Special Considerations During Pregnancy and After Delivery

Last Updated: February 29, 2024

Summary Recommendations

- Pregnant people should be counseled about the increased risk for severe disease from SARS-CoV-2 infection and the measures they can take to protect themselves and their families from infection.
- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** withholding COVID-19 vaccination from pregnant or lactating individuals specifically because of pregnancy or lactation **(AIII)**.
- If hospitalization for COVID-19 is indicated for a pregnant patient, care should be provided in a facility that can conduct maternal and fetal monitoring, when appropriate.
- General management of COVID-19 in pregnant patients should include:
 - · Fetal and uterine contraction monitoring based on gestational age, when appropriate
 - · Individualized delivery planning
 - A multispecialty, team-based approach that may include consultation with obstetric, maternal-fetal medicine, infectious disease, pulmonary-critical care, and pediatric specialists, as appropriate
- The Panel **recommends against** withholding COVID-19 treatment from pregnant or lactating individuals specifically because of pregnancy or lactation (AIII).
- In general, the therapeutic management of pregnant patients with COVID-19 should be the same as for nonpregnant patients, with a few exceptions (AIII). Notable exceptions include:
 - The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated **(AIII)**.
 - There is insufficient evidence for the Panel to recommend either for or against the use of therapeutic anticoagulation in pregnant patients with COVID-19 who do not have evidence of venous thromboembolism. See <u>Antithrombotic</u> <u>Therapy in Patients With COVID-19</u> for more information.
- For details regarding therapeutic recommendations and pregnancy considerations, see <u>Therapeutic Management of</u> <u>Nonhospitalized Adults With COVID-19</u>; <u>Therapeutic Management of Hospitalized Adults With COVID-19</u>; <u>Pregnancy</u>, <u>Lactation</u>, and <u>COVID-19 Therapeutics</u>; and the individual drug sections.
- Data on the use of COVID-19 therapeutic agents in pregnant and lactating people are limited. When making decisions
 about treatment, pregnant or lactating people and their clinical teams should use a shared decision-making process
 and consider several factors, including the severity of COVID-19, the risk of disease progression, and the safety of
 specific medications for the fetus, infant, or pregnant or lactating individual. For detailed guidance on using the Panelrecommended COVID-19 therapeutic agents during pregnancy, see <u>Pregnancy, Lactation, and COVID-19 Therapeutics</u>.
- The decision to feed the infant breast milk while the lactating patient is receiving therapeutic agents for COVID-19 should be a collaborative effort between the patient and the clinical team, including infant care providers. The patient and the clinical team should discuss the potential benefits of the therapeutic agent and evaluate the potential risk of pausing lactation on future breast milk delivery to the infant. For more information, see <u>Pregnancy, Lactation, and COVID-19 Therapeutics</u>.

Each recommendation in the Guidelines receives a rating for the strength of the recommendation (A, B, or C) and a rating for the evidence that supports it (I, IIa, IIb, or III). See <u>Guidelines Development</u> for more information.

Epidemiology of COVID-19 in Pregnancy

Although the overall risk of severe illness is low, pregnant people with COVID-19 are at a higher risk of severe disease than nonpregnant people.¹ After adjustments have been made for age, race/ethnicity, and underlying medical conditions, pregnant women have significantly higher rates of intensive care unit (ICU) admission (10.5 vs. 3.9 cases per 1,000 cases; adjusted risk ratio [aRR] 3.0; 95% CI, 2.6–3.4),

mechanical ventilation (2.9 vs. 1.1 cases per 1,000 cases; aRR 2.9; 95% CI, 2.2–3.8), extracorporeal membrane oxygenation (0.7 vs. 0.3 cases per 1,000 cases; aRR 2.4; 95% CI, 1.5–4.0), and death (1.5 vs. 1.2 cases per 1,000 cases; aRR 1.7; 95% CI, 1.2–2.4).

An ongoing systematic review and meta-analysis of 435 studies also described increased odds of ICU admission and mechanical ventilation among pregnant and recently pregnant patients with COVID-19 when compared with nonpregnant patients of reproductive age.^{2,3} Compared with pregnant women and recently pregnant women without COVID-19, pregnant women with COVID-19 were at a higher risk of preterm birth and stillbirth.

A national cohort study in the United States evaluated whether severe maternal morbidity, as defined by the Centers for Disease Control and Prevention (CDC), was associated with SARS-CoV-2 infection during pregnancy.⁴ The study reported that among the 93,624 pregnant individuals who delivered, 4.8% were infected with SARS-CoV-2 at some point during pregnancy. Among the cases of SARS-CoV-2 infection, 59.5% occurred early in pregnancy, 13.5% occurred 7 to 30 days before delivery, and 27% occurred <7 days before delivery. The adjusted risk of severe maternal morbidity was 2.22 times higher for pregnant individuals who were infected <7 days before delivery and 1.67 times higher for those who were infected 7 to 30 days before delivery, when compared with the risk for pregnant individuals who delivered and had not been infected with SARS-CoV-2 during pregnancy. The study also reported that at the time of hospitalization for delivery, severe maternal morbidity was associated with younger (15–25 years) and older maternal (>35 years) ages, non-Hispanic Black race, lower household income and educational attainment, pre-existing medical conditions, and diagnosed pregnancy complications.

Obstetric and Perinatal Outcomes in Patients With COVID-19

An observational cohort study at 33 U.S. hospitals evaluated the maternal characteristics and outcomes across disease severity for all of the pregnant patients who had a singleton gestation and a positive result on a SARS-CoV-2 virologic test.⁵ The data suggested that adverse perinatal outcomes were more common in patients with severe or critical disease than in asymptomatic patients with SARS-CoV-2 infection, including an increased incidence of cesarean delivery (59.6% vs. 34.0% of patients; aRR 1.57; 95% CI, 1.30–1.90), hypertensive disorders of pregnancy (40.4% vs. 18.8%; aRR 1.61; 95% CI, 1.18–2.20), and preterm birth (41.8% vs. 11.9%; aRR 3.53; 95% CI, 2.42–5.14). The perinatal outcomes for those with mild to moderate illness were similar to those observed among asymptomatic patients with SARS-CoV-2 infection.

Among 1,249,634 delivery hospitalizations in the United States from March 2020 through September 2021, women with COVID-19 had an increased risk of stillbirth, which was defined as fetal death at >20 weeks' gestation (aRR 1.90; 95% CI, 1.69–2.15).⁶ The risk of stillbirth was higher during the time period that Delta was the dominant variant in the United States (aRR 4.04; 95% CI, 3.28–4.97) than during the pre-Delta period (aRR 1.47; 95% CI, 1.27–1.71).

A retrospective cohort analysis collected data from 14,104 pregnant or recently postpartum individuals who delivered at U.S. hospitals that participated in the Gestational Research Assessments for COVID-19 (GRAVID) study.⁷ Compared with pregnant individuals who did not have SARS-CoV-2 infection, patients with COVID-19 during pregnancy had an increased risk of meeting the composite endpoint of maternal death or severe morbidity related to hypertensive disorders of pregnancy, postpartum hemorrhage, or infection. Eighty percent of the patients in this cohort tested positive for SARS-CoV-2 infection during the third trimester. The primary composite endpoint occurred in 13.4% of patients who had COVID-19 during pregnancy or within 6 weeks postpartum and in 9.2% of those who did not have COVID-19 (aRR 1.41; 95% CI, 1.23–1.61).

When compared with those who did not have a positive SARS-CoV-2 test result, pregnant patients who had SARS-CoV-2 infection prior to 28 weeks' gestation had a subsequent increased risk of fetal/neonatal death (aRR 1.97; 95% CI, 1.01–3.85), preterm birth at <37 weeks (aRR 1.29; 95% CI, 1.02–1.63), and hypertensive disorders of pregnancy with delivery at <37 weeks' gestation (aRR 1.74; 95% CI, 1.19–2.55).⁸ There were no significant differences between these groups of patients in the risk of preterm birth at <34 weeks, any major congenital abnormalities, or a size for gestational age of less than the 5th or 10th percentiles. There were also no significant differences between these groups in the rates of gestational hypertension overall or preeclampsia with severe features. These data suggest that those with SARS-CoV-2 infection early in gestation may also have an increased risk of subsequent adverse pregnancy outcomes.

Vertical Transmission of COVID-19

Although vertical transmission of SARS-CoV-2 is possible, current data suggest that it is rare.⁹ A review of 101 infants born to 100 women with SARS-CoV-2 infection at a single U.S. academic medical center found that 2 infants (2%) had indeterminate SARS-CoV-2 polymerase chain reaction (PCR) results, which were presumed to be positive. However, the infants exhibited no evidence of clinical disease. It is reassuring that the majority of the infants received negative PCR results after rooming with their mothers and breastfeeding directly (the mothers in this study practiced appropriate hand and breast hygiene).

Data collected by the CDC as part of the Surveillance for Emerging Threats to Mothers and Babies Network showed that among 4,038 infants born to people with COVID-19, for whom laboratory testing information was available and who were tested during the delivery hospitalization, 227 infants (5.6%) had positive PCR results for SARS-CoV-2.¹⁰

The published data to date were largely collected prior to the emergence of the Omicron variants. The risk of vertical transmission may vary based on viral dynamics and the transmissibility of the circulating variants in a community. However, the variant-specific factors associated with vertical transmission have not been determined. For additional information on vertical transmission and infants born to people with SARS-CoV-2 infection, see Special Considerations in Children.

Racial and Ethnic Disparities Among Pregnant People With COVID-19

Between January 22 and June 7, 2020, the CDC received reports of 8,207 women who were pregnant at the time of their COVID-19 diagnosis. Among these women, 46% were reported to be Hispanic, and 22% were reported to be Black.¹¹ Those proportions were higher than the proportions of Hispanic (24%) and Black (15%) women who gave birth in 2019, suggesting that pregnant people who are Hispanic or Black may be disproportionately affected by SARS-CoV-2 infection. It is important to note that these disparities are related to social determinants of health, current and historic inequities in access to health care and other resources, and structural racism. The American College of Obstetricians and Gynecologists (ACOG) has <u>published guidance</u> on addressing health equity during the COVID-19 pandemic.

Prevention of COVID-19 in Pregnancy

Pregnant people should be counseled about the increased risk for severe disease from SARS-CoV-2 infection and the measures they can take to protect themselves and their families from infection. Nonpharmacologic measures include practicing physical distancing, washing hands regularly, and wearing a face covering as per guidance from the CDC.

COVID-19 Vaccines

The COVID-19 Treatment Guidelines Panel (the Panel) recommends against withholding COVID-19 vaccination from pregnant or lactating individuals specifically because of pregnancy or lactation (AIII). COVID-19 Treatment Guidelines

Pregnant people should be counseled about the benefits of COVID-19 vaccination, which include a decreased risk of severe disease and hospitalization for the pregnant person and a decreased risk of hospitalization for the infant in the first 6 months of life.¹² The Society for Maternal-Fetal Medicine, the ACOG, and the CDC recommend that all eligible people, including pregnant and lactating individuals and those planning to become pregnant, receive COVID-19 vaccines as recommended.¹³⁻¹⁵ The CDC has published up-to-date guidance regarding COVID-19 vaccination, including guidance for administering vaccines to pregnant and lactating individuals.¹⁶ COVID-19 vaccines can be administered regardless of trimester and in concert with other vaccines recommended during pregnancy.¹⁴

Pregnant people were not included in the initial COVID-19 vaccine studies. However, a growing body of observational data supports the efficacy and safety of administering COVID-19 vaccines to this population. At this time, the mRNA vaccines BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) are recommended for pregnant or lactating individuals. The adjuvanted vaccine NVX-CoV2373 (Novavax) can also be used.^{14,15} For the most up-to-date clinical recommendations, see the <u>CDC</u> guidelines on using COVID-19 vaccines. The ACOG and the Society for Maternal-Fetal Medicine provide guidance for counseling pregnant and lactating patients about COVID-19 vaccination.^{13,14}

Efficacy

A prospective cohort study of 131 subjects at 2 academic medical centers compared the immunogenicity and reactogenicity of the mRNA COVID-19 vaccines in pregnant and lactating women and nonpregnant controls.¹⁷ The study also compared vaccine-generated immunity to the immune response to natural SARS-CoV-2 infection among pregnant participants. Maternal immunoglobulin G antibody levels were similar after vaccination in pregnant and lactating women and in nonpregnant controls, and the antibody response did not differ by trimester of vaccination. Vaccinated pregnant women had significantly higher levels of antibodies than pregnant women who had had natural SARS-CoV-2 infection during the previous 4 to 12 weeks.

Antibody Transfer to the Neonate

The available data indicate that vaccine-derived antibodies are passively transferred to the neonate during pregnancy and lactation.¹⁸ A case control study that was conducted at 20 pediatric hospitals in 17 states in the United States from July 1, 2021, to January 17, 2022, assessed the relationship between maternal vaccination with a 2-dose mRNA COVID-19 vaccine during pregnancy and pediatric hospitalization for COVID-19.¹² In this study, 379 infants aged <6 months were hospitalized. Among these infants, 176 had COVID-19 and were considered case infants. The remaining 203 infants did not have COVID-19 and were considered control infants. Sixteen percent of the mothers of the case infants had received 2 doses of COVID-19 vaccine during pregnancy compared with 32% of the mothers of control infants.

Maternal completion of a 2-dose primary mRNA COVID-19 vaccination series during pregnancy led to a decrease in the number of infant hospitalizations for COVID-19 during the first 6 months of life (61% decrease; 95% CI, 31% to 78%).¹² There were no statistically significant differences between the case infants and control infants in the presence of underlying medical conditions or the occurrence of premature birth. Of the 43 case infants who were admitted to the ICU, 88% had mothers who were unvaccinated. These data further support the CDC's recommendation for COVID-19 vaccination in people who are pregnant, breastfeeding, or trying to become pregnant or who might become pregnant in the future.¹⁶

Safety

A study that used data from 3 vaccine safety reporting systems in the United States reported that the frequency of adverse events among 35,691 vaccine recipients who identified as pregnant was similar to the frequency observed among nonpregnant patients.¹⁹ Local injection site pain, nausea, and vomiting were reported slightly more frequently in pregnant people than in nonpregnant people. Other systemic reactions were reported more frequently among nonpregnant vaccine recipients, but the overall *COVID-19 Treatment Guidelines*

reactogenicity profile was similar for pregnant and nonpregnant patients.

From December 2020 to June 2021, a total of 22,953 pregnant people in the United States were enrolled in the COVID-19 Vaccine Pregnancy Registry.²⁰ An analysis that compared historic cohorts with people who received a COVID-19 vaccine during pregnancy found no increased risk of spontaneous abortion; major birth defects; or pregnancy-associated outcomes, including stillbirth, preterm birth, hypertensive disorders of pregnancy, neonatal ICU admission, or maternal ICU admission.²¹

Managing COVID-19 in Pregnancy

In pregnant patients, as in nonpregnant patients, SARS-CoV-2 infection can present as asymptomatic or presymptomatic disease or with a wide range of clinical manifestations, from mild symptoms to severe disease and respiratory failure that requires ICU admission. The illness severity, underlying comorbidities, and clinical status of pregnant patients who have symptoms compatible with COVID-19 should be assessed to determine whether in-person evaluation for potential hospitalization is needed.

If hospitalization for COVID-19 is indicated, care should be provided in a facility that can conduct maternal and fetal monitoring, when appropriate. General management of COVID-19 in pregnant patients should include:

- Fetal and uterine contraction monitoring based on gestational age, when appropriate
- Individualized delivery planning
- A multispecialty, team-based approach that may include consultation with obstetric, maternal-fetal medicine, infectious disease, pulmonary-critical care, and pediatric specialists, as appropriate

In general, the recommendations for managing COVID-19 in nonpregnant patients also apply to pregnant patients.

Therapeutic Management of COVID-19 in the Setting of Pregnancy

To date, most SARS-CoV-2-related clinical trials have excluded individuals who are pregnant or lactating. In cases where lactating and pregnant individuals have been included in studies, only a small number have been enrolled. This makes providing evidence-based recommendations on the use of anti-SARS-CoV-2 therapies in these vulnerable patients difficult and potentially limits their treatment options. When possible, pregnant and lactating individuals should not be excluded from clinical trials of COVID-19 therapeutic agents or vaccines.

The Panel **recommends against** withholding COVID-19 treatments from pregnant or lactating individuals specifically because of pregnancy or lactation (AIII).

Data on the use of COVID-19 therapeutic agents in pregnant and lactating people are limited. Pregnancy is a risk factor for severe COVID-19. Studies have demonstrated that pregnant individuals are at increased risk of ICU admission, mechanical ventilation, and death, as well as poor obstetric and neonatal outcomes.¹⁴ When making decisions about treatment, pregnant or lactating people and their clinical teams should use a shared decision-making process and consider several factors, including the severity of COVID-19, the risk of disease progression based on the person's comorbidities, and the safety of specific medications for the fetus, infant, or pregnant or lactating individual.

For details regarding therapeutic recommendations and pregnancy and lactation considerations, see <u>Therapeutic Management of Nonhospitalized Adults With COVID-19</u>; <u>Therapeutic Management of Hospitalized Adults With COVID-19</u>; <u>Pregnancy, Lactation, and COVID-19</u> Therapeutics; and the individual drug sections. In general, the therapeutic management of pregnant patients with COVID-19

should be the same as for nonpregnant patients, with a few exceptions (AIII). Notable exceptions include:

- The Panel **recommends against** the use of **molnupiravir** for the treatment of COVID-19 in pregnant patients unless there are no other options and therapy is clearly indicated (AIII). For more information regarding the use of molnupiravir in pregnant patients, see <u>Pregnancy, Lactation, and COVID-19 Therapeutics</u>.
- Pregnant patients were not included in most of the clinical trials that evaluated therapeutic anticoagulation in the setting of COVID-19, and there is a potential for increased maternal risks if bleeding occurs during pregnancy. Therefore, there is insufficient evidence for the Panel to recommend either for or against the use of therapeutic anticoagulation in pregnant patients with COVID-19 who do not have evidence of venous thromboembolism.

Timing of Delivery

The ACOG provides <u>detailed guidance</u> on the timing of delivery and the risk of vertical transmission of SARS-CoV-2.

In most cases, the timing of delivery should be dictated by obstetric indications rather than maternal diagnosis of COVID-19. For people who had suspected or confirmed COVID-19 early in pregnancy and who recovered, no alteration to the usual timing of delivery is indicated.

After Delivery

Therapeutic management in postpartum patients should follow guidelines for nonpregnant patients. However, the use of anticoagulant therapy in the immediate postpartum period should be individualized, as there may be an increased risk of bleeding, especially after an operative delivery.

The majority of studies have not demonstrated the presence of SARS-CoV-2 in breast milk; therefore, breastfeeding is not contraindicated for people with laboratory-confirmed or suspected SARS-CoV-2 infection.²² Precautions should be taken to avoid transmission to the infant, including practicing appropriate hand hygiene, wearing face coverings, and performing proper pump cleaning before and after breast milk expression.

The decision to feed the infant breast milk while the lactating patient is receiving therapeutic agents for COVID-19 should be a collaborative effort between the patient and the clinical team, including infant care providers. The patient and the clinical team should discuss the potential benefits of the therapeutic agent and evaluate the potential risk of pausing lactation on future breast milk delivery to the infant.

Specific guidance on the postdelivery management of infants born to individuals with known or suspected SARS-CoV-2 infection, including breastfeeding recommendations, is provided by the <u>American Academy of Pediatrics</u>.

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