

CLINICAL PEARL UPDATE

April 2021



mRNA COVID-19 Vaccine Safety in Pregnant Persons

Recent NEJM study adds to existing research suggesting mRNA vaccine benefits outweigh potential risks in pregnancy

Background

The Phase III clinical trials upon which the FDA determined Emergency Use Authorization for the 3 U.S. authorized COVID-19 vaccines did not specifically include pregnant and lactating persons. Because this subpopulation was not a defined inclusion criteria, obtaining clear and consensus guidance on vaccinating pregnant people against COVID-19 has been difficult. The respective vaccine EUA Fact Sheets for Providers, derived from these clinical trials, unilaterally state “Available data on [Manufacturer] COVID-19 Vaccine administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy.”¹

To date, pregnancy has not been a contraindication or precaution to COVID-19 vaccination. Rather, pregnant individuals have the opportunity to engage in shared clinical decision making with their healthcare providers and may choose to receive any currently authorized COVID-19 vaccine with informed consent.

In the time since each of these COVID-19 vaccines have received authorization, the number of self-identified pregnant individuals who have opted to receive a vaccine has grown, allowing for the Centers for Disease Control and Prevention (CDC) to aggregate data on this patient subpopulation through the dedicated **V-safe COVID-19 Vaccine Pregnancy Registry**.

While official recommendations around vaccinating in pregnancy found in these vaccines’ EUA Fact Sheets for Providers remain equivocal, the collective body of evidence gathered and assessed to date suggests that poor pregnancy outcomes – namely, miscarriage – have **not** occurred at higher incidence rates among COVID-19 vaccine recipients in comparison to typical background rates (15% miscarriage rate reported to V-Safe Pregnancy Registry as of February 18th, 2021 vs. 26% background miscarriage rate²).³

V-Safe COVID-19 Vaccine Pregnancy Registry

The **V-Safe after Vaccination Health Checker** is a voluntary smartphone based tool that prompts vaccine recipients to report post-vaccination effects directly to the CDC, through regularly scheduled text message and web survey based prompts.

Through this V-Safe tool, more than **94 thousand participants** have indicated that they were pregnant at the time they received COVID-19 vaccination, as of 04/19/2021. Of this self-identified group of pregnant vaccine recipients, over **4.6 thousand** individuals have been contacted and additionally enrolled in the **V-Safe COVID-19 Vaccine Pregnancy Registry**, which allows the CDC to make specific health check-ins throughout gestation and again at set time-points after delivery.⁴

This robust health monitoring applied to pregnant vaccine recipients is cultivating data that was unavailable at the initial time these COVID-19 vaccines were authorized for emergency use, and may soon provide the basis for consensus recommendations on vaccinating pregnant individuals against COVID-19.

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Abridged Chronology of Historical Bulletins Regarding COVID-19 Vaccination of Pregnant Persons

- 01/07/2021: CDC updates its [COVID-19 vaccine guidance for pregnant people](#) to acknowledge that “Based on how these vaccines work in the body, experts believe they are unlikely to pose a specific risk for people who are pregnant. However, there are currently limited data on the safety of COVID-19 vaccines in pregnant people.” This guidance recognizes both that the COVID-19 disease places pregnant persons at increased risk for severe illness *and* that data regarding COVID-19 vaccination in pregnant persons is limited. Ultimately, the CDC states that being vaccinated is a personal choice, and while all U.S. authorized COVID-19 vaccines may be offered to pregnant persons, individuals should retain the autonomy to choose if and when they are vaccinated.⁵
- 01/08/2021: World Health Organization (WHO) issues a [recommendation](#) to “[Withhold] BNT162b2 in pregnancy, unless the benefit of vaccinating a pregnant woman outweighs the potential vaccine risks, such as in health workers at high risk of exposure and pregnant women with comorbidities placing them in a high-risk group for severe COVID-19.” WHO does acknowledge that the Pfizer-BioNTech vaccine is not a live virus, and as such would not in theory pose a significant threat to pregnant persons.⁵
- 01/25/2021: WHO issues a similar [recommendation](#) regarding Moderna’s COVID-19 vaccine, recommending against its use in pregnant individuals unless they are higher risk for severe COVID-19. The same concession is made regarding the Moderna vaccine’s morphology and its unlikelihood to pose a threat to mother or fetus.⁵
- 01/27/21: The American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) issue a [joint statement](#) that “ACOG and SMFM continue to stress that both COVID-19 vaccines currently authorized by the U.S. Food and Drug Administration (at the time only the 2 mRNA vaccines were authorized) should not be withheld from pregnant individuals who choose to receive the vaccine.” This is largely in response to the WHO recommendations to withhold vaccines from pregnant people unless they are at high risk of exposure or severe COVID-19.⁵

Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons⁶

Published 04/21/2021, in the [New England Journal of Medicine](#)

From 12/14/20 – 2/28/21, researchers assessed data from the **V-Safe after Vaccination Health Checker** surveillance system, the **V-Safe Pregnancy Registry**, and the **Vaccine Adverse Event Reporting System (VAERS)** to characterize the initial safety of mRNA COVID-19 vaccines in pregnant persons.

Calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against COVID-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the COVID-19 pandemic.

FINDINGS

- **V-Safe after Vaccination Health Checker**
 - Total vaccine recipients identified as pregnant: 35,691.
 - Age range: 16 to 54 years.
 - Vaccine effects reported among pregnant persons vs nonpregnant persons:

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- More frequent: Injection-site pain.
- Less frequent: headache, myalgia, chills, and fever.
- **V-safe Pregnancy Registry**
 - Enrolled: 3958 participants.
 - Completed pregnancy: 827.
 - Live birth: 712 (86.1%).
 - Pregnancy Loss 115 (13.9%).
 - Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%).
 - No neonatal deaths were reported.
- **VAERS**
 - Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases).

CONCLUSIONS

“Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA COVID-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes.”⁶

Additional Data

The following data on COVID-19 vaccination in pregnant persons were presented at the 03/01/2021 meeting of the Advisory Committee on Immunization Practices (ACIP).³

Notably, while miscarriage was the most frequently reported pregnancy-specific adverse event to VAERS, rates among COVID-19 vaccinated individuals were not beyond the expected known background rates based on presumed COVID-19 vaccine doses administered to pregnant women.

V-safe pregnancy registry outcomes of interest in COVID-19 vaccinated pregnant women as of February 18, 2021*

Outcomes	Background rates [†]	V-safe pregnancy registry overall
Pregnancy outcome		
Miscarriage (<20 weeks)	26%	15% [†]
Stillbirth (≥ 20 weeks)	0.6%	1%
Pregnancy complications		
Gestational diabetes	7-14%	10%
Preeclampsia or gestational hypertension [§]	10-15%	15%
Eclampsia	0.27%	0%
Intrauterine growth restriction	3-7%	1%
Neonatal		
Preterm birth	10.1%	10%
Congenital anomalies [†]	3%	4%
Small for gestational age [^]	3-7%	4%
Neonatal death	0.38%	0%

* <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-02/28-03-01/05-covid-Shimabukuro.pdf> Figure 1

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