Pregnancy, fetal, and newborn outcomes following a first booster dose of COVID-19 vaccine during pregnancy

CITF Scientific Meeting
Vancouver, Canada
March 8-10, 2023

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Disclaimer

The results from this study are unpublished and currently undergoing review with a journal

Conflicts and Disclosures

Conflicts

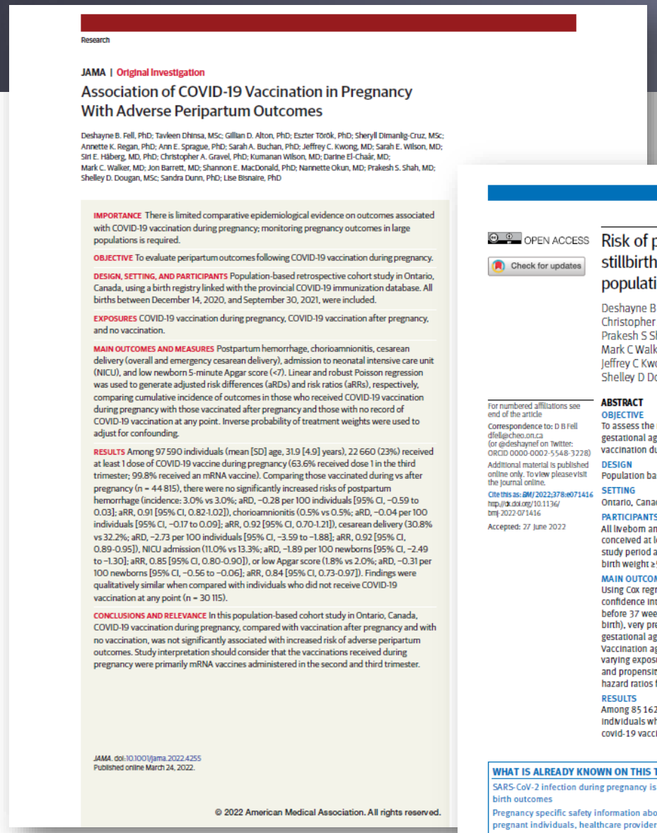
I have no conflicts to declare

COVID-19 illness during pregnancy

- COVID-19 illness during pregnancy is associated with adverse outcomes
  - Internationally, many studies have documented increased ICU admission, mechanical ventilation, maternal death, and other adverse outcomes in pregnant people as a result of COVID-19 during pregnancy
  - Increased risk of adverse pregnancy and birth outcomes, including preterm birth, stillbirth, small-for-gestational-age at birth, and other pregnancy complications have also been documented

Villar J, et al. Lancet. 2023 Feb 11;401(10375):447-457; Villar J, et al. JAMA Pediatr. 2021 Aug 1;175(8):817-826; McClymont E, et al. JAMA. 2022 May 24;327(20):1983-1991.

COVID-19 vaccination during pregnancy



Research

JAMA | Original Investigation

Association of COVID-19 Vaccination in Pregnancy With Adverse Peripartum Outcomes

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IMPORTANCE There is limited comparative epidemiological evidence on outcomes associated with COVID-19 vaccination during pregnancy; monitoring pregnancy outcomes in large populations is required.

OBJECTIVE To evaluate peripartum outcomes following COVID-19 vaccination during pregnancy.

DESIGN, SETTING, AND PARTICIPANTS Population-based retrospective cohort study in Ontario, Canada, using a birth registry linked with the provincial COVID-19 immunization database. All births between December 14, 2020, and September 30, 2021, were included.

EXPOSURES COVID-19 vaccination during pregnancy, COVID-19 vaccination after pregnancy, and no vaccination.

MAIN OUTCOMES AND MEASURES Postpartum hemorrhage, chorioamnionitis, cesarean delivery (overall and emergency cesarean delivery), admission to neonatal intensive care unit (NICU), and low newborn 5-minute Apgar score (<7). Linear and robust Poisson regression was used to generate adjusted risk differences (aRDs) and risk ratios (aRRs), respectively, comparing cumulative incidence of outcomes in those who received COVID-19 vaccination during pregnancy with those vaccinated after pregnancy and those with no record of COVID-19 vaccination at any point. Inverse probability of treatment weights were used to adjust for confounding.

RESULTS Among 97 590 individuals (mean [SD] age, 31.9 [4.9] years), 22 660 (23%) received at least 1 dose of COVID-19 vaccine during pregnancy (63.6% received dose 1 in the third trimester; 99.8% received an mRNA vaccine). Comparing those vaccinated during vs after pregnancy (n = 44 815), there were no significantly increased risks of postpartum hemorrhage (incidence: 3.0% vs 3.0%; aRD, −0.28 per 100 individuals [95% CI, −0.59 to 0.03]; aRR, 0.91 [95% CI, 0.82-1.02]), chorioamnionitis (0.5% vs 0.5%; aRD, −0.04 per 100 individuals [95% CI, −0.17 to 0.09]; aRR, 0.92 [95% CI, 0.70-1.21]), cesarean delivery (30.8% vs 32.2%; aRD, −2.73 per 100 individuals [95% CI, −3.59 to −1.88]; aRR, 0.92 [95% CI, 0.89-0.95]), NICU admission (11.0% vs 13.3%; aRD, −1.89 per 100 newborns [95% CI, −2.49 to −1.30]; aRR, 0.85 [95% CI, 0.80-0.90]), or low Apgar score (1.8% vs 2.0%; aRD, −0.31 per 100 newborns [95% CI, −0.56 to −0.06]; aRR, 0.84 [95% CI, 0.73-0.97]). Findings were qualitatively similar when compared with individuals who did not receive COVID-19 vaccination at any point (n = 30 115).

CONCLUSIONS AND RELEVANCE In this population-based cohort study in Ontario, Canada, COVID-19 vaccination during pregnancy, compared with vaccination after pregnancy and with no vaccination, was not significantly associated with increased risk of adverse peripartum outcomes. Study interpretation should consider that the vaccinations received during pregnancy were primarily mRNA vaccines administered in the second and third trimester.

JAMA. doi:10.1001/jama.2022.4255
Published online March 24, 2022.

RESEARCH

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Risk of preterm birth, small for gestational age at birth, and stillbirth after covid-19 vaccination during pregnancy: population based retrospective cohort study

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Additional material is published online only. To view please visit the journal online.

Cite this as: BMJ 2022;378:e071416 http://dx.doi.org/10.1136/bmj-2022-071416

Accepted: 27 June 2022

ABSTRACT

OBJECTIVE
To assess the risk of preterm birth, small for gestational age at birth, and stillbirth after covid-19 vaccination during pregnancy.

DESIGN
Population based retrospective cohort study.

SETTING
Ontario, Canada, 1 May to 31 December 2021.

PARTICIPANTS
All livebom and stillborn infants from pregnancies conceived at least 4 2 weeks before the end of the study period and with gestational age ≥20 weeks or birth weight ≥500 g.

MAIN OUTCOME MEASURES
Using Cox regression, hazard ratios and 95% confidence intervals were estimated for preterm birth before 37 weeks (overall and spontaneous preterm birth), very preterm birth (<32 weeks), small for gestational age at birth (<10th centile), and stillbirth. Vaccination against covid-19 was treated as a time varying exposure in the outcome specific risk window, and propensity score weighting was used to adjust hazard ratios for potential confounding.

RESULTS
Among 85 162 births, 43 099 (50.6%) occurred in individuals who received one dose or more of a covid-19 vaccine during pregnancy—42 979 (99.7%) received an mRNA vaccine. Vaccination during pregnancy was not associated with any increased risk of overall preterm birth (6.5% among vaccinated *v* 6.9% among unvaccinated; adjusted hazard ratio 1.02, 95% confidence interval 0.96 to 1.08), spontaneous preterm birth (3.7% *v* 4.4%; 0.96, 0.90 to 1.03), or very preterm birth (0.59% *v* 0.89%; 0.80, 0.67 to 0.95). No increase was found in risk of small for gestational age at birth (9.1% *v* 9.2%; 0.98, 0.93 to 1.03) or stillbirth (0.25% *v* 0.44%; 0.65, 0.51 to 0.84). Findings were similar by trimester of vaccination, mRNA vaccine product, and number of doses received during pregnancy.

CONCLUSION
The findings suggest that vaccination against covid-19 during pregnancy is not associated with a higher risk of preterm birth, small for gestational age at birth, or stillbirth.

WHAT IS ALREADY KNOWN ON THIS TOPIC
- SARS-CoV-2 infection during pregnancy is associated with adverse maternal and birth outcomes
- Pregnancy specific safety information about covid-19 vaccination is important for pregnant individuals, healthcare providers, and policy makers to guide decision making
- Evidence from large comparative studies about pregnancy outcomes after covid-19 vaccination during pregnancy is limited

WHAT THIS STUDY ADDS
- No association was found between immunisation with an mRNA covid-19 vaccine during pregnancy and increased risk of preterm birth, spontaneous preterm birth, very preterm birth, small for gestational age at birth, or stillbirth
- These findings can help inform evidence based decision making about the risks and benefits of covid-19 vaccination during pregnancy

Introduction
Infection with SARS-CoV-2 during pregnancy has been associated with higher risks of admission to hospital, admission to an intensive care unit, and death for pregnant individuals.[1 2] Furthermore, SARS-CoV-2 infection has been associated with a higher risk of preterm birth,[3 5] fetal growth restriction,[4] postpartum haemorrhage,[4] and stillbirth.[4] Many countries recommend covid-19 vaccination during pregnancy,[7] which has been shown to be effective against covid-19 in pregnant individuals[8] as well as their newborns[9 10]; however, vaccine coverage among pregnant individuals remains lower than among women of reproductive age.[11 12]

Safety concerns about covid-19 vaccination during pregnancy remains a potential obstacle to improving coverage. As of July 2022, results published from epidemiological studies are reassuring—two case-control studies of covid-19 vaccination in early pregnancy found no association with spontaneous abortion.[33 34] Our recent study of pregnancies to 30 September 2021, including 22 660 individuals vaccinated during the second or third trimester, did not show any association with adverse peripartum outcomes such as postpartum haemorrhage or low Apgar scores.[35] However, fewer studies have examined risk of adverse birth outcomes associated with prenatal covid-19 vaccination. A population based birth registry

- Receiving the ***primary*** COVID-19 vaccines series during pregnancy:
  - Reduces the risk of COVID-19 illness in pregnant individuals and their offspring
  - Has not been associated with increased risk of clinically serious acute adverse events in pregnant people or with any elevated risks of adverse maternal and neonatal outcomes

- Only a small number of studies to-date have evaluated outcomes following receipt of the ***third dose*** in pregnancy

Objective

- To assess risk of adverse pregnancy, fetal, and neonatal outcomes following a third dose (first booster dose) of COVID-19 vaccine during pregnancy (vs. no third dose during pregnancy) among individuals who had completed their primary COVID-19 vaccine series before pregnancy

Data sources

- BORN Ontario Birth Registry collects data on:
  - All live births and stillbirths ≥20 weeks from birth hospitals (>100 hospitals), midwifery practice groups, birthing centres
  - Integrated mother-baby records
  - Detailed sociodemographic, health-related, and pregnancy-related data, including birth outcomes

- Birth registry linked with the provincial COVID-19 vaccination registry (COVaxON):
  - All immunizations, regardless of setting
  - Dates of all doses, vaccine type/product

Murphy et al. IJE 2021; 50(5):1416-1417h. doi: 10.1093/ije/dyab033

Study design & population

- Retrospective cohort study
- Pregnant individuals with expected date of delivery between December 20, 2021 and August 31, 2022:
  - Had completed both doses of their primary COVID-19 vaccine series before the date of their last menstrual period (LMP)
  - Became eligible to receive a third dose any time before the end of their pregnancy (i.e., dose 2 date + 168 days)

Exposure groups

- **Vaccinated group**: Received a third COVID-19 vaccine dose between the LMP date up to 1 day before delivery (or end of outcome-specific risk window)
- **Unvaccinated group**: Completed primary COVID-19 vaccine series before the LMP date, were eligible for a third dose before the end of pregnancy, but did not receive a third dose during pregnancy

Outcomes

- **Pregnancy outcomes**
  - Hypertensive disorders of pregnancy
  - Placental abruption
  - Cesarean delivery
  - Emergency cesarean delivery
  - Chorioamnionitis
  - Postpartum hemorrhage

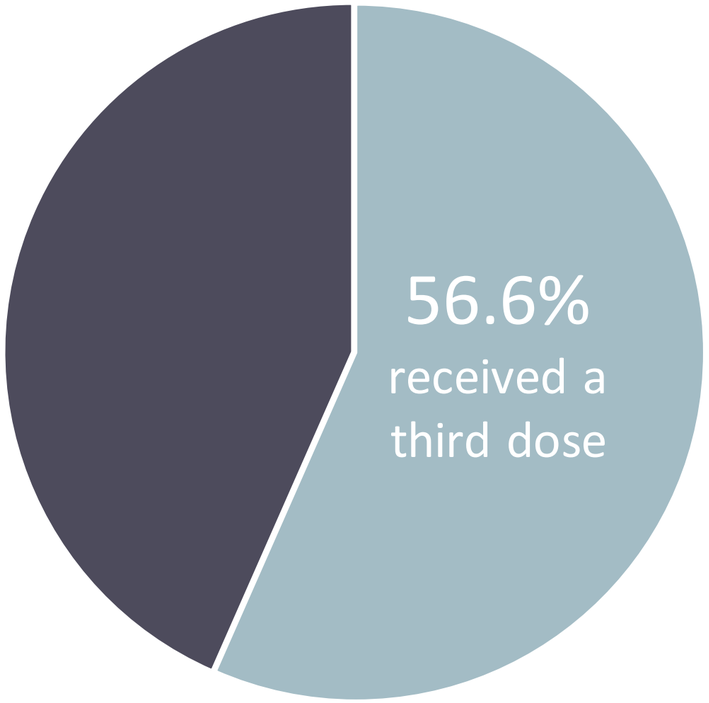
- **Fetal and neonatal outcomes**
  - Stillbirth (antepartum or intrapartum) at ≥20 weeks
  - Preterm birth (<37 weeks)
    - Very preterm birth
    - Spontaneous/clinician-initiated preterm birth
  - Neonatal intensive care unit (NICU) admission >24 hours
  - Newborn 5-minute Apgar score <7
  - Small-for-gestational-age (SGA) birth (<10th percentile)

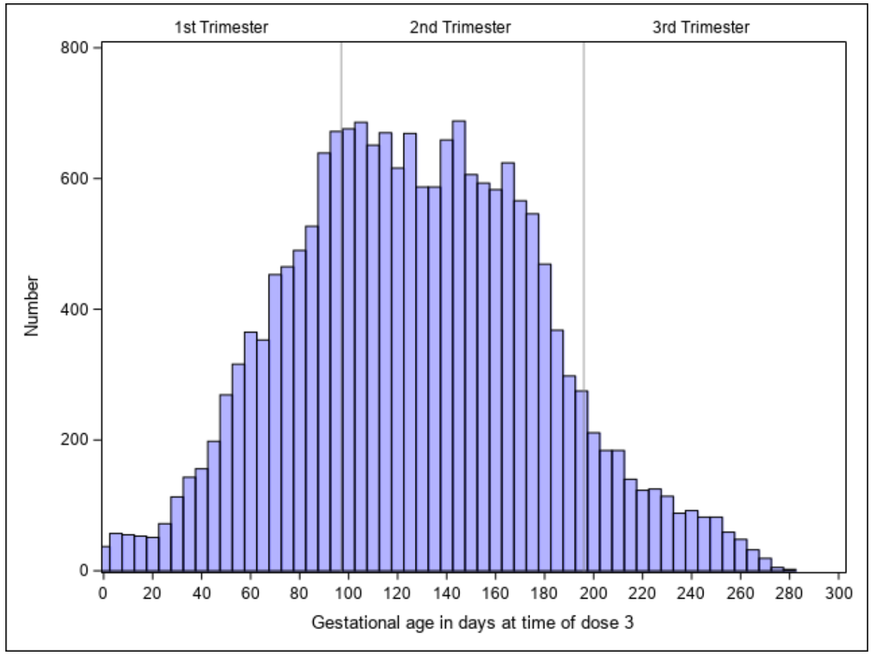
Analytical approach

- Propensity score methods:
  - Computed predicted probability of receiving a third dose of COVID-19 vaccine during pregnancy
  - Propensity scores used to develop inverse probability of treatment weights (IPTW)
- Multiple imputation to account for missing values (5 imputation datasets)
- Follow-up:
  - Starts at 20 weeks (T_0)
  - Ends at the occurrence of an outcome of interest or end of the outcome-specific risk window, whichever occurs first
- Extended Cox proportional hazards models with time-varying exposure
- Subgroup analyses: by mRNA vaccine product and trimester of third dose

Among **32,689** live births and stillbirths corresponding to **32,125** unique pregnancies during the study period

- **18,491 (56.6%)** live births and stillbirths were born to individuals who received a third COVID-19 vaccine dose during pregnancy
  - Individuals received dose 3 at a median of 196 days (28 weeks) after dose 2





Gestational timing (trimester) of dose 3 received during pregnancy

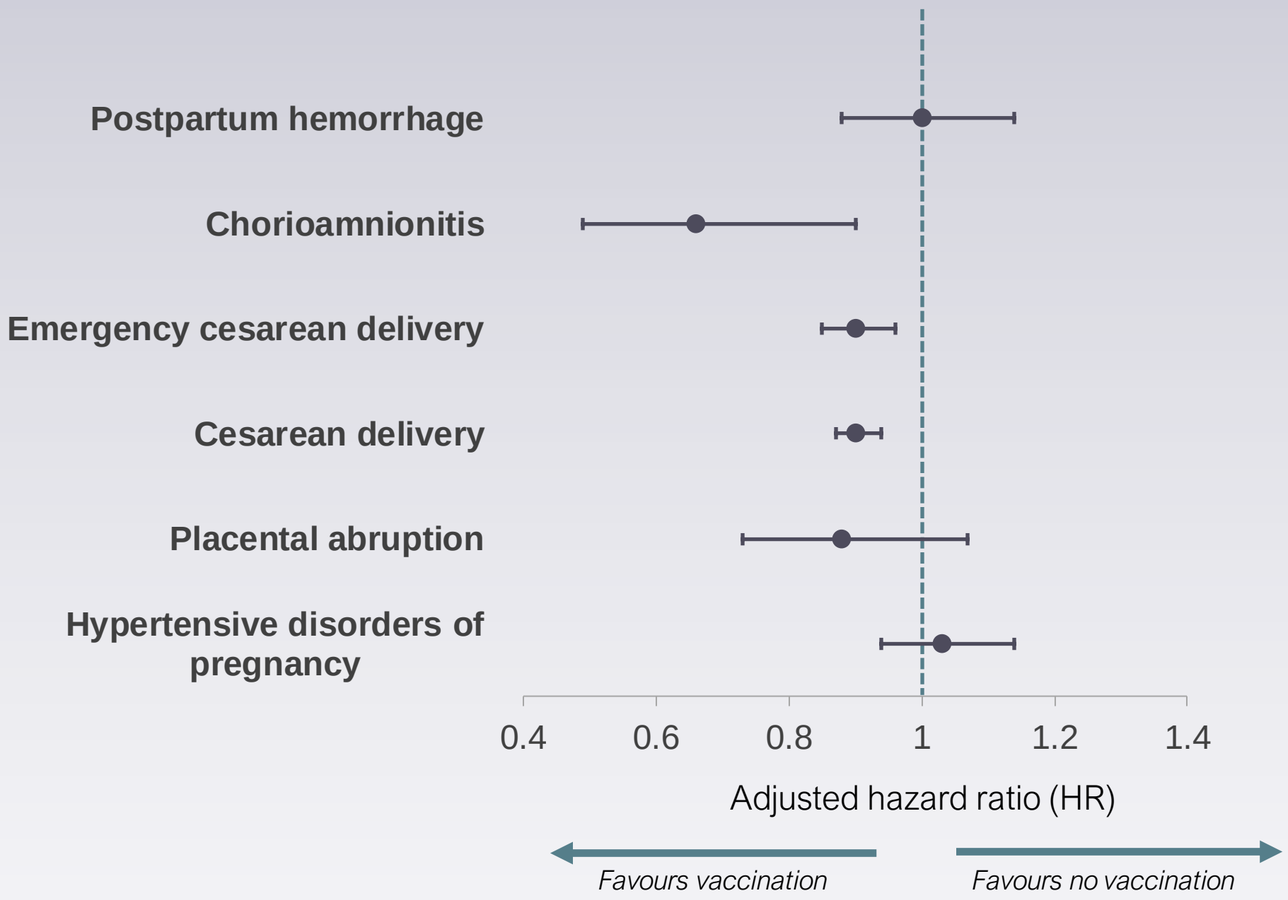
Characteristics of study population

		
 Maternal age at delivery ≥ 30 years	80.7%	66.3%
 Smoking during pregnancy	1.8%	4.3%
 Living in neighbourhoods with higher median family income (quintile 4&5)	44.3%	35.2%

Those who received a third COVID-19 vaccine dose during pregnancy were ***more likely*** to be:

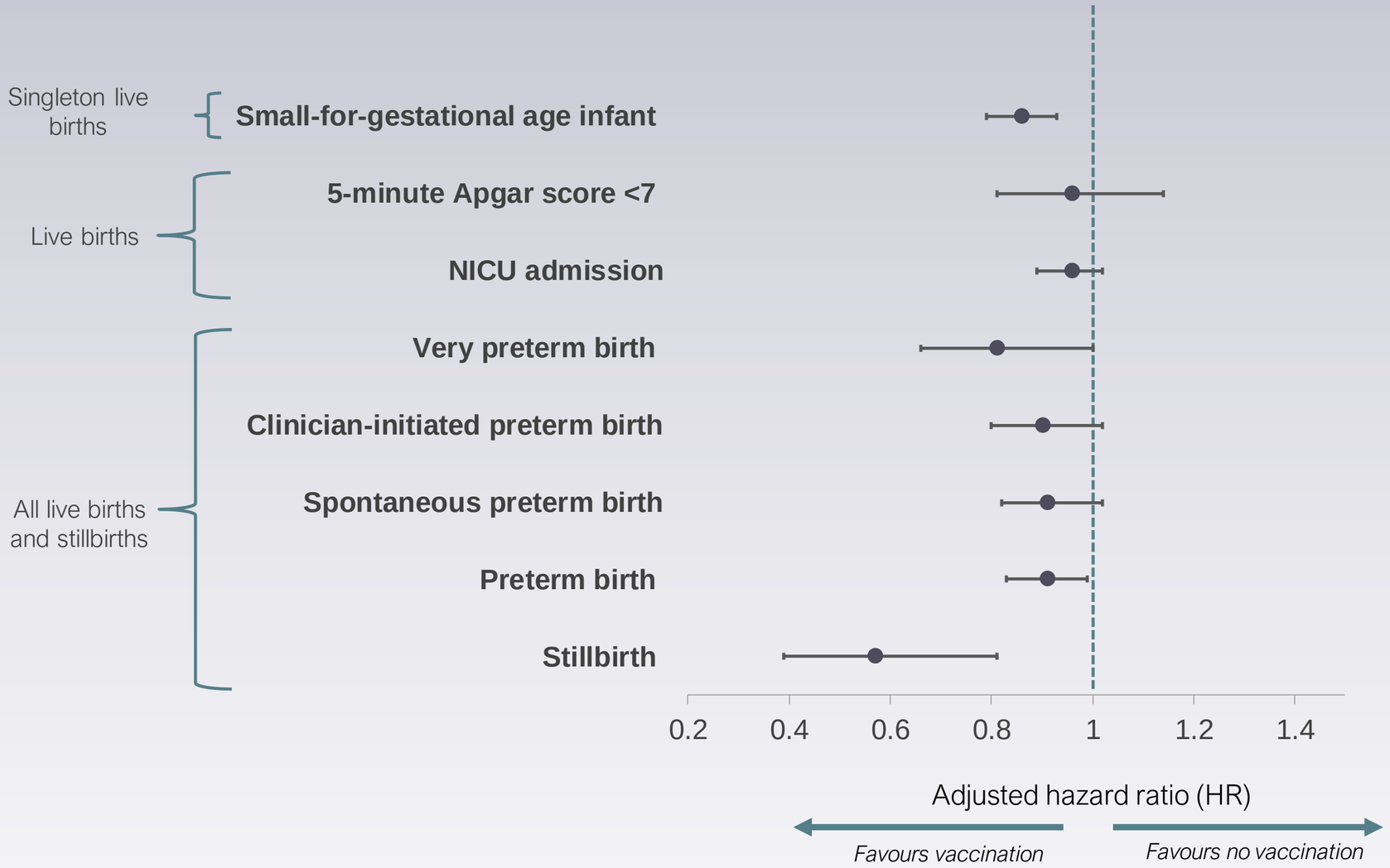
- 30 years of age and older
- Non-smoker
- Living in higher income neighbourhoods

Pregnancy outcomes



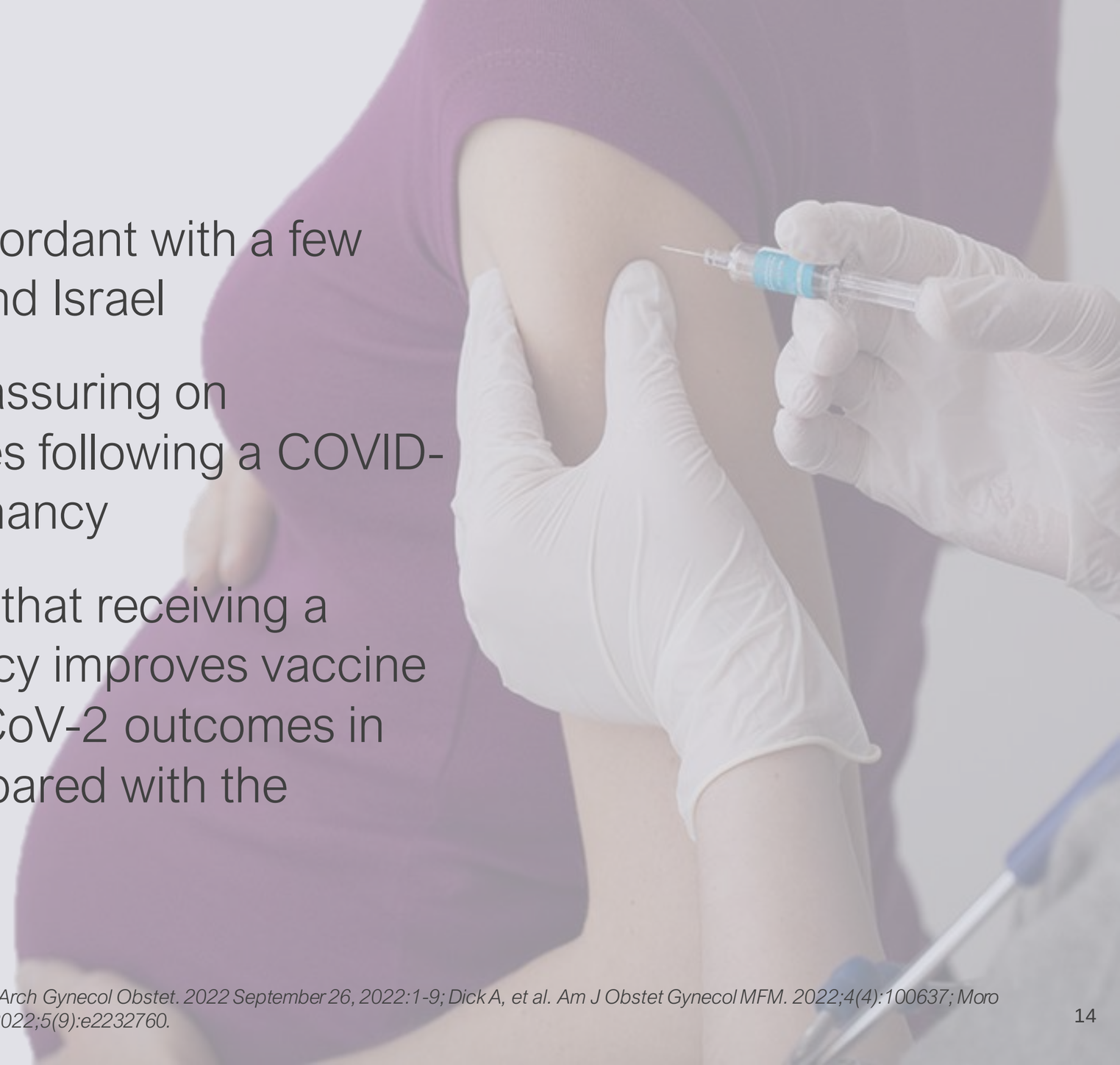
- Receipt of a third COVID-19 vaccine dose during pregnancy was ***not associated*** with any increased risk of:
  - Postpartum hemorrhage
  - Chorioamnionitis
  - Cesarean and emergency cesarean delivery
  - Placental abruption
  - Gestational hypertensive disorder

Fetal and neonatal outcomes



- Receipt of a third COVID-19 vaccine dose during pregnancy was ***not associated*** with any increased risk of adverse fetal and neonatal outcomes
- Associations were similar in subgroup analyses stratified by mRNA vaccine product and trimester of vaccination

- Results of this study are concordant with a few other studies from the U.S. and Israel
- Safety evidence to-date is reassuring on pregnancy and birth outcomes following a COVID-19 booster dose during pregnancy
- Emerging evidence suggests that receiving a booster dose during pregnancy improves vaccine effectiveness against SARS-CoV-2 outcomes in mothers and newborns, compared with the primary series alone



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Acknowledgements

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VACCINE SURVEILLANCE REFERENCE GROUP | GROUPE DE RÉFÉRENCE SUR LA SURVEILLANCE DES VACCINS

COVID-19 IMMUNITY TASK FORCE | GROUPE DE TRAVAIL SUR L'IMMUNITÉ FACE À LA COVID-19

- Funded by the Public Health Agency of Canada through the COVID-19 Immunity Task Force
- Ontario Ministry of Health for granting access to the COVaxON database
- Maternal-newborn hospitals and midwifery practice groups in Ontario for providing maternal-newborn data to BORN Ontario
- BORN Ontario staff for their assistance with data extraction, linkage, code review, and results review

Lessons learned

- Data linkage agreements
- Collaboration between data entities (BORN and COVaxON)
- Established Registry with robust data in near real-time
- Diverse project team
- Effective KT strategy with key organizations

Data linkage

Capacity

Diversity

Partnership

Communication

- Detailed individual patient-level data
- Complexity of studies
- Trolls and unpleasant emails/comments
- Changes of pandemic (new variants, number of doses)