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Timing of influenza vaccination during pregnancy

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The United States Advisory Committee on Immunization Practices (ACIP), the Centers for Disease Control and Prevention, and the American College of Obstetricians and Gynecologists recommend influenza vaccination at any time during pregnancy for persons who are or might become pregnant or postpartum during the influenza season.[1] Influenza vaccination is safe during pregnancy and has a well-described safety profile for the pregnant person and developing fetus.[1] Vaccination is important because pregnant people are at increased risk of hospitalization with influenza[2], and this has been particularly

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CRediT authorship contribution statement

Samantha M. Olson: Writing – review & editing, Writing – original draft, Visualization, Methodology, Conceptualization. **Leila C. Sahni:** Writing – review & editing, Methodology, Conceptualization. **Julie A. Boom:** Writing – review & editing, Methodology, Conceptualization. **Fatimah S. Dawood:** Writing – review & editing, Methodology, Conceptualization. **Flor M. Muñoz:** Writing – review & editing, Methodology, Conceptualization. **Sascha R. Ellington:** Writing – review & editing, Supervision, Methodology, Conceptualization.

observed during the second and third trimesters.[1] In addition, infants are at high risk, with children aged 0–4 years and particularly infants in the first 6 months of life consistently representing the highest pediatric influenza-associated hospitalization rates (laboratory-confirmed influenza hospitalizations: https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html)

The objective of this clinical perspective is to summarize current ACIP recommendations for influenza vaccination during pregnancy for the prevention of influenza among pregnant persons and infants aged 0–6 months, to demonstrate how recent data continue to support vaccination guidance and to discuss future considerations for vaccination timing.

Updated recommendations

In August 2021, ACIP updated guidance to accommodate earlier influenza vaccination in July or August for certain groups of pregnant people, and these considerations have remained through the current 2023-2024 influenza vaccination guidelines.[1] Seasonal influenza vaccines might be available in July or August, but for most people aged ≥6 months, ACIP recommends that the influenza vaccine be given in September or October to optimize protection before the influenza season. However, the current ACIP recommendations state that vaccination during July and August can be considered for pregnant people in their third trimester to protect themselves and their young infants. For pregnant people in their first or second trimester, influenza vaccination during July and August should be avoided because of possible waning of protection during the influenza season.[1] For this group, waiting to vaccinate until September or October is preferable unless there is concern that vaccination later in the season might not be possible.[1]

These recommendations followed accumulating evidence that vaccination during pregnancy reduces the risk of influenza and associated severe outcomes in young infants who are not eligible for vaccination until 6 months old.[1,3,4] Although the primary goal of maternal influenza vaccination is to protect the pregnant person, vaccination during pregnancy also provides protection to infants <6 months against influenza and associated severe outcomes during the influenza season. The timing of influenza vaccination during pregnancy to optimize infant protection must account for the timing of influenza virus circulation, which varies and is not predictable, and the timing of annual influenza vaccine availability, which depends on production and lot release timelines, which vary each season. Furthermore, the pregnant person's gestational age, the duration the infant will be exposed to circulating influenza viruses while <6 months old, and waning vaccine effectiveness for both the pregnant person and the infant are additional important considerations.

In a recent study, our research showed vaccination during pregnancy reduced influenza-associated hospitalizations and emergency department visits by 52% among infants during the first 2 months of life.[3] Further, maternal vaccination during the third trimester of pregnancy reduced influenza illness during the infants' first 6 months by 52%. Although still beneficial, maternal vaccination during the first or second trimesters of pregnancy reduced infant influenza illnesses by only 17%. Therefore, protection of infants born during the influenza season may be higher when mothers are vaccinated later in pregnancy.

Studies have shown that maternal antibody concentrations increase approximately 2 weeks following vaccination and peak between 2 and 6 weeks postvaccination.[4,5] Levels of maternal antibodies in the infant at birth are closely associated with the pregnant person's immune response, and antibody concentrations from first- and second-trimester vaccination may wane before childbirth, whereas maternal antibody levels in infants wane over the first 6 months of life. Optimal timing of maternal vaccination for the benefit of the infant would allow time for maximal maternal antibody response and sufficient time for transplacental antibody transfer before birth. Furthermore, because of the seasonal nature of influenza, vaccination during the first and second trimesters of pregnancy is considered optimal to protect the pregnant person and infant born during intraseasonal months. In our analysis, we did not estimate effectiveness among infants aged 3–5 months, but evidence suggests maternal antibodies may wane at 3–4 months.

To visualize the complexity of timing in pregnancy and provide a model to consider when determining the optimal timing of influenza vaccination in pregnancy, we present a figure showing the length of a pregnancy (Figure, *solid line*) and the first 6 months of an infant's life (Figure, *dotted line*). Theoretically, persons who become pregnant in September—November may be vaccinated before influenza circulation to provide protection during pregnancy (Figure, orange *solid line*). Infants born to these pregnant people will be approximately 4–6 months old during the subsequent season and will be at increased risk until they are age-eligible for vaccination around December—February (Figure, orange *dotted line*).

Vaccination may be later in pregnancy for persons with pregnancies beginning from March to May (Figure, blue *solid line*). Infants born to these individuals from December to February are at increased risk and will not be eligible for their vaccination during their first influenza season (Figure, blue *dotted line*). Infants born to pregnant people vaccinated during the third trimester could have the highest maternal antibody levels, depending on the timing of maternal vaccination relative to the infant's birth.

Optimal timing of influenza vaccination during pregnancy may offer protection for the pregnant person and the infant. Counseling pregnant people on these benefits may increase vaccine uptake. Timing for other vaccines recommended during pregnancy differs but may overlap with influenza vaccination timing. Similar to influenza, the COVID-19 vaccine is recommended at any time to protect the pregnant person and their infant. Tetanus-diphtheria and pertussis vaccination is recommended between the 27th and 36th gestational week, whereas respiratory syncytial virus (RSV) vaccination is recommended between the 32nd and 36th gestational week during the RSV season.

Determining the optimal timing of vaccination to achieve desirable antibody kinetics and transfer from a pregnant person to an infant may lead to maternal immunization schedules with optimal protection for the pregnant person and infant from pathogens with fall and winter seasonality. Future influenza research may investigate the use of 2 doses in the pregnant or postpartum person depending on the timing of their pregnancy and waning vaccine effectiveness for the pregnant person and the infant.

Existing evidence on the effectiveness of influenza vaccination during pregnancy for the prevention of influenza-associated illnesses in infants during the first 6 months of life supports current ACIP recommendations. Additional studies to understand the optimal timing may lead to updated vaccination recommendations.

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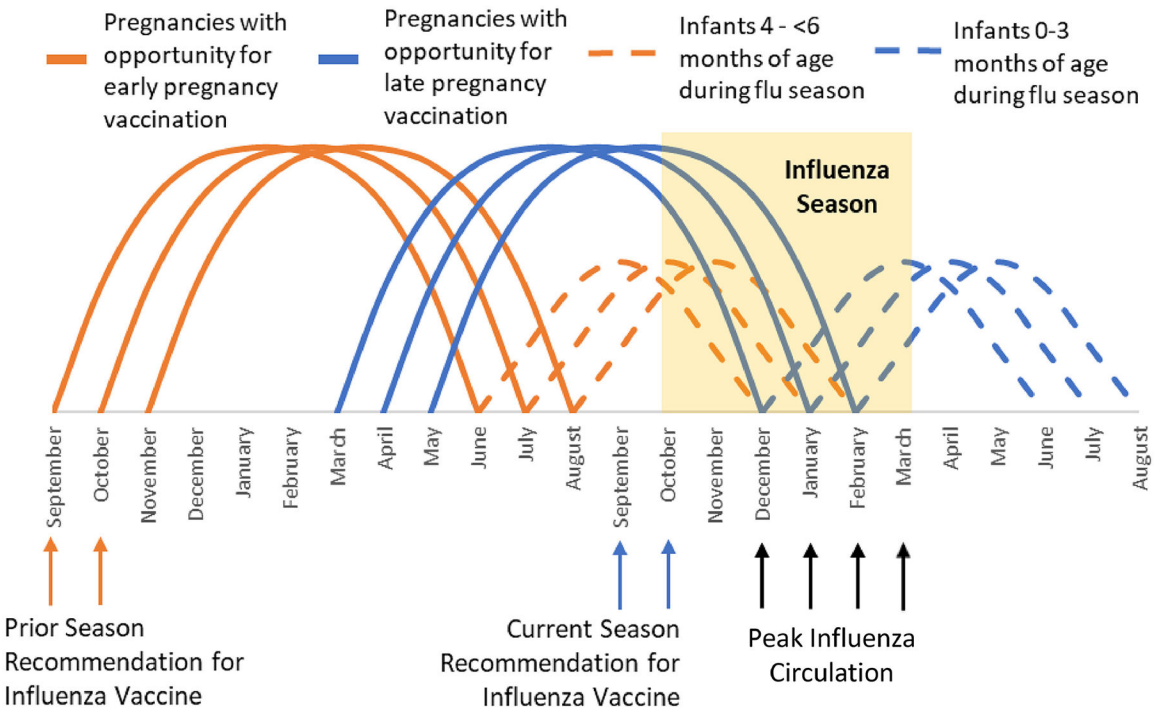

FIGURE. Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality