GLOBAL VACCINE DATA NETWORK (GVDN) | GLOBAL COVID VACCINE SAFETY (GCoVS)

Assessing the Safety of Maternal Immunization in Observational and Real-World Data

Lessons Learned from a Global Study

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SECTION 01

01

Introduction.

Study rationale, design, objectives, and analytic approach.

THE RATIONALE

COVID-19 vaccine trials excluded pregnant women — evidence had to come from observational studies.

Pregnant women are at increased risk of severe complications from COVID-19 disease — making maternal immunization an important strategy for protecting both mother and fetus.

Pregnant women were excluded from COVID-19 vaccine trials. As a result, evidence on the safety of vaccination in pregnancy has relied primarily on observational studies.

Most prior studies were single-country, with short follow-up and limited comparability. Detecting rare outcomes and assessing generalisability required coordinated, multi-database analyses.

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GVDN PARTNER SITES

First coordinated multi-database cohort study of COVID-19 vaccine safety in pregnancy.

STUDY DESIGN & OBJECTIVES

Multiple countries, one protocol, federated design.

DESIGN	Multi-site observational retrospective cohort	POPULATION	Pregnant women aged 14–54	PREGNANCY PERIOD	28 days pre-LMP → 1 day pre-delivery Evaluated based on GA at end of pregnancy
EXPOSURE	At least one COVID-19 vaccination during pregnancy period	OUTCOMES	17 core · 25 exploratory · 27 AESI	COVARIATES	34 covariates e.g. SES, high-risk medical conditions

PRIMARY OBJECTIVE	Does COVID-19 vaccination during pregnancy increase the risk of pre-specified pregnancy, fetal, or neonatal outcomes?
SECONDARY EXPOSURES	Brand, dose, interval, co-administration, trimester of first vaccination
SUBGROUP ANALYSES	Prior vaccination or infection, maternal age, health status, LMP certainty

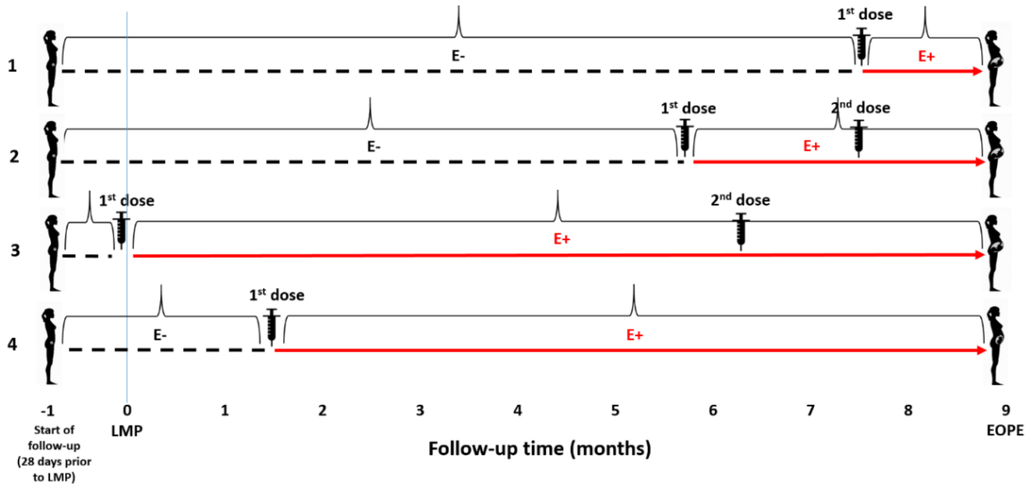
ANALYTIC APPROACH

Cox proportional hazards, three covariate adjustment levels.

MODEL

Extended Cox PH with time-varying exposure

GA used as primary timescale



COVARIATE ADJUSTMENT LEVELS

Unadjusted
Provides a baseline

Exposure + outcome only

↓

Harmonised
Prioritises between-site comparison

Unadjusted + all of: Age, SES, high-risk conditions, calendar week

↓

Maximal
Prioritises within-site confounding

Harmonised + any of: Urban-rural, infections and other complications, parity, trimester at first ANC visit, smoking, history of complications, prior COVID-19 and non-COVID-19 vaccination.

META-ANALYSIS

Random effects

SECTION 02

02

The Data.

Descriptive and analytic cohorts.

> These results are **preliminary, unpublished, and subject to change** — please do not cite or share without permission.

TOTAL COHORT

Participation from 12 sites*, 10 countries, 5 continents

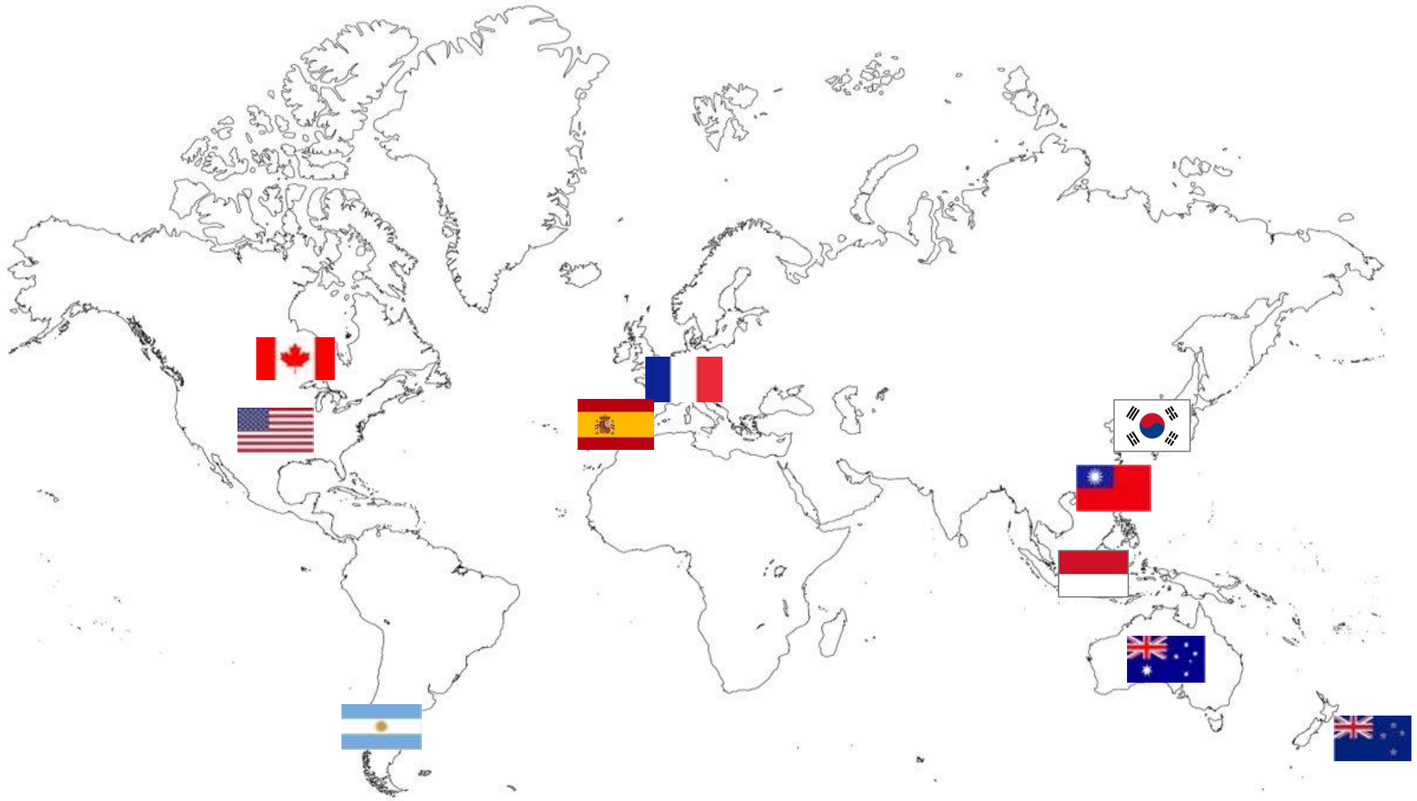
*Data currently collected from 10 out of 12 sites

3.2M
Pregnancies

2.8M
Births

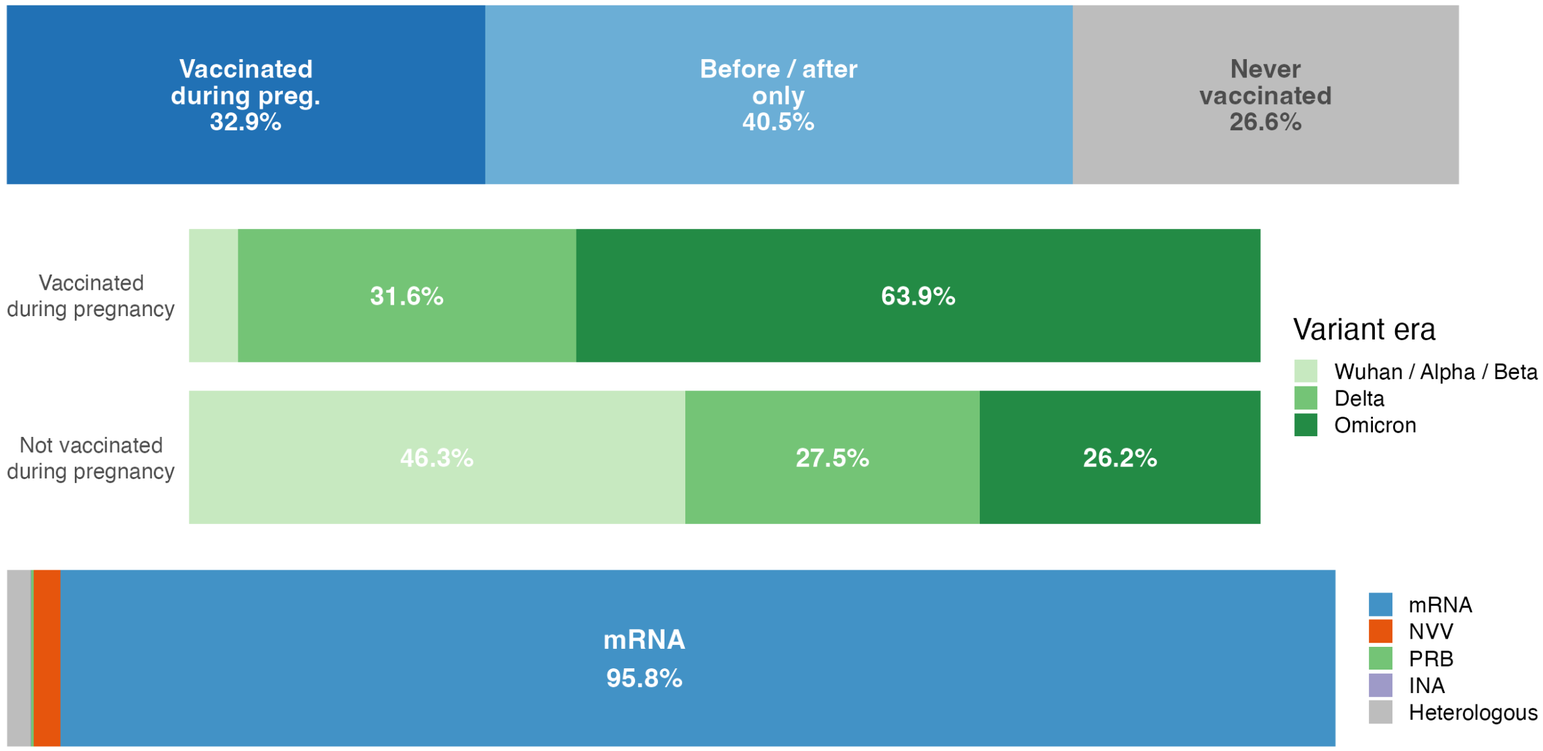
2.2M
Liveborn infants

2.5yrs
December 2020 – June 2023



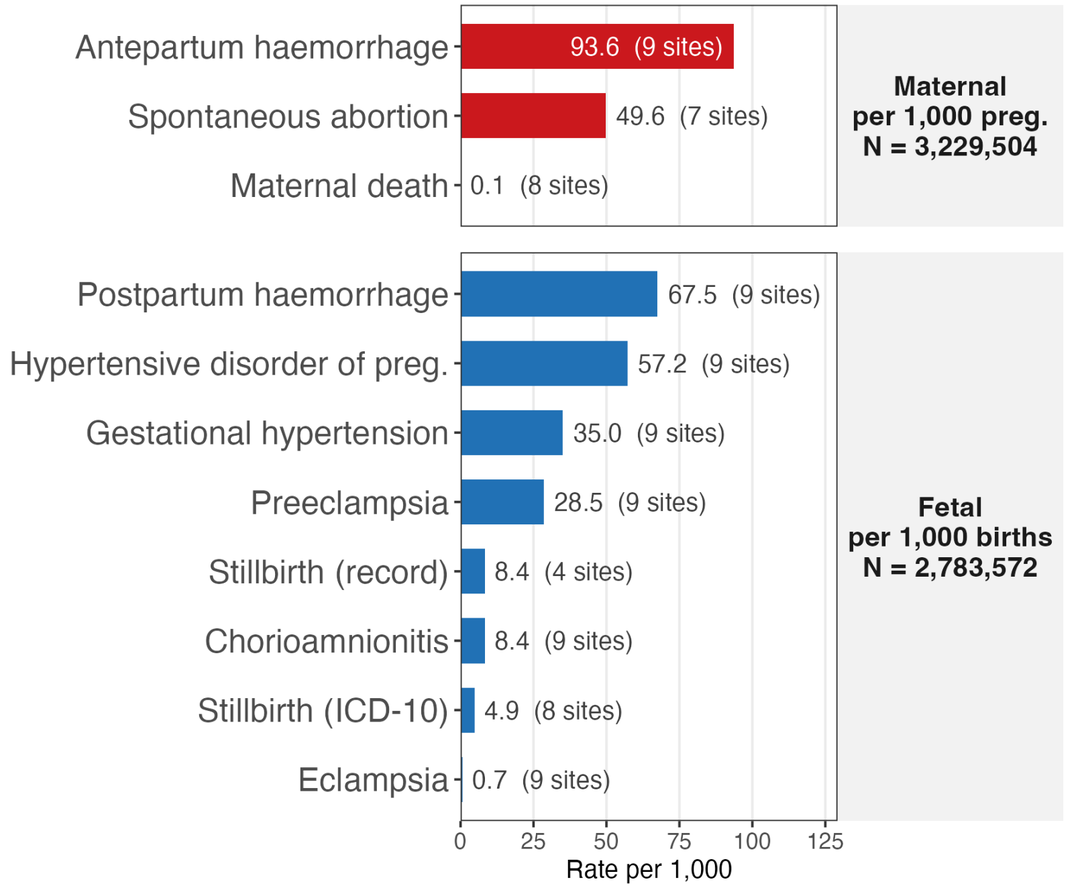
VACCINATIONS

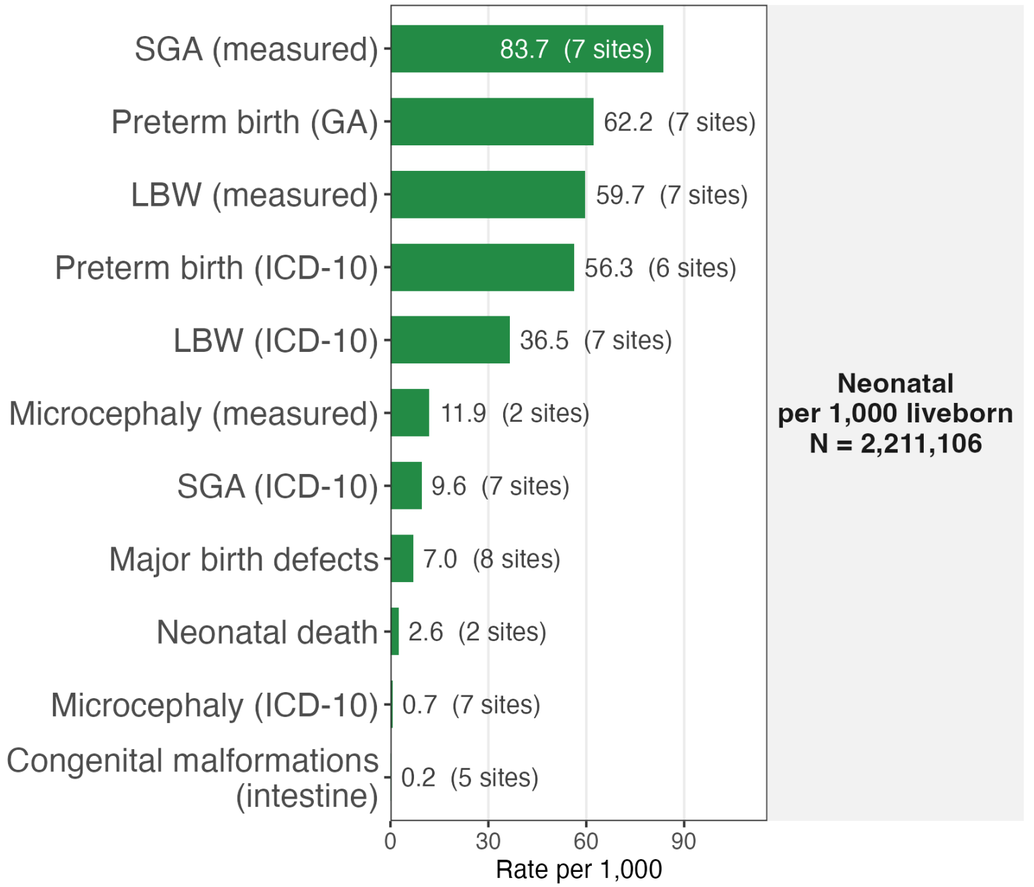
33% vaccinated during pregnancy, predominantly mRNA, during the Delta / Omicron eras



CORE OUTCOMES

Over 1.5 million core pregnancy outcomes





ANALYTIC COHORT

Exclusions are applied to obtain an analytic dataset

- Sites with analysis still in progress (1/10 sites)
- Pregnancies with (i) incomplete / inaccurate pregnancy period, (ii) missing COVID-19 vaccination data (date, brand, dose number), or (iii) missing core covariate data (age, SES, high risk status)
- Any site-specific exclusions

*Korea did not contribute towards neonatal outcome analyses due to low linkage proportion

Canada	France	Indonesia	Korea	New Zealand	Spain (x2)	Taiwan	United States
Dec 2020–Dec 2022	Jan 2021–Dec 2022	Jan 2020–Jul 2023	Feb 2021–Dec 2022	Mar 2021–Dec 2022	Jan 2021–Jun 2023	Mar 2021–Sep 2022	Dec 2020–Sep 2022
233,724 pregnancies	1,398,127 pregnancies	2,821 pregnancies	416,693 pregnancies	104,444 pregnancies	49,359 pregnancies	267,485 pregnancies	289,550 pregnancies
99.1% included	91.6% included	88.7% included	91.6% included	100.0% included	60.9% included	98.6% included	74.9% included
45.9% vaccinated	35.6% vaccinated	26.7% vaccinated	19.1% vaccinated	43.3% vaccinated	12.7% vaccinated	54.8% vaccinated	13.0% vaccinated

Overall analytic dataset (9 sites)

3,064,545	90.1%	32.1%	437,592	519,732	440,012
			142.8	198.4	215.0
pregnancies	included	vaccinated	maternal · per 1k preg.	fetal · per 1k births	neonatal · per 1k liveborn

Slides 12-22 contained results that are unpublished and have therefore been redacted

What we learned - 5 key takeaways.

NO. 01 No evidence of increased preterm birth risk following COVID-19 vaccination — consistent across definitions, covariate adjustment levels, secondary exposures, and subgroups

NO. 02 The impact of covariate adjustment differed substantially across outcomes — there needs to be a balance between harmonised and targeted adjustment strategies.

NO. 03 Heterogeneity is here to stay — we need to embrace it, learn from it, and plan accordingly. Multi-site studies are an important step towards this.

NO. 04 Working within a federated network is challenging — requires extensive planning, coding, site buy-in, and support. But the more we do it, the easier it gets (e.g. established CDMs)

NO. 05 Maternal immunisation studies require pregnancy-specific methods — e.g. time-varying exposures, appropriate handling of gestational age, and mitigation of fixed cohort bias

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Questions