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COVID-19 Vaccines and Pregnancy

By Erin Wilson, MPH and Rebecca Dekker, PhD, RN of EvidenceBasedBirth.com

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Question: What vaccines are available?

Answer: In the U.S., there are three vaccines being administered. The Pfizer/BioNTech and Moderna vaccines are *messenger RNA* (mRNA) vaccines. These were the first vaccines to become available in the U.S., mostly because so much research had been done to develop this method prior to the pandemic. So, although these are the first ever mRNA vaccines used in the U.S., this technique has been worked on by scientists since the 1990s. The pandemic brought increased attention and funding that allowed scientists to improve upon this existing technology and make it available. There is currently another mRNA vaccine being used in African countries against the Ebola virus. COVID-19 mRNA vaccines are two-doses that deliver one or more coronavirus genes into human cells, essentially giving the body temporary instructions to make harmless spike proteins to stimulate immunity. The result is that the body can produce its own antibodies against COVID-19.

The Pfizer/BioNTech mRNA vaccine was approved by the FDA in August 2021 for all people 16 years and older. This approval is the first of its kind for an mRNA vaccine. The Moderna mRNA vaccine is currently approved under an Emergency Use Authorization (EUA) for adults 18 and older.

The Pfizer vaccine is also available to 12 to 15-year-olds under an EUA. Per the CDC, this vaccine is recommended to all people 12 years and older including those who are pregnant, lactating, trying to become pregnant, or planning to become pregnant soon.

More recently, on November 2, 2021, the CDC recommended the Pfizer/BioNTech pediatric vaccine for to 5 to 11-year-olds. The pediatric vaccine is one third the dose of the adult version (10 micrograms versus 30 micrograms). Also, like the adult version of the Pfizer vaccine, it is administered as two doses that are three weeks apart. The pediatric vaccine is currently approved under an EUA.

The Johnson and Johnson vaccine is made using the viral vector method. This technology has been used in vaccine development since the 1970s, and relies on a harmless virus (the vector) to deliver the vaccine. In the one-dose viral vector COVID-19 vaccines, a gene for the viral spike protein is inserted into another inactive virus to deliver the gene to human cells. This causes the immune system to recognize the virus and quickly respond by producing antibodies.

Use of the Johnson and Johnson vaccine was briefly suspended when data showed an increased risk of a rare adverse event involving low platelet count and blood clots in vaccine recipients under 50 years old who identified as women. On April 23, 2021, the FDA and CDC recommended that use of the vaccine continue due to benefits outweighing the risks. According to the CDC, pregnant people and those under 50 are still eligible to receive this vaccine but should be educated on the alternative (mRNA) vaccines that are also available.[1]

Then, on December 16, 2021, the CDC released newer data, showing a higher risk of blood clotting than previously known. Those with the highest risk are people who identify as women between the ages of 30 and 49. The updated risk is 1 per 100,000 people in this demographic. Overall, the rate of the rare blood clotting condition is 3.8 per 1 million people who received this vaccine.[2] Additionally, data have increasingly shown that the Johnson and Johnson vaccine offers significantly less protection than the other available vaccines. Given this new information, the CDC is now recommending the mRNA vaccines over the Johnson and Johnson vaccine. The Johnson and Johnson vaccine is not being removed from market in the U.S., and it will still be available to anyone who prefers this option.[3]

Question: How effective are the different vaccines at preventing COVID-19?

Answer: This is a very difficult question to answer due to newly evolving COVID-19 variants and disease distribution. The more contagious a variant is, and the more people who are spreading it, can change the answers to this question. Initial vaccine efficacy was shown to be around 95% for the mRNA vaccines (Pfizer BioNTech and Moderna) and 72% for the viral vector vaccine (Johnson and Johnson), but these numbers only capture how the vaccines performed under the controlled conditions of a clinical trial. The initial *efficacy* differs from the vaccines' real-world *effectiveness* and does not account for factors such as newer variants, vaccine response in different people, and how protection may lessen or change over time. Even as these numbers evolve, it's important to note that all the available vaccines remain extremely effective at preventing severe disease, hospitalization, and death. These definitions may help you as you read other articles and interpret data:

Vaccine efficacy is defined as the percent decrease in disease incidence in a vaccinated group versus an unvaccinated group in optimal conditions (such as in a randomized control trial).

Vaccine effectiveness measures a vaccine's ability to prevent any undesired outcome such as infection, severe disease, hospitalization, or death in real world conditions.

For more information on this topic, including the latest information on vaccine efficacy and effectiveness, visit:

Yale Medicine Vaccine Article (https://bit.ly/3pxvBN0)

Vaccine Efficacy and Effectiveness-CDC (https://bit.ly/2ZoQpeF)

Question: What is the available evidence on COVID-19 vaccination in pregnancy and while lactating?

Answer: When the vaccines were first rolled out in late 2020 and early 2021, no official U.S. recommendations were given for or against vaccination during pregnancy/lactation. This is primarily because pregnant and lactating people were

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not included in the first COVID-19 vaccine trials. Some of the first pregnant and lactating vaccine recipients were healthcare workers. Then in April 2021, pregnant people in the U.S. general population were offered the vaccine.

The CDC tracks pregnant people who receive a COVID-19 vaccine and, as of December 6, 2021, there were 178,661 self-reported pregnant people who completed the CDC's "v-safe after vaccination health checker." Of this group, 7,200 vaccinated pregnant people enrolled in the "v-safe pregnancy registry" to be followed throughout their pregnancies and beyond. In this group, there was no significant increase in the rate of pre-term birth, miscarriage, placental abnormalities, or congenital anomalies compared to the general population. So far, most v-safe pregnancy registry participants received their vaccines in the third trimester of pregnancy.[4]

A study published in the American Journal of Obstetrics and Gynecology (AJOG) in March 2021 compared vaccine response in 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 non-pregnant). All participants in this study received an mRNA vaccine, with about half receiving Pfizer/BioNTech and half receiving Moderna. Immune responses were similar in the three groups (pregnant, lactating, and non-pregnant). In the pregnant study group, the immune responses of participants did not differ based on when they received the vaccine in pregnancy, and the vaccine generated higher antibody levels than seen in natural COVID-19 infection. Immune protection from vaccine-generated antibodies passed to babies through the placenta and human milk, and these antibodies were detected in cord blood and human milk samples.[5]

Researchers are continuing to publish many smaller studies about vaccination in lactating people. Early data show that antibodies to the COVID-19 virus successfully transfer from vaccinated parents to babies who are ingesting human milk. Small studies have also demonstrated that, while antibodies do successfully transfer, the components of the mRNA COVID-19 vaccines do not transfer via human milk.[6] While this research is encouraging, and in line with other vaccines given during pregnancy, more information is needed to determine if the antibodies transferred in human milk and cord blood sufficiently protect babies from COVID-19.

Question: Are the vaccines approved for use during pregnancy?

Answer: In response to the growing body of evidence demonstrating the safety of COVID-19 vaccines for pregnant and lactating people, many major organizations began recommending vaccination for this population in August 2021. This list currently includes the Federal Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), American College of Obstetricians and Gynecologists (ACOG), American College of Nurse Midwives (ACNM), the Society for Maternal Fetal Medicine (SMFM), and the National Institute for Health and Care Excellence in the United Kingdom (NICE), among others. Also in August 2021, the FDA granted full approval to the Pfizer/BioNTech vaccine for all individuals 16 years and older. The approval does not specifically state that pregnant people are included, but it does not exclude them. At the time this handout was written, the Moderna and Johnson and Johnson vaccines remain approved under Emergency Use Authorization (EUA).

Question: Does COVID-19 cause more serious disease in pregnancy? What are the known risks of vaccinating during pregnancy compared to the known risks of COVID-19 during pregnancy?

Answer: Pregnant people with COVID-19 infection are at higher risk for more severe disease—especially for those who are unvaccinated. A recent study by the National Institute of Health Research (NIHR) showed that 99.5% of pregnant people admitted to the hospital with COVID-19 were unvaccinated. When compared with non-pregnant people, pregnant people with COVID-19 were at an increased risk of intensive care admission, respiratory support, and pneumonia.[7]

Two other known risks of COVID-19 in pregnancy are pre-term birth and preeclampsia. In 2021, researchers analyzed California Vital Statistics birth certificate records of more than 200,000 births and found a 60% increased risk in very pre-term birth (giving birth at <32 weeks of pregnancy) in participants with a COVID-19 diagnosis. Additionally, there was a 40% increased risk in pre-term birth (giving birth at <36 weeks of pregnancy), and a 10% increased risk in early term birth (giving birth between 37 weeks 0 days and 38 weeks 6 days of pregnancy) in participants with a COVID-19 diagnosis. These increased risks are relative to the control or non-COVID-19 group.[8]

Also in 2021, researchers reviewed 28 different studies made up of 790,954 pregnant people, 15,524 of which were diagnosed with COVID-19. The risk of developing preeclampsia was 1.58 times higher in the COVID-19 group as compared to the pregnant people without COVID-19. Both symptomatic and asymptomatic COVID-19 infections resulted in significantly higher rates of preeclampsia, though the rate was slightly higher in symptomatic cases.[9]

A study published in the New England Journal of Medicine in April 2021, and updated in October 2021, provides the most comprehensive data thus far about people who received an mRNA COVID-19 vaccine during pregnancy. This data was gathered from three CDC sources-the 'v-safe after vaccination health checker', the v-safe pregnancy registry, and VAERS (the Vaccine Adverse Event Reporting System). The data showed that compared with non-pregnant people who were vaccinated, pregnant people who received an mRNA vaccine were more likely to report injection site pain and less likely to report other systemic reactions including headache, fever, chills, and muscle pain. Pregnant people were also more likely to report nausea and vomiting after their second dose of vaccine, but they were not more likely

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to report any other serious vaccine reactions as compared to non-pregnant people. There were no significant differences in the rates of adverse pregnancy outcomes including pregnancy loss, pre-term birth, and small for gestational age newborns between vaccinated pregnant people in the study group and pre-pandemic rates of these events.[10]

Another study, currently published as a letter to the editor on October 20, 2021, in the New England Journal of Medicine, looked at the early (first trimester) miscarriage rate in pregnant people who received a COVID-19 vaccine during pregnancy and pregnant people who did not. The study took place in Norway and researchers reviewed the records of about 18,000 pregnant people-about 14,000 of whom had ongoing pregnancies and about 4,000 of whom had early miscarriages-from Norwegian registry data. The study found no evidence of increased early pregnancy loss in the participants who received a COVID-19 vaccine, adding to the increasing evidence of the safety of COVID-19 vaccines in pregnancy.[11]

Question: Has research demonstrated a link between COVID-19 and infertility?

Answer: There is no evidence that demonstrates a link between COVID-19 vaccination and infertility for egg-carriers. Theories about a possible connection come from what some believe is a structural similarity of the SARS-CoV-2 spike protein and syncitin-1, a protein that helps form the placenta and is necessary for the development of an embryo in utero. This misleading theory, circulated by a known anti-vaccination group, proposed that an immune response against the spike protein could also cause an immune response against syncitin-1, thus potentially impacting pregnancy. However, experts in immunology, infectious disease, and pregnancy have refuted this idea.

A study published in September 2021 studied this idea in people already undergoing in vitro fertilization for fertility treatment. Study participants were divided into three groups: 1) those who had COVID-19 antibodies from prior natural infection, 2) those who had COVID-19 antibodies from prior vaccination, and 3) those who did not have antibodies from infection or vaccination. All vaccinated participants received one of the two available mRNA vaccine regimens. In the study, 143 unique frozen embryo transfers (FETs) were analyzed. Standard screening and protocols for FET were followed. The researchers found no difference in pregnancy success rates between the three groups.[12]

Another study explored this theory by directly comparing the placentas of birthing people who had received the COVID-19 mRNA vaccine in pregnancy versus those who had not received the vaccine. In this study, researchers at Northwestern University examined the placentas of 84 vaccinated people and 116 unvaccinated people shortly after giving birth. All study participants had negative COVID-19 polymerase chain reaction (PCR) tests. The vaccinated group did not have a higher rate of placental abnormalities as compared to the unvaccinated group. The study, published in Obstetrics and Gynecology in August 2021, further refutes theories of any association between COVID-19 vaccines and placental health, and adds to the growing body of evidence that COVID-19 mRNA vaccines are safe in pregnancy and the preconception period.[13]

Another much discussed topic regarding fertility is the possible association between COVID-19 vaccination and changes in menstrual cycles. The United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHPRA) has received over 30,000 reports of such events to their yellow card surveillance system—a self-reporting system similar to VAERS in the United States. Reproductive health experts suggest that these changes are likely hormonal and the result of the body's immune response from vaccination, rather than a reaction to specific components of the vaccine. These reports have come from both mRNA and viral vector vaccine recipients, and most people who reported these changes had their abnormal menstrual cycles return to normal after one cycle. More research is needed to investigate this possible link. For anyone tracking their menstrual cycles in hopes of preventing or achieving pregnancy, this is a potentially important consideration.[14]

Question: What can we expect in terms of future research about vaccination in pregnancy?

Answer: A study called "Preg-CoV" is the first randomized trial to directly study COVID-19 vaccination in pregnancy. The study is currently taking place in the United Kingdom at the National Institute of Health Research (NIHR) Southampton Clinical Research Facility and is enrolling pregnant people between the ages of 18-44 and in weeks 13-34 of pregnancy. The primary goal of the study is to determine the best timing between doses for the mRNA COVID-19 vaccines in pregnancy. Study scientists will analyze blood and human milk samples from pregnant study participants, as well as blood samples from babies born to study participants. Scientists hope the results will help us understand how vaccines can protect pregnant people and how that protection can potentially transfer to newborns. Initial results are expected at the end of 2021.[15]

Question: Is there a new recommendation regarding booster shots for pregnant people?

Answer: In September 2021, the FDA announced an Emergency Use Authorization (EUA) for booster doses of the Pfizer/BioNTech vaccine. Another EUA for Moderna and Johnson and Johnson booster doses followed shortly after in October 2021. This approval also allowed for the mixing of vaccines, such that the booster dose may be a different brand than the primary vaccine dose(s).[16] At first, only more vulnerable populations including people over 65, immunocompromised individuals, and people living or working in high-risk environments were approved to receive booster doses.

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Then, on December 9, 2021, the recommendation was extended to all people 18 years and older. Per a webinar that we attended on December 1, 2021, taught by Kara Polen at the CDC, this recommendation includes pregnant and lactating people as well as those wanting to become pregnant soon.[17] The American College of Obstetricians and Gynecologists (ACOG) also updated their Practice Advisory on December 3, 2021 to include pregnant and recently pregnant people in their booster dose recommendation.[18]

At this time, booster doses are available to anyone 16 years and older. The Pfizer/BioNTech vaccine is the only option approved for 16 and 17-year-olds. All available brands can be given to those 18 years and older. The CDC updated their guidance on December 17, 2021, recommending the mRNA vaccines over the Johnson and Johnson option. You can view the CDC's guide on boosters here: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/booster-shot.html (https://bit.ly/3J9JqbU)

A NOTE FROM EBB

The research on vaccines (including the research on booster doses) is rapidly changing, and new studies may be published that update some of the current evidence written about in this handout. Below is a list of resources that may be helpful to pregnant people and those trying to conceive in navigating vaccination decisions:

- COVID-19 and Pregnancy CDC Page (https://bit.ly/3mevXGn)
- NIH-How COVID-19 Affects Pregnancy (https://bit.ly/3pL1OQO)
- Preg-CoV Trial Information (https://bit.ly/3bd2dmE)

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18. ACOG Practice Advisory. COVID-19 Vaccination Considerations for Obstetric-Gynecologic Care. Updated online December 3, 2021.