Monthly Public Health Webinar

RSV Vaccine During Pregnancy (to protect the infant)

October 12, 2023

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Department of Health and Human Services

PPT Slides Will Be Posted to our Healthcare Provider Resources Website

- https://www.dhhs.nh.gov/programs-services/disease-prevention/infectious-disease-control/bidc-resources-healthcare-providers

Healthcare Providers and Public Health Partners Call Presentations

Filter by Keyword:

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Sort Results by: Date Filed (New-Old)

Result Count: 5 | 10 | 25

Healthcare Providers and Public Health Partners Call Presentation, August 10, 2023

Topics:

- Nirsevimab (Beyfortus™)
- RSV Vaccines

Document Format: *PDF* | ***Tags:*** *HCP Calls*

Date Filed: *08/10/2023*

Post-Acute COVID Syndrome (PACS) a.k.a. Post-Acute Sequelae of COVID (PASC) a.k.a. Long COVID, Post-COVID, Long Haul Presentation

Document Format: *PDF* | ***Tags:*** *HCP Calls*

Date Filed: *07/13/2023*

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FDA NEWS RELEASE

FDA Authorizes Updated Novavax COVID-19 Vaccine Formulated to Better Protect Against Currently Circulating Variants

Share | Tweet | Linkedin | Email | Print

For Immediate Release: October 03, 2023

https://www.fda.gov/news-events/press-announcements/fda-authorizes-updated-novavax-covid-19-vaccine-formulated-better-protect-against-currently

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Use of COVID-19 Vaccines in the United States

Interim Clinical Considerations

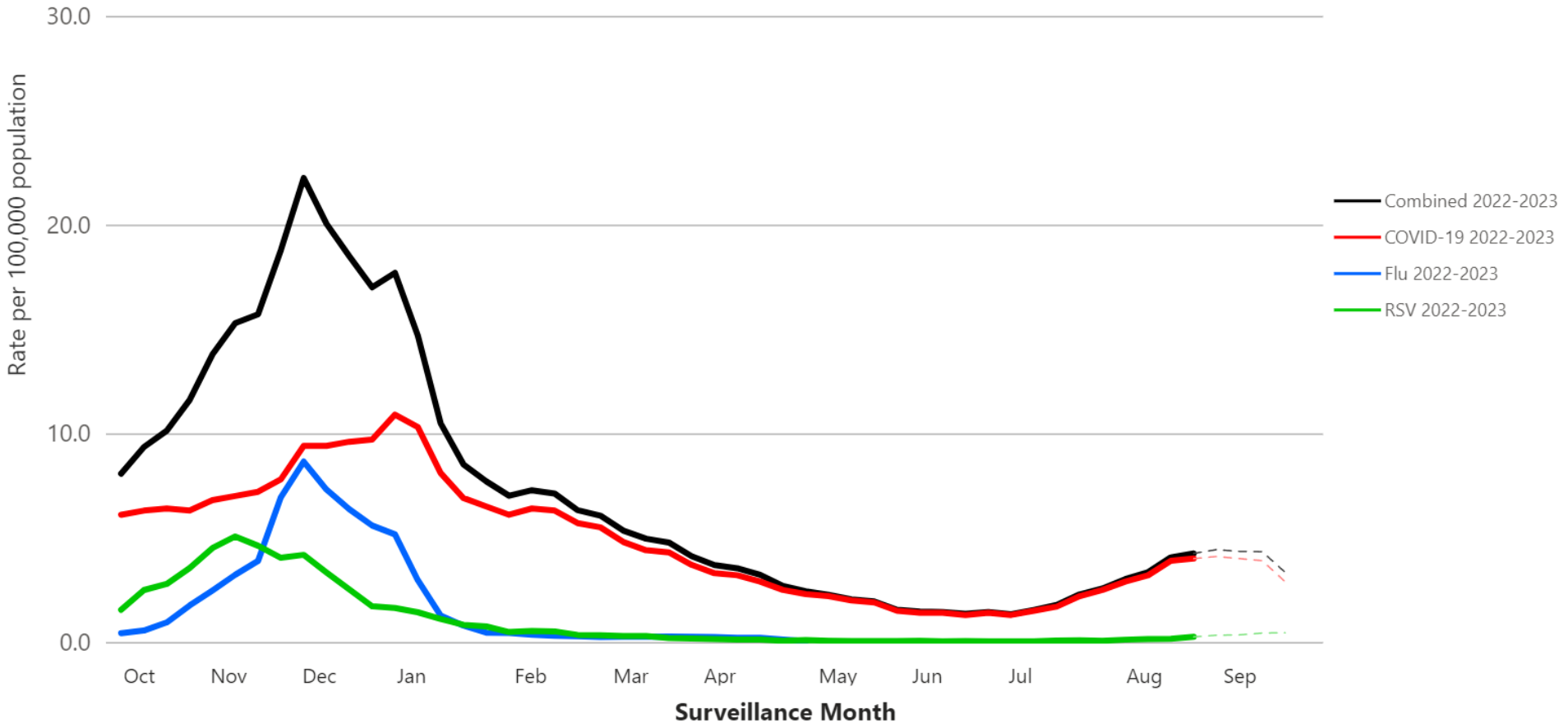
Print

Summary of recent changes (last updated October 6, 2023):

- The updated 2023–2024 formulation of Novavax COVID-19 Vaccine is recommended for people ages 12 years and older as follows:
  - Initial vaccination: 2 doses of updated (2023–2024 Formula) Novavax COVID-19 Vaccine
  - Previously vaccinated with any Original monovalent or bivalent COVID-19 vaccine (Moderna, Novavax, Pfizer-BioNTech, Janssen): 1 dose of updated (2023–2024 Formula) Novavax Vaccine
- People who are moderately or severely immunocompromised may receive 1 or more additional updated (2023–2024 Formula) Novavax vaccine doses.
- People ages 12 years and older have the option of receiving either the updated (2023–2024 Formula) mRNA (Moderna, Pfizer-BioNTech) or updated (2023–2024 Formula) Novavax vaccine.

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

Weekly Rates of COVID-19, RSV, and Influenza Hospitalizations in the U.S.



Data last updated: October 4, 2023. | **Accessibility:** Right click on the graph area to display options such as show data as table and copy visual.

https://www.cdc.gov/surveillance/resp-net/dashboard.html

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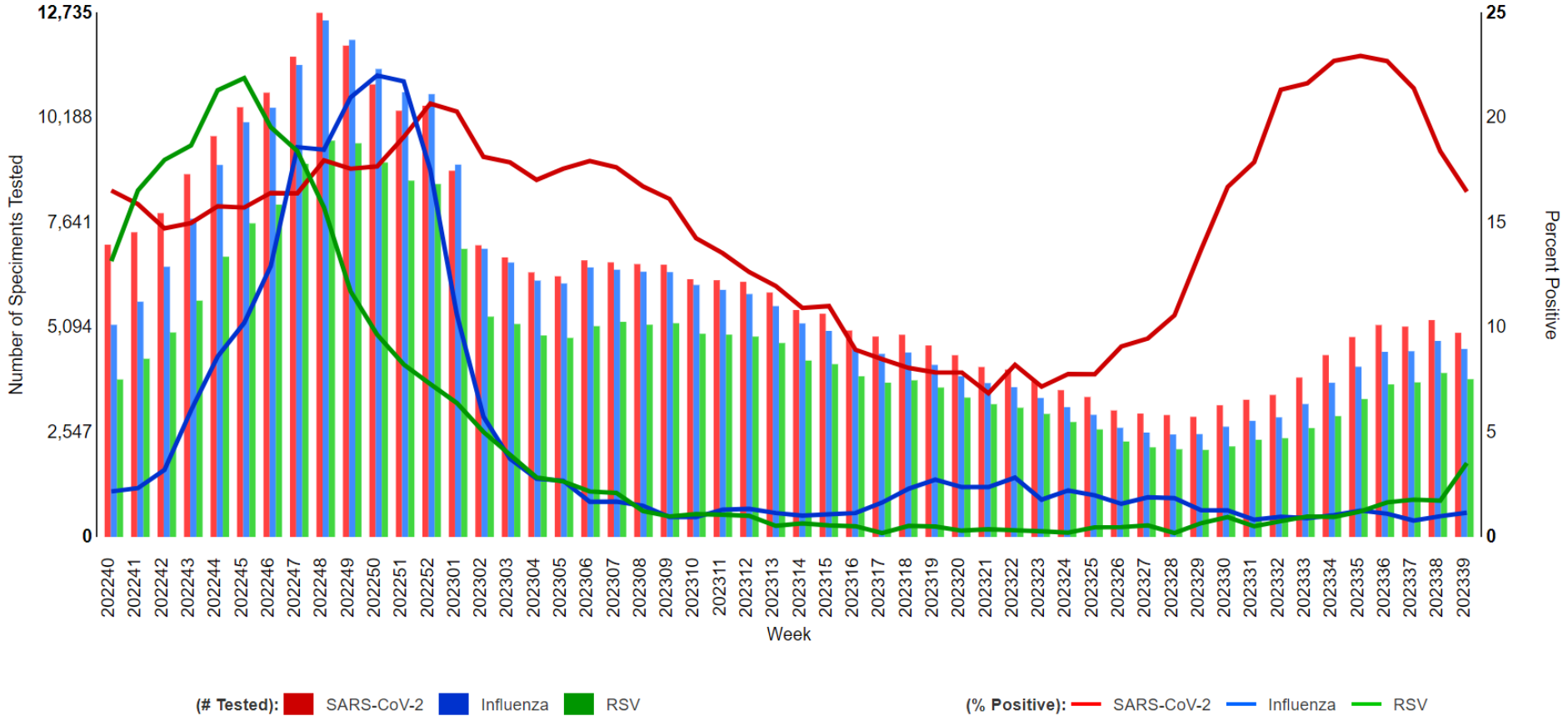
Emergency Department Testing for COVID-19, RSV and Influenza in the U.S.



https://www.cdc.gov/surveillance/resp-lens/dashboard.html

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RSV is the leading cause of hospitalization in U.S. infants[1]

- Most (68%) infants are infected in the first year of life and nearly all (97%) by age 2 years[2]
- 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 conditions[3]

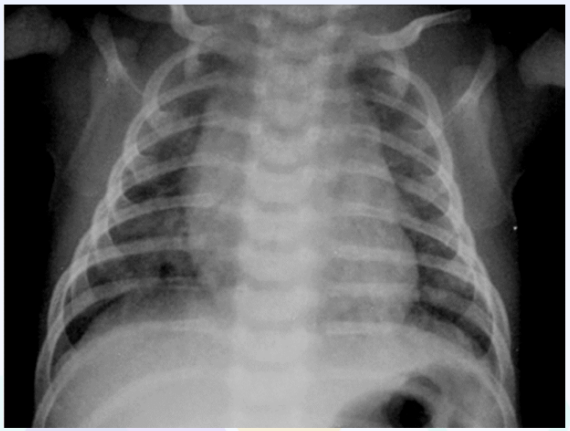


Image: Goncalves et al. Critical Care Research and Practice 2012

[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; [5]CDC NVSN data

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

Background: RSV Vaccines and Nirsevimab

- Two RSV vaccine products currently available:
  - GSK: Adjuvanted recombinant prefusion F-protein vaccine
  - Pfizer: Non-adjuvanted recombinant prefusion F-protein vaccine
- Both the GSK and Pfizer RSV vaccines can be administered to adults 60 years of age or older
- Only the Pfizer RSV vaccine is recommended for use during pregnancy
- Nirsevimab is a long-acting recombinant human monoclonal antibody that targets and binds the RSV F-protein inhibiting viral fusion and host cell entry
  - Administered directly to infants and young children under 2 years of age
  - Prevents RSV lower respiratory tract infection/disease (LRTI/LRTD) through passive immunization

ACIP Recommendations: Nirsevimab

- ALL Infants aged <8 months born during or entering their first RSV season are recommended to receive one dose of nirsevimab

- Children aged 8-19 months who are at increased risk of severe RSV disease and entering their second RSV season are recommended to receive one dose of nirsevimab

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

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

- Adults aged 60+ years of age MAY receive a single dose of an RSV vaccine using shared clinical decision-making (based on a discussion between the healthcare provider and patient)

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

ACIP Recommendations: RSV Vaccine During Pregnancy

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

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

Background: RSV Vaccine During Pregnancy

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

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

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

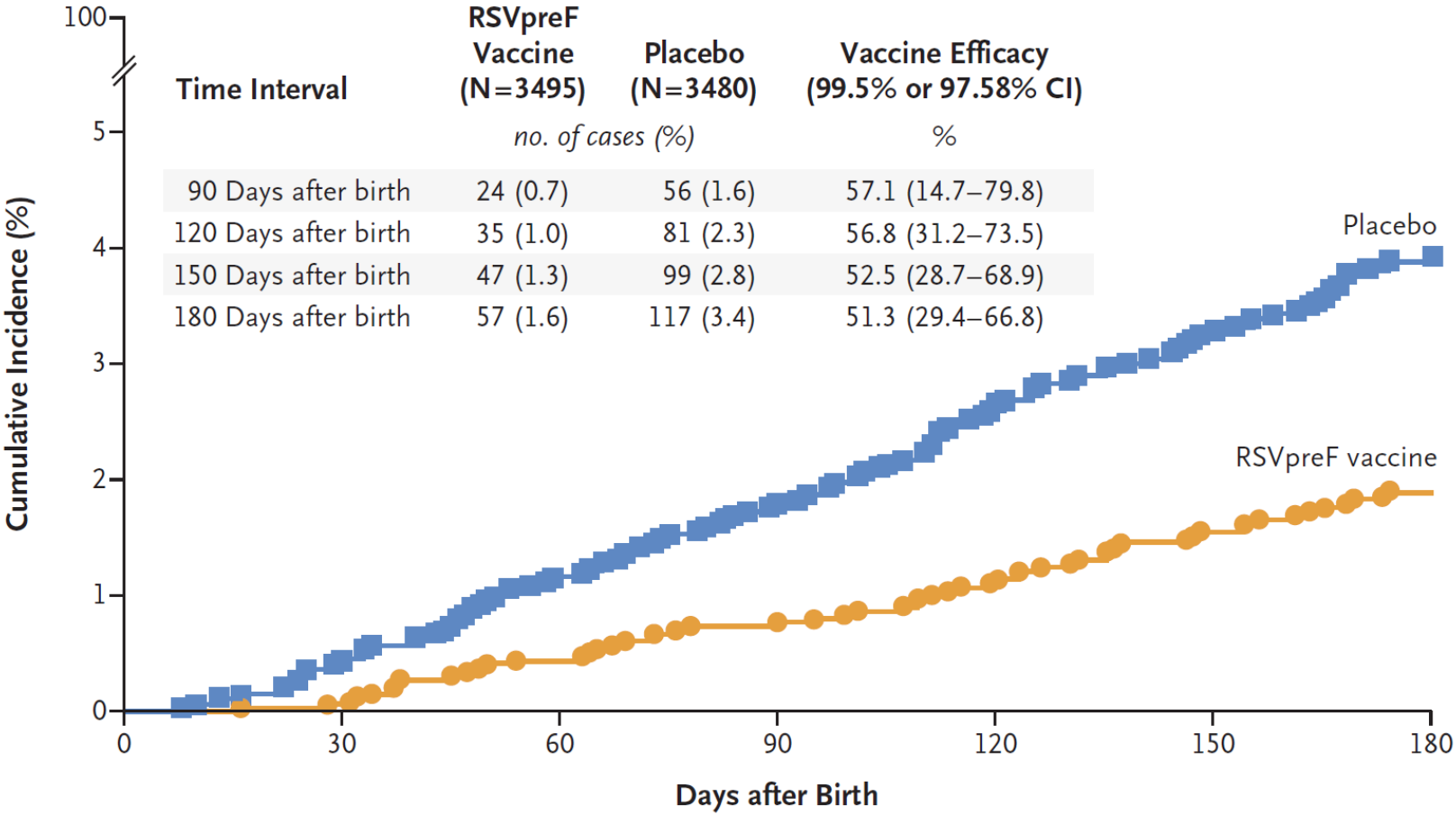
	Clinical Trial Dosing Interval (24-36 weeks gestation)
Medically attended RSV-associated LRTI	**51.3%** (95% CI: 29.4% – 66.8%)
Severe medically attended RSV-associated LRTI	**69.4%** (95% CI: 44.3% – 84.1%)
Hospitalization for RSV-associated LRTI	**56.8%** (95% CI: 10.1% – 80.7%)

LRTI: Lower Respiratory Tract Infection

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

B Medically Attended RSV-Associated Lower Respiratory Tract Illness

Time Interval	RSVpreF Vaccine (N=3495)	Placebo (N=3480)	Vaccine Efficacy (99.5% or 97.58% CI)
	no. of cases (%)		%
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)



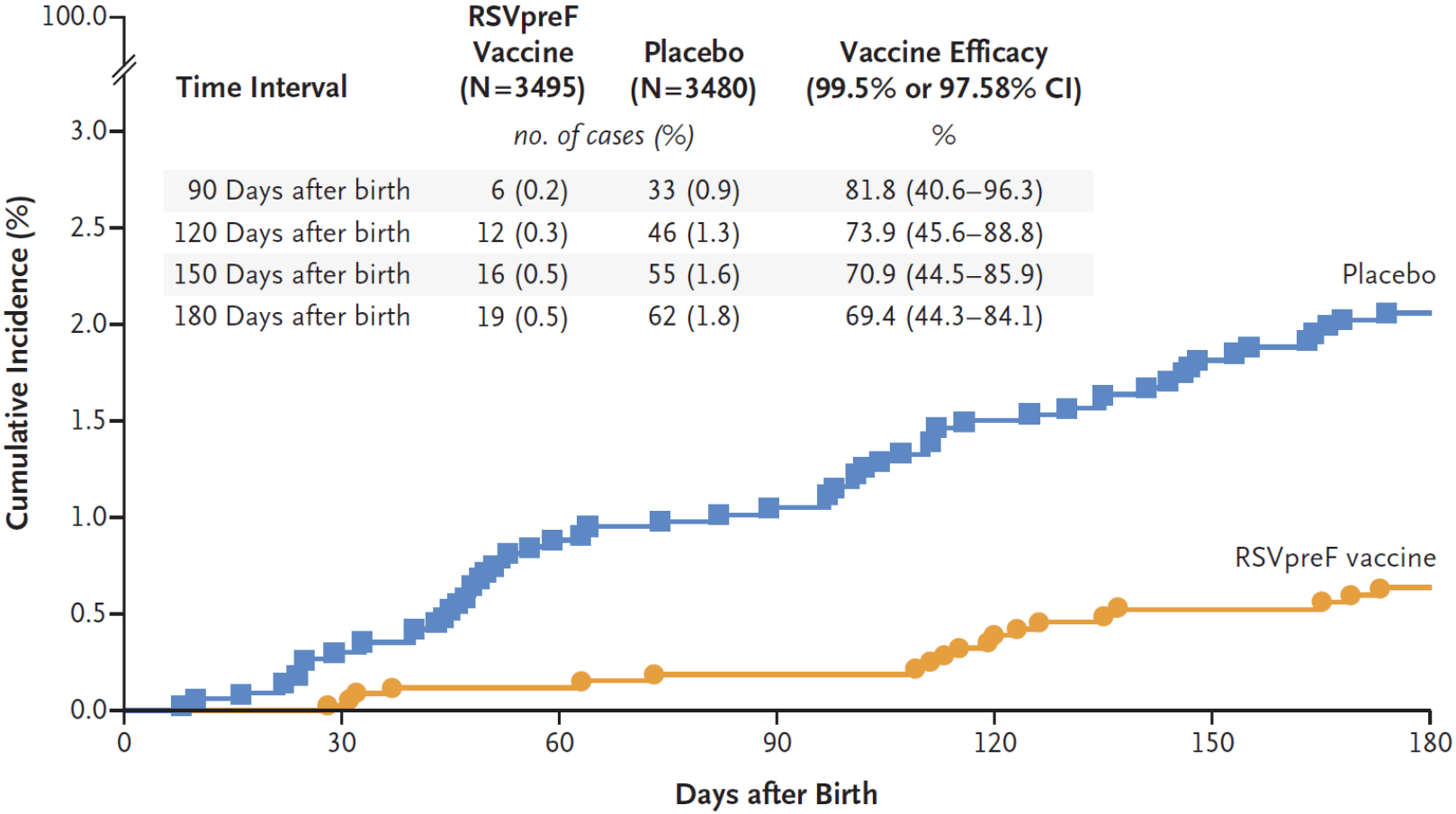
No. at Risk

Placebo	3480	3288	2964	2879	2804	2738	2700
RSVpreF vaccine	3495	3348	3035	2968	2898	2845	2792

https://www.nejm.org/doi/full/10.1056/NEJMoa2216480

A Medically Attended Severe RSV-Associated Lower Respiratory Tract Illness

Time Interval	RSVpreF Vaccine (N=3495)	Placebo (N=3480)	Vaccine Efficacy (99.5% or 97.58% CI)
	no. 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)



No. at Risk

Placebo	3480	3292	2973	2899	2833	2776	2749
RSVpreF vaccine	3495	3349	3042	2981	2916	2867	2820

https://www.nejm.org/doi/full/10.1056/NEJMoa2216480

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

	Clinical Trial Dosing Interval (24-36 weeks gestation)
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LRTI: Lower Respiratory Tract Infection

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

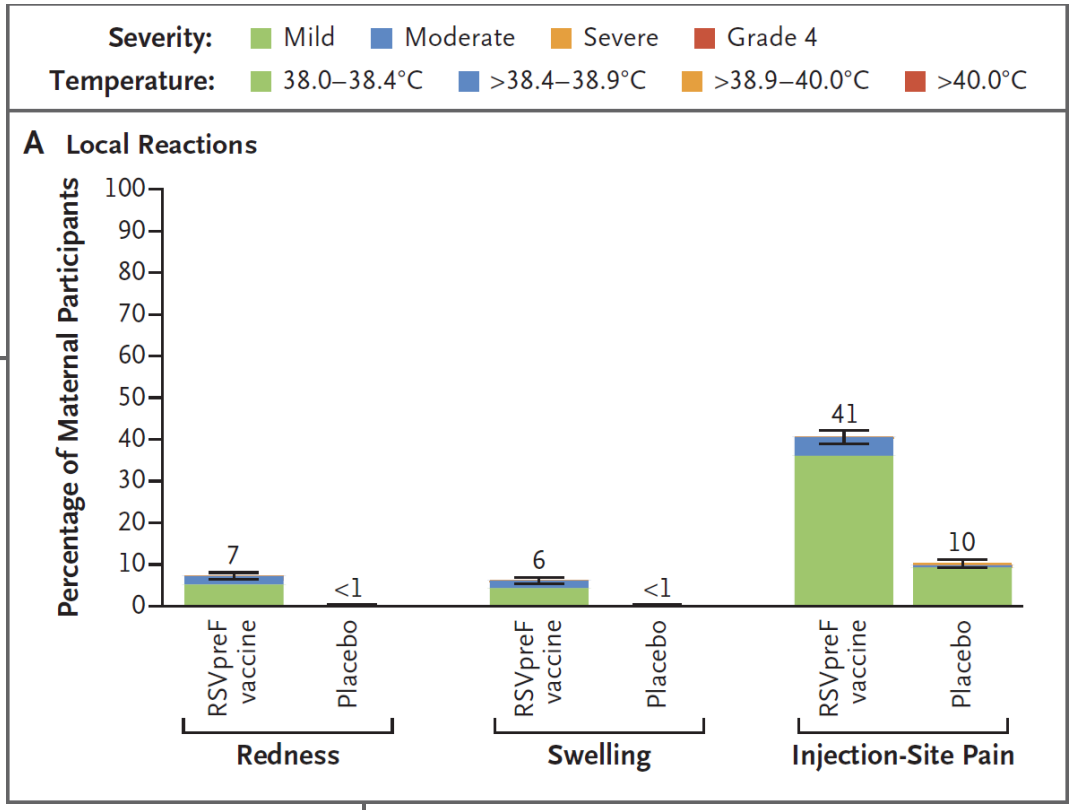
Vaccine Efficacy for Selected **Infant** Clinical Endpoints Between 0 – 180 Days of Life

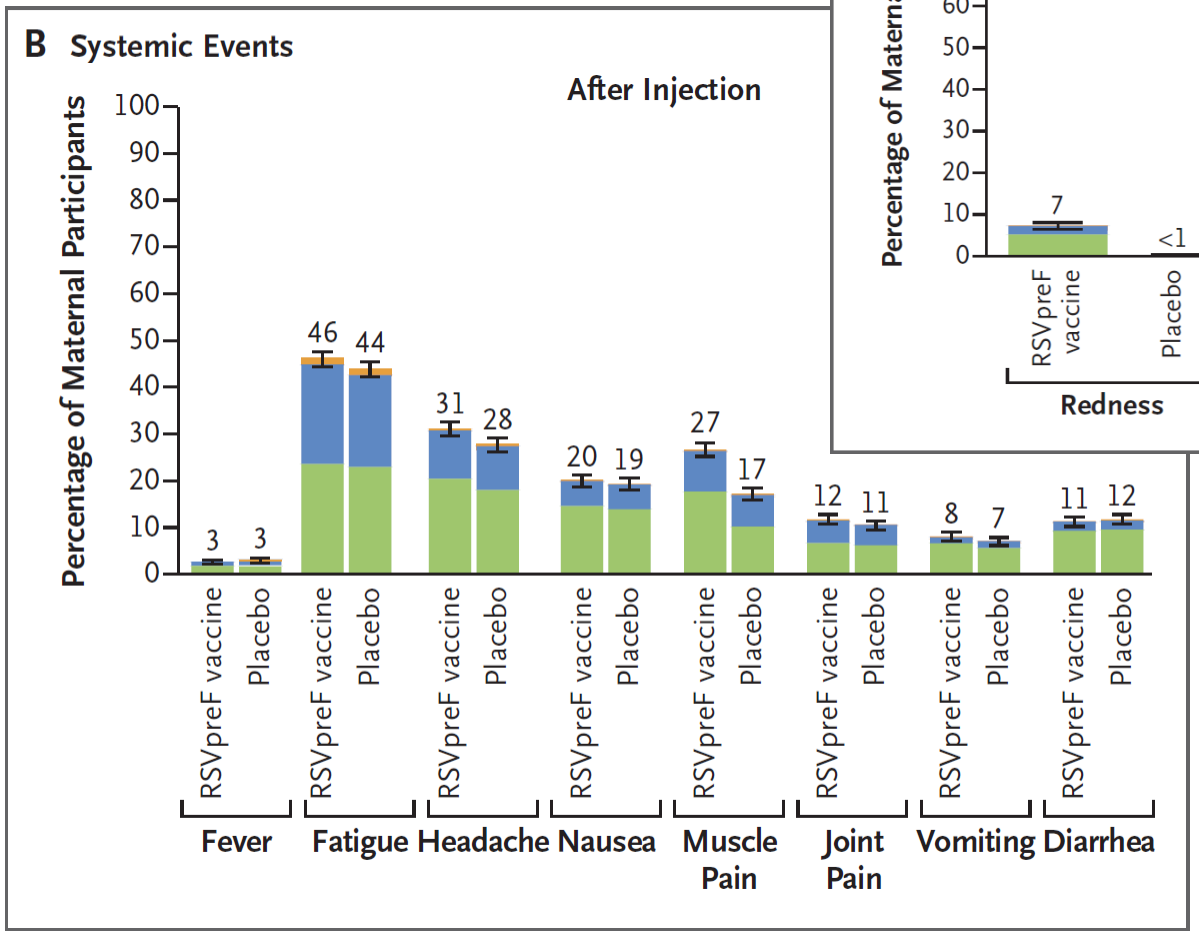
	Clinical Trial Dosing Interval (24-36 weeks gestation)	FDA Approved Dosing Interval (32-36 weeks gestation)
Medically attended RSV-associated LRTI	**51.3%** (95% CI: 29.4% – 66.8%)	**57.3%** (95% CI: 29.8% – 74.7%)
Severe medically attended RSV-associated LRTI	**69.4%** (95% CI: 44.3% – 84.1%)	**76.5%** (95% CI: 41.3% – 92.1%)
Hospitalization for RSV-associated LRTI	**56.8%** (95% CI: 10.1% – 80.7%)	**48.2%** (95% CI: -22.9% – 79.6%)

LRTI: Lower Respiratory Tract Infection

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

Reactogenicity During Pregnancy





https://www.nejm.org/doi/full/10.1056/NEJMoa2216480

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

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

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

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

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

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https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

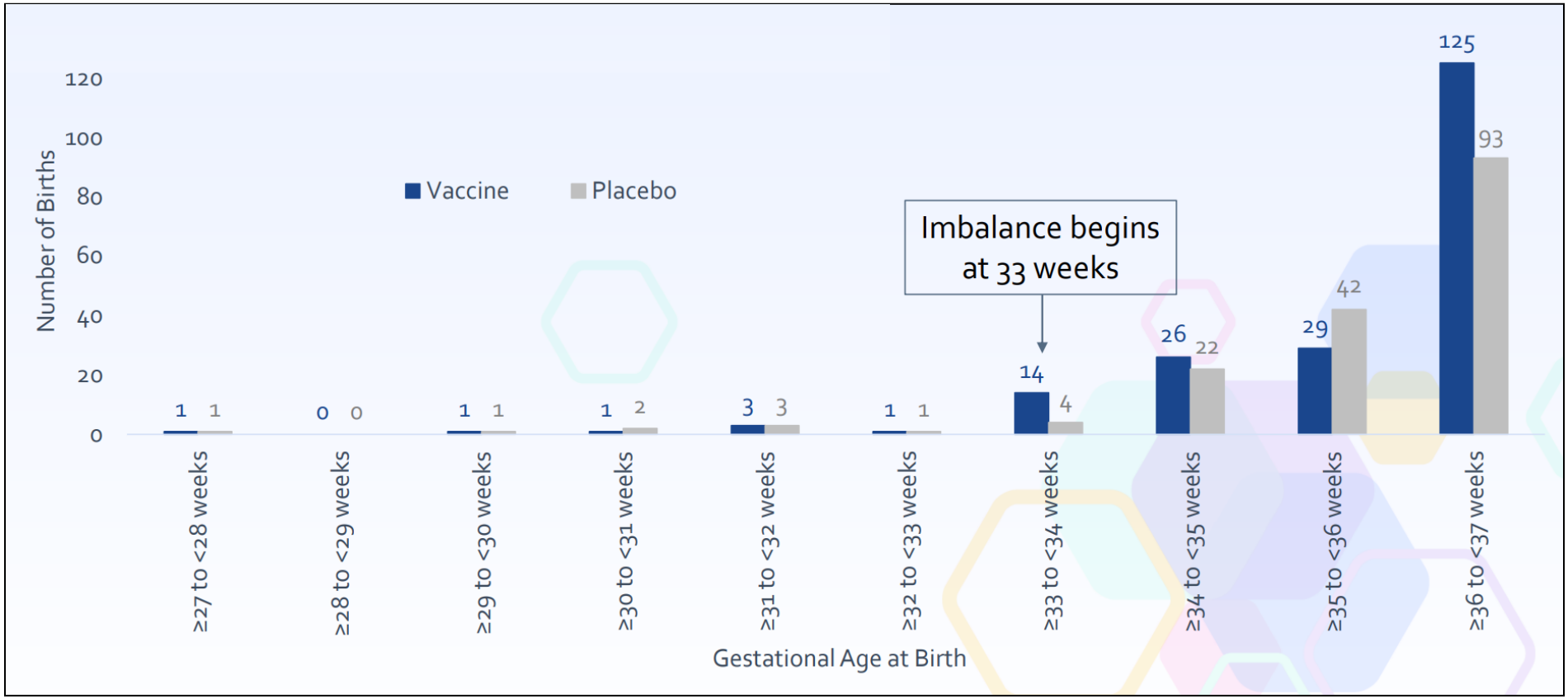
Relative Risk (95% CIs) for Select Adverse Outcomes (Vaccine vs. Placebo Groups)

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

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

https://www.cdc.gov/vaccines/acip/recs/grade/pfizer-RSVpreF-pregnant-people-etr.html
https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

Preterm Birth (Birth at <37 Weeks Gestation) Imbalance Began at 33 Weeks with Clinical Trial Dosing Interval (24 – 36 Weeks Gestation)



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

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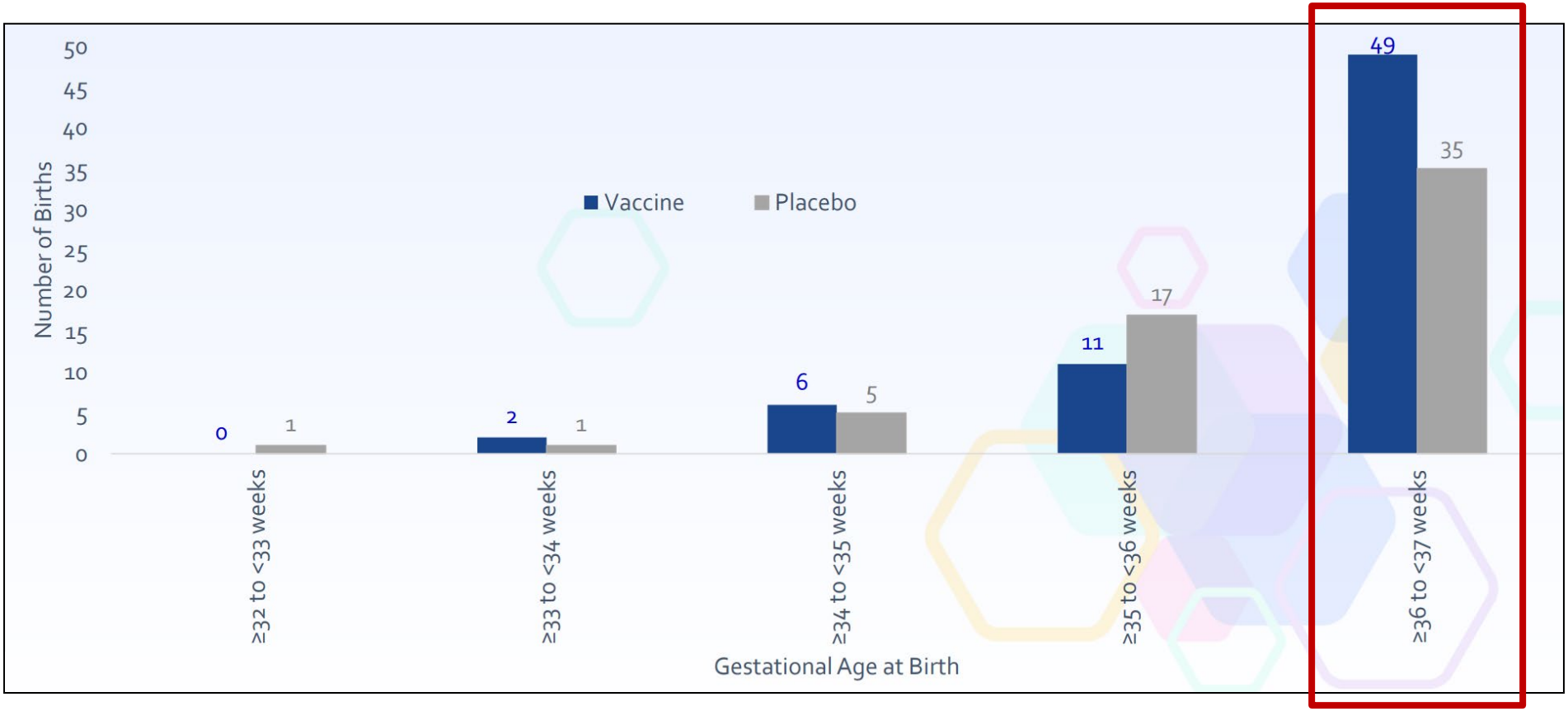
Preterm Birth (Birth at <37 Weeks Gestation) Imbalance Less Prominent with FDA Approved Dosing Interval (32 – 36 Weeks Gestation)



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

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

Preterm birth rates in maternal RSV vaccine clinical trials: GSK

- Trial of a similar GSK maternal RSV vaccine (stabilized prefusion F protein vaccine without an adjuvant) was halted due to an imbalance of preterm births

Outcome	Vaccine group, n (%) N=3,496	Placebo group, n (%) N=1,739	Relative Risk (95% CI)
Preterm birth <37 weeks	238 (6.81%)	86 (4.95)	1.38 (1.08, 1.75)
Neonatal death	13 (0.37%)	3 (0.17%)	2.16 (0.62, 7.55)

- Imbalance of neonatal deaths was a consequence of preterm birth imbalance
- Imbalance in preterm births was seen in low and middle-income countries (RR: 1.57, 95% CI: 1.17, 2.10) but not high-income countries (RR: 1.04, 95% CI: 0.68, 1.58)
- Imbalance was observed from April-December 2021, but not consistently after December 2021
- Reason for the imbalance remains unclear

Study vaccine given at $24^{0/7}$ to $34^{0/7}$ weeks gestation

Vaccines and Related Biological Products Advisory Committee February 28 - March 1, 2023 Meeting Briefing Document- Sponsor GSK (fda.gov)

https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Mat-Ped-Fleming-Dutra-508.pdf

ACIP Work Group Summary on Preterm Birth Imbalance

- When using the full trial dosing interval (24–36 weeks gestation), most preterm births (60%) were >30 days after vaccination, and no known biologic mechanism for vaccines to cause preterm birth, particularly >30 days after vaccination
- When assessed among those vaccinated during the approved interval (32–36 weeks gestation), data on preterm birth were reassuring to the Work Group
  - Imbalance in preterm birth was still present but lessened
  - Most infants born preterm in the vaccine group (72%, 49/68) were born at 36 weeks
  - In the United States (largest contributing country in the trial), imbalance in preterm births reversed:
    - Trial dosing interval: 5.7% in vaccine vs. 5.3% in placebo recipients
    - Approved dosing interval: 4.0% in vaccine vs. 4.4% in placebo recipients
- Majority of the Work Group felt the approved dosing interval (32–36 weeks gestation) reduces the potential risk of preterm birth and the potential for complications from preterm birth, which is their major safety concern

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

Additional Maternal Adverse Events (Clinical Trial Dosing Interval Results)

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

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

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

Additional ACIP Clinical Recommendations

- Simultaneous administration with other recommended vaccines (e.g., Tdap, influenza, COVID-19) is allowed/permissible
- "Additional data are needed to determine whether additional seasonal doses during subsequent pregnancies are indicated"
- Nirsevimab is recommended for infants born <14 days after maternal RSV vaccination because ~14 days are needed after maternal vaccination for antibody development and transplacental transfer (i.e., nirsevimab is recommended for all infants born at <34 weeks gestation)
- Nirsevimab "may be considered" for infants born to vaccinated mothers in rare circumstances when the potential incremental benefit of administration is warranted (based on clinical judgement)

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

Additional ACIP Clinical Recommendations

- Infants and children 8 – 19 months of age who are at increased risk for severe RSV and entering their 2nd RSV season are recommended to receive nirsevimab regardless of maternal RSV vaccination

- Administration of both maternal RSV vaccine during pregnancy and infant nirsevimab is NOT needed for most infants – there is no data currently available directly comparing efficacy between these two products

- "Providers who care for pregnant persons should discuss the relative advantages and disadvantages of both maternal RSV vaccination and nirsevimab and consider patient preferences when determining whether to vaccinate the pregnant person or to rely on administration of nirsevimab to the infant…"

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

Advantages and Disadvantages of Maternal Vaccination vs. Nirsevimab

Maternal RSV Vaccine

Advantages

- Provides protection immediately after birth
- Might be more resistant to potential viral mutations

Disadvantages

- Protection is potentially reduced if fewer antibodies are produced or transferred from pregnant person to baby
- Potential risk for preterm birth and/or hypertensive disorders of pregnancy

Infant Nirsevimab

Advantages

- Protection may wane slower than protection from maternal RSV vaccine
- Direct receipt of antibodies rather than relying on transplacental transfer
- No risk for adverse pregnancy outcomes

Disadvantages

- Potentially limited availability this RSV season
- Requires infant injection

https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w

New Immunizations to Protect Against Severe RSV

Who Does It Protect?	Type of Product	Is It for Everyone in Group?
 Adults 60 and over	RSV vaccine	Talk to your doctor first
 Babies	RSV antibody given to baby	All infants entering or born during RSV season. Small group of older babies for second season.
	OR	
 Babies	RSV vaccine given during pregnancy	Can get if you are 32–36 weeks pregnant during September–January

www.cdc.gov/rsv

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

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ACIP Recommendations

- **RSV vaccines**:
  - Pregnancy: https://www.cdc.gov/mmwr/volumes/72/wr/mm7241e1.htm?s_cid=mm7241e1_w
  - Adults 60 years of age and older: https://www.cdc.gov/mmwr/volumes/72/wr/mm7229a4.htm
- **Nirsevimab monoclonal antibody**:
  - https://www.cdc.gov/mmwr/volumes/72/wr/mm7234a4.htm
- **COVID-19 vaccines**:
  - https://www.cdc.gov/mmwr/volumes/72/wr/mm7242e1.htm?s_cid=mm7242e1_w
  - https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html
- **Influenza vaccines**:
  - https://www.cdc.gov/mmwr/volumes/72/rr/rr7202a1.htm

Q&A