4, 60.1)



MALRI = medically-attended lower respiratory infection.

Zar HG, et al. Presented at: IDWEEK 2024; October 16-19, 2024; Los Angeles, CA. Abstract 166.

Phase 2b/3 Study on the Efficacy and Safety of Clesrovimab in Healthy Preterm and Full-Term Infants

Findings:

- The proportions of patients with AEs, including injection-site and systemic AEs, drug-related AEs, and serious AEs were comparable between the clesrovimab and placebo groups
- There were no treatment-related deaths or deaths attributed to RSV disease

Participants with AEs	Clesrovimab N[a] = 2,409 n (%)	Placebo N[a] = 1,202 n (%)
Overall Solicited and Unsolicited AEs *(Days 1-365 postdose)*		
≥ 1AE	1,816 (75.4)	918 (76.4)
Drug-related AE	587 (24.4)	296 (24.6)
Any SAE	278 (11.5)	149 (12.4)
Drug-related SAE[b]	1(0.0)	1(0.1)
Death[c]	7 (0.3)	3 (0.2)

Key Takeaways: A single dose of clesrovimab given before or during the first RSV season was efficacious in reducing RSV-associated MALRI and RSV-associated hospitalization in healthy preterm and full-term infants and was generally well tolerated with a safety profile comparable to placebo.

AE = adverse event.

Zar HG, et al. Presented at: IDWEEK 2024; October 16-19, 2024; Los Angeles, CA. Abstract 166.

Phase 3 Trial Evaluating Safety, Efficacy, and PK of Clesrovimab in Infants and Children at Increased Risk for Severe RSV

Incidence of RSV-Associated Endpoints (Season 1: Days 1-150)

RSV-associated endpoint	Clesrovimab n = 443			Palivizumab n = 437		
	Number of events	Total follow-up time (months)[a]	Incidence rate, % over 5 months[b] (95% CI)[c]	Number of events	Total follow-up time (months)[a]	Incidence rate, % over 5 months[b] (95% CI)[c]
MALRI requiring ≥1 indicator of LRI or severity[d]	14	1946.9	3.6% (2.0, 6.0)	12	1969.5	3.0% (1.6, 5.3)
Hospitalization[e]	5	1968.9	1.3% (0.4, 3.0)	6	1987.3	1.5% (0.6, 3.3)

Safety Outcomes (Season 1: Days 1-150)

	Clesrovimab N = 445[a]		Palivizumab N = 450		% Difference vs. palivizumab
	n	(%)	n	(%)	Estimate (95% CI)[b]
Overall AEs *(following any dose)*					
≥1 AE	323	(72.6)	344	(76.4)	-3.9 (-9.6, 1.9)
Drug-related AE[c]	120	(27.0)	127	(28.2)	-1.3 (-7.1, 4.6)
SAE	99	(22.2)	110	(24.4)	-2.2 (-7.7, 3.4)
Drug-related SAE[c]	0	(0.0)	2	(0.4)	-0.4 (-1.6, 0.4)
Death	8	(1.8)	4	(0.9)	0.9 (-0.7, 2.7)
AESI *(days 1-42 postdose 1)*					
Rash	3	(0.7)	1	(0.2)	0.5 (-0.6, 1.8)
Anaphylaxis/Hypersensitivity	0	(0.0)	0	(0.0)	0.0 (-0.8, 0.9)

None of the deaths were considered related to study intervention and were largely attributable to underlying condition/comorbidities or another clearly identifiable cause. Analysis of these events did not identify any patterns or trends.

Key Takeaways:

- Clesrovimab was well tolerated in infants and young children at increased risk for severe RSV disease
- In season 1, the safety profile of clesrovimab 105 mg was generally comparable to that of palivizumab
- The incidences of RSV-associated MALRI and RSV-associated hospitalization were comparable between participants who received a single dose of clesrovimab and those who received monthly palivizumab in their first RSV season

AESI = adverse event of special interest; PK = pharmacokinetics; SAE = serious adverse event. Zar HG, et al. Presented at: IDWEEK 2024; October 16-19, 2024; Los Angeles, CA. Abstract 167.

Summary – Part 1

- RSV PreF maternal vaccine, nirsevimab, and palivizumab all licensed for use this season
- All these modalities protect infants in the first 6 months of life
- Nirsevimab real-world data shows effective protection
- Maternal PreF vaccine is not associated with higher preterm births

ClinicalTrials.gov. Updated July 17, 2023. Accessed March 3, 2025. https://www.clinicaltrials.gov/study/NCT04767373

Summary – Part 2

- Clesrovimab should be available in near future as additional option for infants
- Grandparents should be encouraged to get their RSV vaccines
- A strong recommendation for mAb/vaccine is needed from you!
- Older infants and young children are the target of current live-attenuated, RNA, and other vaccines

Panel Discussion: Strategies for Improving Immunization Rates

Patsy Stinchfield, RN, MS, CPNP

Independent Consultant
Immediate Past President
National Foundation for Infectious Diseases (NFID)
Victoria, MN

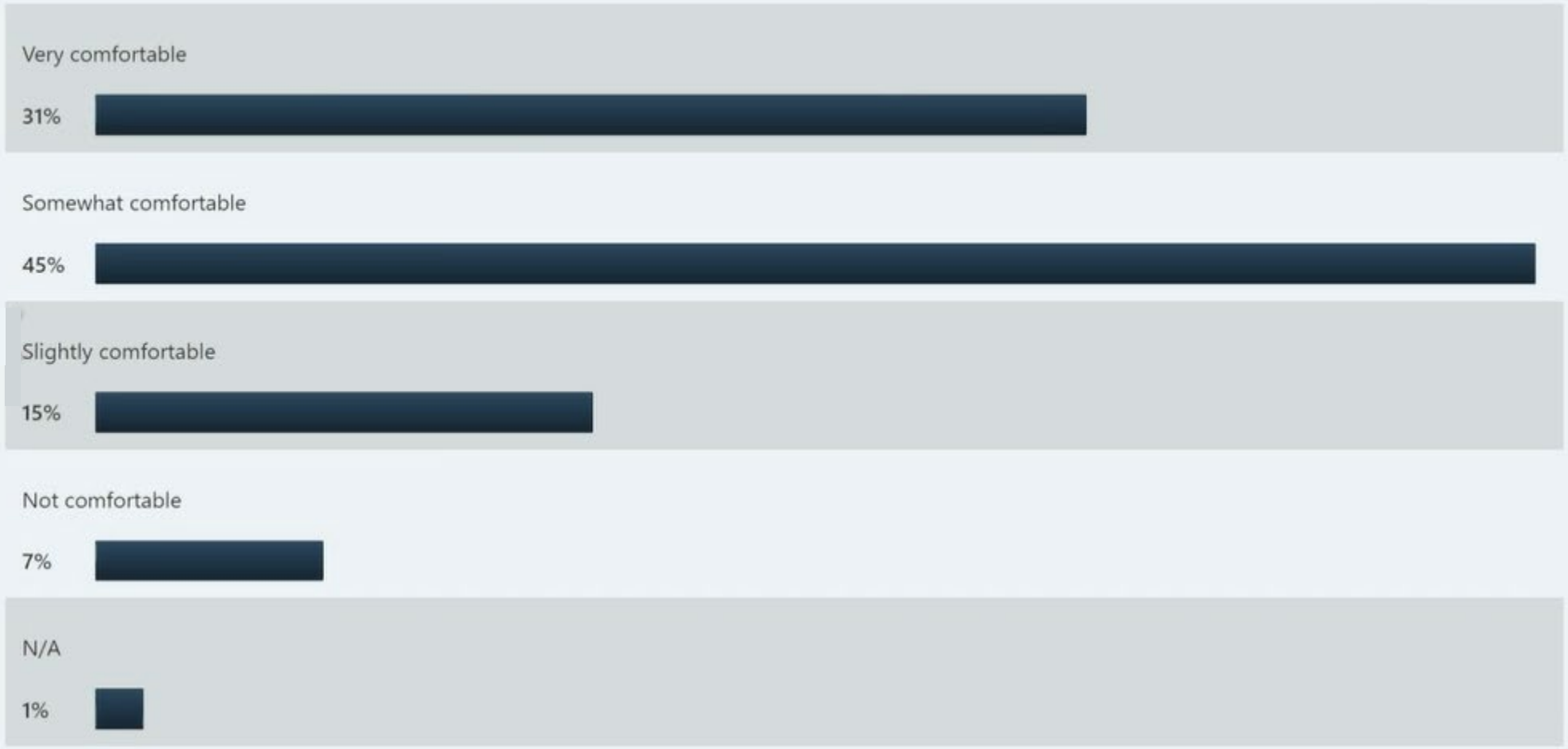
Live Audience Poll #1

How comfortable are you addressing parental concerns/hesitancy regarding pediatric RSV immunization?

- Very comfortable
- Somewhat comfortable
- Slightly comfortable
- Not comfortable
- N/A

Live Audience Poll #1 Results

How comfortable are you addressing parental concerns/hesitancy regarding pediatric RSV immunization?



Wheel of KNOWLEDGE

Most Parents Vaccinate on Schedule

Pro-Vaccine	Vaccine Hesitant	Anti-Vaccine
Acceptors	Vaccine- hesitant	Rejector
Agree with or do not question vaccines	Are unsure about, delay, or choose only some vaccines	Completely reject vaccines
Child fully immunized	Child under-immunized	Child un-immunized
Believe vaccines are safe	Concerned vaccine side effects outweigh benefits	Very concerned about vaccine side effects
Believe vaccines work	Concerned vaccines might not prevent disease	Doubt vaccines work
High trust in provider	Desires a trustworthy provider	Low or no trust
Interest in vaccine info from provider	Interest in vaccine info from provider	No interest in vaccine info
K entry '23-'24= 93% (↓ from 95%)	~10-30%	3.3% ↑ From 3% '22

Opel DJ, et al. *Pediatrics.* 2014;133(3):526-530.

Addressing Immunization Hesitancy

- How do you talk with families who are hesitant about immunization practices that are "new"?
- What strategies do you find helpful in building trust?
- Are there specific communication approaches you find most successful when discussing immunizations?

Live Audience Poll #2

Overall, what are the biggest barriers you encounter regarding implementation/uptake of pediatric passive RSV immunization? *(Select all that may apply)*

1. Lack of awareness
2. Parental/caregiver hesitancy
3. Clinician hesitancy
4. Limited access or availability at the point of care
5. Documentation issues
6. Collaboration/workflow challenges
7. Other, N/A

Live Audience Poll #2 Results

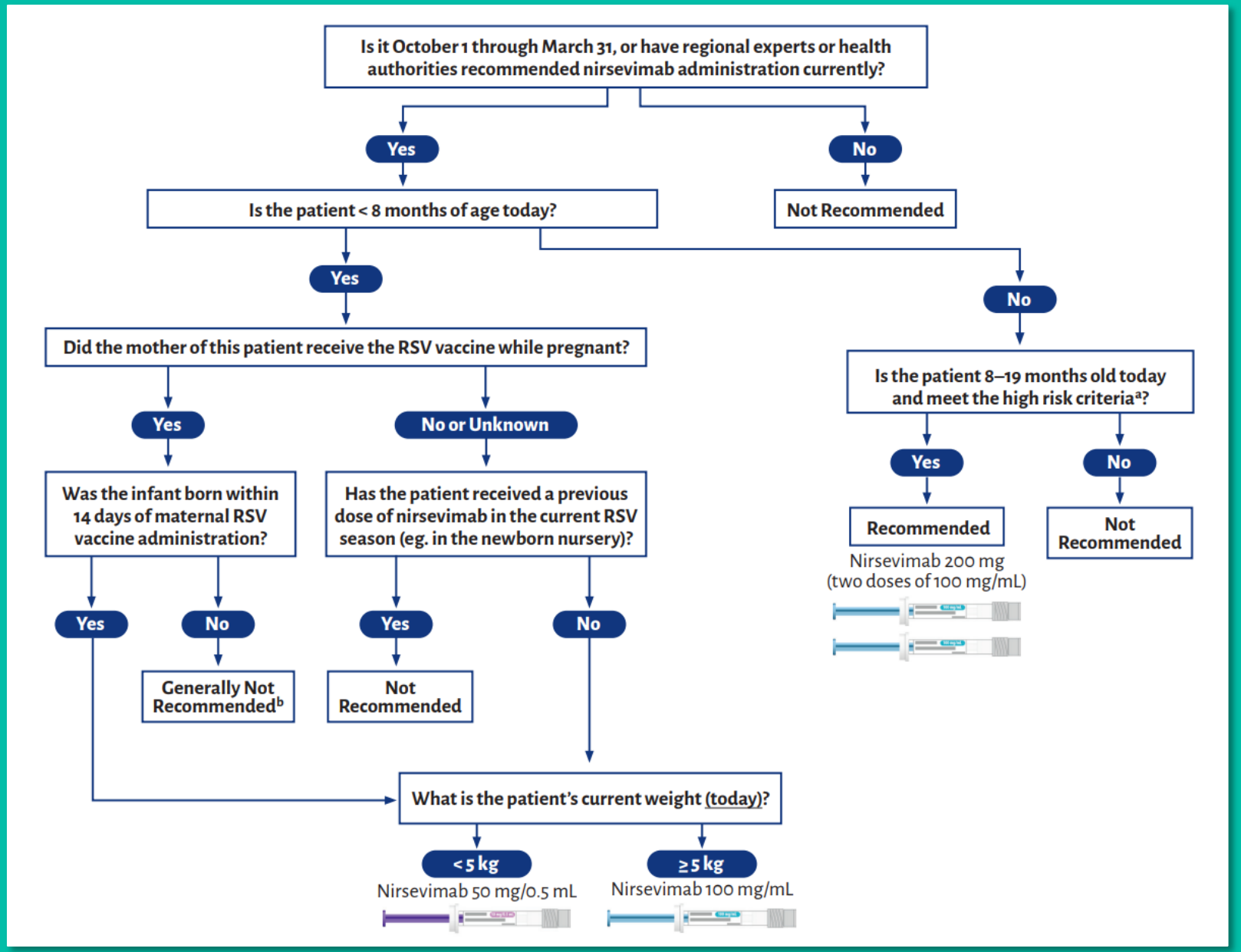
What are the biggest barriers you encounter regarding implementation/uptake of pediatric passive RSV immunization?

Wheel of KNOWLEDGE

Administration Timing Guide

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

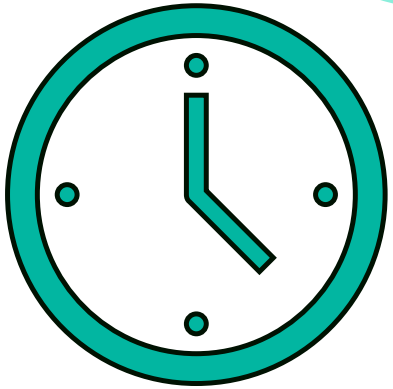
AAP Resource



RSV = respiratory syncytial virus. American Academy of Pediatrics (AAP). Accessed February 24, 2025. https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/nirsevimab-administration/

Emerging Questions Regarding Timing

- "Shortly before or during RSV season": How is that decided in your practice; in your state?
- If Mom was vaccinated less than 14 days before baby was born, how is that documented? What is your next step with the baby?
- What other timing tips can you share?



Interprofessional Strategies for Management

- Who are you partnering with for successful uptake?
- How are peds clinics and birth centers communicating if Mom has been immunized?
- For babies with higher-risk conditions, how is that communicated?
- What is working in your area?

Educate With Reliable Resources

CDC

Pinkbook webinar and series

National Foundation for Infectious Diseases

Immunization and clinical vaccinology course

Children's Hospital of Philadelphia

Vaccine Education Center

CDC National Immunization Awareness Month Educational Resources for Parents and Patients

Children's MINNESOTA The Kid Experts

Comfort Promise program

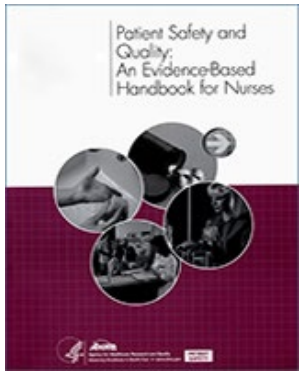
Immunize.org

VACCINATE YOUR FAMILY

NIC

2025 conference in Sept

voices for vaccines



Chapter 44: Tools and Strategies for Quality Improvement and Patient Safety

Scan to watch a REEL REVIEW reinforcing what you've learned today!