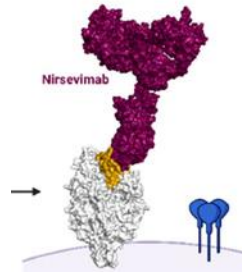
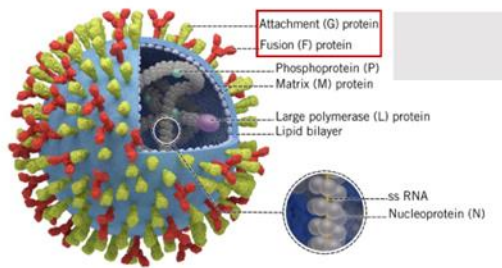


Update on Immunization Practices for Prevention of Severe RSV Infection



Pablo J. Sánchez, MD



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

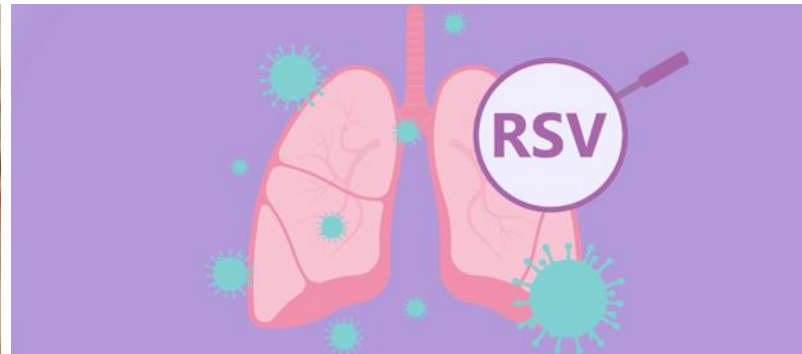


THE OHIO STATE UNIVERSITY
COLLEGE OF MEDICINE

Partners for Kids Webinar, Columbus, OH; 9/12,2024

DISCLOSURE STATEMENT

Dr. Pablo Sánchez has no financial relationship to disclose.



Update on RSV: Objectives

- Describe the epidemiology of RSV: THE Problem!
- Describe the prophylaxis options to limit severe RSV disease in infants and high-risk children:
 - Infant passive immunization: nirsevimab
 - Maternal RSV vaccine

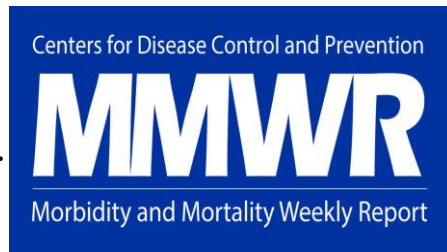


RSV Prevention: Outline

- The process of approval: FDA, CDC
- RSV: The Problem and the Virus
- Preventive strategies:
 - **Nirsevimab** (Beyfortus™)
 - **Maternal prefusion F protein-based RSV vaccine** (Abrysvo™)
- Recommendations CDC and AAP (and NCH!)
- Implementation

RSV Prevention: The Process!

- **VRBPAC** (Vaccines and Related Biological Products Advisory Committee) → **FDA**
- **AMDAC** (Antimicrobial Drugs Advisory Committee) → **FDA**
- **ACIP** (Advisory Committee on Immunization Practices) → **CDC**
- **MMWR**: publication makes it final!



*Griffin et al. NEJM, 2020

**Kampmann et al NEJM, 2023

RSV Prevention

- **Nirsevimab (Beyfortus™):***

- Recommended by the Antimicrobial Drugs Advisory Committee (AMDAC), approved by FDA on July 17, 2023
- Recommended by ACIP (10-0) and CDC on August 3, 2023
- MMWR published on August 25, 2023



- **Maternal prefusion F Protein-based RSV vaccine (recombinant RSVpreF vaccine, Abrysvo™):****

- Approved by FDA on August 21, 2023
- Recommended by ACIP (11-1) / CDC on 9/22/2023
- MMWR published on October 6, 2023

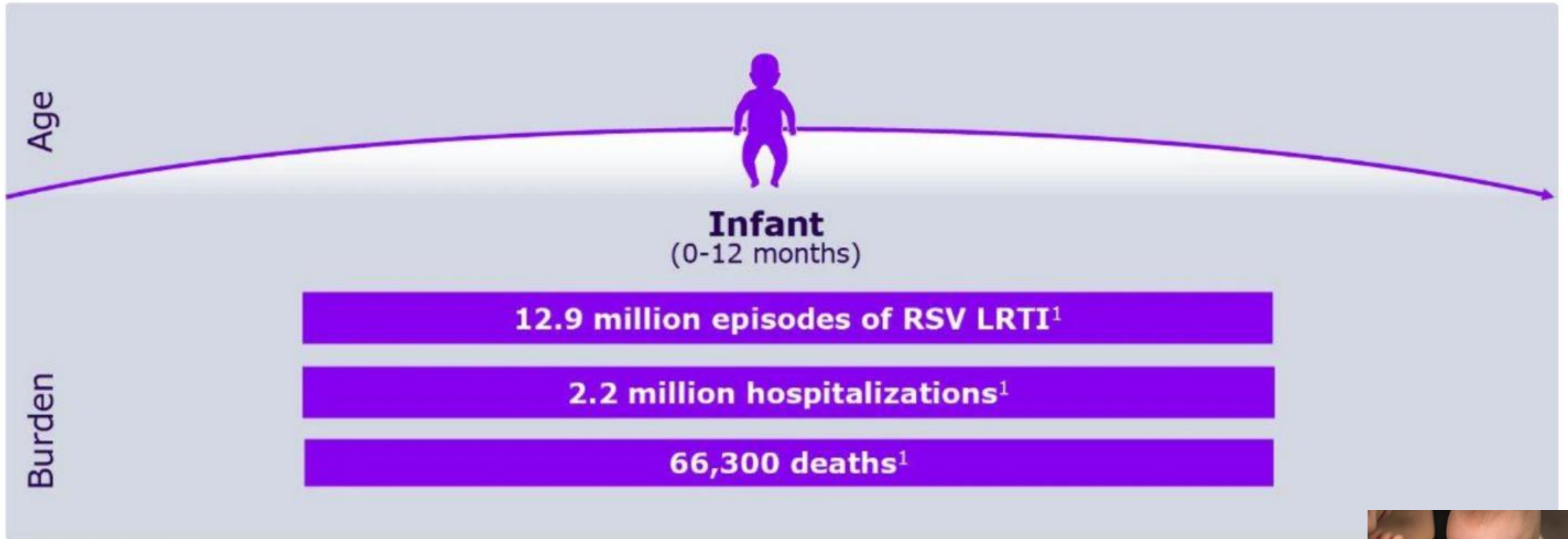


*Griffin et al. NEJM, 2020; Hammitt et al. NEJM 2022; Jones et al. MMWR 2023

**Kampmann et al. NEJM, 2023; Fleming-Dura et al. MMWR, 2023



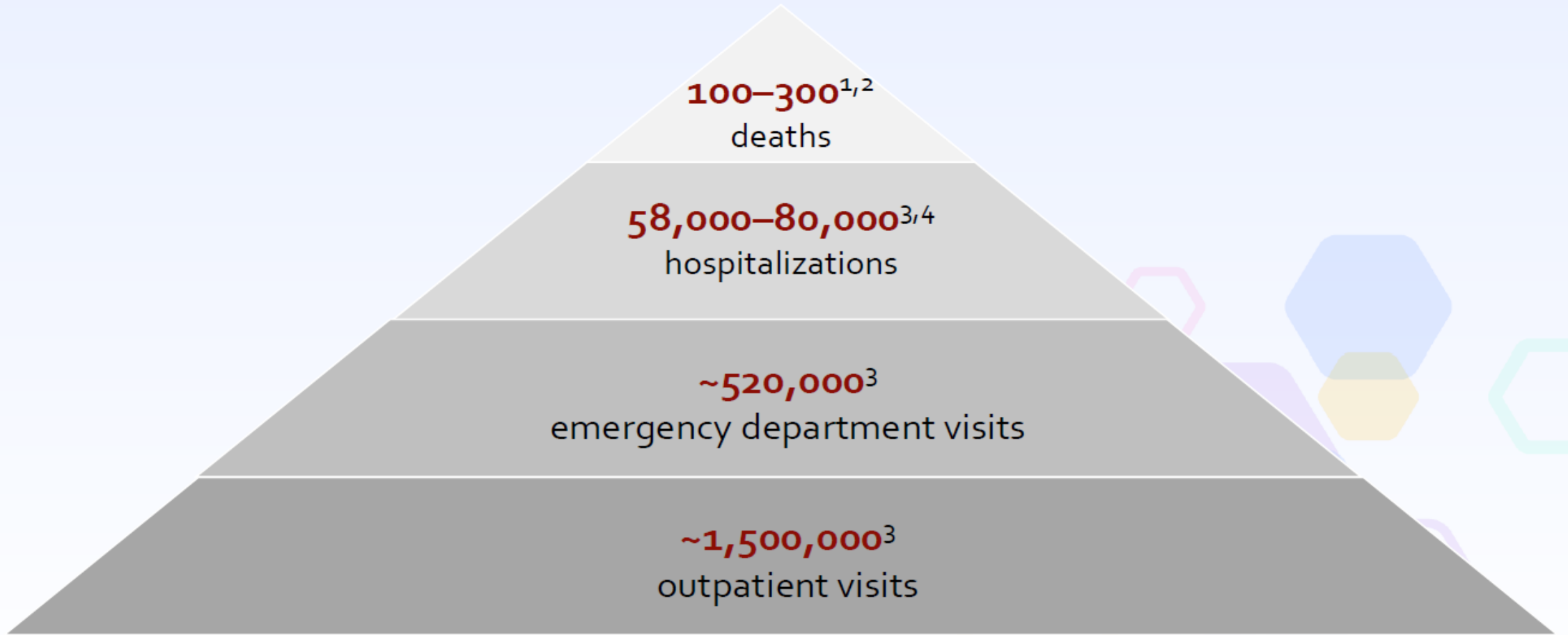
RSV Causes Substantial Disease Burden for Newborns and Infants Globally



Based on 2019 global data.



Each year in U.S. children aged less than 5 years, RSV is associated with...



¹Thompson et al, JAMA, 2003; ²Hansen et al, JAMA Network Open, 2022; ³Hall et al, NEJM, 2009; ⁴McLaughlin et al, J Infect Dis, 2022 (*estimate 80,000 hospitalizations in infants <1y)

RSV is the leading cause of hospitalization in U.S. infants¹

- Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2 years²
- 2-3% of young infants will be hospitalized for RSV^{3,4,5}
- RSV is a common cause of lower respiratory tract infection in infants
- Highest RSV hospitalization rates occur in first months of life and risk declines with increasing age in early childhood^{3,5}
- 79% of children hospitalized with RSV aged <2 years had no underlying medical conditions³

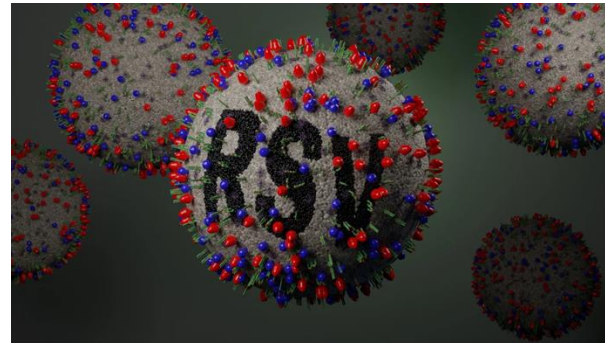


Image: Goncalves et al. Critical Care Research and Practice 2012

¹[Suh et al. JID 2022.](#) ²[Glezen et al, Arch Dis Child, 1986;](#) ³[Hall et al, Pediatrics, 2013;](#) ⁴[Langley & Anderson, PIDJ, 2011;](#) ⁵CDC NVSN data

RSV: NCH

	RSV		
	Positive	Total	Percent Positive
9/7/2024	3	240	1%
8/31/2024	6	220	3%
8/24/2024	0	168	0%
8/17/2024	2	164	1%
8/10/2024	0	155	0%
8/3/2024	0	173	0%
7/27/2024	0	118	0%
7/20/2024	0	174	0%
7/13/2024	3	153	2%
7/6/2024	1	126	1%
6/29/2024	1	151	1%
6/22/2024	1	153	1%
6/15/2024	1	154	1%
6/8/2024	2	161	1%
6/1/2024	1	204	0%
5/25/2024	1	184	1%
5/18/2024	3	191	2%
5/11/2024	2	200	1%
5/4/2024	8	239	3%
4/27/2024	1	208	0%
4/20/2024	2	200	1%
4/13/2024	7	166	4%
4/6/2024	1	208	0%
3/30/2024	11	203	5%
3/23/2024	6	223	3%
3/16/2024	10	250	4%
3/9/2024	10	262	4%
3/2/2024	11	285	4%
2/24/2024	25	302	8%
2/17/2024	28	299	9%



**This season: 2024-2025
“Start” nirvesimab
on October 1, 2024**

Last Season: 2024-2024:
“Start” on November 1
Started nirsevimab on 10/25/2023
Stopped March 8, 2024

<https://nationwidechildrens.sharepoint.com/sites/A10011/MicrobiologyImmunserologyUpdates/Forms/AllItems.aspx?id=%2Fsites%2FA10011%2FMicrobiologyImmunserologyUpdates%2FNationwideChildrensWeeklyRespiratoryReport%2Epdf&parent=%2Fsites%2FA10011%2FMicrobiologyImmunserologyUpdates&p=true&ga=1>



Evolution of AAP Statements Regarding RSV Prophylaxis

Volume 134, Issue 2

August 2014



FROM THE AMERICAN ACADEMY OF PEDIATRICS | POLICY STATEMENT | AUGUST 01 2014

Updated Guidance for Palivizumab Prophylaxis Among Infants and Young Children at Increased Risk of Hospitalization for Respiratory Syncytial Virus Infection

COMMITTEE ON INFECTIOUS DISEASES AND BRONCHIOLITIS GUIDELINES COMMITTEE; Michael T. Brady, MD; Carrie L. Byington, MD; H. Dele Davies, MD; Kathryn M. Edwards, MD; Mary Anne Jackson, MD; Yvonne A. Maldonado, MD; Dennis L. Murray, MD; Walter A. Orenstein, MD; Mobeen H. Rathore, MD; Mark H. Sawyer, MD; Gordon E. Schutze, MD; Rodney E. Willoughby, MD; Theoklis E. Zaoutis, MD; Shawn L. Ralston, MD; Allan S. Lieberthal, MD; H. Cody Meissner, MD; Brian K. Alverson, MD; Jill E. Baley, MD; Anne M. Gadomski, MD; David W. Johnson, MD; Michael J. Light, MD; Nizar F. Maraqa, MD; Eneida A. Mendonca, MD; Kieran J. Phelan, MD; Joseph J. Zorc, MD; Danette Stanko-Lopp, MA; Sinsi Hernández-Cancio, JD

Pediatrics (2014) 134 (2): 415–420.

<https://doi.org/10.1542/peds.2014-1665>

Dec 2005

'12 Red Book
Mar 2013

AAP Policy Statement: Modified recommendations

for use of palivizumab for prevention of RSV

no major changes
Policy Statement retired
2012 RB reaffirmed

Evolution of AAP Statements Regarding RSV Prophylaxis

Morbidity and Mortality Weekly Report

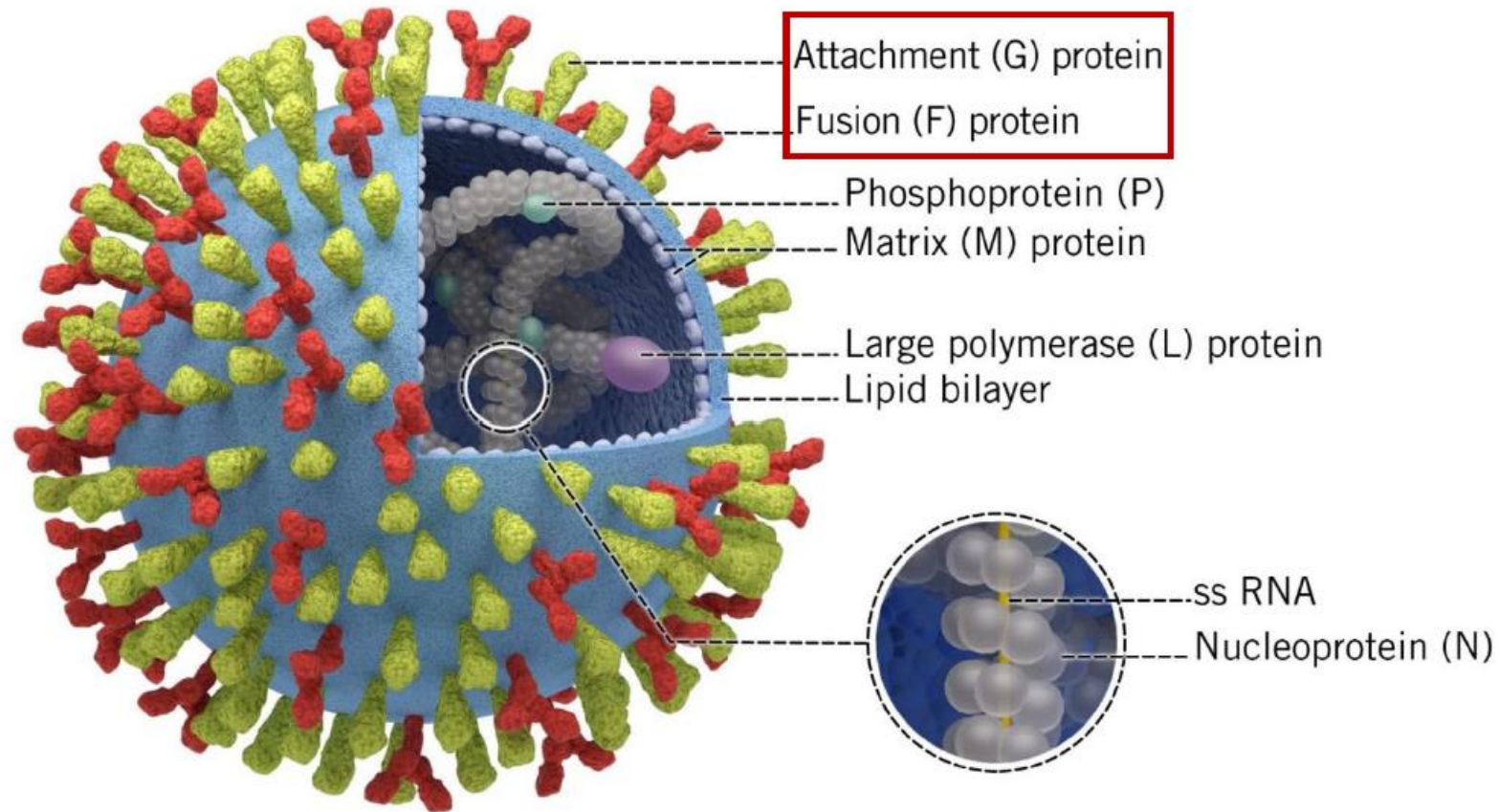
Use of Nirsevimab for the Prevention of Respiratory Syncytial Virus Disease Among Infants and Young Children: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

Jefferson M. Jones, MD¹; Katherine E. Fleming-Dutra, MD¹; Mila M. Prill, MSPH¹; Lauren E. Roper, MPH¹; Oliver Brooks MD²; Pablo J. Sánchez, MD³; Camille N. Kotton, MD⁴; Barbara E. Mahon, MD¹; Sarah Meyer, MD⁵; Sarah S. Long, MD⁶; Meredith L. McMorrow, MD¹

US Department of Health and Human Services | Centers for Disease Control and Prevention | MMWR | August 25, 2023 | Vol. 72 | No. 34

	for use of palivizumab for prevention of RSV
'12 Red Book	no major changes
Mar 2013	Policy Statement retired
	2012 RB reaffirmed

RSV – virion structure

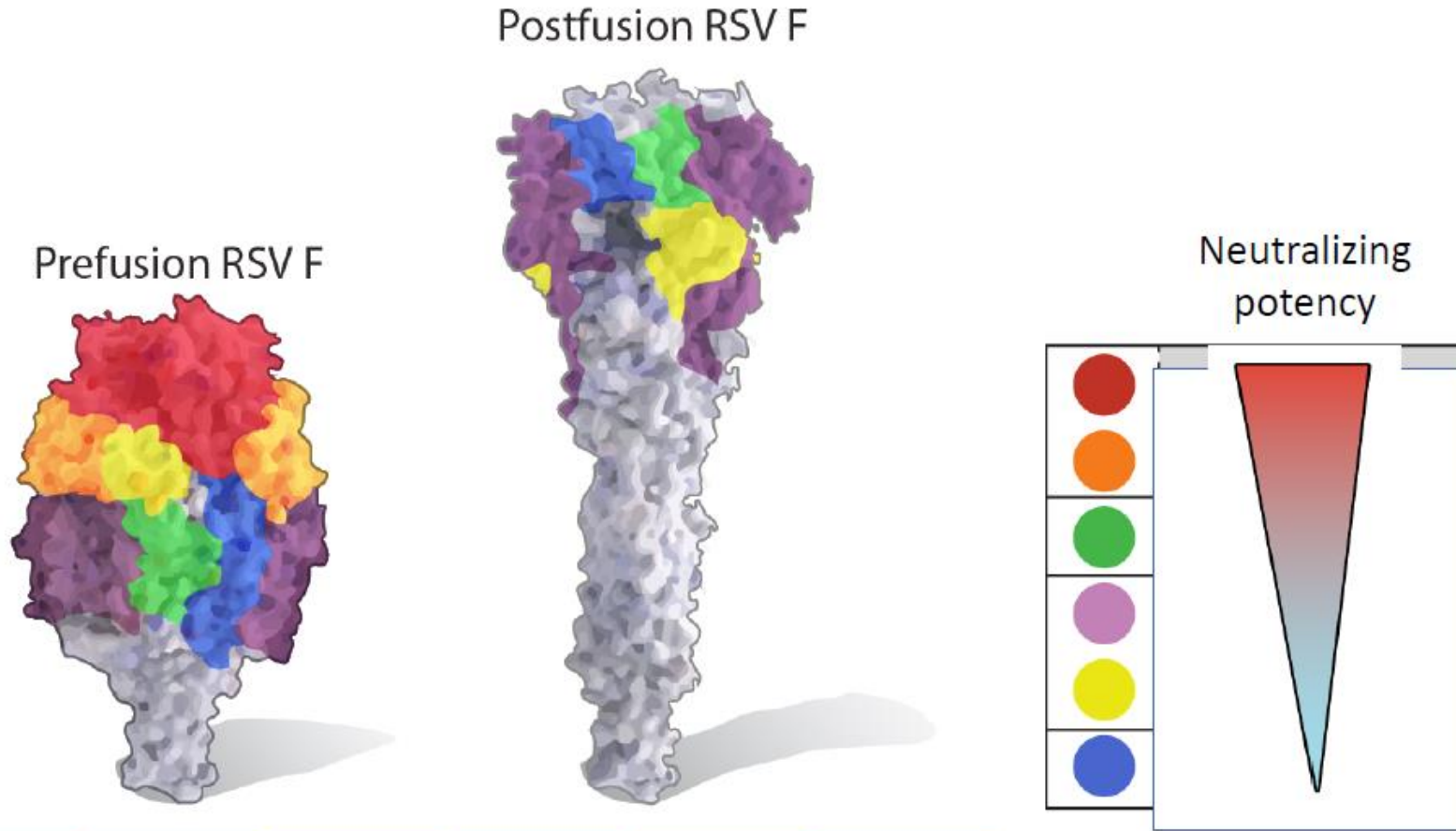


1955: Morris and coworkers: “chimpanzee coryza agent (CCA)”

1957: Chanock and coworkers: isolated virus from 2 children with lower respiratory tract disease

F glycoprotein: primary function is to mediate fusion of the viral and host cell membranes.

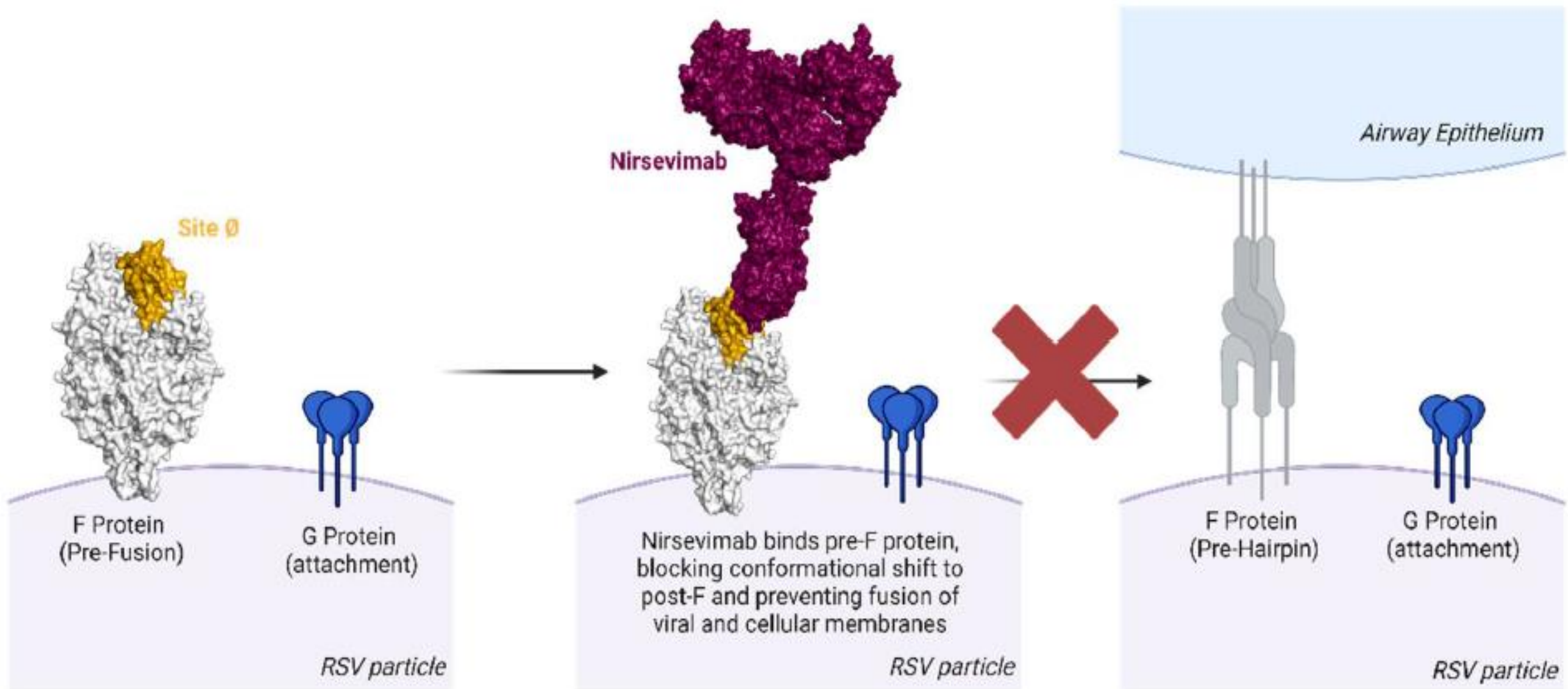
The fusion (F) protein exists in two or more structural forms, which bind different antibodies



SITE Ø SITE I SITE II SITE III SITE IV SITE V

Current Opinion in Virology

Nirsevimab: Mechanism of Action



Nirsevimab: Mechanism and Duration of Action

- Nirsevimab (Beyfortus™): recombinant human immune globulin G1 kappa monoclonal antibody that binds to the prefusion conformation of the RSV fusion protein resulting in enhanced neutralizing activity compared with palivizumab
- Modification of the Fc region promotes extension of the half-life
- Clinical trials demonstrated efficacy through at least 150 days and only needs to be administered once per season*
- No decline in efficacy; administered intramuscularly

[*Repeat dosing after cardiopulmonary bypass](#)

Nirsevimab: Clinical Trials

- **Griffin et al. NEJM 2020: Phase 2b**
 - 1453 preterm infants: 29-34 weeks GA; 2016-2017
 - Randomized to nirsevimab (50 mg IM; n=969) or placebo (2:1; n=484) at start of RSV season
 - Primary endpoint: medically attended RSV-associated lower respiratory tract infection (MALRI) through 150 days
 - Secondary: RSV hospitalization
 - **MALRI incidence 70% (95% CI, 52-81) lower** with nirsevimab (2.6% [n=25] vs. 9.5% [n=8]; p<0.001)
 - **RSV hospitalization: 78% lower** (95% CI, 51.9-90.3) (0.8% [n= 8] vs. 4.1% [n=20]; p<0.001)
 - Adverse effects: 2.3% (nirsevimab) vs. 2.1% (placebo)

Nirsevimab: Clinical Trials

- **Hammitt et al. NEJM 2022: Phase 3 (MELODY)**
 - 1490 infants: ≥ 35 weeks GA; 2019-2020 RSV season
 - Randomized (2:1) to nirsevimab (50 mg IM; n=994) or placebo (n=496) at start of RSV season
 - Primary endpoint: medically attended RSV-associated lower respiratory tract infection (**MALRI**) through 150 days
 - MALRI incidence: nirsevimab (1.2% [n=12] vs. 5% [n=25]; $p < 0.001$)
 - **Efficacy 74.5%** (95% CI, 49.6-87.1; $p < 0.001$)
 - Secondary: **RSV hospitalization**
 - RSV hospitalization: 0.6% (n= 6) vs. 1.6% (n=8); $p = 0.07$
 - **Efficacy 62.1%** (95% CI, -8.6-86.8)
 - Serious adverse events: 6.8% (nirsevimab) vs. 7.3% (placebo)

Nirsevimab: Clinical Trials

- **Muller et al. NEJM 2023: Phase 3 (MELODY – full enrollment)**
 - 3012 infants: ≥ 35 weeks GA (31 countries)
 - Randomized (2:1) to nirsevimab (50 or 100 mg IM; n=1998) or placebo (n=996) at start of RSV season



The NEW ENGLAND
JOURNAL of MEDICINE

[SPECIALTIES](#) ▾ [TOPICS](#) ▾ [MULTIMEDIA](#) ▾ [CURRENT ISSUE](#) ▾ [LEARNING/CME](#) ▾ [AUTHOR CENTER](#) [PUBLICATIONS](#) ▾

CORRESPONDENCE



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

Published April 5, 2023 | N Engl J Med 2023;388:1533-1534 | DOI: 10.1056/NEJMc2214773 | [VOL. 388 NO. 16](#)

Nirsevimab: Clinical Trials

- **Muller et al. NEJM 2023: Phase 3 (MELODY – full enrollment); cont.**
 - Medically attended RSV-associated lower respiratory tract infection (**MALRI**) through 150 days:
 - Nirsevimab 1.2% [n=24] vs. placebo 5.4% [n=54])
 - **Efficacy 76.4%** (95% CI, 62-85.2)
 - **RSV hospitalization:**
 - 0.4% [n=9] vs. 2% [n=20]
 - **Efficacy 76.8%** (95% CI, 49.4-89.4)
 - **Severe MALRI:**
 - 0.3 % (n=7) vs 1.7% (n=17)
 - **Efficacy: 78.6%** (95% CI, 48.8-91.0)
 - Adverse events: 1.3% (nirsevimab) vs. 1.5% (placebo)



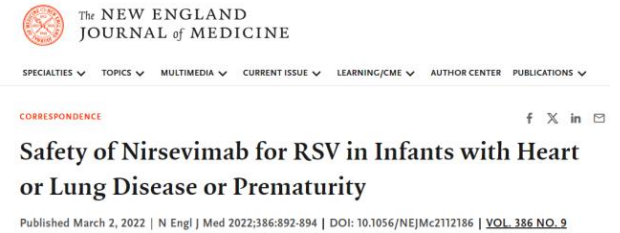
Nirsevimab: Clinical Trials

- **Dagan et al. JPIDS 2024: MELODY – 2nd season**
 - 3012 infants: ≥35 weeks GA (31 countries)
 - Randomized to nirsevimab or placebo
 - 2796 (93%) infants completed follow-up through 2nd RSV season
 - **2nd season: No enhancement of RSV disease**

Disease Event (<i>n</i> [%])	First RSV Season (Through 151 Days Post-dose)		Second RSV Season ^b (362–511 Days Post-dose)	
	Nirsevimab (<i>N</i> = 2009)	Placebo (<i>N</i> = 1003)	Nirsevimab (<i>N</i> = 1944)	Placebo (<i>N</i> = 967)
Events due to RSV				
Medically attended RSV LRTI ^c	24 (1.2)	54 (5.4)	19 (1.0)	10 (1.0)
Medically attended RSV LRTI with hospitalization ^c	9 (0.4)	20 (2.0)	3 (0.2)	3 (0.3)
Medically attended RSV LRTI (very severe) ^d	7 (0.3)	17 (1.7)	3 (0.2)	3 (0.3)
Medically attended RSV-associated LRTI on any test result ^{e,f}	34 (1.7)	75 (7.5)	35 (1.8)	20 (2.1)
Hospitalization for any respiratory illness due to RSV on any test result ^{f,g}	15 (0.7)	26 (2.6)	10 (0.5)	6 (0.6)

Nirsevimab: Clinical Trials

- **Domachowske et al. NEJM 2022: Phase 2-3 (MEDLEY)**



- 925 infants:
 - Preterm infants ≤ 35 weeks GA: n=615
 - Congenital heart disease (CHD) or Chronic Lung Disease of Prematurity (CLD): n=310
- Randomized to nirsevimab (50/100 mg IM; n=406; 208 [CHD-CLD] or palivizumab (n=206; 98 [CHD-CLD]) at start of RSV season
- Medically attended RSV-associated lower respiratory tract infection (MALRI) through 150 days:
 - Nirsevimab 0.6% (4/616) vs. palivizumab 1.0% (3/309)
- Day 151: serum nirsevimab levels similar in both cohorts and MELODY trial

Nirsevimab: Clinical Trials

- **Domachowske et al. NEJM 2022: Phase 2-3 (MEDLEY); cont.**
 - 925 infants:
 - Preterm infants ≤ 35 weeks GA: n=615
 - Congenital heart disease (CHD) or Chronic Lung Disease of Prematurity (CLD): n=310
 - **Adverse events:**
 - Preterm cohort: 1.5% of nirsevimab group and 1.9% of palivizumab group
 - CHD/CLD cohort: 1.9% of nirsevimab group and 2.0% of palivizumab group
 - Heparin-induced thrombocytopenia (nirsevimab, n=1)
 - 5 deaths: 2 Preterm; 3 CHD-CLD (nirsevimab); 1 CHD-CLD (palivizumab) - unrelated

Nirsevimab: Clinical Trials

- **Domachowske et al. JPIDS 2023: MEDLEY Season 2**
 - 262 infants:
 - Congenital heart disease (CHD) or Chronic Lung Disease of Prematurity (CLD)
 - Original nirsevimab cohort: nirsevimab (200 mg) followed by placebo
 - Original palivizumab cohort: randomized (1:1) to nirsevimab (200 mg) vs. palivizumab
 - 42 P/P; 40 P/N; 180 N/N
 - Adverse events: Similar across treatment groups
 - P/P: 29 (69%); P/N: 29 (72.5%); N/N: 126 (70%)
 - No RSV LRI
 - No deaths and no AEs of special interest (hypersensitivity; immune complex disease, thrombocytopenia)

Nirsevimab: Clinical Trials

- **Drysdale et al. NEJM 2023: HARMONIE (pragmatic)**
 - 8058 infants:
 - <12 months of age, GA \geq 29 weeks (France, Germany, UK)
 - Randomized (1:1) to nirsevimab (n=4021) or standard care (n=4021) before or during RSV season (2022-2023)
 - Primary endpoint: **RSV hospitalization**
 - Nirsevimab 0.3% (n=11) vs. standard care 1.5% (n=19)
 - **Efficacy: 83.2%** (95% CI, 67.8-92.0); p<0.001
 - Secondary outcome: **“very severe” RSV hospitalization** (O₂ sat<90%, O₂)
 - Nirsevimab 0.1% (n=5) vs. standard care 0.5% (n=19)
 - **Efficacy: 75.7%** (95% CI, 32.8-92.9); p=0.004
 - Adverse events: 2.1%



Nirsevimab Efficacy Estimates (ACIP/CDC)

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%)

*Pooled phase 2b (excluding underdosed) and phase 3 trial estimate comparing nirsevimab arm to placebo arm

Nirsevimab: “Real-World” Effectiveness Against RSV Hospitalization

- CDC New Vaccine Surveillance Network (7 pediatric academic centers):
 - **90% effectiveness**
- Spain (9 hospitals in Valencia, Murcia, Valladolid):
 - **70%-84% effectiveness**
- Spain (Navarre, population-based, 1177 infants, 92% coverage):
 - **88% effectiveness**
- Luxembourg: 84% coverage in maternity wards
 - Decreased RSV hospitalization and PICU admissions in infants <6 months old
- France (ENVIE): **83% effectiveness**
- Spain (Galicia): **82% effectiveness**

MMWR 2024; Lopes-Lacort et al. Euro Surveill 2024
Ezpeleta et al. Vaccines 2024; Ernst et al. Euro Surveill 2024;
Assad et al. NEJM 2024; Ares-Gomez, Lancet ID 2024



TDAP AND
FLU VACCINES
DURING
PREGNANCY

**THE BEST
SHOT**



2022-2023 Influenza Season

- Inactivated Influenza (IIV)
 - 47.2%
- Pertussis (Tdap)
 - 55.4%
- COVID-19
 - 27.3%
- Vaccine Hesitancy increased since the 2019-2020 season



THE BEST SHOT



RSV vaccine: 54% very likely to receive.

Saper et al. Pediatrics 2024

RSV Prevention

- **Nirsevimab (Beyfortus™):***

- Recommended by the Antimicrobial Drugs Advisory Committee (AMDAC), approved by FDA on July 17, 2023
- Recommended by ACIP (10-0) and CDC on August 3, 2023
- MMWR published on August 25, 2023



- **Maternal prefusion F Protein-based RSV vaccine (recombinant RSVpreF vaccine, Abrysvo™):****

- Approved by FDA on August 21, 2023
- Recommended by ACIP (11-1) / CDC on 9/22/2023
- MMWR published on October 6, 2023



*Griffin et al. NEJM, 2020; Hammitt et al. NEJM 2022; Jones et al. MMWR 2023

**Kampmann et al. NEJM, 2023; Fleming-Dura et al. MMWR, 2023

The NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

APRIL 20, 2023

VOL. 388 NO. 16

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

B. Kampmann, S.A. Madhi, I. Munjal, E.A.F. Simões, B.A. Pahud, C. Llapur, J. Baker, G. Pérez Marc, D. Radley, E. Shittu, J. Glanternik, H. Snaggs, J. Baber, P. Zachariah, S.L. Barnabas, M. Fausett, T. Adam, N. Perreras, M.A. Van Houten, A. Kantele, L.-M. Huang, L.J. Bont, T. Otsuki, S.L. Vargas, J. Gullam, B. Tapiero, R.T. Stein, F.P. Polack, H.J. Zar, N.B. Staerke, M. Duron Padilla, P.C. Richmond, K. Koury, K. Schneider, E.V. Kalinina, D. Cooper, K.U. Jansen, A.S. Anderson, K.A. Swanson, W.C. Gruber, and A. Gurtman, for the MATISSE Study Group*



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Primary Endpoints:

Vaccine Efficacy by Cumulative Days after Birth for Two Primary Endpoints

Administered at
24-36 weeks of
pregnancy

RSV-Positive Severe MA-LRTI	Maternal Vaccine Group (as Randomized)		Vaccine Efficacy ^b (%) (CI [*])
	RSVpreF 120 µg (N ^a =3495)	Placebo (N ^a =3480)	
Time Interval	Number of Cases (%)	Number of Cases (%)	
90 Days after birth	6 (0.2)	33 (0.9)	81.8 (40.6, 96.3)
120 Days after birth	12 (0.3)	46 (1.3)	73.9 (45.6, 88.8)
150 Days after birth	16 (0.5)	55 (1.6)	70.9 (44.5, 85.9)
180 Days after birth	19 (0.5)	62 (1.8)	69.4 (44.3, 84.1)
RSV-Positive MA-LRTI			
Time Interval	Number of Cases (%)	Number of Cases (%)	Vaccine Efficacy ^b (%) (CI [*])
90 Days after birth	24 (0.7)	56 (1.6)	57.1 (14.7, 79.8)
120 Days after birth	35 (1.0)	81 (2.3)	56.8 (31.2, 73.5)
150 Days after birth	47 (1.3)	99 (2.8)	52.5 (28.7, 68.9)
180 Days after birth	57 (1.6)	117 (3.4)	51.3 (29.4, 66.8)

*99.5% CI for 90 days, 97.58% CI for 120/150/180 days. CI LB >20% for all time points.

Abbreviations: RSV = respiratory syncytial virus. a. N = number of participants (at risk) in the specified group. These values are used as the denominators for the percentage calculations. b. Vaccine efficacy was calculated as $1 - (P / [1 - P])$, where P is the number of cases in the RSVpreF group divided by the total number of cases. The confidence interval was adjusted using Bonferroni procedure and accounting for the primary endpoints results.



RSVpreF Vaccines

- Pfizer 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%)
- GSK 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 (Pfizer) for 32-36 weeks with postmarketing surveillance to assess preterm birth and hypertensive disorders of pregnancy

RSVpreF Vaccine (Pfizer): Post-marketing

Son et al JAMA Network Open 2024

- Retrospective, observational cohort: 2023-2024 RSV season
- 2 NYC hospitals: women delivered at ≥ 32 wks from 9/2023-1/2024
- 2973 women: 35% vaccinated at 32-36 wks
 - 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)

Maternal RSVpreF Vaccine: Effect Estimates, Benefits

OUTCOME	Vaccine Efficacy (95% CI): 32-36 weeks pregnancy
Medically attended RSV-associated lower respiratory tract infection (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)

Use of the Pfizer Respiratory Syncytial Virus Vaccine During Pregnancy for the Prevention of Respiratory Syncytial Virus–Associated Lower Respiratory Tract Disease in Infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

Katherine E. Fleming-Dutra, MD^{1,*}; Jefferson M. Jones, MD^{1,*}; Lauren E. Roper, MPH¹; Mila M. Prill, MSPH¹; Ismael R. Ortega-Sanchez, PhD¹; Danielle L. Moulia, MPH¹; Megan Wallace, DRPH¹; Monica Godfrey, MPH¹; Karen R. Broder, MD²; Naomi K. Tepper, MD³; Oliver Brooks, MD⁴; Pablo J. Sánchez, MD⁵; Camille N. Kotton, MD⁶; Barbara E. Mahon, MD¹; Sarah S. Long, MD⁷; Meredith L. McMorro, MD¹

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



October 6, 2023



EARLY RELEASE

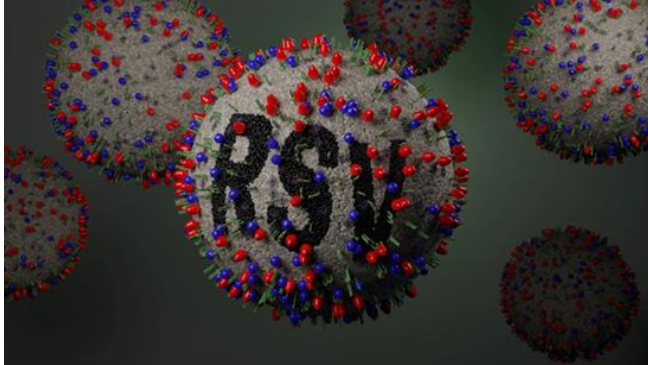


Use of the Pfizer Respiratory Syncytial Virus Vaccine During Pregnancy for the Prevention of Respiratory Syncytial Virus–Associated Lower Respiratory Tract Disease in Infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

RSVpreF Vaccine

- Pregnant women: 32-36 weeks' gestation
 - “Seasonal” - September through January (most of USA)
 - May be administered with other vaccines
 - Prevention of RSV lower respiratory tract disease and severe lower respiratory tract disease in infants (≥ 34 weeks gestation) from birth to 6 months of age
 - From time of maternal vaccination, 14 days or more needed for development and transplacental transfer of maternal antibodies
-

RSV PROPHYLAXIS



When it's more than just a cold.

RSV symptoms:

- Tugging at the neck to try to get air
- Fast breathing
- Flared nostrils
- Belly breathing



**RECOMMENDATIONS:
2024-2025: KICK-OFF OCTOBER 1!**

Nirsevimab Recommendations

- Infants <8 months born during or entering their 1st RSV season (November 1, 2024), including those previously recommended to receive palivizumab
 - Must be <8 months old on day of nirsevimab administration
- Children aged 8-19 months (on day of nirsevimab administration) who are at increased risk of severe RSV disease and entering their 2nd RSV season, including those previously recommended to receive palivizumab
- 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

Nirsevimab Recommendations: 1st Season

- Infants <8 months born during or entering their 1st RSV season (age at nirsevimab administration <8 months):
 - The mother did not receive RSV vaccine during pregnancy
 - The mother's RSV vaccination status is unknown
 - The infant was born within 14 days of maternal RSV vaccination

Nirsevimab Recommendations: 1st Season*

- If an infant was born towards the end of March and did not receive nirsevimab, can they receive nirsevimab in October?
 - **YES**
- If a standard risk infant was born last March and received nirsevimab and will be <8 months of age in October, can they receive another dose of nirsevimab?
 - **NO**, as it will be the infant's 2nd RSV season and not “high-risk”

*AAP, Nirsevimab Frequently Asked Questions, 9/2024

Nirsevimab: 2nd RSV Season and High Risk

- Children aged 8-19 months (on day of nirsevimab administration)
- 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
- Severe immunocompromise
- 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

Timing of Nirsevimab

- In the first week of age for infants born shortly before and during the RSV season: birth hospitalization or outpatient setting
- Others: shortly before and during the RSV season
- Most of USA: October through March (pre-pandemic)
- Can adjust based on local epidemiology
- Infants with prolonged birth hospitalization: shortly before or promptly after discharge (NOT during NICU stay!)
- Can be co-administered with routine childhood vaccines

RSVpreF Vaccine + Nirsevimab

- Infant may receive nirsevimab after maternal vaccination:
 - Mothers who may not mount an adequate immune response to vaccination (e.g., immunocompromised) or have conditions associated with reduced transplacental antibody transfer (HIV-infected)
 - Substantial risk for severe RSV disease: hemodynamically significant congenital heart disease, intensive care admission and requiring oxygen at discharge
 - Post cardiopulmonary bypass, ECMO

Nirsevimab Post-Cardiopulmonary Bypass and ECMO

- Additional dose after surgery/ECMO during RSV season *if age-eligible*
- First RSV season:
 - If performed ≤ 90 days after receiving nirsevimab, additional dose based on body weight at the time of the additional dose
 - If performed > 90 days after receiving nirsevimab, additional dose of 50 mg regardless of body weight.
- Second RSV season:
 - If performed ≤ 90 days after receiving nirsevimab, additional dose of 200 mg regardless of body weight.
 - If performed > 90 days after receiving nirsevimab, additional dose of 100 mg regardless of body weight.

Nirsevimab: Indications and Dosage

Advisory Committee on Immunization Practices (ACIP) Recommendations

Eligible Population	Dosage (Single Dose)	Timing
All neonates and infants < 8 months (1 st season)	Weight < 5 kg: 50 mg IM Weight ≥ 5 kg: 100 mg IM	Typical RSV Season in Ohio[#]: November through March
High-risk* 8-19 months (2 nd season)	200 mg IM, regardless of body weight	Duration of action is at least 150 days; administration at start of season will provide protection throughout season

* See AAP and ACIP guidance for defined high risk population

Post-COVID-19 pandemic RSV seasons have been more variable than usual, adjust administration timing based on local RSV-activity if needed

[Storage and Handling](#)



[Jones JM et al. MMWR Morb Mortal Wkly Rep. 2023 Aug 25;72\(34\):920-925.](#)

Nirsevimab: Storage and Handling

- Prefilled syringes
- Store refrigerated at 36 - 46° F (2 - 8° C)
- May be at room temperature for 8 hours 68 - 77° F (20 - 25° C)
- 50 mg doses will be in purple syringes and 100 mg in blue syringes



50 mg by
IM injection



100 mg by
IM injection

Vaccine Administration Errors (VAERS):

34 reports of adult vaccine given to children <2 years of age
(31 infants <8 mo)



27 Pfizer, 7 GSK

1 infant with CHD had cardiopulmonary arrest within 24 hours (GSK)



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Nirsevimab: Adverse Reactions/Reporting

- Adverse reactions that occurred more frequently than placebo:
 - Rash (0.9%)
 - Injection site reactions (0.3%)
- Reporting Adverse Reactions
 - If administered alongside vaccines: report to VAERS
 - If administered alone: report to FAERS (MedWatch)
- ImpactSIIS
 - Documentation of nirsevimab administration will occur in ImpactSIIS per ODH



Nirsevimab: Challenges

- CDC: nirsevimab included in childhood immunization schedule and Vaccines for Children program
- Approximately 10% of birthing hospitals participate in VFC
- Bundled payment model for newborn care
 - Hepatitis B vaccine more feasible to cover at ~\$13-16/dose
 - Will nirsevimab be included in bundled payments?
- Critical to ensure documentation of maternal receipt (and date) of RSV vaccine
- Critical to ensure documentation of in-hospital nirsevimab administration in records sent to primary care provider

..... Nirsevimab: \$495/dose; \$395/VFC
Pre-F RSV vaccine: \$295

Vaccines For Children (VFC) Program

VFC-enrolled practices will be able to order nirsevimab from the Ohio Department of Health for the 2024-2025 season.

This season, practices will be able to order nirsevimab through VFC even if they do not have commercial nirsevimab stock. This provision will be in place until August 2025.

If not a VFC-enrolled practice, work with your local health department to ensure patients have access to nirsevimab.

Covered Nirsevimab Billing Codes

CPT Codes for Medication and Administration

90380	Respiratory syncytial virus, monoclonal antibody, seasonal dose; 0.5 mL dosage, for intramuscular use
90381	Respiratory syncytial virus, monoclonal antibody, seasonal dose; 1 mL dosage, for intramuscular use.
96380	Administration of respiratory syncytial virus, monoclonal antibody, seasonal dose by intramuscular injection, <u>with counseling</u> by physician or other qualified health care professional
96381	Administration of respiratory syncytial virus, monoclonal antibody, seasonal dose by intramuscular injection

AAP website with
billing info and
helpful vignettes



Reimbursement from Commercial Insurance

Due to inclusion in the CDC's routine immunization schedule, insurances are required to cover nirsevimab without cost sharing

Major commercial policies reference CDC/ACIP guidance for nirsevimab coverage

During the 2023-2024 season NCH and DCH received expected reimbursement from all major commercial insurances

Nirsevimab Administrations to Patients at Nationwide Children's Hospital

Expected to begin
October 1st

- This will protect infants throughout the anticipated RSV season (November – March)

Outpatient:

- Primary care clinics
- Specialty clinics (pulmonary, complex care, BPD, cardiology, and ID)*

Inpatient:

- Neonates being discharged from NCH NICUs
- Other qualifying admitted patients at discharge

*Other outpatient clinics can make patient specific requests for doses

PARTNERS
FOR KIDS®



Nirsevimab Administrations to Patients at Dayton Children's Hospital

Expected to begin
October 1st

- This will protect infants throughout the anticipated RSV season (November – March)

Outpatient

- RSV prevention clinic
 - [Referral form](https://www.childrensdayton.org) for clinic at [childrensdayton.org](https://www.childrensdayton.org)
 - For high-risk patients only
- DCH primary care, kids express, and specialty clinics with high-risk patients

Inpatient

- Neonates being discharged from DCH NICU

PFK RSV Prevention Resource Page

[PFK RSV Prevention Page](#)

- Resource links for providers and patients
- Partners For Kids developed resources
 - News and updates
 - Recorded webinar
- Regularly updated with new information as it becomes available

Pharmacy Updates

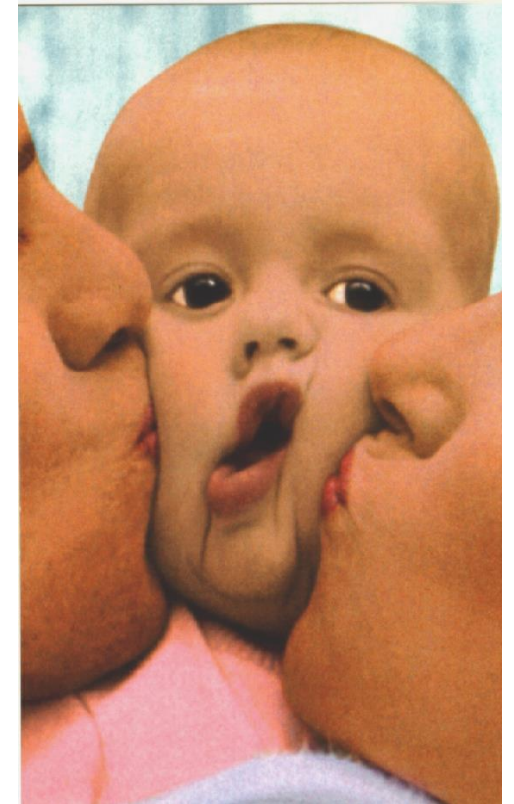
Respiratory Syncytial
Virus (RSV) Prevention
Resource

Read More



RSV Prevention

- Spread by contact (rarely droplet)
- Portal of entry: eye/nose
- Stress handwashing!
- Avoid the exposure!



Immunize today for a healthier tomorrow



Let's
RISE

Routine Immunizations on
Schedule for Everyone
(RISE)

Nationwide Children's Hospital Center for Perinatal Research



NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.™

Pablo J. Sánchez, MD
*Center for Perinatal Research
NEO-ID Clinic (614.722.4452)*

700 Children's Drive | Columbus, Ohio | 43205
P 614.355.6638 | F 614.355.5899 | C 214.621.1068
Pablo.Sanchez@NationwideChildrens.org



RESEARCH SAVES BABIES!