

Pregnancy and Influenza Vaccination: Making an Informed Choice

by

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Part I – Influenza, Pregnancy, and Vaccinations

Lucia, a first-time pregnant mother, let out a sigh as she sank into her couch. She had just returned from her pregnancy support group, which usually helped to calm her nerves, but today was different. After the session, she overheard some of the other expectant parents talking about people they knew catching the flu. This made Lucia nervous; she had contracted the influenza virus and been sick with the flu (i.e., the disease caused by influenza virus infection) before she was pregnant but had no idea how it might affect her now. Lucia ultimately just wanted to make an informed choice about influenza vaccination that was best for the fetus she was carrying and herself. After some thought she decided to learn more about the interplay between pregnancy and the influenza virus to better understand the symptoms of infection, risks during pregnancy, and how she might prevent infection from influenza. She did some research online and this is what she found:

Although there are four types of influenza viruses (influenza A–D), influenza A is most common in humans and causes a highly contagious respiratory illness. While influenza B can also be the cause of seasonal influenza epidemics in humans, influenza A is more virulent and usually has more severe disease outcomes (Nuwarda et al., 2021). Influenza viruses have glycoproteins hemagglutinin (HA) and neuraminidase (NA) on their surface, which help the virus enter and infect cells. Symptoms of infection usually include fever, body aches, headaches, fatigue, and cough but severe cases can lead to hospitalization and death (Nuwarda et al., 2021; Yu et al., 2022). Pregnant individuals are considered at high risk for flu, which could be caused by a weakening in the immune response and the stress pregnancy puts on the cardiac and respiratory systems (Rand & Olson-Chen, 2023; Yu et al., 2022). Additionally, contraction of the influenza virus during pregnancy is linked with increased risk of hospitalizations, intensive care unit admissions, maternal mortality, and pregnancy loss. Influenza A can also affect the fetus and newborn potentially causing preterm labor, congenital anomalies, and newborn mortality (Yu et al., 2022). The most effective prevention strategy is maternal influenza vaccination (CDC, 2024d).

The information Lucia found was quite concerning. She was nervous to leave the house in case she came into contact with the virus. She remembered briefly reading about influenza vaccinations the last time she was immunized but was eager to learn more; specifically, more about the safety and efficacy for her and the growing fetus. Lucia turned to the Centers for Disease Control and Prevention (CDC) website for more information:

The CDC and Advisory Committee on Immunization Practices (ACIP) recommend influenza vaccination during any trimester of pregnancy. The most effective flu prevention strategy is maternal influenza vaccination (CDC, 2024d). Studies show that vaccination reduces the risk of flu by almost half in pregnant individuals, which closely matches the effectiveness of the influenza vaccine in non-pregnant adults during flu seasons (Thompson et al., 2014). They also provide evidence that pregnant people who receive an influenza vaccination have a 40% reduced risk of influenza associated hospitalization (Thompson et al., 2019). Importantly, studies show even greater protection to the infant once they are born, protecting them from two-thirds of influenza virus infections (Regan & Munoz, 2021).

The CDC has also conducted studies that support the safety of influenza vaccination for pregnant individuals (CDC, 2024e). Quotes summarizing key findings are below:

- Review of reports to the Vaccine Adverse Event Reporting System (VAERS) found no evidence to suggest a link between pregnancy complications or adverse fetal outcomes among pregnant women and flu shots (CDC, 2024e).
- A large study using Vaccine Safety Datalink (VSD) data from three flu seasons (2012–13, 2013–14, 2014–15) found no increased risk for spontaneous abortion (miscarriage) after flu vaccination during pregnancy (CDC, 2024e).
- A large study using VSD data found no increased risk for adverse pregnancy events (like chorioamnionitis, pre-eclampsia, or gestational hypertension) for pregnant women who received the flu vaccine from 2002 to 2009 when compared to pregnant women who were not vaccinated (CDC, 2024e).
- A VSD study examined stillbirth rates in pregnant women aged 14–49 years between 2007 and 2015 and did not find a significant association between influenza vaccination during pregnancy and stillbirth (CDC, 2024e).

After this research, Lucia decided that receiving an influenza vaccine would be the best choice for her and her baby, but she still wasn't quite sure how they worked and which kind would be the best for her situation. To help answer these questions, she turned back to her laptop and continued reading:

All influenza vaccines in the U.S. protect against four strains, two influenza A viruses and two influenza B viruses. There are several types of influenza vaccines that are approved for certain populations (CDC, 2024a; Nypaver et al., 2021). Inactivated vaccines—those with virus that cannot replicate—are Food and Drug Administration (FDA) recommended for people 6 months and older. Live attenuated vaccines—those that contain virus that can replicate but are weakened—are FDA approved for those who are not pregnant or immunocompromised, ages 4–49. Finally, recombinant vaccines are FDA approved for adults over the age of 18. These vaccines are produced using slightly different strategies which are shown in Figure 1 below (see next page).

Questions

1. Why are pregnant individuals considered high risk for influenza?
2. How do disease outcomes differ for an individual who contracts influenza during pregnancy versus contracting influenza when they are not pregnant?
3. How does influenza vaccine efficacy compare between pregnant and non-pregnant individuals?
4. What is one piece of evidence Lucia found that supports the safety of influenza vaccination during pregnancy?

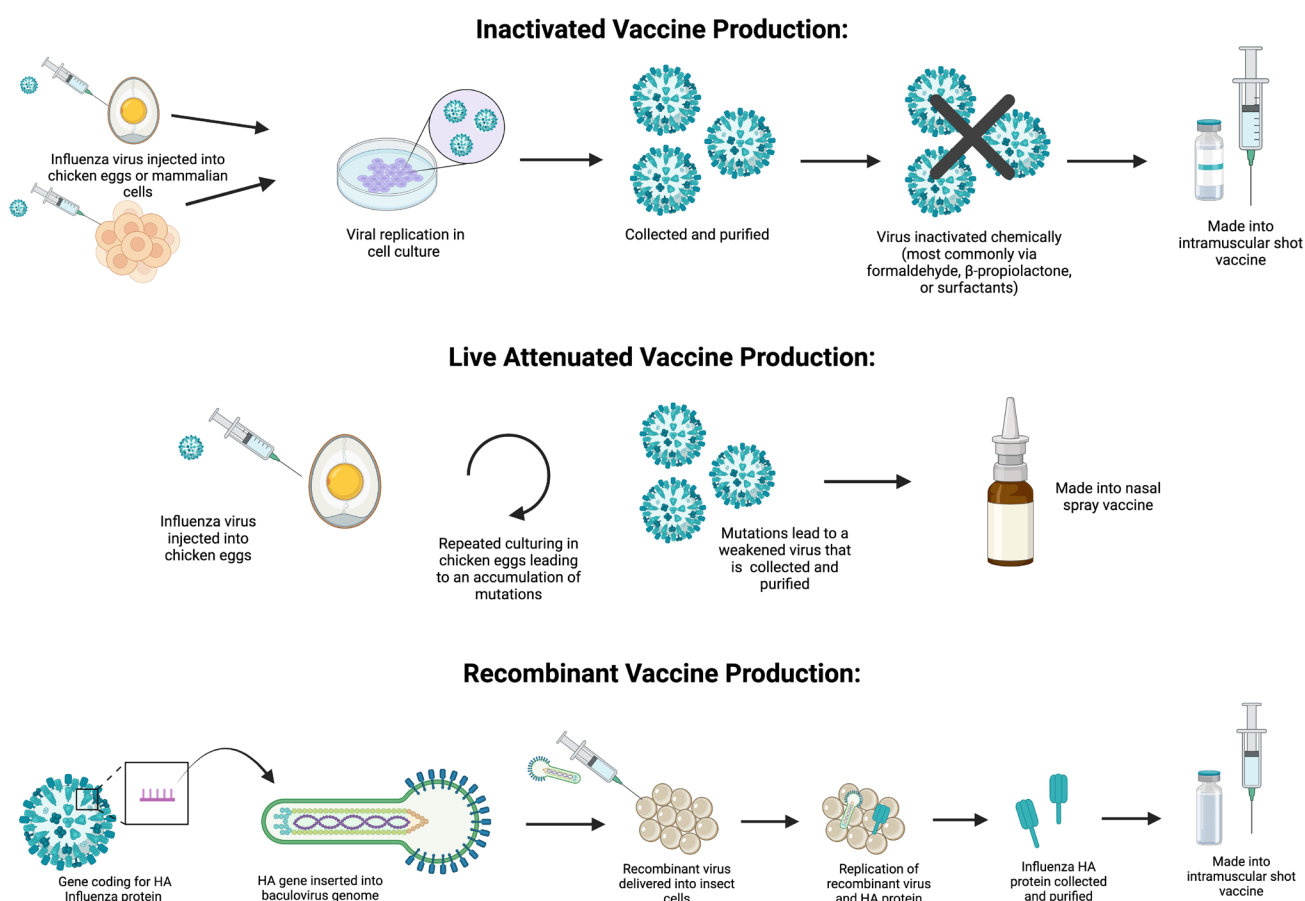


Figure 1. Three main types of influenza vaccines and how they are produced. *Credit:* Created in Biorender.com.

5. Using Figure 1 above, complete Table 1 below to compare the influenza vaccine types.

Table 1. Vaccine comparison.

	<i>Inactivated</i>	<i>Live Attenuated</i>	<i>Recombinant</i>
<i>What is/are the part(s) of the virus found in this vaccine that the immune system responds to?</i>			
<i>How is/are the part(s) of the virus amplified during the production of this vaccine?</i>			
<i>Is this vaccine safe for individuals who are immunocompromised?</i>			

6. Using what you have learned from Lucia's research, help her make an informed choice:

- Which vaccine would you recommend for Lucia during her pregnancy?
- Why might this be the best option?

Part II – The Immune Response and Passive Immunity

Lucia's research led her to decide to get an inactivated influenza vaccine, but she was still curious about how the vaccine worked and wanted to learn more. She decided to investigate how her immune system would respond to different vaccines and how they would directly protect her body from the flu.

The immune response to influenza vaccine is an active immune process, very similar to its response to a natural viral infection. Figure 2 [see below] shows how inactivated influenza vaccines (IIV) are recognized by antigen presenting cells (APC) such as macrophages and dendritic cells (DC). These immune cells ingest the inactivated virus via phagocytosis and break it down into smaller pieces (antigen). They then present the antigen on class II major histocompatibility complexes (MHC II) which allows for the recognition of exogenous (foreign) antigen by a helper T cell's T cell receptor. Since the whole virus is used in this vaccine a variety of antigens may be recognized. From this interaction, helper T cells can become activated and secrete cytokines, small proteins or peptides that help regulate immune cell function. As a result of helper T cell cytokines and B cell receptor (BCR) activation by components of the virus, B cells are activated. Once B cells are activated, they can differentiate into either short- or long-lived plasma cells that make antibodies to this particular antigen or become memory B cells which provide immunologic memory to future infection from the same pathogen (Akkaya et al., 2020). The memory B cells produced in response to the vaccine allow the body to remember and recognize the influenza virus when encountered naturally and eliminate the pathogen before the virus can cause serious illness.

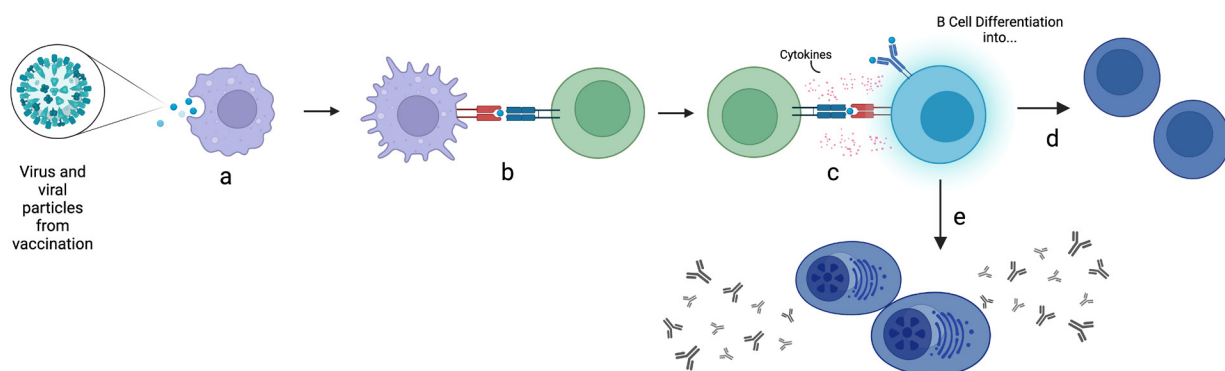


Figure 2. Immune response to inactivated influenza vaccine. Credit: Created in BioRender.com.

Figure 1 [see above, previous page] shows that the same is true for influenza recombinant vaccines, except only a specific protein is presented to the immune system (Incacare, 2021). The HA surface protein will stimulate an immune response to this specific viral-protein rather than a response to many different viral components. In future influenza encounters, the HA protein will be recognized and the host will have a quick, strong immune response against the HA protein, causing the elimination of the pathogen.

Live attenuated influenza vaccines (LAIV) can also activate an immune response through the mechanisms described above; however, these vaccines are more likely to induce an additional pathway of immune memory. In these vaccines, the virus is able to replicate in host cells, typically in the nasal passage and upper respiratory tract. Infected epithelial cells will then present endogenous antigen—antigen made within an infected cell—on class I major histocompatibility complexes (MHC I). Antigen presented on MHC I can cause the activation of cytotoxic T cells which function to kill the infected cells. By killing infected cells, it prevents the spread of the disease. Concurrently, APCs, helper T cells, plasma cells, and memory B cells can elicit a response to build up immunity and memory.

Although both IIV and LAIV can induce B cell and antibody responses, only LAIV has been shown to activate antibodies in the mucosal lining of the nasal cavity and upper respiratory tract where influenza infection typically starts. Hence, mucosal antibodies induced by LAIV reflect the mechanisms which define mucosal vaccination protection (Thwaites et al., 2023).

Questions

7. Describe the interactions between immune cells and viral particles using points a–e in Figure 2 above (see previous page).
 - a.
 - b.
 - c.
 - d.
 - e.
8. Draw the interaction between immune cells and live attenuated vaccine components that can lead to the activation of cytotoxic T cells.

As Lucia finished reading about vaccination and the immune system, she thought to herself, “It’s great that the vaccine would protect me, but how would it affect my developing baby?” So, she continued her research:

The placenta is an organ that develops during pregnancy and functions to provide nutrients and oxygen to the developing fetus (Cleveland Clinic, 2022.). It also helps to remove fetal waste products and facilitates placental circulation through it. Maternal antibodies, such as those made through influenza vaccination, can be transferred through the placenta to the fetus. This mechanism is called passive immunity. Rather than making antibodies like the pregnant person does as a part of active immunity, the fetus simply acquires them from the pregnant person. The fetus will then have immunity to influenza for as long as they have antibodies (around 6 months). After birth, a neonate is still very vulnerable to infection. To combat this, maternal antibodies can be passed through breastmilk (Albrecht & Arck, 2020; Lagousi et al., 2022). These antibodies end up in the infant’s intestinal mucosal membrane and protect against infection. Therefore, maternal vaccination not only benefits the pregnant individual, but also can provide immunity to the fetus and newborn through passive immunity.

Questions

9. Define passive immunity.
10. How does passive immunity differ from active immunity?
11. Consider what you know about how vaccination during pregnancy would impact the offspring:
 - a. How does a fetus receive immunity to influenza?
 - b. How might a newborn receive immunity to influenza?
 - c. Are the processes described in (a) and (b) above examples of active or passive immunity?

Part III – Vaccine Coverage and Health Equity

After her extensive research, Lucia was fairly confident about her decision. If she were to get an inactivated influenza vaccine, she would protect herself from the virus and pass immunity on to her baby. However, Lucia's doctor never mentioned the importance of influenza vaccination during pregnancy. She was curious how other pregnant parents in her group were thinking about it.

“Hey, I was wondering if any of you have gotten an influenza vaccine this season?” Lucia texted in her expectant parent group chat and anxiously awaited a response. *Ding!* Lucia quickly grabbed her phone. It buzzed in her hand as more messages appeared from others in the group.

Person 1: No, I normally do but I was worried it might hurt my baby.

Person 2: I have never gotten the vaccine before, and I've always been fine.

Person 3: I want to keep my pregnancy natural, so no.

Person 4: I did! My doctor recommended it!

Person 5: I also did, to protect my baby.

Person 6: Oh... I haven't even thought about it.

Lucia found these responses interesting. Her research had shown that vaccines are effective during pregnancy and could benefit both the pregnant person and the offspring before and after birth. So why were there so many different responses from the pregnancy group?

On Lucia's way into the hospital for her scheduled influenza vaccine, she noticed a pamphlet with the following vaccination coverage data (see Figure 3 below):

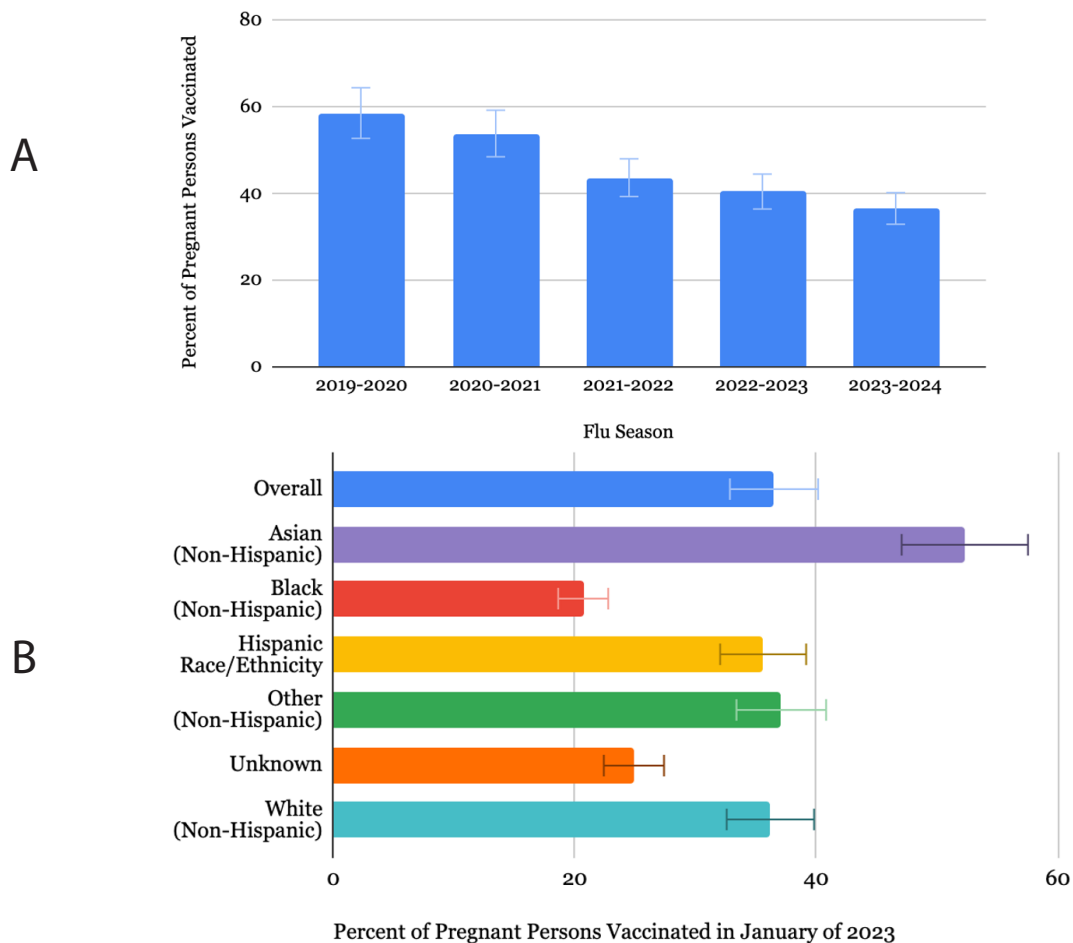


Figure 3. Influenza vaccination coverage. Panel A: Vaccination coverage for pregnant persons in the U.S. over the past 5 years. Panel B: Vaccination coverage for pregnant persons within the U.S. in January of 2023 separated by racial group (modified from CDC, 2025b).

After seeing Figure 3, Lucia realized that she and her friends were not the only ones questioning vaccination during pregnancy. She recognized that many pregnant people are not getting vaccinations, especially in the past few years. The pamphlet said that vaccine hesitancy describes the reasons why individuals may not get vaccinated. She wanted to understand vaccine hesitancy more so she read an excerpt from a review article published by the Pediatric Clinics of North America (Rand & Olson-Chen, 2023). She was especially curious about vaccine hesitancy among pregnant individuals:

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%). 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. 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.

The pamphlet Lucia read also said that vaccination hesitancy often correlates with social determinants of health.

Social determinants of health are the non-medical factors that influence health outcomes. They are the conditions in which people are born, grow, work, live, and age, and the wider set of forces and systems shaping the conditions of daily life. These forces and systems include economic policies and systems, development agendas, social norms, social policies, and political systems (WHO, n.d.).

She was curious to learn more about social determinants of health and the related issues of health equity and vaccine hesitancy, so she spent a few minutes on the CDC website reading the following:

- What is Health Equity: <<https://www.cdc.gov/health-equity/what-is/index.html>>
- Partnering for Vaccine Equity: <<https://www.cdc.gov/vaccine-equity/php/about/index.html>>

It now made sense to Lucia that social determinants of health affect the reasons why pregnant individuals may not get influenza vaccinations. She recognized that addressing these factors directly could bring about more vaccination coverage and the achievement of health equity.

Even though many pregnant people end up not getting the influenza vaccination, Lucia walked out of her appointment feeling very happy with her decision to get one. She felt at ease and much less anxious about the safety of the fetus and the possibility of contracting influenza. She was proud of the diligence and time she put into reading about vaccine function and safety. Most importantly, Lucia was eager to encourage her friends to take similar actions.

Questions

12. Regarding health equity and social determinants of health:
 - a. How would you define health equity in your own words?
 - b. What are some examples of social determinants of health?
 - c. How do the concepts of health equity and social determinants of health relate to one another?

13. Using your understanding of social determinants of health:

- What do Figure 3A and 3B show?
- What are some reasons why pregnant people may not get vaccinated?
- What are possible benefits and drawbacks of disaggregating data by race and ethnicity?

14. Figure 4 shows data collected by the CDC in 2022. Using this figure and the research you have done, explain how social determinants of health may affect vaccine coverage.

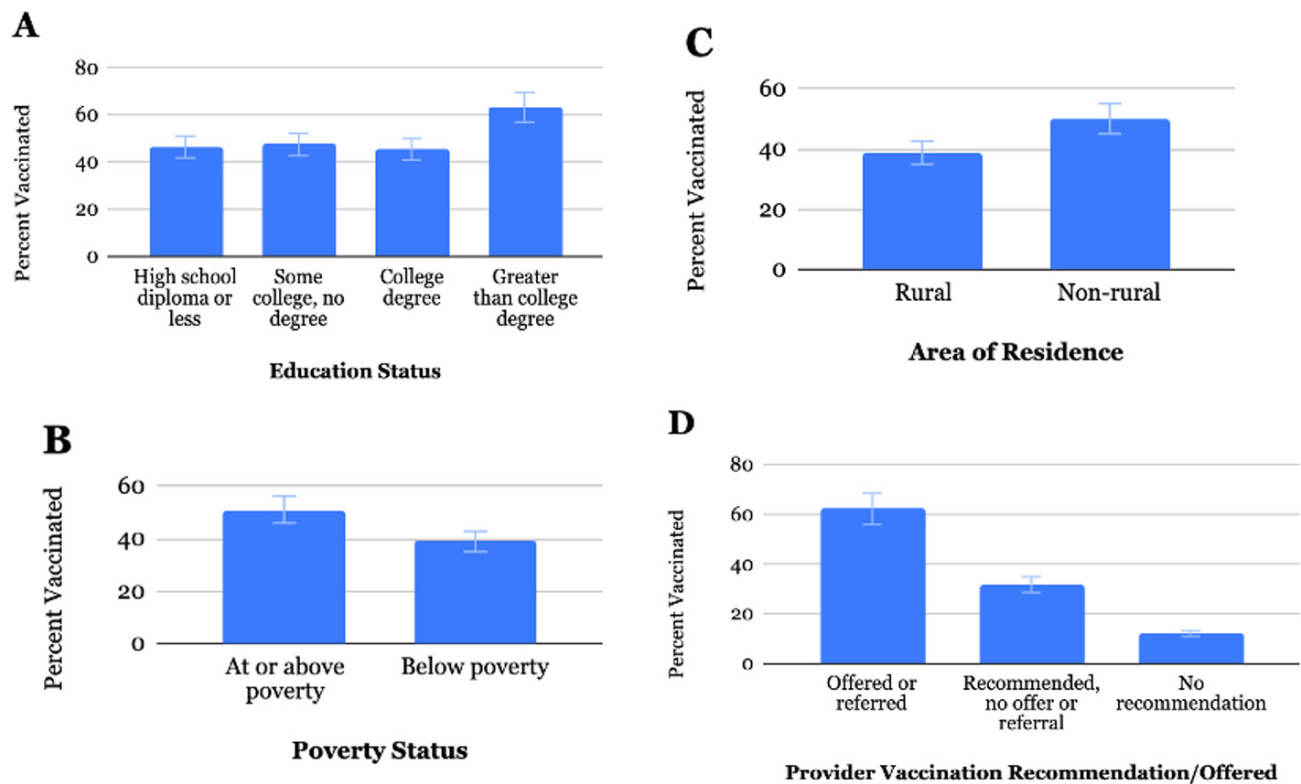


Figure 4. Influenza vaccine coverage among different groups of pregnant individuals. (Modified from CDC, 2024c.)

15. What are some ways societal institutions (e.g., national and local governments, health care systems) can mitigate vaccine hesitancy?
16. Why are mitigation strategies for vaccine hesitancy important?
17. In Lucia's situation she had the time and inclination to do her own research about influenza vaccinations in order to make an informed choice.
 - a. How might someone's final decision about influenza vaccination be different without the information gained through Lucia's research?
 - b. What can be done to increase vaccine coverage for those who do not have the ability or time to do their own research?
 - c. How might you, as an individual or within your profession, help close gaps in health equity?

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