Society for Maternal•Fetal Medicine
High-risk pregnancy experts

SMFM: Provider Considerations for Engaging in COVID-19 Vaccine Counseling With Pregnant and Lactating Patients
8.23.2021 (last published 8.13.21)

SMFM recommends that pregnant and lactating people be vaccinated against COVID-19. The Centers for Disease Control and Prevention (CDC) state that "COVID-19 vaccination is recommended for all people aged 12 years and older, including people who are pregnant, lactating, trying to get pregnant now, or might become pregnant in the future."

What should be considered when counseling a pregnant person regarding COVID-19 vaccination?

SMFM, the CDC, and other organizations representing maternal and public health professionals recommend that pregnant, postpartum, and lactating people and those considering pregnancy receive the COVID-19 vaccination. Vaccination is the best method to reduce maternal and fetal complications of SARS-CoV-2 infection. Counseling to support the recommendation for vaccination should include available data on vaccine efficacy, as well as data on vaccine safety during pregnancy and lactation. Provider counseling has been shown to have a significant positive impact on patient vaccination.

Maternal and obstetrical risk of disease

Data indicate that pregnancy is an independent risk factor for severe COVID-19 disease. Although the absolute risk of severe morbidity and mortality remains low, reports have demonstrated that pregnancy is independently associated with a 3-fold increased risk for ICU admission, a 2.4-fold increased risk for needing ECMO, and a 1.7-fold increased risk of death due to COVID-19, compared with symptomatic nonpregnant patients. Pregnant patients with comorbidities (body mass index greater than 35 kg/m^2, diabetes, and heart disorders) and those older than age 35 also appear to have a particularly elevated risk of adverse maternal outcomes. Other conditions the CDC has identified as increasing the risk for severe illness from SARS-CoV-2 infection include cancer, chronic kidney disease, chronic obstructive pulmonary disease, heart conditions, immunocompromised state from organ transplant, sickle cell disease, and smoking. Hispanic, Latinx, and Black patients are disproportionately affected by severe maternal morbidity and mortality and have a disproportionately higher incidence of COVID-19 infection and death. These disparities, caused by social determinants of

health that act as barriers to health and well-being, have become more apparent and exaggerated during this crisis.

Data also indicate an increased rate of adverse obstetric outcomes, including cesarean delivery, preterm birth, and possibly stillbirth in pregnant patients with symptomatic SARS-CoV-2 infection.

Vaccine mechanism and administration

There are currently three COVID-19 vaccines authorized for use in the United States. Two are mRNA vaccines (Pfizer-BioNTech BNT162b2 and Moderna mRNA 1273 vaccines), and one is an adenoviral-vector vaccine (Janssen [a pharmaceutical company of Johnson & Johnson] Biotech Ad26.COV2.S). None of the currently authorized vaccines contain live virus. The U.S. Food and Drug Administration (FDA) approved the Pfizer-BioNTech COVID-19 Vaccine for use in individuals 16 years of age and older, and will now be marketed as Comirnaty. The vaccine continues to be authorized for individuals 12 to 15 years of age.

The Pfizer and Moderna vaccines contain mRNA, a genetic material that encodes the SARS-CoV-2 spike S protein. Both RNA vaccines elicit neutralizing antibody responses to the S-protein. They are not live vaccines, and data suggest rapid degradation (approximately 10 to 20 days) of the mRNA by normal cellular processes. There is no risk of genetic modification to people receiving the vaccine.

The Janssen Biotech (J&J) one-dose vaccine uses an adenovirus that has been modified so that it can no longer multiply in humans and cannot cause disease to carry the gene for the coronavirus spike S protein into the host cell. Once inside the host cell, the gene harnesses the cell's machinery to produce more spike protein. The spike protein is then expressed on the host cell membrane, triggering both antibody and cell-mediated immune responses. The risk of genetic modification from adenovector vaccines is also low; viral DNA carrying the gene encoding the coronavirus spike protein enters the host nucleus to be transcribed but is not integrated into the host's DNA.

On April 13, 2021, the US FDA and CDC jointly recommended a pause to use of the Janssen Biotech (J&J) vaccine due to reports of a rare, severe type of blood clot called cerebral venous sinus thrombosis (CVST) occurring in combination with low levels of blood platelets (thrombocytopenia). The FDA and CDC confirmed that a total of 15 cases of thrombosis with thrombocytopenia syndrome (TTS) had been reported to the Vaccine Adverse Event Reporting System (VAERS), including the original six reported cases. All of the cases occurred in women between the ages of 18 and 59, with a median age of 37 years. Reports indicated symptom onset between 6 and 15 days after vaccination. None of the reported cases to date have occurred in pregnant people.

After reviewing the data, the CDC and FDA concluded that the chance of developing CVST and TTS following vaccination with the Janssen Biotech (J&J) vaccine is very low and that the benefits of the vaccine outweigh the risks. Both agencies recommended that use of the Janssen Biotech (J&J) vaccine resume effective April 23, 2021. The following warning is now included for the Janssen Biotech (J&J) vaccine:

> *Reports of adverse events following use of the Janssen COVID-19 Vaccine under emergency use authorization suggest an increased risk of thrombosis involving the cerebral venous sinuses and other sites (including but not limited to the large blood vessels of the abdomen and the veins of the lower extremities) combined with thrombocytopenia and with onset of symptoms approximately one to two weeks after vaccination. Most cases of thrombosis with thrombocytopenia reported following the Janssen COVID-19 Vaccine have occurred in females ages 18 through 49 years; some have been fatal. The clinical course of these events shares features with autoimmune heparin-induced thrombocytopenia. In individuals with suspected thrombosis with thrombocytopenia following the Janssen COVID-19 Vaccine, the use of heparin may be harmful and alternative treatments may be needed. Consultation with hematology specialists is strongly recommended. The American Society of Hematology has published considerations relevant to the diagnosis and treatment of thrombosis with thrombocytopenia following the Janssen COVID-19 Vaccine.*

Although TTS after vaccination has not been reported in pregnant people, obstetric clinicians should have a high degree of suspicion of TTS in pregnant people who report central nervous system symptoms or who have signs of VTE or thrombocytopenia within 30 days of vaccination. In this setting, immediate evaluation with a complete blood count and imaging (tailored based on symptoms) is recommended, with additional evaluation pending results of the initial clinical evaluation. Heparin (unfractionated or low molecular weight) must be avoided.

SMFM recommends following the CDC guidelines for vaccine administration. Vaccination should be offered regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection. Viral or serologic testing for acute or prior infection, respectively, is not recommended for the purpose of vaccine decision-making. Vaccination should not be given if the recipient is acutely ill.

A pregnancy test prior to vaccination is not recommended. Available data also do not indicate the need to delay attempting pregnancy following vaccination. There are no data to guide timing of vaccination during pregnancy; therefore, the vaccine should be offered independent of trimester.

Efficacy of vaccine

Data based on results from clinical trials indicate that the efficacy of the Pfizer vaccine after the second dose is 95.0% (95% CI, 90.3%–97.6%), and the efficacy of the Moderna vaccine after the second dose is 94.1% (95% CI, 89.3%–96.8%). Available

data demonstrate that both mRNA COVID-19 vaccines (Pfizer and Moderna) are highly effective in producing vaccine-induced antibody titers in pregnant and lactating women. Observational data demonstrate that the clinical effectiveness of mRNA vaccines in pregnant people is high, with an adjusted hazard ratio of 0.22 (95% CI 0.11-0.43). Patients should be counseled about the importance of completing the 2-dose series for optimal protection. It takes 2 weeks following the second dose to be considered fully vaccinated.

Data based on clinical trials indicate that the Janssen (J&J) one-dose vaccine is 72% (95% CI) effective at preventing moderate to severe disease, 85% effective in preventing severe disease, and 100% effective in preventing COVID-19–related hospitalization and death 28 days after vaccination.

The data regarding the vaccine's effectiveness against SARS-CoV-2 mutations (variants) is ongoing. The CDC and FDA are developing guidance as this situation evolves. CDC guidance for vaccinated persons also continues to evolve. SMFM recommends that vaccinated persons refer to the CDC website for updated recommendations on masks and physical distancing.

Table 1. Authorized and Approved Vaccines

	Age	Dose schedule	Efficacy	Technology
Pfizer-BioNTech/ Comirnaty (approved)	≥12 years ≥16 years	2 doses/ 21 days	95% after 2nd dose	mRNA
Moderna	≥18 years	2 doses/ 28 days	94.1% after 2nd dose	mRNA
Janssen Biotech (J&J)*	≥18 years	1 dose	72% moderate; 85% severe; 100% COVID-related hospitalization and death	Adenovector

*Female individuals younger than age 50 years, including those who are pregnant, lactating, and postpartum individuals, can receive any FDA-authorized COVID-19 vaccine available to them. However, they should be aware of the rare risk of thrombosis with thrombocytopenia syndrome after receiving the Janssen (J&J) vaccine and be counseled that other FDA-authorized COVID-19 vaccines are available.

Boosters

Currently, the CDC is recommending that moderately to severely immunocompromised people receive an additional dose of an mRNA vaccine. The CDC list includes people who have:

- Been receiving active cancer treatment for tumors or cancers of the blood
- Received an organ transplant and are taking medicine to suppress the immune system
- Received a stem cell transplant within the last 2 years or are taking medicine to suppress the immune system
- Moderate or severe primary immunodeficiency (such as DiGeorge syndrome, Wiskott-Aldrich syndrome)
- Advanced or untreated HIV infection
- Been receiving active treatment with high-dose corticosteroids or other drugs that may suppress the immune response

Although full vaccination is still providing stable and highly effective protection against hospitalizations and severe outcomes, a decrease in vaccine effectiveness against SARS-CoV-2 infection over time has been observed. Because the current protection against severe disease, hospitalization, and death could diminish in the months ahead, especially among those who are at higher risk for complications or were vaccinated during the earlier phases of the vaccination rollout, the U.S. Department of Health and Human Services (HHS) has developed a plan to begin offering booster shots beginning the week of September 20. Individuals would receive a booster shot starting 8 months after an individual's second dose. This plan is subject to the FDA conducting an independent evaluation and determination of the safety and effectiveness of a third dose of the Pfizer and Moderna mRNA vaccines and CDC's Advisory Committee on Immunization Practices (ACIP) issuing booster dose recommendations based on a thorough review of the evidence.

Fetal considerations

Counseling should weigh the risks of disease, the theoretical risk of harm, and the potential benefits to the fetus. Available safety data for mRNA vaccines in pregnancy include Developmental and Reproductive Toxicology (DART) data from Pfizer and Moderna, limited data from pregnant persons inadvertently enrolled in clinical trials, and data collected from the CDC's v-safe program. None of the data have indicated safety concerns or risks to pregnancy.

In a recent cohort study, maternal antibodies to SARS-CoV-2 were found to have crossed the placenta after infection during pregnancy, and cord blood antibody concentrations correlated with maternal antibody concentrations. These findings, which have been replicated in other cohorts, demonstrate the potential for maternal antibodies to transfer to the fetus and provide neonatal protection. They also suggest the need for further data to determine if SARS-CoV-2 antibodies are protective against newborn

infection, the concentration needed to achieve protection, and whether vaccine-elicited antibodies are similar to naturally acquired antibodies.

Another recent study showed the transfer of vaccine-induced IgG to the neonate, with higher umbilical cord blood titers achieved with longer intervals from vaccination. Boosting following the second vaccine dose resulted in augmented IgG levels in the cord blood. These findings point to the ability of maternal mRNA vaccination to induce immunologic protection to neonates through antibody transfer in utero and during lactation.

What safety data are available about the vaccines and pregnancy?

Despite SMFM's advocacy efforts, pregnant and lactating people have been excluded in the recent vaccine trials; therefore, there are no clinical trial data on the safety of the COVID-19 vaccines in pregnant people. The CDC's Advisory Committee on Immunization Practices (ACIP) reports that preclinical studies have been reassuring. Individual decision-making needs to balance these theoretical risks with the risks associated with delayed vaccination and the possibility of maternal SARS-CoV-2 infection.

To date, more than 139,000 pregnant people have self-reported within the CDC v-safe program, and the types and frequency of self-reported acute side effects do not appear to differ from those in the general population. Moreover, more than 3,900 of these individuals have been followed longitudinally in a registry devoted specifically to pregnancy outcomes, such as miscarriage and stillbirth, pregnancy complications, maternal ICU admission, adverse birth complications, neonatal death, infant hospitalizations, and birth defects.

Published findings indicate that more than 35,000 participants (aged 16 to 54 years) in the CDC v-safe program (the v-safe surveillance system, the v-safe Vaccine Pregnancy Registry, and VAERS) identified as pregnant from December 14, 2020 to February 28, 2021 and received an mRNA COVID-19 vaccine. Over 3,900 participants have been enrolled in the specific v-safe Vaccine Pregnancy Registry, with 827 completed pregnancies registered. Vaccine reactions were similar among pregnant individuals compared with nonpregnant women. Adverse pregnancy outcomes of completed pregnancies (including spontaneous abortion, stillbirth, preterm birth, small size for gestational age, congenital anomalies, and neonatal death) all fell within the normative ranges expected based on the medical literature and background rates.

A recent study of 2,456 pregnant people enrolled in the CDC v-safe pregnancy registry who were vaccinated preconception or before 20 weeks of gestation shows that miscarriage rates following vaccination were similar to the background incidence of miscarriage.

Available data from the Janssen Biotech (J&J) vaccine also include developmental and reproductive toxicity (DART) data and 8 pregnancies inadvertently enrolled in clinical trials. Further, previous vaccine trials using adenovirus vectors in pregnant patients, eg, Ebola vaccine, have not demonstrated adverse pregnancy outcomes.

Safety monitoring in pregnant people is ongoing, and the Janssen Biotech (J&J) vaccine will be included in future vaccine safety surveillance activities. Pfizer and Janssen are planning clinical trials in pregnant volunteers.

What are the expected side effects, and are they harmful?

Postvaccination signs and symptoms are typically mild to moderate in severity and occur within the first 3 days of vaccination (the day of vaccination and the following two days, with most occurring the day after vaccination) and resolve within 1 to 2 days. More frequent and severe signs and symptoms follow the second dose. Pregnant patients who experience fever following vaccination should be counseled to take acetaminophen.

Allergic reactions, including anaphylaxis, have been reported but are rare (4.7 per million for Pfizer-BioNTech and 2.5 per million for Moderna) following COVID-19 vaccination in nonpregnant individuals. Management of anaphylaxis in pregnant individuals is the same as in nonpregnant individuals. For more information on the management of anaphylaxis after COVID-19 vaccination, see the CDC website.

The vaccines may be administered to persons with underlying medical conditions who have no contraindications to vaccination. Persons with HIV infection, other immunocompromising conditions, or who take immunosuppressive medications or therapies might be at increased risk for severe COVID-19. These individuals may still receive the vaccines unless otherwise contraindicated. For more information on vaccination in persons with underlying medical conditions, see the CDC website.

CDC Resources

Healthcare workers:

https://www.cdc.gov/coronavirus/2019-ncov/hcp/vaccination.html

Safety monitoring:

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety.html

CDC vaccine guidance:

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations-process.html#groups-considered

https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html#pregnant

CDC v-safe:

https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/vsafe.html