# Maternal RSV vaccine safety surveillance

## Advisory Committee on Immunization Practices (ACIP)
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# Disclaimer

- The findings and conclusions in this presentation are those of the author and do not necessarily represent the official position of the CDC
- The use of product trade names is for identification purposes only

# Topics

- Background
- CDC vaccine safety monitoring for Pfizer RSV vaccines in pregnancy:
  - Vaccine Adverse Event Reporting System (VAERS)
  - V-Safe
  - Vaccine Safety Datalink (VSD)
- Summary

# Key points up front

- In clinical trials among pregnant persons at 24–36 weeks' gestation, more preterm births were noted among Pfizer RSV vaccine recipients compared to placebo (differences not statistically significant)
- Post-licensure safety surveillance of the Pfizer RSV vaccine in pregnant persons was initiated during the 2023-2024 season
- The patterns of reported local and systemic (e.g., headache) symptoms in V-safe and VAERS after maternal Pfizer RSV vaccine were consistent with its pre-licensure safety profile
- Among reports received in VAERS after maternal Pfizer RSV vaccine, the most frequent adverse events reported were pregnancy-specific conditions (e.g., preterm delivery), as expected for a vaccine recommended at 32-36 weeks' gestational age
- Preliminary findings in the VSD observed that the incidence of preterm births is 4.1% among pregnant persons who received Pfizer RSV vaccine during the 2023-2024 respiratory season. This was within the expected range of the incidence of preterm births at 32-36 weeks' gestation (3.1 - 6.1%) before introduction of this vaccine
- CDC and FDA will continue to monitor maternal RSV vaccine safety in VAERS, V-safe and VSD

# Background

- In clinical trials among pregnant persons at 24–36 weeks' gestation, more preterm births were noted among Pfizer RSV vaccine recipients compared to placebo, but the differences were not statistically significant
  - To avoid the potential risk of preterm birth before 32 weeks' gestation, FDA approved the maternal Pfizer RSV vaccine (Abrysvo) for use in pregnant persons at 32 through 36 weeks' gestational age[1]
- The label for Pfizer RSV vaccine notes potential risk of preterm birth under warnings and precautions section[1]
- In addition, more hypertensive disorders of pregnancy were observed among vaccine recipients compared to placebo recipients, but the differences were not statistically significant
- Post-licensure safety surveillance of the new Pfizer RSV vaccine in pregnant persons is of great importance to ensure maternal Pfizer RSV safety at the population level and the benefits of using the vaccine in pregnant persons to protect infants from RSV LRTD outweigh possible risks

RSV: respiratory syncytial virus; LRTD: lower respiratory tract disease

[1] https://www.fda.gov/media/168889/download

# VAERS is the nation's early warning system for vaccine safety

CDC + FDA

VAERS

**Vaccine Adverse Event Reporting System**

Co-managed by
CDC and FDA
https://vaers.hhs.gov/

# VAERS ADVERSE EVENT REPORTING SYSTEM (VAERS)

**Strengths**

- National data
- Accepts reports from anyone
- Rapidly detects safety signals
- Can detect rare adverse events
- Data available to public

**Limitations**

- Reporting bias
- Inconsistent data quality and completeness
- Lack of unvaccinated comparison group
- Generally cannot assess causality

- VAERS accepts all reports from all reporters without making judgments on causality or judging clinical seriousness of the event
- As a hypothesis generating system, VAERS identifies potential vaccine safety concerns that can be studied in more robust data systems

# Approaches to analyzing VAERS data

- For more than a decade VAERS has been used as part of vaccine safety surveillance for vaccines used in pregnancy (e.g., influenza, Tdap, COVID-19)[1,2]
  - Descriptive analysis
  - Clinical review of individual reports
  - Aggregate descriptions of automated data (e.g., counts of reported adverse events)
  - Calculation of reporting rates for pregnancy outcomes (if doses of a vaccine administered in pregnancy or vaccination coverage data are available)
- Clinical review of infant's medical records at birth and for the first 3 months of life (enhanced surveillance)

[1]Moro et al. Obstetrics & Gynecology 140(3):p 421-427, September 2022. https://journals.lww.com/greenjournal/Fulltext/2022/09000/Safety_of_Booster_Doses_of_Coronavirus_Disease.11.aspx

[2]Moro et al. Vaccine. 34(20):p2349-2353, April 2016. https://www.sciencedirect.com/science/article/pii/S0264410X16300329?via%3Dihub

# Characteristics of maternal Pfizer RSV vaccine reports submitted to VAERS (as of June 3, 2024)

| Characteristics | N (%) |
|---|---|
| Number of reports | **121** |
| Maternal deaths | 0 |
| Pregnancy-specific adverse event(s) reports | 52 (43) |
| Maternal age in years, median (range) [1] | 32 (21-41) |
| Maternal age ≥ 35 years | 24 (20) |
| Onset interval in days from vaccination to adverse event, median (interquartile range) | 1 (0,4) |
| Gestational age[2] in weeks at time of vaccination, median (range) | 34 (9,37) |
| **Type of reporter** | |
| Patient/relative[3] | 60 (50) |
| Provider | 36 (30) |
| Vaccine manufacturer | 19 (16) |
| Other | 6 (5) |

[1] Age not provided in 15 reports; [2] Gestational age at vaccination available for 90 reports; unknown for 31 reports
[3] Pregnant persons represented 70% of those who reported a preterm delivery
From October 2023 through March 2024 an estimated 320,400 pregnant persons received RSV vaccine (Peacock. Implementation and Uptake of Nirsevimab and Maternal RSV Vaccine. Advisory Committee on Immunization Practices. June 28, 2024.

# Most frequently reported MedDRA Preferred Terms[1] among reports (n=121) to VAERS following Pfizer RSV vaccination in pregnant persons (as of June 3, 2024)

| Rank | MedDRA PT (not mutually exclusive) | N (%) |
|---|---|---|
| 1 | Premature delivery | 29 (24) |
| 2 | Premature labor | 18 (15) |
| 3 | Caesarean section | 18 (15) |
| 4 | Uterine contractions during pregnancy | 16 (13) |
| 5 | Headache | 15 (12) |
| 6 | Nausea | 13 (11) |
| 7 | Fever | 13 (11) |
| 8 | Vomiting | 12 (10) |
| 9 | Pain | 11 (9) |
| 10 | Preterm premature rupture of membranes | 10 (8) |

[1] Medical Dictionary for Regulatory Activities Preferred Terms (https://www.meddra.org/how-to-use/basics/hierarchy); MedDRA PTs not mutually exclusive

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# Adverse events among pregnant persons following Pfizer RSV vaccination in VAERS (as of June 3, 2024)

| Adverse event | N (%) |
|---|---|
| **Pregnancy specific** | **52 (43)** |
| Premature delivery (< 37 weeks' gestation) | 37 (31) |
| High blood pressure/gestational hypertension[1] | 4 (3) |
| Infant death[2] | 1 (1) |
| Stillbirth (≥ 20 weeks' gestation) | 3 (2) |
| Delivery/labor/contractions | 3 (2) |
| Premature rupture of membranes | 2 (2) |
| Other[3] | 2 (2) |
| **Non-pregnancy specific** | **69 (57)** |
| General disorders and administration site conditions (mostly injection site and systemic reactions) | 41 (34) |
| Vaccination errors[4] | 21 (17) |
| Infections and infestations | 3 (2) |
| Neurological disorders (Bell's palsy)[6] | 2 (2) |
| Other[4] | 5 (4) |

[1] One report of thrombocytopenia that met Brighton level 2 criteria was reported in a patient with elevated blood pressure following vaccination
[2] 35-week infant with anoxic brain injury and neonatal death after emergent C-section, resuscitation, and hospital transfer 4 days after vaccination
[3] Other includes one report each of premature infant incorrectly classified as preterm (37w), a patient who underwent labor at 37 weeks, 6 days
[4] Vaccination errors included: eight reports of vaccine given outside recommended gestational period, six given outside season, three reports of an additional dose of RSV given during same season, before approval in two, subcutaneous route in one, storage issue for Covid-19 vaccine, not RSV. Three reports of adverse events with vaccination errors
[5] Other includes two reports of no adverse event, and one each of diarrhea, infant with jaundice, and a report of rash
From October 2023 through March 2024, an estimated 320,400 pregnant persons received RSV vaccine (Peacock. Implementation and Uptake of Nirsevimab and Maternal RSV Vaccine. Advisory Committee on Immunization Practices. June 28, 2024.
**[6] No verified cases of Guillain-Barre Syndrome reported**

# Preterm deliveries (as of June 3, 2024)

| Classification[1] | N |
|---|---|
| Late preterm (34-36 weeks) | 27 |
| Early preterm (≥ 32 - <34 weeks) | 7 |
| Very preterm (28 - < 32 weeks) | 0 |
| Extremely preterm (< 28 weeks) | 0 |
| Unknown gestational age | 3 |
| Total | 37** |

[1] Based on ACOG and WHO definitions

## Risk factors and clinical information[2]

- 22 reported a medical condition or complication that increased risk for preterm delivery (e.g., elevated blood pressure, history of preterm delivery)
- 12 had insufficient information (no medical records)
- 3 uncomplicated pregnancies (no reported factors)
- 8 deliveries were induced

[2] Median maternal age at vaccination was 33 years (range 25-40 years); median onset interval from vaccination to preterm birth was 3 days (range 0-31 days)

From October 2023 through March 2024, an estimated 320,400 pregnant persons received RSV vaccine (Peacock. Implementation and Uptake of Nirsevimab and Maternal RSV Vaccine. Advisory Committee on Immunization Practices. June 28, 2024.

# Characteristics and outcomes of infants born to Pfizer RSV recipients

| Characteristics | N (%) |
|---|---|
| Number of infants[1] | 75 |
| Premature at birth (< 37 weeks)[2] | 38 (51) |
| Gestational age at birth (weeks) [3], median (range) | 36 (32 – 41) |
| Infants at term | 33 (44) |
| Sex | |
| Male | 32 (43) |
| Female | 34 (45) |
| Unknown sex | 9 (12) |
| Infant deaths[4] | 1 |
| Infant born with low birth weight (< 2,500 g) | 16 (21) |
| NICU admission[5] | 24 |
| Condition or reason for admission in NICU (not mutually exclusive)<br>Respiratory distress<br>Prematurity<br>Fetal distress<br>Unknown | <br>10 (42)<br>7 (29)<br>1 (4)<br>9 (38) |

[1] 66 infants born of a single pregnancy; 6 from 3 twin pregnancies; 3 data not reported
[2] Includes 6 infants from three twin pregnancies
[3] Gestational age at birth unknown for 4 reports
[4] 35-week infant with anoxic brain injury and neonatal death after emergent C-section, resuscitation, and hospital transfer 4 days after vaccination
[5] NICU admission unknown in 20 (39%) reports
From October 2023 through March 2024, an estimated 320,400 pregnant persons received RSV vaccine (Peacock. Implementation and Uptake of Nirsevimab and Maternal RSV Vaccine. Advisory Committee on Immunization Practices. June 28, 2024.

# VAERS Summary

- Among reports received, local and systemic symptoms (e.g., headache) were frequently reported in VAERS after Pfizer RSV vaccine consistent with pre-licensure studies in pregnant persons
- In clinical trials among pregnant persons at 24–36 weeks' gestation, more preterm births were noted among Pfizer RSV vaccine recipients compared to placebo
- The label for Pfizer RSV vaccine notes potential risk of preterm birth under warnings and precautions section
- Patients (pregnant persons) were the most common reporters (50%) overall and represented 70% of those who reported a preterm delivery
- Reports of pregnancy specific conditions (e.g., preterm delivery) were not unexpected for the Pfizer RSV vaccine, which is recommended at 32-36 weeks' gestation in pregnancy

# V-safe

# In Fall 2023 V-safe expanded to include RSV vaccine

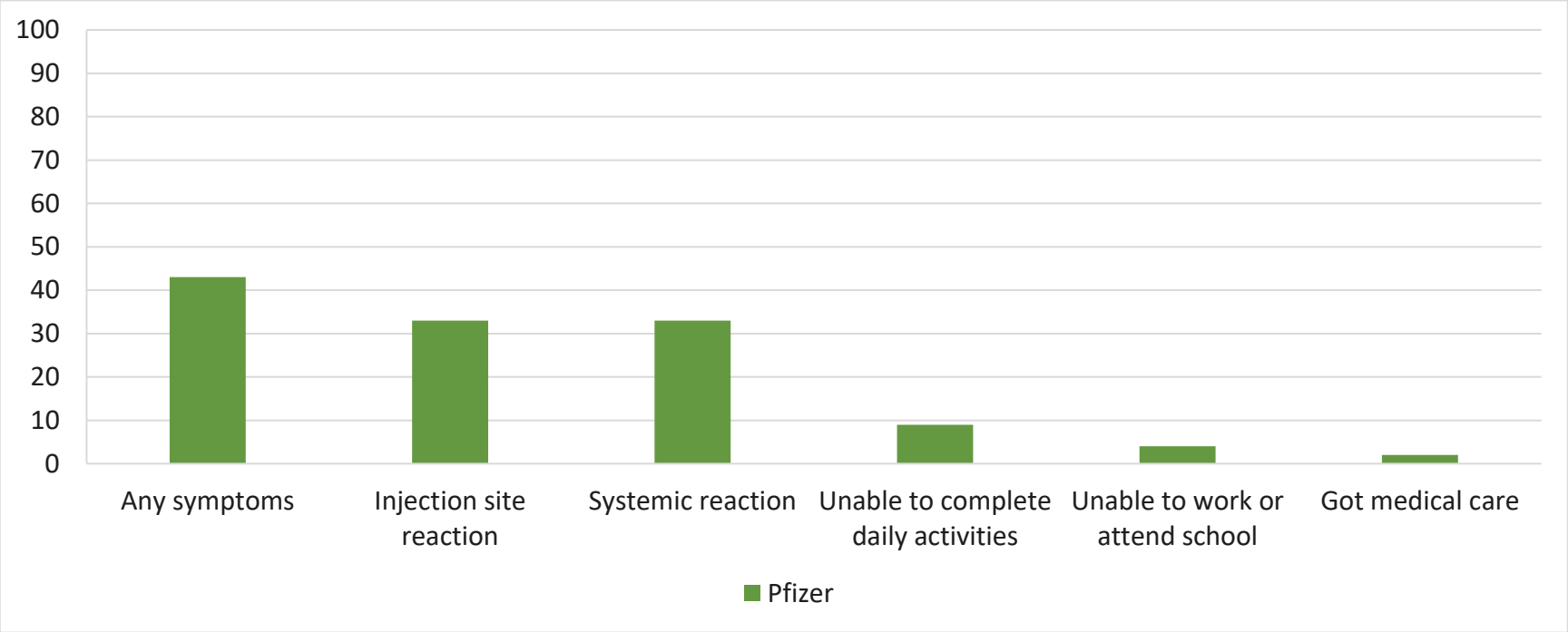
- Surveys sent daily during the first week after vaccination, then weekly through week 6
- Daily surveys solicit adverse events and health impacts after vaccination
  - Local reactions (e.g., pain, redness, swelling)
  - Systemic reactions (e.g., fatigue, headache, muscle pain)
  - Health impacts (e.g., unable to perform normal daily activities, missed school or work, or received medical care)
  - Additional questions for persons who reported immunocompromise at vaccination
- Weekly surveys solicit new symptoms or conditions after vaccination
- Maternal RSV protocol includes additional questions about current and prior pregnancies

# Characteristics of persons aged 16-49 years with reported RSV vaccination during pregnancy*

| Characteristic | % |
|---|---|
| **Age group, years** | |
| 16-34 | 58.4 |
| 35-49 | 41.6 |
| **Immunocompromised** | **2** |
| **Vaccine(s) co-administered** | **12** |
| COVID-19 | 5.8 |
| Influenza | 0.7 |
| Tetanus | 4 |
| Other | 1.3 |

* For 1,116 V-safe participants aged 16-49 years enrolled in the maternal RSV protocol with ≥1 completed daily survey during August 21, 2023 – May 20, 2024

# Reactions and health impacts reported for persons aged 16-49 years with reported RSV vaccination during pregnancy (n=1,116)*

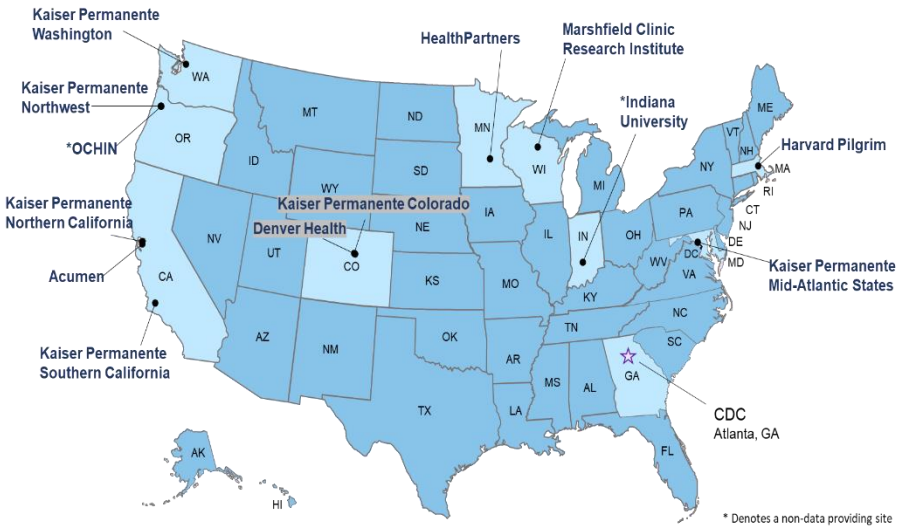



* For 1,116 V-safe participants aged 16-49 years enrolled in the maternal RSV protocol with ≥1 completed daily survey during August 21, 2023 – May 20, 2024

# Vaccine Safety Datalink

# Vaccine Safety Datalink (VSD) 2024

- Collaborative project between CDC and integrated healthcare organizations
- Monitors safety of vaccines used in the US, primarily through real-world data of rare and serious events following vaccination
- Includes data on ~15.5 million individuals across all sites annually
- ~ 115,000 annual live births
- Data is organized using a common data model with standardized coding systems



# VSD Prenatal RSV Vaccine Surveillance

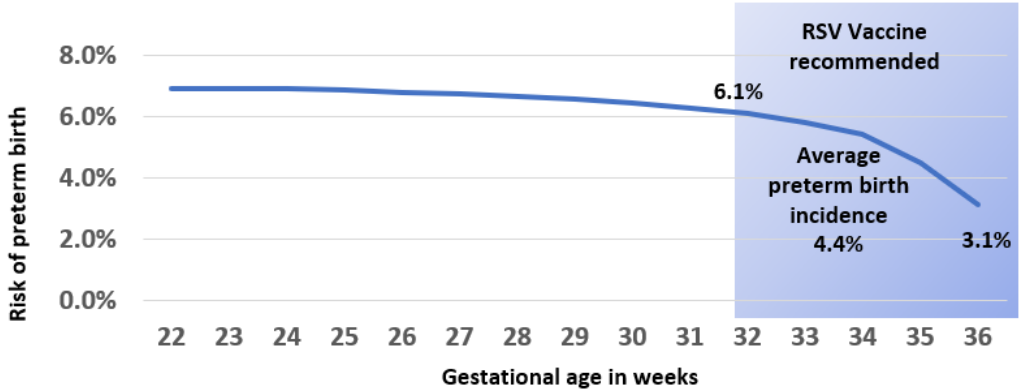
- Determine cumulative *historical* incidence rates of preterm birth among singleton pregnancies in the VSD reaching specified gestational ages from 22–36 weeks during 2017–2022

- Determine incidence of preterm births in RSV vaccinated pregnant persons[1,2]

[1]For RSV vaccines administered at 30 to less than 37 weeks' gestation
[2]Pfizer RSV should be administered at 32 through 36 weeks' gestation
https://www.fda.gov/media/168889/download

# Preterm births in VSD – Historical incidence of preterm births and preterm births following RSV vaccine during pregnancy at 9 VSD sites

**Incidence of preterm births among singleton pregnancies in the VSD reaching specified gestational ages from 22–36 weeks during 2017–2022**




- In VSD, 10,295 RSV vaccines were administered at 30 to less than 37 weeks gestational age among pregnant persons during 2023–2024 respiratory season with 427 preterm births among vaccinees.
- **The preterm birth incidence was 4.1% which is *within the expected range* (3.1–6.1%) based on historical data.**

# VSD 1:1 Matched analysis (ongoing)[1]

- Pregnant persons, RSV vaccinated: unexposed at same gestational week
- Create propensity scores to account for confounding
- Outcomes
  - Acute safety outcomes (e.g., anaphylaxis, Guillain-Barré syndrome)
  - Preterm birth
  - Stillbirth
  - Preeclampsia/eclampsia/HELLP*
- 2023-2024 analysis pending, data available later this year

*Hemolysis, elevated liver enzymes, low platelet count

[1] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-09-22/02-Mat-Peds-DeSilva-508.pdf

# Summary

- Local and systemic symptoms were reported to V-safe following Pfizer RSV vaccine in pregnant persons, with a frequency similar to that observed in pre-licensure trials; few pregnant people in V-safe reported medical care for symptoms1
- Among reports received in VAERS after maternal Pfizer RSV vaccine, the most frequent adverse events reported were local and systemic symptoms (e.g., headache) and pregnancy specific conditions (e.g., preterm delivery), as expected for a vaccine recommended for pregnant persons at 32-36 weeks' gestation
- Post-licensure vaccine safety data from VAERS and V-safe during first season after maternal Pfizer RSV vaccine are consistent with the pre-licensure safety profile
- Preliminary findings in the VSD observed that the incidence of preterm births is 4.1% among pregnant persons who received Pfizer RSV vaccine during the 2023-2024 respiratory season. This was within the expected range of the incidence of preterm births at 32-36 weeks' gestation (3.1 - 6.1%) before introduction of this vaccine
- CDC and FDA will continue to monitor maternal RSV vaccine safety in VAERS, V-safe and VSD

[1] https://www.fda.gov/vaccines-blood-biologics/abrysvo

# Acknowledgements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- National Center for Immunization and Respiratory Diseases
  - Coronavirus and Other Respiratory Viruses Division

# Closing Slide / Disclaimer

## The findings and conclusions in this presentation are those of the authors and not necessarily represent the official position of CDC

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