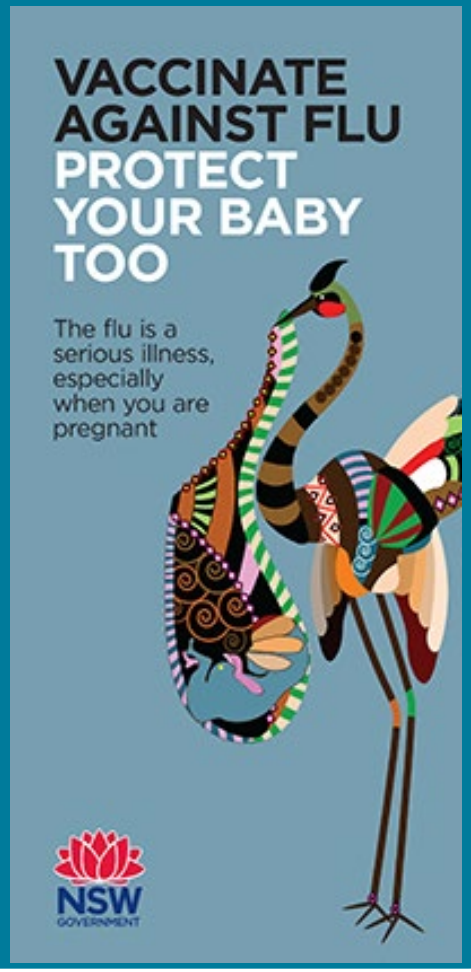
Lessons Learned from Maternal Vaccines Already Implemented

Janet A. Englund, M.D.
Professor of Pediatrics
Seattle Children's Hospital
University of Washington
Fred Hutchinson Cancer Research Center
Seattle, WA USA



Advertisement for Maternal Flu Vaccine from NSW, Australia

Consequences of Maternal Immunization on Fetal Outcomes
IABS
June 8-9
Zurich, Switzerland

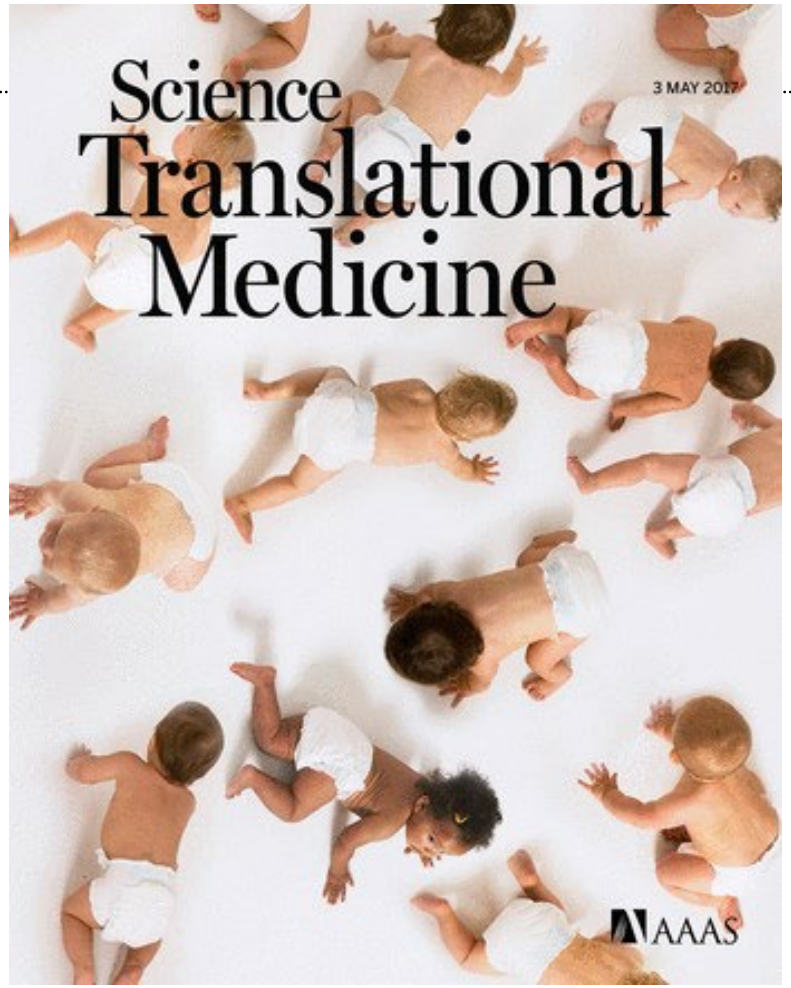
Fred Hutch Cancer Center
UNIVERSITY of WASHINGTON
Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

DISCLOSURES

My institution has received research support for clinical studies from GSK, Pfizer, Shionogi and AstraZeneca.

I have served as a consultant for Cidara, Merck, GSK, Meissa Vaccines, Moderna, and Pfizer.

I support influenza, RSV, and COVID-19 vaccination for healthcare workers including pregnant persons at my institution.



Fred Hutch Cancer Center

UNIVERSITY of WASHINGTON

Seattle Children's HOSPITAL • RESEARCH • FOUNDATION

Lessons Learned…..

OUTLINE

- **Background**
- **Tetanus**
- **Pertussis combination vaccines (Tdap)**
- **Influenza**
- **COVID-19**

IMMUNIZATION DURING PREGNANCY: IT'S NOT NEW !

- **Historical: pre-1950's:** benefits of smallpox vaccine, diphtheria toxoid, whole cell pertussis vaccine described
- **1960's-present**: Benefit of routine **tetanus toxoid** immunization during pregnancy
- **1980's**: Lack of data halted most maternal vaccination programs
- **2009-10: Pandemic influenza A/H1N1** outbreak demonstrated risk of flu during pregnancy and benefits of maternal flu vaccine in women and infants in industrialized and later in LMIC countries
- **2012-2015**: **Maternal Tdap** given in response to pertussis epidemic and neonatal pertussis deaths, with benefit of maternal Tdap demonstrated for infants in US/UK
- **2020-2023**: **SARS-CoV-2 pandemic:** High risk during pregnancy, with vaccine recommended in many countries with benefit in pregnant persons and their infants
- **2024: RSV PreF protein** vaccine licensed & recommended during pregnancy to benefit infants

PUBLIC HEALTH IMPLICATIONS OF MATERNAL IMMUNIZATION:
Opportunities for Intervention

- Maternal immunization with vaccines such as **tetanus toxoid vaccine** has been successfully implemented worldwide in antenatal care
- Benefit for all persons **able to access care**: increased emphasis on IMPROVING access and frequency of antenatal care by WHO and national public health organizations
- Maternal immunization is a **cost-effective** modality but requires integration of vaccine and clinical arms of health care
- **Not a replacement** for pediatric vaccination after birth

FACTORS AFFECTING TRANSPLACENTAL TRANSPORT OF MATERNAL ANTIBODY TO THE INFANT

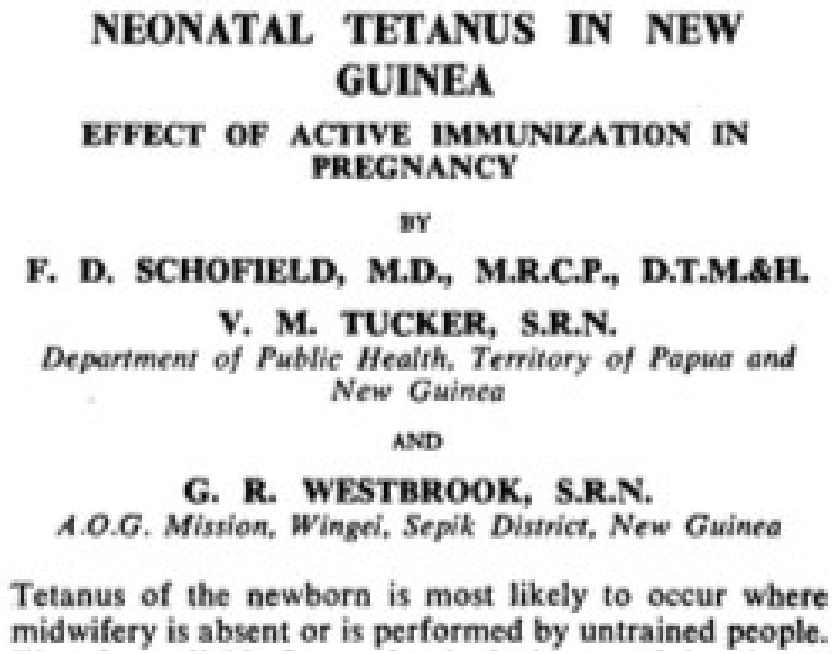
- Maternal health, nutrition
- Placental abnormalities
  - Malaria
  - HIV infection
- Time:
  - gestational age of infant
  - time between vaccination and delivery
- Maternal IgG level:
- IgG subclass:
  IgG1 = IgG3 > IgG4 > IgG2

Infant born in Nepal during maternal immunization trial

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

NEONATAL TETANUS: A PREVENTABLE DISEASE

- Important cause of neonatal death worldwide for centuries
  - 1980: 30% of all deaths in first year of life in many developing countries
- 1961: Landmark study in New Guinea demonstrated benefit of maternal immunization with tetanus toxoid
  (Schofield et al, Brit Med J 1961,2: 785-9)
  - Excellent protection of mothers and infants via maternal immunization
- 1989: World Health Organization first set goal to eliminate neonatal tetanus using maternal immunization – renewed X 3; added adolescent immunization later as adjunct



NEONATAL TETANUS IN NEW GUINEA

EFFECT OF ACTIVE IMMUNIZATION IN PREGNANCY

BY

F. D. SCHOFIELD, M.D., M.R.C.P., D.T.M.&H.

V. M. TUCKER, S.R.N.

Department of Public Health, Territory of Papua and New Guinea

AND

G. R. WESTBROOK, S.R.N.

A.O.G. Mission, Wingei, Sepik District, New Guinea

Tetanus of the newborn is most likely to occur where midwifery is absent or is performed by untrained people.

BMJ 1961; 2:785

Maternal tetanus vaccination is effective in reducing neonatal mortality

Bulletin of the World Health Organization, **58** (6): 927-930 (1980)

Reduction of neonatal tetanus by mass immunization of non-pregnant women: duration of protection provided by one or two doses of aluminium-adsorbed tetanus toxoid*

R. E. BLACK,[1] D. H. HUBER,[2] & G. T. CURLIN[3]

Outcome: Death during first 14 days of life in mothers receiving Tet Tox VX vs Cholera Tox VX

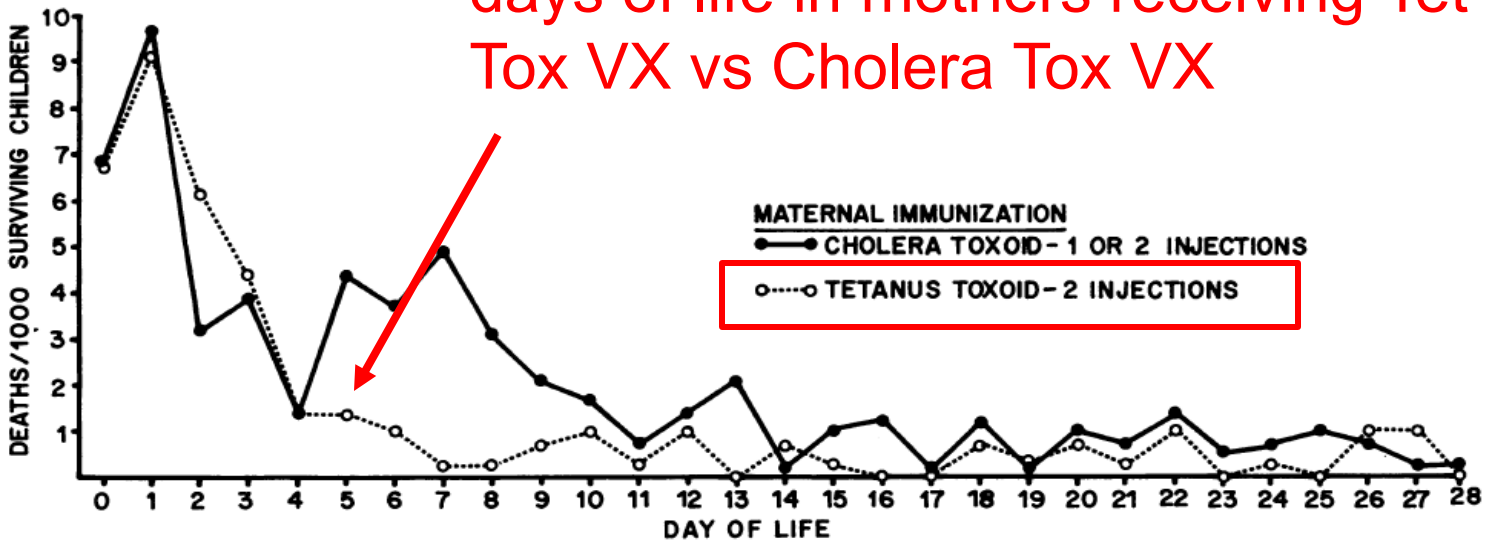


Fig. 1. Neonatal death rates by age of death following maternal immunization with one or two doses of cholera or two doses of tetanus/diphtheria toxoids.

e Children's
SEARCH • FOUNDATION

Maternal tetanus vaccination is effective in reducing neonatal mortality

Bulletin of the World Health Organization, **58** (6): 927-930 (1980)

Reduction of neonatal tetanus by mass immunization of non-pregnant women: duration of protection provided by one or two doses of aluminium-adsorbed tetanus toxoid*

R. E. BLACK,[1] D. H. HUBER,[2] & G. T. CURLIN[3]

Note: Minimal safety evaluations during mass vaccine campaign

Outcome: Death during first 14 days of life in mothers receiving Tet Tox VX vs Cholera Tox VX

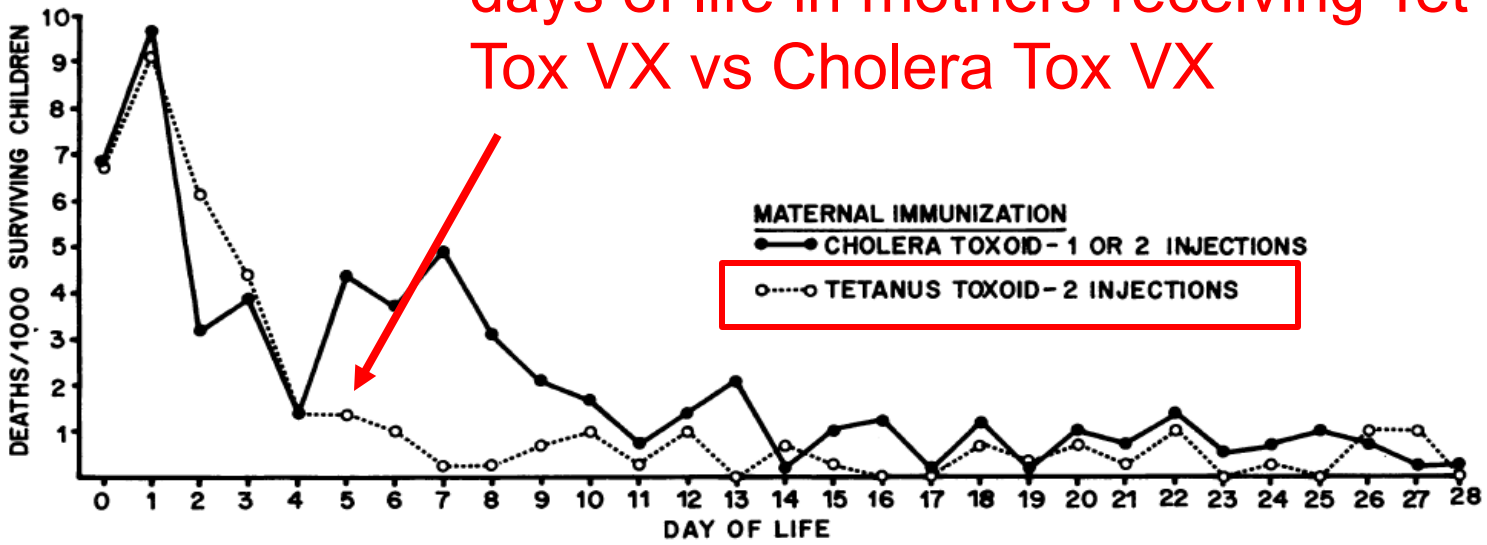


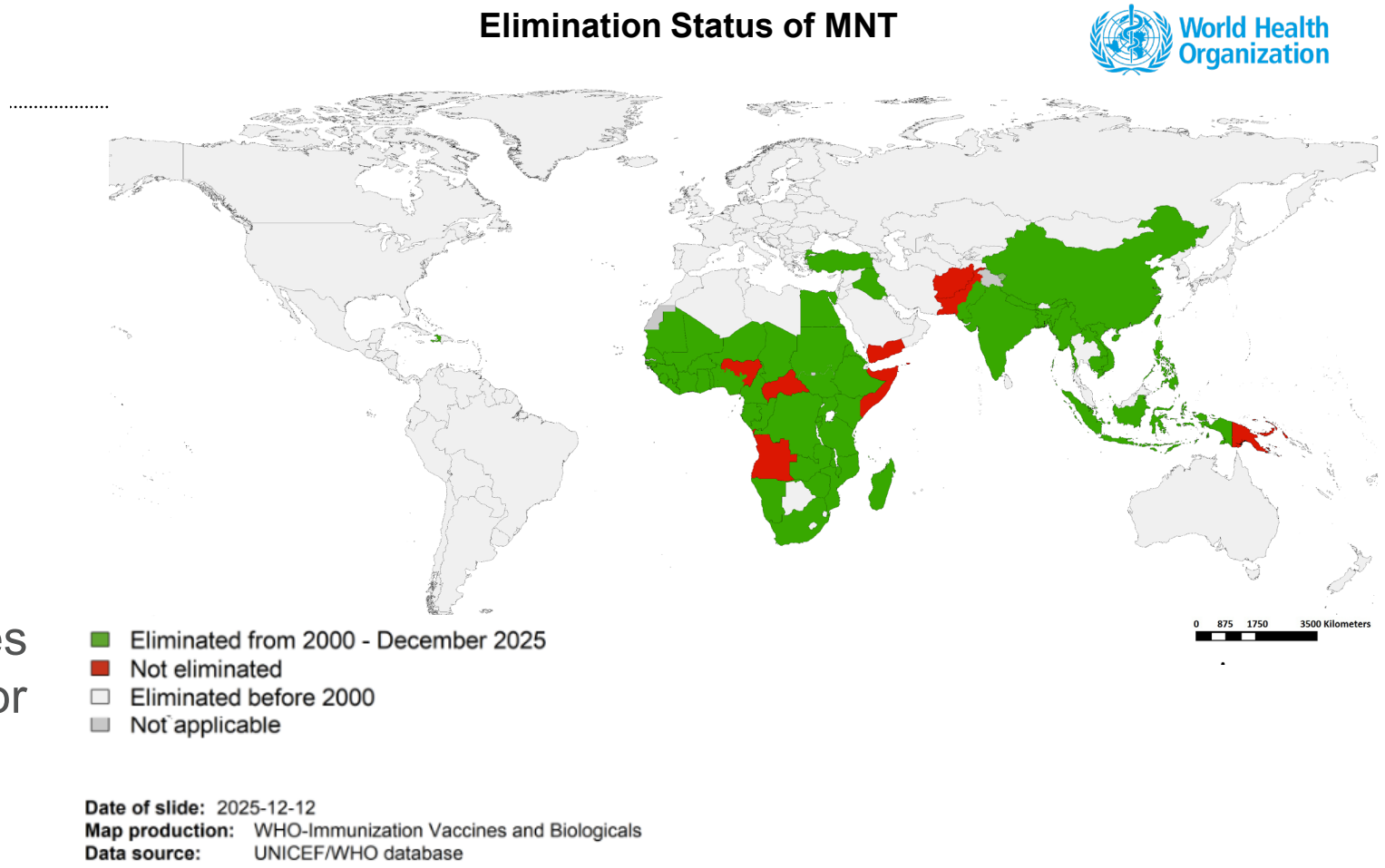
Fig. 1. Neonatal death rates by age of death following maternal immunization with one or two doses of cholera or two doses of tetanus/diphtheria toxoids.

MATERNAL IMMUNIZATION TO PREVENT NEONATAL TETANUS: 51/59 Countries Eliminated Maternal-Neonatal Tetanus (MNT) 2025

Current “TT2” strategy: 2 doses of TT in pregnancy plus 3 doses in women of childbearing age reduced rate of neonatal tetanus by 96%

In 1999: 59 countries had not eliminated maternal-neonatal tetanus (MNT)

By end of 2025, only 8 of 59 countries had ongoing MNT (51/59 validated for achieving MNT elimination)



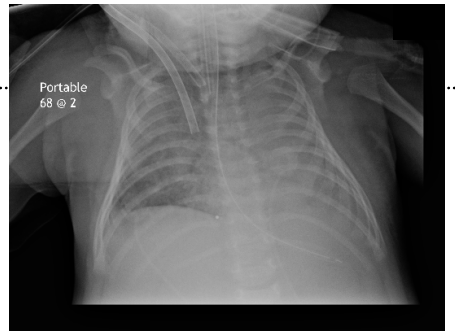
*https://www.who.int/initiatives/maternal-and-neonatal-tetanus-elimination-(mnte)/progress-towards-global-mnt-elimination
accessed June 3, 2026

*8 Remaining: Afghanistan, Angola, Central African Republic, Nigeria, Pakistan, Papua New Guinea, Somalia, Yemen

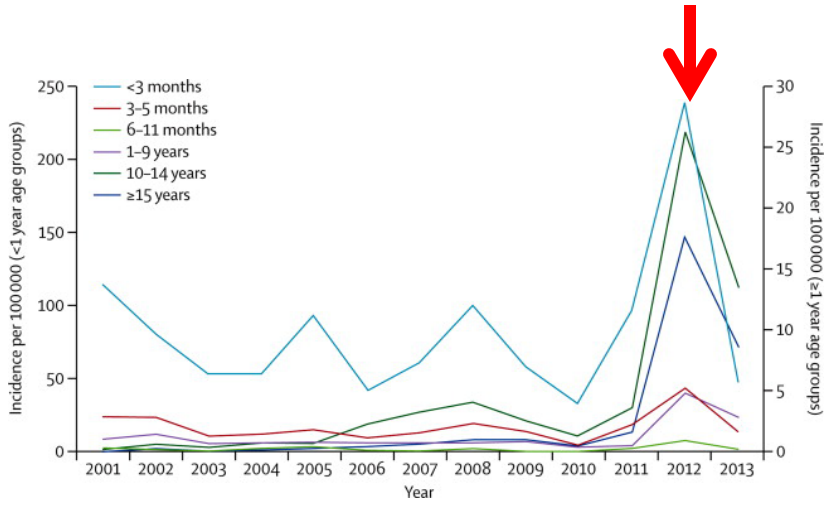
2018: estimate of 25,000 neonatal deaths

Maternal Pertussis Immunization*

- Pertussis disease most serious in youngest infants < 3 months
- US and UK Medicines and Healthcare Regulatory Agency recommended acellular pertussis combination vaccine in pregnancy beginning in 2012, with immediate decrease in infant cases/deaths that has persisted (Amirthalingam CID 2016 suppl)
- Acellular pertussis combination vaccines recommended for pregnant persons since 2015 in multiple countries outside the US and UK, including Australia, New Zealand, Latin America, Belgium, Spain.



Maternal Pertussis Vx
Introduced in UK Oct. 2012



*Amirthalingam G et al. Effectiveness of maternal pertussis vaccination in England: an observational study. Lancet 2014; 384:1521

Countries with recommendation for pertussis immunization during pregnancy* and changes in maternal pertussis uptake globally**

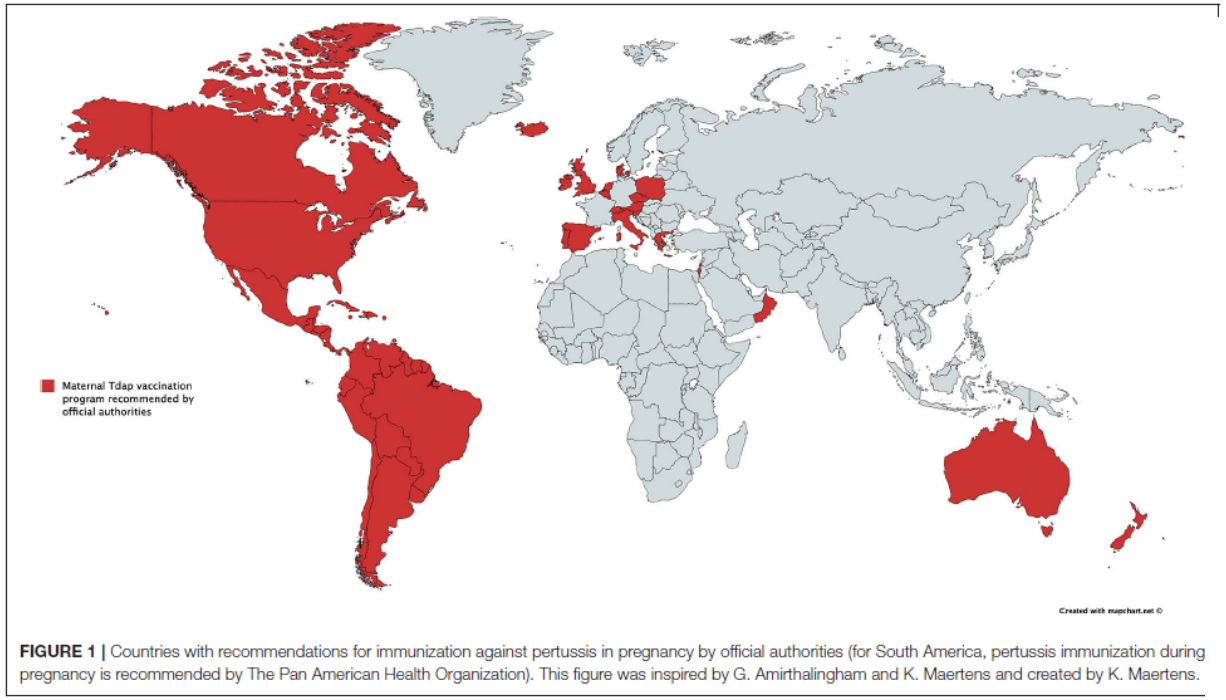


FIGURE 1 | Countries with recommendations for immunization against pertussis in pregnancy by official authorities (for South America, pertussis immunization during pregnancy is recommended by The Pan American Health Organization). This figure was inspired by G. Amirthalingham and K. Maertens and created by K. Maertens.

*AbuBaya 2020 Front Immunology

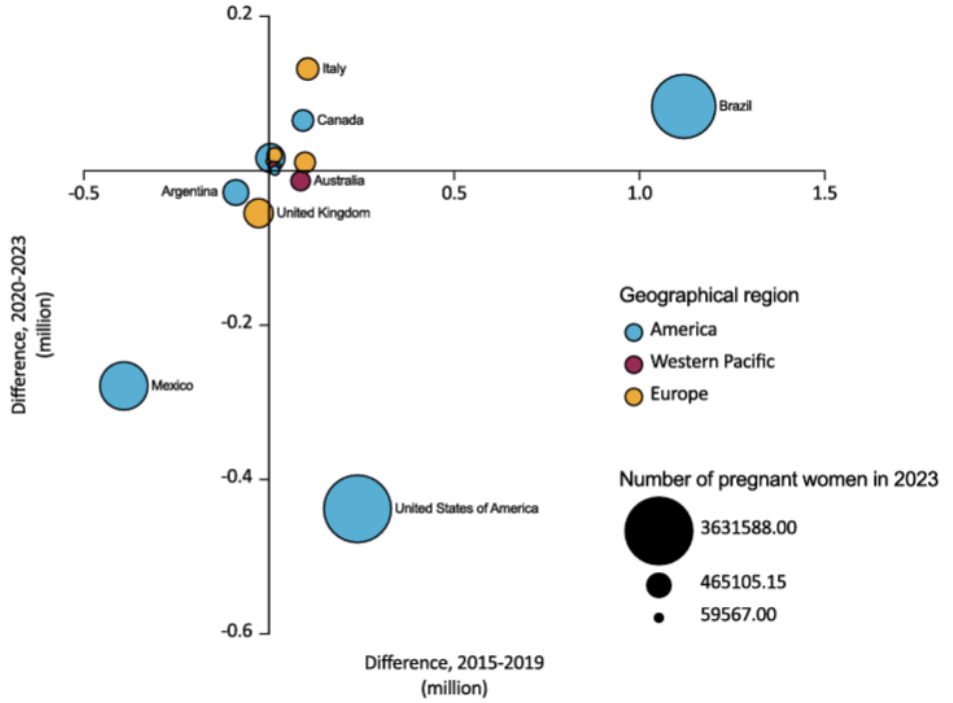
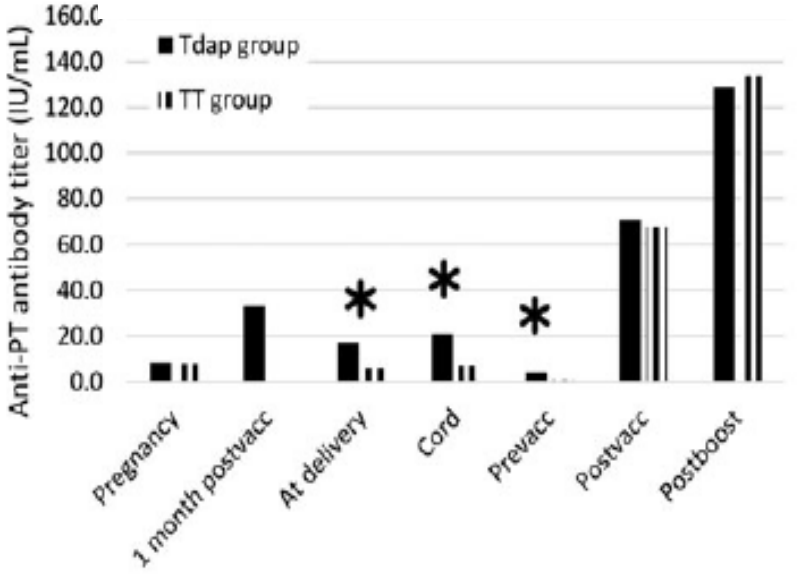


***Fig. 5*: Differences in numbers of pregnant women vaccinated Tdap from 2015 to 2019 and 2020 to 2023, by country and territory.** Fig. 5 describes differences in numbers of pregnant women vaccinated Tdap, exploring which country and territory explain more about the global and regional trends.

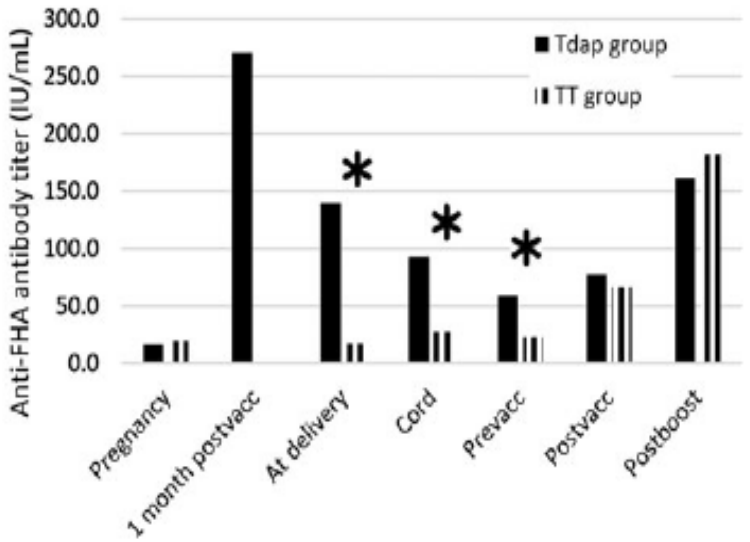
**Zhang et al. EClin Med 2025

Examples of potential interference of some pertussis antibodies following maternal vx but not post booster dose- Viet Nam (Maertens et al, 2016)

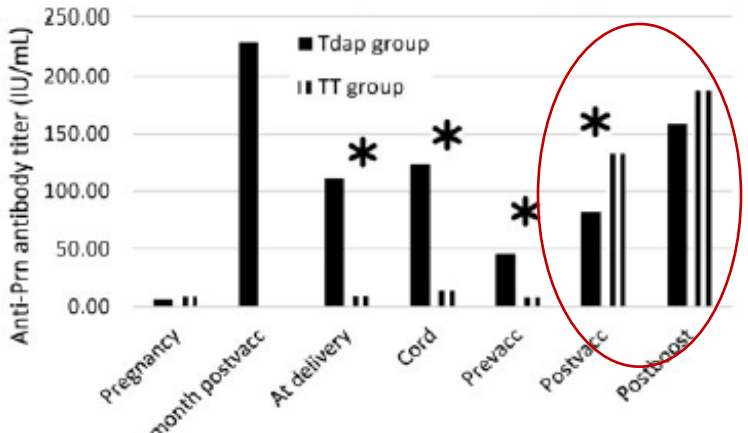
Anti-PT Antibodies



Anti-FHA Antibodies



Anti-PRN Antibodies



In babies born to mothers receiving Tdap:

- Higher infant **PT** and **FHA** Ab levels at birth (cord) and pre-vx; similar Ab levels post-vx
- Higher infant **PRN** Ab levels in cord and prevx but <u>LOWER</u> post vx. After booster dose, Ab were similar

***CID 2016; 64**

Impact of Pertussis Maternal Immunization on Infants: Interference

Maternal pertussis vaccine may affect infant response to Tdap or DPT

- Pertussis vaccine antibodies **persist** in infants born to immunized women for many 4 months (Englund et al Pediatrics 1995; Maertens et al CID 2016)

- **Concern of interference** with infant DTaP vaccines early in life: some Ag have more interference; perhaps more important with first dose, and concerning potentially with earlier administration of first DTP/DTaP dose - given at 6 weeks compared to 3 M (Barug et al Lancet ID 2019)

- **Booster doses result in similar infant antibody responses**: Similar infant response after booster DTaP dose in babies born to maternal vaccine recipients vs controls (Munoz 2014; Maertens 2016; Rice 2019)

Systematic Review of Maternal Tdap Immunization: Safety *

Analysis of 91 studies and 14,000 papers, including 62 new studies 2020-2026

- conducted by the Vaccine Integrity Project at Univ. Minnesota's Center for Infectious Disease Research and Policy (without pharma sponsorship)
- Systematic review available online 2026.

Table 1. Review question in patient, intervention, comparator, outcome (PICO) format based on the existing recommendation

			Outcomes	
Population	**Intervention**	**Comparator**	**Safety**	**Effectiveness**
Pregnant populations (gestational age 27-36 weeks), regardless of prior vaccination	Any Tdap vaccine licensed in the U.S. (alone or in combination)	No Tdap	Stillbirth Miscarriage Preterm birth Eclampsia, preeclampsia, hypertensive disorders of pregnancy Congenital anomalies Fetal/neonatal development	Immunogenicity Rates of tetanus, diphtheria, and pertussis infection in adults and infants Disease severity in adults and infants

Safety and effectiveness of tetanus-diphtheria-acellular pertussis (Tdap) vaccination during pregnancy: a systematic review and meta-analysis. Vaccine Integrity Project. Accessed May 13, 2026. https://vaxintegrity.cidrap.umn.edu/sites/default/files/FINAL%20REPORT%20Tdap%20Vaccine%20in%20Pregnancy%20Evidence%20Review.pdf

Review: https://www.contemporaryobgyn.net/view/comprehensive-review-of-tdap-vaccine-during-pregnancy-confirms-infant-protection-maternal-safety

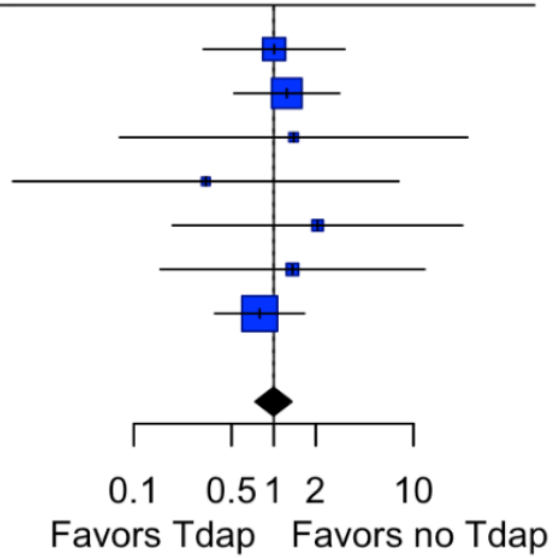
Systematic Review of Maternal Tdap Immunization: Safety *

Safety: Rates of preterm birth and low birth weight were similar

Figure 5a: Estimates of the risk of preterm births from RCTs

Study	Tdap Events	Tdap Total	No Tdap Events	No Tdap Total	Weight (%)	Risk Ratio (95% CI)	Risk of Bias
Haidara 2024	8	133	4	67	16.4	1.01 [0.31; 3.23]	Low
Perrett 2020	11	341	9	346	29.4	1.24 [0.52; 2.95]	Low
Sompagdee 2020	4	87	0	13	2.7	1.39 [0.08; 24.37]	Some concerns
Hoang 2016	0	52	1	51	2.2	0.33 [0.01; 7.84]	High
Halperin 2018	2	134	1	138	3.9	2.06 [0.19; 22.45]	Moderate
Munoz 2014	3	33	1	15	4.7	1.36 [0.15; 12.05]	Low
Shakib 2013	8	134	38	505	40.7	0.79 [0.38; 1.66]	Serious
Total (95% CI)		**914**		**1135**	**100.0**	**1.00 [0.74; 1.35]**	

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 1.57$, df = 6 (P = 0.9548); $I^2 = 0.0\%$



https://vaxintegrity.cidrap.umn.edu/sites/default/files/FINAL%20REPORT%20Tdap%20Vaccine%20in%20Pregnancy%20Evidence%20Review.pdf

Systematic Review of Maternal Tdap Immunization: Safety Demonstrated*

- **Benefits**:
  - Significantly reduced risk of lab-confirmed pertussis in infants
  - Estimate prevention of 146 cases/100,000 infants; 95% VE against fatal pertussis
- **Safety**
  - No increased risks of preeclampsia, eclampsia, gestational diabetes, or chorioamnionitis.
  - Birth outcomes, rates of preterm birth and low birth weight similar
  - Relative risk reduction for stillbirth (RR 0.82), although risk overall very low – not meaningful

CONCLUSIONS: Robust safety outcomes across pregnancy

Safety and effectiveness of tetanus-diphtheria-acellular pertussis (Tdap) vaccination during pregnancy: a systematic review and meta-analysis. Vaccine Integrity Project. Accessed June 4, 2026. https://vaxintegrity.cidrap.umn.edu/sites/default/files/FINAL%20REPORT%20Tdap%20Vaccine%20in%20Pregnancy%20Evidence%20Review.pdf

Influenza Vaccine for Pregnant Persons: WHO, 2022

World Health Organization

Organisation mondiale de la Santé

Weekly epidemiological record

Relevé épidémiologique hebdomadaire

13 MAY 2022, 97th YEAR / 13 MAI 2022, 97e ANNÉE
No 19, 2022, 97, 185–208
http://www.who.int/wer

Contents

Vaccines against influenza: WHO position paper – May 2022

Vaccins antigrippaux: note de synthèse de l'OMS – mai 2022

- **High risk of severe disease**
- **Safety** of seasonal influenza vaccine throughout pregnancy
- **Effectiveness** of preventing influenza in the women as well as in their young infants.

WHO Position Paper – May 2022 Vaccines Against Influenza. Wkly Epidm Rec 2022, #19. 97; 185-208

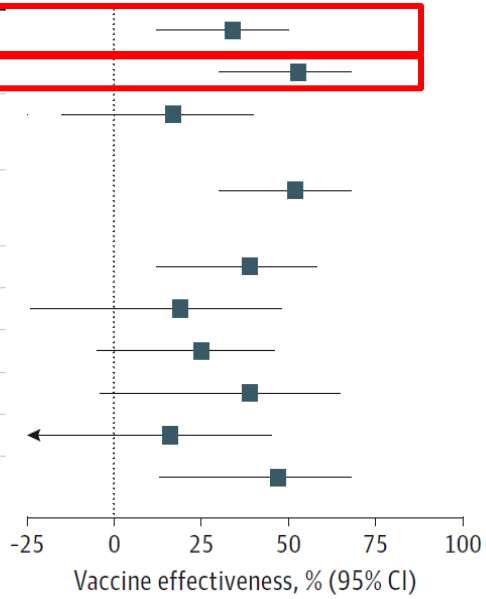
How to implement influenza vaccination in pregnant women, 2016 WHO Manual: https://iris.who.int/bitstream/handle/10665/250084/WHO-IVB-16.06-eng.pdf?sequence=1

Maternal Flu Vaccine Prevents Hospitalization and ED visits for Flu in young children: VE from seven US sites*

JAMA Pediatr. 2024;178(2):176-184.

Figure 2. Effectiveness of Maternal Influenza Vaccination During Pregnancy Against Influenza Hospitalizations and Emergency Department (ED) Visits in Infants

Infants <6 mo of age	Vaccinated mothers, No./total No. (%)		Effectiveness of maternal vaccination against influenza illness in infants, % (95% CI)
	Infants with influenza illness	Control infants	
Overall effectiveness of maternal vaccination	94/223 (42)	1913/3541 (54)	34 (12 to 50)
Infants <3 mo of age	49/106 (46)	1293/2147 (60)	53 (30 to 68)
Mother vaccinated during first or second trimester of pregnancy	59/188 (31)	1009/2637 (38)	17 (-15 to 40)
Mother vaccinated during third trimester of pregnancy	35/164 (21)	904/2532 (36)	52 (30 to 68)
Hospital admission	55/125 (44)	1416/2541 (56)	39 (12 to 58)
ED visit	39/98 (40)	497/1000 (50)	19 (-24 to 48)
Influenza A	70/157 (45)	1913/3541 (54)	25 (-5 to 46)
H1N1	21/53 (40)	1913/3541 (54)	39 (-4 to 65)
H3N2	42/87 (48)	1913/3541 (54)	16 (-29 to 45)
Influenza B	25/67 (37)	1913/3541 (54)	47 (13 to 68)



*Sahni et al JAMA Peds

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

Effectiveness of Maternal Influenza Vaccine to Mothers and Infants in Clinical Trials in Nepal, Mali, and South Africa*

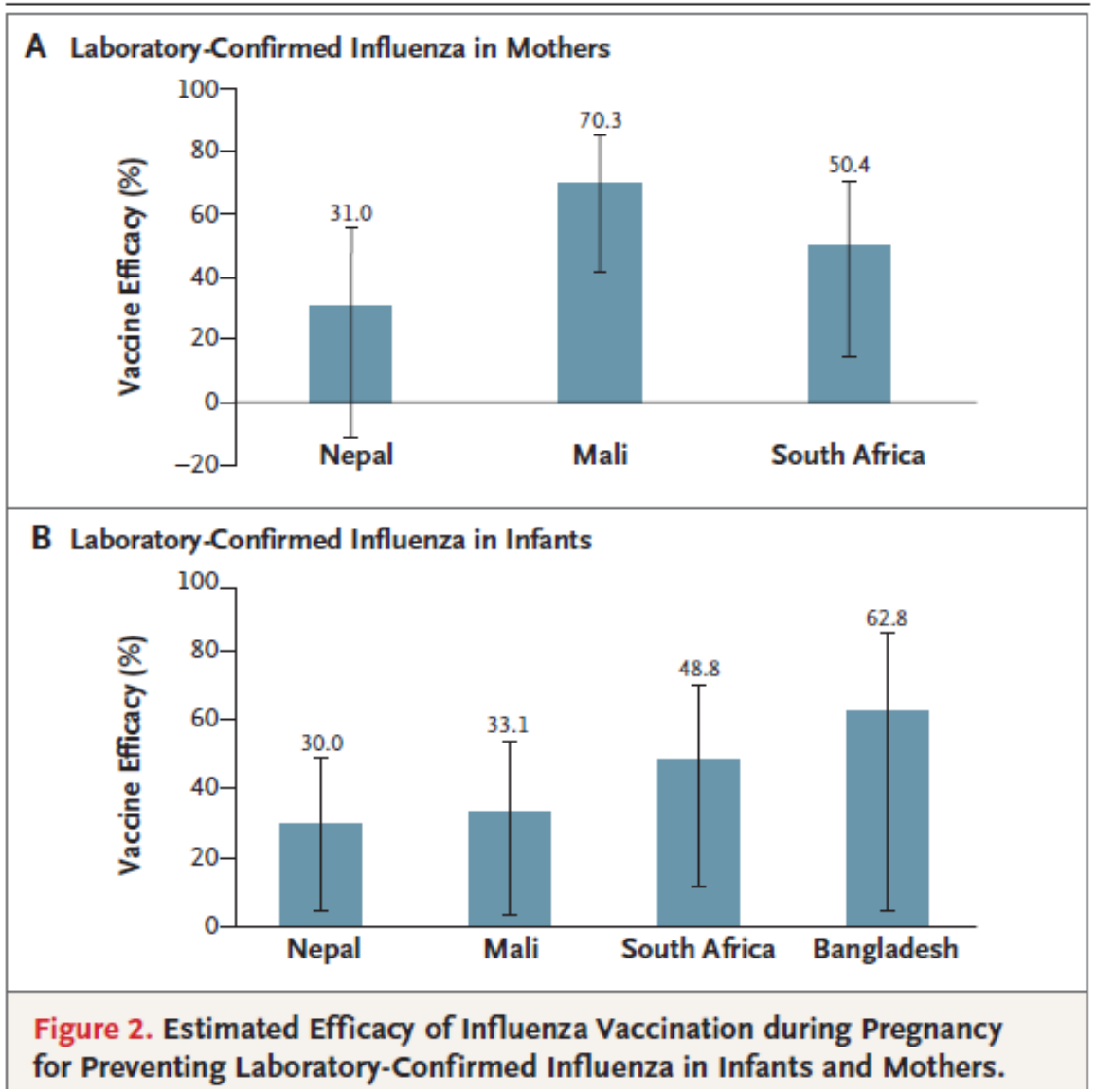
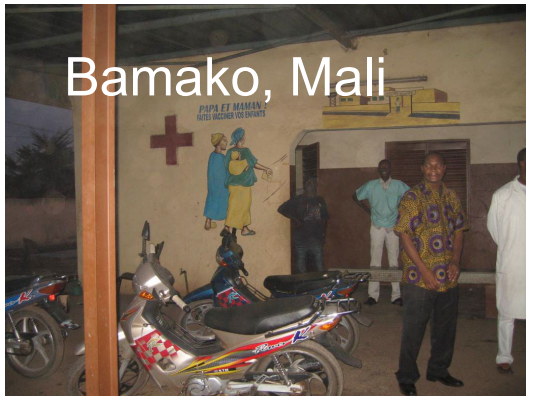


Figure 2. Estimated Efficacy of Influenza Vaccination during Pregnancy for Preventing Laboratory-Confirmed Influenza in Infants and Mothers.



*Omer NEJM 2017

INFLUENZA VACCINES IN PREGNANCY: Systematic Review, 2023*

Wolfe DM, *et al. BMJ Open* 2023;**13**:e066182. doi:10.1136/bmjopen-2022-066182

Methods: Search of electronic databases through 2021 searched for associations of pregnancy and maternal serious adverse events (SAEs) and adverse birth outcomes, using GRADE to assess evidence

Results: 63 studies reviewed (24 cohort, 5 case-control); 34 pandemic vaccines, other combination of seasonal/pandemic vaccines

- No sig. association: Preterm birth, spontaneous abortion, SGA birth
- No sig association: Stillbirth, congenital anomalies, maternal non-obstetric SAE

Conclusion:

- Seasonal influenza vaccination during pregnancy not associated with adverse birth outcomes or maternal non-obstetric SAE, with evidence of very low certainty.
- Appropriate control of confounding and temporal biases should be considered in future studies.

Examples of Recent Influenza Maternal Vaccine Safety Assessments

No significant association of maternal influenza vaccinations and:

- Fetal loss (Regan et al: Maternal influenza vaccination and associated risk of fetal loss: A claims-based prospective cohort study. Vaccine 2024)
- Birth defects (Malange et al: Influenza vaccination during early pregnancy and risk of major birth defects, US Birth Defects Study To Evaluate Pregnancy exposures, 2014–2019. Vaccine 2025)
- Congenital heart disease (Palmsten et al: Influenza vaccination during pregnancy and risk of selected major structural congenital heart defects, National Birth Defects Prevention Study, 2006-2011. Birth Defects Res 2023)
- Birth outcomes in Nicaragua (Arrioloa et al: Association of influenza vaccination during pregnancy with birth outcomes in Nicaragua. Vaccine 2017)
- Sequential flu vaccination in two pregnancies (Getahun et al: Safety of the seasonal influenza vaccine in 2 successive seasons. JAMA Network Open 2024).

COVID-19 INFECTION RECOGNIZED TO BE HAZARDOUS IN PREGNANCY EARLY IN PANDEMIC: 2020*

Update: Characteristics of Symptomatic Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status — United States, January 22–October 3, 2020

Weekly / November 6, 2020 / 69(44);1641–1647

Study of 409,462 symptomatic women of whom 23,434 (5.7%) were pregnant

Outcome	aRR (95% CI) pregnant vs non-pregnant individuals
ICU admission	3.0 (2.6-3.4)
Ventilator use	2.9 (2.2-3.8)
ECMO	2.4 (1.5-4.0)
Death	1.5 (1.2-2.4)

MMWR Morb Mortal Wkly Rep 2020;69:1641–1647
http://dx.doi.org/10.15585/mmwr.mm6944e3external icon

COVID-19 mRNA vaccine given during pregnancy is safe and protects infants against disease

Newborn and Early Infant Outcomes Following Maternal COVID-19 Vaccination During Pregnancy[1]

Sarah C. J. Jorgensen, PharmD, MPH; Samantha S. M. Drover, PhD; Deshayne B. Fell, PhD; Peter C. Austin, PhD; Rohan D'Souza, MD, PhD; Astrid Guttmann, MDCM, MSc; Sarah A. Buchan, PhD; Sarah E. Wilson, MD; Sharifa Nasreen, PhD; Kevin L. Schwartz, MD, MSc; Mina Tadrous, PharmD, PhD; Kumanan Wilson, MD, MSc; Jeffrey C. Kwong, MD, MSc

In this population-based cohort study in Ontario, Canada, maternal mRNA COVID-19 vaccination during pregnancy was associated with lower risks of SNM, neonatal death, and NICU admission

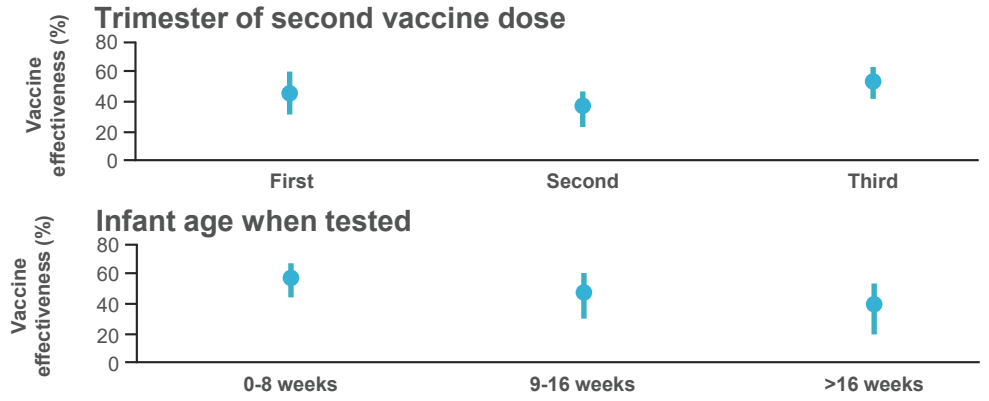
*Jorgensen SCJ, et al. JAMA Pediatr. 2023 Dec 1;177(12):1314-1323.

Maternal mRNA covid-19 vaccination during pregnancy and delta or omicron infection or hospital admission in infants: test negative design study[2]

Sarah C J Jorgensen, Alejandro Hernandez, Deshayne B Fell, Peter C Austin, Rohan D'Souza, Astrid Guttmann, Kevin A Brown, Sarah A Buchan, Jonathan B Gubbay, Sharifa Nasreen, Kevin L Schwartz, Mina Tadrous, Kumanan Wilson, Jeffrey C Kwong

Infant VE of mRNA COVID-19 vaccines during pregnancy[2]

Effectiveness of the primary mRNA covid-19 vaccine series during pregnancy against omicron infection in infants younger than six months of age.



*Jorgenson SCJ et al. *BMJ* 2023; 380 doi: https://doi.org/10.1136/bmj-2022-074035

COVID-19 Vaccine Policies on Pregnancy: Varied Worldwide (COMIT, 2022*)

COMIT Covid-19 Maternal Immunization Tracker

Berman Institute of Bioethics
Johns Hopkins University
Center for Immunization Research

The COMIT policy tracker was developed with support from the Bill & Melinda Gates Foundation and Wellcome.

CITATION

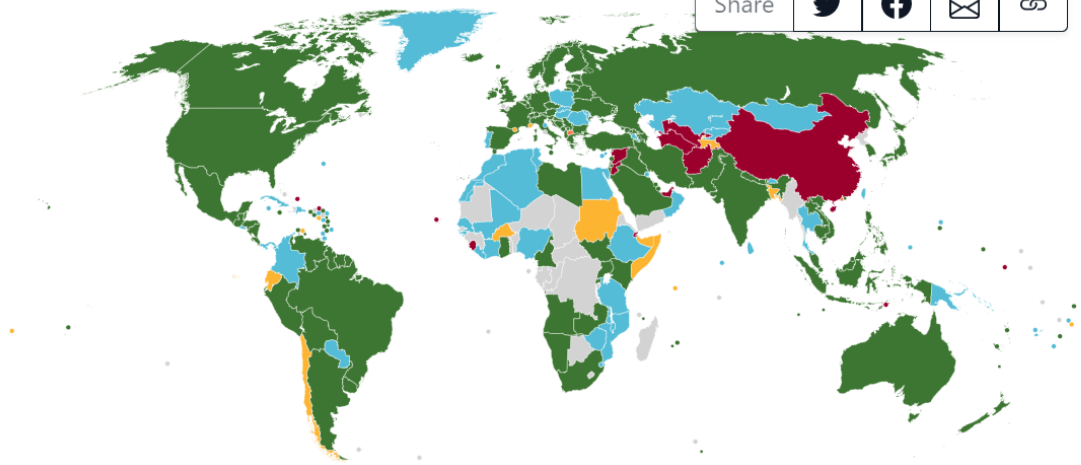
Berman Institute of Bioethics & Center for Immunization Research, Johns Hopkins University. Covid-19 Maternal Immunization Tracker (COMIT). www.comitglobal.org. Accessed: 5/4/2022, 4:01:14 PM.

CONTACT

If you have questions or comments, or would like to notify us of any technical issues you are experiencing with COMIT, please get in touch. We welcome and appreciate your valuable feedback.

COVID-19 Maternal Immunization Tracker

Share



108	58	14	2	14	28
Recommended for some or all	Permitted	Permitted with qualifications	Not recommended but with exceptions	Not recommended	No position found

World Health Organization

Public Health Authority | Global

Most recent vaccine policy positions

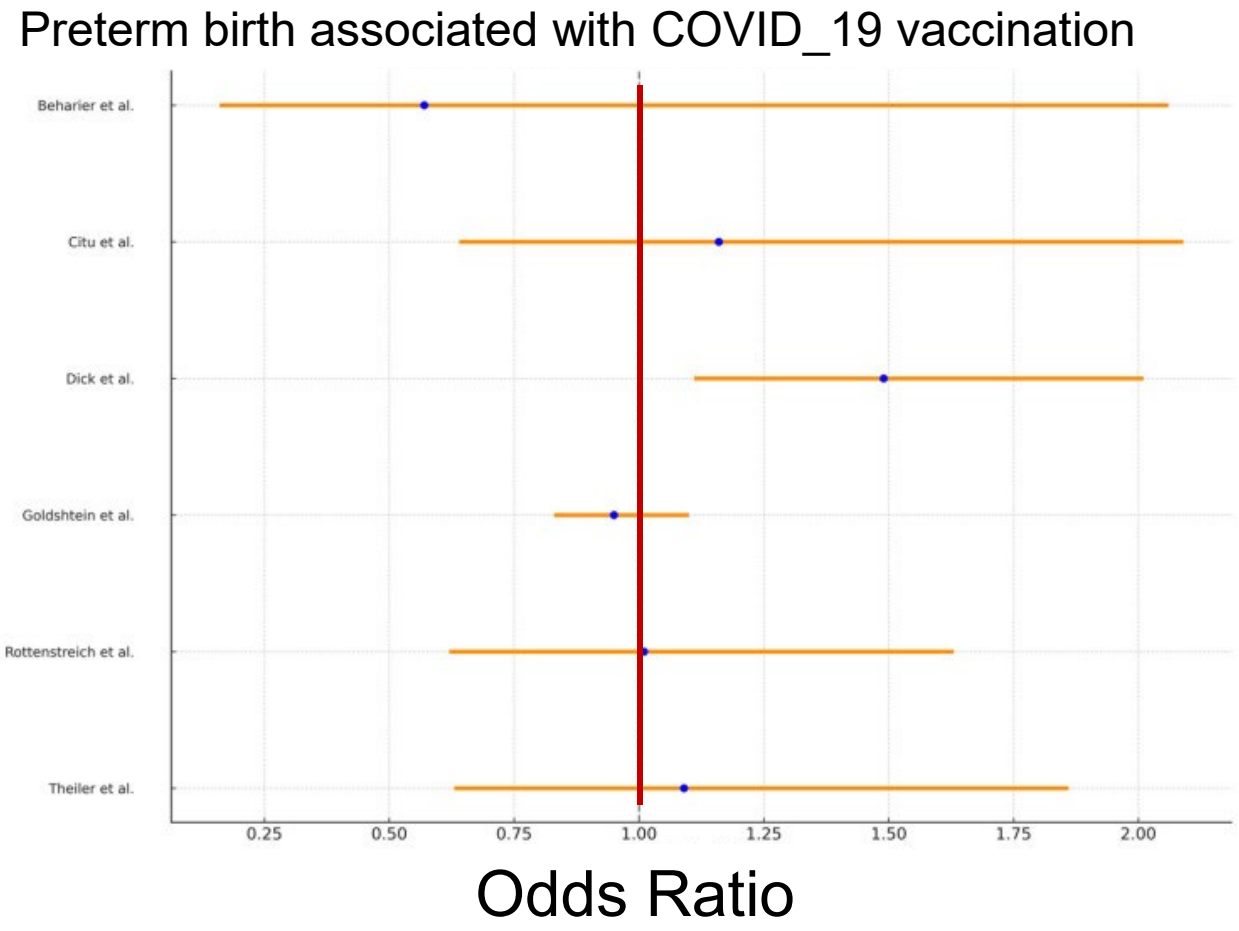
Name	Pregnancy	Lactation
Bharat Biotech Covaxin	●	●
Johnson & Johnson Janssen COVID-19 vaccine	●	●
Moderna COVID-19 vaccine	●	●
Novavax Covovax, TAK-019	●	●
Oxford-AstraZeneca Vaxzevria, Covishield	●	●
Pfizer/BioNTech Comirnaty	●	●
Sinopharm BIBP-CorV	●	●
Sinovac CoronaVac	●	●

Last reviewed on 2022-04-19

*https://www.comitglobal.org/explore/public-health-authorities/pregnancy

COVID-19 vaccines given in pregnancy not associated with preterm births *

Meta-analysis of 6 studies & 35,612 patients from publications in 2021-2022



Conclusions:

- No sig. risk for preterm birth
- No sig. risk of adverse pregnancy outcomes
- No sig. risk of neonatal complications

Uta et al. Vaccines 2024

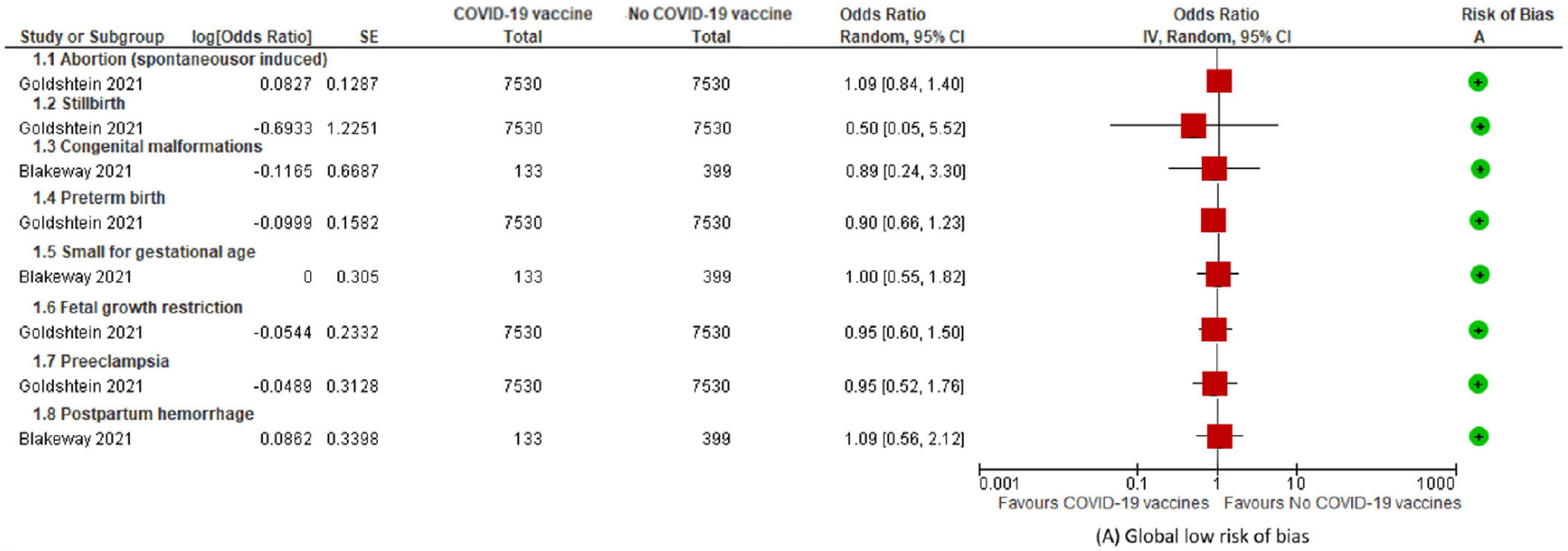
Safety of COVID-19 Vaccines during Pregnancy: Systematic Review and Meta-analysis (Ciapponi et al, 2023)

Systematic review of 8837 records/71 studies involving 17 million pregnancies

- 37/71 studies were cohort studies;12 surveillance studies; 6/71 studies in LMIC studies
- 9 studies selected for inclusion (US, UK, Israel)

Results:

- **Adverse pregnancy outcomes, reactogenicity: did not exceed background rates**
- **Exception: Postpartum hemorrhage reported by 2 studies but comparison with non-exposed pregnant persons found non-stat sig. differences (OR 1.09; 95% CI 0.56-2.12)**



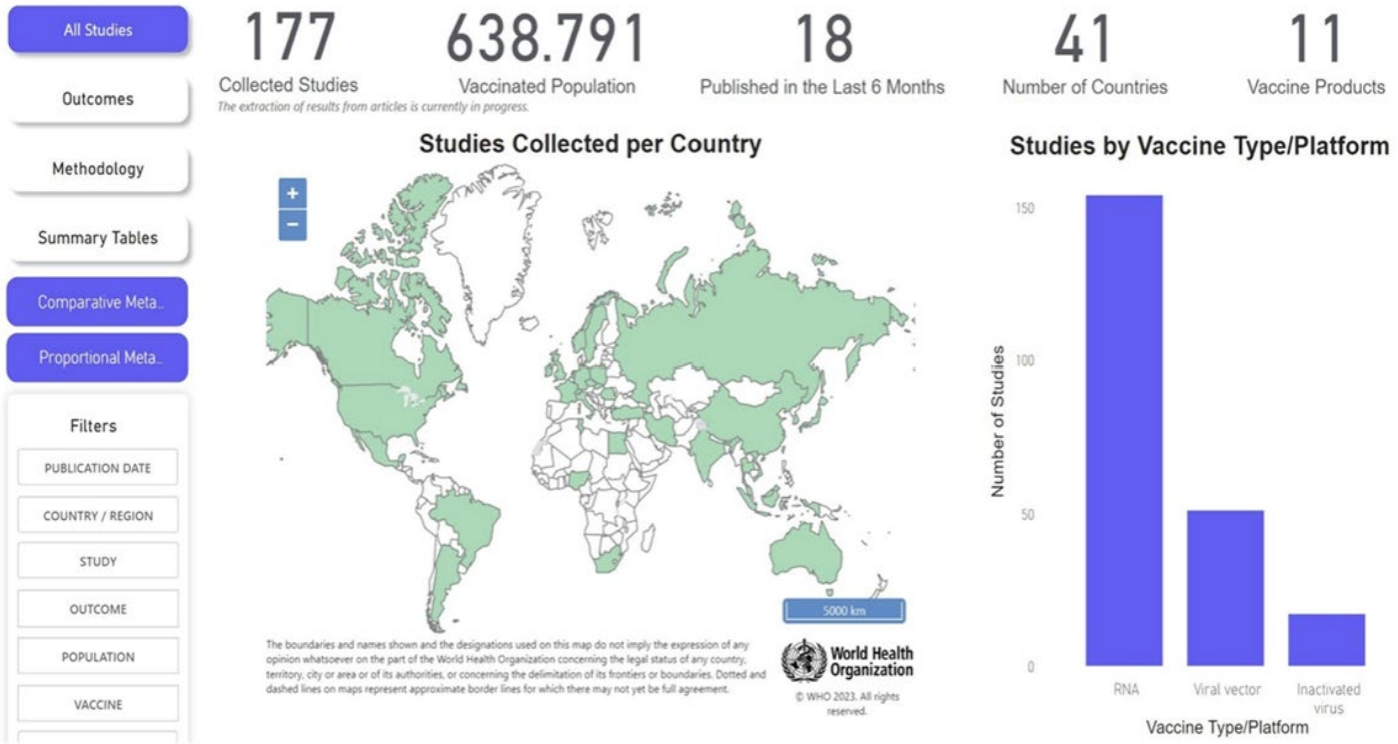
Vaccine 41 (2023) 3688–3700

Fig. 2. Forest plots of pregnancy outcomes comparing exposure with no exposure to COVID-19 vaccines.

“Living” Systematic Review on Safety and Effectiveness of COVID-19 Vaccine during Pregnancy (2024*)

Conclusion: No safety concerns

- **No associations** between COVID-19 vaccination during pregnancy with > = 1 dose vx and adverse maternal-pregnancy- and infant-related outcomes, regardless of trimester and vx type
- **Outcomes** included miscarriage, gestational diabetes, hypertensive disorders, congenital anomalies, Apgar score at 5 minutes < 7, prematurity, SGA, NICU or hospitalization and respiratory distress
- **Observed stat. significant reductions** in stillbirth with mRNA/viral vector vaccines administered in early stages of pregnancy and in emergency C/S with mRNA vx



First trimester COVID-19 mRNA vaccines NOT associated with risk of major congenital malformations*

JAMA Network Open. 2025;8(10):e2538039. doi:10.1001/jamanetworkopen.2025.38039

Review of medical records registry "Mother–Child Epi-Meres" in France:

- Review from Apr 2021-Jan 2022; followup through Dec. 2024
- Assessment of major congenital malformations in 13 organ systems and 75 individual diagnostic criteria
- Evaluation of **527, 564 eligible live born infants, of which** 130,338 or 24.7% born to mothers who received ≥ 1 doses of COVID-19 vaccine during 1st trimester

CONCLUSION: No increased risk of major congenital malformations observed overall or by organ system or for any of 75 individual malformations.

*Bernard, Duchemin, et al. JAMA Netwk Open 2025 Oct

COVID-19 Vaccine as a Model: Maternal Ab Transplacental Transfer to Infants

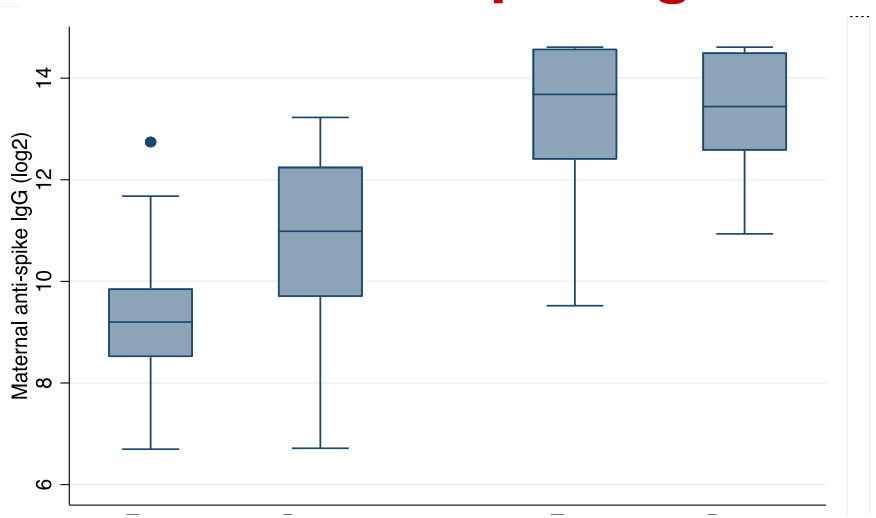
What do we know about impact on pregnancy, maternal health/placental function and the impact on maternal Ab active transfer after vaccination?

Maternal COVID-19 vaccine immunization serves as model for:

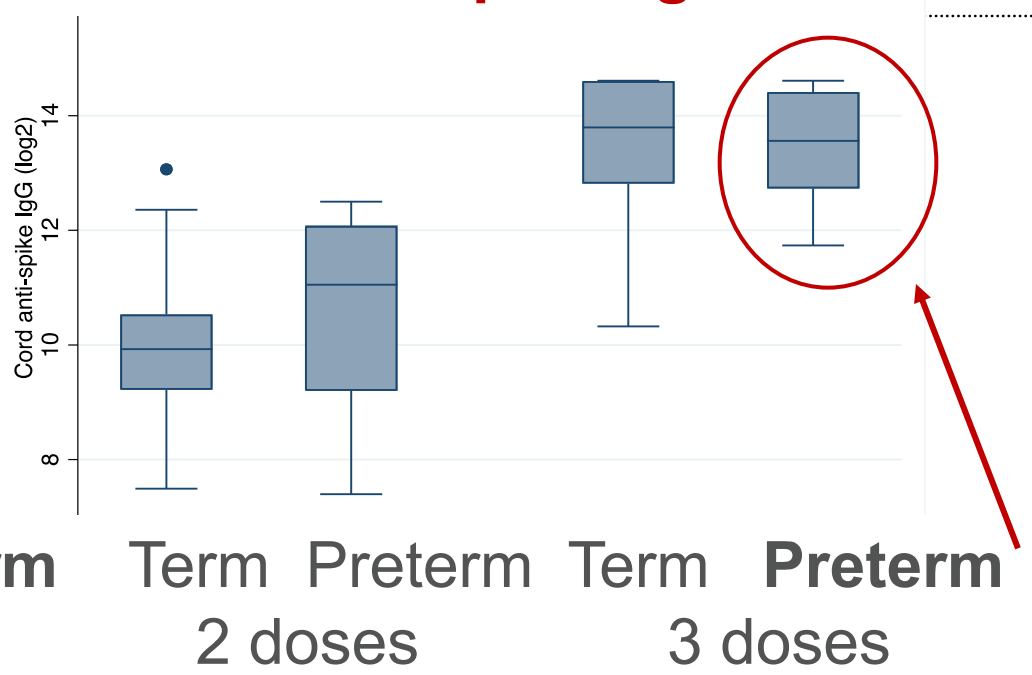
- Impact on major congenital malformations
- Impact on premature delivery
- Maternal Ab transfer in:
  - Preterm infants
  - Intrauterine growth retardation/small for gestational age infants
  - Preeclampsia/maternal hypertension
  - Multiple gestations

More doses of COVID-19 vaccine prior to/ during pregnancy can improve Ab levels in both term and preterm infants *

MATERNAL Spike IgG Ab



CORD Spike IgG Ab



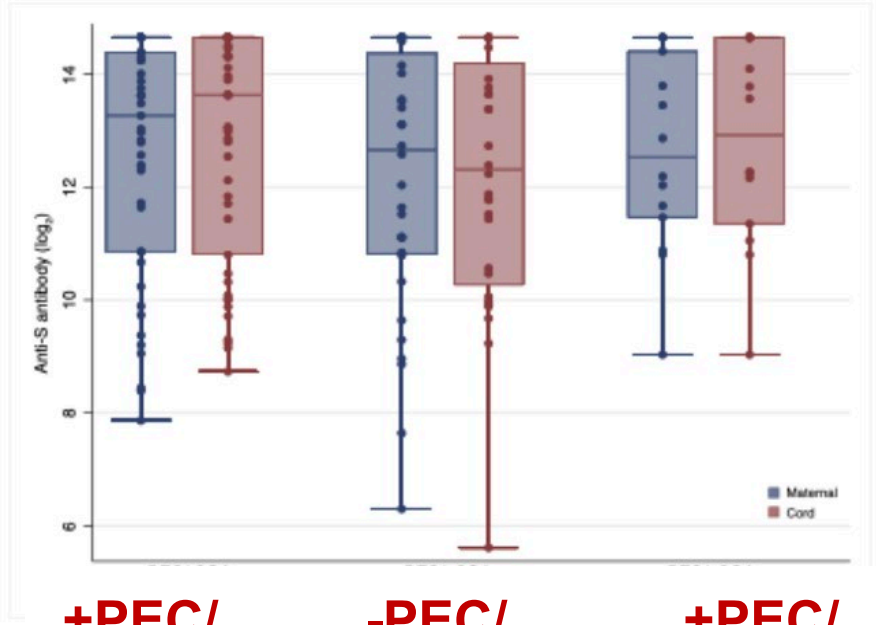
Boxplot showing the distribution of anti-spike IgG in 189 term and 28 preterm mat/cord pairs, by preterm status and number of doses of COVID-19 mRNA vaccine prior to delivery.

*Kachikis JAMA Netwk Open 2023

UNIVERSITY of WASHINGTON

Transplacental SARS-CoV-2 Ab Transfer in Pregnancy Is Similar with Pre-eclampsia and/or SGA infants*

PEC = Preeclampsia
SGA=Small for Gestational Age



Kung et al, PIDJ 2025;44;s43

Table. Maternal / cord anti-spike AB

	Total n=93	+PEC/ -SGA n=47	-PEC/ +SGA n=32	+PEC +SGA n=14	P-value
Mat. anti-S	5460 (4022, 7412)	5970 (3854, 9249)	4514 (2533, 8045)	6248 (3106, 12570)	0.75
Cord anti-S	6157 (4601, 8240)	7170 (4778, 10759)	4642 (2675, 8055)	7046 (3454, 14374)	0.38
Ratio	1.1 (1.0, 1.3)	1.2 (1.1, 1.4)	1.0 (0.8, 1.4)	1.1 (1.0, 1.3)	0.69

**Note: Geometric mean concentrations (95% confidence intervals); mat. & cord anti-spike IgG compared using Kruskal Wallis test;
ratio calculated as cord anti-spike IgG divided by maternal anti-spike IgG and compared using one-way ANOVA**

UNIVERSITY of WASHINGTON

(*Pediatr Infect Dis J* 2025;44:S43–S45

Paradigm Shift of Research During Pregnancy*

https://www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit/ethical considerations#:~:text=The%20revised%20document%20states%20that,for%20Research%20Involving%20Humans%202022

Kachikis A, Eckert LO, Englund JA. Chapter 1. In: Leuridan EE, Nunes MC, Jones CE, editors. Maternal Immunization: Academic Press; 2020.

* Ethical considerations for including women as research participants. Committee Opinion No. 646. *Obstet Gynecol.* 2015; 126:e100–7.

Challenges remaining for maternal immunization….

Acknowledgements:

A. Kachikis,MD, L. Eckert MD, H. Chu, MD, A. Greninger, MD, PhD,, E. Klein, MD, K. Lacombe, MS, S. Vora, MD, A Waghmare, MD, and Peds ID Research Team - Seattle Children's Hospital, and Univ. Washington
K. Edwards, MD, N. Halasa, MD, MPH - Vanderbilt University
F. Munoz, MD, P. Piedra, W.P. Glezen, MD - Baylor College of Medicine
J. Tielsch, PhD, J. Katz, PhD - Johns Hopkins
K. Neuzil, Lead of SAGE RSV Working Group (Formerly NIH) and Gates Fndn

Funding: NIAID, CDC, PATH, AstraZeneca, MedImmune, Moderna, Thrasher, Pfizer, Bill and Melinda Gates Fndn, Gates Ventures.

HOSPITAL • RESEARCH • FOUNDATION

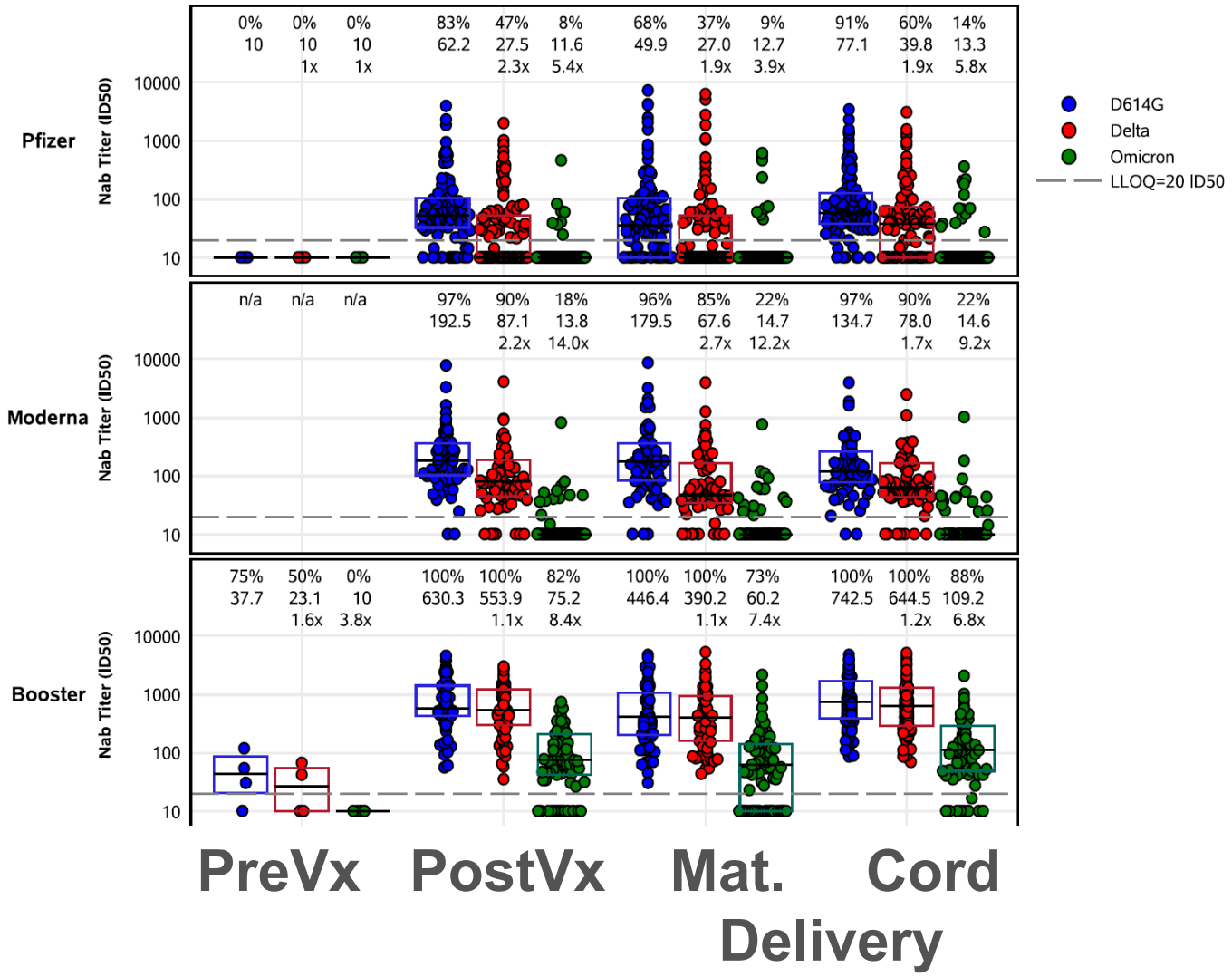
Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION

Vaccines recommended or being considered to be administered during pregnancy – 2026*

Vaccines – licensed or used	Maternal benefit	Fetal/neo-natal benefit	Timing during pregnancy	Safety concerns
Tetanus	✓	✓	Third trimester	None identified
Influenza-inactivated	✓	✓	Any trimester	None identified
Pertussis- Acellular	✓	✓	2nd-3rd trimester	None identified
Meningococcal conj.	✓	No data	If necessary	None identified
Polio – for Outbreaks; inactivated or oral vx	✓	No data	If necessary	Prefer inactivated but no safety concerns identified with live vx
RSV F protein	Min. data	✓	Studied only after 24 wks gestation	Acceptable safety profile; preterm birth with GSK vx; ? hypertension
COVID-19 Vaccines	✓	✓	**Through-out pregnancy**	**Safety confirmed in mother and infants up to 2 yrs of age**
UNDER INVESTIGATION Group B streptococcus	✓	✓	Under study =potentially early	No data
Cytomegalovirus	Possibly	✓	No data	No data
Hepatitis E (licensed in China)	✓	✓	No data	?Preterm/stillbirth
Others: Ebola, MPox	✓	✓	No data	?

*Adapted from Englund, Kachikis PIDJ 2024

COVID-19 Booster vaccination during pregnancy enhances maternal binding and neutralizing Ab responses and Ab transfer to the newborn*



Demonstrated good SARS CoV-2 neutralizing Ab activity in sera from pregnant immunized women and cord by study vaccine:

- pre-vx
- post vx
- delivery maternal
- cord blood

*Munoz et al & DMID 21-004 Study Group, Vaccine 41; 5296. 2023

COVID-19 Maternal Ab in Twin Pregnancies: Impact of Chorionicity on Transplacental Ab Transfer *

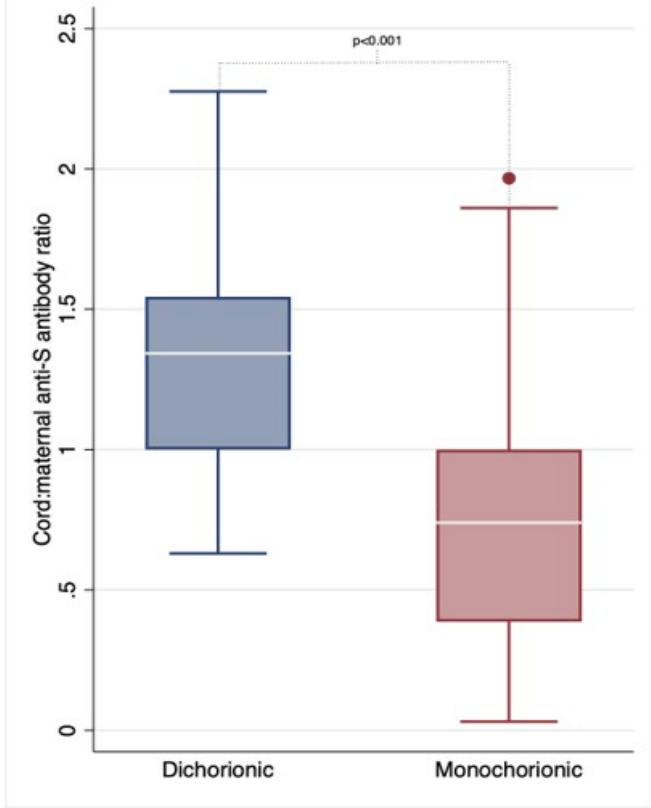
Methods

- Enrolled and obtained blood from 27 mat/cord dichorionic and 13 monochorionic triads from 2021-2023
- Sera/plasma assessed for anti-Spike Ab using Roche Elecsys immunoassay

Conclusions

- Both mono- and dichorionic twin infants benefit from maternal immunization
- After adjusting for time from vaccination to delivery, cord:maternal antibody ratios are significantly higher in dichorionic pregnancies,

Boxplot of cord to maternal anti-S in dichorionic and monochorionic pregnancies



Abbreviation: anti-S = anti-Spike antibody

* Stolarczuk et al, INMIS 2024 Mtg

Seattle Children's
HOSPITAL • RESEARCH • FOUNDATION