

Maternal Vaccination and Vaccine Hesitancy



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KEYWORDS

- Prenatal care • Vaccination • Vaccination hesitancy • Tdap vaccine
- Influenza vaccine • COVID-19 vaccine

KEY POINTS

- Influenza, Tdap, and COVID-19 vaccines are safe to give during pregnancy.
- These vaccines provide protection to newborns via transplacental transfer and prevent maternal morbidity caused by influenza and COVID-19.
- Obstetric care providers should stock vaccine in their office to increase vaccination rates.
- Obstetric care providers and their office staff should continue to offer vaccines even if a pregnant person refused the vaccine previously.
- Vaccine safety is the most common concern for patients; future studies in vaccine communication and counseling for obstetric care providers are needed.

INTRODUCTION

Vaccination is an essential part of the care of pregnant patients. No adverse fetal impacts have been identified with inactivated virus, toxoid, or bacterial vaccines. Live-attenuated vaccines should be reserved for the postpartum period.¹ The American College of Obstetrics and Gynecology (ACOG) recommends that both inactivated influenza vaccine and Tdap are given during every pregnancy and that all pregnant individuals are vaccinated against COVID-19. Specifically, the influenza vaccine is recommended during each influenza vaccination season as soon as it becomes available. It can be given in any trimester. The ideal window to receive Tdap extends from 27 to 36 weeks gestation to maximize passive antibody transfer for the newborn.¹ COVID vaccine, including boosters, is recommended any time during pregnancy when a patient is eligible. The most recent US estimates of pregnancy vaccination rates, from 2019 to 2020, showed 61.2% of pregnant people received the influenza vaccine, 56.6% received Tdap, and 40.3% received both vaccines.² COVID-19 rates of full vaccination among pregnant people were last reported to be above 70%, with the

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majority of people now fully vaccinated before pregnancy.³ Significant racial disparities in full vaccination coverage for COVID remain, with 89.5% of Asians being fully vaccinated before or during pregnancy, 67.9% among White, and 58.1% among Black pregnant people.³

For influenza and Tdap vaccine, the highest vaccination rates were among those who received a provider offer or referral for vaccination. Racial and ethnic disparities in pregnancy vaccination rates are particularly notable for the Tdap vaccine with 35.8% coverage among Hispanic women and 38.8% among Black women compared with 65.5% of White women. Data from the Pregnancy Risk Assessment Monitoring Systems survey showed that after adjustment for factors including maternal age, marital status, education, prenatal care utilization, and smoking, Black women were 30% less likely to receive the influenza vaccine compared with non-Hispanic White women.⁴ In addition, women living in rural areas were less likely to receive influenza vaccination during pregnancy.⁵ Overall, approximately 40% of pregnant people do not receive influenza and Tdap vaccines, which leaves them vulnerable to maternal and neonatal infection. An analysis of National Health Interview Survey (NHIS) data from 2012 to 2018 showed that the strongest predictor of vaccination during pregnancy was having health insurance, followed by having a higher income and greater level of education.⁶

DISCUSSION

Influenza

Pregnancy increases the risk of morbidity and mortality related to influenza infection; it is associated with physiologic changes including decreased lung capacity and increased cardiac output that leave patients vulnerable to the impacts of influenza infection.⁷ This was particularly notable during the H1N1 pandemic when pregnant people were more likely to be hospitalized and also more likely to die from the infection compared with those who were not pregnant.⁸

Large cohorts of pregnant patients have been followed after inactivated influenza vaccination. There is no association between vaccination and adverse pregnancy outcomes including cesarean delivery, preterm birth, or infant medical conditions up to 6 months of age.⁹ Longitudinal prospective studies of influenza vaccination in pregnancy following children up to 7 years of age found no increase in congenital malformations, malignancies, or neurocognitive delays.⁷

Prior studies have shown that inactivated influenza vaccine is effective in reducing hospitalization in pregnancy by an average of 40%.¹⁰ Not only does the vaccine prevent maternal infection but also transplacental influenza antibody transfer occurs and provides protection for newborns who cannot receive the vaccine before 6 months of age.^{7,8} A recent meta-analysis showed that maternal influenza vaccination was associated with an overall reduction of influenza infection in infants of 34%.¹¹ In addition, administration of the influenza vaccine during pregnancy is associated with a decreased risk of preterm birth and low birth weight infants.¹²

Despite the value of vaccination, pregnant people have low influenza vaccination rates. Health care workers effect the decisions of patients when they are considering influenza vaccination. They can play an important role in protecting pregnant people and their infants from a vaccine-preventable disease. Understanding and communicating the safety and efficacy of influenza vaccine is essential.⁷

Tdap

The ACOG recommends that all pregnant patients receive a Tdap vaccine during each pregnancy to prevent pertussis in infants¹ as the infant pertussis vaccination series

does not begin until 2 months of age. When Tdap vaccine is given as early as possible in the 27 to 36 weeks of gestation window, it benefits the neonate by passive transfer of antibodies across the placenta.¹

A large retrospective cohort found that the maternal Tdap vaccination was highly protective against pertussis infection in infants, particularly in the first 2 months of life.¹³ There was 91.4% effectiveness among infants during the first 2 months and 69% during the first year of life. The protection from hospitalization was 94% and from pertussis-related death was 95%. Providing Tdap immunization during pregnancy is even more effective for protecting newborns compared with “cocooning,” in which people with close contact to the infant are vaccinated (eg, postpartum maternal vaccination) as a form of infant protection.¹³

A systematic review of 1.4 million pregnant patients who received the Tdap vaccine investigated its safety. Those receiving the vaccine had no increased risk for adverse birth outcomes, including preterm birth. The study found a slightly higher incidence of chorioamnionitis in those who received Tdap; fever following the vaccine was reported in up to 3% of pregnant patients.¹⁴ Risk ratios for chorioamnionitis were small and did not seem to be clinically relevant. A more recent retrospective review of 5 years of birth data in Ontario, Canada, found no association with chorioamnionitis or other adverse events.¹⁵

COVID-19

Following the release of the initial COVID-19 vaccines in December 2020, multiple national and international societies representing obstetric and reproductive health care providers released a unified statement supporting public health measures to combat COVID-19, which included the emergency authorized use of COVID-19 vaccines in pregnancy. The group also urged the inclusion of pregnant people in vaccine trials.¹⁶ In July 2021, the centers for disease control and prevention (CDC) released new data on the safety of COVID-19 vaccination in pregnancy, and at this time, the ACOG officially announced a strong recommendation for the COVID-19 vaccine in pregnancy.¹⁷

A systematic review of mRNA COVID-19 vaccines given during pregnancy included more than 48,000 subjects and demonstrated that both the Pfizer-BioNTech and Moderna vaccines can prevent SARS-CoV-2 infection in pregnant people.¹⁸ The most common adverse reactions were similar to the general population and included pain at the injection site, fatigue, and headache. In a systematic review, pregnant people who received COVID-19 vaccine during pregnancy did not have a higher risk of adverse pregnancy or neonatal outcomes compared with unvaccinated pregnant people.¹⁹

In addition to effectiveness in prevention of maternal COVID-19 during pregnancy, the vaccine has been associated with a decrease in the stillbirth rate.²⁰ In a systematic review, antibody responses were rapid after the first vaccine dose. After the second dose, antibody responses were stronger and associated with better transplacental antibody transfer. Longer intervals between first vaccination dose and delivery were also associated with higher antibody fetal IgG measured in cord blood and a better antibody transfer ratio.¹⁸ Maternal completion of the two-dose COVID-19 vaccination series during pregnancy was associated with a decrease in hospitalization among infants less than 6 months of age.²¹ In addition, vaccinations conferred protective immunity to newborns through breast milk.¹⁹ COVID-19 vaccination in pregnancy has clearly demonstrated both maternal and neonatal benefit, though future studies are needed to clarify optimal timing as well as utility of repeat vaccination during pregnancy.

Vaccination Disparities and Reasons for Hesitancy

Numerous factors contribute to lower uptake of influenza vaccine among Black nonpregnant adults that carry over into vaccine hesitancy during pregnancy; the key factors include attitudes and beliefs, knowledge, lack of access, trust in health care providers and vaccines, risk perception, and racial discrimination.²² Historical medical injustices and ongoing racial discrimination contribute to mistrust of the health care system.²³ For pregnant people, research has shown that compared with White women, Black and Hispanic women were less confident in vaccine safety and efficacy and less likely to trust information from health care providers and public health authorities.²⁴ Black women were the least confident in the safety of the maternal influenza and Tdap vaccine. This is important, as women with higher confidence in vaccine safety and efficacy for themselves and their infant, as well as those with higher perceived risk of influenza and pertussis disease had greater intention to receive flu and Tdap vaccines (four to nine times greater odds of vaccine acceptance).^{25,26} In addition, those pregnant for the first time were less sure of their vaccine knowledge and intentions than those with prior children. In a meta-analysis of factors that influence maternal vaccination in pregnancy believing there was potential for vaccine-induced harm had a negative influence on seasonal influenza vaccine uptake (OR 0.22, 95% CI 0.11–0.44) and reduced the odds of being vaccinated fivefold.²⁵ Prior influenza vaccination is a strong predictor of influenza vaccination during pregnancy²⁷; the odds of receiving an influenza vaccine during pregnancy are three to five times greater if an individual receives an influenza vaccine outside of pregnancy. Factors specifically associated with increased Tdap vaccination include receiving an influenza vaccination, having the vaccine available on-site at the obstetrician's office, and having a higher number of prenatal care visits.^{28,29}

A health care provider recommendation is one of the strongest predictors of immunization during pregnancy for both influenza and Tdap.^{28,30} A meta-analysis of factors that influence vaccine decision-making for pregnant women found the odds of receiving a pertussis or influenza vaccination are 10 to 12 times higher among pregnant women who received a provider recommendation.²⁵ Black women historically report a lower rate of being recommended or offered influenza vaccine during pregnancy,³¹ and among those offered, Black women are less likely to receive the vaccine compared with other women.² In addition, receipt of a provider offer or referral for Tdap during pregnancy was lower among Black than among Hispanic women and White women in 2020. Among those with a provider offer for Tdap vaccination, coverage was lowest for Hispanic women, followed by Black women, and White women.²

Influenza Vaccine Hesitancy

In a 2016 survey of obstetric providers, the most commonly reported reasons for vaccine refusal were patients' belief that influenza vaccine makes them sick (48%), belief they are unlikely to get a vaccine-preventable disease (38%), general worries about vaccines (32%), desire to maintain a natural pregnancy (31%), and concern that their child could develop autism as a result of vaccination during pregnancy (25%).³² The extrapolation of autism fears to vaccination in pregnancy highlights the potential impact of vaccine safety misinformation. Many obstetric providers believed that stressing the potential harm of disease to the newborn was most effective in conversations with patients. The patient concerns reported by providers match those that have been reported directly by patients.³³ Specifically, patients worry about side effects for themselves and potential harm for their fetus; some have concerns about vaccine ingredients, such as mercury, and some believe the vaccine is not effective at preventing influenza disease.³⁴

COVID Vaccine Hesitancy Reasons

Because pregnant people were not included in COVID-19 vaccine clinical trials, the advice regarding receipt of COVID vaccine for pregnant people changed rapidly over the course of 2020 to 21. During the early years of the pandemic, pregnant patients who were Black, Hispanic, younger, with lower education, prior refusal of the influenza vaccine, or who were not counseled about the COVID vaccination had lower vaccine acceptance.^{19,35}

Studies have examined reasons for COVID vaccine hesitancy during pregnancy, some of which are the same as those for nonpregnant patients, and some of which are specific to pregnancy. Most commonly, women who are hesitant report lack of information about vaccine safety during pregnancy,³⁵ on fetal development, and on later child well-being.³⁶ Conversely, the predictors of vaccine acceptance include confidence in vaccine safety and effectiveness, worrying about COVID-19, compliance to mask guidelines, trust of public health agencies, and positive attitudes toward routine vaccines.³⁷

Specific Issues Related to Pregnancy

Specific issues related to pregnancy care offer opportunities to increase vaccination rates. For most patients, office visits during pregnancy are frequent, with 12 to 14 visits recommended during a healthy pregnancy. Visits tend to be monthly during the first 4 to 28 weeks, then every other week from 28 to 36 weeks gestation, and weekly thereafter. During the COVID-19 pandemic, a shift toward telemedicine visits occurred to limit exposure to the virus; some offices recommended 6 or fewer in-person visits during pregnancy, with alternate visits offered virtually.^{38,39} The first prenatal visit is longer and more comprehensive, allowing an opportunity to discuss healthy living and health care, including vaccinations, during pregnancy.⁴⁰ The influenza vaccine is often offered at the first prenatal visit is seasonally appropriate, and some offices combine the 28-week glucose test for diabetes with an opportunity to give the Tdap vaccine. If patients refuse either the influenza or Tdap vaccine, vaccination can be discussed again at future visits as patients are seen frequently.

Increasing evidence shows that many parents make decisions about vaccines for their children during pregnancy, or even before conception.^{41–43} One study of low-income pregnant women found that half considered pregnancy to be the best time to receive information about childhood vaccination and were most likely to indicate the nurse who gave them vaccines as the person with whom they would like to discuss childhood vaccines.⁴⁴ More research is needed to assess the feasibility of having discussions of childhood vaccines in the obstetric office as well as the willingness of obstetric nurses and providers to take on this role.

Evidence to Overcome Vaccine Hesitancy/Increase Rates

Several approaches aimed at increasing maternal vaccination rates during pregnancy have been successful (**Table 1**). As noted above, a provider recommendation is the most important predictor of vaccine uptake for pregnant people.⁴⁵ However, there is a gap in communication training for obstetric providers, with little or no training available in how best to communicate with vaccine-hesitant patients.⁴⁶ Regarding specific communication techniques, studies show that message framing (loss- or gain-framed) in isolation is not an effective intervention.^{47,48} In a survey of obstetricians, the most commonly reported strategies used to address refusal were stating that it is safe to receive vaccines in pregnancy (96%), explaining that not getting the vaccine puts the fetus or newborn at risk (90%) or not getting the vaccine puts the pregnant

Intervention	Evidence
Provider recommendation	++
Stocking vaccines in practice	++
Standing orders	+
Group prenatal care	+
Offering vaccination more than once	+
Provider prompt	+
Multifaceted QI intervention	+
Patient education	+/-
Patient reminders	+/-

Strong evidence (++); Some evidence (+); No evidence (-).

person's health at risk (84%).³² The strategy perceived as most effective was stating that not getting vaccinated puts the fetus or newborn at risk. In addition, it is necessary to continue to offer vaccine despite refusal; in one study, 20% of pregnant people who received influenza vaccine had previously refused it.⁴⁹ Emphasizing the need for vaccination more than once helps patients realize its importance.

In a systematic review that examined interventions to increase influenza vaccination rates, educational interventions aimed at pregnant people resulted in higher rates in half of studies.⁵⁰ Many interventions have been tried, including pamphlets, text messages, video, and apps for pregnant individuals.^{48,51-54} Two studies using educational pamphlets increased vaccination rates; the pamphlets discussed flu vaccine safety and the benefit of the vaccine to the pregnant person and the infant.^{51,55} Educational text messaging⁵⁶ and video-based education⁵⁴ did not improve rates. It remains unclear how best to educate pregnant individuals to increase vaccine uptake and how to combat misinformation.

Several studies of mothers have found that information focusing on the benefit and safety of vaccines given to pregnant people to protect their infant is beneficial and preferred to information about protecting the pregnant person.^{55,57} A different approach is to target-specific concerns; an app-based intervention that provided videos based on parent needs was well received by pregnant people, even among those who were vaccine hesitant; this has not yet been shown to increase vaccination rates.⁵⁸ Patients use CDC and pregnancy Websites for vaccine information, but they value information from their providers.⁵⁹

Other practice-based interventions that can be effective include changing the model of care to group visits, offering reminders to patients, prompting providers, and having standing orders in place. Stocking vaccines in the practice is also associated with increased uptake,⁶⁰ so patients do not have to make separate appointments or travel to off-site locations for vaccination. A study of group prenatal care found a much higher rate of influenza vaccine uptake (62% vs 38%) in the group model compared with traditional care group.⁶¹ The increase was attributed to both more patient education and social support.

Reminders for pregnant patients to return for vaccines have been shown to be effective in one study. Specifically, text message reminders in the fall increased influenza vaccination uptake during pregnancy.⁵³ In a public health campaign, Text4Baby, computerized reminders that pregnant people sign up for online, increased influenza vaccination during pregnancy, particularly for those whose provider had not

recommended the vaccine.⁶² Such reminders can serve as a way to message patients who have fewer health care visits.

Office-based interventions have the potential to increase vaccination rates. In one study, a prompt to the provider from the electronic health record was associated with a dramatic increase in Tdap vaccination at 32 weeks gestation; this occurred at a time when recommendations changed from offering the vaccine from postnatal to prenatal, so the prompt was not tested alone.⁶³ In addition, standing orders have been shown to be effective for both Tdap and influenza vaccine.^{64,65} Given that many electronic health record (EHRs) have checklists to indicate specific tests done during pregnancy, using such a list or other easily visible documentation has the potential to serve as a reminder to staff and providers as well.

More than one approach is likely necessary to dramatically increase rates, as is needed for childhood and adolescent vaccines.⁶⁶ One example of combining multiple interventions is the AFIX-OB intervention.⁶⁷ This program was modeled after the CDCs AFIX QI program. It provided QI strategies (eg, standing order, EHR reminder), technical assistance with immunization champions, incentives, and practice-based tools. The program was successful in increasing rates of influenza and Tdap vaccination rates in two states. It is important to see if such interventions can be scaled-up to affect a larger population in a cost-effective way.

SUMMARY

Vaccination during pregnancy is critical for both maternal and neonatal protection as many vaccines cannot be administered until 2 to 6 months after birth. Although pregnant patients were excluded from many initial vaccination safety studies, growing safety data are reassuring for inactivated influenza, Tdap, and COVID-19 vaccination. There are known racial disparities in vaccination rates, with Black women often having lower rates compared with women of other races; efforts must be made to make health care during pregnancy equitable. Vaccine hesitancy has many potential sources, but effective strategies to overcome hesitancy include directed obstetric provider recommendations, improved access, and continuing to offer vaccine. Additional research is needed specifically focused on communication with vaccine-hesitant pregnant patients.

CLINICS CARE POINTS

- Personal vaccination recommendations from obstetric providers are crucial.
- Vaccination discussions that focus on the safety and benefit for the infant are preferred by pregnant individuals.
- Providers should offer vaccines even if previously refused as patients may be more accepting later in pregnancy.
- Stocking vaccine in the obstetric provider office is needed to increase rates.
- Standing orders can be used as an effective way to increase vaccination rates.
- A multipronged approach that includes effective communication as well as workflow changes is likely needed to increase vaccination rates for pregnant individuals.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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