RSV Prevention in Infants and Young Children

Empowering Pediatric NPs to Lead Early Protection

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Molecular Virology and Microbiology
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Texas Children's Hospital
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Disclosures

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Asuncion Mejias, MD, PhD, has a relevant financial relationship in the form of:

Advisory Board for AstraZeneca; Enanta Pharmaceuticals, Inc.; Merck & Co., Inc.; Moderna, Inc.; Pfizer; and Sanofi.

Grant/Research Support from Merck & Co., Inc.

Speaker for Pfizer and Sanofi.

Disclosures

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Flor M. Munoz, MD, has a relevant financial relationship in the form of:

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Consultant for Sanofi.

Planning Committee and Reviewers

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Goals for Today

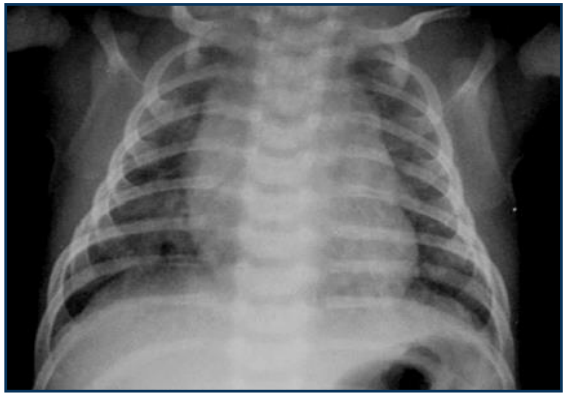
During this presentation, we will learn that…

- **The burden of RSV-related morbidity and mortality** is significant among all infants and at-risk young children
- **Recent clinical trials provide evidence** on the safety and efficacy of passive immunization as novel strategies for preventing RSV in pediatric populations
- **HCPs can use current guidance** to develop and implement care plans, ensuring appropriate use of RSV monoclonal antibodies for all infants, along with best practices for counseling parents and caregivers

RSV Burden and Unmet Needs in Infants

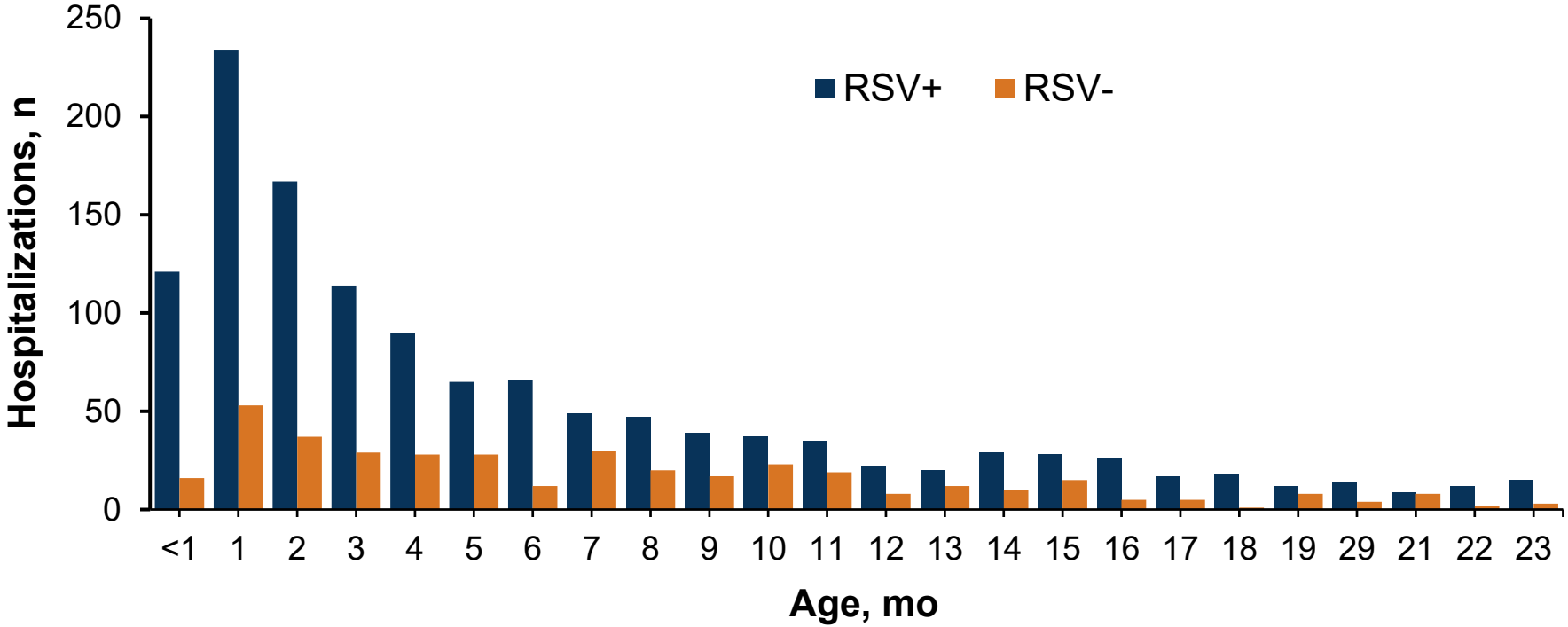
RSV Is the Leading Cause of Hospitalization in US Infants[1-7]

- Most (68%) infants are infected in the first year of life
  - Nearly all (97%) by age 2 years
- 2%-3% of young infants will be hospitalized for RSV
- RSV is a common cause of LTRI in infants
- Highest RSV hospitalization rates occur in the first months of life
  - Risk declines with increasing age in early childhood
- 79% of children hospitalized with RSV aged <2 years had no underlying medical conditions



1. Suh M et al. *J Infect Dis*. 2022;226(suppl 2):S195-S212. 2. Glezen WP et al. *Am J Dis Child*. 1986;140:543-546. 3. Hall CB et al. *Pediatrics*. 2013;132:e341-e348.
4. Langley GF, Anderson LJ. *Pediatr Infect Dis J*. 2011;30:510-517. 5. https://www.cdc.gov/nvsn/php/about/index.html.
6. Gonçalves A et al. *Crit Care Res Pract*. 2012:2012:861867. 7. Rha B et al. *Pediatrics*. 2020;146:e20193611.

RSV Hospitalizations by Month of Age: NCH 2013-2015[1]



1. Garcia-Mauriño C et al. *Pediatr Infect Dis J*. 2018;37:514-519.

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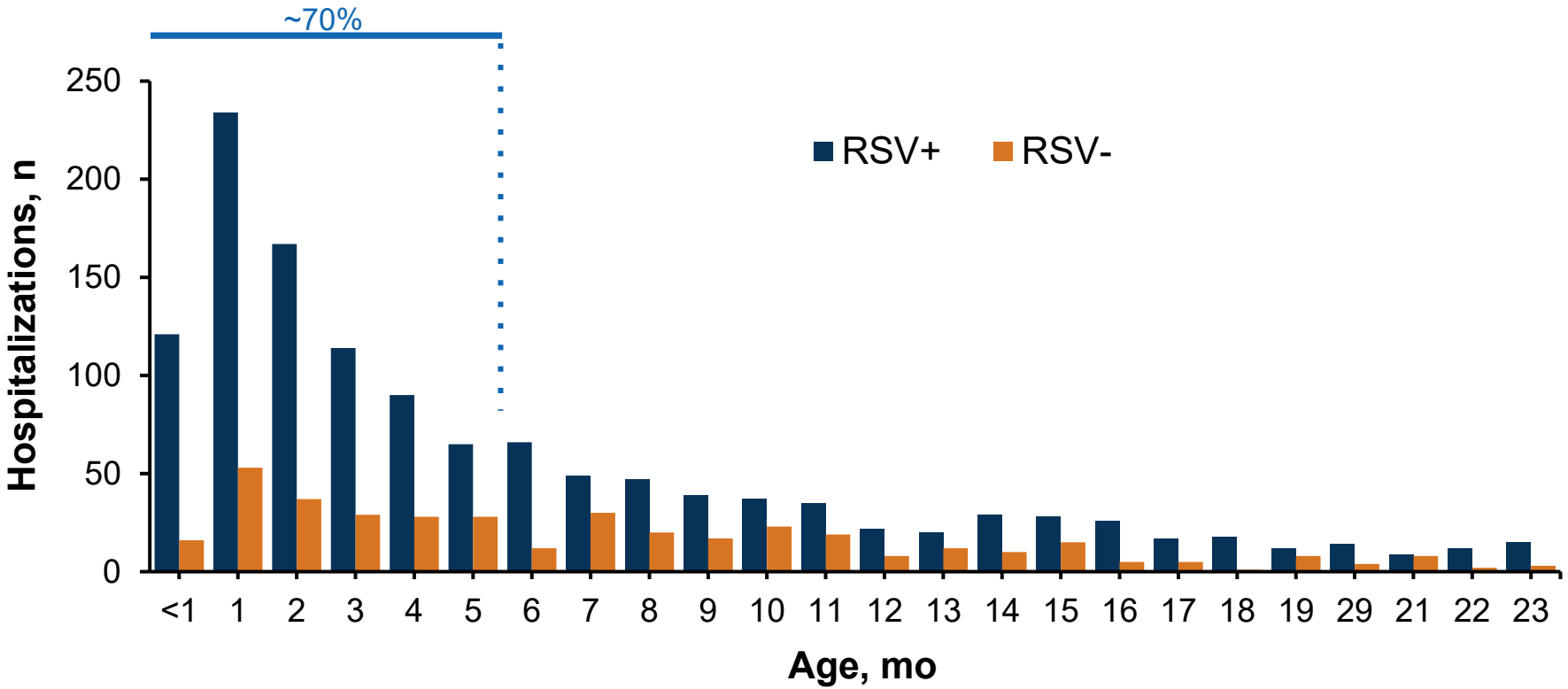

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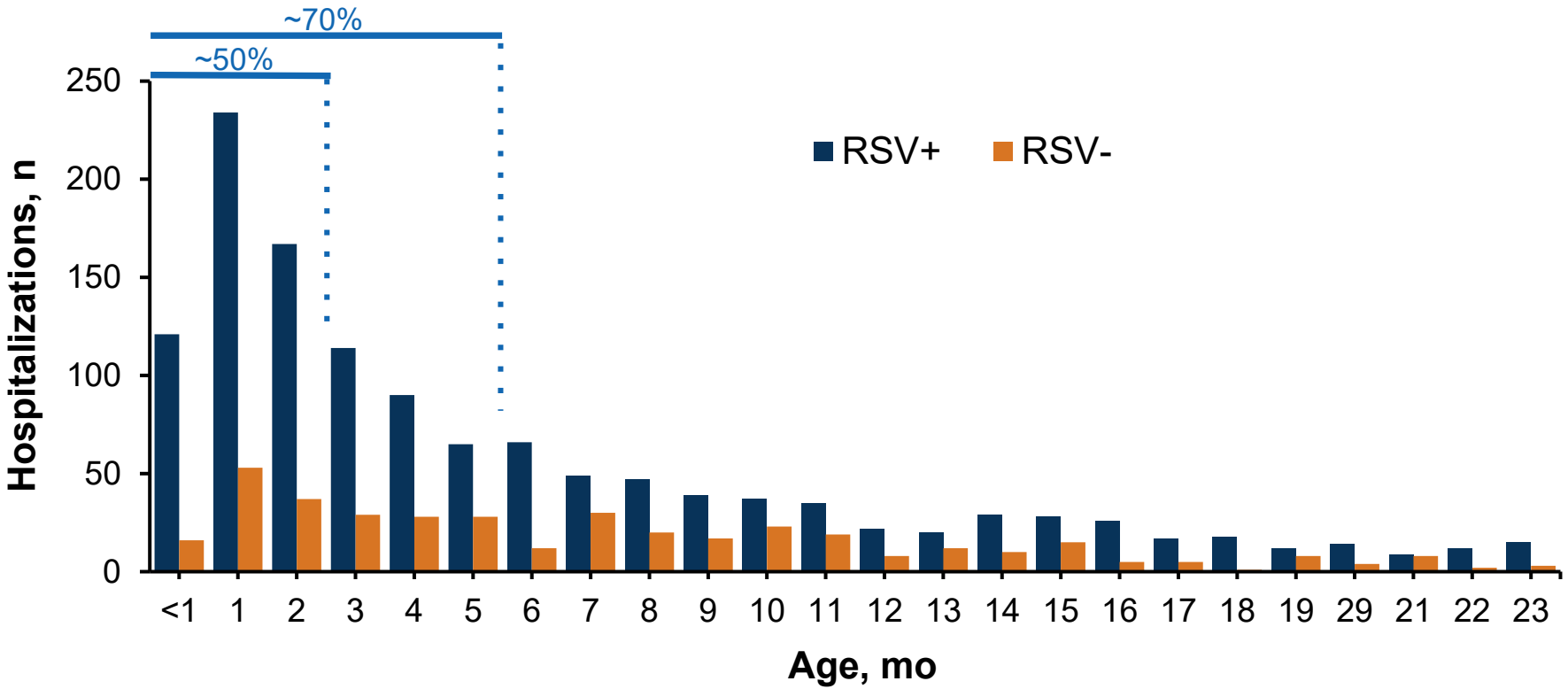

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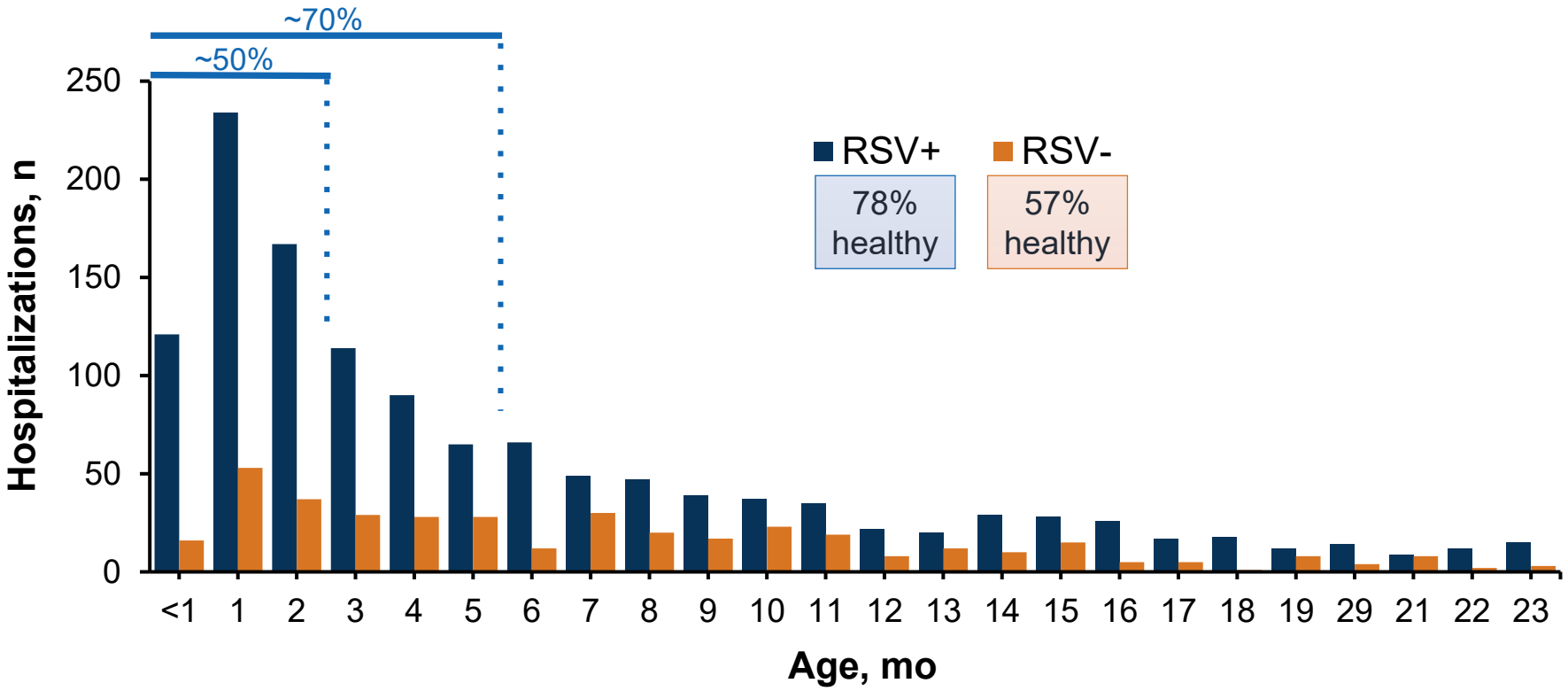

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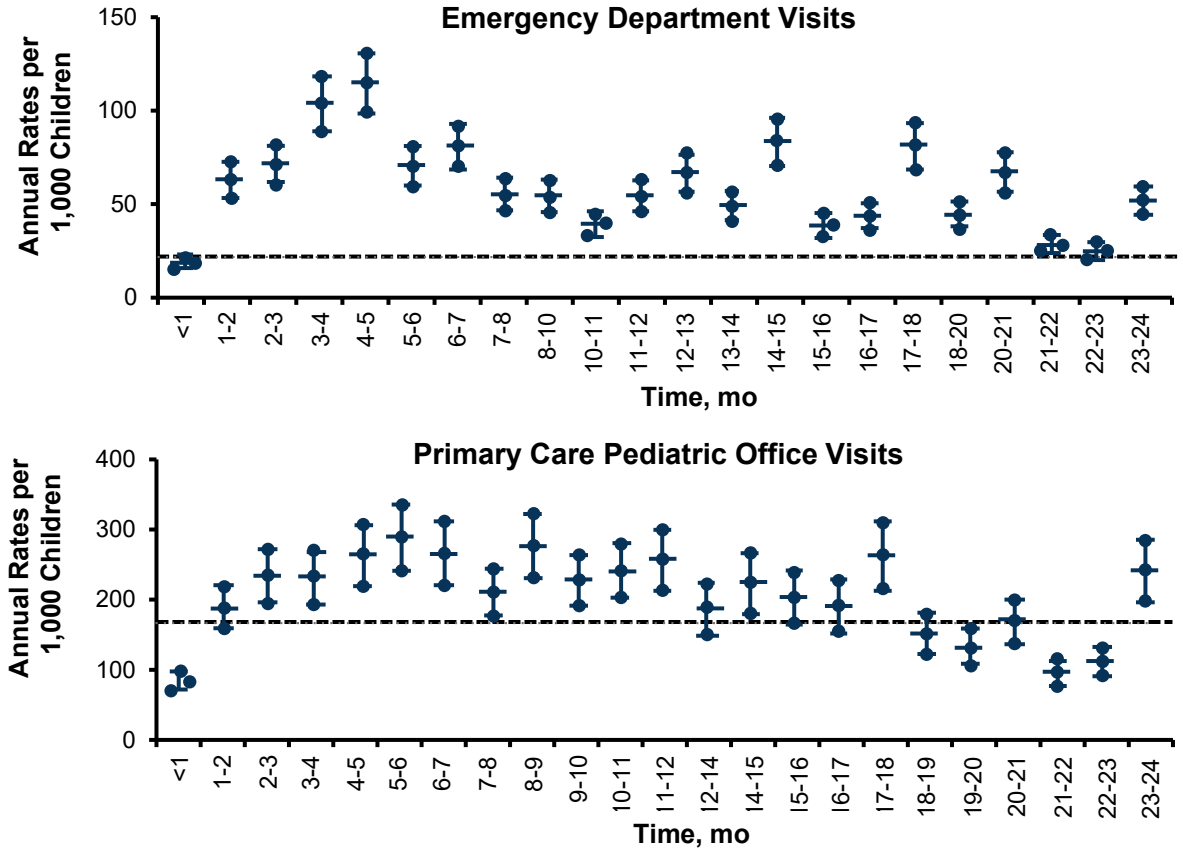
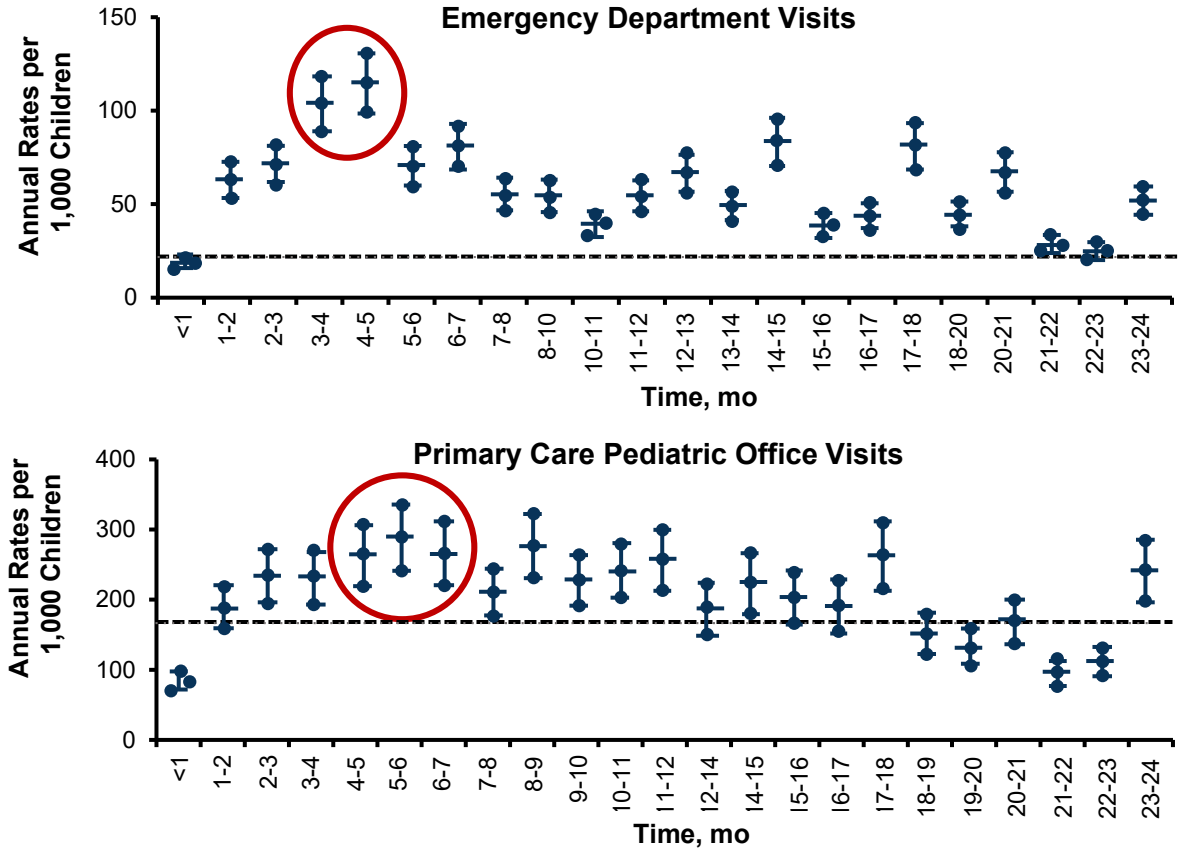
RSV Outpatient Visits in Children <24 Months of Age[1]



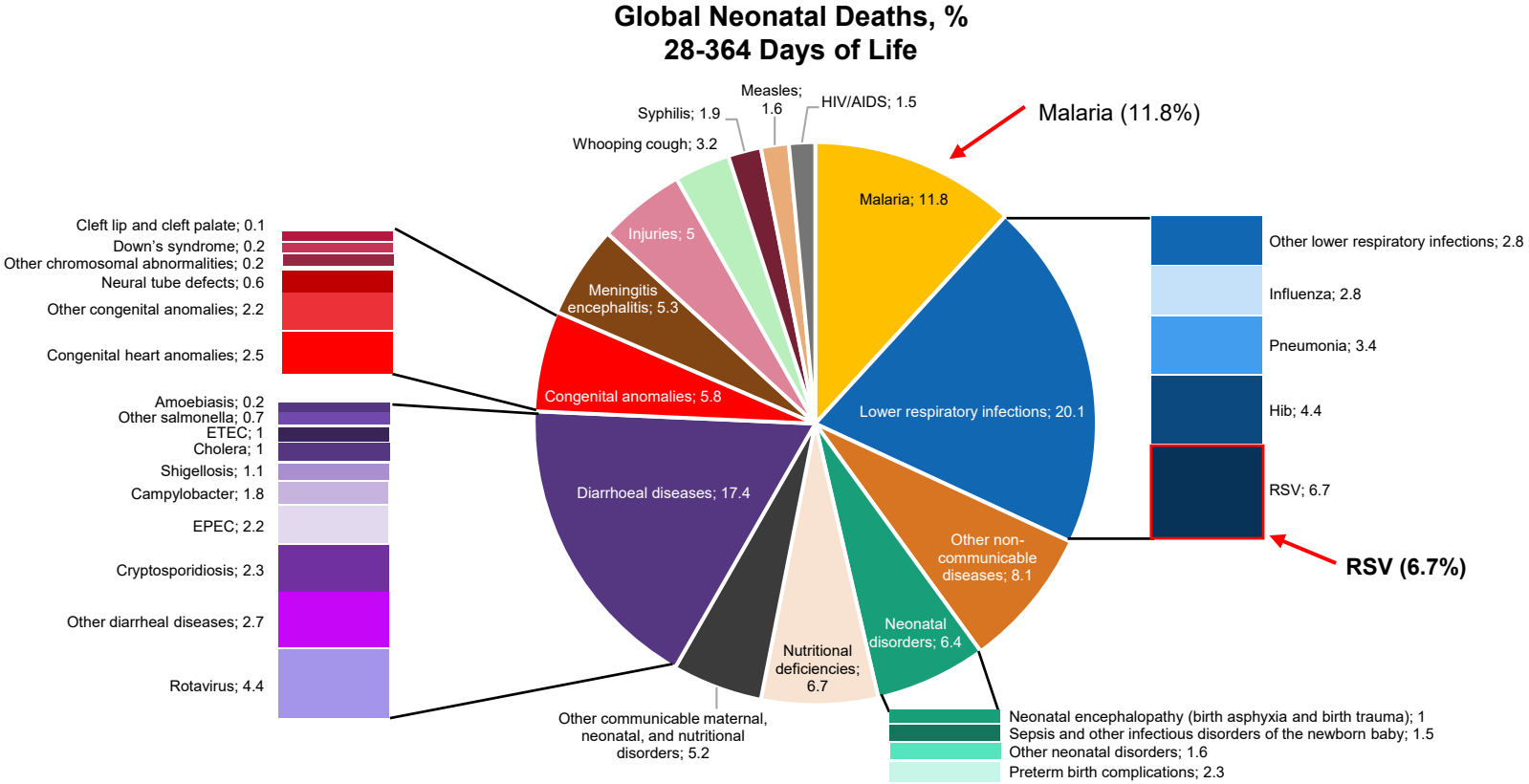
1. Lively JY et al. *J Pediatric Infect Dis Soc*. 2019;8:284-286.

RSV Outpatient Visits in Children <24 Months of Age[1]



1. Lively JY et al. *J Pediatric Infect Dis Soc*. 2019;8:284-286.

Global RSV Disease Burden[1]

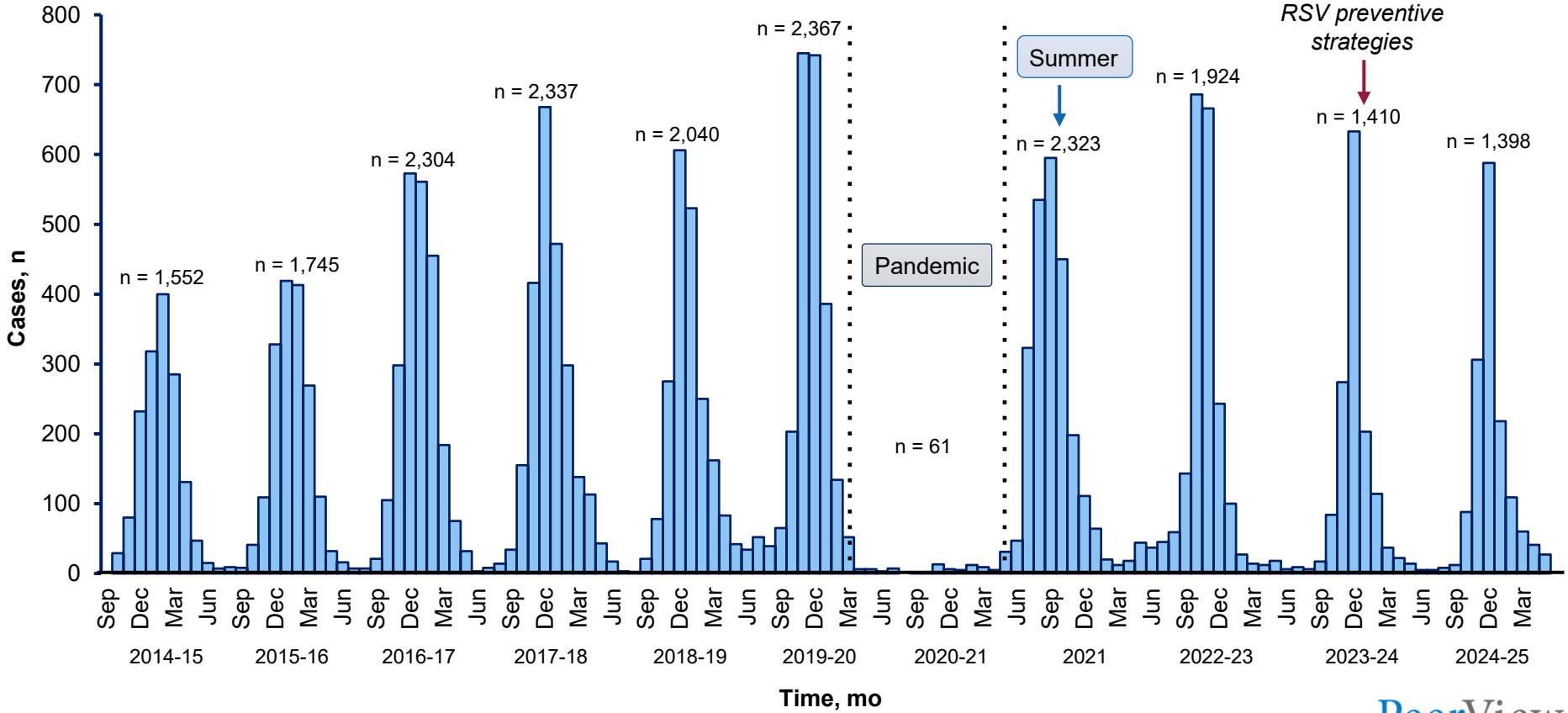


RSV kills more children under the age of 1 year than any other single pathogen (except malaria)

1. Lozano R et al. *Lancet*. 2012;380:2095-128.

Changes in RSV Seasonality

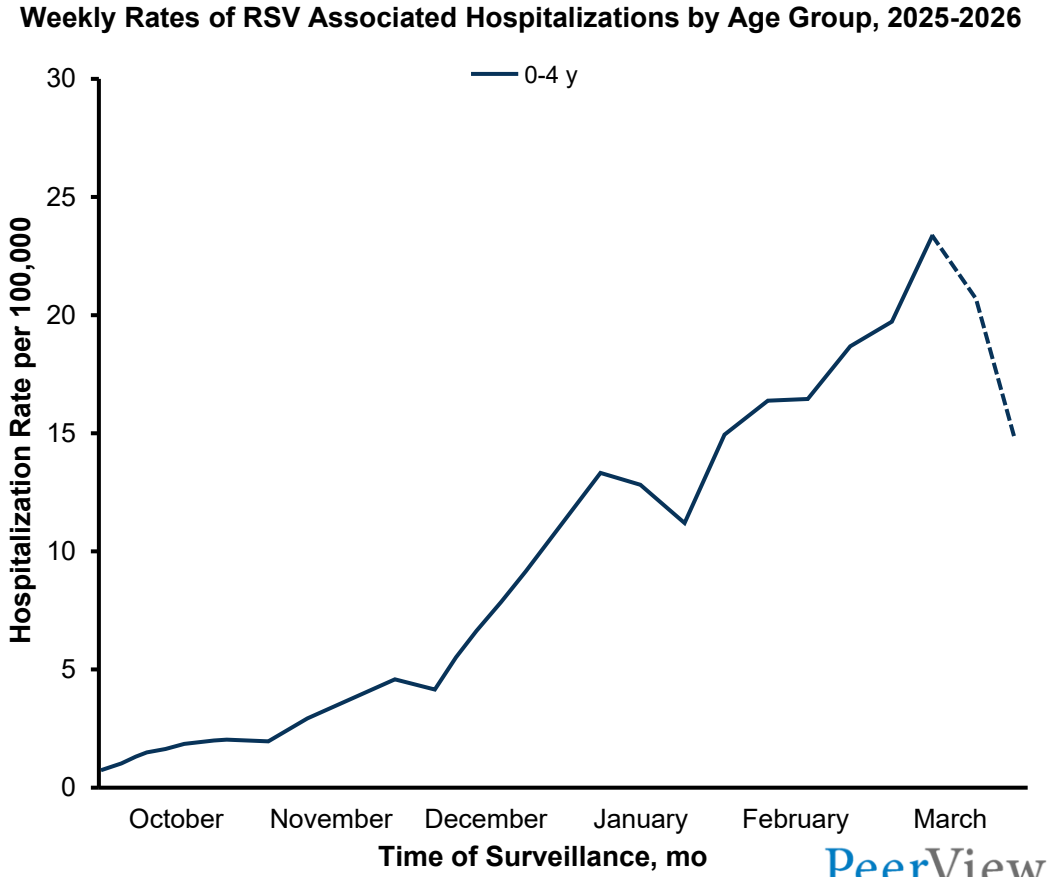
RSV Circulation: Nationwide Children's Hospital 2014-2025[1]



1. https://www.nationwidechildrens.org/specialties/laboratory-services/for-providers/pathogen-surveillance-reports-antibiograms.

RSV Hospitalizations in Young Children in the U.S. During the 2025-2026 RSV Season[1]

RSV activity has persisted late in the season across many parts of the United States, with hospitalizations among infants and young children (particularly those under age 4 years) just now starting to decline in mid-March 2026



1. https://www.cdc.gov/rsv/php/surveillance/rsv-net.html.

RSV-Associated Morbidity Beyond Bronchiolitis

Challenge Question 1

What long-term morbidity is commonly associated with infants and children who have had an RSV infection?

1. Chronic ear infections
2. Delayed motor development
3. Type 1 diabetes
4. Wheezing and asthma

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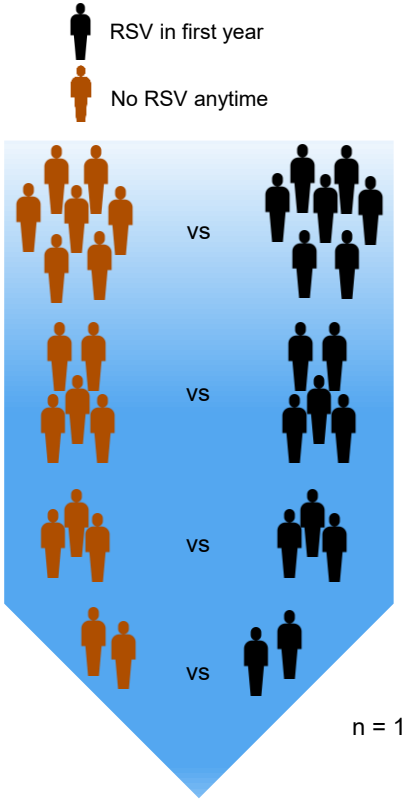
1. Chronic ear infections
2. Delayed motor development
3. Type 1 diabetes
4. **Wheezing and asthma**

The correct answer here is wheezing and asthma.

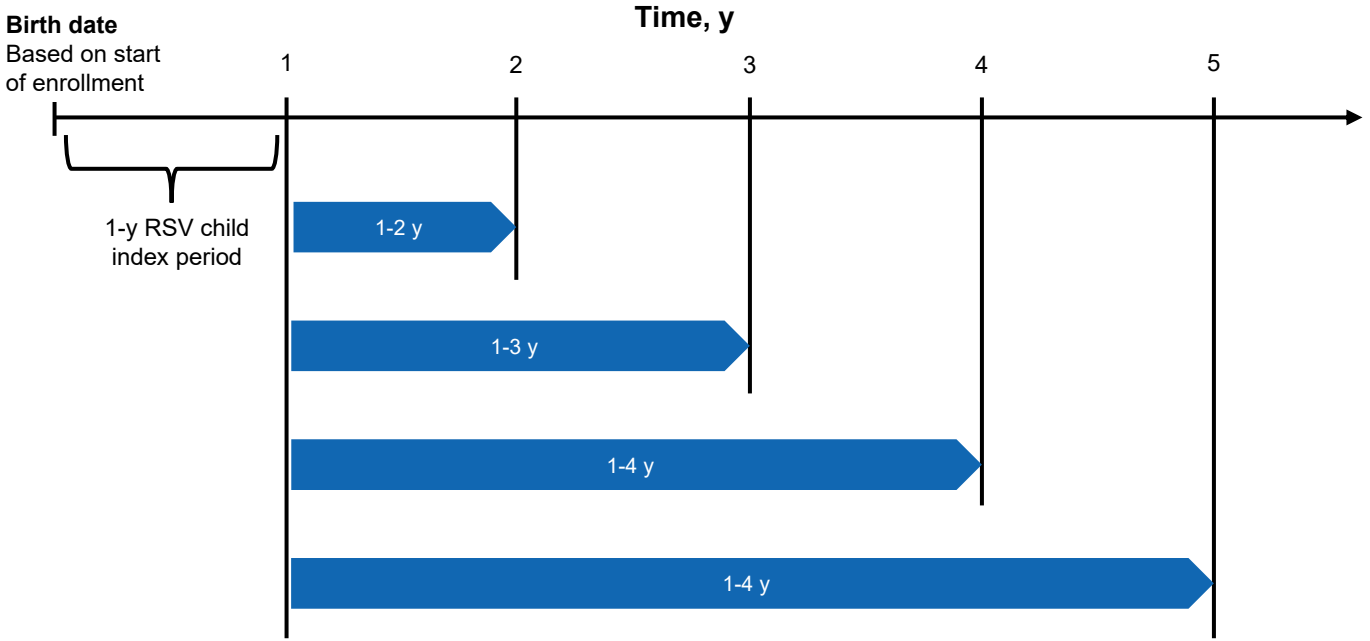
Let's talk about the incidence of post-RSV wheezing and asthma in infants and children in the United States.

Post-RSV Wheezing/Asthma in the United States, 2010-2016[1]



n = 124,894 pairs

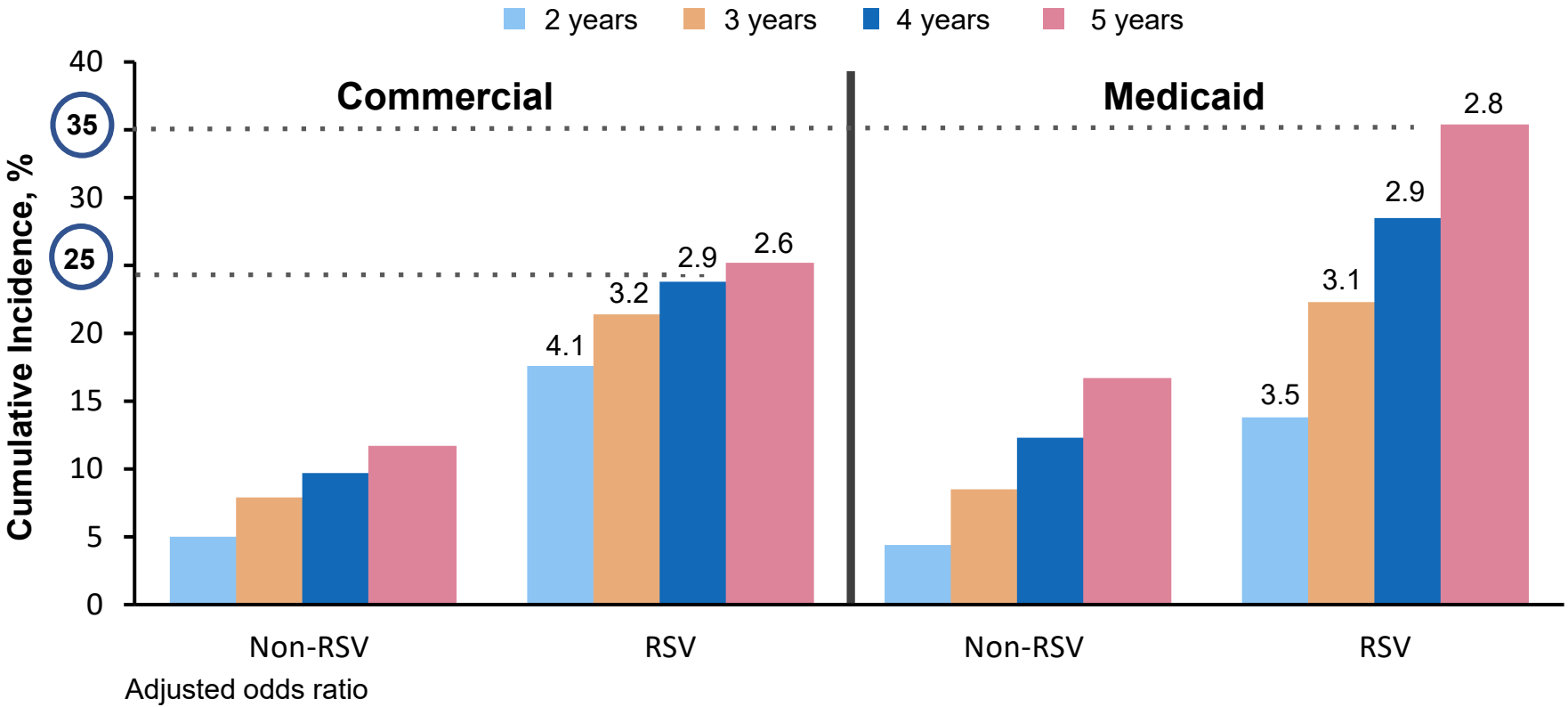
Attrition due to longer enrollment requirement



Follow-Up Period

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

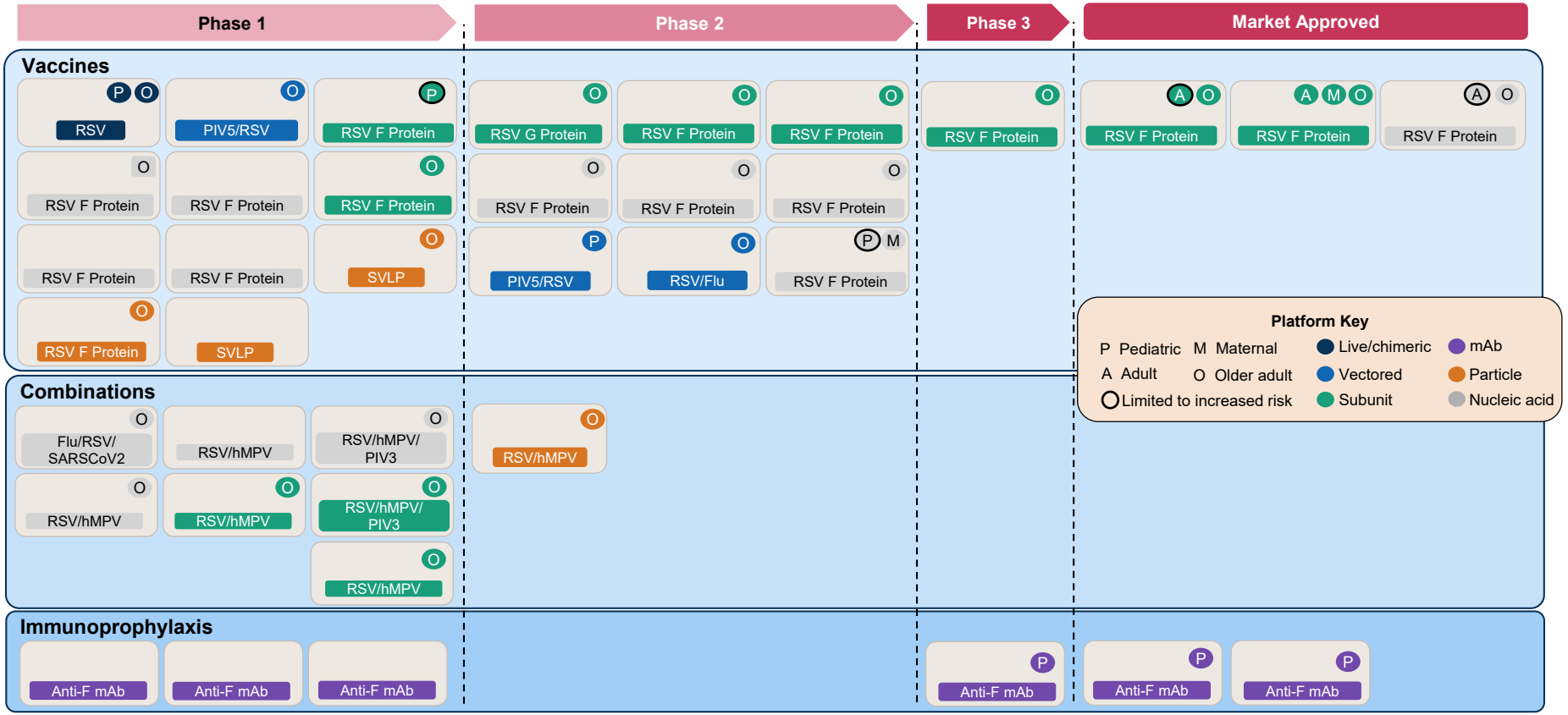
Cumulative Incidence of Post-RSV Recurrent Wheezing/Asthma[1]



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

Evidence Behind Maternal Vaccination and Monoclonal Antibodies for RSV Prevention

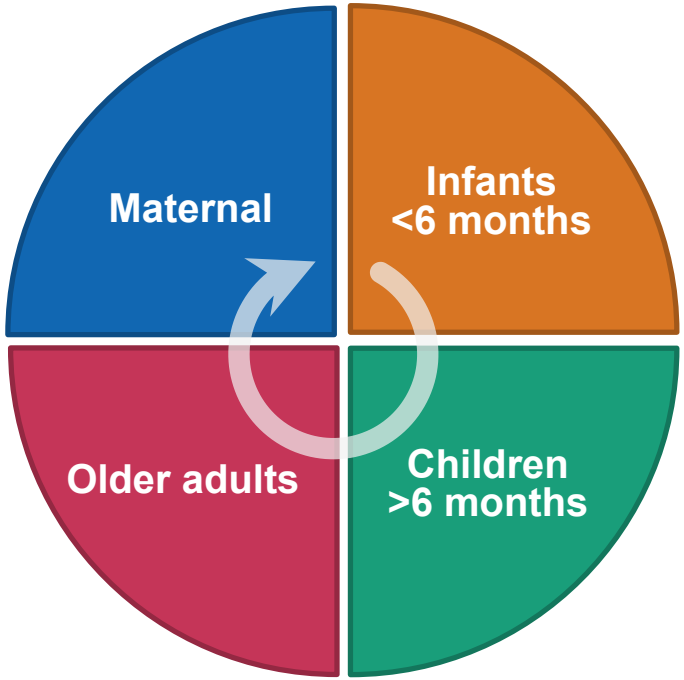
RSV Vaccine and Monoclonal Antibody (mAb) Snapshot[1]



1. https://www.path.org/our-impact/resources/rsv-vaccine-and-mab-snapshot.

PeerView

Target Populations for RSV Vaccine Types[1]



1. Mejias A et al. *Ann Allergy Asthma Immunol*. 2020;125:36-46.

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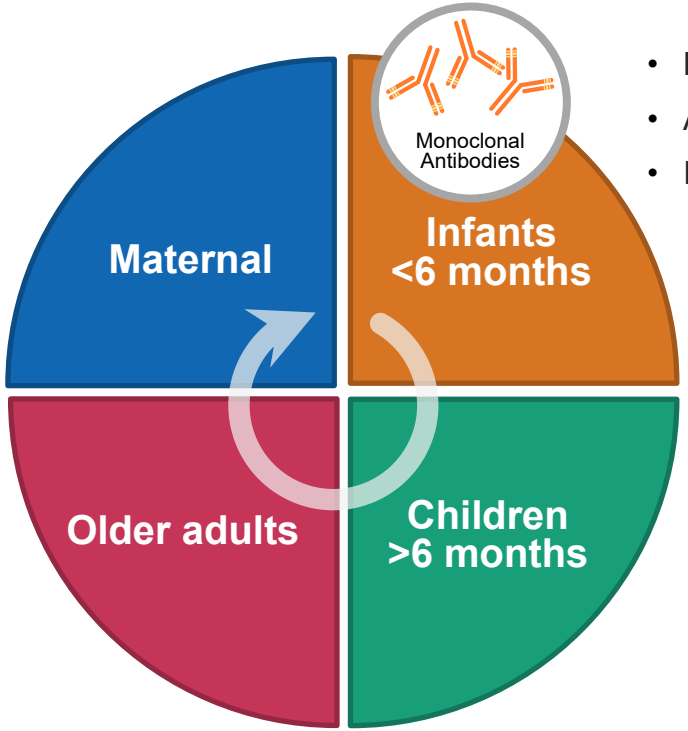

- Protection from severe disease
- Antigen naïve
- Immature immune system

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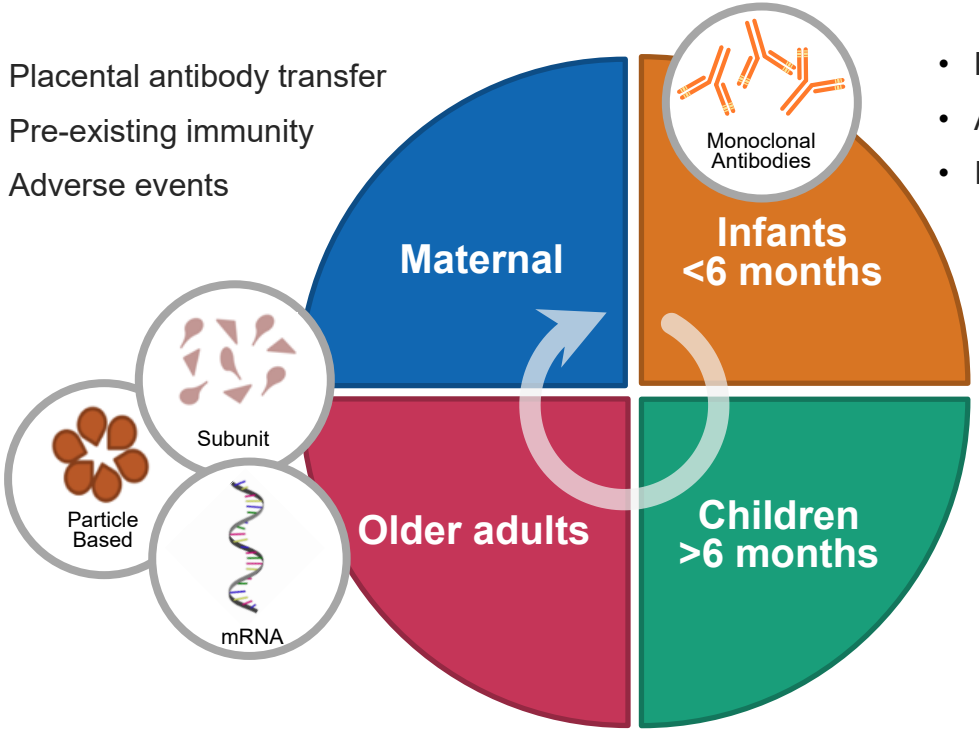
Target Populations for RSV Vaccine Types[1]

- Placental antibody transfer
- Pre-existing immunity
- Adverse events



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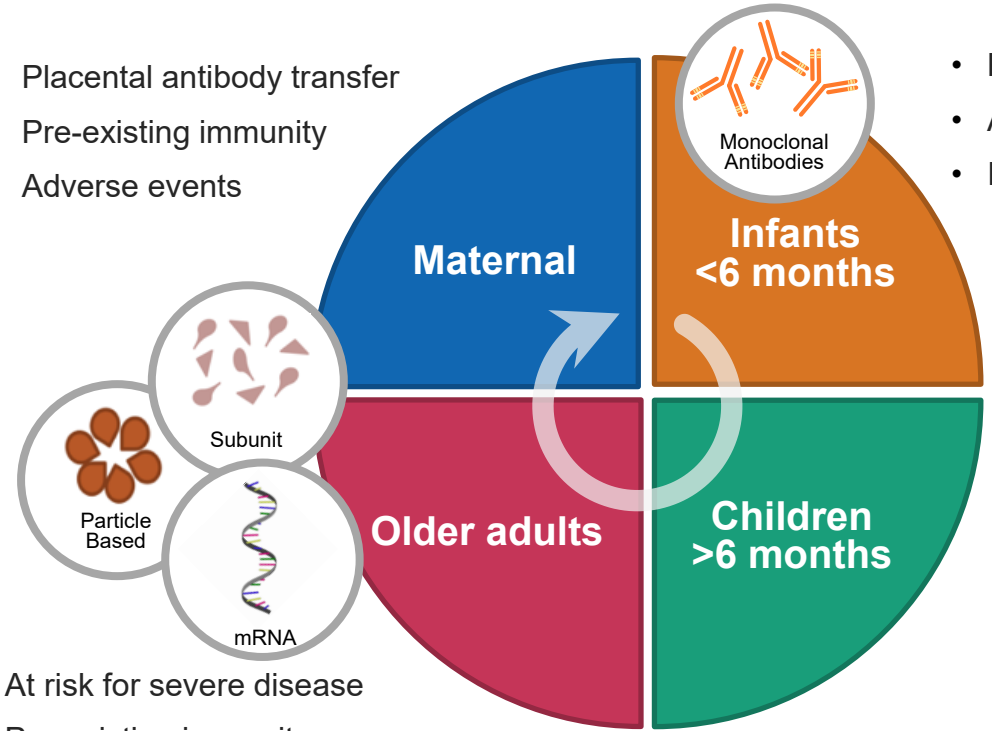

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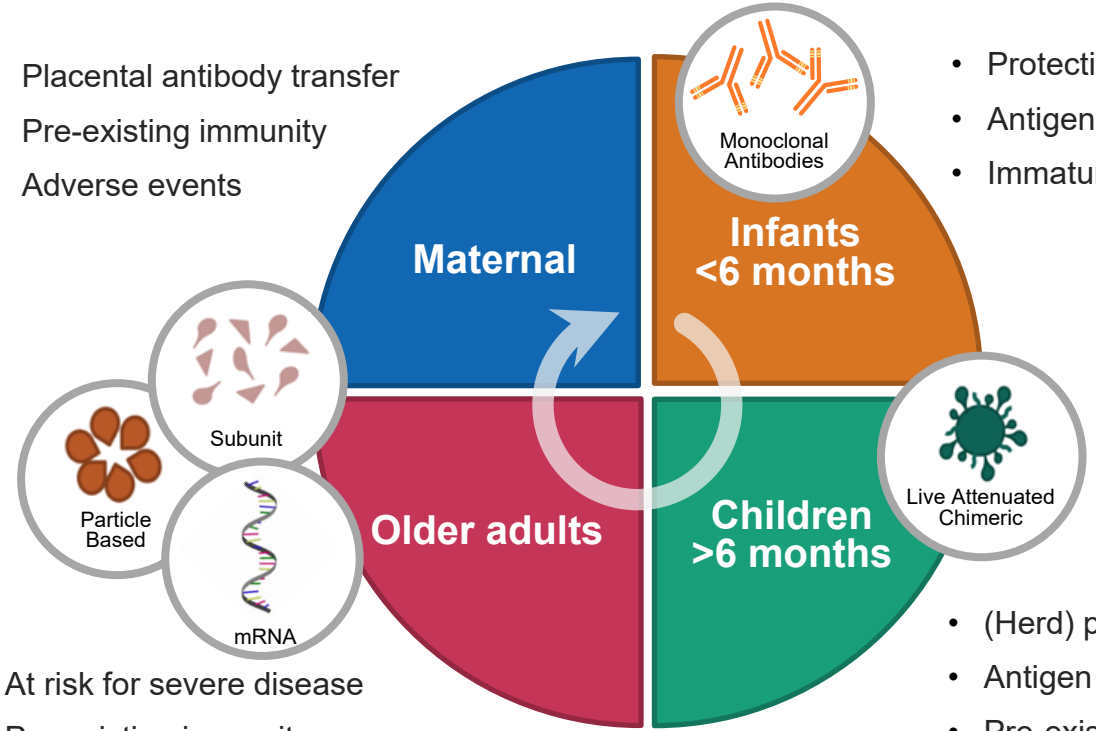

- Protection from severe disease
- Antigen naïve
- Immature immune system

- At risk for severe disease
- Pre-existing immunity
- Immunosenescence

- (Herd) protection
- Antigen naïve (<2 years)
- Pre-existing immunity

1. Mejias A et al. *Ann Allergy Asthma Immunol*. 2020;125:36-46.

Why Did It Take So Long to Develop Vaccines for RSV? Why Do We Have Different Options Now?

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- Peak of severe disease in young infants: rationale for passive immunization
- 1960s: formalin-inactivated vaccine legacy

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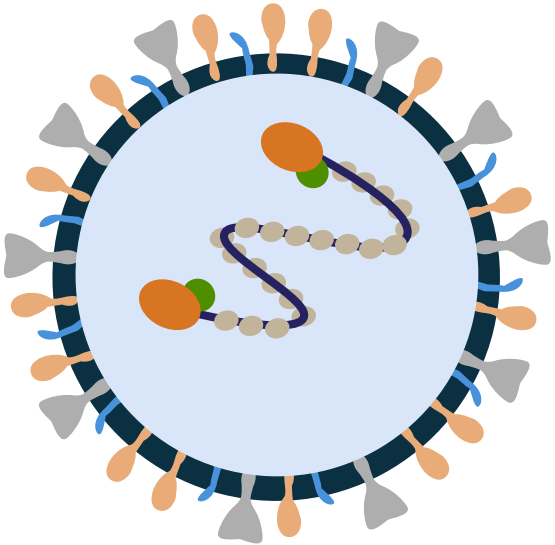
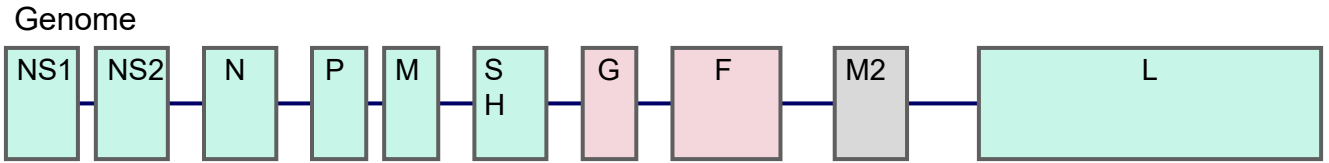
- Global impact of RSV (morbidity and mortality)
- RSV PreF structure solved in 2013

RSV: The Virus





1. Mejias A et al. *Vaccine*. 2017;35:496-502.

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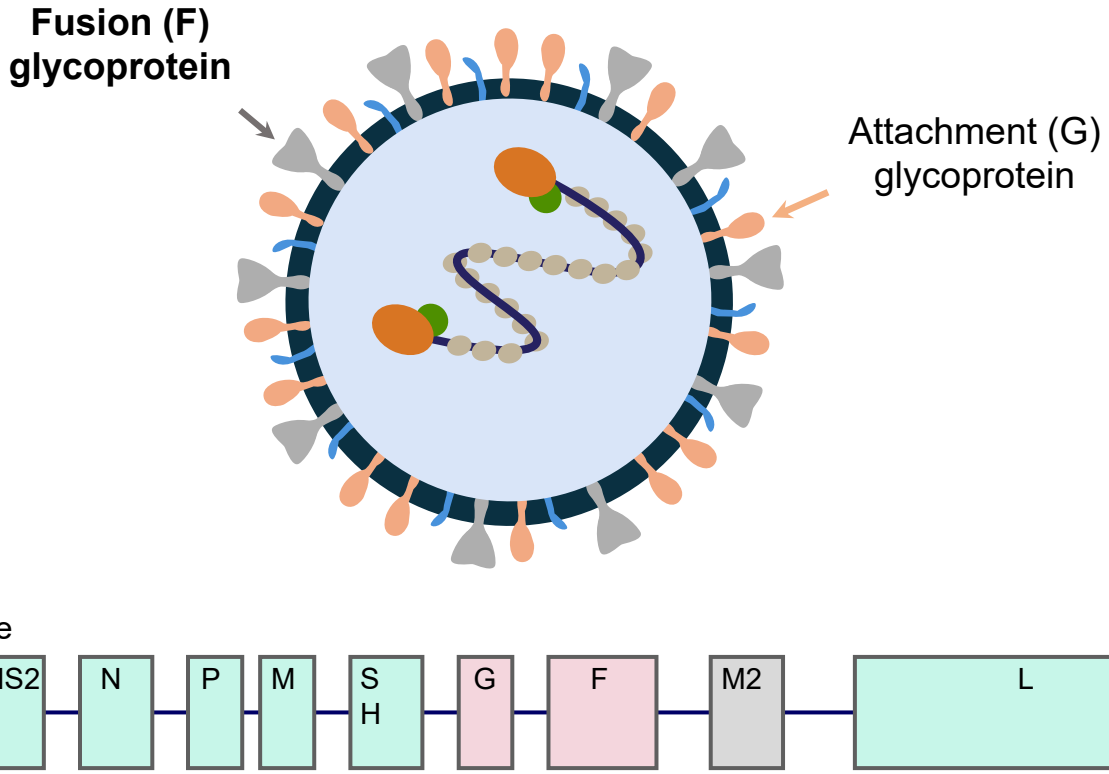

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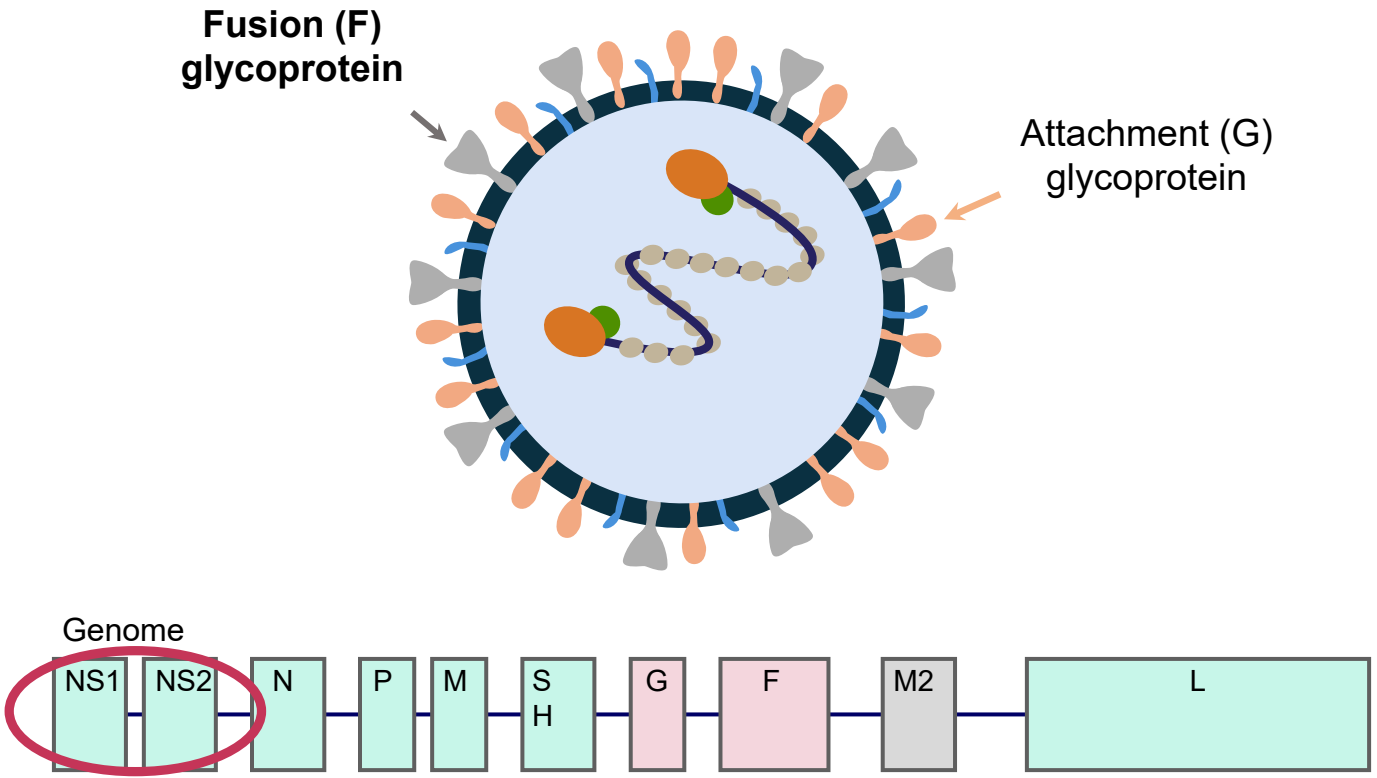

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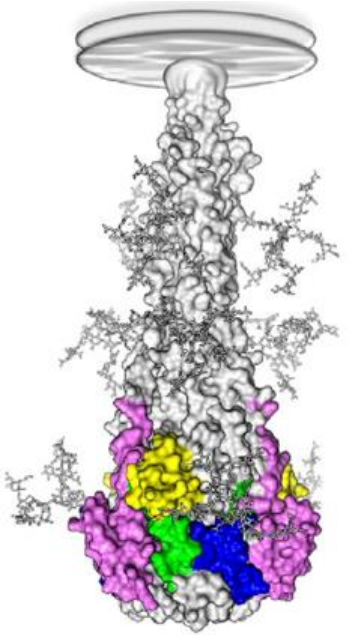
RSV PreF and PostF Antigenic Sites

Postfusion RSV F

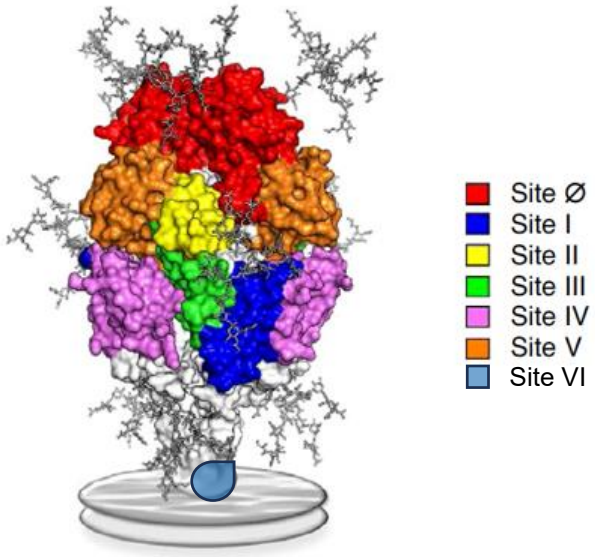


1. Graham B. *Curr Opin Immunol*. 2019:59:57-64.

RSV PreF and PostF Antigenic Sites

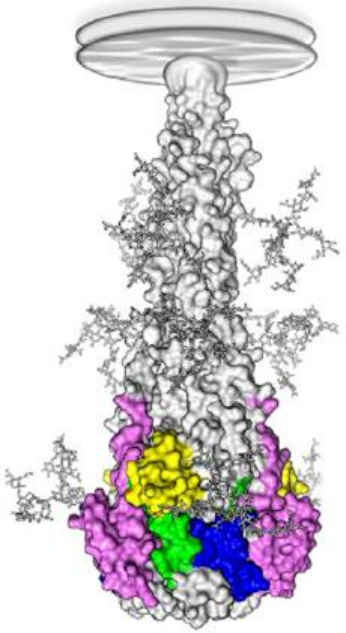
Antibodies that bind to pre-F are more efficient at neutralizing RSV than those against post-F

Prefusion RSV F



Structured-based vaccines

Postfusion RSV F



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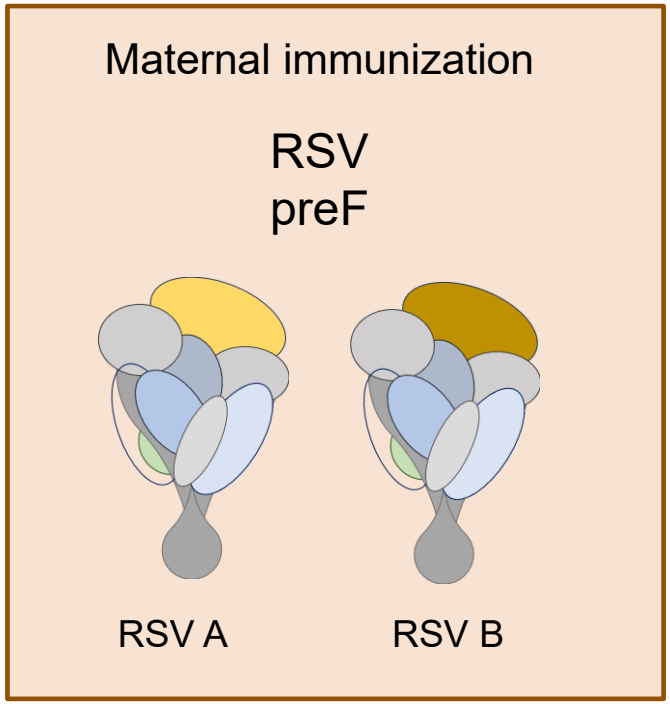
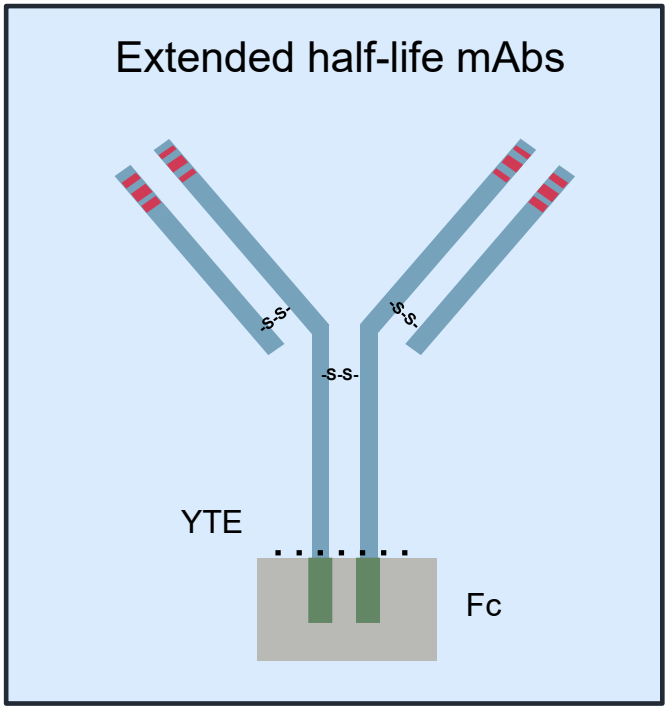
RSV Preventive Strategies for Young Infants





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

Rationale for Passive Immunization Against RSV in Young Infants

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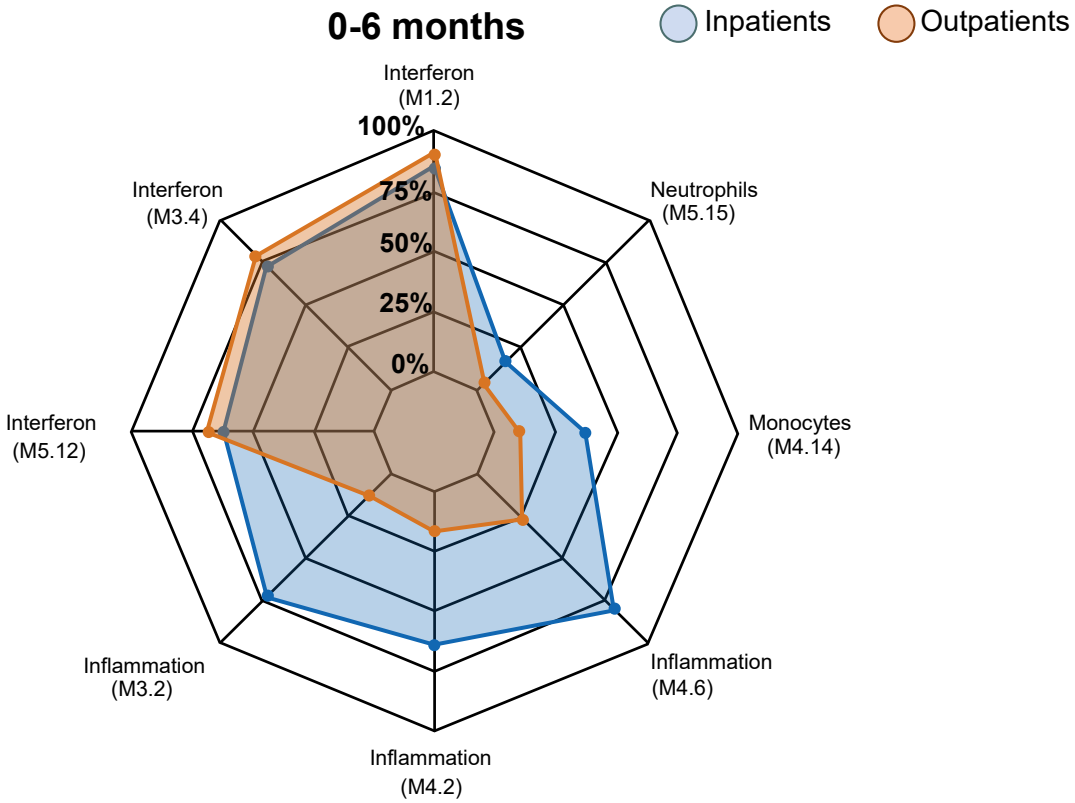
Impaired innate (IFN) immune responses

Rationale for Passive Immunization Against RSV in Young Infants

Impaired innate (IFN) immune responses

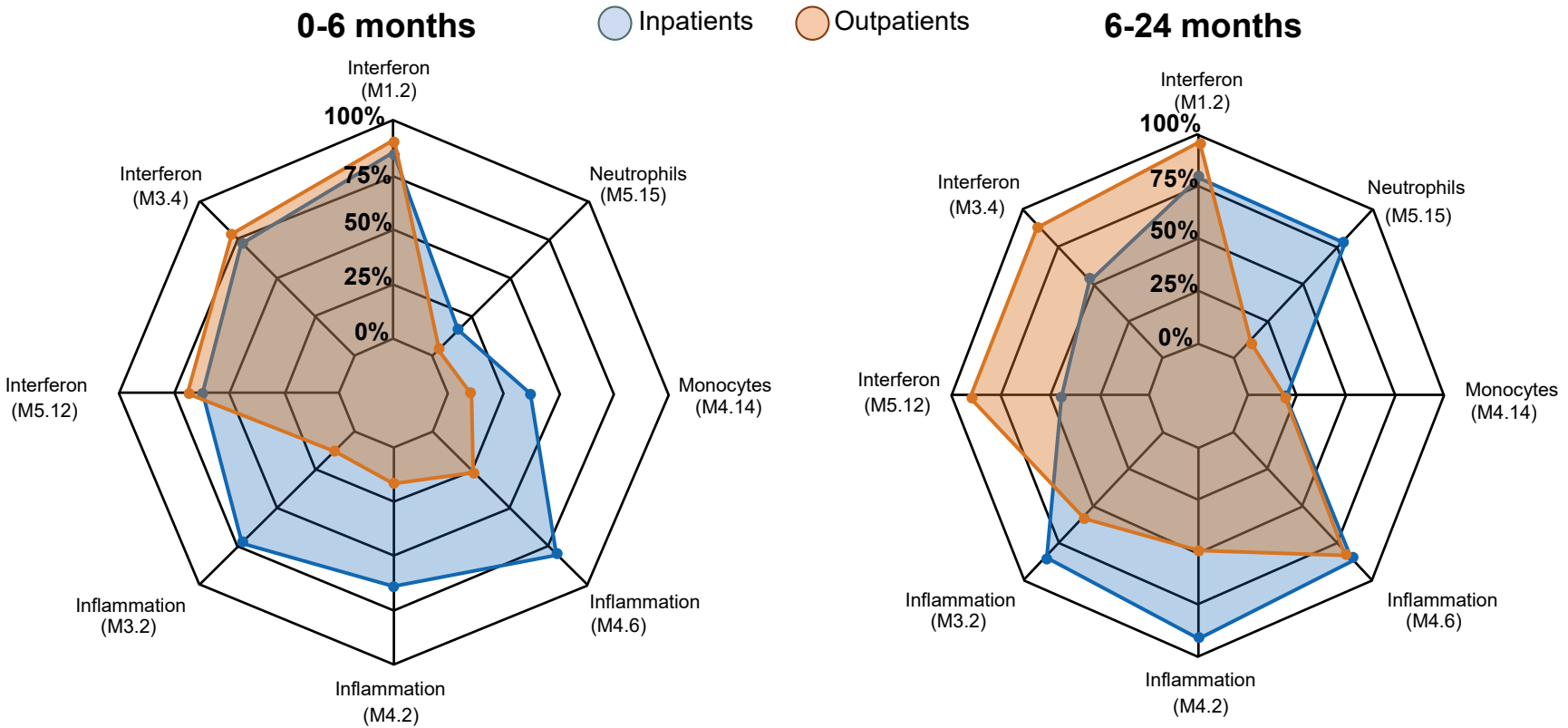
Inadequate antibody responses

RSV Immune Responses: Age and Disease Severity



1. Heinonen S et al. *Sci Transl Med*. 2020;12:eaaw0268.

RSV Immune Responses: Age and Disease Severity



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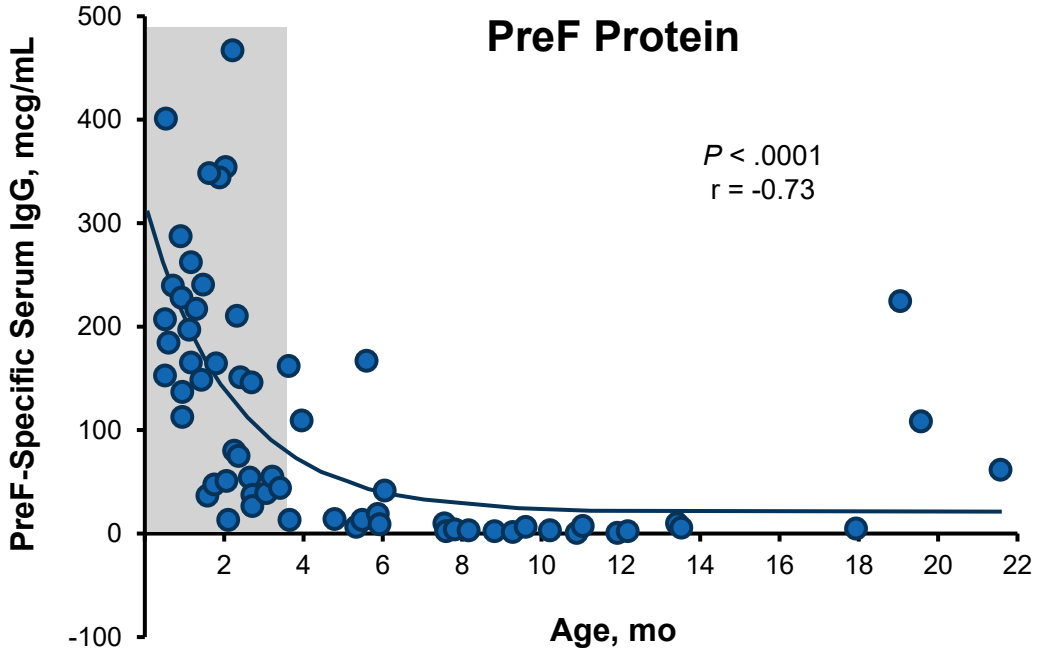
PeerView

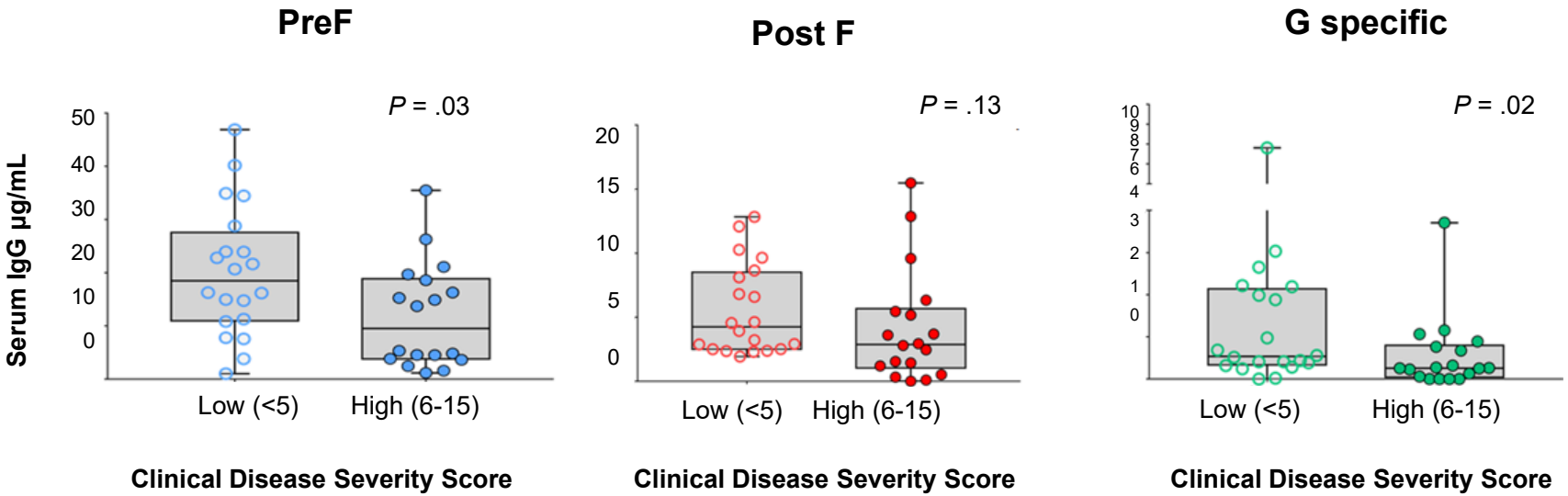
Maternal and Infant Antibody Responses

Serum IgG Antibodies Against RSV Glycoproteins Inversely Correlate With Age



n = 65; 45 hospitalized patients and 20 outpatients.
Spearman (r) correlation is indicated.
Nonlinear regression, one phase decay (shaded values).
1. Capella C et al. *J Infect Dis*. 2017;216:1398-1406.

Patients With Low Severity Scores Had Higher PreF- and G-Specific IgG Antibodies

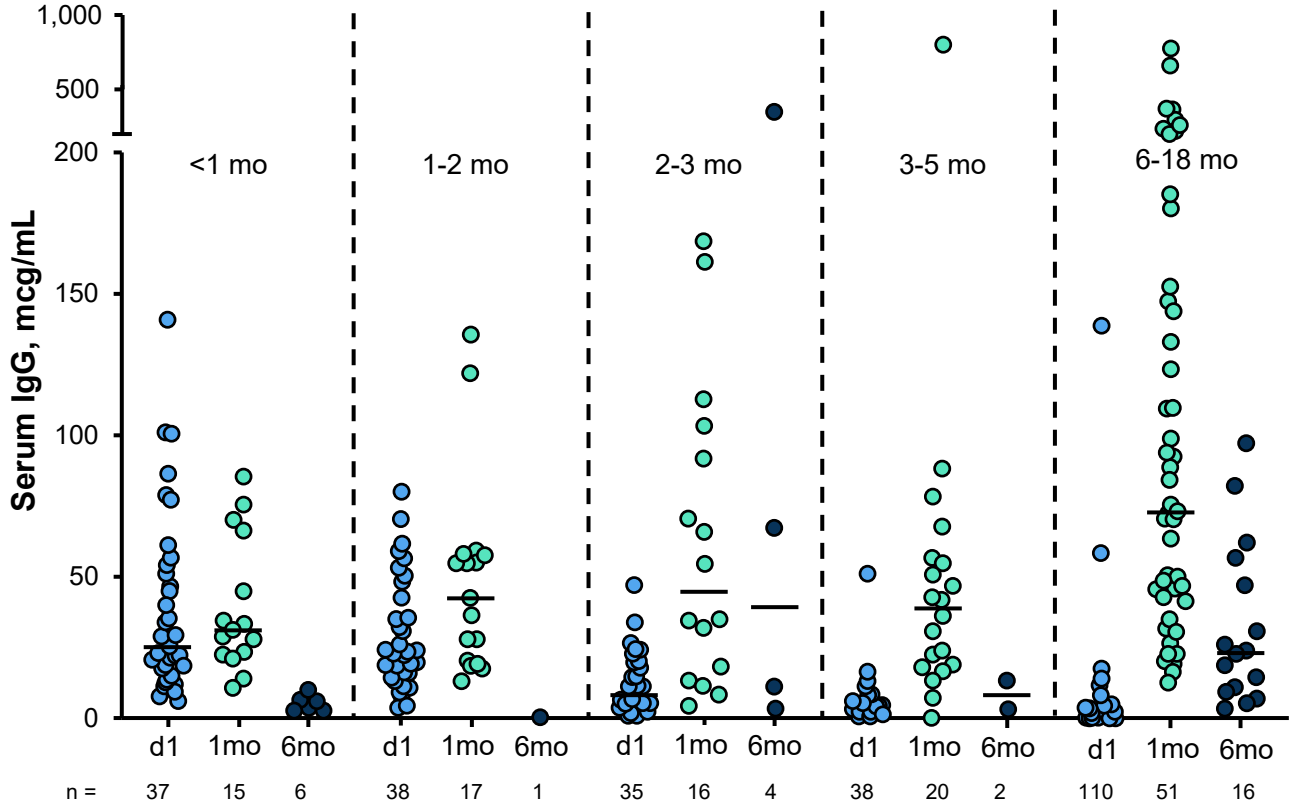


Patients ≤6 months of age.
n = 38 hospitalized patients.
Mann-Whitney, median (IQR).
1. Capella C et al. *J Infect Dis*. 2017;216:1398-1406.

PreF Antibody Concentrations During Acute RSV Infection and at 1 Month and 6 Months Impact of Age

1. Mejias A et al. RSVVW 2024.

PreF Antibody Concentrations During Acute RSV Infection and at 1 Month and 6 Months Impact of Age



1. Mejias A et al. RSVVW 2024.

PeerView

Maternal Vaccination Against RSV

MATISSE: Phase 3 Trial of RSVpreF Vaccine in Pregnancy

- **Phase 3 double-blind RCT: 120 µg RSVpreF (A/B) non-adjuvanted or placebo (1:1)**
  - Single dose
  - Second to third trimester 24-36 weeks gestation
- **Primary endpoints assessed through 90 to 180 days after birth**
  - Severe MA RSV-LRTIs in infants
  - MA RSV-LRTIs in infants

18 countries
2 seasons
7,420 maternal
7,307 infants

1. Kampmann B et al. *N Engl J Med*. 2023;388:1451-1464.

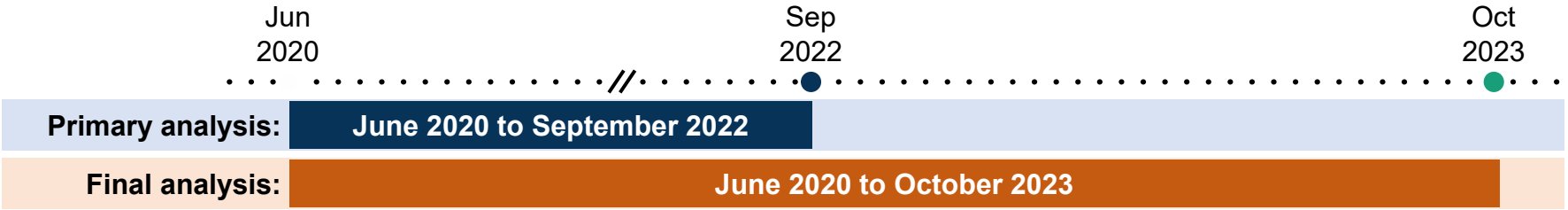
MATISSE: Study Outcomes and Timeline[1]

Maternal participants:
Safety 6 months after delivery

7,386
(+29 more than primary analysis)

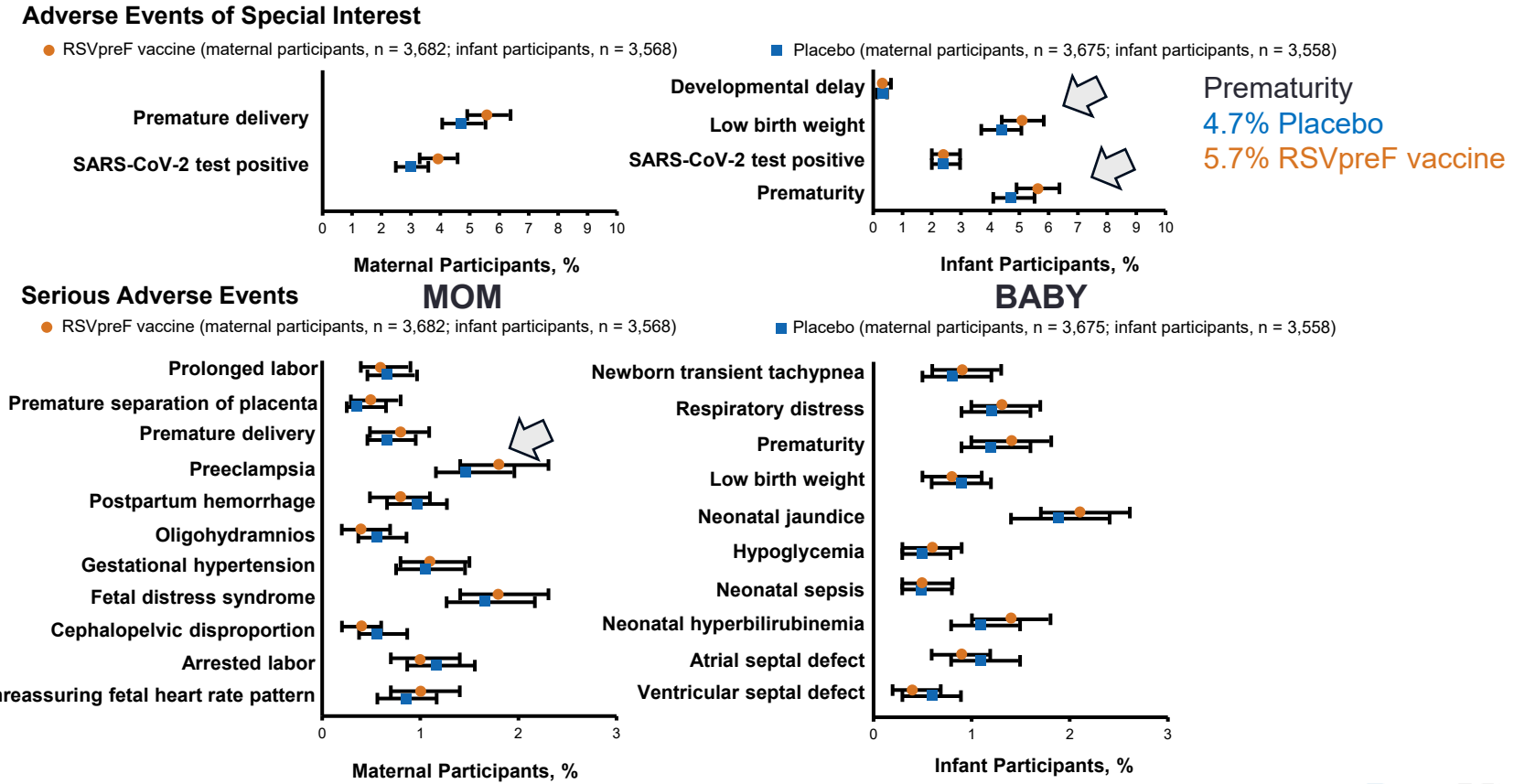
Infant participants:
Safety and respiratory surveillance up to 2 years

7,307
(181 more than primary analysis)



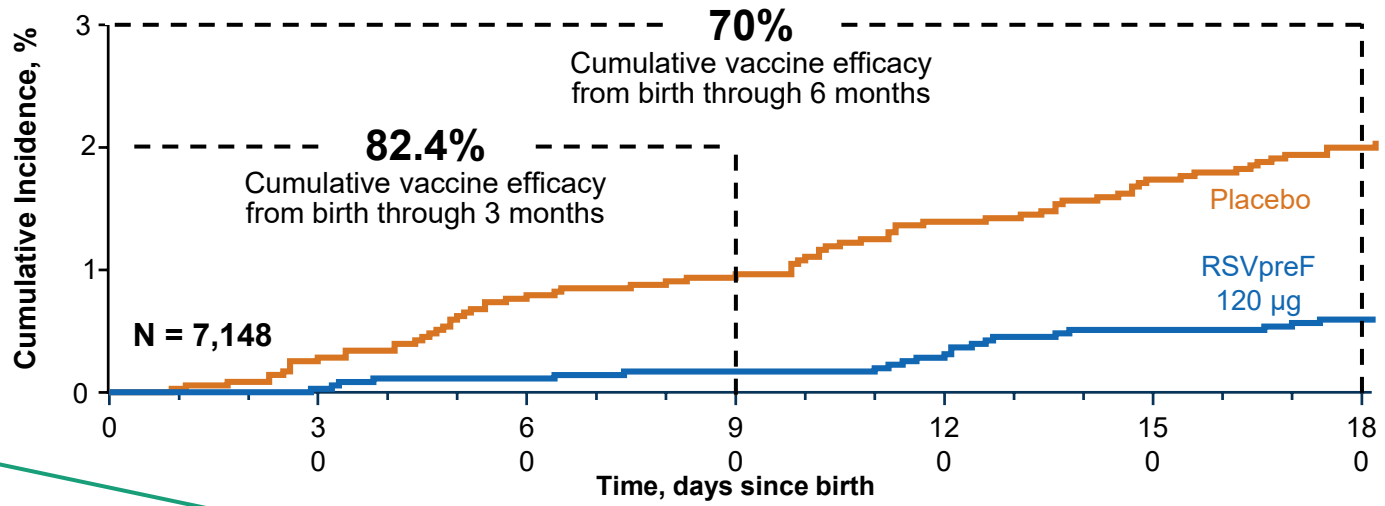
1. Simoes EA et al. *Obstet Gynecol*. 2025;145:157-167.

MATISSE: No Difference in AESI or SAE[1]



1. Kampmann B et al. *N Engl J Med.* 2023;388:1451-1464.

MATISSE Final Analysis: Efficacy By Month Against Severe RSV-Associated MALRTI in Infants From Birth to 6 Months of Age



High efficacy against severe disease from birth

Cumulative cases	RSVpreF 120 µg	1	4	6	13	18	21
	Placebo	10	28	34	49	61	70
Incremental cases	RSVpreF 120 µg	1	3	2	7	5	3
	Placebo	10	18	6	15	12	9
Incremental vaccine efficacy[2]		**90.0**	**83.3**	**66.7**	**53.8**	**58.3**	**66.7**

1. Simões EAF et al. *Obstet Gynecol*. 2025;145:157-167. 2. Simões EAF et al. *Obstet Gynecol*. 2025;145:157-167; Erratum forthcoming April 2025.

Imbalance of Preterm Birth Observed in Clinical Trials for the RSVpreF Vaccine in Pregnant Persons[1]

In clinical trials, maternal RSV vaccine was administered at 24-36 weeks' gestation, and more preterm births and hypertensive disorders of pregnancy were observed among pregnant people who received maternal RSV vaccine (RSVpreF) vs placebo, but the **differences were not statistically significant**

- *Data were insufficient to establish or exclude a causal relationship*

FDA approved maternal RSV vaccine (RSVpreF) for use in pregnant persons at 32-36 weeks' gestation to avoid the potential risk of preterm birth at <32 weeks' gestation

ACIP judged **the benefits** of RSV vaccine (RSVpreF) at 32-36 weeks' gestation to **outweigh the potential risk for preterm birth and hypertensive** disorders of pregnancy

1. Fleming-Dutra KE et al. *MMWR Morb Mortal Wkly Rep.* 2023;72:1115-1122.

Maternal RSV Vaccine Safety: First Season Analysis of Preterm Birth and Those Small for Gestational Age[1-3]

- Preliminary findings from the first season of maternal RSV vaccine in a Vaccine Safety Datalink (VSD) study found that **maternal RSV vaccine during 32 to 36 weeks' gestation was not associated with an increased risk of preterm birth or small for gestational age[1]**
  - The RSV workgroup felt that these data were very reassuring

	Matched Pairs, N	Events in Those RSV Vaccinated, N (%)[c]	Events in Those Unvaccinated and Matched, N (%)[c]	Risk Ratio (95% CI)
Preterm birth[a]	13,965	563 (4.0)	628 (4.5)	0.90 (0.80-1.00)
SGA at birth[b]	11,819	799 (6.8)	774 (6.5)	1.03 (0.94-1.14)

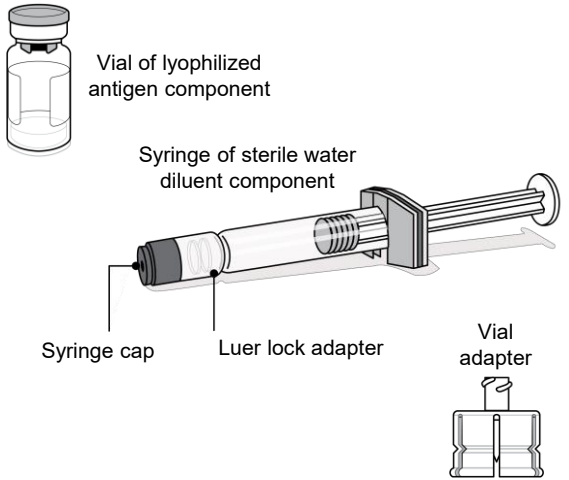
[a] Preterm birth = birth <37 weeks gestational age. [b] SGA at birth = "small for gestational age"; birthweight <10th percentile for gestational age compared with a US reference population.
[c] Events only included through date of censoring when unvaccinated pair crosses over to vaccinated.

1. https://www.cdc.gov/acip/grade/pfizer-RSVpreF-pregnant-people.html. 2. https://www.cdc.gov/acip/downloads/slides-2024-10-23-24/03-RSV-Mat-Peds-DeSilva-508.pdf.
3. Talge NM et al. *Pediatrics*. 2014;133:844-853.

RSV Vaccine Products Currently Indicated for Pregnant Persons[1]

RSVpreF
Recombinant bivalent prefusion F protein vaccine

Requires reconstitution (kit)
Dose: 0.5 mL IM
FDA approved: August 2023
Indicated for individuals who are
pregnant at 32-36 weeks gestational age
or individuals ≥18 y



1. Abrysvo (respiratory syncytial virus vaccine) Prescribing Information. https://labeling.pfizer.com/ShowLabeling.aspx?id=19589.

Maternal Vaccine Effectiveness: 2023-2024 Season[1-4]

Study	Country/ Coverage	Study Design	Sample Size	Effectiveness
Son M et al 2024	USA/ coverage 33%-44%	Retrospective; 2 NYC hospitals	1,026/2,973	• Effectiveness not assessed • No increased risk of prematurity or perinatal outcomes
MSAL 2024	Argentina/ coverage 62%	Surveillance network for Argentina (IRAG)	854 458 RSV+/396(-)	• Hospitalizations; 0-3 mo: **67%;** <6 mo: **62%** • Severe disease (<6 mo): **70%**
Marc GP et al 2025	Argentina/ coverage 62%	Multicenter, 12 hospitals (6 provinces)	505 286 RSV+/219(-)	• Hospitalizations; 0-3 mo: **79%;** <6 mo: **71%** • Severe disease (<6 mo): **77%** • Deaths: 0 and 3 in vaccinees vs nonvac
Gentile A et al 2025	Argentina/ coverage 62%	Multicenter, 4 public hospitals	187 91 RSV+/96(-)	• Hospitalizations; 0-3 mo: **79%;** <6 mo: **68%** • Oxygen use reduced by 3 d (4 vs 7) • LOS reduced by 3 d (5 vs 8)

MATISSE RCT efficacy (hospitalization): **68%** 0-3 mo; **57%** <6 mo and for severe disease: **82%** 0-3 mo; **70%** <6 mo

1. Son M et al. *JAMA Netw Open.* 2024;7:e2419268. 2. Vazquez. Sociedad Latinoamericana de Vacunología 2025.
3. Marc GP et al. *Lancet Infect Dis*. 2025;25:1044-1054. 4. Gentile A et al. *Pediatr Infect Dis J.* 2025;44:988-994.

Challenge Question 2

Your 28-year-old patient who is 33 weeks and 4 days pregnant presents for a routine OB visit in November and asks if she should get the RSV vaccine today. How do you respond to her question?

1. She should wait until she is 38 weeks pregnant to get vaccinated
2. She can receive the RSVpreF vaccine
3. She can receive the RSVpreF3 vaccine
4. She can receive the mRNA-1345 vaccine

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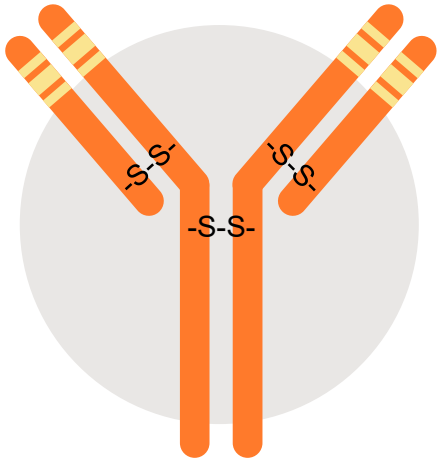
1. She should wait until she is 38 weeks pregnant to get vaccinated
2. **She can receive the RSVpreF vaccine**
3. She can receive the RSVpreF3 vaccine
4. She can receive the mRNA-1345 vaccine

The correct answer here is that she can receive the RSVpreF vaccine, based on her weeks of gestation and because it is the only RSV vaccine to date to be studied for and approved in this population.

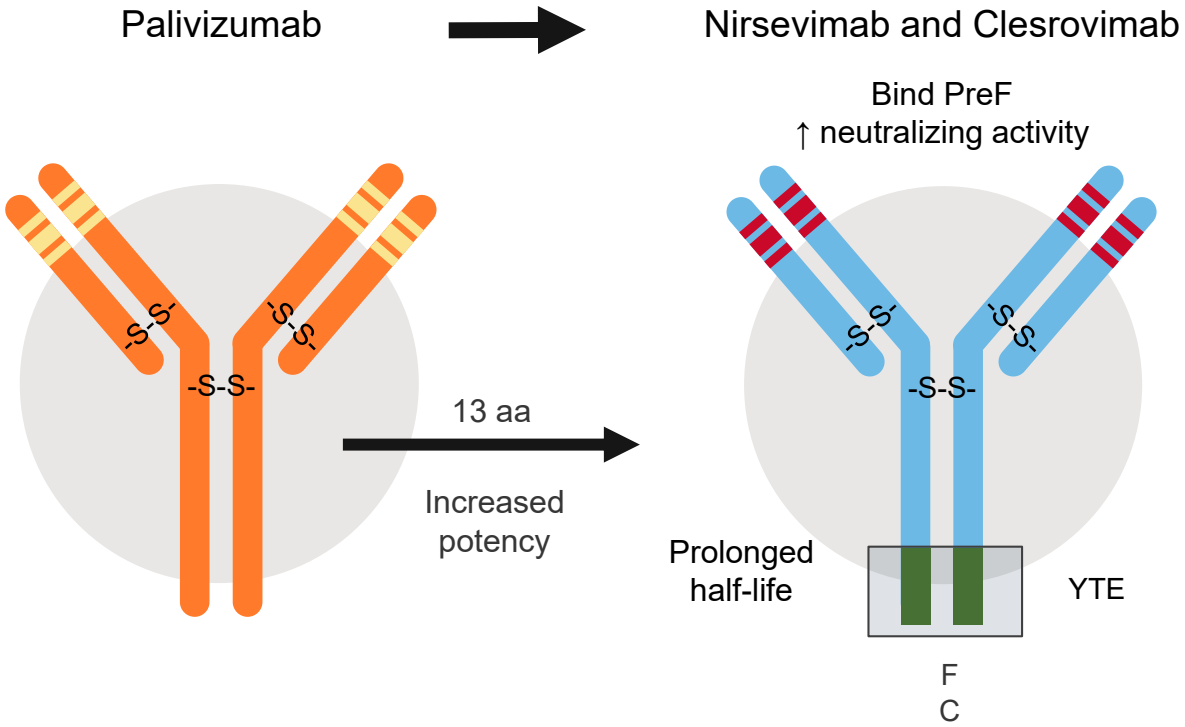
Development of Anti-RSV Monoclonal Antibodies

Advances on Anti-RSV Neutralizing Monoclonal Antibodies

Palivizumab



Advances on Anti-RSV Neutralizing Monoclonal Antibodies

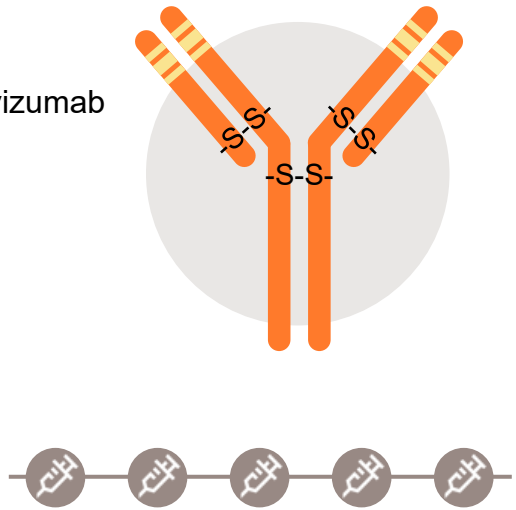


Reinventing the Role of mAbs for Prevention of RSV

1. Courtesy of Dr. Ramilo.

Reinventing the Role of mAbs for Prevention of RSV

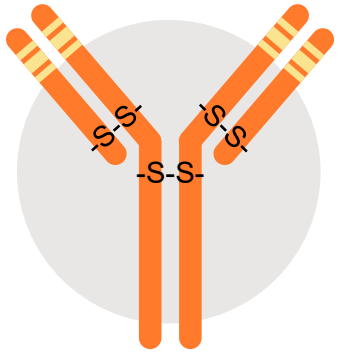
Palivizumab

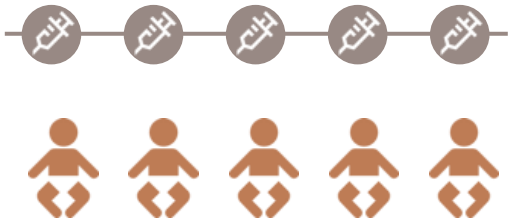


1. Courtesy of Dr. Ramilo.

Reinventing the Role of mAbs for Prevention of RSV

Palivizumab

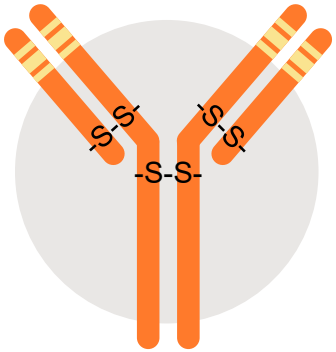


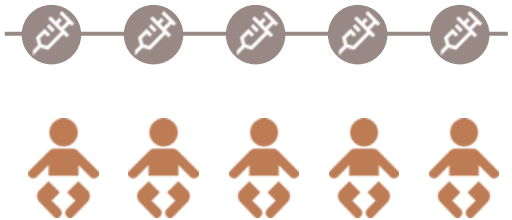


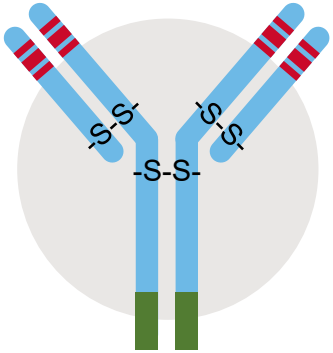
1. Courtesy of Dr. Ramilo.

Reinventing the Role of mAbs for Prevention of RSV

Palivizumab





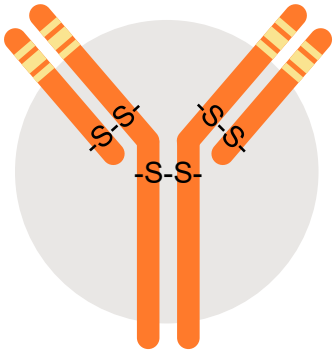


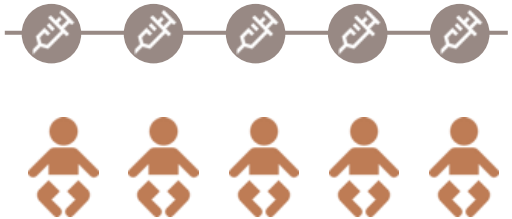
Nirsevimab
Clesrovimab

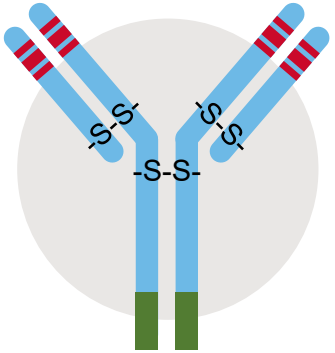
1. Courtesy of Dr. Ramilo.

Reinventing the Role of mAbs for Prevention of RSV

Palivizumab







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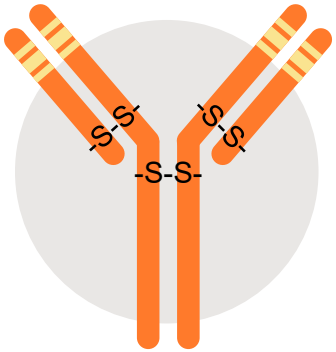
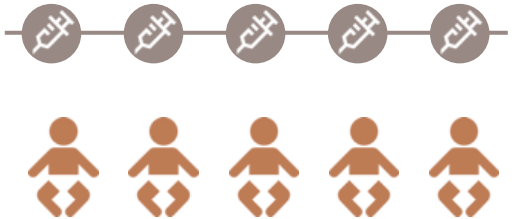
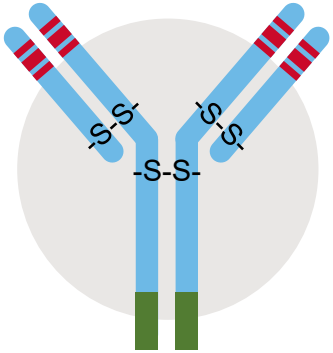
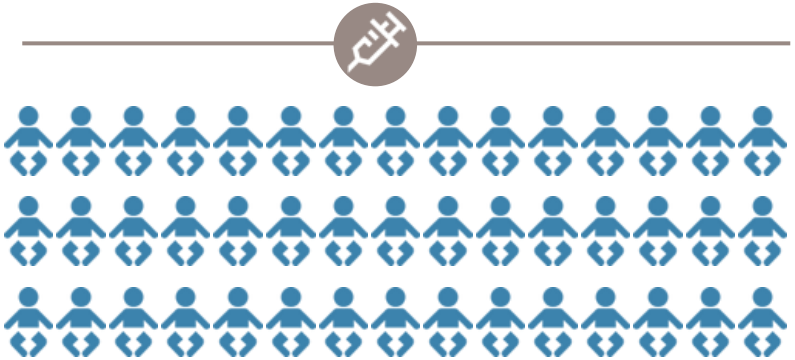






Nirsevimab
Clesrovimab



1. Courtesy of Dr. Ramilo.

Efficacy and Safety of Monoclonal Antibodies

Challenge Question 3

You are seeing a healthy 5-day old infant for her first well baby visit. She was born December 1 at 39 weeks and 6 days. Her mother did not receive the maternal RSV vaccine during pregnancy and would like to know if her baby can get the RSV monoclonal antibody?

1. Yes, but the baby can only receive nirsevimab
2. Yes, but the baby can only receive clesrovimab
3. Yes, the baby can receive either nirsevimab or clesrovimab
4. No, the baby is not considered high risk

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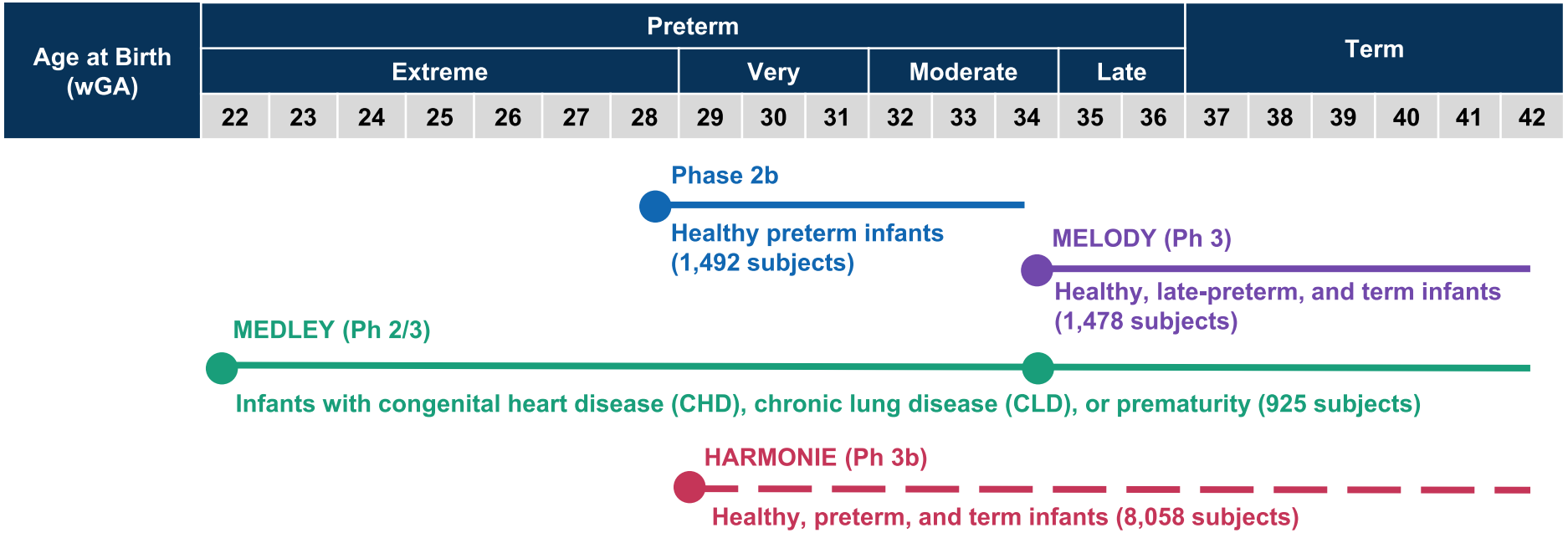
1. Yes, but the baby can only receive nirsevimab
2. Yes, but the baby can only receive clesrovimab
3. **Yes, the baby can receive either nirsevimab or clesrovimab**
4. No, the baby is not considered high risk

The correct answer here is that the baby is indicated for an RSV monoclonal antibody because she was born during RSV season and her pregnant parent did not receive the RSV vaccine.

As we'll discuss, both nirsevimab and clesrovimab are approved for all infants <8 months old born during or entering their first RSV season.

Nirvesimab Is Designed to Protect All Infants From RSV[1-4]

Clinical Development Program



1. Griffin MP et al. *N Engl J Med.* 2020;383:415-425. 2. Hammitt LL et al. *N Engl J Med.* 2022;386:837-846.
3. Domachowske JB, et al. *N Engl J Med.* 2022;386:892–894. 4. Drysdale SB et al. *N Eng J Med.* 2023;389:2425–2435.

Nirsevimab: Safety Profile Across Broad Infant Population

	Phase 2b 29 to <35 wGA		MELODY All Subjects ≥35 wGA		MEDLEY Season 1 Preterm		MEDLEY Season 1 CHD/CLD		MEDLEY[a] Season 2 CHD/CLD		
	Placebo (n = 479)	Nirsevimab (n = 968)	Placebo (n = 996)	Nirsevimab (n = 1,998)	Palivizumab (n = 206)	Nirsevimab (n = 406)	Palivizumab (n = 98)	Nirsevimab (n = 208)	Pali/Pali (n = 42)	Pali/Nirs (n = 40)	Nirs/Nirs (n = 180)
Serious adverse events, %	16.9	11.2	7.4	6.3	5.3	6.9	20.4	19.2	0	10	9.4
Adverse events of grade 3 or higher, %	12.5	8.0	3.8	3.1	3.4	3.4	13.3	14.4	2.4	10	7.8
Adverse events of special interest, %	0.6	0.5	0	0.2	0	0.2	0	0.5	0	0	0
Deaths, n	3	2	0	4	0	2	1	3	0	0	0

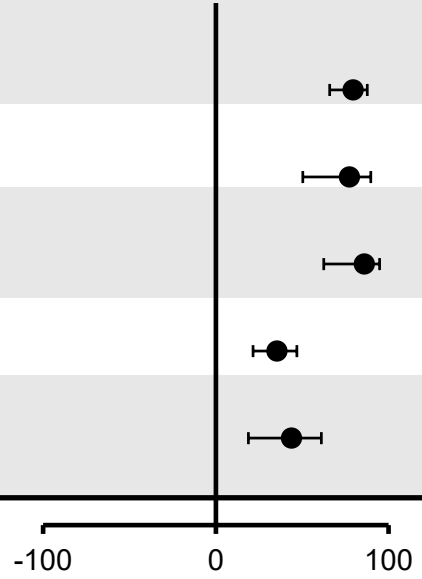
- None of the serious adverse events or deaths were considered related to nirsevimab
- Overall, incidence of nirsevimab antidrug antibody was low across studies with no safety concerns
- Nirsevimab had a favorable safety profile with similar types and frequencies of adverse events compared with placebo or palivizumab groups

[a] Groups' labels indicate which product the participants received in both seasons (season 1/season 2).

1. Griffin MP et al. *N Engl J Med.* 2020;383:415-425. 2. Muller WJ et al. *N Engl J Med*. 2023;388:1533-1534. 3. Domachowske JB, et al. *N Engl J Med.* 2022;386:892-894. 4. Domachowske JB et al. *J Pediatric Infect Dis Soc.* 2023;12:477-480. 5. Hammitt LL et al. *N Engl J Med*. 2022;386:837-846.

Nirsevimab: Consistent Efficacy Across RSV Confirmed MA-LRTIs of Different Severities[1]

	Placebo (n = 786) n (%)	Nirsevimab (n = 1,564) n (%)	Efficacy, %	95% CI[a]	*P*[b]
RSV confirmed MA-LRTIs[b]	51 (6.5)	19 (1.2)	**79.5**	65.9-87.7	<.0001
RSV confirmed MA-LRTIs with hospitalization[b]	21 (2.7)	9 (0.6)	**77.3**	50.3-89.7	.0002
RSV confirmed MA-LRTIs (very severe)[c]	18 (2.3)	5 (0.3)	**86.0**	62.5-94.8	<.0001
Medically attended all-cause LRTI	149 (19.0)	191 (12.2)	**35.4**	21.5-46.9	<.0001
Medically attended all-cause respiratory illness with hospitalization	51 (6.5)	57 (3.6)	**43.8**	18.8-61.1	<.0022



[a] Estimated based on Poisson regression with robust variance (including study as a covariate); not corrected for multiplicity.
[b] Included imputation of missing data. [c] Defined as those cases requiring supplemental oxygen or intravenous fluids (exploratory endpoint).
1. Simões EAF et al. *Lancet Child Adolesc Health.* 2023;7:180-189.

Nirsevimab: Effectiveness Against RSV Hospitalization 2023-24 Season[1-7]

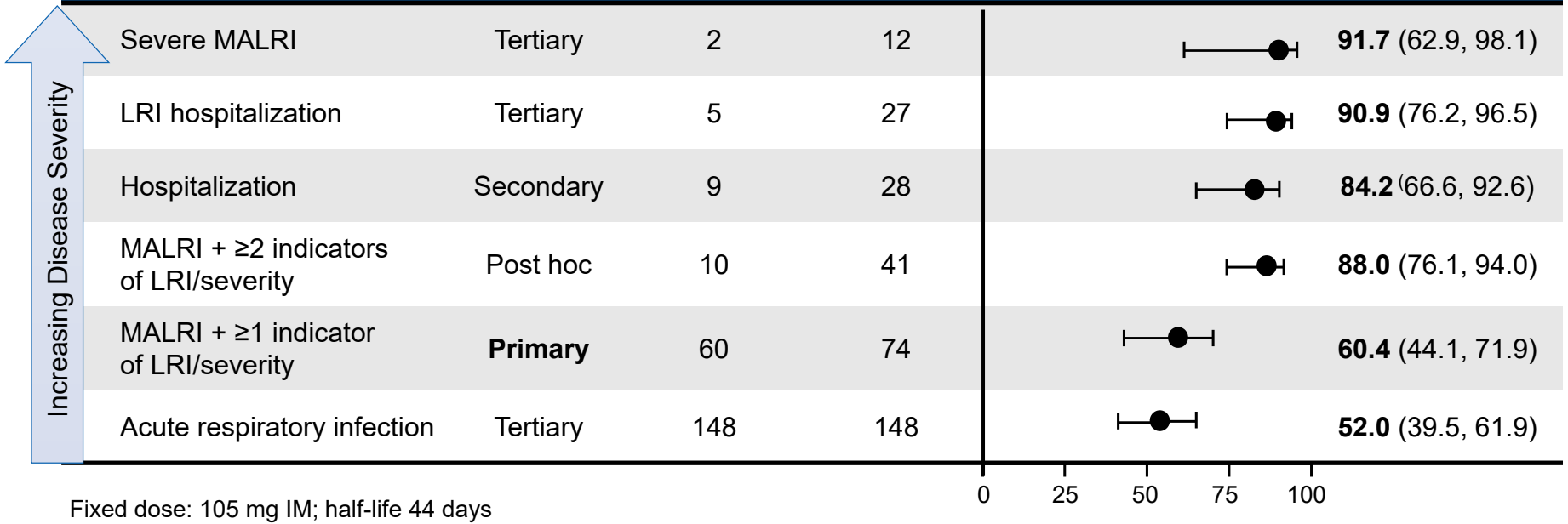
Study	Country/ Coverage	Study Design	Sample size	Effectiveness
Moline HR et al 2024	USA/ coverage <40%[a]	7 pediatric academic centers; Test negative study design	n = 699 infants (407 cases/292 control)	**90%** (75%-96%)
Lopez-Lacort M et al 2024	Valencia, Spain/ coverage ~89%	9 pediatric hospitals; test negative study design	n = 166/15,765 (95 cases/71 control)	**84%** (77%-90%)
Ares-Gomez S et al 2024	Galicia, Spain/ coverage 92%	Population based; https://www.nirsegal.es/en	n = 46/9,408 (30 cases/16 control)	**82%** (77%-90%)
Coma E et al 2024	Cataluna, Spain/ coverage 82%	Population based; case control	n = 26,525 (23,127 cases/3,398 control)	**88%** (77%-92%)
Assad Z et al 2024	France/ coverage 15%	ENVIE (multicenter); matched case/control 2:1	n = 1,035 (690 cases/345 control)	**83%** (73%-89%)
Ernst C et al 2024	Luxembourg/ coverage 84%	4 maternity hospitals; pre and post nirsevimab	n = 1,277 (232 vs 72)	**70%**
Torres JP et al 2025	Chile/ coverage 94%	Population based; https://nirse.isci.cl	n = 154,173	**76%** (69%-81%)

[a] https://www.cdc.gov/rsvvaxview.

1. Moline HR et al. *MMWR Morb Mortal Wkly Rep*. 2024;73:209-214. 2. López-Lacort M et al. *Euro Surveill*. 2024;29:2400046. 3. Ares-Gomez S et al. *Lancet Infect Dis*. 2024;24:817-828. 4. Coma E et al. *Arch Dis Child*. 2024;109:736-741. 5. Assad Z et al. *N Engl J Med*. 2024;391:144-154. 6. Ernst C et al. *Euro Surveill*. 2024;29:2400033. 7. Torres JP et al. *Lancet Infect Dis*. 2025;25:1189-1198.

Clesrovimab: Phase 2b/3 Study to Evaluate Efficacy and Safety in Healthy Preterm and Full-Term Infants (CLEVER)[1]

RSV-Associated Endpoint	Endpoint	Clesrovimab Cases, n (n = 2,398)	Placebo Cases, n (n = 1,201)	Efficacy (through Day 150), % (95% CI)
Severe MALRI	Tertiary	2	12	**91.7** (62.9, 98.1)
LRI hospitalization	Tertiary	5	27	**90.9** (76.2, 96.5)
Hospitalization	Secondary	9	28	**84.2** (66.6, 92.6)
MALRI + ≥2 indicators of LRI/severity	Post hoc	10	41	**88.0** (76.1, 94.0)
MALRI + ≥1 indicator of LRI/severity	**Primary**	60	74	**60.4** (44.1, 71.9)
Acute respiratory infection	Tertiary	148	148	**52.0** (39.5, 61.9)



Fixed dose: 105 mg IM; half-life 44 days

1. Zar HJ et al. *N Engl J Med*. 2025;393:1292-1303.

Clesrovimab: Phase 3 Study to Evaluate Efficacy and Safety in High-Risk and Preterm Infants (SMART Season 1 Data)

RSV-Associated Endpoint	Clesrovimab n = 443			Palivizumab n = 437		
	Events, n	Total Follow-Up Time, months[a]	Incidence rate, % over 5 months[b] (95% CI)[c]	Events, n	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	1,946.9	**3.6%** (2.0, 6.0)	12	1,969.5	**3.0%** (1.6, 5.3)
Hospitalization[e]	5	1,968.9	**1.3%** (0.4, 3.0)	6	1,987.3	**1.5%** (0.6, 3.3)

[a] One month was defined as 30 days. [b] Five months were defined as 150 days. [c] Confidence intervals were estimated by exact Poisson confidence limits. [d] Defined as: RSV PCR positive and cough or difficulty breathing and at least 1 of the following: wheezing, chest wall indrawing/retractions, rales/crackles, hypoxemia, tachypnea, or dehydration due to respiratory symptoms.
[e] Defined as: RSV PCR positive and hospital admission for respiratory illness.

1. Zar HJ et al. *N Engl J Med*. 2025;393:1343-1345.

Clesrovimab: Early Read-Out on the Phase 3 SMART Trial Season 2 Data Is Positive[1,2]

Phase 3 trial	• Evaluated clesrovimab in infants/children at increased risk for severe RSV across two seasons
Randomization	• Randomized 1:1 to receive one clesrovimab dose or monthly palivizumab • An additional open-label higher clesrovimab dose available in season 2 for eligible participants
Efficacy	• Respiratory symptoms: 3.2% vs 3.4% • RSV hospitalization: 1.0% vs 1.7% • Season 2 MALRI: 7.3%; hospitalization: 3%
Safety	• Similar AE profile vs palivizumab • Common: irritability, somnolence, injection site reactions
Regulatory path	• Data under review for expanded clesrovimab use in high-risk children during their second season

1. https://www.contemporarypediatrics.com/view/clesrovimab-shows-promise-in-high-risk-infants-across-2-rsv-seasons.
2. https://vohnetwork.com/news/pharma/merck-reports-positive-phase-3-smart-data-for-enflonsia-in-high-risk-children-through-second-rsv-season.

Guidance on Monoclonal Antibody Dosing

Population	Nirsevimab Dose[1,2]	Clesrovimab Dose[3]
All infants younger than 8 months born during or entering their first RSV season	**Weight <5 kg:** 50 mg IM **Weight ≥5 kg:** 100 mg IM	105 mg IM, **regardless of body weight**
Infants and children aged 8 through 19 months who are • At increased risk of severe RSV and • Entering their second RSV season	200 mg IM, **regardless of body weight**	*Not yet approved for this indication*

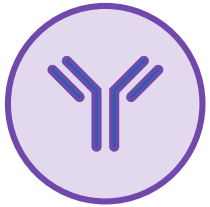
1. Jones JM et al. *MMWR Morb Mortal Wkly Rep*. 2023;72:920-925. 2. Yonts et al. *Pediatrics*. 2024;154:e2024068310.
3. Moulia. *MMWR Morb Mortal Wkly Rep*. 2025;74:508.

Translating Evidence Into Pediatric Practice

The Goal is RSV Protection for All Infants[1-7]

Vaccination in Pregnancy

Maternal **RSVpreF vaccine** for use during pregnancy



Long-Acting mAbs

Extended half-life **monoclonal antibodies** for infants

Available protection strategies for ALL infants

- **Recombinant RSVpreF vaccine (single dose)**
  - Approved and recommended: summer/fall 2023

- **Nirsevimab long-acting mAb (single dose)**
  - Approved and recommended: summer 2023
- **Clesrovimab long-acting mAb (single dose)**
  - Approved and recommended: summer 2025

1. Vittucci. *Global Pediatrics*. 2024;7:100130. 2. Chatterjee. *Infect Dis Ther*. 2021;10:5. 3. cdc.gov/rsv/infants-young-children/index.html. 4. Griffin. *N Engl J Med*. 2020;383:415. 5. Hammitt. *N Engl J Med*. 2022;386:837. 6. Jones. *MMWR Morb Mortal Wkly Rep*. 2023;72:920. 7. Moulia. *MMWR Morb Mortal Wkly Rep*. 2025;74:508.

Allison, a 34-Year-Old Pregnant Person

Routine OB Visit: November 4, 2025

- Allison is a gestational surrogate who is 37w5d pregnant
- She received her RSV vaccine at 34w5d
- She is being induced tomorrow because of consistently elevated blood pressure

Patient History

Medical
- Currently 37 weeks pregnant, BP elevated

Social
- No tobacco, no alcohol

Family
- Non-contributory

Data from today's visit
- BP 144/96 mmHg, HR 78 bpm, temp 97.6º F, height 5'5", weight 153 lb
- Most recent CMP and CBC WNL
- GBS negative

Current Medications
- Daily prenatal vitamin

Allison, a 34-Year-Old Pregnant Person

Routine OB Visit: November 4, 2025

- Allison is a gestational surrogate who is 37w5d pregnant
- She received her RSV vaccine at 34w5d
- She is being induced tomorrow because of consistently elevated blood pressure

Patient History

53 lb

Will the baby need an RSV monoclonal antibody after delivery?

Recommendations for RSV Monoclonal Antibodies in Infants[1]

RSV Monoclonal Antibodies (mAbs) for Infants Born During RSV Season

An infant RSV mAb is recommended for infants <8 months of age who are born during or are entering their first RSV season (typically fall through spring) if:

- The infant's birth parent did not receive RSV vaccine during pregnancy, or
- The RSV vaccination status of the infant's birth parent is unknown, or
- The infant was born within 14 days of RSV vaccination during pregnancy

The child's age on the day the infant RSV mAb is administered should be used to determine if the child is eligible for immunization

Except in rare circumstances, an infant RSV antibody is **not** needed for most infants who are born ≥14 days after the pregnant person received RSV vaccine

1. https://www.cdc.gov/rsv/hcp/vaccine-clinical-guidance/infants-young-children.html.

Brycen, a 3-Week-Old Healthy Infant

Clinic Visit: December 14, 2025

- Here for well-child visit, newborn, 8-28 days old
- Parents are hesitant about any form of vaccination or antibody treatments for their child, preferring “a more natural approach” to healthcare

Patient History

Medical

- None; born at 40 weeks

Social

- Non-contributory

Family

- Mother, 28, unvaccinated against RSV during pregnancy

Data from today’s visit

- Weight 8 lb 11 oz (51st percentile)
- Height 20.25” (30th percentile)
- Head circumference 14.96” (95th percentile)
- Temperature 99.6º F
- Pulse 120 bpm
- RR 27 bpm

Brycen, a 3-Week-Old Healthy Infant

Clinic Visit: December 14, 2025

- Here for well-child visit, newborn, 8-28 days old
- Parents are hesitant about any form of vaccination or antibody treatments for their child, preferring “a more natural approach” to healthcare

Patient History

How would you counsel Brycen’s family on the efficacy and safety of RSV monoclonal antibodies for healthy infants born during RSV season?

- RR 27 bpm

Educating Families About RSV Immunoprophylaxis

Family Education on RSV Risks and Prevention

- **Informational materials**: Provide families with printed or digital resources explaining the risks of RSV and how immunoprophylaxis works
- **Open communication**: Engage families in conversations about RSV risk factors, prevention, and the importance of immunoprophylaxis
- **Follow-up education**: Schedule follow-up appointments or calls to reinforce educational points and answer any questions

Make the recommendation!
2024 CDC survey data show that lack of provider recommendation was the most common reason families declined either maternal RSV immunization or infant mAb[1]

Reliable Resources to Share With Families

- **AAP RSV Discussion Guide Infographic**
  https://downloads.aap.org/AAP/PDF/15ChildhoodGuide_RSV_Family.pdf
- **HealthyChildren.org: RSV: When It's More Than Just a Cold**
  https://www.healthychildren.org/English/health-issues/conditions/chest-lungs/Pages/RSV-When-Its-More-Than-Just-a-Cold.aspx
- **HealthyChildren.org: RSV, Flu & COVID: How Are These Respiratory Illnesses Different?**
  https://www.healthychildren.org/English/health-issues/conditions/COVID-19/Pages/How-is-the-Flu-Different-From-COVID-19.aspx

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

Using Culturally Responsive Communication

Active listening

Understand cultural values and beliefs that may influence the family's perception of RSV prevention

Language and literacy considerations

Use plain language and translated materials to reach non-English–speaking families

Overcoming hesitancy and improving confidence in immunoprophylaxis

Address concerns about new preventive measures, using data and testimonials to build trust

Sandra, a 36-Year-Old Pregnant Person

Routine OB Visit: March 11, 2026

- Sandra is 35w1d pregnant today
- She is interested in receiving the maternal RSV vaccine because she heard that RSV is still prevalent in her community

Patient History

Medical

- Currently 35 weeks pregnant, no other medical history

Social

- No tobacco, no alcohol

Family

- Non-contributory

Data from today's visit

- BP 120/80 mmHg, HR 64 bpm, temp 97.6º F, height 5'7", weight 162 lb
- Most recent CMP and CBC WNL
- GBS positive

Current Medications

- Daily prenatal vitamin

Sandra, a 36-Year-Old Pregnant Person

Routine OB Visit: March 11, 2026

- Sandra is 35w1d pregnant today
- She is interested in receiving the maternal RSV vaccine because she heard that RSV is still prevalent in her community

Patient History

2 lb

Would you administer the maternal RSV vaccine to Sandra today?

AAP and ACOG Recommendations for RSV Vaccination During Pregnancy[1,2]

Maternal RSV Vaccination With RSVpreF

Pregnant at 32w0d through 36w6d gestation from September through January in most of the continental United States and have not received RSV vaccine in previous pregnancy[a]:

one dose RSVpreF

- Administer RSV vaccine regardless of previous RSV infection
- *Subsequent pregnancies*: Additional RSVpreF doses not recommended; no data are available to inform whether additional doses are needed in subsequent pregnancies; infants born to pregnant women who received RSVpreF during a previous pregnancy should receive nirsevimab or clesrovimab

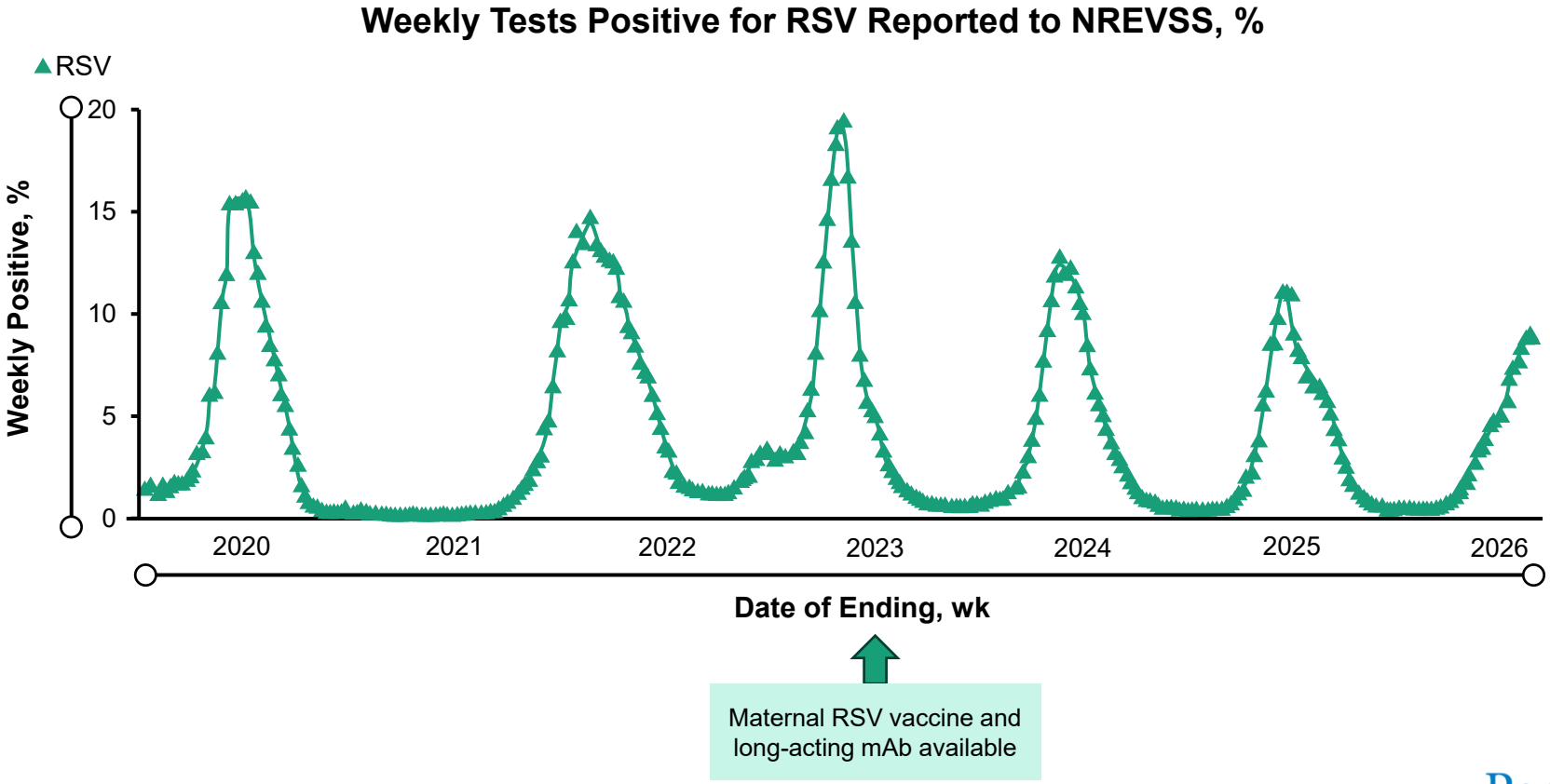
Either maternal RSV vaccination with RSVpreF or infant immunization with nirsevimab or clesrovimab is recommended to prevent severe RSV disease in infants

All other pregnant women: RSV vaccine not recommended

[a] Providers in jurisdictions with RSV seasonality that differs from most of the continental United States (eg, Alaska, jurisdictions with tropical climate) should follow guidance from public health authorities (eg, CDC, health departments) or regional medical.pdf. centers on timing of administration based on local RSV seasonality.

1. https://downloads.aap.org/AAP/PDF/AAP-Immunization-Schedule.
2. https://www.acog.org/news/news-releases/2025/08/acog-releases-updated-maternal-immunization-guidance-covid-influenza-rsv.

Impact of RSV Prevention Strategies in the United States, 2023-2026[1]



1. https://www.cdc.gov/nrevss/php/dashboard/index.html.

Conclusions

- RSV is a leading cause of severe LTRI and hospitalization in infants worldwide
- Disease burden extends beyond acute bronchiolitis, with potential long-term respiratory sequelae
- Young infants are uniquely vulnerable for many reasons
- Prevention strategies include
  - Vaccination during pregnancy
  - Long-acting monoclonal antibodies for all infants (first season) and at-risk young children (second season)
- Optimizing outcomes requires coordinated implementation, timely counseling, and appropriate selection of preventive strategies across care settings