

RSVpreF Vaccine Safety Surveillance in Pregnancy from The Vaccine Safety Datalink

Malini DeSilva, MD, MPH

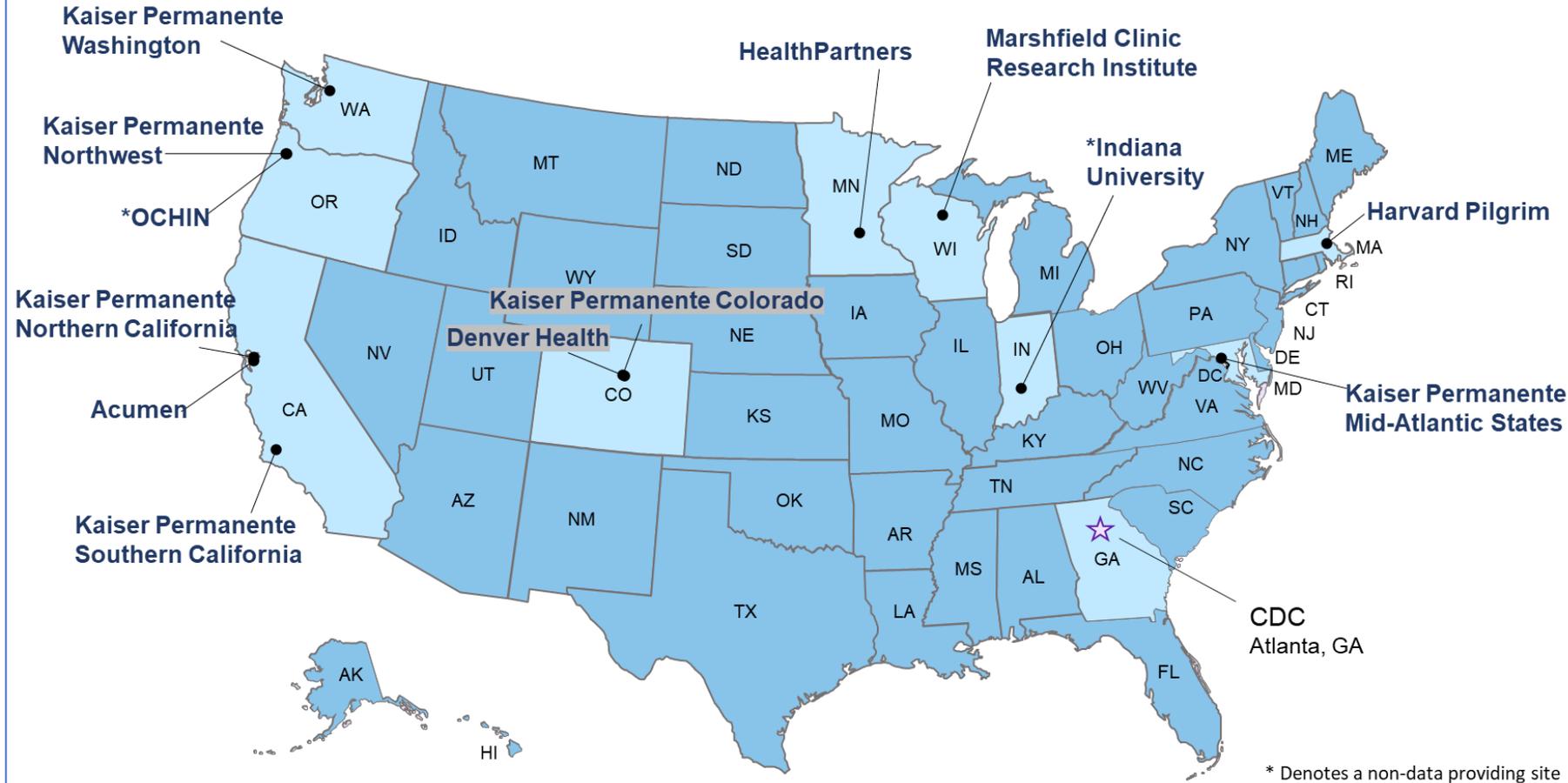
ACIP meeting

September 22, 2023



Vaccine Safety Datalink (VSD), 2023

- Collaborative project between CDC and integrated healthcare organizations
- Monitors safety of vaccines used in the U.S., 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



Vaccine Safety Datalink (VSD) data structure

- **Distributed data model – each VSD site creates standardized data files**
 - Define cohort
 - Vaccines
 - Diagnoses & procedures from inpatient/outpatient/emergency
 - Birth and death files
- **Dynamic pregnancy episode file – validated algorithms for identifying ongoing & completed pregnancies, updated weekly**
 - Pregnancy start, last menstrual period (LMP)
 - Gestational age
 - Pregnancy outcome (when available)
- **Mom-baby linkage**
- **Ancillary drug or lab files available ad-hoc for specific studies**
- **Automated data files supplemented with chart review, as needed**

ORIGINAL
ARTICLES



Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine



Maternal Influenza Vaccine and Risks for Preterm or Small for Gestational Age Birth

James D. Nordin, MD, MPH¹, Elyse Olshen Kharbanda, MD, MPH¹, Gabriela Vazquez Benitez, PhD¹, Heather Lipkind, MF
Claudia Vellozzi, MD, MPH³, and Frank DeStefano, MD, MPH³, on behalf of the Vaccine Safety Datalink*

CORRESPONDENCE

Evaluation of Acute Adverse Events after Covid-19 Vaccination during Pregnancy

ELSEVIER

journal homepage: www.elsevier.com/locate/vaccine

Maternal Tdap vaccination and risk of infant morbidity

Malini DeSilva^{a,*}, Gabriela Vazquez-Benitez^a, James D. Nordin^a, Heather S. Lipkind^b, Nicola P. Klein^c,
T. Craig Cheetham^d, Allison L. Naleway^e, Simon J. Hambidge^f, Grace M. Lee^g, Michael L. Jackson^h,
Natalie L. McCarthyⁱ, Elyse O. Kharbanda^a

Original Investigation

Evaluation of the Association of Maternal Pertussis Vaccination With Obstetric Events and Birth Outcomes

Elyse O. Kharbanda, MD, MPH; Gabriela Vazquez-Benitez, PhD; Heather S. Lipkind, MD, MS;
Nicola P. Klein, MD, PhD; T. Craig Cheetham, PharmD, MS; Allison Naleway, PhD; Saad B. Omer, PhD;
Simon J. Hambidge, MD, PhD; Grace M. Lee, MD, MPH; Michael L. Jackson, PhD; Natalie L. McCarthy, MPH;
Frank DeStefano, MD, MPH; James D. Nordin, MD, MPH

Tdap vaccination during pregnancy and risk of chorioamnionitis and related infant outcomes

Victoria Greenberg^{a,*}, Gabriela Vazquez-Benitez^b, Elyse O. Kharbanda^b, Matthew F. Daley^c,
Hung Fu Tseng^d, Nicola P. Klein^e, Allison L. Naleway^f, Joshua T.B. Williams^g, James Donahue^h,
Lisa Jacksonⁱ, Eric Weintraub^j, Heather Lipkind^k, Malini B. DeSilva^l

Original Investigation | Public Health

COVID-19 Booster Vaccination in Early Pregnancy and Surveillance for Spontaneous Abortion

Elyse O. Kharbanda, MD, MPH; Jacob Haapala, MPH; Heather S. Lipkind, MD, MS; Malini B. DeSilva, MD, MPH; Jingyi Zhu, PhD; Kimberly K. Vesco, MD, MPH;
Matthew F. Daley, MD; James G. Donahue, DVM, PhD; Darios Getahun, MD, PhD; Simon J. Hambidge, MD, PhD; Stephanie A. Irving, MHS; Nicola P. Klein, MD, PhD;
Jennifer C. Nelson, PhD; Eric S. Weintraub, MPH; Joshua T. B. Williams, MD; Gabriela Vazquez-Benitez, PhD



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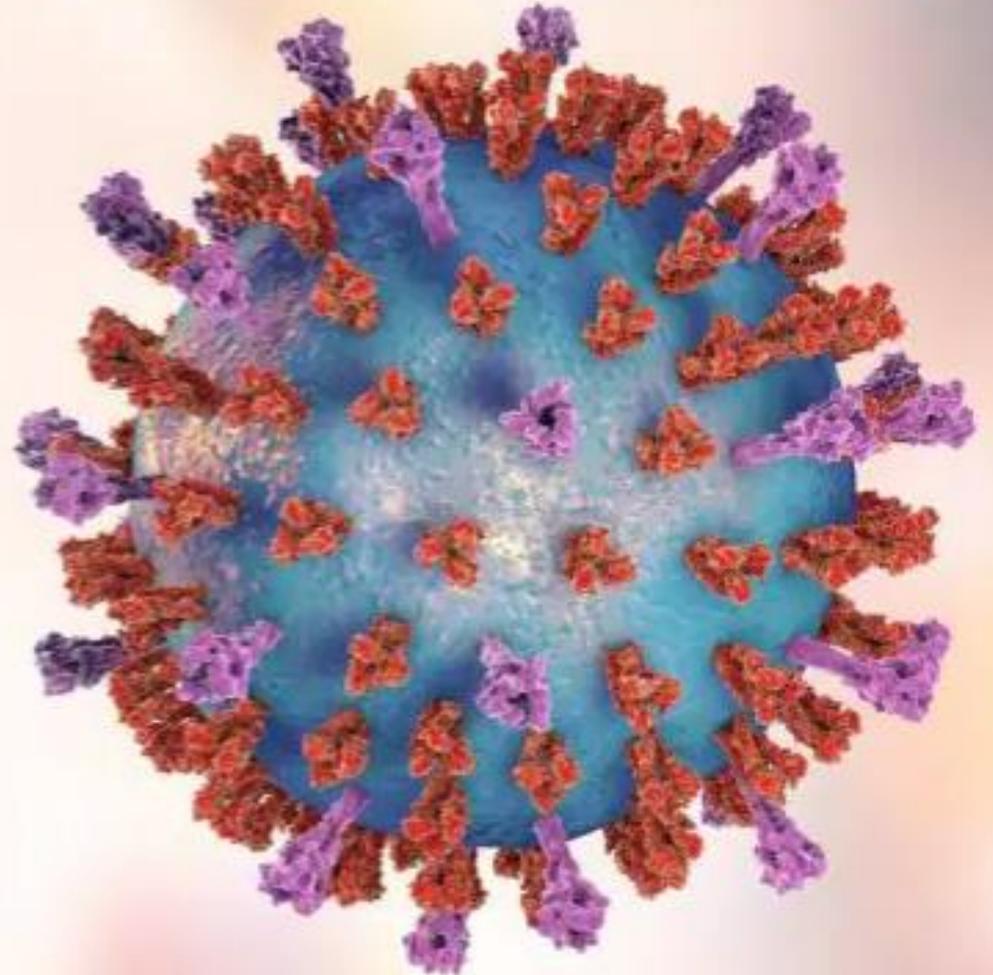


First Trimester Influenza Vaccination and Risks for Major Structural Birth Defects in Offspring

Elyse Olshen Kharbanda, MD, MPH¹, Gabriela Vazquez-Benitez, PhD¹, Paul A. Romitti, PhD², Allison L. Naleway, PhD³,
T. Craig Cheetham, PharmD⁴, Heather S. Lipkind, MD, MS⁵, Nicola P. Klein, MD, PhD⁶, Grace Lee, MD, MPH⁷,
Michael L. Jackson, PhD, MPH⁸, Simon J. Hambidge, MD, PhD⁹, Natalie McCarthy, MPH¹⁰, Frank DeStefano, MD, MPH¹⁰, and
James D. Nordin, MD, MPH¹, for the Vaccine Safety Datalink

Prenatal RSVpreF Vaccine Background

- RSVpreF (Pfizer) effective against severe RSV-associated LRTI in infants
- RSVpreF clinical trial data on safety in pregnant persons
 - Injection site pain most common reactogenicity event
 - Imbalance in preterm births in vaccinated group
 - Most late preterm (34–<37 weeks)
 - Most occurred >30 days after vaccination
 - Most prominent in a single country
- GSK RSV prenatal vaccine clinical trial halted due to imbalance in preterm birth in vaccinated



Goal & Challenges

Prenatal RSVpreF Vaccine Surveillance

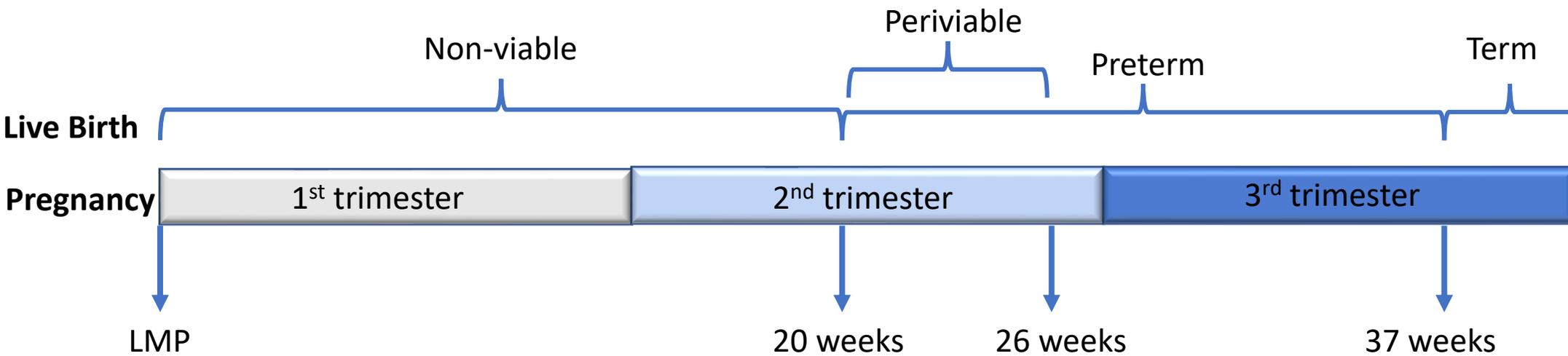
- **Goal:** To evaluate the safety of RSVpreF vaccine administered during pregnancy in the VSD's large, real-world population
- **Challenges:**
 - Vaccine uptake
 - Healthy vaccinee bias
 - Uncertain recommendations for RSVpreF use & administration
 - Coadministration of COVID-19, influenza, Tdap

Pregnancy Outcomes



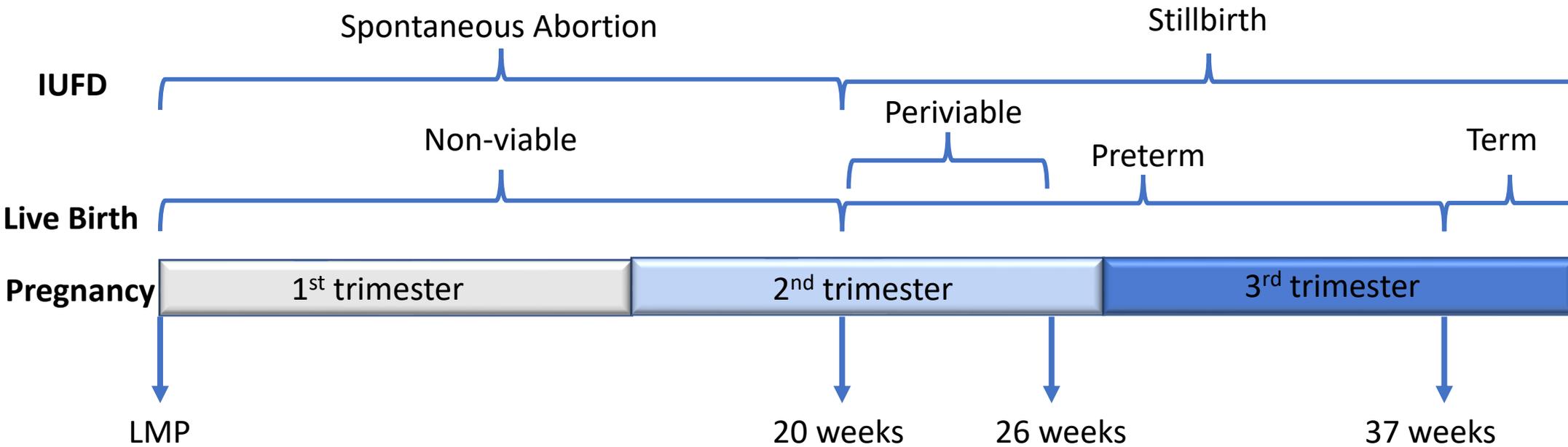
LMP = Last menstrual period

Pregnancy Outcomes



LMP = Last menstrual period

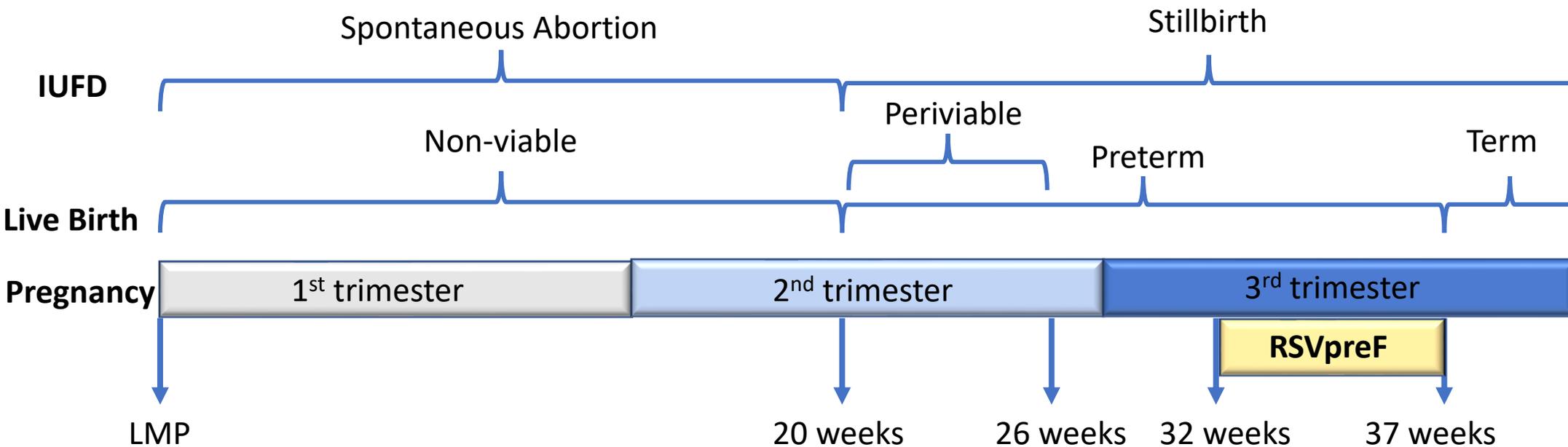
Pregnancy Outcomes



LMP = Last menstrual period

IUFD = Intrauterine Fetal Demise

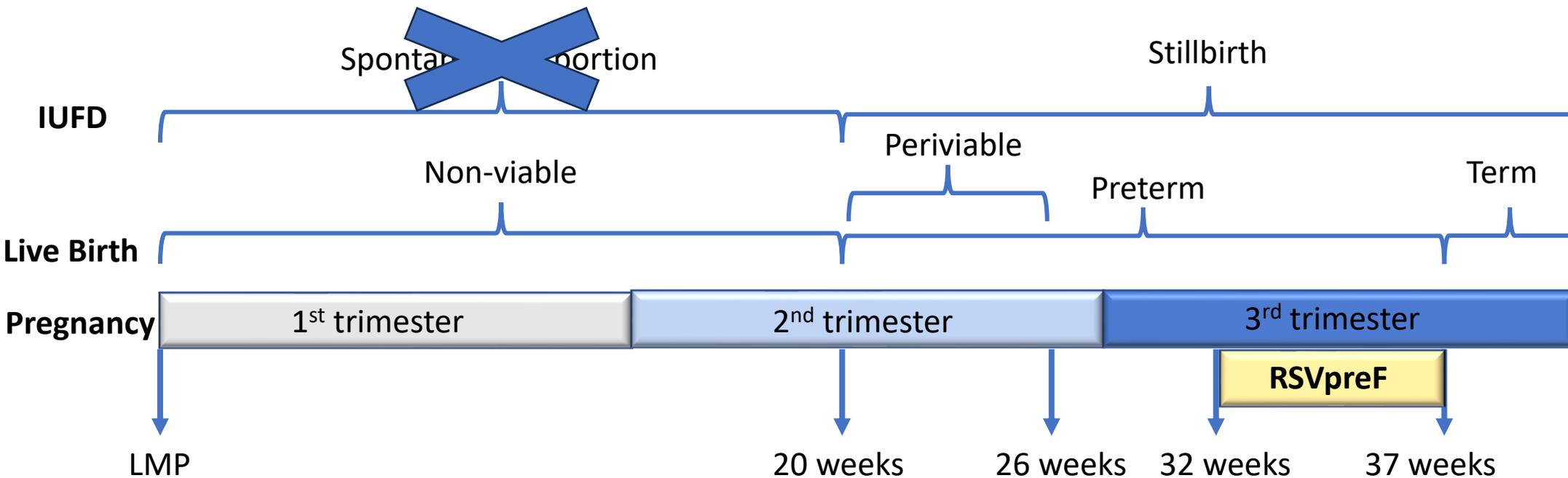
Pregnancy Outcomes



LMP = Last menstrual period

IUFD = Intrauterine Fetal Demise

Pregnancy Outcomes



Prenatal RSVpreF Surveillance

- Bimonthly surveillance
- Use validated algorithms applied to electronic health data in VSD to identify pregnant persons 16–49 years at ≥ 20 weeks' gestation
 - Exclude pregnancies: ending in therapeutic abortion, multiple gestation, and with insufficient information to date pregnancy
- Exposure: RSVpreF vaccination ≥ 28 weeks gestation
- Match 1:1, vaccinated: unvaccinated
 - VSD Site & gestational age
 - Create propensity scores to account for confounding using readily available variables (e.g., age, pregnancy start date, race, ethnicity, medical comorbidities)

Adverse outcomes evaluated

- Acute outcomes
 - Use algorithm developed for other VSD safety surveillance and modified for pregnant population
 - Diagnoses associated with outpatient, emergency department, and hospital encounters
 - Chart confirmation for selected outcomes
- Pregnancy related and birth outcomes
 - Preeclampsia/eclampsia – ICD-10 codes
 - Preterm birth – gestational age at birth
 - Stillbirth – ICD-10 codes with chart review confirmation

Acute Outcomes

Outcome	Risk window(s) (days)	VSD Background rate/10,000*
Anaphylaxis	0–1	n/a
Fever	1–7	3.3
Malaise / fatigue	1–7	11.4
Skin and soft tissue or local allergic reactions	1–7	7.0
Acute disseminated encephalomyelitis	1–21, 1–42	0
Acute myocardial infarction	1–21, 1–42	0.3
Appendicitis	1–21, 1–42	0.6
Bell's Palsy	1–21, 1–42	0.8
Cerebral venous sinus thrombosis (CVST)	1–21, 1–42	0.1
Disseminated intravascular coagulation (DIC)	1–21, 1–42	0.3
Guillain-Barré syndrome	1–21, 1–42	0
Immune thrombocytopenic purpura (ITP)	1–21, 1–42	7.6
Lymphadenopathy / lymphadenitis	1–21, 1–42	4.6

*Identified from unvaccinated pregnant persons, COVID-19 medically attended acute outcomes 1–7 or 1–21 day evaluation

Acute Outcomes, continued

Outcome	Risk window (d)	Background rate/10,000*
Myocarditis / pericarditis	1-21, 1-42	0
Pulmonary embolism (PE)	1-21, 1-42	0.1
Seizure	1-21, 1-42	0.8
Stevens-Johnson syndrome or toxic epidermal necrolysis	1-21, 1-42	n/a
Stroke, hemorrhagic	1-21, 1-42	0.4
Stroke, ischemic	1-21, 1-42	0.4
Thrombosis with thrombocytopenia syndrome (TTS)	1-21, 1-42	n/a
Thrombotic thrombocytopenic purpura (TTP)	1-21, 1-42	n/a
Transverse myelitis	1-21, 1-42	n/a
Trigeminal neuralgia and related disorders	1-21, 1-42	0.1
Venous thromboembolism (VTE)	1-21, 1-42	0.4

*Identified from unvaccinated pregnant persons, COVID-19 medically attended acute outcomes 1- 21 day evaluation

Pregnancy related and birth outcomes

Outcome	Risk window	Pfizer phase 3 RSVpreF trial, n (%) [¥]
Preeclampsia and eclampsia	1-21, 1-42	68/3682 (1.8) [¥]
Preterm birth (<37 w)	Up to 37 weeks	126/2494 (5.1) ^Δ
Stillbirth	1-21, 1-42	10/3682 (0.3) [¥]

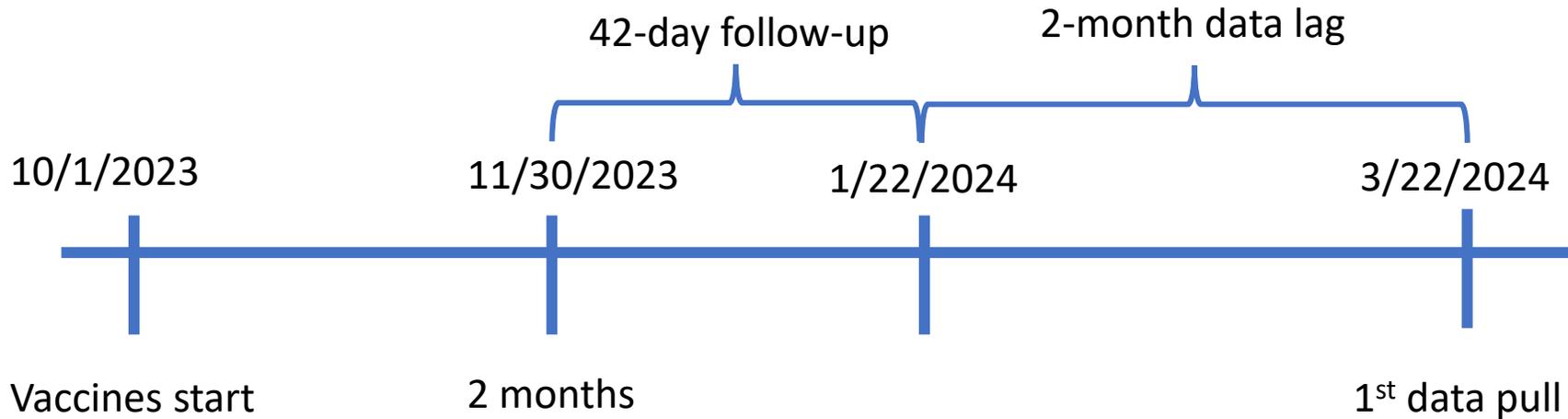
[¥] RSVPreF Phase 3 clinical trial: [Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants | NEJM](#)

^ΔPreterm birth rate in high-income countries (Slide 23 [Evidence to Recommendations Framework: \(cdc.gov\)](#))

Prenatal RSVpreF Surveillance Analysis

- Risk ratios with corresponding 95% CI using Poisson distribution with robust variance using generalized estimating equation (GEE)
- Censoring within risk windows when no longer at risk, due to pregnancy outcome, or if an unvaccinated match is vaccinated
- Adjustments for known confounders
- If preterm births signal detected, exploration into etiology
- Sensitivity Analysis: alternative matching strategies
- Exploratory: Coadministration of Tdap and RSVpreF

Example timeline



Repeat analyses every 60 days/2 months

Our Team

HealthPartners

- Malini DeSilva
- Elyse Kharbanda
- Jacob Haapala
- Gabriela Vazquez-Benitez
- Leslie Kuckler
- Robyn Kaiser
- Jingyi Zhu
- Sunita Thapa
- Sheryl Kane
- Nicole Trower

Weill Cornell Medicine

- Heather Lipkind

Kaiser Northwest

- Kimberly Vesco

CDC

- Eric Weintraub
- Elizabeth Quincer

Other VSD sites

- Acumen
- Denver Health
- Harvard Pilgrim
- Indiana University
- Kaiser Permanente Northwest
- Kaiser Permanente Colorado
- Kaiser Permanente Southern California
- Kaiser Permanente Northern California
- Kaiser Permanente Washington
- Kaiser Permanente Mid-Atlantic States
- Marshfield Clinic
- OCHIN