COVID-19: VACCINATION FOR WOMEN WHO ARE PREGNANT OR LACTATING

A Rapid Guidance Summary from the Penn Medicine Center for Evidence-based Practice
Last updated May 24, 2021. All links rechecked May 24 unless otherwise noted.

This Rapid Guidance Summary is a description of existing guidance and evidence reviews from a variety of sources that was in effect at the time of publication. It should not be used or interpreted as a clinical practice guideline, but instead can be used in development of local recommendations and policies.

Key questions answered in this summary

- Should women who are pregnant, breastfeeding, or attempting to conceive be vaccinated against COVID-19?

Please see the separate CEP Rapid Guidance Summary for information on effects of vaccines on fertility and pregnancy outcomes.

Summary of major recommendations

- Guidelines note there is limited clinical evidence on the safety or effectiveness of COVID-19 vaccines in women who are pregnant or breastfeeding, but postmarketing studies are finding that rates of adverse events in pregnant women are similar to rates in women who are not pregnant. There is also evidence that COVID-19 disease is associated with worse outcomes for patients who are pregnant.
- There is some evidence that maternal antibodies are transferred across the placenta and through breastmilk, with possible protective effects to the fetus and infant.
- Public health agencies and professional specialty societies consistently recommend shared decision-making to best balance the risks of vaccination with the risks of remaining unvaccinated. They do not consider pregnancy or breastfeeding to be a contraindication to COVID-19 vaccination.
- Women of childbearing age may be at increased risk of thrombosis and thrombocytopenia syndrome (TTS) following vaccination with an adenovirus vaccine. Some organizations state a preference for mRNA vaccines in these patients. *Please see the CEP Rapid Guidance Summary on thrombotic events with adenovirus vaccines.*
- The consensus of guidance from US medical centers consistently supports the US societies' recommendations for shared decision-making and offering vaccination to women who are pregnant or breastfeeding.

Public health agency and professional society guidelines on COVID-19 vaccination of women who are pregnant

Source	Recommendations
PHE May 20	Although clinical trials on the use of COVID-19 vaccines during pregnancy are not advanced, the available data do not indicate any harm to pregnancy. JCVI has therefore advised that women who are pregnant should be offered vaccination at the same time as non-pregnant women, based on their age and clinical risk group. There is now extensive post-marketing experience of the use of the Pfizer BioNTech and Moderna vaccines in the USA where over 100,000 pregnant women have been vaccinated, mainly with these 2 vaccines, with no safety signals being raised so far. There have been no specific safety concerns from any brand of COVID-19 vaccine in relation to pregnancy but more research is needed and there is more safety data available for the Pfizer BioNTech and Moderna vaccines which is why these 2 vaccines are currently the preferred vaccines to offer to pregnant women. Clinicians should discuss the risks and benefits of vaccination with the woman, who should be told about the limited evidence of safety for the vaccine in pregnancy.
RCOG May 14	The latest advice from the Joint Committee on Vaccination and Immunisation (JCVI) is that COVID-19 vaccines should be offered to pregnant women at the same time as the rest of the population, based on their age and clinical risk group. Women should discuss the benefits and risks of having the vaccine with their healthcare professional and reach a joint decision based on individual circumstances. *CEP NOTE: RCOG and RCM have published a decision aid leaflet for women considering vaccination.*
SOGC May 4	Pregnant individuals should be offered vaccination at any time during pregnancy or while breastfeeding if no contraindications exist. SOGC supports the use of all available COVID-19 vaccines approved in Canada in any trimester of pregnancy and during breastfeeding in accordance with regional eligibility. The decision to be vaccinated is based on the individual's personal values, as well as an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding. Individuals should not be precluded from vaccination based on pregnancy status or breastfeeding.
NACI May 3	NACI recommends that a complete vaccine series with a COVID-19 vaccine (preferably with an mRNA vaccine) may be offered to pregnant individuals in the authorized age group if a risk assessment deems that the benefits outweigh the potential risks for the individual and the fetus, and if informed consent includes discussion about the evidence on the use of COVID-19 vaccines in this population. (Discretionary Recommendation)
SMFM Apr. 29	SMFM strongly recommends that pregnant and lactating people have access to the COVID-19 vaccines and that they engage in a discussion about potential benefits and unknown risks with their healthcare providers regarding receipt of the vaccine. 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 or within 14 days from receiving another vaccine. 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.
ACOG Apr. 28	ACOG recommends that pregnant individuals have access to COVID-19 vaccines. Individuals considering a COVID-19 vaccine should have access to available information about the safety and efficacy of the vaccine, including information about data that are not available. A conversation between the patient and their clinical team may assist with decisions regarding the use of vaccines approved under EUA for the prevention of COVID-19 by pregnant patients. Important considerations include: • the potential efficacy of the vaccine • the risk and potential severity of maternal disease, including the effects of disease on the fetus and newborn • the safety of the vaccine for the pregnant patient and the fetus. While a conversation with a clinician may be helpful, it should not be required prior to vaccination, as this may cause unnecessary barriers to access. Pregnancy testing should not be a requirement prior to receiving any EUA-approved vaccine.

	Pregnant patients who decline vaccination should be supported in their decision. Regardless of their decision to receive or not receive the vaccine, these conversations provide an opportunity to remind patients about the importance of other prevention measures such as hand washing, physical distancing, and wearing a mask. Expected side effects should be explained as part of counseling patients, including that they are a normal part of the body's reaction to the vaccine and developing antibodies to protect against COVID-19 illness. Women under age 50 including pregnant individuals can receive any FDA-authorized COVID-19 vaccine available to them. However, they should be aware of the rare risk of TTS (thrombosis with thrombocytopenia syndrome) after receipt of the Janssen COVID-19 vaccine and that other FDA-authorized COVID-19 vaccines are available (i.e., mRNA vaccines).

Public health agency and professional society guidelines on COVID-19 vaccination of women who are lactating

Source	Recommendations
NACI May 3	A complete vaccine series with a COVID-19 vaccine may be offered to individuals in the authorized age group who are breastfeeding, if a risk assessment deems that the benefits outweigh the potential risks for the individual and the infant, and if informed consent includes discussion about the limited evidence on the use of COVID-19 vaccines in this population. (Discretionary Recommendation)
ACOG Apr. 28	COVID-19 vaccines should be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP.
SOGC May 3	Pregnant individuals should be offered vaccination at any time during pregnancy or while breastfeeding if no contraindications exist. SOGC supports the use of all available COVID-19 vaccines approved in Canada in any trimester of pregnancy and during breastfeeding in accordance with regional eligibility. The decision to be vaccinated is based on the individual's personal values, as well as an understanding that the risk of infection and/or morbidity from COVID-19 outweighs the theorized and undescribed risk of being vaccinated during pregnancy or while breastfeeding. Individuals should not be precluded from vaccination based on pregnancy status or breastfeeding.
PHE May 20	There is no known risk associated with giving non-live vaccines whilst breastfeeding. JCVI advises that breastfeeding women may be offered vaccination with any suitable COVID-19 vaccine. The developmental and health benefits of breastfeeding should be considered along with the woman's clinical need for immunisation against COVID-19, and at the same time, the woman should be informed about the absence of safety data for the vaccine in breastfeeding women.
RCOG May 14	You should not stop breastfeeding in order to be vaccinated against COVID-19. *CEP NOTE: RCOG and RCM have published a decision aid leaflet for women considering vaccination.*
SMFM Apr. 29	Vaccination is recommended for lactating persons. Counseling should balance the lack of data on vaccine safety and a person's individual risk for infection and severe disease. The theoretical risks regarding the safety of vaccinating lactating people do not outweigh the potential benefits of the vaccine.

Evidence reviews on vaccines and pregnancy

Reviewer	Findings
NACI May 3	The safety and efficacy of authorized COVID-19 vaccines in pregnancy have not yet been established, however safety data are accumulating from post marketing surveillance. Pregnant individuals were excluded from the mRNA and viral vector COVID-19 vaccine clinical trials. Currently, there are limited data on the safety of COVID-19 vaccine from animal developmental and reproductive toxicity studies. Emerging research suggests that COVID-19 mRNA vaccination during pregnancy results in comparable antibody titers to those generated in non-pregnant women. Maternal IgG humoral response to mRNA COVID-19 vaccines transfers across the placenta to the fetus, leading to a significant and potentially protective, antibody titer in the neonatal bloodstream. The evidence of pregnancy as an independent risk factor for severe COVID-19 is evolving. A rapid review of evidence from OECD member countries found a low certainty of evidence of at least a two-fold increase in hospitalization due to COVID-19 for pregnancy (any stage). Early studies consistently show that both anti-spike IgG and IgA are present in breastmilk after maternal vaccination with mRNA vaccines. In one small cohort study, mRNA from COVID-19 vaccines was undetectable in breastmilk 4-48 hours post-vaccination.
SOGC May 4	Most pregnant individuals who become infected with SARS-CoV-2 will have mild-to-moderate symptoms and many can be asymptomatic. However, both Canadian and international data from large studies spanning multiple jurisdictions demonstrate that approximately 7-11% of pregnant individuals will require hospitalization for COVID-related morbidity and between 1-4% of pregnant individuals require admission to an intensive care unit (ICU). Compared to non-pregnant individuals with COVID-19, pregnant individuals are at increased risk of admission to hospital, critical care and invasive ventilation compared to age-matched peers. The risk of severe morbidity from COVID-19 in pregnant individuals appears to be associated with risk factors including age ≥ 35 years old, asthma, obesity, preexisting diabetes, preexisting hypertension and heart disease. In addition, both Canadian and US data show an increased risk of preterm birth associated with COVID-19 infection in pregnancy which will cause consequent morbidity to the infant related to prematurity. Pregnant and breastfeeding individuals were excluded from the available Phase II and Phase III studies for the Pfizer-BioNTech and Moderna COVID-19 vaccines. However, for Pfizer-BioNTech, there were 23 individuals (12 in the vaccine arm and 11 in the placebo arm) who reported pregnancies during the trial and are being followed for pregnancy outcomes with no reports of adverse effects to date. For the Moderna trials, there were 13 individuals (6 in the vaccine and 7 in the placebo group) who reported pregnancies during the trial without reports of adverse effects to date. US data reporting on nearly 4,000 pregnant individuals who received either the Pfizer-BioNtech vaccine or the Moderna vaccine reported no differences in the rates of adverse pregnancy and neonatal outcomes for those individuals who were pregnant and compared to pre-pandemic rates. The Developmental and Reproductive Toxicity animal studies for the Moderna and Pfizer-BioNTech vaccines are ongoing. According to the World Health Organization and the American College of Obstetricians & Gynecologists, no major safety signals have been identified. Similarly, breastfeeding individuals were also excluded from the Phase III trials available at present. Therefore, there is no data on the safety of COVID-19 vaccines in lactating individuals or the effects of mRNA vaccines on the breastfed infant or on milk production. Because mRNA vaccines are not considered live virus vaccines, they are not hypothesized to be a risk to the breastfeeding infant.
SMFM Apr. 29	Recent 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 from COVID-19, compared to symptomatic nonpregnant patients. Pregnant patients with comorbidities (body mass index higher than 35 kg/m2, diabetes, and heart disorders) and those older than age 35 also appear to have a particularly elevated risk of adverse maternal outcomes. Data also indicate an increased rate of adverse obstetric outcomes, including cesarean delivery, preterm birth, and possibly stillbirth among pregnant patients with symptomatic SARS-CoV-2 infection. Counseling should also 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

Reviewer	Findings
	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. 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, over 85,000 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 3900 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.

Medical center guidance on COVID-19 vaccination of women who are pregnant or lactating

Center	Recommendation
Penn Medicine Not dated	If you are planning to become pregnant, you can receive the vaccine. The FDA also allows pregnant women to receive the vaccine. However, pregnant women were not studied in the vaccine trials, so there is not much information about the use of the vaccine among this group. If you are pregnant, we and the Society for Maternal-Fetal Medicine recommend that you discuss getting the vaccines with your provider. If you are breastfeeding, you can still get the vaccine and do not need to stop breastfeeding.
Washington May 21	Pregnant and breastfeeding women should get the vaccine once it is available to them. We know that: • Pregnant or breastfeeding women were not included in the COVID-19 clinical trials. • The risk of maternal or fetal harm from an mRNA vaccine is unknown but thought to be low. • COVID-19 disease carries an increased risk in pregnancy. This is particularly true for patients with obesity or other medical conditions.
Mayo May 19	If you are pregnant or breastfeeding, you may choose to get a COVID-19 vaccine. While further research is needed, early findings suggests that getting an mRNA COVID-19 vaccine during pregnancy poses no serious risks. The findings are based on data from the CDC's coronavirus vaccine safety monitoring system. If you have concerns, talk to your health care provider about the risks and benefits. Keep in mind that the mRNA COVID-19 vaccines don't alter your DNA or cause genetic changes.
Johns Hopkins May 13	COVID-19 vaccines currently authorized by the FDA should not be withheld from pregnant individuals who choose to receive the vaccine. We strongly recommend that women talk with their doctor to discuss all factors about the vaccine and their pregnancy. While there are many unanswered questions about the vaccines for pregnant women, Johns Hopkins Medicine agrees with and supports the recommendations of the ACIP, ACOG, and SMFM.

Center	Recommendation
Michigan Not dated	With the information currently available, we at believe the benefit of receiving the COVID-19 vaccine is greater than the risks of getting COVID-19 for women who are pregnant, breastfeeding or trying to conceive. There is no specific safety information about the COVID-19 vaccine in pregnancy because pregnant women were not included in the early studies. However, most scientists, doctors and national organizations support pregnant women receiving the vaccine because the risks of COVID-19 in pregnancy can be severe. Additionally, the Academy of Breastfeeding Medicine does not recommend stopping breastfeeding for people who get the COVID-19 vaccine and the American College of Obstetrics and Gynecology advises that it is not necessary to delay pregnancy after completing both doses of the vaccine. To help make your decision about receiving the vaccine, be sure to speak with your health care provider.
Yale Not dated	The available data shows the Pfizer, Moderna and Johnson & Johnson vaccines are safe. These vaccines were not specifically studied for safety in pregnant participants during the initial clinical trials. However, experts are continuing to study the impact of the vaccine and we hope to have more data soon. Please note, pregnancy is not a contraindication to any of the available vaccines. CDC and ACIP said the vaccine should be offered to pregnant and lactating people. As of April 5, 2021, more than 77,000 V-Safe participants indicated they were pregnant at the time they received the COVID-19 vaccine. V-Safe is a CDC program designed to track vaccine side effects. A recent evaluation of V-Safe data published in The New England Journal of Medicine found that while many pregnant vaccine recipients reported common side effects such as pain at the injection site, they found no obvious safety issues stemming from the mRNA vaccines. Researchers will continue to study any long-term impacts.

Guidance sources

ACIP–Advisory Committee on Immunization Practices (USA)
ACOG–American College of Obstetricians and Gynecologists
CDC–Centers for Disease Control and Prevention (USA)
FDA–US Food and Drug Administration
JCVI– Joint Committee on Vaccination and Immunisation (UK)
NACI– National Advisory Committee on Immunization (Canada)
PHE–Public Health England
RCM–Royal College of Midwives (UK)
RCOG–Royal College of Obstetricians and Gynaecologists (UK)
SMFM–Society for Maternal-Fetal Medicine
SOGC–Society of Obstetricians and Gynaecologists of Canada

Update history (key additions and changes only)

December 24, 2020: Initial report.

May 24, 2021: All guidance updated, December 3 JCVI guidance withdrawn, new table of evidence reviews, revised conclusions.

About this report

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site (http://www.uphs.upenn.edu/cep) for further details on the methods for developing these reports.

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