Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
BACKGROUND: COVID-19 infection in pregnancy is associated with a higher risk of progression to severe disease, but vaccine uptake by pregnant women is hindered by persistent safety concerns. COVID-19 vaccination in pregnancy has been shown to reduce stillbirth, but its relationship with preterm birth is uncertain.

OBJECTIVE: This study aimed to measure the rate of COVID-19 vaccine uptake among women giving birth in Melbourne, Australia, and to compare perinatal outcomes by vaccination status.

STUDY DESIGN: This was a retrospective multicenter cohort study conducted after the June 2021 government recommendations for messenger RNA COVID-19 vaccination during pregnancy. Routinely collected data from all 12 public maternity hospitals in Melbourne were extracted on births at ≥20 weeks’ gestation from July 1, 2021 to March 31, 2022. Maternal sociodemographic characteristics were analyzed from the total birth cohort. Perinatal outcomes were compared between vaccinated and unvaccinated women for whom weeks 20 to 43 of gestation fell entirely within the 9-month data collection period. The primary outcomes were the rates of stillbirth and preterm birth (spontaneous and iatrogenic) in singleton pregnancies of at least 24 weeks’ gestation, after exclusion of congenital anomalies. Secondary perinatal outcomes included the rate of congenital anomalies among infants born at ≥20 weeks’ gestation and birthweight ≤third centile and newborn intensive care unit admissions among infants born without congenital anomalies at ≥24 weeks’ gestation. We calculated the adjusted odds ratio of perinatal outcomes among vaccinated vs unvaccinated women using inverse propensity score-weighting regression adjustment with multiple covariates; \( P<.05 \) was considered statistically significant.

RESULTS: Births from 32,536 women were analyzed: 17,365 (53.4%) were vaccinated and 15,171 (47.6%) were unvaccinated. Vaccinated women were more likely to be older, nulliparous, nonsmoking, not requiring an interpreter, of higher socioeconomic status, and vaccinated against pertussis and influenza. Vaccination status also varied by region of birth. Vaccinated women had a significantly lower rate of stillbirth compared with unvaccinated women (0.2% vs 0.8%; adjusted odds ratio, 0.18; 95% confidence interval, 0.09–0.37; \( P<.001 \)). Vaccination was associated with a significant reduction in total preterm births at <37 weeks (5.1% vs 9.2%; adjusted odds ratio, 0.60; 95% confidence interval, 0.51–0.71; \( P<.001 \)), spontaneous preterm birth (2.4% vs 4.0%; adjusted odds ratio, 0.73; 95% confidence interval, 0.56–0.96; \( P=.02 \)), and iatrogenic preterm birth (2.7% vs 5.2%; adjusted odds ratio, 0.52; 95% confidence interval, 0.41–0.65; \( P<.001 \)). Infants born to vaccinated mothers also had lower rates of admission to the neonatal intensive care unit. There was no significant increase in the rate of congenital anomalies or birthweight ≤3rd centile in vaccinated women. Vaccinated women were significantly less likely to have an infant with a major congenital anomaly compared with the unvaccinated group (2.4% vs 3.0%; adjusted odds ratio, 0.72; 95% confidence interval, 0.56–0.94; \( P<.02 \)). This finding remained significant even when the analysis was restricted to women vaccinated before 20 weeks’ gestation.

CONCLUSION: COVID-19 vaccination during pregnancy was associated with a reduction in stillbirth and preterm birth, and not associated with any adverse impact on fetal growth or development. Vaccine coverage was substantially influenced by known social determinants of health.

Key words: cohort studies, COVID-19, pregnancy outcome, premature birth, stillbirth, vaccination

Introduction

Pregnancy is an independent risk factor for severe COVID-19 infection, with pregnant people having higher rates of hospitalization, intensive care unit admission, and mortality compared with nonpregnant adults.\(^1\) COVID-19 infection during pregnancy also increases the risk of serious adverse perinatal outcomes, including stillbirth, preterm birth, cesarean delivery, and preeclampsia.

An effective vaccine against SARS-CoV-2 became available globally from early 2021,\(^2\) with the Australian rollout commencing in March 2021.\(^3\) By the end of 2021, vaccine uptake in the eligible Australian population was 85 per 100.\(^4\) It is now well-established that the messenger RNA (mRNA) COVID-19 vaccine is safe and protective against severe COVID-19 disease in pregnancy,\(^5\)--\(^8\) but this confidence was not present at the launch of the vaccine program because of the exclusion of pregnant women from early clinical trials.\(^9\) It was not until June 9, 2021 that Australian health authorities changed their advice on vaccination in pregnancy from cautiously recommending deferral to the postpartum period, to clearly recommending vaccination with an mRNA vaccine during pregnancy.\(^10\) The change in health advice was met with vaccine
COVID-19 infection in pregnancy is associated with a higher risk of progression to severe disease, but vaccine uptake by pregnant women is hindered by persistent safety concerns. COVID-19 vaccination in pregnancy has been shown to reduce stillbirth, but its relationship with preterm birth is uncertain. Most of the published literature on COVID-19 vaccination in pregnancy has methodological limitations, including fixed-cohort bias and time-varying exposure. We conducted this multicenter study to provide robust evidence on messenger RNA (mRNA) COVID-19 vaccination and perinatal outcomes including stillbirth, preterm birth, and congenital anomalies.

Key findings
The adjusted odds of stillbirth, preterm birth, and neonatal intensive care admission were markedly reduced among infants born to COVID-19—vaccinated women compared with those born to unvaccinated women. Both spontaneous and iatrogenic preterm births were reduced among vaccinated women. COVID-19 vaccination during pregnancy was not associated with an increase in congenital anomalies or fetal growth restriction.

What does this add to what is known?
Our analysis confirmed a strong relationship between the COVID-19 mRNA vaccine and lower stillbirths and iatrogenic and spontaneous preterm births. We provided further evidence to endorse the safety of the mRNA vaccine during pregnancy and to promote the benefits of reduced stillbirth and preterm birth. Vaccine coverage was not distributed equally in our population and was influenced by known social determinants of health. In addition to its impact on reducing severe COVID-19 illness, vaccination may have been a proxy for other biological and social determinants of health in our pregnant population.

In Melbourne, Australia, data collection on maternal COVID-19 vaccination status was mandated by the Department of Health and Aged Care for all births from July 1, 2021. These vaccination data were collected by a collaboration of 12 Melbourne public maternity hospitals under a research protocol established to monitor the effect of the pandemic on clinical quality indicators. Data from the Collaborative Maternity and Newborn Dashboard (CoMaND) for the COVID-19 pandemic were used here to assess the perinatal outcomes associated with vaccination in pregnancy, including preterm birth, stillbirth, and congenital anomalies.

Materials and Methods

Institutional review board approval
This study was given ethical approval from the human research ethics committees of Austin Health (Ref. HREC/64722/Austin-2020) and Mercy Health (Ref. 2020-031).

Study population
We extracted routinely collected data on births at ≥20 weeks of gestation from all 12 public maternity hospitals in Melbourne from July 1, 2021 to March 31, 2022. Data on pregnancies that ended before 20 weeks are not collected in our routine maternity data collection and were not available for this study. Approximately 80% of all hospital births in Melbourne occur in these study sites. Births in exclusively private hospitals and planned home births outside of publicly funded home-birth programs were not captured. However, women planning a private hospital or home birth would typically be transferred to a public hospital if they were at risk of preterm birth <31 weeks or required tertiary maternal—fetal medicine care.

Outcome measures
Our analysis was performed with several denominator groups according to the outcomes of interest.

Total births cohort
Sociodemographic characteristics. We used the total number of women giving birth from July 1, 2021 to March 31,
2022 to compare the characteristics of those with and without at least 1 dose of a COVID-19 vaccine before or during pregnancy. The characteristics included: maternal age, body mass index (BMI) in kg/m², smoking status, need for an English interpreter, maternal region of birth, socioeconomic status (assigned by residential postcode), parity, diabetes mellitus (none, gestational, preexisting, not tested), influenza vaccination status, pertussis vaccination status, plurality, gestation at first antenatal visit ≤12 weeks, and geographic remoteness.

Vaccination status by the week of birth. To examine temporal patterns in the uptake of COVID-19 vaccine following the health authority recommendations, we measured the weekly proportion of births to women who had received ≥1 doses of the mRNA COVID-19 vaccine before or during pregnancy.

Choropleth maps of Socio-Economic Indexes for Areas (SEIFA) and vaccination rates were generated in Tableau (version 2022.3; Salesforce, San Francisco, CA). Data on the specific brand of vaccine were not collected, but the Pfizer COVID-19 vaccine was the most available during the study period.

Calculated last menstrual period cohort

We used the calculated calendar week of the last menstrual period (LMP), rather than calendar week of birth, to define the vaccine-exposed and unexposed groups to ensure that any woman birthing from 20 to 43 weeks’ gestation would be captured in the birth data, thus avoiding “fixed cohort bias.”

Perinatal outcomes at ≥24 weeks. Perinatal outcomes were calculated from the singleton cLMP cohort following exclusion of congenital anomalies, terminated pregnancies, and births <24 weeks’ gestation. Calculation was performed using an “all births” denominator (live births and stillbirths). These outcomes included:

1. Stillbirths: total, term, and preterm <37 weeks.
2. Preterm birth <37 weeks: total, spontaneous, and iatrogenic. An iatrogenic birth was defined as any birth without spontaneous onset of labor (ie, induced labor or no labor).
3. Fetal growth restriction (FGR): defined as birthweight ≤3rd centile using Australian population sex-specific birthweight charts.
4. Apgar score <7 at 5 minutes.
5. Special-care nursery admission.
6. Neonatal intensive care unit (NICU) admission.
7. Mode of birth: induction of labor, prelabor cesarean delivery, cesarean delivery after labor onset, unassisted vaginal birth, instrumental vaginal birth (forceps/vacuum).
8. Born before arrival: refers to the rate of planned hospital births that occur before arrival, including unplanned births at home, in transit, or other locations.
9. Severe postpartum hemorrhage: estimated blood loss ≥1000 mL.
10. Iatrogenic birth for fetal compromise: total, ≥37 weeks, <37 weeks. An iatrogenic birth was an induction of labor or cesarean delivery before labor onset. Indications for induction of labor and cesarean delivery were coded according to the Australian Institute of Health and Welfare’s Metadata Online Registry (METEOR), which defines fetal compromise as “suspected or actual fetal compromise, and intrauterine growth restriction.” Any documentation of suspected FGR, antepartum abnormal cardiotocography,
“fetal distress” (without labor), reduced fetal movements, oligohydramnios, abnormal umbilical artery Doppler studies, or placental insufficiency prompted inclusion in this classification. All outcomes other than congenital anomalies and stillbirths were also calculated using live births as the denominator. Iatrogenic births for fetal compromise were only calculated using the live births denominator.

COVID-19 infections during pregnancy were collected and analyzed for the main outcomes of congenital anomalies, stillbirth, and preterm birth according to vaccination status.

**Statistical analysis**

No sample size calculation was performed because this was a cohort defined by the vaccination period. Analyses of secondary outcomes were considered exploratory, and no adjustments for multiple comparisons were made. Continuous variables in both determinants and safety analyses were presented with mean and standard deviation. Categorical variables were presented as counts and percentages. Statistical analyses were conducted using Stata, version 17 (StataCorp, College Station, TX), and 2-sided $P$ values <.05 were considered statistically significant.

**Determinants of COVID-19 vaccination uptake**

We performed multiple imputation by chained equations to minimize the bias from missing data in our dataset and created 5 imputed datasets. Factors associated with antenatal COVID-19 vaccination were analyzed using multivariable Poisson regression, with covariates selected on the basis of subject matter knowledge. Results of the regression analyses were presented as incidence rate ratio. The hospital-specific rates of vaccination uptake were summarized and reported as forest plots.

**Perinatal outcomes**

We used inverse-probability-weighted regression adjustment (IPWRA) of the Stata “teffects” suite of commands to balance the baseline difference in the population by COVID-19 vaccination status. The IPWRA also accounts for the missing data. We adjusted for the following covariates: maternal age, BMI at first antenatal visit, maternal region of birth, need for interpreter (proxy indicator for primary language and categorized as “yes” or “no”), parity, socioeconomic status (using quintiles of SEIFA for maternal postcode), diabetes mellitus status (non, gestational, preexisting, not tested), and smoking in pregnancy status. These covariates were chosen for their known impact on the risk of adverse pregnancy outcomes (maternal age, BMI, parity, diabetes mellitus status, smoking, maternal region of birth) or their association with access to public health information and engagement in antenatal care (socioeconomic status, need for interpreter, maternal region of birth). Adjusted analyses were performed using logistic regression, and results were presented as odds ratios (ORs).

**Sensitivity analyses**

We performed unadjusted and adjusted logistic regression analysis without IPWRA to check the consistency of the directions of associations between COVID-19 vaccination and maternal and perinatal outcomes.

We performed a sensitivity analysis for congenital anomalies by excluding women who were first vaccinated at ≥20 weeks because the biologically relevant period of exposure for teratogenesis is in early pregnancy.

To examine the impact of time-varying exposure and the “healthy vaccinee” effect on preterm birth and stillbirth, we performed a Cox regression analysis excluding women who received their first dose of a COVID-19 vaccine at ≥24 weeks’ gestation, and adjusted for pertussis vaccination status. We used Kaplan–Meier curves to plot the cumulative hazard of the outcomes of interest. The proportionality of the hazards of control and exposed cohorts was tested using Schoenfeld residuals.

**FIGURE 2**

Flowchart of study cohorts

![Flowchart of study cohorts](image-url)
Results
There were 33,018 infants born to 32,536 women during the study period. The numbers of inclusions and exclusions for the various cohorts are shown in the study flowchart in Figure 2. The weekly percentages of births to vaccinated women are shown in Figure 3. By the end of the study period, 85% of women giving birth had received at least 1 dose of the COVID-19 vaccine before or during pregnancy (Figure 3).

Sociodemographic characteristics of vaccinated vs unvaccinated groups
Of the 32,536 women giving birth during the 9-month study period, 17,365 (53.4%) had received at least 1 dose of the mRNA COVID-19 vaccine and 15,171 (46.6%) had not. The characteristics of vaccinated and unvaccinated groups are shown in Table 1. Vaccinated women were significantly older, and more often nulliparous, nonsmoking, not requiring an interpreter, of higher socioeconomic status, and vaccinated against pertussis and influenza (P<.05 for all variables). Vaccination status also varied by region of birth. Choropleth maps of postcodes showing socioeconomic status and vaccination coverage are shown in Supplemental Figure 1. Forest plots of vaccination coverage by hospitals are provided in Supplemental Figure 2.

Perinatal outcomes in the calculated last menstrual period cohort
After exclusions, 12,679 participants remained in the cLMP cohort (Figure 2). Of these, 9927 had received at least 1 dose of the COVID-19 vaccine during pregnancy, and of these, 94.1% also received a second dose. A documented gestation at first and second vaccine dose was available for 98.3% and 92.7% of the vaccinated groups, respectively. The median gestational age at the first dose was 24 weeks (interquartile range, 19–28 weeks) and 28 weeks (interquartile range, 24–32 weeks) for the second dose (Figure 5). No data on third or subsequent vaccine doses were available.

The perinatal outcomes with “all births” and “live births” denominators are presented in Tables 2 and 3, respectively.

Primary outcomes
The vaccinated group had a significantly lower rate of stillbirth compared with the unvaccinated group (0.2% vs 0.8%; adjusted OR [aOR], 0.18; 95% confidence interval [CI], 0.09–0.37; P<.001) (Table 2). When stratified by gestational age, this difference was statistically significant only for preterm stillbirths (0.1% vs 0.7%; aOR, 0.12; 95% CI, 0.05–0.31; P<.001). This finding remained robust in the sensitivity analysis (Supplemental Table).

The vaccinated group also had a significantly lower rate of preterm birth (5.1% vs 9.2%; aOR, 0.60; 95% CI, 0.51–0.71; P<.001), which was significant for both spontaneous preterm birth (2.4% vs 4.0%; aOR, 0.73; 95% CI, 0.56–0.96; P=.02) and iatrogenic preterm birth (2.7% vs 5.2%; aOR, 0.52;
### TABLE 1
Maternal characteristics by COVID-19 vaccination status among total birth cohort

| Maternal characteristics | Vaccinated N=17,365 | | Unvaccinated N=15,171 | Multiple imputed dataset |
|--------------------------|---------------------|-----|-----------------------|--------------------------|
|                          | n                   | %   | n                     | %                       | Denominator | IRR^a | Pvalue |
| Maternal age group, y    |                     |     |                       |                         |             |       |        |
| <25                      | 1477                | 8.5 | 1915                  | 12.6                    | 32,536      | 0.91  | .005   |
| 25–29                    | 3223                | 18.6| 3377                  | 22.3                    | Ref         |       |        |
| 30–34                    | 7224                | 41.6| 5823                  | 38.4                    | 1.12        | <.001 |        |
| 35–39                    | 4487                | 25.8| 3327                  | 21.9                    | 1.18        | <.001 |        |
| ≥40                      | 954                 | 5.5 | 729                   | 4.8                     | 1.19        | <.001 |        |
| Parity                   |                     |     |                       |                         |             |       |        |
| 0                        | 7783                | 44.8| 6259                  | 41.3                    | 32,535      | 1.09  | <.001 |
| ≥1                       | 9582                | 55.2| 8911                  | 58.7                    | Ref         |       |        |
| Plurality                |                     |     |                       |                         |             |       |        |
| Singleton                | 17,102              | 98.5| 14,936                | 98.5                    | 32,536      | Ref   |       |
| Multifetal pregnancy     | 263                 | 1.5 | 235                   | 1.6                     | 1.00        | .96   |        |
| BMI categories           |                     |     |                       |                         |             |       |        |
| <18                      | 193                 | 1.2 | 173                   | 1.2                     | 30,824      | 0.99  | .90    |
| 18–24                    | 7651                | 46.3| 6477                  | 45.3                    | Ref         |       |        |
| 25–29                    | 4892                | 29.6| 4322                  | 30.0                    | 1.00        | .97   |        |
| 30–34                    | 2228                | 13.5| 1950                  | 13.6                    | 1.03        | .27   |        |
| 35–39                    | 947                 | 5.7 | 860                   | 6.0                     | 1.04        | .26   |        |
| ≥40                      | 603                 | 3.7 | 528                   | 3.7                     | 1.08        | .092  |        |
| Smoking in pregnancy     |                     |     |                       |                         |             |       |        |
| Nonsmokers               | 16,883              | 97.2| 14,270                | 94.1                    | 32,536      |       |        |
| Smokers                  | 482                 | 2.8 | 901                   | 5.9                     | 0.71        | <.001 |        |
| Region of birth          |                     |     |                       |                         |             |       |        |
| Americas                 | 317                 | 1.8 | 209                   | 1.4                     | 32,352      | 1.05  | .37    |
| Australia                | 8916                | 51.7| 7898                  | 52.3                    | Ref         |       |        |
| North Africa and Middle East | 661         | 3.8 | 829                   | 5.5                     | 0.89        | .005  |        |
| Northeast Asia           | 600                 | 3.5 | 447                   | 3.0                     | 1.01        | .76   |        |
| Northwest Europe         | 616                 | 3.6 | 373                   | 2.5                     | 1.09        | .050  |        |
| Oceania                  | 527                 | 1.6 | 633                   | 4.2                     | 0.90        | .018  |        |
| Southeast Asia           | 1525                | 8.8 | 1042                  | 6.9                     | 1.12        | <.001 |        |
| Southern and Central Asia | 3426         | 19.9| 2758                  | 18.3                    | 1.03        | .17   |        |
| Southern and Eastern Europe | 249       | 1.4 | 390                   | 2.6                     | 0.71        | <.001 |        |
| Sub-Saharan Africa       | 426                 | 2.5 | 510                   | 3.4                     | 0.89        | .022  |        |
| Interpreter required     |                     |     |                       |                         |             |       |        |
| Not required             | 16,645              | 95.9| 14,413                | 95.0                    | 32,536      |       |        |
| Required                 | 720                 | 4.2 | 758                   | 5.0                     | 0.96        | .27   |        |

SEIFA quintile

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023. (continued)
95% CI, 0.41–0.65; \( P < .001 \). These findings remained robust in the sensitivity analysis (Supplemental Table). The hazard ratio plots for preterm birth and stillbirth that excluded women vaccinated at \( \geq 24 \) weeks, adjusted for pertussis vaccination status, are shown in Figure 6.

### Secondary outcomes

The rate of major congenital anomalies was significantly lower in the vaccinated group than in the unvaccinated group (2.4% vs 3.0%; aOR, 0.80; 95% CI, 0.57–1.13; \( P = .21 \)) (Supplemental Table).

There was also a significant reduction in admissions to the NICU in the vaccinated group (2.4% vs 4.1%; aOR, 0.70; 95% CI, 0.53–0.91; \( P = .007 \)). This trend toward lower NICU admissions was observed in the sensitivity analysis, but with a \( P \) value \( > .05 \).

There was no difference in the rate of severe FGR between the vaccinated and unvaccinated groups. The vaccinated group had a significantly higher rate of induction of labor and iatrogenic births for fetal compromise at term gestation, but significantly lower rate of iatrogenic birth for fetal compromise at preterm gestations and lower rate of prelabor cesarean deliveries (Table 3). There was no significant difference in other birth outcomes such as postpartum hemorrhage, vaginal births, or births before arrival to hospital.

### Subgroup analysis of stillbirth and preterm birth by COVID-19 infection during pregnancy and vaccination status

There were 1078 women with a COVID-19 infection during pregnancy in the total study cohort; of these, 518 women

---

**TABLE 1**

Maternal characteristics by COVID-19 vaccination status among total birth cohort (continued)

| Maternal characteristics | Vaccinated N=17,365 | Unvaccinated N=15,171 | Multiple imputed dataset
|--------------------------|---------------------|------------------------|--------------------------|
|                          | n | % | n | % | Denominator | IRR \( ^{a} \) | \( P \) value |
| 1 (most disadvantaged)   | 3288 | 19.1 | 3551 | 23.7 | 32,181 | 0.94 | .005 |
| 2                        | 2466 | 14.4 | 2223 | 14.8 | Ref | 1.00 | .96 |
| 3                        | 4283 | 24.9 | 3899 | 26.0 | Ref | 1.05 | .039 |
| 4                        | 3980 | 23.2 | 3124 | 20.8 | Ref | 1.07 | .007 |
| 5 (most advantaged)      | 3159 | 18.4 | 2208 | 14.7 | Ref | 0.93 | .19 |

**Remote of residence**

|                          | n | % | n | % | Denominator |
|--------------------------|---|---|---|---|-------------|
| Regional                 | 304 | 1.8 | 358 | 2.4 | 32,536 |
| Metropolitan location    | 17,061 | 98.3 | 14,813 | 97.6 | 0.93 | .19 |

**Gestation at first antenatal visit**

|                          | n | % | n | % | Denominator |
|--------------------------|---|---|---|---|-------------|
| \( \leq 12 \) wk         | 12,252 | 70.6 | 10,656 | 70.2 | 32,536 |
| \( > 12 \) wk            | 5113 | 29.4 | 4515 | 29.8 | 0.99 | .58 |

**Antenatal influenza vaccine**

|                          | n | % | n | % | Denominator |
|--------------------------|---|---|---|---|-------------|
| Nonvaccinated            | 3815 | 22.2 | 4899 | 32.9 | 32,081 |
| Vaccinated               | 13,362 | 77.8 | 10,005 | 67.1 | 1.24 | <.001 |

**Antenatal pertussis vaccine**

|                          | n | % | n | % | Denominator |
|--------------------------|---|---|---|---|-------------|
| Nonvaccinated            | 1415 | 8.2 | 3114 | 20.8 | 32,280 |
| Vaccinated               | 15,860 | 91.8 | 11,891 | 79.3 | 1.74 | <.001 |

**Diabetes mellitus**

|                          | n | % | n | % | Denominator |
|--------------------------|---|---|---|---|-------------|
| None                     | 13,012 | 75.0 | 11,555 | 76.2 | 32,527 |
| Gestational diabetes mellitus | 4088 | 23.6 | 3299 | 21.8 | 1.03 | .10 |
| Preexisting diabetes mellitus | 197 | 1.1 | 143 | 0.9 | 1.10 | .17 |
| Not tested for gestational diabetes mellitus | 64 | 0.4 | 169 | 1.1 | 0.61 | <.001 |

BMI, body mass index; IRR, incidence rate ratio; SEIFA, Socio-Economic Indexes for Areas.

\( ^{a} \) IRR adjusted for maternal age, maternal smoking status, need for interpreter, socioeconomic index for areas, country of birth, parity and diabetes mellitus status.

*Hui. Reduction in stillbirth and preterm birth in COVID-19–vaccinated women. Am J Obstet Gynecol 2023.*
were in the cLMP cohort (Table 4). The crude OR of COVID-19 infection was significantly lower in the vaccinated group (3.6% vs 5.9%; OR, 0.59; 95% CI, 0.49–0.71; P < .0001). There was also a significant reduction in preterm birth among COVID-19–infected women who had been vaccinated during pregnancy (2.3% vs 7.0%; OR, 0.32; 95% CI, 0.12–0.80; P = .015) (Table 4). The number of infected cases was too low to allow adjustment for covariates.

Comment
Principal findings
Our multicenter cohort study confirms the safety and benefits of COVID-19 vaccination in pregnancy and adds new insights into the relationship between vaccination and preterm birth. Vaccinated women had significantly lower rates of stillbirth and preterm birth compared with unvaccinated women and did not have higher rates of congenital anomalies or FGR. Of note, our study shows that COVID-19 vaccination during pregnancy is associated with significantly lower rates of both spontaneous and iatrogenic preterm birth, even after excluding women vaccinated at ≥ 24 weeks’ gestation.

Results in the context of what is known
Our finding on congenital anomalies provides additional reassuring safety data on COVID-19 vaccination in pregnancy. We have strengthened the existing evidence base by showing that there was no increase in the rate of congenital anomalies for women vaccinated before 20 weeks’ gestation, when the risk of teratogenesis would be expected to be higher.

The significantly lower rate of stillbirths is in accordance with previously published studies, but our results are remarkable for the magnitude of the difference. Our aOR of 0.18 is much lower than that of any of the 7 individual studies included in the recent meta-analysis, which reported ORs of 0.50 to 1.50.12 This difference was even more profound in the preterm stillbirths, in which vaccination was associated with a 1-in-1000 risk of preterm stillbirth as opposed to 7-in-1000 without vaccination.

It makes biological sense that vaccination reduces stillbirth given the strong association between severe COVID-19 infection and increased risk of stillbirth.1 However, because of the observational study design, we can only infer a causal relationship between vaccination and fewer stillbirths, presumably mediated by the significant reduction in the odds of COVID-19 infection. However, the burden of COVID-19 infection in the unvaccinated cohort did not seem high enough to account for the entire effect of vaccination on stillbirths. Although we controlled for multiple covariates, and performed a sensitivity analysis on pertussis vaccination status, we speculate that other relevant unmeasured factors associated with COVID-19 vaccination persist, such as health literacy or health care-seeking behavior (the “healthy vaccinee” bias).18 The significantly higher rates of term induction of labor and better adherence to universal gestational diabetes mellitus screening in the vaccinated group suggest important variations in obstetrical care that may have contributed to the difference in perinatal outcomes.

Our study provides strong evidence to support the association between COVID-19 vaccination and reduction in iatrogenic and spontaneous preterm births. The reduction in iatrogenic preterm birth may be because of prevention of complications directly related to COVID-19 infection such as pre-eclampsia or severe maternal respiratory morbidity, whereas the reduction in spontaneous preterm birth may be because of prevention of complications directly related to COVID-19 infection or other nonspecific immune effects. Furthermore, unmeasured confounders may also be responsible for the reduction in preterm births, as discussed above for stillbirths.

The sociodemographic characteristics of our unvaccinated cohort mirror the findings from the United Kingdom.
showing variation in vaccination uptake by socioeconomic status, age, and region of birth. In multicultural Melbourne, public health messaging to non-English speaking communities had notable flaws, including incorrect and out-of-date translations of vaccine communications. This may have contributed to a lack of access to accurate vaccine safety information and a lack of trust in the health authorities among certain ethnic groups.

Clinical implications
Our data give us strong evidence to confidently endorse the safety of the mRNA vaccine for our local pregnant population and to promote the benefits of reduced stillbirth and preterm birth.

TABLE 2
Primary and secondary outcomes among all births (live births and stillbirths)

| Primary and secondary outcomes | Vaccinated | Unvaccinated | Unadjusted odds ratio (IPWRA) | Adjusted odds ratio* (IPWRA) |
|--------------------------------|------------|--------------|-------------------------------|-----------------------------|
|                                | n (%)      | n (%)        | OR L U                        | aOR L U                     |
| Singleton cLMP cohort >20 wk   | N=9927     | N=2752       |                               |                             |
| Congenital anomalies           | 236 2.4    | 83 3.0       | 0.79 0.62 1.01 .06            | 0.72 0.56 0.94 .02          |
| Singleton cLMP cohort excluding congenital anomalies, TOP, and births <24 wk | N=9682     | N=2607       |                               |                             |
| Stillbirths                     |            |              |                               |                             |
| Stillbirths >37 wk              | 6 0.1      | 3 0.1        | 0.54 0.13 2.15 .38            | 0.38 0.09 1.55 .18          |
| Stillbirths <37 wk              | 9 0.1      | 18 0.7       | 0.13 0.06 0.30 .00            | 0.12 0.05 0.31 .00          |
| Preterm birth <37 wk            |            |              |                               |                             |
| Total                           | 495 5.1    | 239 9.2      | 0.56 0.48 0.65 .00            | 0.60 0.51 0.71 <.001        |
| Spontaneous                     | 234 2.4    | 104 4.0      | 0.61 0.48 0.76 .00            | 0.73 0.56 0.96 .02          |
| Iatrogenic                      | 261 2.7    | 135 5.2      | 0.52 0.42 0.64 .00            | 0.52 0.41 0.65 <.001        |
| Newborn outcomes                |            |              |                               |                             |
| Fetal growth restriction        | 237 2.5    | 63 2.4       | 1.01 0.77 1.33 .93            | 1.07 0.79 1.44 .68          |
| SCN admission                   | 907 9.4    | 281 10.8     | 0.87 0.77 0.99 .03            | 0.92 0.80 1.06 .27          |
| NICU admission                  | 236 2.4    | 106 4.1      | 0.60 0.48 0.75 .00            | 0.70 0.53 0.91 .01          |
| 5-min Apgar score <7            | 170 1.8    | 80 3.1       | 0.57 0.44 0.74 .00            | 0.72 0.51 1.01 .06          |
| Intrapartum outcomes            |            |              |                               |                             |
| Induction of labor              | 3589 37.1  | 835 32       | 1.16 1.09 1.23 .00            | 1.11 1.04 1.18 .001         |
| Unassisted vaginal births       | 4738 48.9  | 1378 52.9    | 0.93 0.89 0.97 .00            | 0.98 0.94 1.02 .38          |
| Instrumental vaginal births     | 1533 15.8  | 338 13.0     | 1.22 1.09 1.36 .00            | 1.08 0.96 1.21 .22          |
| Cesarean delivery —no onset of labor | 1829 18.9 | 529 20.3     | 0.93 0.85 1.02 .11            | 0.90 0.81 0.99 .04          |
| Cesarean delivery —after onset of labor | 1583 16.4 | 360 13.8     | 1.18 1.06 1.32 .00            | 1.07 1.07 1.21 .27          |
| Born before arrival             | 62 0.6     | 27 1.0       | 0.62 0.39 0.97 .04            | 0.81 0.50 1.31 .39          |
| Severe PPH ≥1000 mL             | 806 8.3    | 205 7.9      | 1.06 0.91 1.23 .45            | 0.97 0.83 1.13 .72          |

aOR, adjusted odds ratio; cLMP, calculated last menstrual period; IPWRA, inverse-probability-weighted regression adjustment; L, lower limit of 95% confidence interval; NICU, neonatal intensive care unit; OR, odds ratio; PPH, postpartum hemorrhage; SCN, special care nursery; TOP, termination of pregnancy; U, upper limit of 95% confidence interval.

*Adjusted for maternal age, metropolitan vs regional residence, smoking status, need for interpreter, body mass index, region of birth, socioeconomic index for postcodes, diabetes mellitus, parity, infant sex, and gestation at first antenatal visit.

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023.
the socioeconomic and cultural diversity of our population. A sensitive, multifaceted approach in partnership with community leaders is required to improve public health communication and remove barriers to vaccination uptake.22

**Research implications**

The significant reduction in stillbirth and preterm birth raises research questions that may lead to improved care outside the pandemic. Biological and social factors responsible for the reduction in spontaneous preterm birth should be investigated, including nonspecific inflammatory-mediated mechanisms for preterm birth and the mitigating effects of vaccination for COVID-19 and other diseases. It is also likely that vaccination status is a proxy for unmeasured social determinants of health, in addition to the well-established demographic factors included in our analysis. This “healthy vaccinee bias” may reflect the quality of the relationship between a pregnant woman and her healthcare provider because personal recommendation by a healthcare practitioner remains one of the most important influences on vaccine uptake.11 It is also correlated with trust in the government.23 Understanding these confounders and developing new metrics to capture them would aid future studies of vaccination in pregnancy and perinatal outcomes.

**Strengths and limitations**

Our large multicenter cohort of all public hospitals captured 80% of total births in Melbourne, including all hospitals that were designated by the government to care for pregnant inpatients with COVID-19. The major strengths of our cohort are its size, timeliness of data collection, avoidance of common methodological biases, and detailed

| TABLE 3 |
| Perinatal outcomes among live births |
|-------------------------------------|
| Singleton cLMP cohort excluding congenital anomalies, TOP, births <24 wk, and stillbirths | Vaccinated N=9667 | Unvaccinated N=2586 | Unadjusted odds ratio (IPWRA) | Adjusted odds ratioa (IPWRA) |
| Preterm birth <37 wk | n (%) | n (%) | OR L U | Pvalue | aOR L U | Pvalue |
| Total | 486 5.0 | 221 8.6 | 0.59 0.50 0.69 | <.001 | 0.64 0.54 0.76 | <.001 |
| Spontaneous | 230 2.4 | 102 3.9 | 0.60 0.48 0.76 | <.001 | 0.72 0.55 0.94 | .017 |
| Iatrogenic | 256 2.7 | 119 4.6 | 0.58 0.47 0.71 | <.001 | 0.58 0.46 0.74 | <.001 |
| Newborn outcomes | | | | | |
| Fetal growth restriction | 236 2.4 | 62 2.4 | 1.02 0.77 1.34 | .899 | 1.08 0.79 1.46 | .63 |
| SCN admission | 907 9.4 | 281 10.9 | 0.86 0.76 0.98 | .023 | 1.08 0.80 1.06 | .27 |
| NICU admission | 236 2.4 | 106 4.1 | 0.60 0.48 0.75 | <.001 | 0.69 0.53 0.91 | .01 |
| 5-min Apgar score <7 | 155 1.6 | 60 2.3 | 0.69 0.51 0.93 | 0.013 | 1.39 0.51 1.01 | .06 |
| Intrapartum outcomes | | | | | |
| Induction of labor | 3584 37.1 | 820 31.7 | 1.17 1.10 1.24 | <.001 | 1.12 1.05 1.19 | .001 |
| Cesarean delivery—no onset of labor | 1826 18.9 | 526 20.3 | 0.93 0.85 1.01 | .094 | 0.90 0.81 0.99 | .04 |
| Unassisted vaginal births | 4728 48.9 | 1360 52.6 | 0.93 0.89 0.97 | .001 | 0.99 1.06 1.03 | .50 |
| Instrumental vaginal births | 1531 15.8 | 338 13.1 | 1.21 1.09 1.35 | .001 | 1.07 0.95 1.20 | .27 |
| Cesarean delivery—after onset of labor | 1583 16.4 | 360 13.9 | 1.18 1.06 1.31 | .003 | 0.30 0.94 1.20 | .30 |
| Born before arrival | 61 0.6 | 26 1.0 | 0.63 0.40 0.99 | .046 | 0.83 0.51 1.35 | .45 |
| Severe PPH ≥1000 mL | 805 8.3 | 205 7.9 | 1.05 0.91 1.22 | .512 | 0.96 0.83 1.13 | .64 |
| Iatrogenic births for fetal compromise | | | | | |
| Iatrogenic birth for fetal compromise | 1853 19.1 | 451 17.4 | 0.46 0.34 0.64 | .00 | 0.49 0.34 0.70 | <.001 |
| Iatrogenic birth for fetal compromise >37 wk | 1751 18.1 | 392 15.1 | 1.19 1.08 1.32 | .00 | 1.11 1.00 1.24 | .040 |
| Iatrogenic birth for fetal compromise <37 wk | 102 1.1 | 59 2.2 | 0.46 0.34 0.64 | .00 | 0.49 0.34 0.70 | <.001 |

aOR, adjusted odds ratio; cLMP, calculated last menstrual period; IPWRA, inverse-probability-weighted regression adjustment; L, lower limit of 95% confidence interval; NICU, neonatal intensive care unit; OR, odds ratio; PPH, postpartum hemorrhage; SCN, special care nursery; TOP, termination of pregnancy; U, upper limit of 95% confidence interval.

a Adjusted for maternal age, metropolitan vs regional residence, smoking status, need for interpreter, body mass index, region of birth, socioeconomic index for postcodes, diabetes mellitus, parity, infant sex, and gestation at first antenatal visit.

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023.
individual patient-level data including gestation at first vaccine dose.

This was a retrospective study using routinely collected maternity data. Only data on first and second doses of the COVID-19 vaccine were collected by hospitals during the study period, thus the uptake of the third dose by pregnant women is unknown. The 1078 women with COVID-19 infection in the total cohort should be considered a minimum estimate of our total COVID-19 caseload. We do not have individual medical record data to determine whether the stillbirths and preterm births in the unvaccinated cohort were the direct result of acute COVID-19 disease. We await the outcomes from the CHO-PAN (Coronavirus Health Outcomes in Pregnancy and Newborns) registry for detailed local information on pregnancy outcomes for women with COVID-19.24

Our maternity data collection only includes birth outcomes from 20 weeks’ gestation. We therefore cannot comment on risk of miscarriage after COVID-19 vaccination, although other large studies have already provided reassuring data on this.25,26 We acknowledge that our findings on the risk of congenital anomalies are limited by the lack of data on early pregnancy. The lower rate of congenital anomalies observed in the vaccinated group may be a result of

TABLE 4
Selected outcomes among women with documented COVID-19 infection by vaccination status

| Outcomes                                                                 | Vaccinated | Unvaccinated | Unadjusted odds |
|--------------------------------------------------------------------------|------------|--------------|----------------|
|                                                                          | N=9927     | N=2752       |                |
|                                                                          | count (%)  | count (%)    | OR L U Pvalue  |
| Singleton cLMP cohort with COVID-19 infection                           | N=355      | N=163        |                |
| Congenital anomalies                                                    | 9 2.5      | 4 2.5        | 1.0 0.3 3.4 .96|
| Singleton cLMP cohort excluding congenital anomalies, TOP, and births <24 wk with COVID-19 infection | N=346      | N=158        |                |
| Stillbirths                                                              | 1 0.3      | 2 1.3        | 0.2 0.0 2.5 .23|
| Total preterm birth <37 wk                                              | 8 2.3      | 11 7.0       | 0.3 0.1 0.8 .02|
| Spontaneous preterm birth                                               | 1 0.3      | 4 2.5        | 0.1 0.0 1.0 .05|
| Iatrogenic preterm birth                                                | 7 2.0      | 7 4.4        | 0.5 0.2 1.3 .14|

cLMP, calculated last menstrual period; L, lower limit of 95% confidence interval; OR, odds ratio; TOP, termination of pregnancy; U, upper limit of 95% confidence interval.

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023.
differences in use of aneuploidy screening, ultrasound scans, and termination of pregnancy for fetal abnormality before 20 weeks. There may have also been a true reduction in the prevalence of congenital anomalies in the vaccinated group because of differences in periconceptional health behaviors, such as the use of folic acid supplementation, preconception optimization of medical conditions, avoidance of teratogens, and dietary quality.\textsuperscript{27}

**Conclusions**

COVID-19 vaccination during pregnancy is strongly associated with lower risks of stillbirth and preterm birth, without any adverse impact on fetal growth or development. Vaccine coverage was not distributed equally in our population and was influenced by known social determinants of health. Our findings highlight both the achievements of our vaccination program and the challenges for maternity care in ensuring equity of health outcomes across our population.

**Acknowledgments**

The health services and individual hospitals contributing to the Collaborative Maternity and Newborn Dashboard for the COVID-19 pandemic are:

- Mercy Health (Mercy Hospital for Women, Werribee Mercy Hospital)
- The Royal Women’s Hospital, The Women’s at Sandringham
- Monash Health (Monash Medical Centre, Casey Hospital, Dandenong Hospital)
- Northern Health (The Northern Hospital)
- Western Health (Joan Kirner Women’s and Children’s Hospital)
- Eastern Health (Box Hill Hospital, The Angliss Hospital)
- Peninsula Health (Frankston Hospital)

We thank the health service data managers and research midwives (Tania Fletcher, RN/RM, Lynn Rigg, MPH, Eleanor Johnson, MPH, Julie Lay, BSc(Hons) BPharm(Hons), Abby Monaghan, RN/RM, Therese McCarthy, BN/BMid, Pauline Hamilton, Roshanee Rebera, BNGiRegMid MHiM) for their assistance with primary data collection and Andrew Goldsack, MD for assistance with coding of the indications for iatrogenic births.

**References**

1. Villar J, Arifi S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. JAMA Pediatr 2021;175:817–26.

2. Polack FP, Thomas SJ, Kitchin N, et al. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. N Engl J Med 2020;383:2603–15.

3. Australian Department of Health. COVID-19 vaccine rollout update. 2021. Available at: https://www.health.gov.au/sites/default/files/documents/2021/04/covid-19-vaccine-rollout-update-30-april-2021.pdf. Accessed May 21, 2022.

4. World Health Organization. COVID-19 vaccination dashboard. May 22. Available at: https://app.powerbi.com/view?r=eyJrIjoiMWNjNzZkNjctZTNIny00YmMxLThxQzQ1NjZjM2MTYxO NzeWlwiC1l6ImY2MTBjMGJ3LWJkBMIjltNhS04MTBIrNTkYi4MGFmYiU5MC5CismMIoNjB9. Accessed May 21, 2022.

5. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary findings of mRNA Covid-19 vaccine safety in pregnant persons. N Engl J Med 2021;384:2273–82.

6. de Freitas Paganoti AC, Alkmin da Costa R, Papageorghiou AT, et al. COVID-19 vaccines confer protection in hospitalized pregnant and postpartum women with severe COVID-19: a retrospective cohort study. Vaccines 2022;10:749.

7. Gray KJ, Bordt EA, Atyeo C, et al. Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study. Am J Obstet Gynecol 2021;225:303.e1–17.

8. Kalafat E, Heath P, Prasad S, O Brien P, Khall A. COVID-19 vaccination in pregnancy. Am J Obstet Gynecol 2022;227:136–47.

9. UKOSS NPEU surveillance reports. COVID-19 vaccination in pregnancy, 2021. Available at: https://www.npeu.ox.ac.uk/ukooss/completed-surveillance/covid-19-vaccination-in-pregnancy. Accessed May 21, 2022.

10. Australian Government Department of Health and Aged Care. Joint statement between RANZCOG and ATAGI about COVID-19 vaccination for pregnant women. June 9 2021. 2021. Available at: https://www.health.gov.au/news/joint-statement-between-ranzcog-and-atagi-about-covid-19-vaccination-for-pregnant-women. Accessed May 21, 2022.

11. Providing care for iatrogenic births. Aust N Z Obstet Gynaecol 2022;62:695–700.

12. Prasad S, Kalafat E, Blakeway H, et al. Systematic review and meta-analysis of the effectiveness and perinatal outcomes of COVID-19 vaccination in pregnancy. Nat Commun 2022;13:2414.

13. Barnett AG. Time-dependent exposures and the fixed-cohort bias. Environ Health Perspect 2011;119:A422–3.

14. Strand LB, Barnett AG, Tong S. Methodological challenges when estimating the effects of season and seasonal exposures on birth outcomes. BMC Med Res Methodol 2011;11:49.

15. Hué L, Marzan MB, Potenza S, et al. Collaborative maternity and newborn dashboard (CoMaND) for the COVID-19 pandemic: a protocol for timely, adaptive monitoring of perinatal outcomes in Melbourne, Australia. BMJ Open 2021;11:e055902.

16. Dobbins TA, Sullivan EA, Roberts CL, Simpson JM. Australian national birthweight percentiles by sex and gestational age, 1998–2007. Med J Aust 2012;197:291–4.

17. Australian Institute of Health and Welfare. Metadata online registry (METeOR). 2017. Available at: https://meteor.aihw.gov.au/content/index.html?item=587046. Accessed August 5, 2021.

18. Ramschmidt C, Wichmann O, Harder T. Frequency and impact of confounding by indication and healthy vaccinee bias in observational studies assessing influenza vaccine effectiveness: a systematic review. BMC Infect Dis 2015;15:429.

19. UK Health Security Agency. COVID-19 vaccine surveillance report week 19, 2022. Available at: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1075155/COVID-19_vaccine_surveillance_report_12_May_2022_week_19.pdf. Accessed May 22, 2022.

20. ABC News. Australia’s official COVID-19 health information translations left to become eight weeks out of date. 2021. Available at: https://www.abc.net.au/news/2021-08-12/covid-19-information-weeks-out-of-date/100369794?utm_campaign=abc_news_web&utm_content=link&utm_medium=content_shared&utm_source=abc_news_web. Accessed May 21, 2022.

21. Centers for Disease Control and Prevention. COVID data tracker. 2022. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccinations-pregnant-women. Accessed May 22, 2022.

22. Moderator, Hui L, Experts, et al. Pregnancy in the time of COVID-19: what are the challenges for maternity care? Clin Chem 2022;68:385–91.

23. Trent M, Seale H, Chughtai AA, Salmon D, Macintyre CR. Trust in government, intention to vaccinate and COVID-19 vaccine hesitancy: a comparative survey of five large cities in the United States, United Kingdom, and Australia. Vaccine 2022;40:2498–505.

24. Coronavirus Health Outcomes in Pregnancy and Newborns (CHOPAN) registry. Australian and New Zealand Clinical Trials Registry. 2022. Available at: https://chopan.psanz.com.au/chopanv. Accessed May 22, 2022.

25. Magnus MC, Gjesing HK, Eide HN, Wilcox AJ, Fell DB, Häberg SE. Covid-19
vaccination during pregnancy and first-trimester miscarriage. N Engl J Med 2021;385:2008–10.

26. Zauche LH, Wallace B, Smoots AN, et al. Receipt of mRNA Covid-19 vaccines and risk of spontaneous abortion. N Engl J Med 2021;385:1533–5.

27. Yee LM, Silver RM, Haas DM, et al. Quality of periconceptional dietary intake and maternal and neonatal outcomes. Am J Obstet Gynecol 2020;223:121.e1–8.

Author and article information

From the Department of Obstetrics and Gynaecology, Melbourne Medical School, The University of Melbourne, Melbourne, Australia (Dr Hui, Mr Barrientos Marzan, and Drs Pritchard, Said, Whitehead, and Walker); Reproductive Epidemiology Group, Murdoch Children’s Research Institute, Melbourne, Australia (Dr Hui and Mr Marzan); Department of Obstetrics and Gynaecology, Mercy Hospital for Women, Mercy Health, Melbourne, Australia (Drs Hui, Potenza, Pritchard, and Walker); Department of Obstetrics and Gynaecology, The Northern Hospital, Northern Health, Melbourne, Australia (Dr Hui); Center for Alcohol Policy Research, La Trobe University, Melbourne, Australia (Mr Marzan); Department of Obstetrics and Gynaecology, Monash Health, Melbourne, Australia (Drs Rolnik, Palmer, and Mol); Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia (Drs Rolnik, Palmer, Sheehan, and Mol); Department of Maternal-Fetal Medicine, Joan Kirner Women’s and Children’s Hospital, Western Health, Melbourne, Australia (Dr Said); Department of Obstetrics and Gynaecology, Royal Women’s Hospital, Melbourne, Australia (Dr Whitehead); Department of Obstetrics and Gynaecology, Box Hill Hospital, Eastern Health, Melbourne, Australia (Dr Sheehan); Department of Obstetrics and Gynaecology, Frankston Hospital, Peninsula Health, Melbourne, Australia (Dr Ford); and Harvard T.H. School of Public Health, Harvard University, Cambridge, MA (Dr Rolnik).

Received June 30, 2022; revised Oct. 25, 2022; accepted Oct. 30, 2022.

L.H. has received research funding from Ferring Pharmaceuticals outside the scope of this work. B.W.M. is a consultant for Guerbet and has received research grants from Guerbet and Merck & Co; K.R.P. has received consultancy fees from Janssen Pharmaceuticals. D.L.R. has received fees from Alexion Pharmaceuticals for participation in advisory boards unrelated to this work. The remaining authors declare no conflict of interest.

This study was funded by the Norman Beischer Medical Research Foundation and the University of Melbourne Department of Obstetrics and Gynaecology. L.H., B.W.M., and K.R.P. are supported by National Health and Medical Research Council’s investigator grants (GNT1196010, GNT11766437, and GNT2009765). The funding bodies had no role in any aspects of the design or conduct of this study.

The findings of this study were presented as a poster communication at the annual scientific meeting of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists, Gold Coast, Australia, October 8–12, 2022.

Data sharing: Nonidentifiable individual participant data are available on request to the Austin Health Human Research Ethics Committee (ethics@austin.org.au) and the Mercy Health Human Research Ethics Committee (ethics@mercy.com.au). The study investigators may contribute aggregate and nonidentifiable individual patient data to national and international researchers whose proposed use of the data has been ethically reviewed and approved by an independent committee and following signing of an appropriate research collaboration agreement with The University of Melbourne.

Corresponding author: Lisa Hui, MBBS, PhD. lisa.hui@unimelb.edu.au
The participating hospitals are indicated by the lettered circles, with their corresponding vaccination rates displayed in Supplemental Figure 2. SEIFA, Socio-Economic Indexes for Areas.

Hui. Reduction in stillbirth and preterm birth in COVID-19–vaccinated women. Am J Obstet Gynecol 2023.
The hospital-level data are grouped here by maternity service level. Level 6 maternity services provide regional/statewide specialized care for high-risk pregnancies, including extremely preterm births and local care for all women and infants; Level 5 services care for normal- to moderate-risk pregnancies, and manage labor and birth from 31 weeks’ gestation; Level 4 services provide local care for women and infants at normal and moderate risk, including planned births from 34 weeks’ gestation. The geographic location of each hospital is indicated in Supplemental Figure S1.

CI, confidence interval.

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023.
### SUPPLEMENTAL TABLE

**Sensitivity analysis for congenital anomalies, stillbirths, preterm births, and nursery admissions among all births**

| Outcomes                                                                 | Vaccinated | Unvaccinated | Unadjusted odds ratio (IPWRA) | Adjusted odds ratioa (IPWRA) |
|--------------------------------------------------------------------------|------------|--------------|------------------------------|-----------------------------|
|                                                                          |            |              | OR L U                        | aOR L U                      |
|                                                                          |            |              | Pvalue                        | Pvalue                      |
| Singleton cLMP cohort vaccinated <20 wk N=2442                             | 2442       | 2668         | n %                           | n %                         |
| Congenital anomalies                                                     | 66         | 83           | 0.87 0.63 1.20 .400           | 0.80 0.57 1.13 .21           |
| Singleton cLMP cohort vaccinated <24 wk excluding congenital anomalies, terminations of pregnancy, and births <24 wk N=2442 | 4665       | n%           | n%                            |                             |
| Stillbirths                                                               |            |              |                              |                             |
| Stillbirths                                                               | 6          | 0.1          | 21 0.8                        | 0.16 0.06 0.39 <.001         |
| Stillbirths >37 wk                                                       | 2          | 0.0          | 3 0.1                        | 0.37 0.06 2.23 .28           |
| Stillbirths <37 wk                                                       | 4          | 0.1          | 18 0.7                        | 0.12 0.04 0.37 <.001         |
| Preterm birth <37 wk                                                     |            |              |                              |                             |
| Total                                                                   | 231        | 239          | 9.2                          | 0.54 0.45 0.64 <.001         |
| Spontaneous                                                             | 114        | 104          | 4.0                          | 0.61 0.47 0.80 <.001         |
| Iatrogenic                                                              | 117        | 135          | 5.2                          | 0.73 0.54 0.99 .046          |
| Newborn outcomes                                                        |            |              |                              |                             |
| SCN admission                                                            | 422        | 281          | 10.9                         | 0.84 0.73 0.97 .016          |
| NICU admission                                                           | 134        | 106          | 4.1                          | 0.71 0.55 0.91 .006          |

aOR, adjusted odds ratio; cLMP, calculated last menstrual period; IPWRA, inverse-probability-weighted regression adjustment; L, lower limit of 95% confidence interval; NICU, neonatal intensive care unit; OR, odds ratio; PPH, postpartum hemorrhage. SCN, special care nursery; TOP, termination of pregnancy; U, upper limit of 95% confidence interval.

---

Adjusted for maternal age, metropolitan vs regional residence, smoking status, need for interpreter, body mass index, region of birth, socioeconomic index for postcodes, diabetes mellitus, parity, infant sex, and gestation at first antenatal visit.

Hui. Reduction in stillbirth and preterm birth in COVID-19—vaccinated women. Am J Obstet Gynecol 2023.