

Prenatal RSVpreF Vaccine Safety 2023–2024 Respiratory Season The Vaccine Safety Datalink (VSD)

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Presentation to ACIP

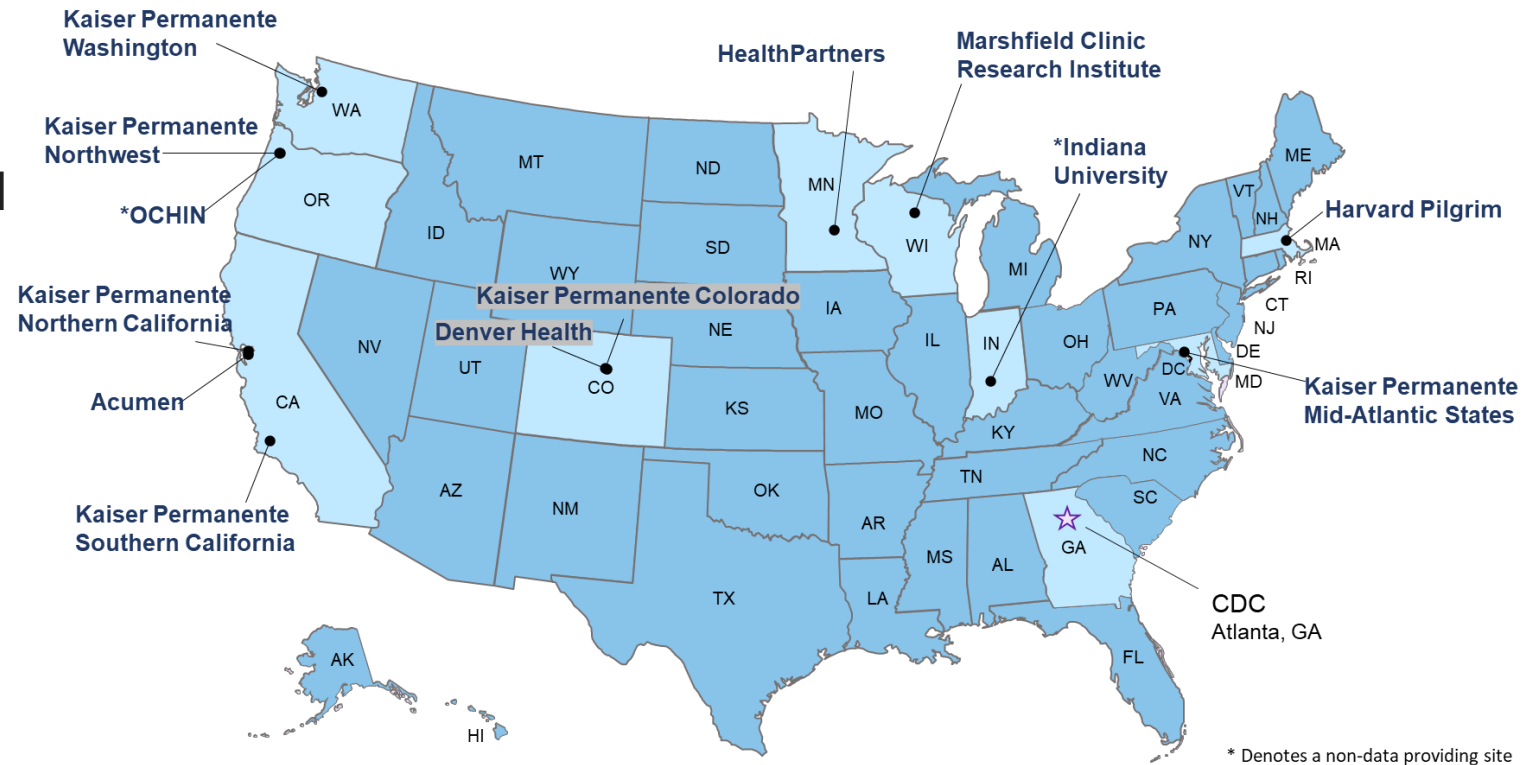
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HealthPartners[®] Institute

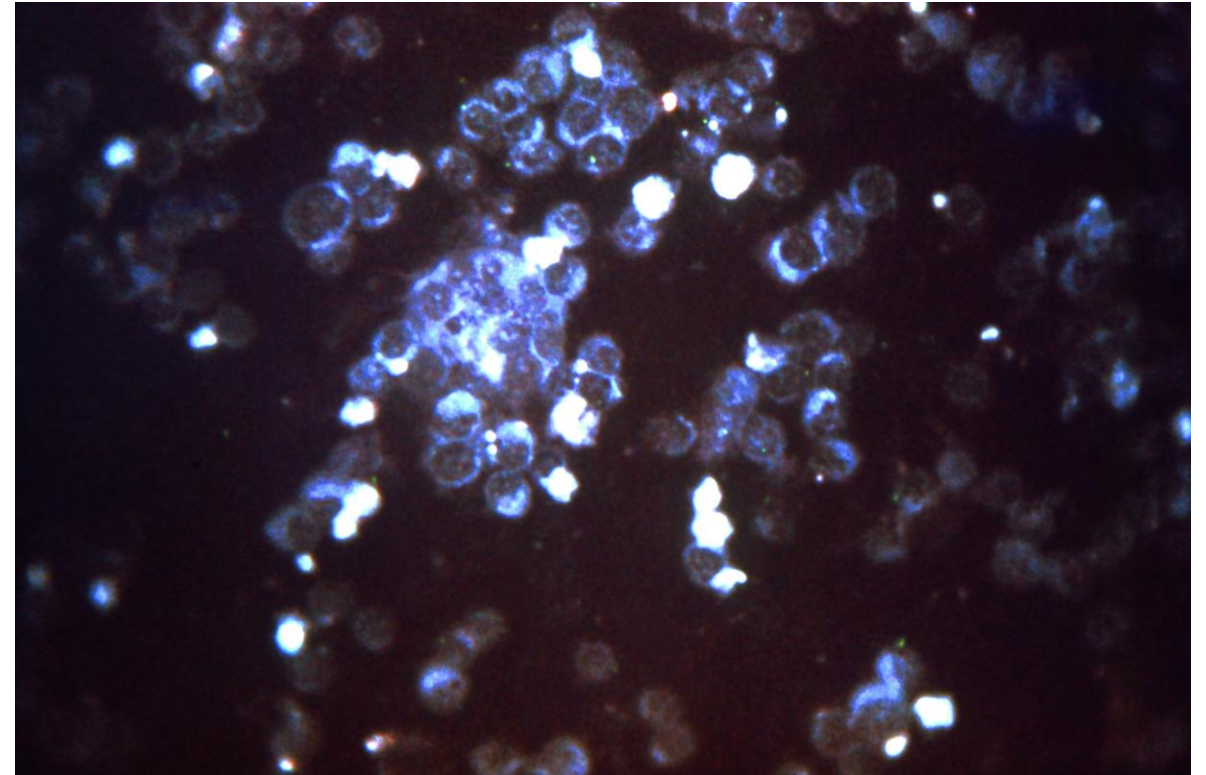
Vaccine Safety Datalink (VSD)

- Collaborative project between CDC and 13 integrated healthcare organizations
- Monitors safety of vaccines used in the U.S., primarily through observational multisite studies
- Includes data on ~15.5 million individuals across all sites annually (~4.5% of U.S. population)
- Annual birth cohort ~ 115,000
- Data is organized using a common data dictionary with standardized coding systems



Prenatal RSVpreF vaccine 2023–2024 season

- **ACIP recommendation 9/22/23:**
 - **32–36 weeks gestation with seasonal administration**
- **RSVpreF clinical trial¹ identified non-significant imbalances among vaccinated compared to placebo in:**
 - **Preterm births**
 - **Gestational hypertension and preeclampsia**



Photomicrograph of RSV using indirect immunofluorescent antibody under fluorescent lighting.

<https://phil.cdc.gov/Details.aspx?pid=6484>

¹Simoes EAF, Center KJ, Tita ATN, et al. Prefusion F Protein-Based Respiratory Syncytial Virus Immunization in Pregnancy. *N Engl J Med*. Apr 28 2022;386(17):1615-1626. doi:10.1056/NEJMoa2106062

Prenatal RSVpreF vaccine safety outcomes

- ❖ **Acute outcomes within 42 days of vaccination**
- ❖ **Preterm birth (birth <37 weeks gestational age)**
- ❖ **Small for Gestational Age (SGA) at birth**
- ❖ **Stillbirth (antepartum)**
- ❖ **Hypertensive disorders of Pregnancy (HDP):**
 - **Gestational hypertension (GHTN)** - New onset HTN after 20 weeks gestation
 - **Preeclampsia** - New onset or worsening chronic HTN after 20 weeks gestation with or without severe features
 - **Eclampsia** - Convulsive manifestation of HDP with no other etiology
 - **HELLP Syndrome** (hemolysis, elevated liver enzymes, and low platelets)

Methods - Target trial emulation design

Recreating a randomized experiment from observational data

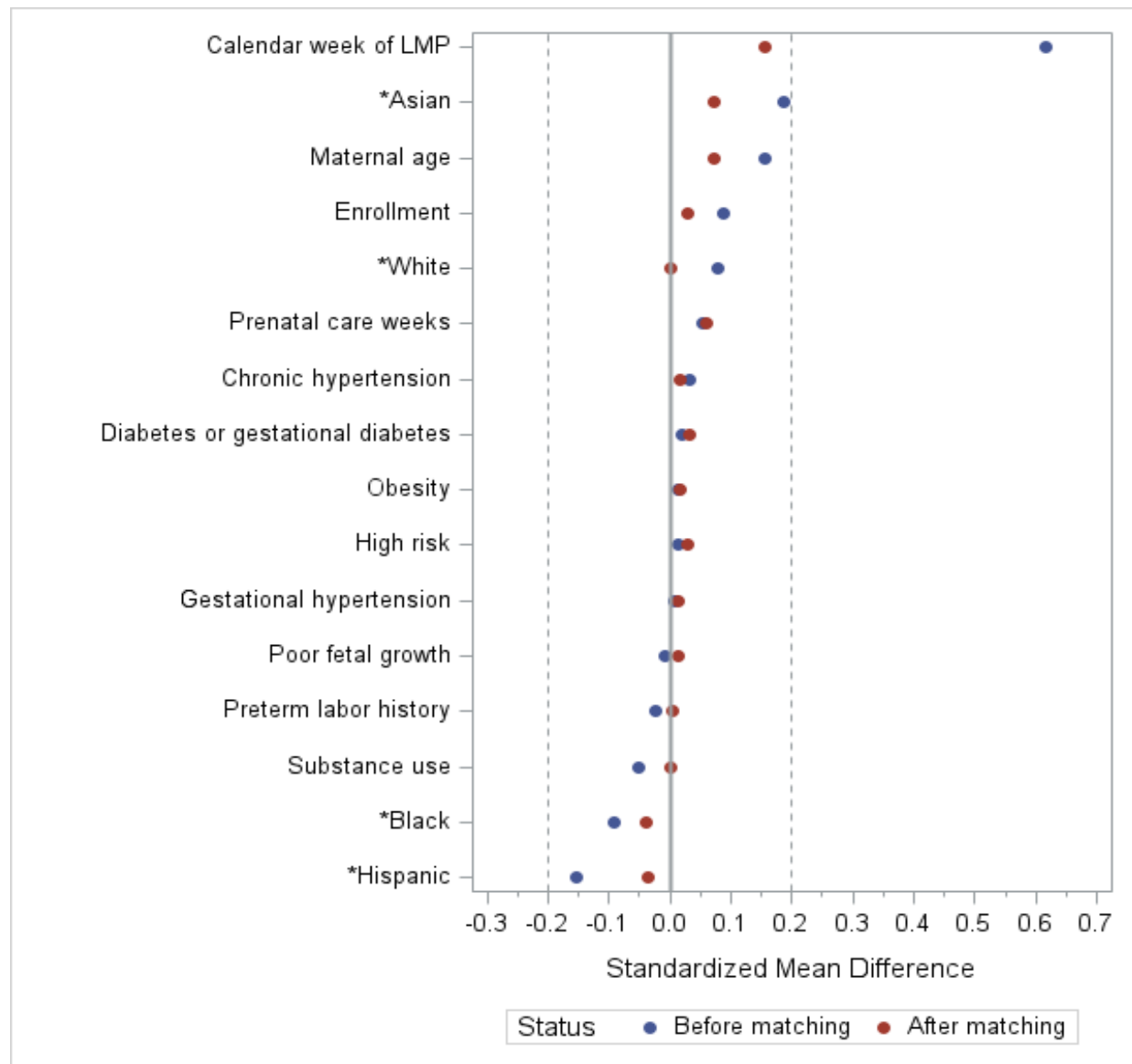
Protocol Component	
Eligibility criteria	Pregnant women 16–49 years with gestational age 32–<37 weeks during 9/22/2023 – 1/31/24 or 2/29/24 for two sites
Treatment strategies	<ul style="list-style-type: none">• RSVpreF vaccination (exposed)• No RSVpreF vaccination (unexposed)
Assignment procedures	Exposed women matched 1:1 to unexposed on: <ul style="list-style-type: none">• VSD site• Propensity to be vaccinated*• Gestational week
Follow-up period	<ul style="list-style-type: none">• Index date (vaccination or gestational day of vaccine for unexposed match) through 2 weeks after pregnancy end• Follow up censored at crossover to RSVpreF vaccination

*Covariates included: Maternal age, calendar week at pregnancy start, # of weeks with prenatal care, race/ethnicity, comorbidities (i.e., HTN, DM, GHTN, GDM, obesity, substance use), history of preterm labor, poor fetal growth, supervision of high-risk pregnancy, enrollment, and gestational week

Analysis

- **Estimated risk ratios with 95% Confidence Interval (CI) using Log binomial model with robust variance with adjustment for nulliparity**
- **For small for gestational age at birth, matched set excluded if infant weight not available for either infant in matched pair**
- **For hypertensive disorders of pregnancy, matched set excluded if onset occurs before or on index date for either woman**

Balance plot before and after matching



SMD = standardized mean differences for variables included in the propensity score before and after matching.

Common way to assess covariate balance after matching

Interpretation: -0.2 to 0.2 = small difference between groups

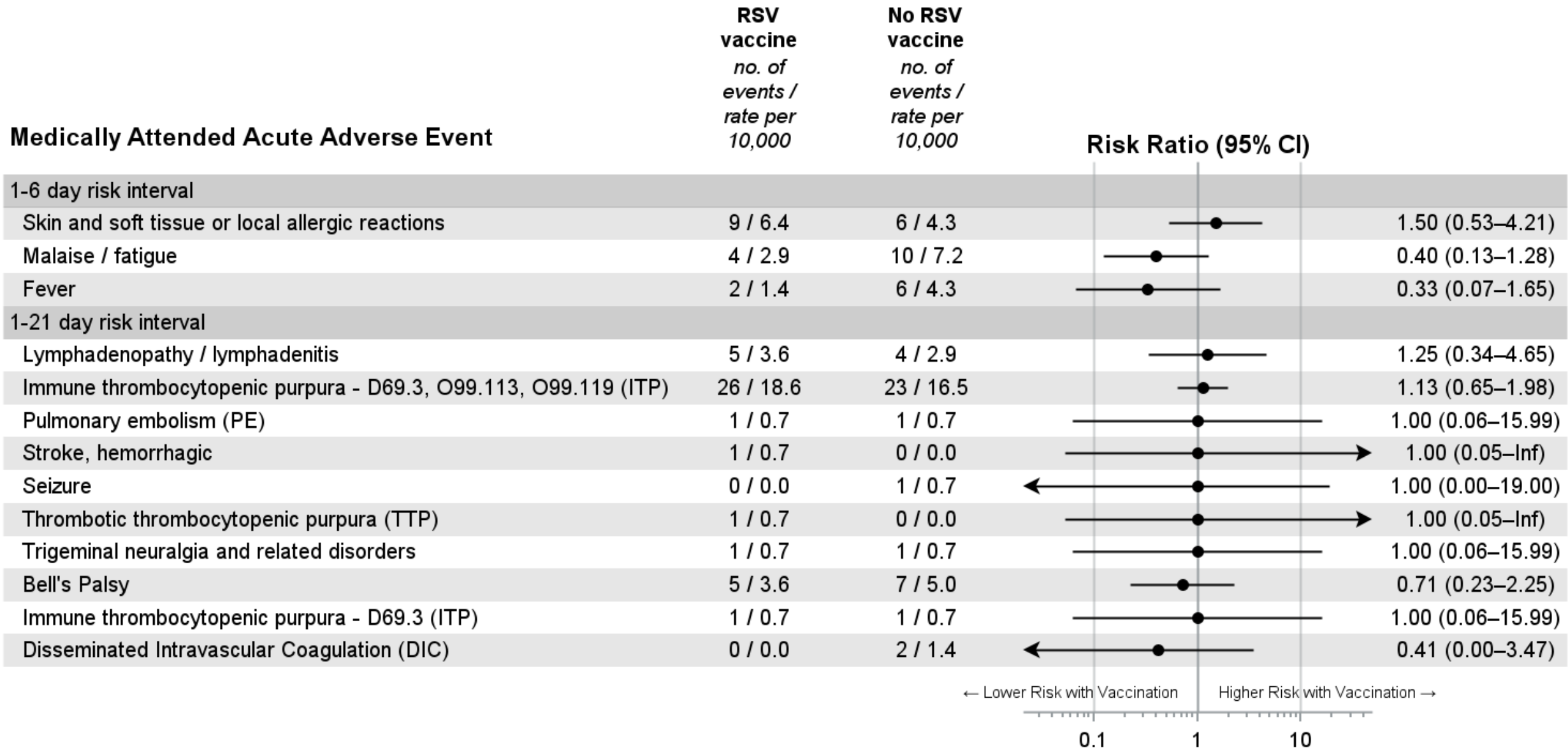
Notes:

- *Race/Ethnicity
- LMP = last menstrual period
- Enrollment = continuous health plan enrollment from 90 prior to LMP through index week
- ICD-10 codes for:
 - High Risk = O09.* (Supervision of care for a high-risk pregnancy)
 - Poor fetal growth = O36.5
 - Preterm labor history = O09.21, Z87.51

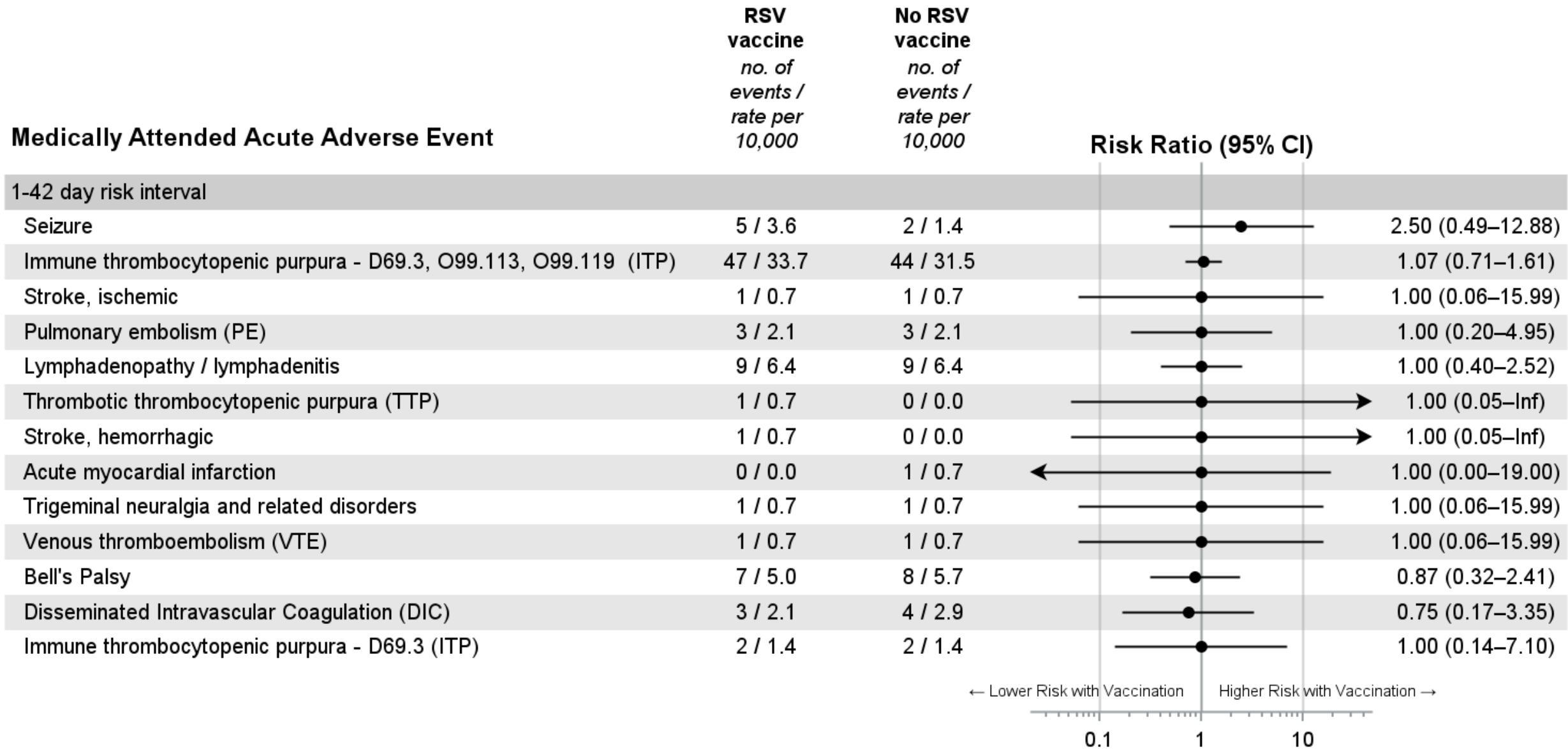
Matched cohort* characteristics, N = 13,966

	RSVpreF Vaccinated, n (%)	Unvaccinated match, n (%)
Age group		
• 16–24 years	1405 (10.1)	1595 (11.4)
• 25–29 years	3151 (22.6)	3439 (24.6)
• 30–34 years	5461 (39.1)	5272 (37.7)
• 35–39 years	3286 (23.5)	3020 (21.6)
• 40–49 years	663 (4.7)	640 (4.6)
Race/Ethnicity		
• Asian	3039 (21.8)	2635 (18.9)
• Black	862 (6.2)	991 (7.1)
• Hispanic	4459 (31.9)	4691 (33.6)
• White	4542 (32.5)	4541 (32.5)
• Other/Unknown	1064 (7.6)	1108 (7.9)
≥1 other vaccine during pregnancy	13758 (98.5)	11315 (81.0)
Nulliparity	5914 (46.4)	4853 (38.7)

1–6 and 1–21 day acute safety outcome risks among pregnant women receiving RSVpreF vaccine and unvaccinated matches



1–42 day acute safety outcome risk among pregnant women receiving RSVpreF vaccine and unvaccinated matches



Preterm birth^a risk among pregnant women receiving RSVpreF vaccine and unvaccinated matches

Matched pairs, N	RSVpreF vaccinated		Unvaccinated match		Adjusted Risk Ratio (95% CI) ^b
	N events*	Preterm birth %	N events*	Preterm birth %	
13,966	563	4.0	627	4.5	0.90 (0.80–1.00)

^aPreterm birth = birth <37 weeks gestational age

^bAdjusted for nulliparity

*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

SGA^a at birth risk in infants born to RSVpreF vaccinated pregnant person or unvaccinated pregnant matches

Matched pairs, N	RSVpreF vaccinated		Unvaccinated match		Adjusted Risk Ratio (95% CI) ^b
	N events*	SGA at birth %	N events*	SGA at birth %	
11,822	799	6.8	774	6.5	0.99 (0.90–1.09)

^aSGA at birth = Small for gestational age at birth; birth weight <10th percentile for gestational age compared with a U.S. reference population¹

^bAdjusted for nulliparity

*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

Note: 11,822 matched pairs with complete infant weight data (85%)

Talge NM, Mudd LM, Sikorskii A, Basso O. United States birth weight reference corrected for implausible gestational age estimates. *Pediatrics*. May 2014;133(5):844-53. doi:10.1542/peds.2013-3285

Stillbirth risk in RSVpreF vaccinated pregnant women or unvaccinated pregnant matches

Matched pairs, N	RSVpreF vaccinated		Unvaccinated match		Adjusted Risk Ratio (95% CI) ^a
	N events*	Stillbirths per 1000	N events*	Stillbirths per 1000	
13,966	11	0.79	10	0.72	1.09 (0.46–2.58)

^aAdjusted for nulliparity

*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

Hypertensive disorders of pregnancy (HDP) risk among pregnant women receiving RSVpreF vaccine and unvaccinated matches, N = 13,474

Outcome	RSVpreF vaccinated		Unvaccinated match		Adjusted Risk Ratio (95% CI) ^a
	N events*	%	N events*	%	
Any HDP	2344	17.4	2056	15.3	1.09 (1.03–1.15)
Eclampsia OR HELLP	40	0.3	50	0.4	0.77 (0.51–1.16)
Preeclampsia	1198	8.9	1021	7.6	1.12 (1.03–1.21)
Gestational hypertension ^b	1069	8.8	939	7.8	1.10 (1.01-1.19)

^aAdjusted for nulliparity

^bMatched pairs = 12104; excludes matched pairs with chronic hypertension

*Events only included through date of censoring when unvaccinated pair crosses over to vaccinated

Evaluation of rates of cesarean delivery, admissions following birth hospitalization, and lengths of stay for patients with hypertensive disorders of pregnancy (HDP) by RSVpreF vaccination status

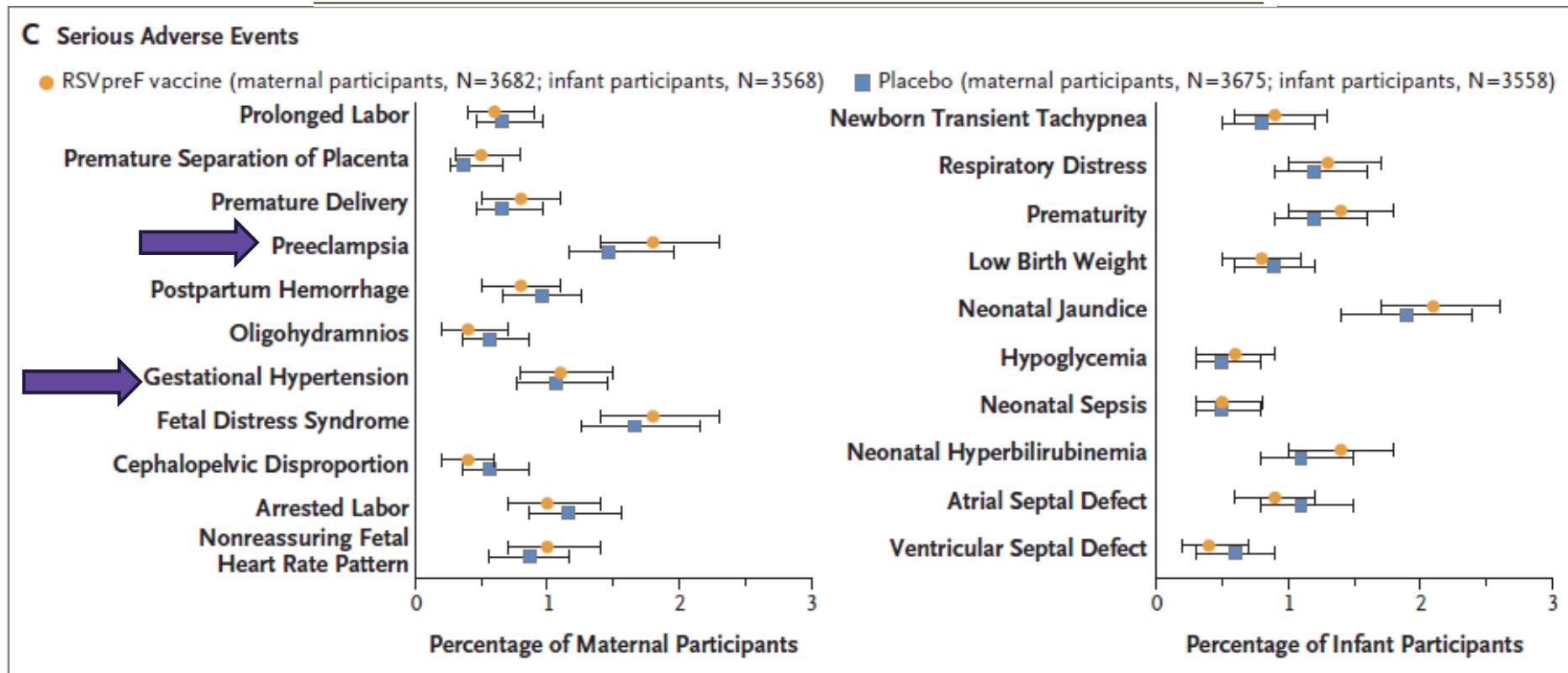
HDP Severity indicator		RSVpreF vaccinated N = 2344	Unvaccinated match N = 2056
		N (%)	N (%)
Cesarean delivery		795 (33.9)	675 (32.8)
HDP admission \leq 14 days following birth hospitalization		184 (7.8)	165 (8.1)
Length of stay >3 days for birth hospitalization			
Infant ^a	Cesarean delivery	125 (17.8)	123 (21.4)
	NSVD	93 (6.8)	70 (5.9)
Mother	Cesarean delivery	384 (49.0)	310 (46.0)
	NSVD	277 (18.3)	245 (17.9)

NSVD = normal spontaneous vaginal delivery

^aMissing: RSVpreF vaccinated = 282 ; Unvaccinated = 300

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

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



Nonadjuvanted Bivalent Respiratory Syncytial Virus Vaccination and Perinatal Outcomes

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- Retrospective observational cohort study of patients who delivered at 32 0/7 weeks' gestation or later at 2 NYC hospitals 9/22/23 – 1/31/24

Table 2. Pregnancy Outcomes Between Patients Who Had RSV Vaccination During Pregnancy Documented in Their Electronic Health Record vs Those Who Did Not

Pregnancy outcome	Patients, No. (%)		OR (95% CI)	aOR (95% CI) ^a	HR (95% CI) ^b
	RSV vaccine (n = 1011)	No RSV vaccine (n = 1962)			
Primary outcome					
Preterm birth <37 weeks' gestation	60 (5.9)	131 (6.7)	0.88 (0.64-1.20)	0.87 (0.62-1.20)	0.93 (0.64-1.34)
Secondary outcomes					
Hypertensive disorders of pregnancy	203 (20.1)	355 (18.1)	1.14 (0.94-1.38)	1.10 (0.90-1.35)	1.43 (1.16-1.77)
Gestational hypertension ^c	153 (15.1)	273 (13.9)	NA	NA	NA
Preeclampsia	67 (6.6)	130 (6.6)	NA	NA	NA
Eclampsia	1 (0.1)	1 (0.1)	NA	NA	NA
HELLP syndrome	2 (0.2)	2 (0.1)	NA	NA	NA
Small-for-gestational age birth weight ^d	107 (10.6)	178 (9.1)	1.19 (0.92-1.52)	1.16 (0.89-1.50)	1.31 (0.97-1.77)
Stillbirth	2 (0.2)	3 (0.2)	1.29 (0.17-7.82)	NA	NA

Abbreviations: aOR, adjusted odds ratio; HELLP, hemolysis, elevated liver enzymes, and low platelets; HR, hazard ratio; NA, not applicable; OR, odds ratio; RSV, respiratory syncytial virus.

^a Multivariable logistic regression model including covariates maternal age, race, ethnicity, insurance type, parity, delivery hospital site, in vitro fertilization pregnancy, pregestational diabetes, and body mass index (calculated as weight in kilograms divided by height in meters squared) greater than 30 at delivery encounter admission.

^b Time-dependent Cox covariate regression model including same covariates as multivariable logistic regression model.

^c The denominator removes patients with diagnosis of preexisting chronic hypertension, 7 patients in each study group.

^d Small for gestational age determined based on gestational age (in weeks) at birth and sex using the Fenton reference.^{16,17}

- Stratified analyses by site and insurance status, association remained among those with private insurance and at 1 of 2 sites

Conclusions from 2023–2024 respiratory season findings

- ❖ RSVpreF vaccine not associated with increased risk for
 - Acute safety outcomes
 - Preterm birth
 - SGA at birth
 - Stillbirth
- ❖ RSVpreF vaccine associated with small but statistically increased risk for HDP
 - Potential residual confounding or outcome misclassification
 - Severity of HDP similar between vaccinated and unvaccinated women based on rates of c-section, admission following birth hospitalization, and length of stay
- ❖ 2024–2025 season analysis pending

Our Team

HealthPartners

- ❖ Malini DeSilva
- ❖ Elyse Kharbanda
- ❖ Jacob Haapala
- ❖ Gabriela Vazquez-Benitez
- ❖ Leslie Kuckler
- ❖ Jingyi Zhu
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- ❖ Nicole Trower

- ❖ VSD site PIs

Weill Cornell Medicine

- Heather Lipkind

Kaiser Northwest

- Kimberly Vesco

CDC

- Eric Weintraub
- Elizabeth Quincer

Hypertensive Disorders of Pregnancy (HDP)

GHTN → preeclampsia → Eclampsia = HELLP

- Onset = 1st HDP diagnosis at or after 20+0 weeks GA
- Evaluate as combined outcome (any HDP) and individual outcomes
- For individual outcomes, only include most severe outcome:

	Hypertensive disorders of pregnancy diagnoses		
Patient	GHTN	Pre-eclampsia	Eclampsia OR HELLP
1		X	
2	X	X	
3	X	X	X
Count	0	2	1

GHTN = gestational hypertension; HELLP = hemolysis, elevated liver enzymes, and low platelet syndrome; GA = gestational age

Acute outcomes

Outcome	Risk window(s) (days)	Background rate/10,000*	RSVpreF clinical trial, N=3682, n (%)**
Anaphylaxis	0–1	n/a	n/a
Fever	1–7	3.3	3%
Malaise / fatigue	1–7	11.4	46%
Skin and soft tissue or local allergic reactions	1–7	7.0	41%
Acute disseminated encephalomyelitis	1–21, 1–42	0	n/a
Acute myocardial infarction	1–21, 1–42	0.3	n/a
Appendicitis	1–21, 1–42	0.6	n/a
Bell's Palsy	1–21, 1–42	0.8	n/a
Disseminated intravascular coagulation (DIC)	1–21, 1–42	0.3	n/a
Guillain-Barré syndrome	1–21, 1–42	0	n/a
Immune thrombocytopenic purpura (ITP)	1–21, 1–42	7.6	n/a
Lymphadenopathy / lymphadenitis	1–21, 1–42	4.6	<0.1%

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

**RSVPreF Phase 3 clinical trial electronic diary for 7 days after vaccination

n/a = not available

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	0/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

Previous VSD studies evaluation HDP

Vaccine	IIV	Tdap	COVID-19	IIV in successive pregnancies
Time period*	6/1/2022–7/31/2009	1/1/2010–11/15/2012	6/1/21 – 1/31/22	1/1/2004 – 12/31/2018
Age of participants	14–49	14–49	16–49	any
GA at exposure	any	<20 weeks	<20 weeks	any
HDP outcomes	ICD-9 codes: • GHTN (642.3, 642.9); vax ≥ 20 weeks GA • Mild preeclampsia (642.4) • Severe preeclampsia or eclampsia (642.5-642.7)	ICD-9 codes occurring ≥20 weeks GA: • GHTN (642.3x, 642.9x) ^a • Preeclampsia (642.4x-642.8x) ^b	ICD-10 codes ≥20 weeks GA–2 wks postpartum: • Gestational HTN (O13.x) • Preeclampsia-eclampsia-HELLP syndrome (O14.x, O15.x, and O16.x)	• Preeclampsia (642.4x, 642.5x, 642.7x; O11.x, O14.x) • Eclampsia (642.6x; O15.x)

*may refer to vaccine administration dates, pregnancy end date, or pregnancy start date

^a 642.3x, 642.4x, 642.9x = 2 outpatient or 1 inpatient diagnosis

^b 642.5x-642.7x = inpatient diagnosis

Inactivated Influenza Vaccine

Table 3. Incidence Rates and Adjusted Hazard Rate Ratios for Adverse Obstetric Events Occurring During Pregnancy or Postpartum Period After Trivalent Inactivated Influenza Vaccination

Outcome	Events After Vaccination:No. of Events (Rate per 1,000 Pregnancies)			Multivariable Analyses*	
	Vaccinated	Unvaccinated	P	Adjusted Hazard Rate Ratio (95% CI)	P
Vaccinated in 1st trimester					
n=21,107		n=40,738			
Mild preeclampsia ^{†,‡,§}	657 (30.0)	1,249 (31.4)	.45	0.94 (0.86–1.04)	.22
Severe preeclampsia or eclampsia ^{†,‡,§}	364 (16.6)	617 (15.5)	.27	1.05 (0.92–1.19)	.51
Vaccinated at 20 weeks or greater					
n=38,038		n=74,192			
Gestational hypertension ^{†,§}	1,663 (44.3)	3,046 (41.9)	.053	1.04 (0.98–1.11)	.19
Gestational diabetes [§]	1,773 (50.1)	3,925 (57.0)	<.001	0.88 (0.83–0.93)	<.001
Chorioamnionitis	1,615 (42.9)	2,861 (39.0)	.002	1.08 (1.02–1.15)	.01
Puerperal infection [§]	363 (9.5)	728 (9.8)	.64	0.96 (0.85–1.09)	.55
Venous complications [§]	21 (0.55)	63 (0.85)	.08	0.64 (0.39–1.05)	.08
Pulmonary embolus [§]	11 (0.20)	17 (0.16)	.56	1.23 (0.58–2.64)	.59
Peripartum cardiomyopathy [§]	13 (0.24)	37 (0.35)	.24	0.66 (0.35–1.24)	.20
Vaccinated in any trimester					
n=74,292		n=144,597			
Mild preeclampsia ^{†,‡,§}	2,338 (18.2)	4,422 (18.2)	.73	0.97 (0.93–1.02)	.30
Severe preeclampsia or eclampsia ^{†,‡,§}	1,189 (9.2)	2,293 (9.4)	.44	0.95 (0.88–1.02)	.14
Proteinuria	400 (5.3)	832 (5.8)	.09	0.88 (0.78–1.00)	.04
Urinary tract infection	1,905 (25.5)	3,655 (26.0)	.57	1.0 (0.94–1.05)	.91

CI, confidence interval.

Women vaccinated in the first trimester and their unexposed matches had a mean follow-up of 6.3 months; for women vaccinated at 20 wk or greater and their unexposed matches, mean follow-up was 2.4 months; for women vaccinated in any trimester and their unexposed matches, mean follow-up was 4.1 months.

* All outcomes adjusted for receipt of medical care in the first trimester, hospitalization before vaccination or index date, and poverty; additional adjustments were outcome-specific.

[†] Also adjusted for diabetes and gestational diabetes.

[‡] Also adjusted for proteinuria.

[§] Also adjusted for obesity.

Tdap

Table 2. Rates of Adverse Gestational and Birth Outcomes and Relative Risks Associated With Receipt of Pertussis Vaccine (Tdap) During Pregnancy

Outcome	No. (%)		Risk Ratios (95% CI)		P Value
	Tdap Exposed	Unexposed	Unadjusted	Adjusted ^a	
Full cohort	26 229	97 265			
Chorioamnionitis	1596 (6.1)	5329 (5.5)	1.11 (1.05-1.17)	1.19 (1.13-1.26)	<.001
Preterm delivery, ≥37 wk	1527 (6.3)	7544 (7.8)	1.01 (0.95-1.06)	1.03 (0.97-1.09)	.33
Small for gestational age, <10th percentile	2214 (8.4)	8086 (8.3)	1.02 (0.97-1.06)	1.00 (0.96-1.06)	.68
Vaccinated at <20 wk gestation	6083	97 265			
Hypertensive disorders	497 (8.2)	7736 (8.0)	1.03 (0.94-1.12)	1.09 (0.99-1.20)	.05
Vaccinated at 27-≤36 wk gestation	11 351	97 265			
Chorioamnionitis	637 (5.6)	5329 (5.5)	1.02 (0.95-1.11)	1.11 (1.03-1.21)	.009
Preterm delivery, <37 wk	602 (5.3)	7544 (7.8)	0.88 (0.81-0.96)	0.88 (0.80-0.95)	.002
Small for gestational age, <10th percentile	978 (8.6)	8086 (8.3)	1.04 (0.97-1.10)	1.03 (0.96-1.10)	.40

Kharbanda EO, Vazquez-Benitez G, Lipkind HS, Klein NP, Cheetham TC, Naleway A, Omer SB, Hambidge SJ, Lee GM, Jackson ML, McCarthy NL, DeStefano F, Nordin JD. Evaluation of the association of maternal pertussis vaccination with obstetric events and birth outcomes. JAMA. 2014 Nov 12;312(18):1897-904. doi: 10.1001/jama.2014.14825. PMID: 25387187; PMCID: PMC6599584.

COVID-19

Table 2. Adverse Pregnancy Outcomes and Adjusted Relative Risks and Hazard Ratios After mRNA Coronavirus Disease 2019 (COVID-19) Vaccination in Pregnancy at Eight U.S. Health Care Organizations in the Vaccine Safety Datalink

Pregnancy Outcome	Sample Size	No. With Outcome (Rate/100 Pregnancies)	Crude HR or RR (95% CI)	aHR or aRR (95% CI)*
Gestational hypertension (analytic cohort, n=39,201)				
No COVID-19 vaccine in pregnancy	30,671	3,042 (9.9)	Ref	Ref
Any mRNA COVID-19 vaccine before 20 wk	8,530	920 (10.8)	1.09 (1.01–1.16)	1.08 (0.96–1.22)
1st trimester	6,807	739 (10.9)	1.09 (1.01–1.18)	1.07 (0.96–1.20)
2nd trimester	3,808	394 (10.3)	1.03 (0.93–1.13)	1.06 (0.88–1.29)
Preeclampsia–eclampsia–HELLP syndrome (analytic cohort, n=41,054)				
No COVID-19 vaccine in pregnancy	32,074	2,710 (8.4)	Ref	Ref
Any mRNA COVID-19 vaccine before 20 wk	8,980	796 (8.9)	1.05 (0.97–1.13)	1.10 (0.97–1.24)
1st trimester	7,173	644 (9.0)	1.06 (0.98–1.15)	1.13 (1.00–1.28)
2nd trimester	3,992	328 (8.2)	0.96(0.86–1.07)	1.06 (0.86–1.29)

Vesco KK, Denoble AE, Lipkind HS, Kharbanda EO, DeSilva MB, Daley MF, Getahun D, Zerbo O, Naleway AL, Jackson L, Williams JTB, Boyce TG, Fuller CC, Weintraub ES, Vazquez-Benitez G. Obstetric Complications and Birth Outcomes After Antenatal Coronavirus Disease 2019 (COVID-19) Vaccination. *Obstet Gynecol*. 2024 Jun 1;143(6):794-802. doi: 10.1097/AOG.0000000000005583. Epub 2024 Apr 17. PMID: 38626447; PMCID: PMC11090513.

IIV in successive pregnancies

- At least 2 successive, singleton births between 1/1/200. 12/31/2018

eTable 3 . Rates and relative risks of adverse outcomes in 2nd pregnancy based on maternal vaccination status in successive pregnancies.

Outcomes in the 2 nd pregnancy	Second pregnancy			
	Rate of adverse events		Relative risk (95% confidence interval) ^a	
	Unvaccinated	Vaccinated	Unadjusted	Adjusted
	in both pregnancies (%) N= 37,176	in both pregnancies (%) N= 44,879		
Preeclampsia/eclampsia	2.95	3.39	1.15 (1.06, 1.24)	1.10 (0.99, 1.21)
Placental abruption	0.99	0.96	0.96 (0.84, 1.11)	1.01 (0.84, 1.21)
Maternal fever (>100.4°F)	0.07	0.06	0.96 (0.56, 1.64)	0.87 (0.47, 1.59)
Preterm birth (PTB)	6.4	4.92	0.77 (0.73, 0.81)	0.83 (0.78, 0.89)
Spontaneous PTB	3.2	2.63	0.82 (0.76, 0.89)	0.88 (0.80, 0.97)
Iatrogenic PTB	3.2	2.28	0.71 (0.66, 0.77)	0.77 (0.69, 0.85)
Preterm PROM	8.41	9.51	1.13 (1.08, 1.18)	1.00 (0.94, 1.06)
Chorioamnionitis	1.69	1.93	1.14 (1.03, 1.26)	1.03 (0.90, 1.18)
Small for gestational age birth	7.11	7.25	1.02 (0.97, 1.07)	0.99 (0.93, 1.05)

Abbreviations: PROM, premature rupture of membrane

^a Analyses were adjusted for maternal age, race and ethnicity, maternal education, smoking, and alcohol use during pregnancy, pre-pregnancy body mass index, gestational weight gain, timing of prenatal care initiation/number of prenatal care visits, maternal comorbidities (chronic hypertension, diabetes mellitus, renal disease, and autoimmune disease), history of adverse perinatal outcomes in a prior pregnancy, month of conception, year of pregnancy, interpregnancy interval, receipt of influenza vaccine during the interpregnancy period, receipt of other vaccines during pregnancy, and Vaccine Safety Datalink site.

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