RESEARCH LETTER

## Spontaneous Abortion Following COVID-19 Vaccination During Pregnancy

COVID-19 infection during pregnancy can be associated with severe maternal morbidity.[1] In the United States, 1 COVID-19 vaccine has been approved and 2 have been authorized for use for pregnant women. To date, data on maternal COVID-19 vaccine safety come primarily from passive surveillance, and studies lack an unvaccinated comparison group.[2,3] Spontaneous abortion has been identified as a priority outcome in studies of maternal vaccine safety,[4] and concerns regarding risks of spontaneous abortion may be a barrier to vaccination during pregnancy. We present findings from case-control surveillance of COVID-19 vaccination during pregnancy and spontaneous abortion.

Supplemental content

**Methods** | The Vaccine Safety Datalink is a collaboration between the Centers for Disease Control and Prevention and 9 health systems, representing approximately 3% of the US population.[5] We applied a validated pregnancy algorithm, which incorporates diagnostic and procedure codes and electronic health record (EHR) data, to identify and assign gestational ages for spontaneous abortions and ongoing pregnancies.[6] Data from 8 health systems (Kaiser Permanente: Washington, Northwest, Northern California, Southern California, and Colorado; Denver Health; HealthPartners; and Marshfield Clinic, Wisconsin) over seven 4-week surveillance periods from December 15, 2020, through June 28, 2021, were included. Ongoing pregnancies between 6 and 19 weeks' gestation were identified on the last day of each 4-week surveillance period (index date) and contributed data to 1 or more surveillance periods. Spontaneous abortions were assigned to a 4-week surveillance period based on

Table 1. Receipt of COVID-19 Vaccine in Prior 28-Day Window, by Baseline Characteristics and Surveillance Period, December 15, 2020, Through June 28, 2021

| | Spontaneous abortions | | Ongoing pregnancy-periods[a] | |
|---|---|---|---|---|
| | No. | COVID-19 vaccine, No. (%) | No. | COVID-19 vaccine, No. (%) |
| All | 250 944 | 20 139 (8.0) | 13 160 | 1128 (8.6) |
| Maternal age group, y | | | | |
| 16-24 | 37 210 | 1325 (3.6) | 1433 | 69 (4.8) |
| 25-34 | 156 166 | 12 451 (8.0) | 6640 | 493 (7.4) |
| 35-49 | 57 568 | 6363 (11.1) | 5087 | 566 (11.1) |
| Race and ethnicity[b] | | | | |
| Asian | 35 938 | 4433 (12.3) | 2028 | 262 (12.9) |
| Black, non-Hispanic | 18 790 | 715 (3.8) | 1079 | 48 (4.4) |
| Hispanic | 86 108 | 5207 (6.0) | 4346 | 322 (7.4) |
| White, non-Hispanic | 81 834 | 7571 (9.3) | 4272 | 373 (8.7) |
| Unknown/other | 28 274 | 2213 (7.8) | 1435 | 123 (8.6) |
| Gestational age group, wk | | | | |
| 6-8 | 57 355 | 5196 (9.1) | 5238 | 482 (9.2) |
| 9-13 | 88 982 | 6067 (6.8) | 6652 | 528 (7.9) |
| 14-19 | 104 607 | 8876 (8.5) | 1270 | 118 (9.3) |
| Antenatal visits | | | | |
| ≥1 | 89 913 | 6850 (7.6) | 3203 | 244 (7.6) |
| ≥2 | 161 031 | 13 289 (8.3) | 9957 | 884 (8.9) |
| Surveillance periods | | | | |
| December 15, 2020-January 11, 2021 | 36 964 | 711 (1.9) | 1767 | 21 (1.2) |
| 2021 | | | | |
| January 12-February 8 | 36 981 | 1696 (4.6) | 2097 | 68 (3.2) |
| February 9-March 8 | 37 030 | 2322 (6.3) | 1871 | 97 (5.2) |
| March 9-April 5 | 37 144 | 4934 (13.3) | 1903 | 204 (10.7) |
| April 6-May 3 | 36 191 | 5654 (15.6) | 1864 | 330 (17.7) |
| May 4-May 31 | 34 545 | 3485 (10.1) | 1811 | 272 (15.0) |
| June 1-June 28 | 32 089 | 1337 (4.2) | 1847 | 136 (7.4) |

[a] Four-week surveillance periods included: December 15, 2020, through January 11, 2021; January 12 through February 8, 2021; February 9 through March 8, 2021; March 9 through April 5, 2021; April 6 through May 3, 2021; May 4 through May 31, 2021; and June 1 through 28, 2021. Unique ongoing pregnancies may be counted in more than one 4-week surveillance period and were identified at the last date of the 4-week period.

[b] Race and ethnicity came from electronic health data, based on self-report. Race and ethnicity is included as both COVID-19 vaccine uptake and rates of spontaneous abortion vary by race and ethnicity.

Table 2. Adjusted Odds Ratios for Receipt of COVID-19 Vaccine Within 28 Days Prior to a Spontaneous Abortion, December 15, 2020, Through June 28, 2021, Across 8 Vaccine Safety Datalink Sites and Among 264 104 Pregnancy-Periods[a]

| | Adjusted odds ratio (95% CI)[b] |
|---|---|
| Full population | 1.02 (0.96-1.08) |
| By gestational age, wk | |
| 6-8 | 0.94 (0.86-1.03) |
| 9-13 | 1.07 (0.99-1.17) |
| 14-19 | 1.08 (0.89-1.29) |
| By vaccine type[c] | |
| mRNA-1273 (Moderna) | 1.03 (0.94-1.11) |
| BNT162b2 (Pfizer-BioNTech) | 1.03 (0.95-1.11) |

[a] See Table 1 footnote a for 4-week pregnancy periods. Unique ongoing pregnancies may be counted in more than 1 surveillance period.

[b] Generalized estimating equation models included gestational age group, surveillance period, maternal age group, number of antenatal visits, site, and race and ethnicity factors and accounted for repeated ongoing pregnancies across surveillance periods.

[c] The Ad26.COV.2.S vaccine is not included due to the small number of exposures.

their outcome date; these spontaneous abortions could have been included in the ongoing pregnancy categories during prior periods (eFigure in the Supplement). Vaccination data came from EHRs, medical and pharmacy claims, and regional or state immunization information systems.

We analyzed the odds of receiving a COVID-19 vaccine in the 28 days prior to spontaneous abortion compared with the odds of receiving a COVID-19 vaccine in the 28 days prior to index dates for ongoing pregnancies. Both spontaneous abortions and ongoing pregnancies were assigned to gestational age groups (6-8, 9-13, and 14-19 weeks), surveillance periods, site, maternal age groups (16-24, 25-34, and 35-49 years), number of antenatal visits (≤1 or ≥2), and race and ethnicity. Generalized estimating equations with binomial distribution and logit link were used to account for repeated ongoing pregnancies across surveillance periods. Analyses by manufacturer and gestational age group were also conducted. Analysis was performed using SAS/STAT software version 9.4 (SAS Institute Inc).

This surveillance was approved by the institutional review boards of all participating sites with a waiver of informed consent.

**Results** | Of 105 446 unique pregnancies, 13 160 spontaneous abortions and 92 286 ongoing pregnancies were identified. Overall, 7.8% of women received 1 or more BNT162b2 (Pfizer-BioNTech) vaccines; 6.0% received 1 or more mRNA-1273 (Moderna) vaccines; and 0.5% received an Ad26.COV.2.S (Janssen) vaccine during pregnancy and before 20 weeks' gestation. The proportion of women aged 35 through 49 years with spontaneous abortions was higher (38.7%) than with ongoing pregnancies (22.3%). A COVID-19 vaccine was received within 28 days prior to an index date among 8.0% of ongoing pregnancy periods vs 8.6% of spontaneous abortions (**Table 1**). Spontaneous abortions did not have an increased odds of exposure to a COVID-19 vaccination in the prior 28 days compared with ongoing pregnancies (adjusted odds ratio, 1.02; 95% CI, 0.96-1.08). Results were consistent for mRNA-1273 and BNT162b2 and by gestational age group (**Table 2**).

**Discussion** | Among women with spontaneous abortions, the odds of COVID-19 vaccine exposure were not increased in the prior 28 days compared with women with ongoing pregnancies. Strengths of this surveillance include the availability of a multisite diverse population with robust data capture. Several limitations should be noted. First, gestational age of spontaneous abortions and ongoing pregnancies were not chart confirmed; pregnancy dating may be inaccurate early in pregnancy. Second, although vaccination status was identified using multiple data sources, the COVID-19 vaccine rollout has been complex and some vaccines may have been missed, potentially biasing findings to the null. Third, data on important confounders, such as prior pregnancy history, were not available. Fourth, it was not possible to assess risks specific to the Ad26.COV.2.S vaccine given the small number of exposures. Despite limitations, these data can be used to inform vaccine recommendations and to counsel patients.

**Elyse O. Kharbanda, MD, MPH**
**Jacob Haapala, MPH**
**Malini DeSilva, MD, MPH**
**Gabriela Vazquez-Benitez, PhD**
**Kimberly K. Vesco, MD, MPH**
**Allison L. Naleway, PhD**
**Heather S. Lipkind, MD, MS**

**Author Affiliations:** HealthPartners Institute, Minneapolis, Minnesota (Kharbanda, Haapala, DeSilva, Vazquez-Benitez); Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon (Vesco, Naleway); Obstetrics and Gynecology, Yale University, New Haven, Connecticut (Lipkind).

**Corresponding Author:** Elyse O. Kharbanda, MD, MPH, HealthPartners Institute, 8170 33rd Ave S, Mail Stop 23301A, Minneapolis, MN 55408 (elyse.o.kharbanda@healthpartners.com).

**Accepted for Publication:** August 26, 2021.

**Published Online:** September 8, 2021. doi:10.1001/jama.2021.15494

**Author Contributions**: Drs Kharbanda and Vazquez-Benitez had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
*Concept and design:* Kharbanda, DeSilva, Vazquez-Benitez, Lipkind.
*Acquisition, analysis, or interpretation of data:* All authors.
*Drafting of the manuscript:* Kharbanda, Vazquez-Benitez, Lipkind.
*Critical revision of the manuscript for important intellectual content:* Haapala, DeSilva, Vazquez-Benitez, Vesco, Naleway, Lipkind.
*Statistical analysis:* Haapala, Vazquez-Benitez.
*Obtained funding:* Kharbanda.
*Supervision:* Kharbanda, Lipkind

**Conflict of Interest Disclosures:** Dr Lipkind reported serving on the Pfizer independent external data monitoring committee for the COVID-19 vaccine. Dr Naleway reported receiving research funding from Pfizer for an unrelated study. Dr Vesco reported receiving research funding from Pfizer for an unrelated study. No other financial conflicts were reported.

**Funding/Support:** This study was funded by contract 200-2012-53526 from the Centers for Disease Control and Prevention (CDC).

**Role of the Funder/Sponsor:** The CDC participated in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

**Disclaimer:** The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC. Mention of a product or company name is for identification purposes only and does not constitute endorsement by the CDC.

**Additional Contributions:** *From the Vaccine Safety Datalink*: We thank Nicola Klein, MD, PhD (Kaiser Permanente Northern California), Matthew Daley, MD (Kaiser Permanente Colorado), Darios Getahun, MD (Kaiser Permanente Southern California), Stephanie Irving, MPH (Kaiser Permanente Northwest), Michael Jackson, PhD (Kaiser Permanente Washington), Joshua Williams, MD, Simon Hambidge, MD, PhD (Denver Health), James Donahue, DVM, PhD (Marshfield Clinic), and Candace Fuller, PhD (Harvard Pilgrim) for providing subject matter expertise, technical assistance, assistance with data collection, and review of the study. We thank Leslie Kuckler, MPH, and Jingyi Zhu, PhD (HealthPartners Institute) for their assistance with data collection. We also thank Eric Weintraub (CDC) and Brad Crane (Kaiser Permanente Northwest) for assistance with data collection and management in addition to administrative and technical support. All persons acknowledged have been compensated by the CDC.

**1**. Ko JY, DeSisto CL, Simeone RM, et al. Adverse pregnancy outcomes, maternal complications, and severe illness among US delivery hospitalizations with and without a coronavirus disease 2019 (COVID-19) diagnosis. *Clin Infect Dis*. 2021; 73(suppl 1):S24-S31. doi:10.1093/cid/ciab344

**2**. Shimabukuro TT, Kim SY, Myers TR, et al; CDC v-safe COVID-19 Pregnancy Registry Team. Preliminary findings of mRNA COVID-19 vaccine safety in pregnant persons. *N Engl J Med*. 2021;384(24):2273-2282. doi:10.1056/NEJMoa2104983

**3**. Kadali RAK, Janagama R, Peruru SR, et al. Adverse effects of COVID-19 messenger RNA vaccines among pregnant women: a cross-sectional study on healthcare workers with detailed self-reported symptoms. *Am J Obstet Gynecol*. 2021;S0002-9378(21)00638-4. doi:10.1016/j.ajog.2021.06.007

**4**. Rouse CE, Eckert LO, Babarinsa I, et al; Global Alignment of Immunization Safety in Pregnancy (GAIA) Abortion Work Group; Brighton Collaboration Abortion Working Group. Spontaneous abortion and ectopic pregnancy: case definition & guidelines for data collection, analysis, and presentation of maternal immunization safety data. *Vaccine*. 2017;35(48 pt A):6563-6574. doi: 10.1016/j.vaccine.2017.01.047

**5**. Baggs J, Gee J, Lewis E, et al. The Vaccine Safety Datalink: a model for monitoring immunization safety. *Pediatrics*. 2011;127(suppl 1):S45-S53. doi:10.1542/peds.2010-1722H

**6**. Naleway AL, Crane B, Irving SA, et al. Vaccine Safety Datalink infrastructure enhancements for evaluating the safety of maternal vaccination. *Ther Adv Drug Saf*. 2021;12:20420986211021233. doi:10.1177/20420986211021233