

**Centers for Disease Control and Prevention**  
National Center for Immunization and Respiratory Diseases



# Effectiveness of Maternal Influenza Vaccination during Pregnancy against Influenza-associated Hospitalizations & ED Visits in Infants <6 Months of Age

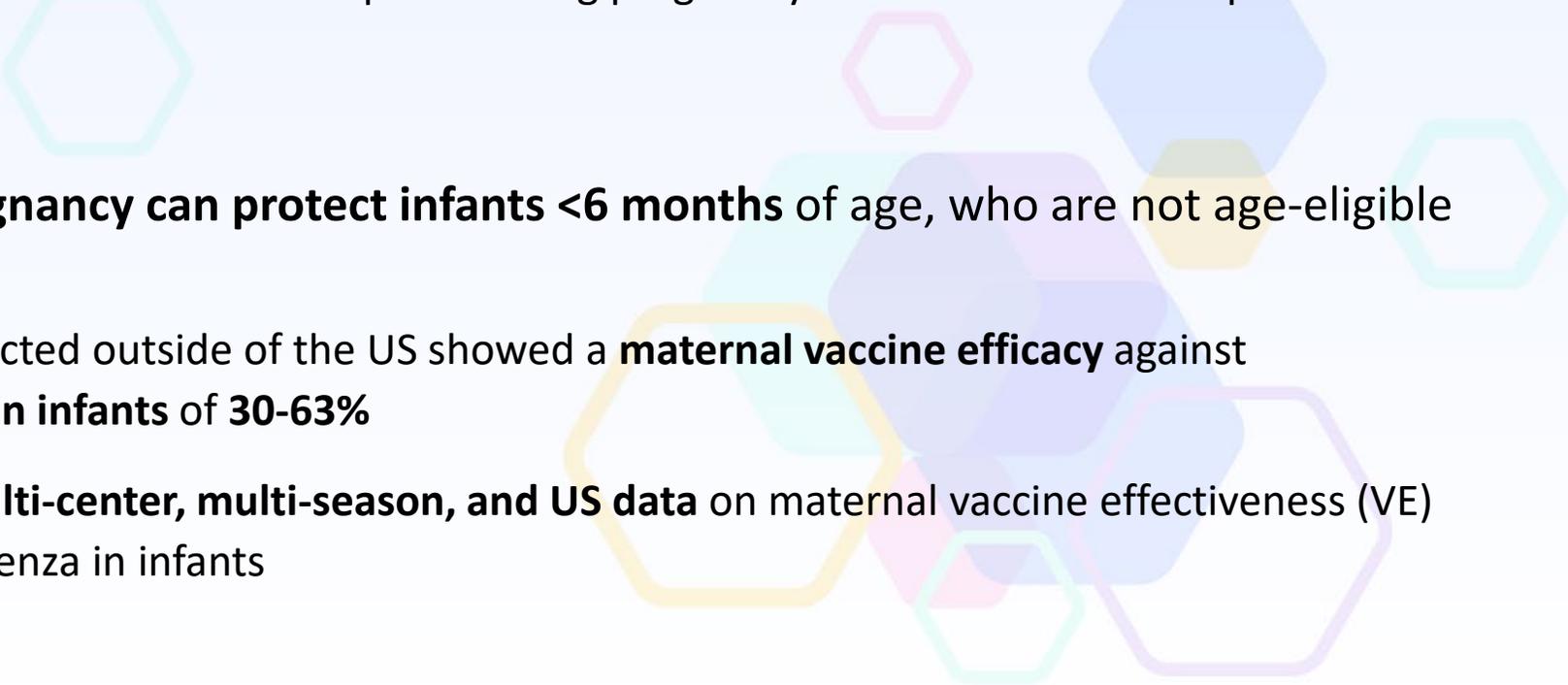
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**Influenza Division**

ACIP Meeting: Influenza Session  
October 25, 2023



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# Background

- **Influenza virus infection during pregnancy** is associated with **severe disease and may be associated with some adverse birth outcomes.**
  - Receipt of **inactivated influenza vaccine** during pregnancy is **safe and effective.**
    - Since the COVID-19 pandemic, influenza vaccination uptake during pregnancy is **~5-15% lower** than pre-pandemic seasons.
  - **Influenza vaccination during pregnancy can protect infants <6 months of age, who are not age-eligible for vaccination.**
    - Randomized control trials conducted outside of the US showed a **maternal vaccine efficacy** against laboratory-confirmed **influenza in infants** of **30-63%**
    - There is a **lack of real-world, multi-center, multi-season, and US data** on maternal vaccine effectiveness (VE) against medically-attended influenza in infants
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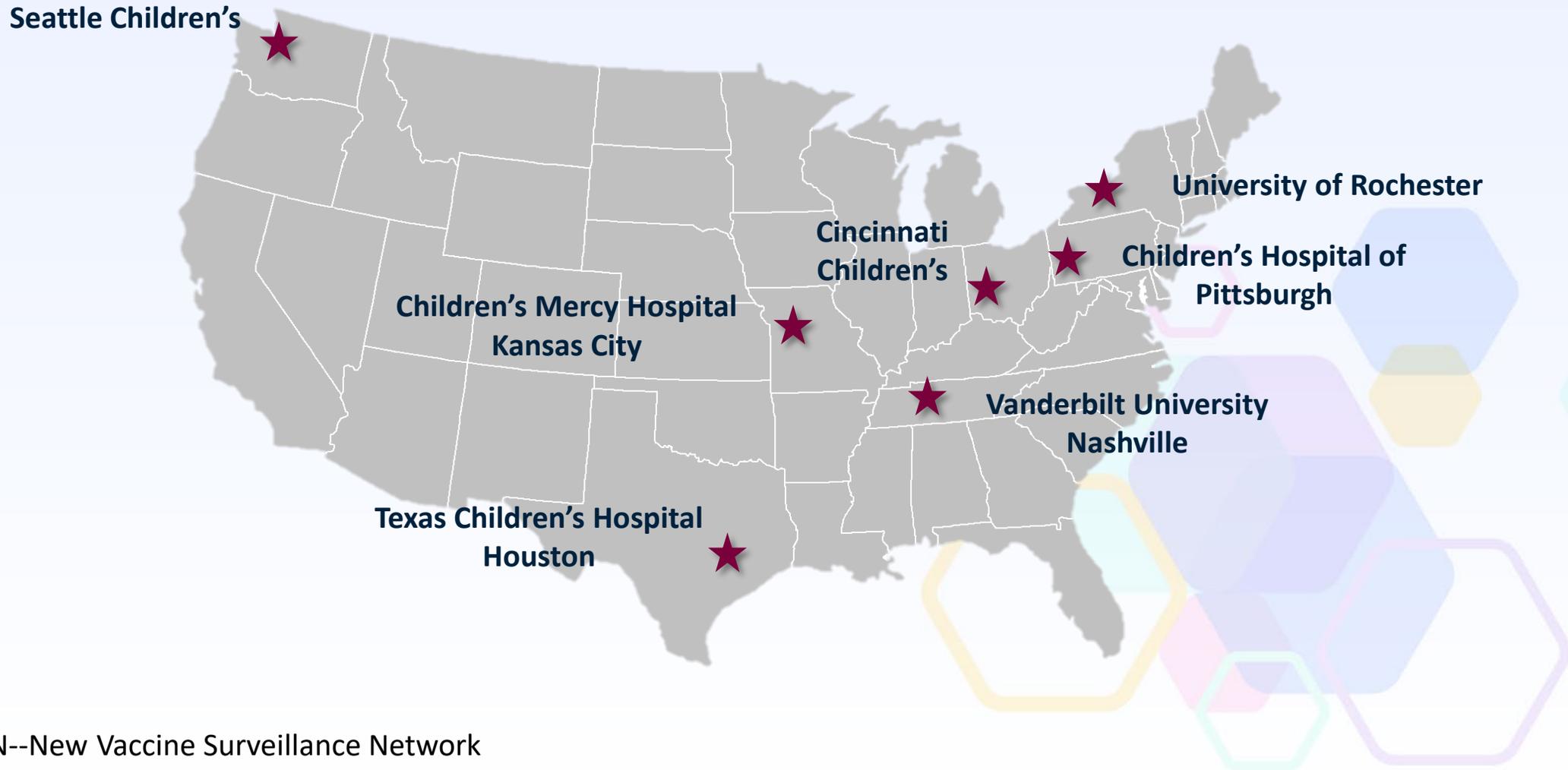
# Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices

- **Current ACIP Wording (As of 2021-2022 Influenza Season):**
  - **Pregnant persons in the third trimester:** Vaccination during July and August can be considered for pregnant persons who are in the third trimester because vaccination might reduce risk for influenza illness in their infants during the first months after birth, when they are too young to receive influenza vaccine (33–36). For pregnant persons in the first or second trimester during July and August, waiting to vaccinate until September or October is preferable, unless there is concern that later vaccination might not be possible.

# Question:

Does maternal influenza vaccination during pregnancy reduce influenza-associated hospitalizations and emergency department (ED) visits in infants <6 months of age?

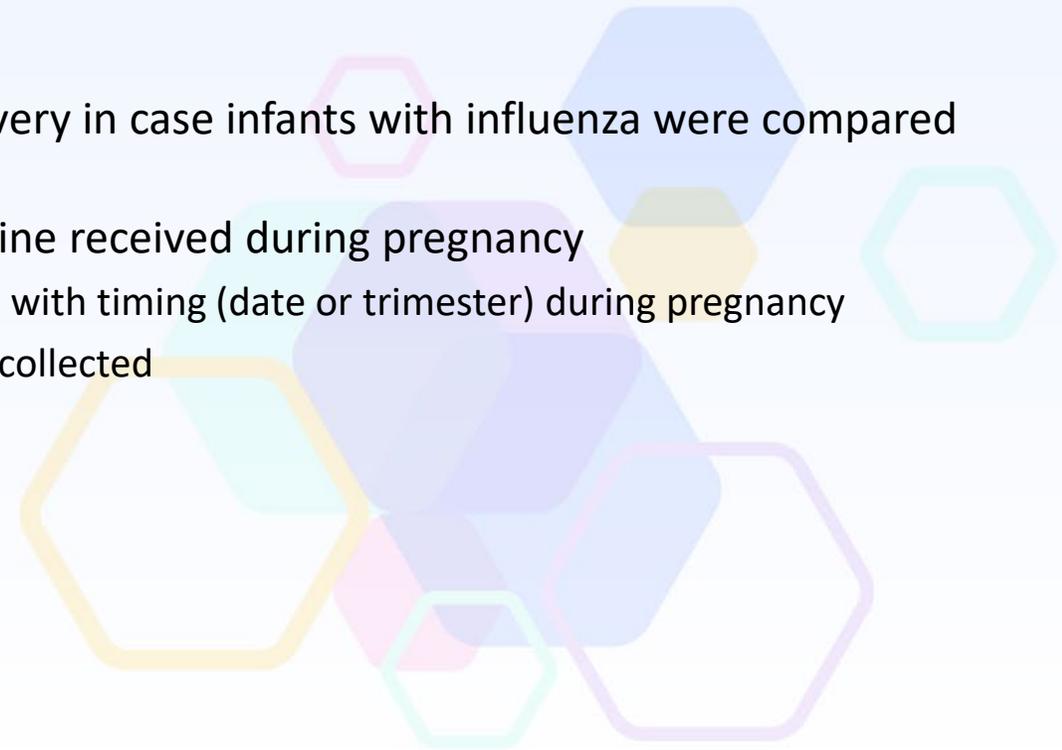
# NVSN\* Pediatric Inpatient & ED Network Sites



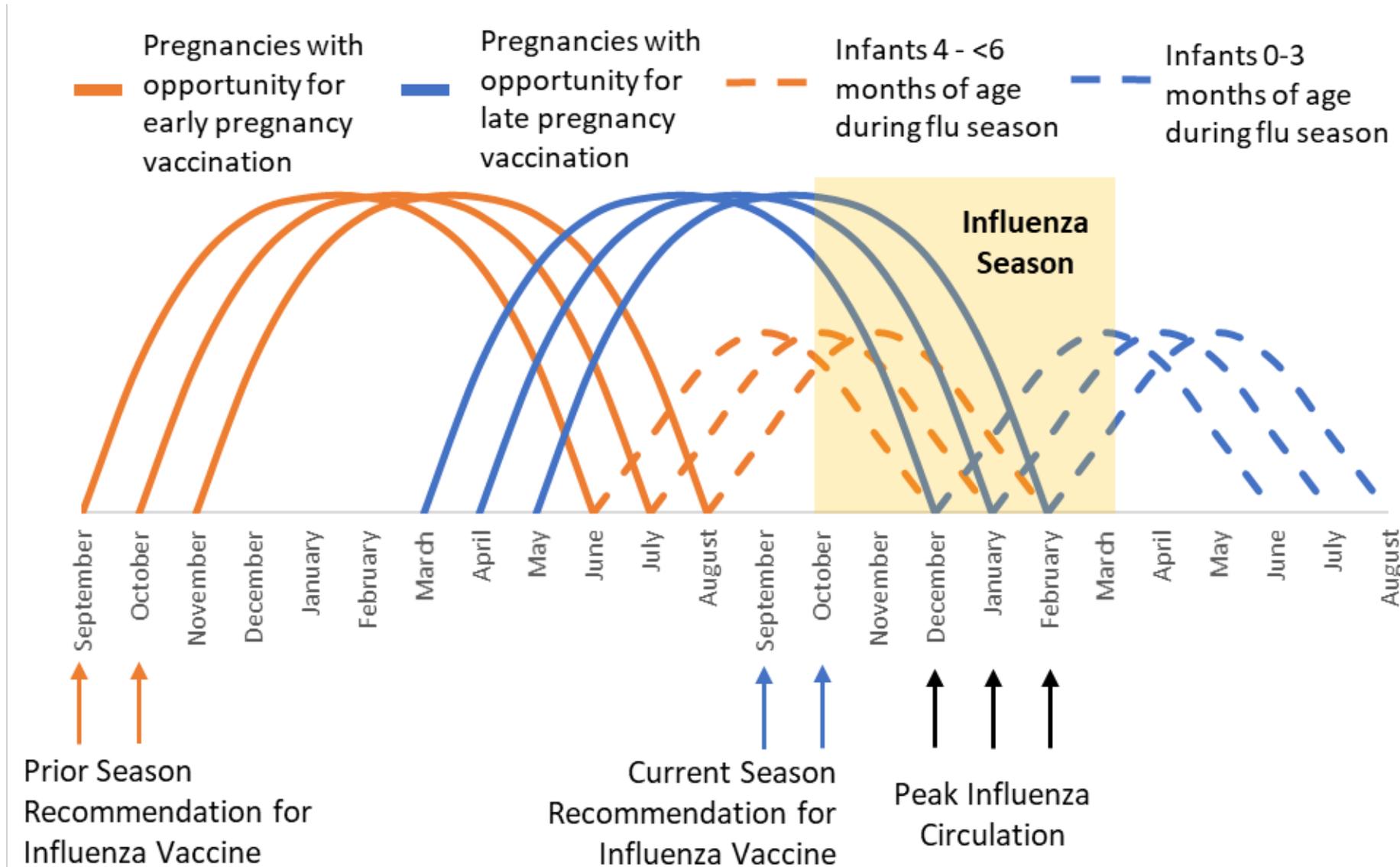
\*NVSN--New Vaccine Surveillance Network

# Methods

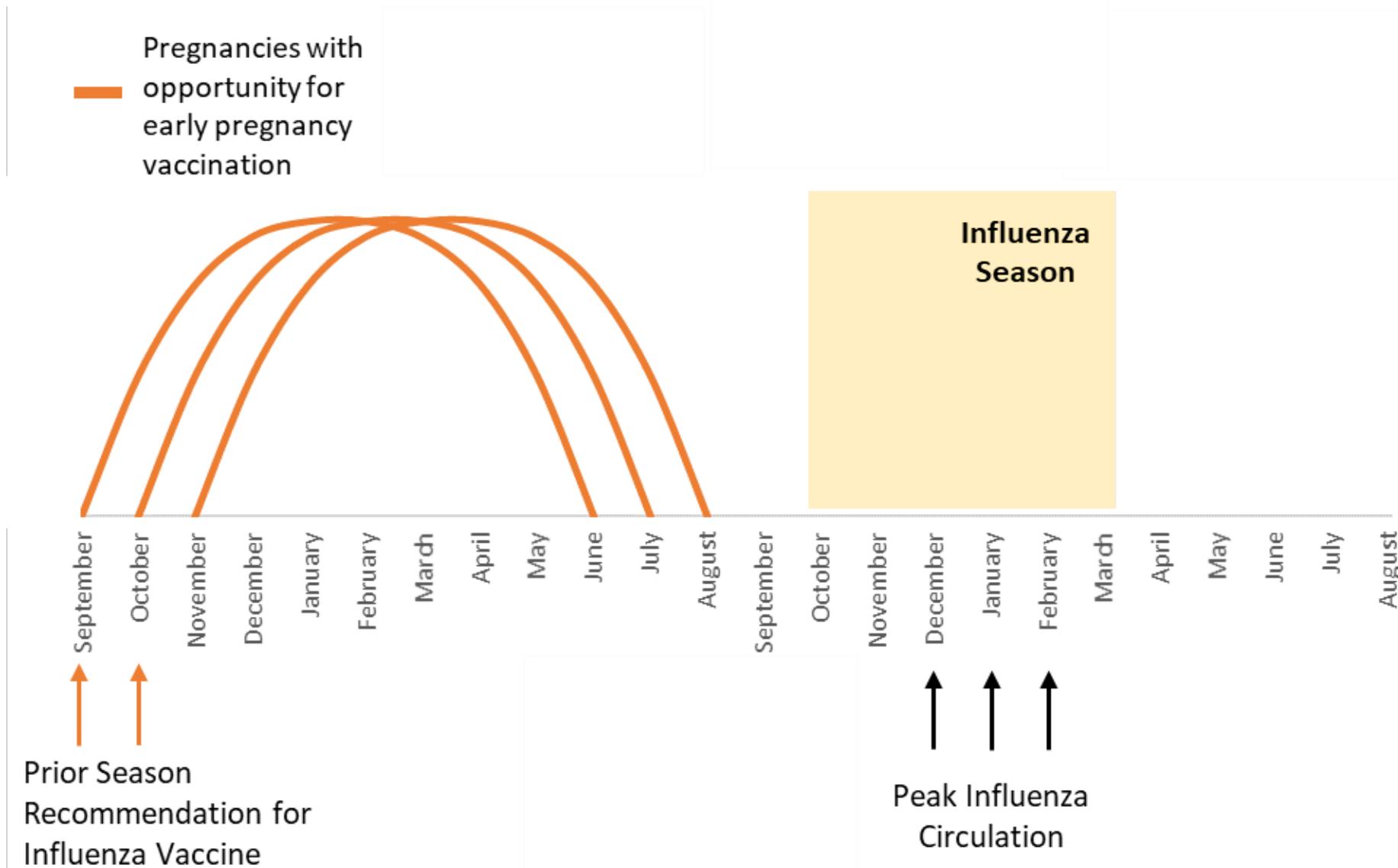
- **Enrollment:** Infants <6 months of age admitted to the hospital or emergency department during 4 influenza seasons (from Fall 2016 through Spring 2020) at 7 pediatric medical centers within the NVSN
- **Cases:**
  - Tested positive for influenza by RT-PCR with acute respiratory illness (ARI) symptoms within 10 days of symptom onset
- **Controls:** Tested negative for influenza with ARI symptoms
- **Design:** Test-negative design
  - Odds of maternal influenza vaccination  $\geq 14$  days prior to delivery in case infants with influenza were compared to control infants with non-influenza respiratory illness
  - **Vaccination status:** Vaccination was defined as influenza vaccine received during pregnancy
    - Documented (registry or providers) or self-reported vaccination with timing (date or trimester) during pregnancy
    - Data on maternal influenza infection during pregnancy was not collected
- **Analysis:**  $VE = (1 - \text{adjusted odds ratio}) \times 100\%$ 
  - Adjusted for infant age, NVSN site, and calendar time



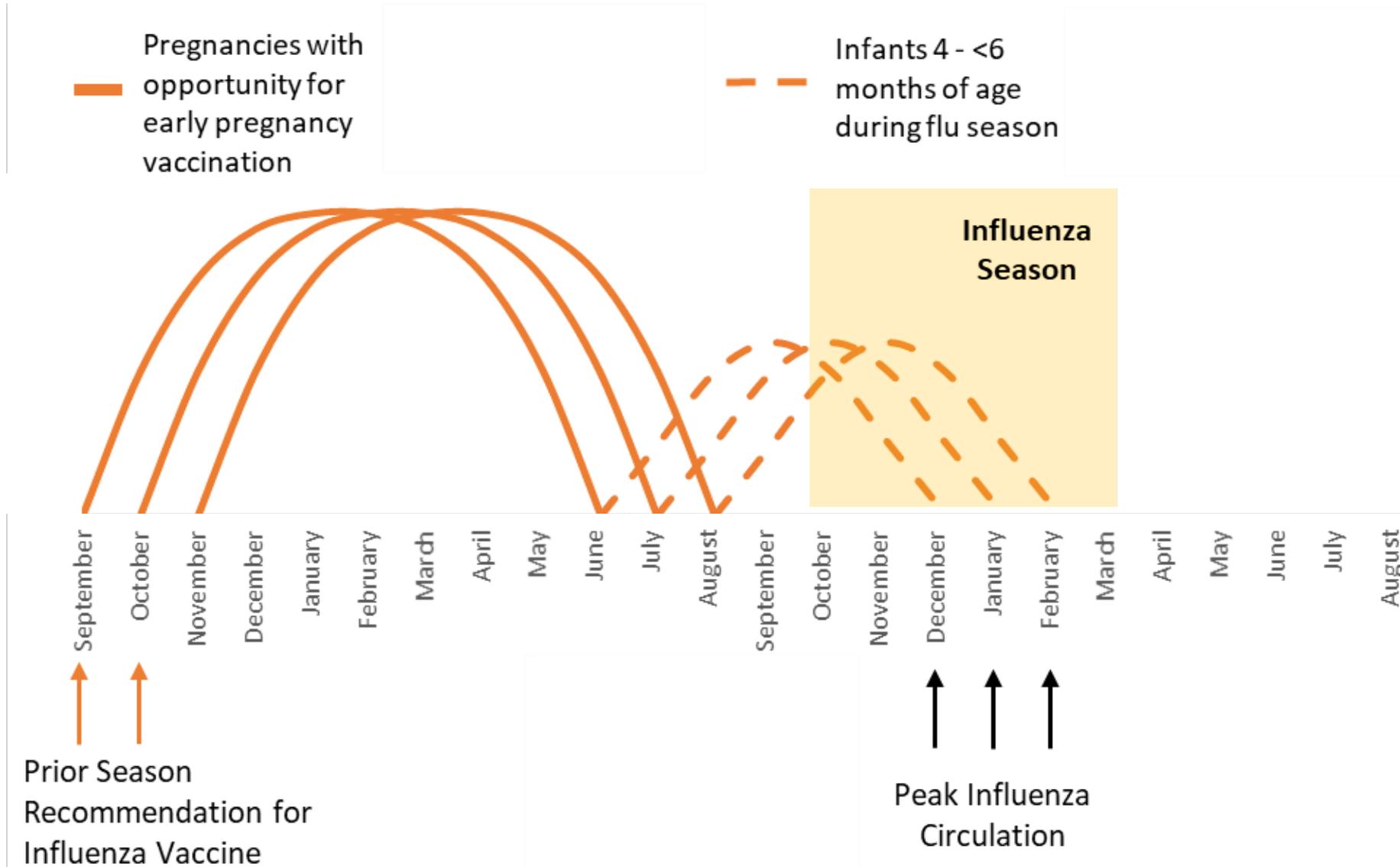
**Figure.** Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality



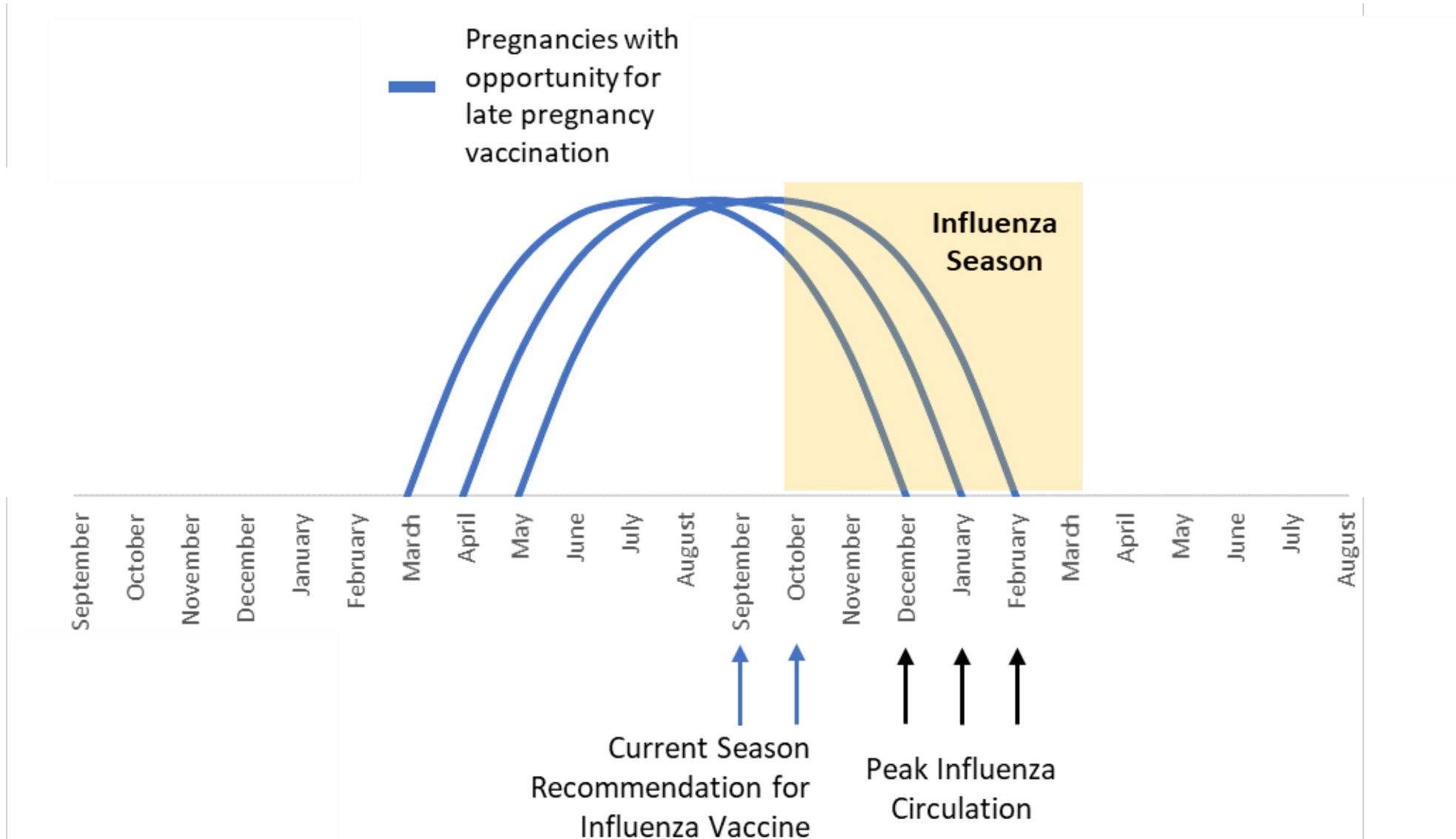
**Figure.** Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality



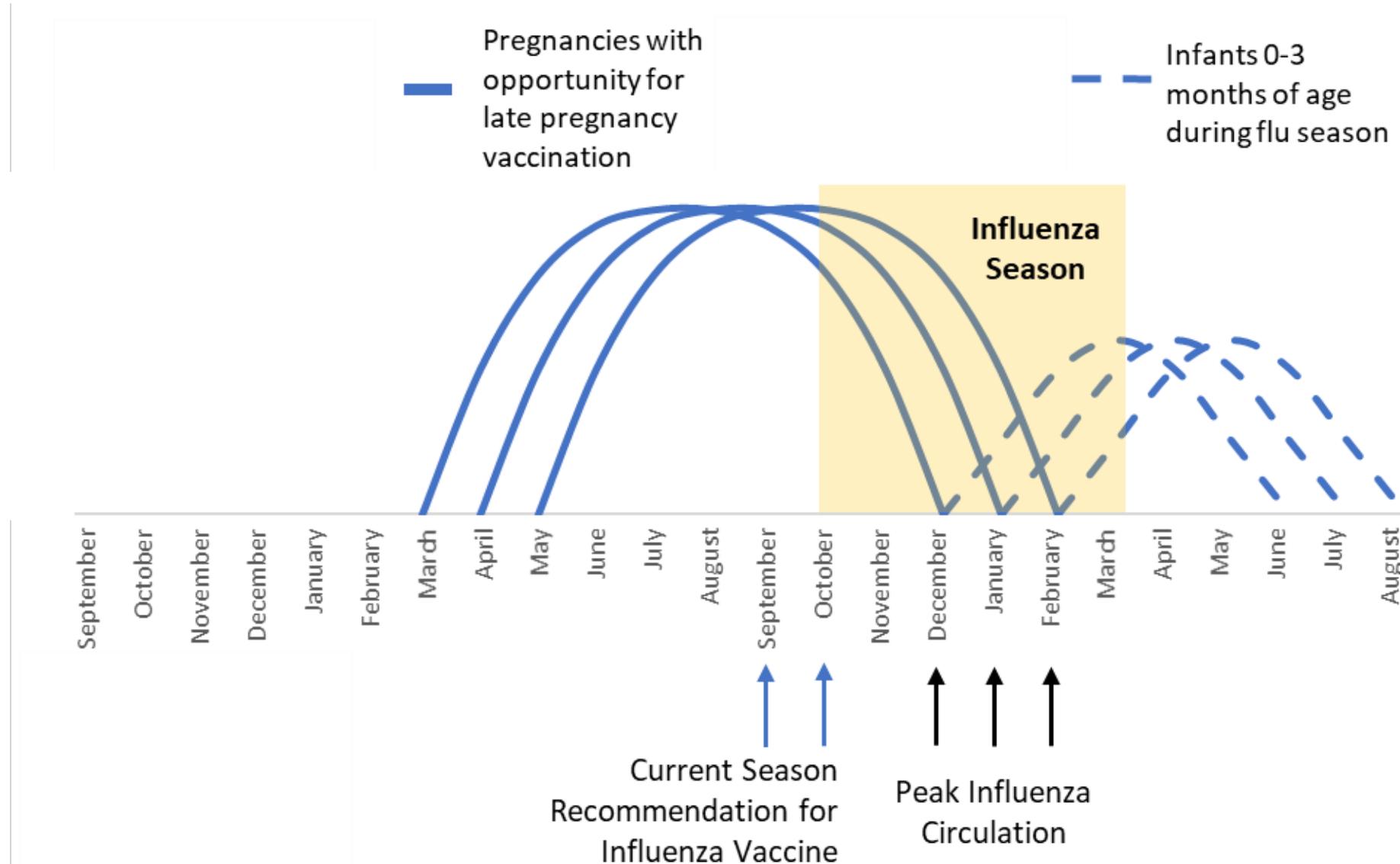
**Figure.** Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality



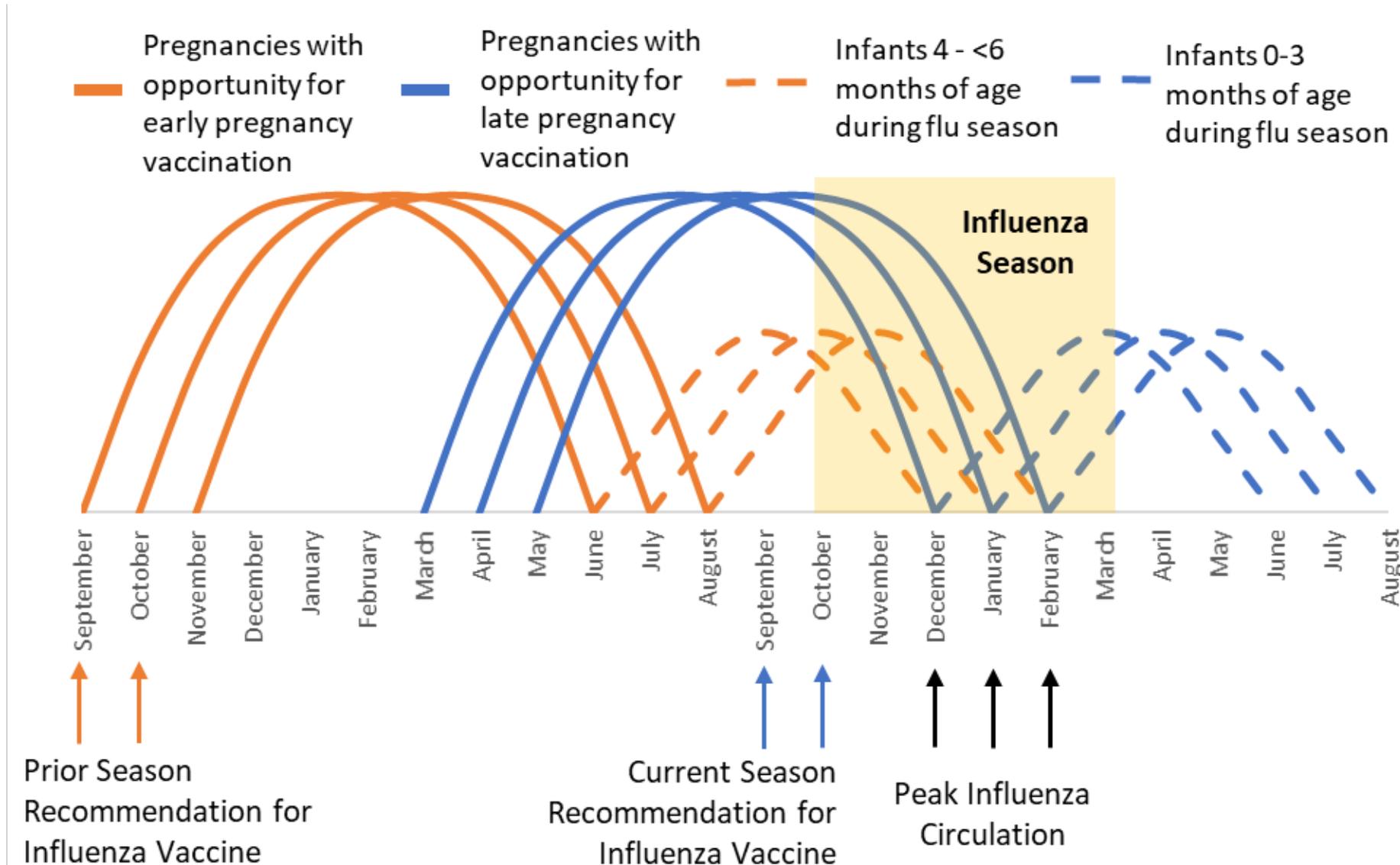
**Figure.** Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality



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



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



# Results



**4,049** infants <6 months of age enrolled between the 2016-2017 through the 2019-2020 flu seasons from 7 pediatric medical institutions

**285** Were excluded (**21** cases, **264** controls)

**92** Born to mothers vaccinated <14 days prior to delivery (8 cases, 84 controls)

**193** Had unknown vaccination timing (13 cases, 180 controls)

**3,764** infants included  
**2,007 (53%)** born to vaccinated mothers  
**1,757 (47%)** born to unvaccinated mothers

**223** case-infants tested positive for influenza

**94 (42%)** born to vaccinated mothers

**129 (58%)** born to unvaccinated mothers

**3,541** control-infants tested negative for influenza

**1,913 (54%)** born to vaccinated mothers

**1,642 (46%)** born to unvaccinated mothers

Characteristic	Case status		Maternal Vaccination Status	
	Case-infants (N=223)	Control-infants (N=3541)	Vaccinated (N=2007)	Unvaccinated (N=1757)
<b>Median age (IQR) – months</b>	3 (2, 5)	2 (1, 4)	2 (1, 4)	3 (2, 4)
<b>Age group – no. (%)</b>				
0-2 months	106 (48)	2147 (61)	1342 (67)	911 (52)
3-5 months	117 (52)	1394 (39)	665 (33)	846 (48)
<b>Female sex – no. (%)</b>	102 (46)	1533 (43)	864 (43)	771 (44)
<b>Race and ethnic group – no./ total no. (%)</b>				
White, non-Hispanic	69/223 (31)	1517/3540 (43)	920/2006 (46)	666/1757 (38)
Black, non-Hispanic	69/223 (31)	695/3540 (20)	302/2006 (15)	462/1757 (26)
Hispanic	64/223 (29)	1008/3540 (28)	585/2006 (29)	487/1757 (28)
Other	21/223 (9)	320/3540 (9)	199/2006 (10)	142/1757 (8)
<b>Breastfeeding at Enrollment</b>	94/223 (42)	1616/3536 (46)	1051/2005 (52)	659/1754 (38)
<b>At least one underlying condition in infants – no./total no. (%)</b>	18 (8)	372 (11)	184 (9)	206 (12)

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<b>Female sex – no. (%)</b>	102 (46)	1533 (43)	864 (43)	771 (44)

**Case-infants and those born to unvaccinated mothers were older than control-infants and those born to vaccinated mothers.**

Characteristic	Case status		Maternal Vaccination Status	
	Case-infants (N=223)	Control-infants (N=3541)	Vaccinated (N=2007)	Unvaccinated (N=1757)

**Infant case status and maternal vaccination status differed by race and ethnic group.**

<b>Race and ethnic group – no./ total no. (%)</b>				
White, non-Hispanic	69/223 (31)	1517/3540 (43)	920/2006 (46)	666/1757 (38)
Black, non-Hispanic	69/223 (31)	695/3540 (20)	302/2006 (15)	462/1757 (26)
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Characteristic	Case status		Maternal Vaccination Status	
	Case-infants (N=223)	Control-infants (N=3541)	Vaccinated (N=2007)	Unvaccinated (N=1757)

**More infants born to vaccinated mothers were breastfeeding on enrollment, and more infants born to unvaccinated mothers had underlying conditions.**

<b>Race and ethnic group – no./ total no. (%)</b>				
White, non-Hispanic	69/223 (31)	1517/3540 (43)	920/2006 (46)	666/1757 (38)
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Characteristic	Case status		Maternal Vaccination Status	
	Case-infants (N=223)	Control-infants (N=3541)	Vaccinated (N=2007)	Unvaccinated (N=1757)
<b>Preterm birth (born &lt;37 weeks gestation) – no./ total no. (%)</b>	37/223 (17)	613/3535 (17)	315/2004 (16)	335/1754 (19)
35-<37 weeks	20/36 (56)	319/600 (53)	167/307 (54)	172/329 (52)
30-34 weeks	14/36 (39)	219/600 (37)	122/307 (40)	111/329 (34)
≤29 weeks	2/36 (6)	62/600 (10)	18/307 (6)	46/329 (14)
<b>NVSN sites– no. (%)</b>				
Nashville	38 (17)	708 (20)	361 (18)	385 (22)
Rochester	14 (6)	358 (10)	213 (11)	159 (9)
Cincinnati	42 (19)	345 (10)	198 (10)	189 (11)
Seattle	26 (12)	359 (10)	281 (14)	104 (6)
Houston	39 (17)	797 (23)	391 (19)	445 (25)
Kansas City	35 (16)	317 (9)	174 (9)	178 (10)
Pittsburgh	29 (13)	657 (19)	389 (19)	297 (17)
<b>Season of enrollment – no. (%)</b>				
2016-2017	49 (22)	778 (22)	462 (23)	365 (21)
2017-2018	60 (27)	829 (23)	429 (21)	460 (26)
2018-2019	45 (20)	986 (28)	560 (28)	471 (27)
2019-2020	69 (31)	948 (27)	556 (28)	461 (26)

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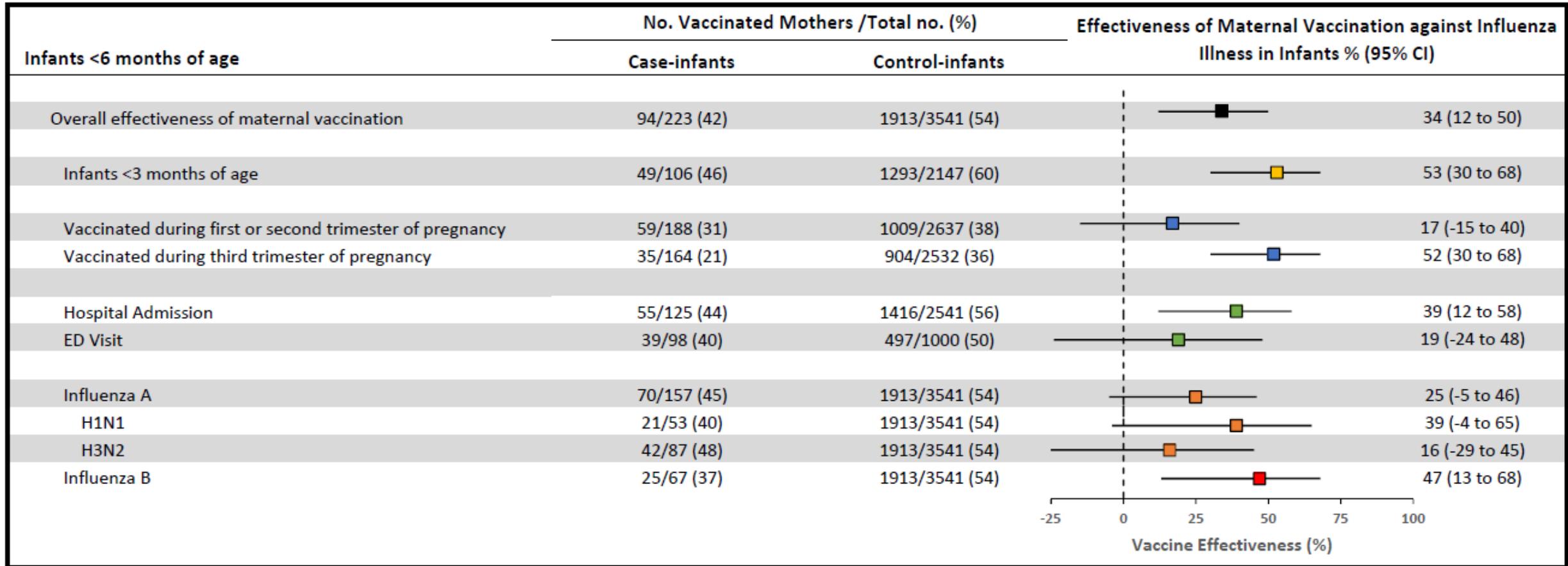
**More infants born to unvaccinated mothers were born preterm.**

Characteristic	Case status		Maternal Vaccination Status	
	Case-infants (N=223)	Control-infants (N=3541)	Vaccinated (N=2007)	Unvaccinated (N=1757)

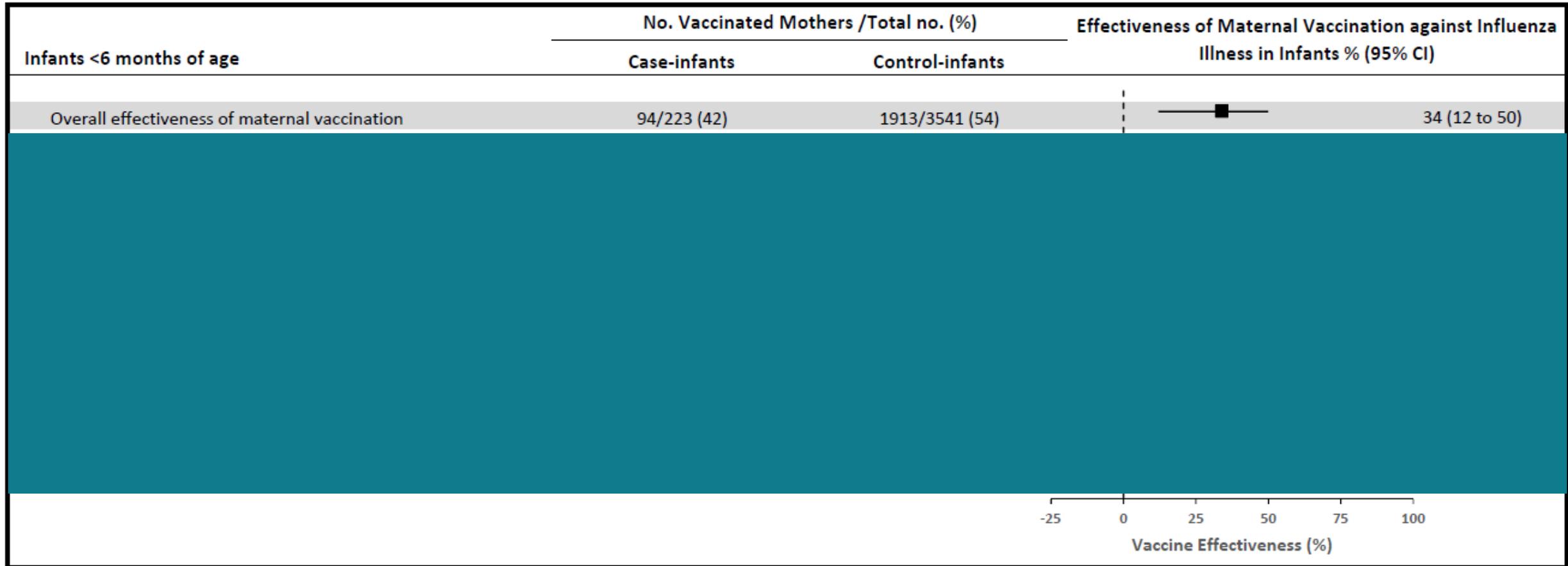
**Vaccination status differed by NVSN site and flu season of enrollment.**

<b>NVSN sites– no. (%)</b>				
Nashville	38 (17)	708 (20)	361 (18)	385 (22)
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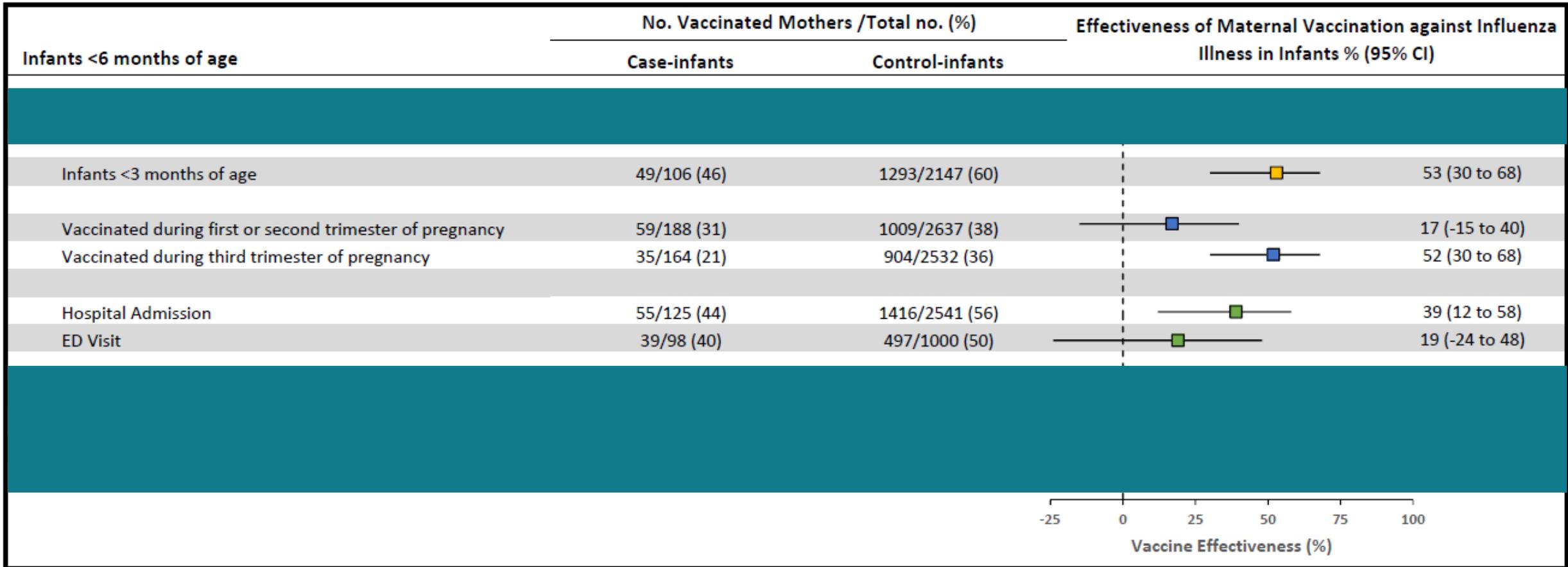
# Maternal Vaccine Effectiveness against Influenza-associated Hospitalizations and Emergency Department Visits in Infants <6 months



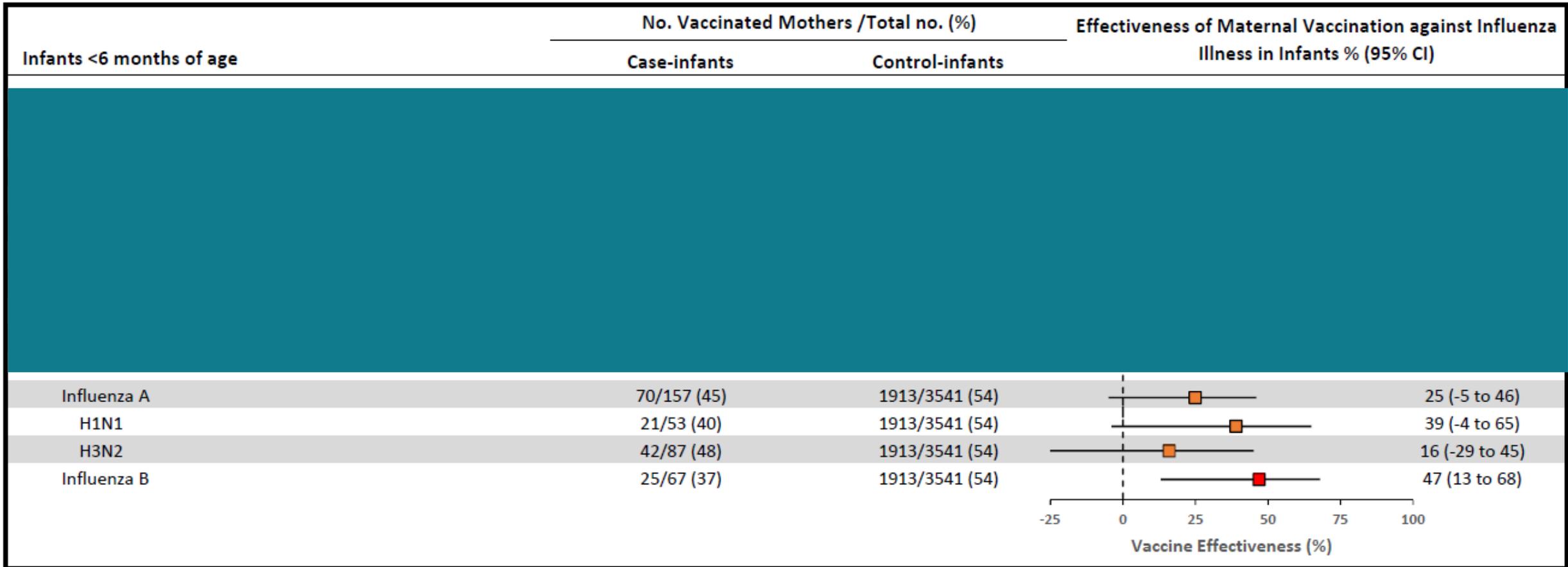
# Overall maternal vaccine effectiveness against influenza hospitalizations and emergency department visits in infants <6 months of age is 34%



# Maternal vaccine effectiveness was higher among infants <3 months, vaccinated during the third trimester, and against hospital admission



**Maternal vaccine effectiveness was consistent** with other VE estimates by influenza type and subtype for the **2016-17 through 2019-20 flu seasons.**





## Summary

### Maternal Vaccine Uptake



**Influenza vaccine uptake** during pregnancy is nationally consistent but **suboptimal**.

### Benefits to Infants



**Maternal vaccination** was associated with **reduced odds of influenza hospitalizations & ED visits** in infants <6 months of age.

### Highest Vaccine Effectiveness



**VE was greatest** among infants <3 months of age, those born to mothers **vaccinated during their third trimester** of pregnancy, and against influenza-associated **hospitalizations**.

### Policy Implications



Currently, there are **no anticipated changes** to **vaccination timing recommendations** during pregnancy.

# Acknowledgments

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