

# CDC PUBLIC HEALTH GRAND ROUNDS

## Maternal Immunization: Current Status and Future Directions



**Event ID: 4157352**

**September 18, 2019**



**U.S. Department of  
Health and Human Services**  
Centers for Disease  
Control and Prevention

# Maternal Vaccination Against Influenza and Pertussis



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Office of the Director, Immunization Services Division

National Center for Immunization and Respiratory Diseases



U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention

# Influenza



pregnant  
women

are at **risk** for serious  
**complications** from flu

- Severe illness
- Pneumonia
- Hospitalization



NO FLU  
ON BOARD

# Influenza Severity in Pregnant Women

- Pregnant women are at increased risk of influenza-related hospitalization compared with the general population
- Risk of influenza-related hospitalization increases later in pregnancy



# Impact of Influenza Among Infants

## Infants aged <6 months:

- Highest rate of influenza-related hospitalizations and deaths of all pediatric age groups
- Five times as likely to be hospitalized and twice the incidence of death vs. children aged 6–23 months



# Pertussis (Whooping Cough)

- Highly contagious, bacterial respiratory infection that can be deadly for infants
- Rapid, high-pitched whoop followed by vomiting and exhaustion
- Infants can have atypical symptoms
- Poorly controlled, despite high vaccination coverage



# Burden of Pertussis in the United States

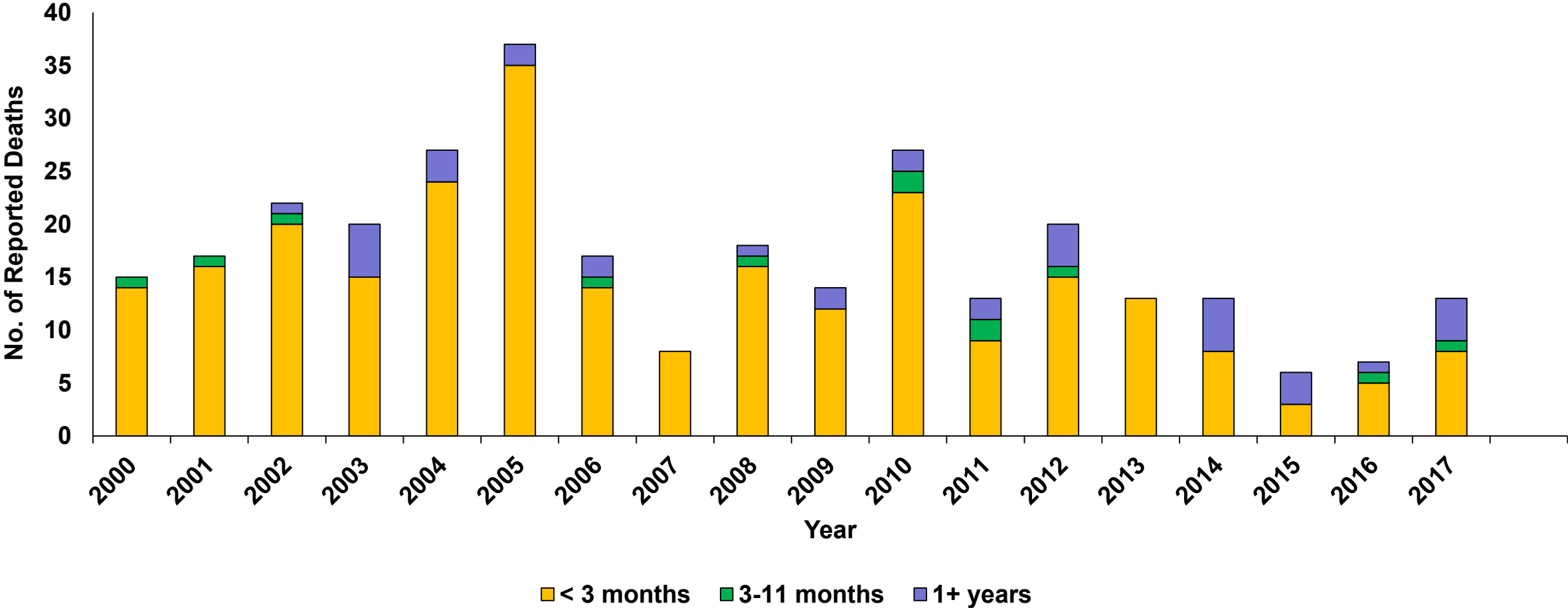


Infants aged <2 months have the **highest incidence rate** of pertussis

Approximately 67% of infants aged <2 months with pertussis need treatment in the **hospital**



# Pertussis Deaths by Age Group, United States, 2000–2017





# Vaccination Recommendations During Pregnancy

**The Advisory Committee on Immunization Practices (ACIP) recommends that all women:**

who are pregnant during flu season receive influenza vaccine (at any time during pregnancy)

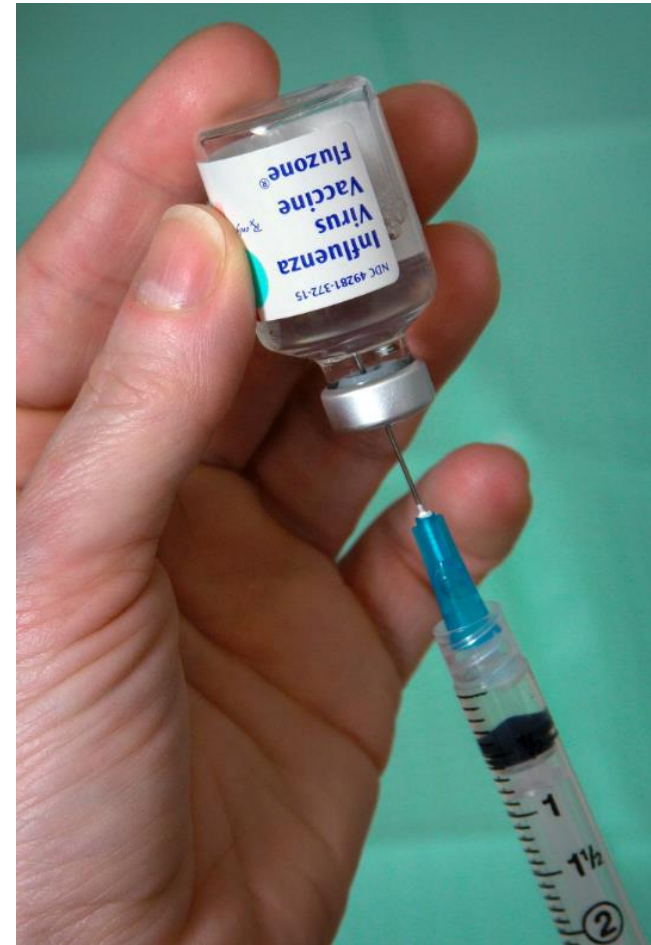
receive tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccine during each pregnancy (preferably during the early part of gestational weeks 27– 36)

# Effectiveness of Influenza Vaccines Given During Pregnancy

Reduces risk of influenza in pregnant women by about 50%, and is 40% effective against influenza-associated hospitalization during pregnancy

Reduces antibiotic use, medical visits, loss of work days

Reduces risk of laboratory-confirmed influenza and influenza hospitalization among infants during the first several months of life



Thompson MG, Kwong JC, Regan AK, et al. *Clin Infect Dis*. 2019;68(9):1444-1453.  
Steinhoff M, Katz J, Englund JA, et al. *Lancet Infect Dis* 2017;17(9):981-9.  
Tapia MD, Sow SO, Tamboura B, et al. *Lancet Infect Dis* 2016;16: 1026–35.3.  
Nunes et al. *Human Vaccines & Immunotherapeutics* 2018; 14(3);758-66.

# Effectiveness of Tdap Vaccines Given During Pregnancy

Tdap during third trimester of pregnancy is 78% effective in preventing pertussis in infants <2 months of age

Infants with pertussis born to vaccinated mothers less likely to be hospitalized or admitted to ICU



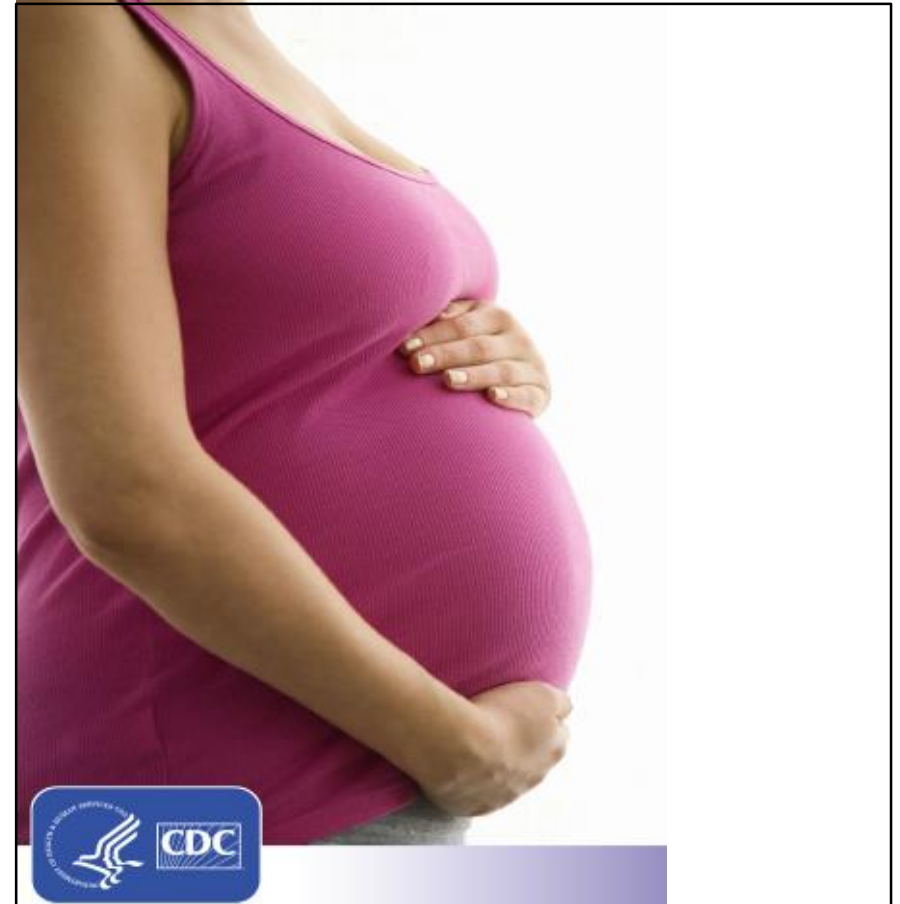
Baxter R, Bartlett J, Fireman B, et al. *Pediatrics*.2017;139 (5).  
Winter K, Nickell S, Powell M, Harriman K. *Clin Infect Dis* 2017;64:3–8.  
Skoff T, Hadler S, Hariri S. *Clin Infect Dis*. 2017; 65 (12):1977-83.

# Safety of Influenza and Tdap Vaccinations During Pregnancy

Two systematic reviews of influenza vaccination show no increased risk for spontaneous abortion, fetal death, or congenital malformations

Tdap in pregnancy does not increase the risk of adverse reactions for the mother or infant

No association between vaccination with either vaccine during pregnancy and risk of infant hospitalization or death in first 6 months of life



Bratton KN, Wardle MT, Orenstein WA, Omer SB. *Clin Infect Dis*. 2015 Mar 1;60(5):e11-9. Epub 2014 Nov 18.

McMillan M, Porritt K, Kralik D, et al. *Vaccine*. 2015; 33: (18):2108-17.

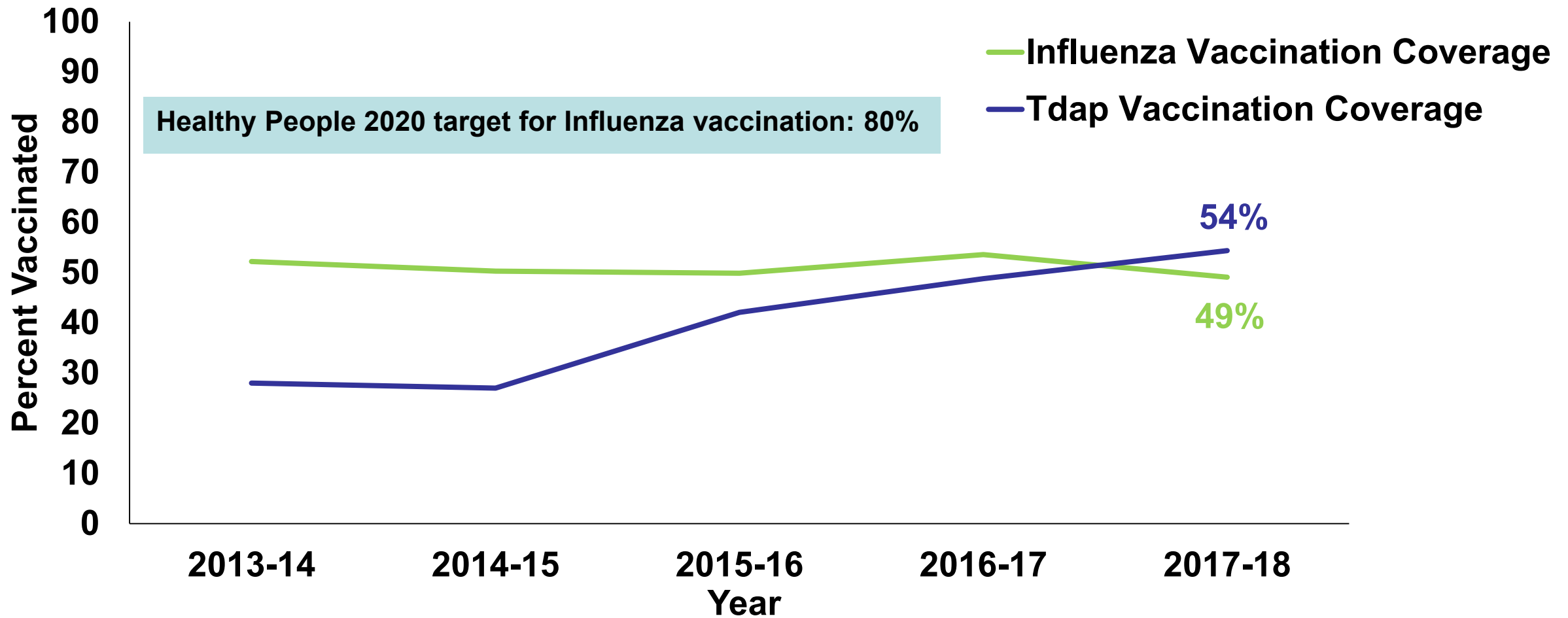
Sukumaran L, McCarthy NL, Kharbanda EO, et al. *JAMA*. 2015;314(15):1581-7.

Munoz FM, Bond NH, Maccato M, et al. *JAMA*.2014;311 (17):1760-9.

Sukumaran L, McCarthy NL, Kharbanda EO, et al. *Pediatrics*. 2018;141(3).

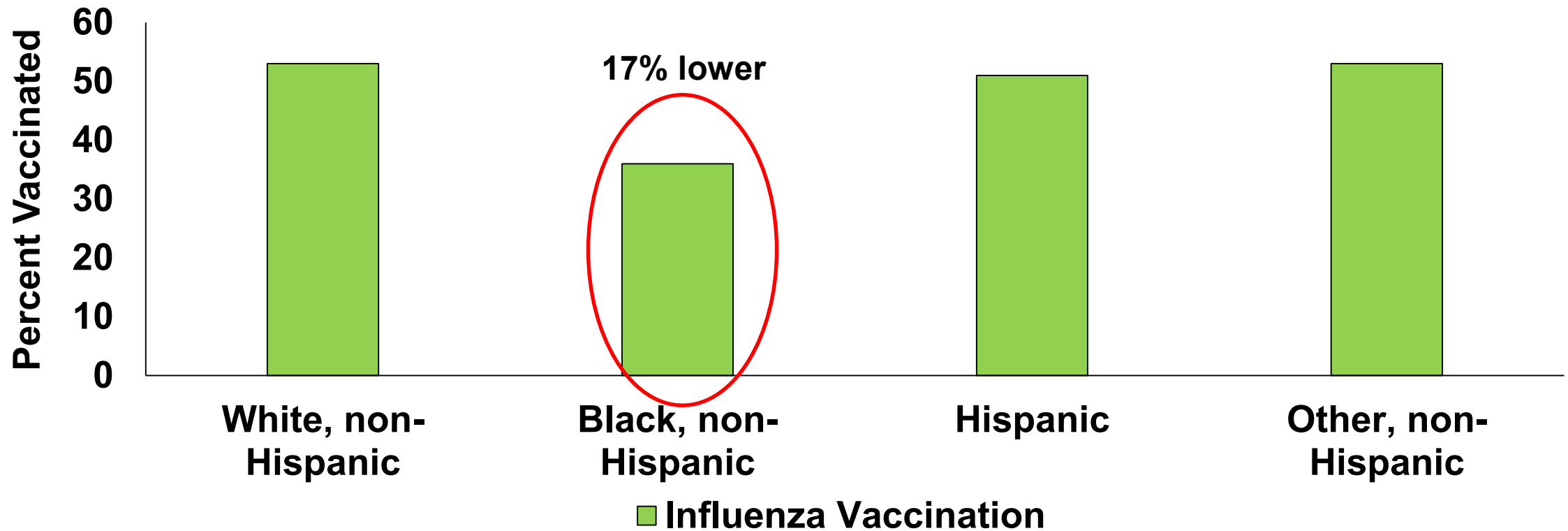
[www.cdc.gov/vaccinesafety/index.html](http://www.cdc.gov/vaccinesafety/index.html)

# Influenza and Tdap Vaccination Coverage Among Pregnant Women, 2013-14 through 2017-18 Influenza Seasons, United States



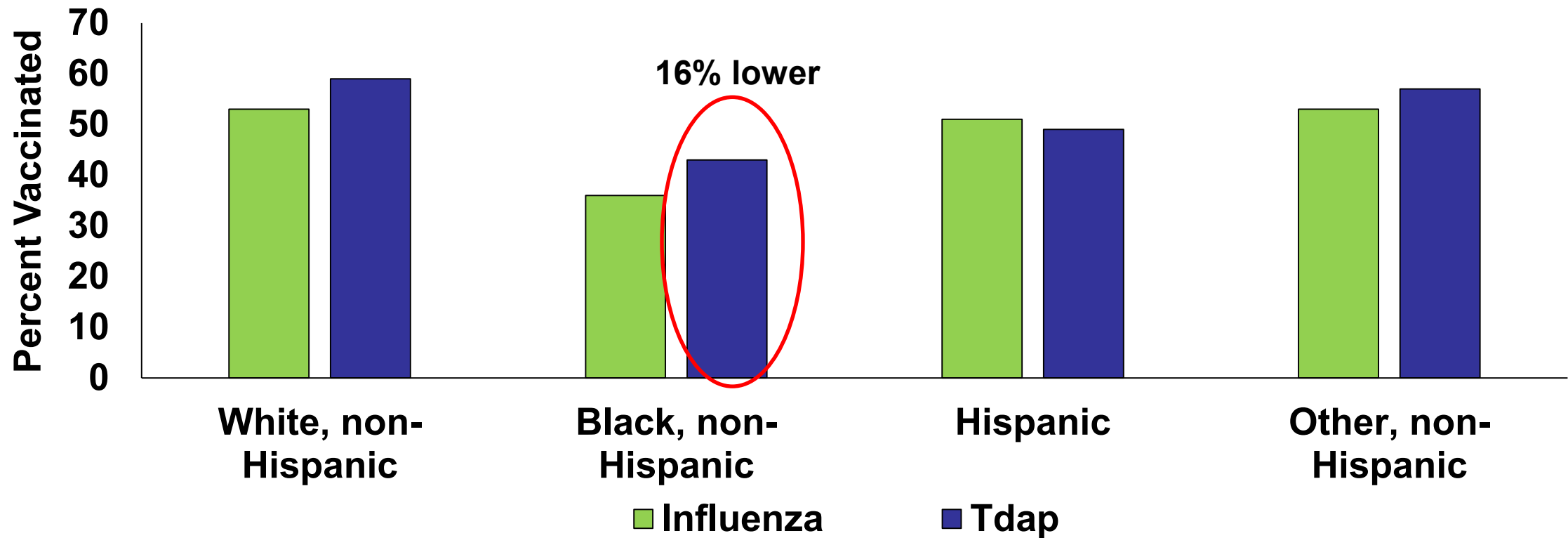
# Disparities in Maternal Vaccination Coverage

**Influenza Vaccination Coverage Among Pregnant Women, by Race and Ethnicity, United States, 2017-2018**



# Disparities in Maternal Vaccination Coverage

Influenza and Tdap Vaccination Coverage Among Pregnant Women, by Race and Ethnicity, United States, 2017-2018



# Vaccination in Pregnant Women by Provider Offer or Recommendation of Vaccine, United States, 2017-2018

**Provider Vaccine Recommendation**

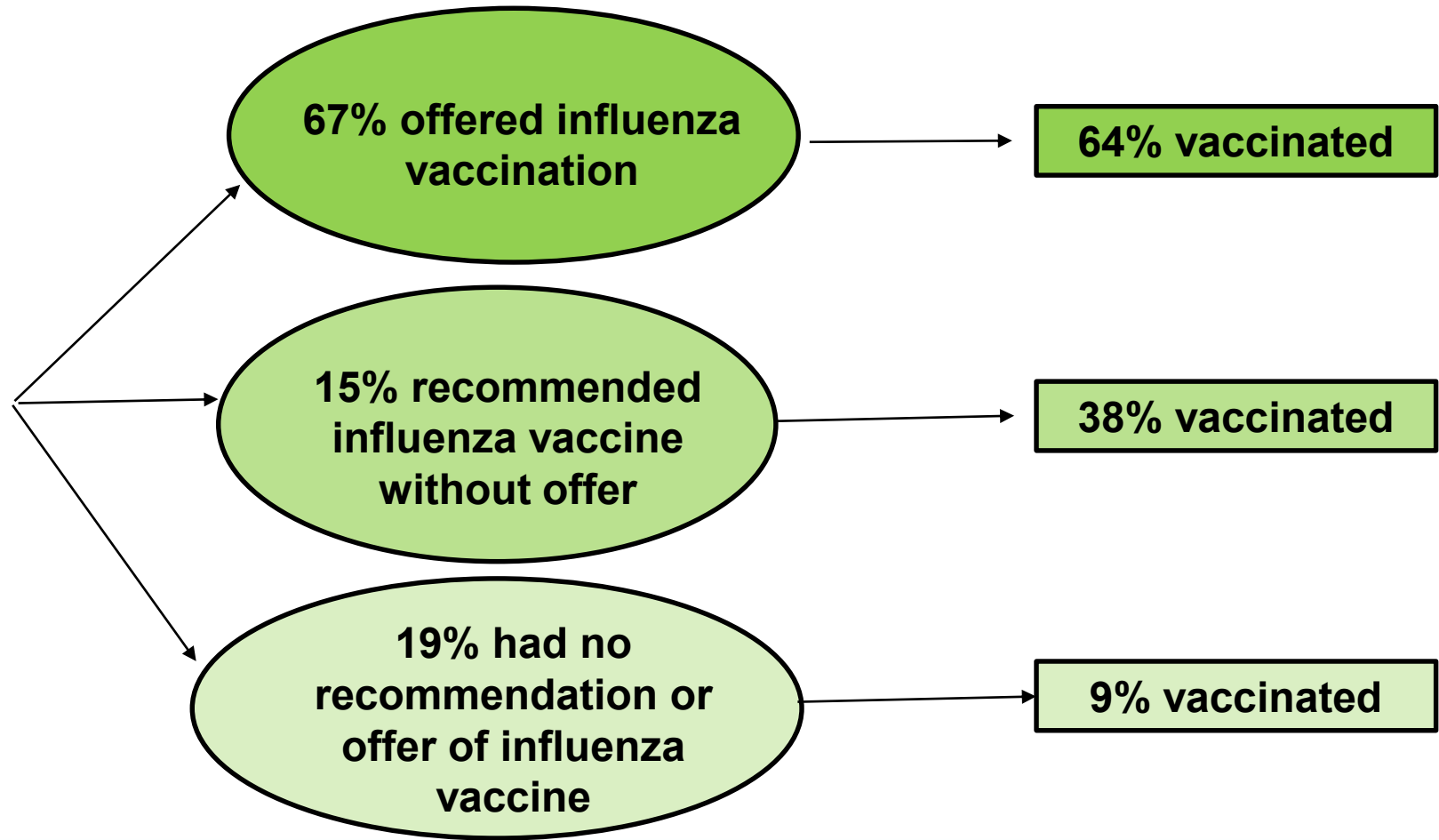


**Provider Vaccine Offer**

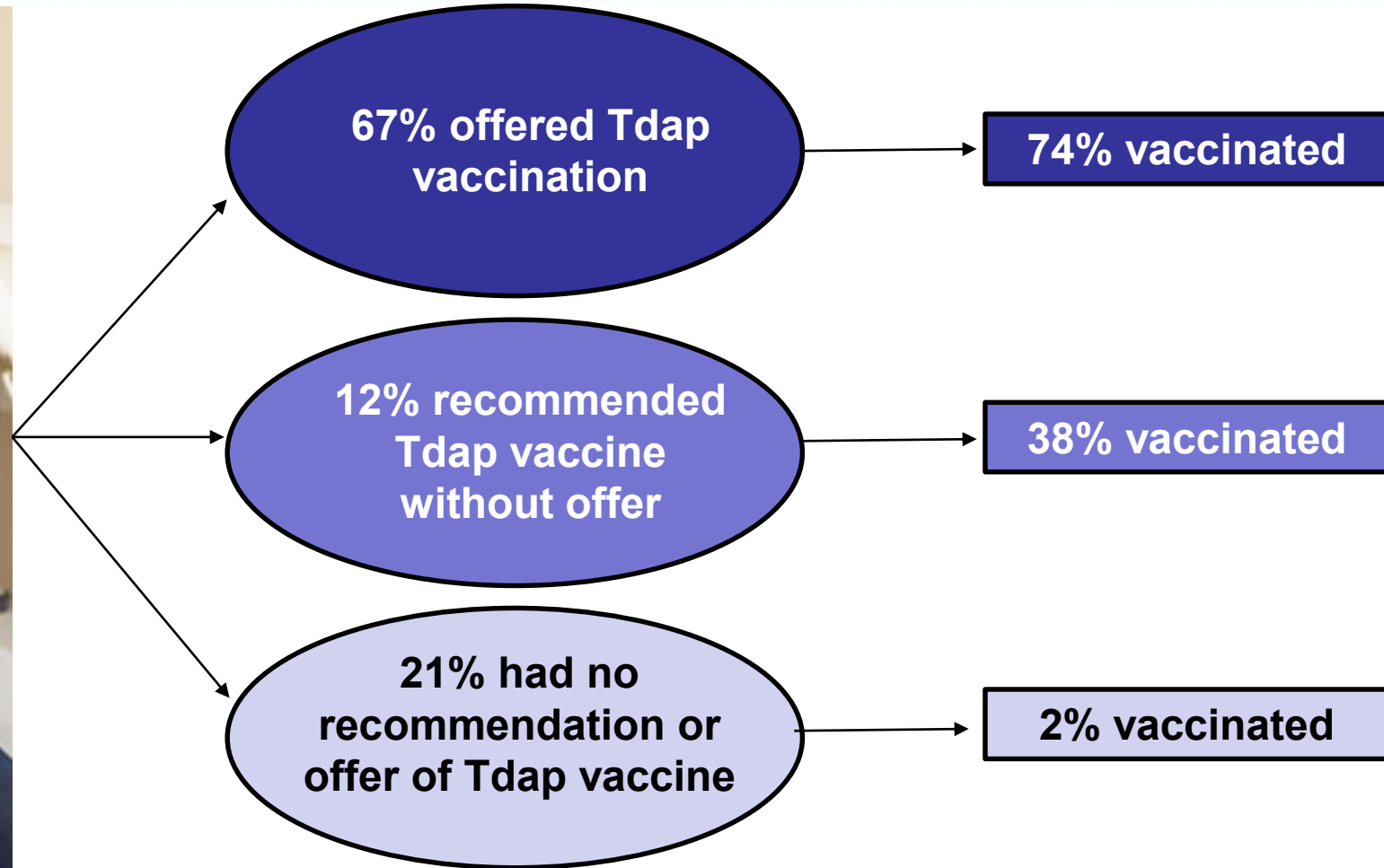




# Influenza Vaccination in Pregnant Women by Provider Offer or Recommendation of Vaccine, United States, 2017-2018



# Tdap Vaccination in Pregnant Women by Provider Offer or Recommendation of Vaccine, United States, 2017-2018



Kahn KE, Black CL, Ding H, et al. *MMWR Morb Mortal Wkly Rep* 2018;67:1055–1059

Tdap: tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine

# Summary

- **Both influenza and pertussis are serious diseases for infants. Influenza is also a serious disease for pregnant women.**
- **Maternal vaccination is effective and safe and can reduce complications, but vaccination coverage is too low.**
- **HCP offering vaccines is strongly associated with vaccination.**



# Helping Clinicians Prioritize Maternal Vaccination



**Laura E. Riley, MD**

*Given Foundation Professor and Chair, Department of Obstetrics and Gynecology*

*Weill Cornell Medicine*

*Obstetrician and Gynecologist-in-Chief at New York Presbyterian Hospital*

# The American College of Obstetricians and Gynecologists



- Founded in 1951, ACOG is the professional organization dedicated to the improvement of women's health.
- In 2005, ACOG called together a Task Force on Immunization.

# Impact of H1N1 Pandemic on Maternal Vaccination

- **2009 H1N1 pandemic**
  - Pregnant women were at high risk of influenza-related complications and death
- **H1N1 influenza vaccination rates for pregnant women increased from 15% to 50%**
  - First significant increase



# ACOG Immunization Program Timeline Since the H1N1 Pandemic

2010

**Immunization Expert Work Group convened to continue momentum from H1N1 pandemic of immunizing pregnant women.**

- **Awarded several multimillion dollar, multiyear immunization grants.**

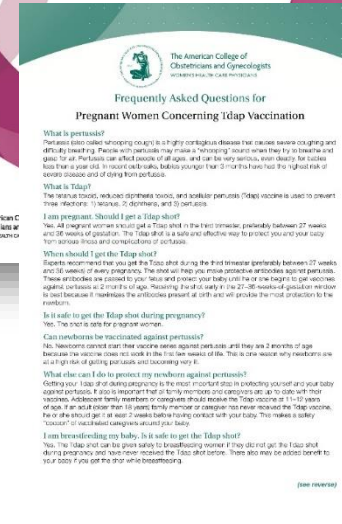
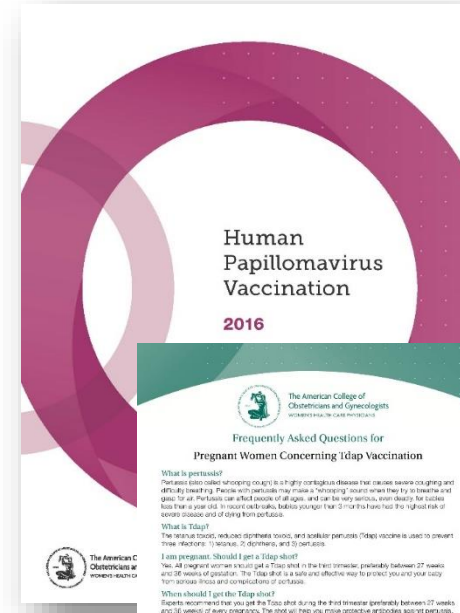
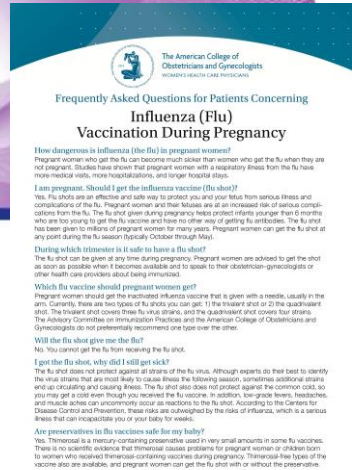
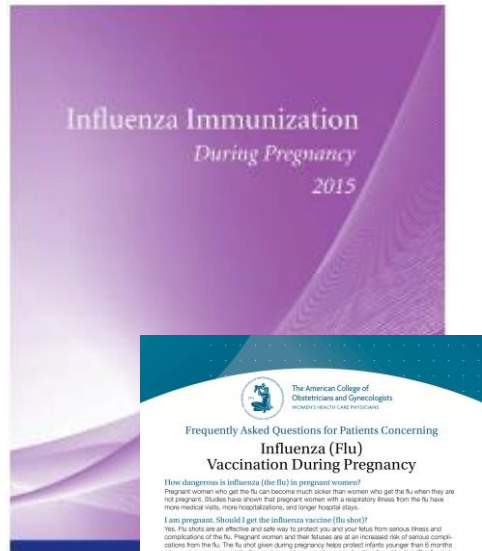
2011

**ACOG's Immunization for Women website developed:**  
[www.immunizationforwomen.org](http://www.immunizationforwomen.org)

2015

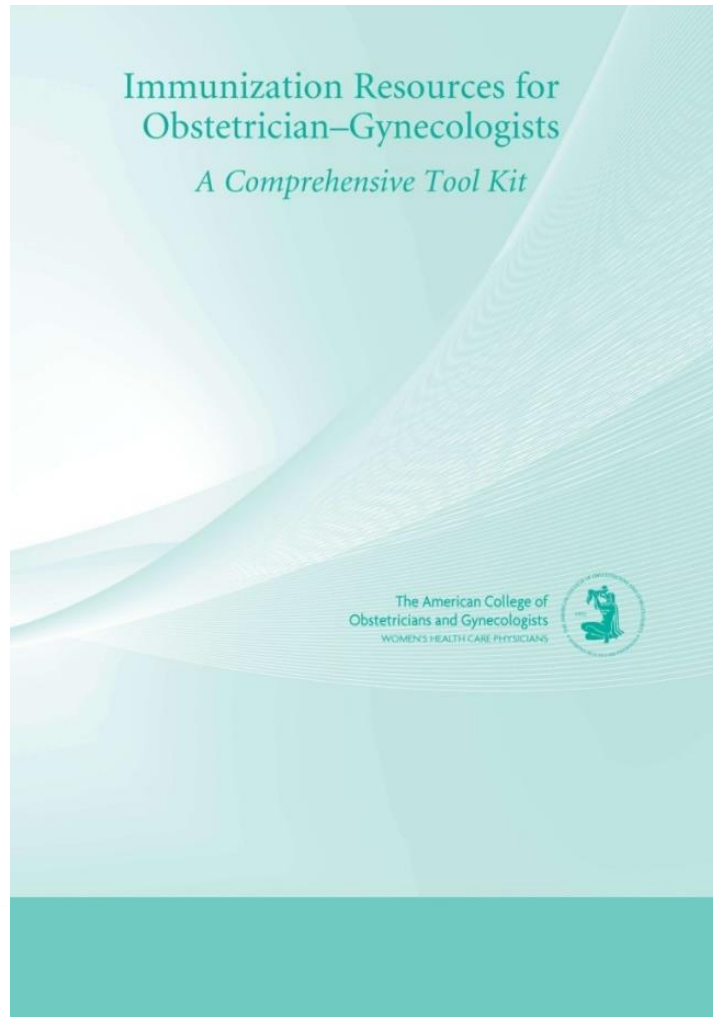
**ACOG partnered with CDC, which resulted in development of immunization tool kits from first round of grants.**

# ACOG Efforts to Improve Adult Immunization Rates: Tool Kits (2011-2018)





# Immunization Resources for Obstetrician-Gynecologists: A Comprehensive Tool Kit\*



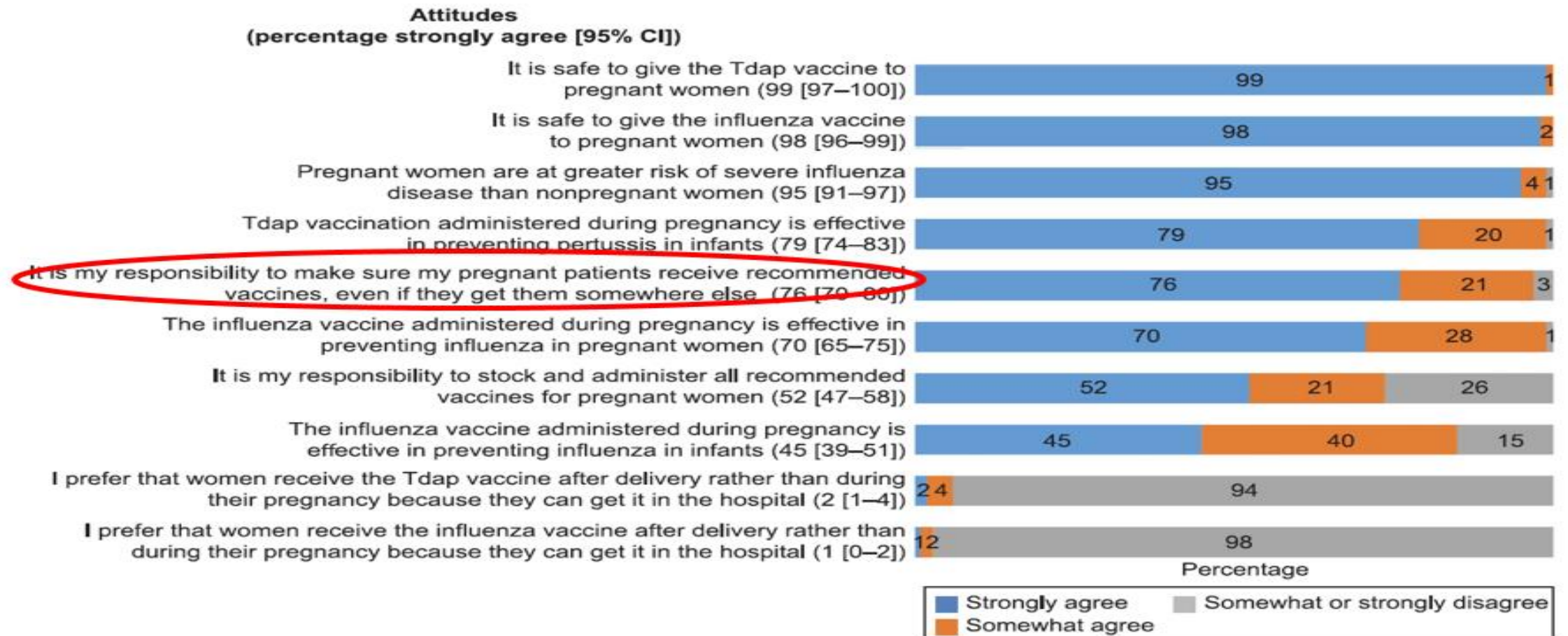
**Promotes immunization assessment, recommendation, administration and documentation as routine part of ob-gyn practice.**

## **Distribution 2013:**

- All 35,000 Ob-Gyns in practice in U.S.
- Residents and Residency Directors
- ACOG District Leadership
- State Maternal and Child Health Directors
- Key CDC Staff
- Partner Organizations

# Attitudes of Ob/Gyn Providers on Vaccinating Pregnant Patients

## Ob/Gyn Survey on Vaccination Practices (n= 331)

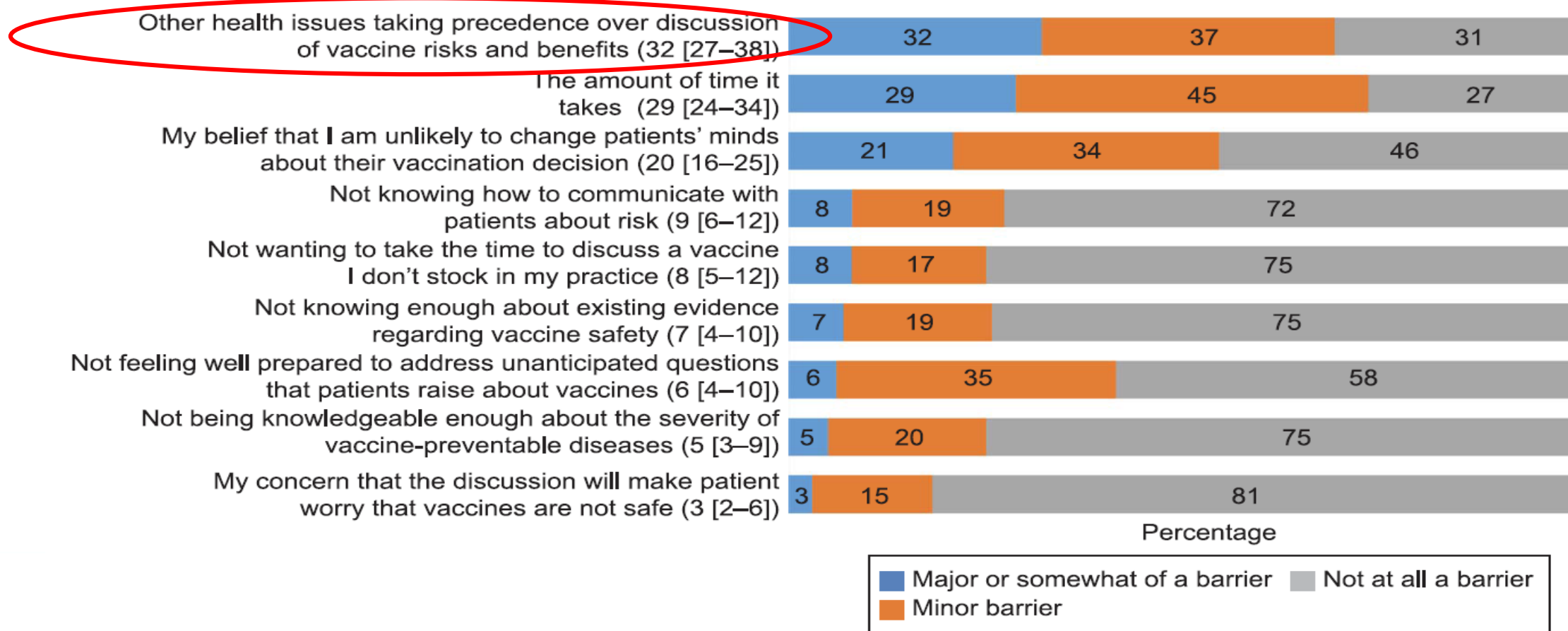


# Barriers Identified to Vaccinating Pregnant Patients

## Ob/Gyn Survey on Vaccination Practices (n= 331)

### Barriers

(percentage of major or somewhat of a barrier [95% CI])





The American College of  
Obstetricians and Gynecologists  
WOMEN'S HEALTH CARE PHYSICIANS

# ACOG COMMITTEE OPINION

Number 741, June 2018

Immunization, Infectious Disease, and Public Health Preparedness Expert Work Group

**Table 1. Summary of Maternal Immunization Recommendations**

Vaccine*	Indicated During Every Pregnancy	May Be Given During Pregnancy in Certain Populations	Contraindicated During Pregnancy	Can Be Initiated Postpartum or When Breastfeeding or Both
Inactivated influenza	X <sup>1,1,2</sup>			X <sup>‡</sup>
Tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap)	X <sup>†,3,4</sup>			X <sup>‡</sup>
Pneumococcal vaccines		X <sup>§,5,6</sup>		X <sup>§,5,6</sup>
Meningococcal conjugate (MenACWY) and Meningococcal serogroup B		X <sup>  ,7</sup>		X <sup>  ,7</sup>
Hepatitis A		X <sup>¶,8</sup>		X <sup>¶,8</sup>
Hepatitis B		X <sup>¶,9,10</sup>		X <sup>¶,9,10</sup>
Human papillomavirus (HPV)**				X <sup>**,11,12</sup>
Measles–mumps–rubella			X <sup>††,13,14</sup>	X <sup>††</sup>
Varicella			X <sup>††,13,15,16</sup>	X <sup>††</sup>

\*An "X" indicates that the vaccine can be given in this window. See the corresponding numbered footnote for details.

<sup>1</sup>Inactivated influenza vaccination can be given in any trimester and should be given with each influenza season as soon as the vaccine is available. The Tdap vaccine is given at 27–36 weeks of gestation in each pregnancy, preferably as early in the 27–36-week window as possible. The Tdap vaccine should be given during each pregnancy in order to boost the maternal immune response and maximize the passive antibody transfer to the newborn. Women who did not receive Tdap during pregnancy (and have never received the Tdap vaccine) should be immunized once in the immediate postpartum period.<sup>1–3</sup>

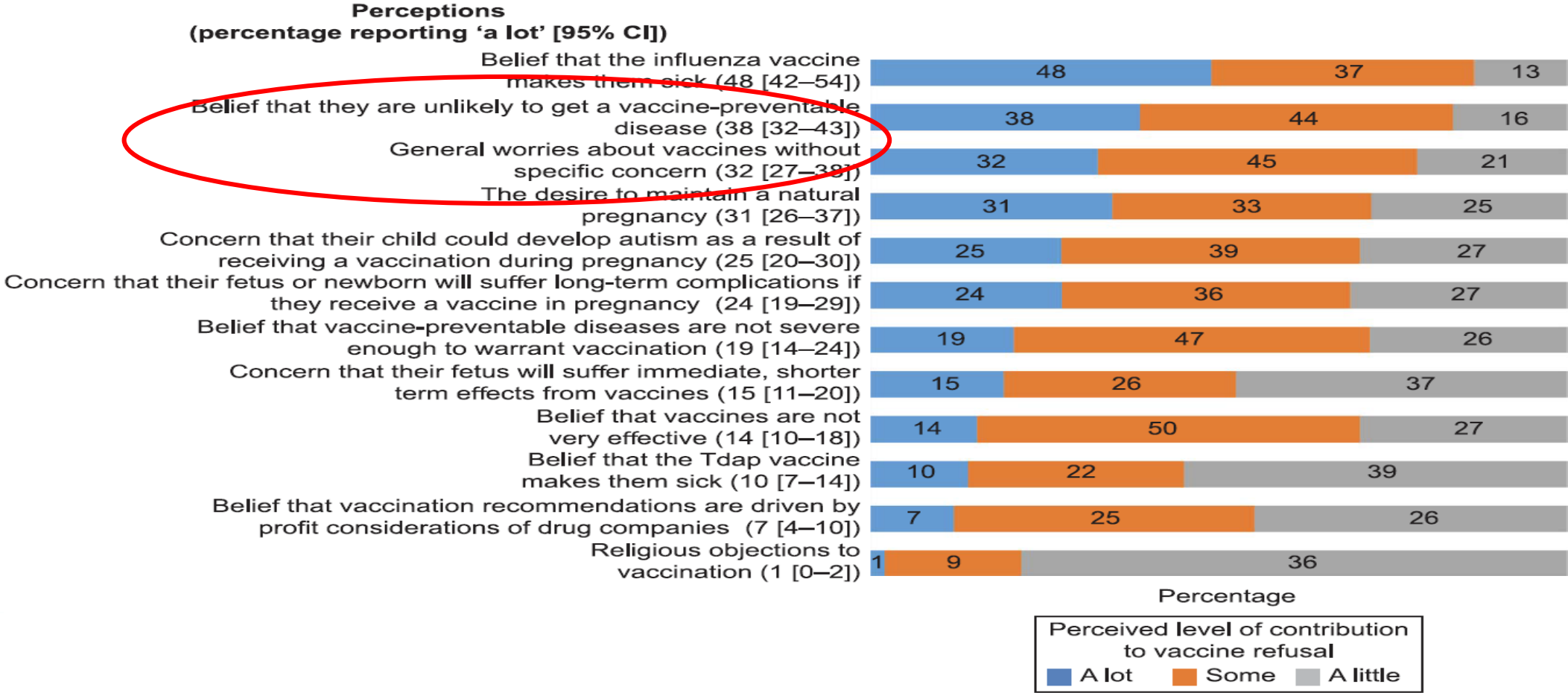
<sup>2</sup>Vaccination during every pregnancy is preferred over vaccination during the postpartum period to ensure antibody transfer to the newborn.<sup>3,4</sup>

<sup>5</sup>There are two pneumococcal vaccines: 1) the 23-valent pneumococcal polysaccharide vaccine (PPSV23) is recommended in reproductive-age women who have heart disease, lung disease, sickle cell disease, and diabetes as well as other chronic illnesses; 2) the 13-valent pneumococcal vaccine (PCV13) is recommended for reproductive-aged women with certain immunocompromised conditions, including human immunodeficiency virus (HIV) infection and asplenia. The PCV13 vaccine should be deferred in pregnant women, unless the woman is at increased risk of pneumococcal disease and after consultation with her health care provider the benefits of vaccination are considered to outweigh the potential risks.<sup>5,6</sup>

<sup>||</sup>Quadrivalent conjugate meningococcal vaccine is routinely recommended for adolescents aged 11–18 years, along with individuals with HIV infection, complement component deficiency (including eculizumab use), functional or anatomic asplenia (including sickle cell disease), exposure during a meningococcal disease outbreak, travel to endemic or hyperendemic areas, or work as a microbiologist routinely exposed to *Neisseria meningitidis*. If indicated, pregnancy should not preclude vaccination. The serogroup B vaccine should be deferred in pregnant women, unless the woman is at increased risk of serogroup B meningococcal disease<sup>7</sup> and, after consultation with her health care provider, the benefits of vaccination are considered to outweigh the potential risks.<sup>7</sup>

# Ob/Gyn Perceptions on Why Women Refuse Vaccines

## Ob/Gyn Survey on Vaccination Practices (n= 331)



# Next Steps to Promote Maternal Immunization

- **Continue to emphasize risk for disease to the fetus or newborn to increase vaccine uptake**
- **Continue to educate about risk of maternal disease complications such as preterm birth, ICU admission for influenza-related morbidity**
- **Introduce education about both maternal and childhood immunization earlier in pregnancy**
- **Partner with others to decrease vaccine hesitancy and refusal**

# How Grady Memorial Hospital Works to Promote and Increase Maternal Immunization



**Denise Jamieson, MD, MPH**

*James Robert McCord Professor and Chair*

Department of Gynecology and Obstetrics

Emory University School of Medicine

# Grady Health System

- **One of the largest public health systems in the U.S.**
- **Safety net institution for medically underserved patients in Atlanta**
- **Approximately 3,000 deliveries per year**
  - 88% Medicaid-eligible
  - 68% non-Hispanic black
  - 23% non-native English speakers
  - 44% inadequate prenatal care utilization
    - ▣ Defined by an index that includes when prenatal care began, and the number of prenatal visits from when prenatal care began until delivery (Kotelchuk index)





# Maternal Vaccination Promotion at Grady

- **Universal provider recommendation**
- **Routine assessment of immunization status**
- **Standing orders**
- **All sites stock influenza and Tdap vaccines**
- **Vaccines provided at no additional charge**



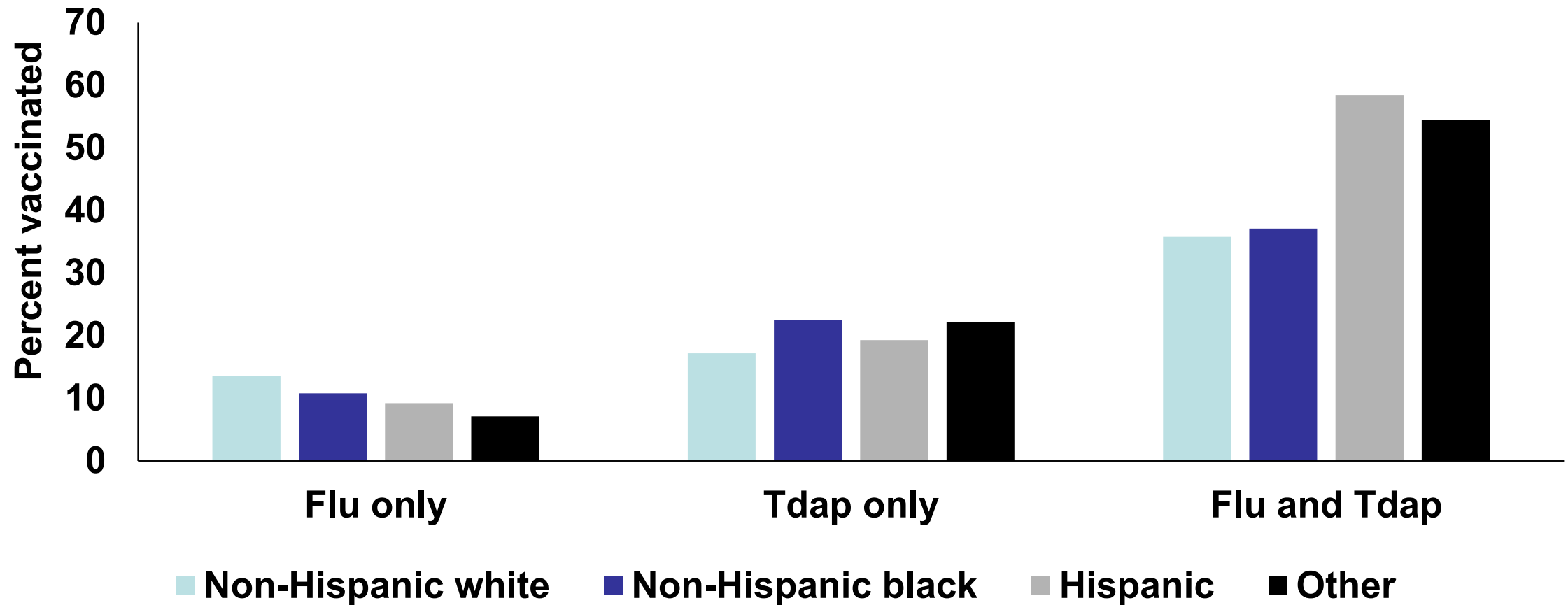
# ACOG Strategies for Effectively Integrating Immunizations into Routine Obstetric-Gynecologic Care

1. **Administer routinely discussed and recommended vaccines.**
2. **Create a culture of immunization by educating and involving all staff in immunization processes.**
3. **Develop a standard process for assessing, recommending, administering, and documenting immunization status of patients.**
4. **Use existing systems and resources to conduct periodic assessments of immunization rates among patients to determine if and where progress is needed.**

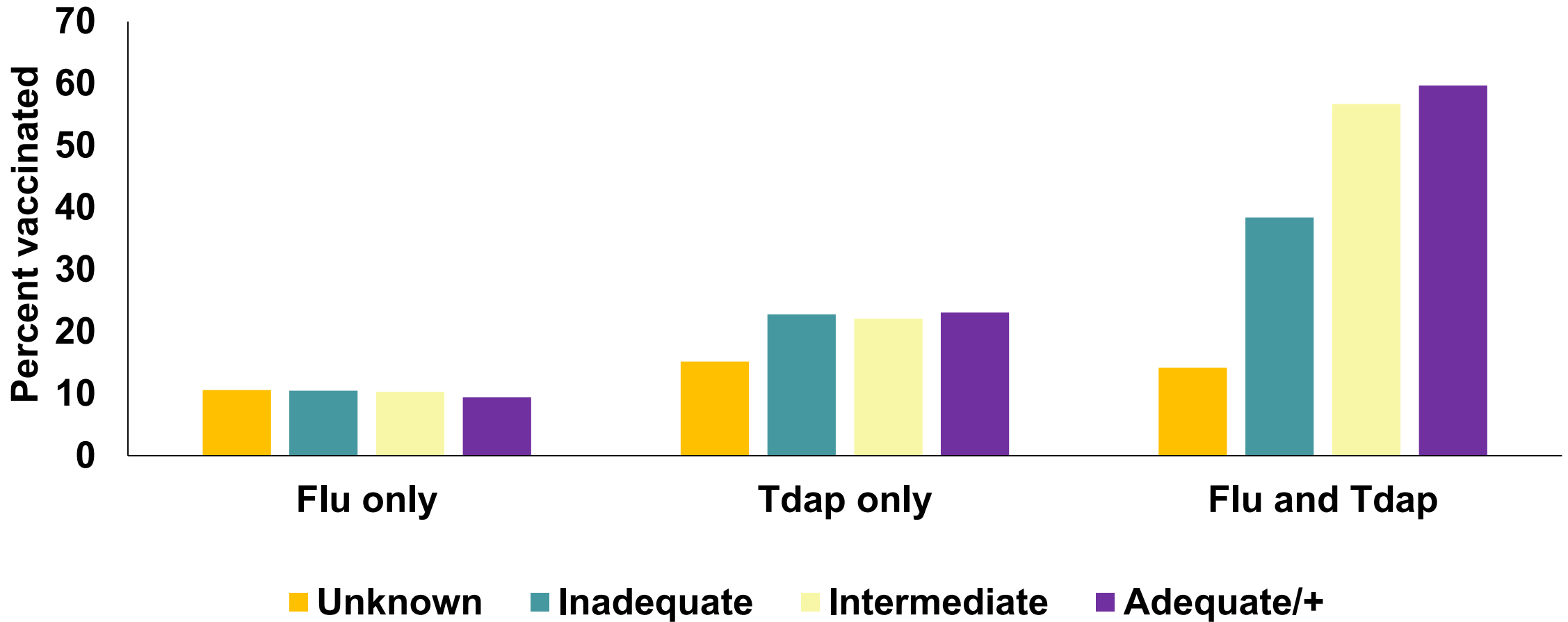
# Assessing Maternal Immunization Rates at Grady

- **Infectious Diseases in Pregnancy (IDPREG) study: Maternal Infections and Outcomes at Grady Memorial Hospital**
- **Retrospective cohort study of around 3,700 deliveries between July 1, 2016 and June 30, 2018**
- **Documented demographic and clinical characteristics of patients, including influenza and Tdap vaccination**

# IDPREG: Influenza and Tdap Vaccination Coverage by Race and Ethnicity, Grady Hospital, July 2016-June 2018



# IDPREG: Influenza and Tdap Vaccination Coverage by Prenatal Care Utilization, Grady Hospital, July 2016-June 2018



# IDPREG Conclusions

- **Rate of receiving both Tdap and influenza vaccination is higher than national average (43% vs 33%).**
- **Hispanic women have highest rates of receiving both influenza and Tdap vaccination.**
- **Vaccination coverage declines with decreasing rates of prenatal care utilization.**
  - >40% of women at Grady had inadequate prenatal care use.

# “Yellow Sheet” Project

## ➤ Goals

- Prospectively track influenza vaccine acceptance in Grady OB/GYN clinic.
- Identify reasons for refusal.
- Develop interventions to improve vaccine coverage.

➤ **All patients seen in clinic from 9/18/2018 through 4/8/2019**

Place patient label here.  
If no label, enter MRN: \_\_\_\_\_

Today's Date: \_\_\_\_\_

Does the patient want the flu shot today? (Please circle one)

Already Received	Flu Vaccine Today	No	Not medically eligible to receive	Unable to consent (e.g. <18 years old)
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↓

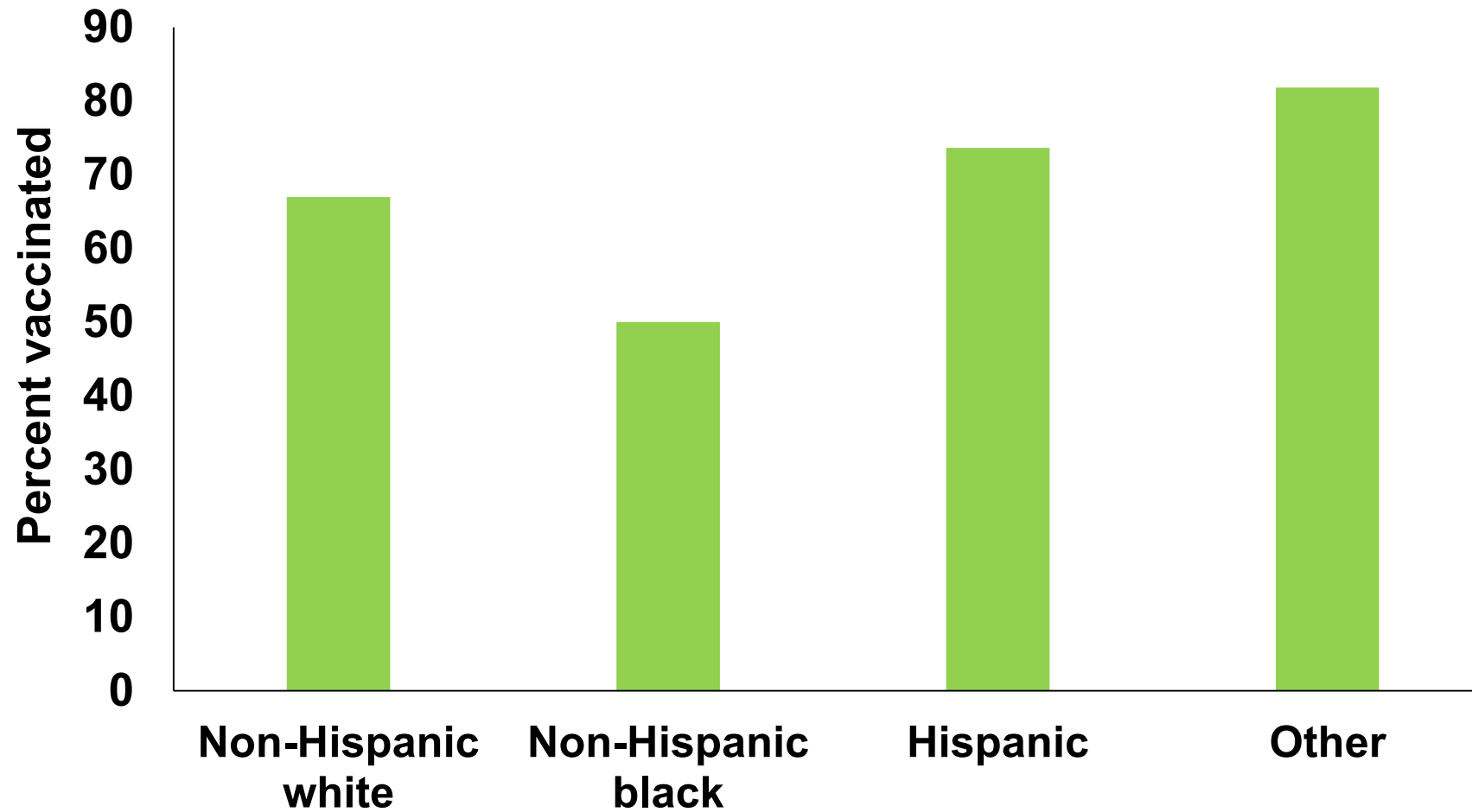
What reasons does the patient state for declining an influenza vaccine today? (Check all that apply):

- I worry about the side effects or harms for me
- I worry about the side effects or harms for my baby (if pregnant)
- I have heard bad things about the flu vaccine
  - Please comment: \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
- I do not normally get a flu vaccine
- I do not think the vaccine is effective in preventing the flu
- I think the vaccine will give me the flu
- I do not think I am at risk of getting the flu
- I do not like shots
- I cannot afford the vaccine
- I will get sick
- Will get next time/later visit
- Other:
  - Please comment: \_\_\_\_\_
  - \_\_\_\_\_
  - \_\_\_\_\_
- Patient declines to give a reason

For administrator use only:

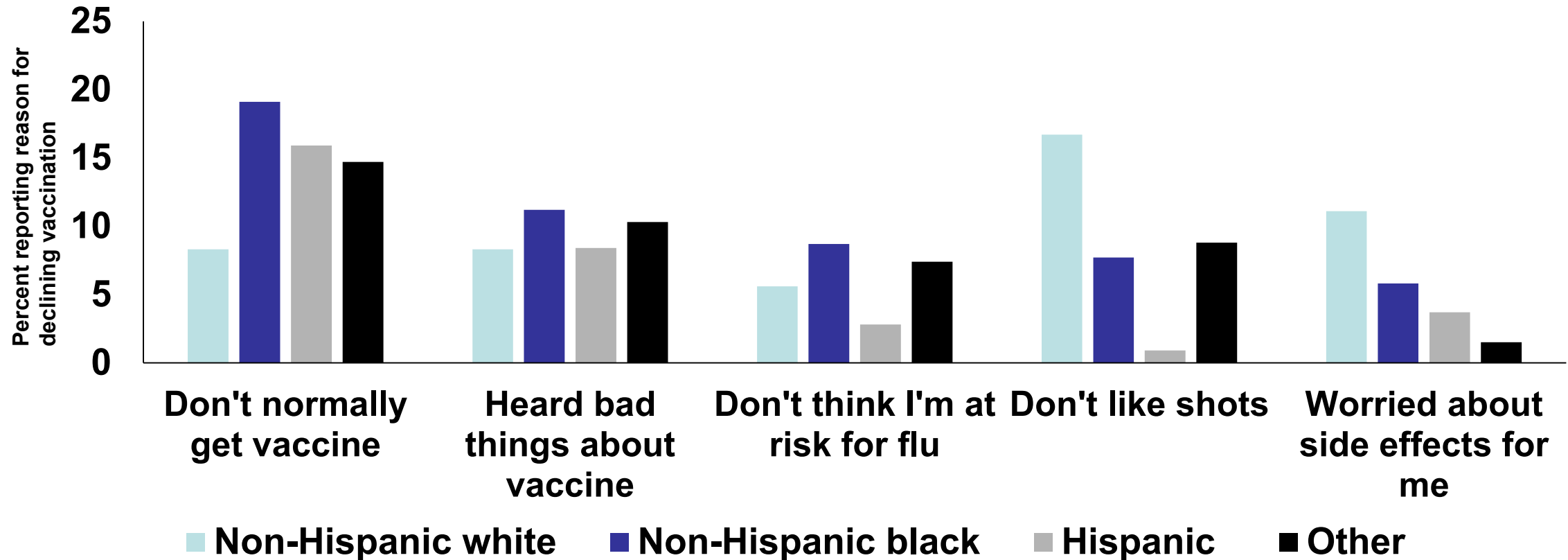
Missing      M    E    Form #: \_\_\_\_\_

# Preliminary Results – Influenza Vaccination of Pregnant Women at Grady Hospital, 9/2018 through 4/2019





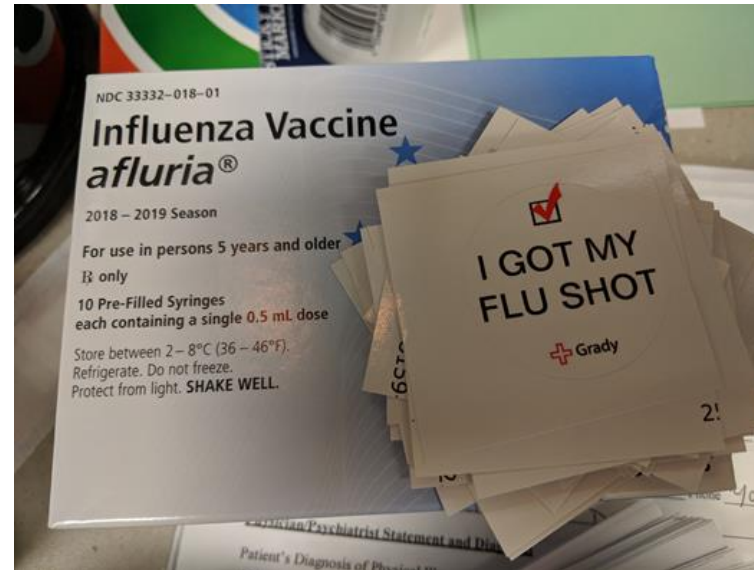
# Top Five Reasons for Influenza Vaccine Refusal Among Pregnant Women



Unpublished data

# Preliminary Results – Influenza Vaccination

Overall vaccination rate for pregnant women at Grady Hospital for the 2018-2019 flu season was 55% (**a 5% increase from the previous two seasons**)



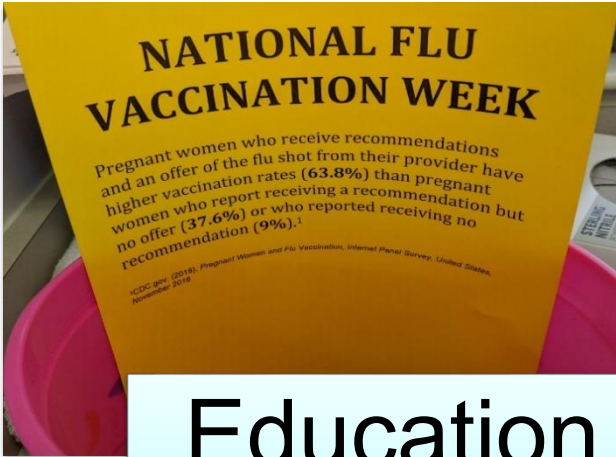
# Keys to Success in Increasing Maternal Immunization



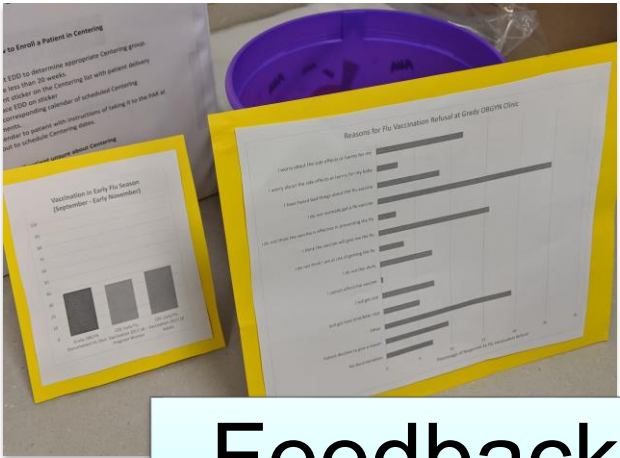
Champions



Incentives



Education



Feedback



Celebration

# Our Grady Team

Sheree Boulet  
Jenna Adams  
Hope Biswas  
Miah Davis  
Kamini Doraivelu  
Emily Goggins  
Lisa Haddad  
Tess Kim  
Mumu Rahman  
Michelle Saums  
Rachel Williams  
Roland Matthews  
Franklyn Geary

INSIDE GRADY | APRIL 2019 EDITION


## OB/GYN FOCUSES ON FIGHTING FLU

At the start of last year's flu season, Grady's OB/GYN Clinic implemented the "Yellow Sheet Project" that aims to collect data on why patients refuse the flu vaccine. The project uses a bright yellow sheet of paper to track whether patients accept or decline the flu vaccine during each visit. If a patient declines the shot, her reasons for declining are also collected. The information from the yellow sheets is then entered into a database and used to track vaccination rates and commonly reported reasons for refusing the vaccine.

"Our intention is to increase vaccination rates, especially in pregnant women, and identify barriers to vaccinations for future flu seasons," said Dr. Denise Jamieson, Emory's associate chief of OB/GYN at Grady.

According to data collected from September 18 to December 15, 2018, only 51% of eligible pregnant patients seen at Grady's OB/GYN clinic received the flu vaccine. Influenza is particularly dangerous in pregnant women given their immunocompromised state, Jamieson said.

"Vaccination not only protects the mother, but also the baby up to six months of age. Even though the vaccine is safe at any stage of pregnancy, nationally vaccination rates in pregnant women have plateaued at 50% for



Dr. Denise Jamieson (center) stands alongside medical students Rachel Williams, Emily Goggins, Jenna Adams, and Tess Kim, who all drive the Yellow Sheet Project.

about the past ten years. We are working hard to beat the national average and protect more of our patients."

Providers counsel patients on the benefits of the vaccine, fill out the yellow sheet, and if given the green light, nurses administer the vaccines. For those who refuse the vaccine, medical students from Emory University School of Medicine prepare and collect yellow sheets documenting reasons for refusal, and then input the data.

"The overarching goal is to improve the quality of care for patients by collecting information on why

they refuse the vaccine, which will enable providers to better target their messages in a way that resonates with patients," Jamieson said.

Patients who refuse the shot often base their decision on habitually skipping the vaccine every season, and a belief that it will make them sick.

"There are a lot of myths and misperceptions about the flu vaccine. The information collected in the Yellow Sheet Project will help us understand patient concerns so we can better counsel patients on the risks and benefits of flu vaccination."

# Accelerating Progress with New Maternal Vaccines



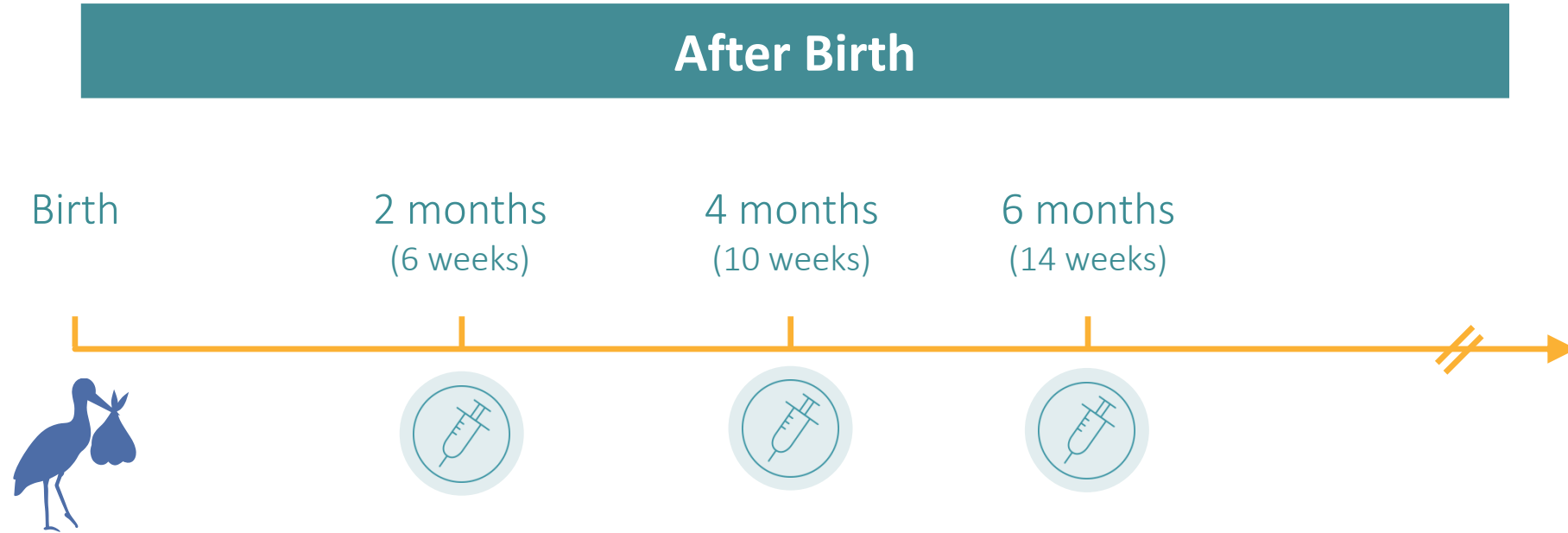
**Saad B. Omer, MBBS, MPH, PhD**

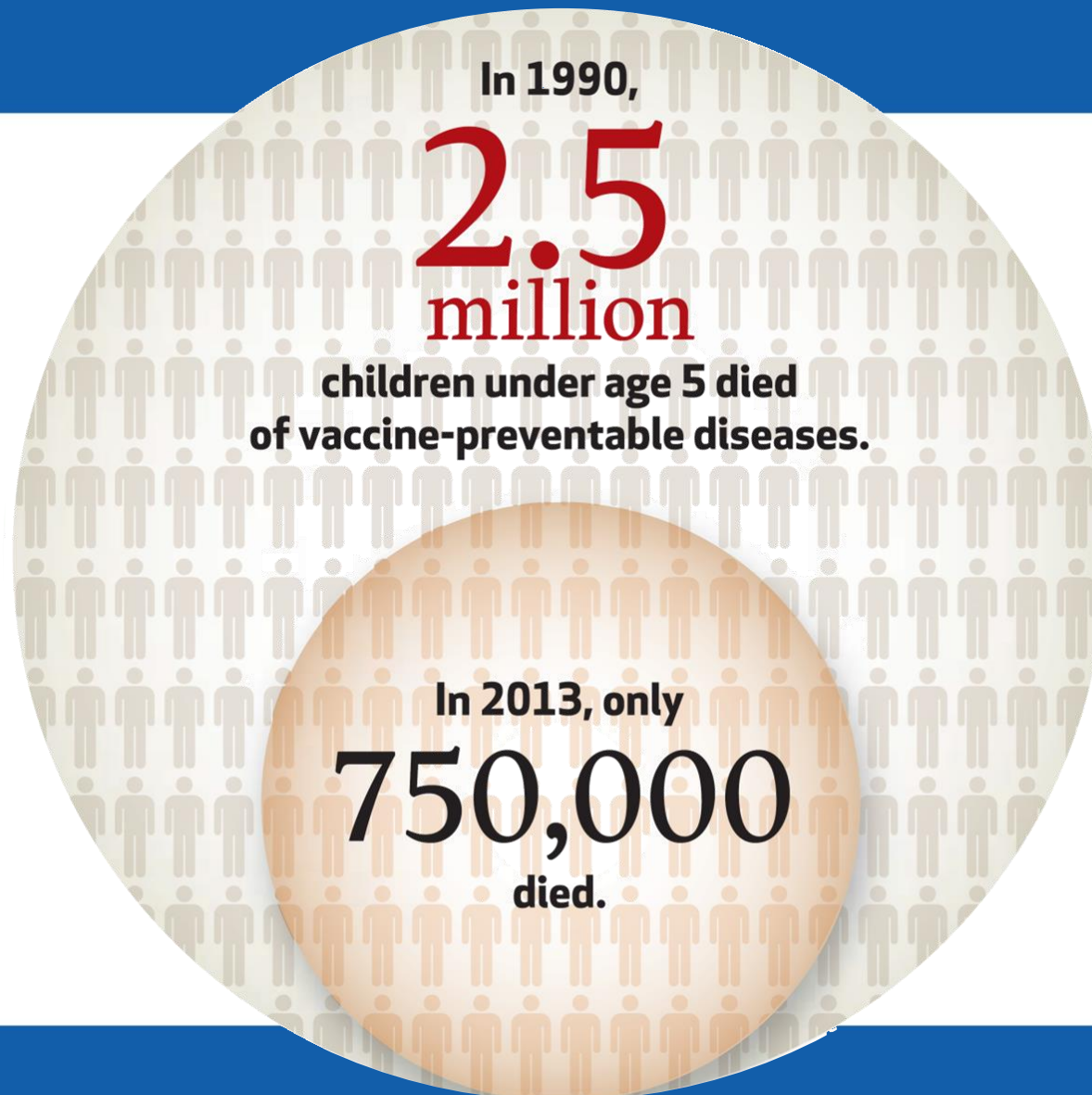
*Director, Yale Institute for Global Health*

*Professor of Medicine, Yale School of Medicine*

*Susan Dwight Bliss Professor of Epidemiology of Microbial Diseases, Yale School of Public Health*

# General Infant Immunization Schedule





In 1990,

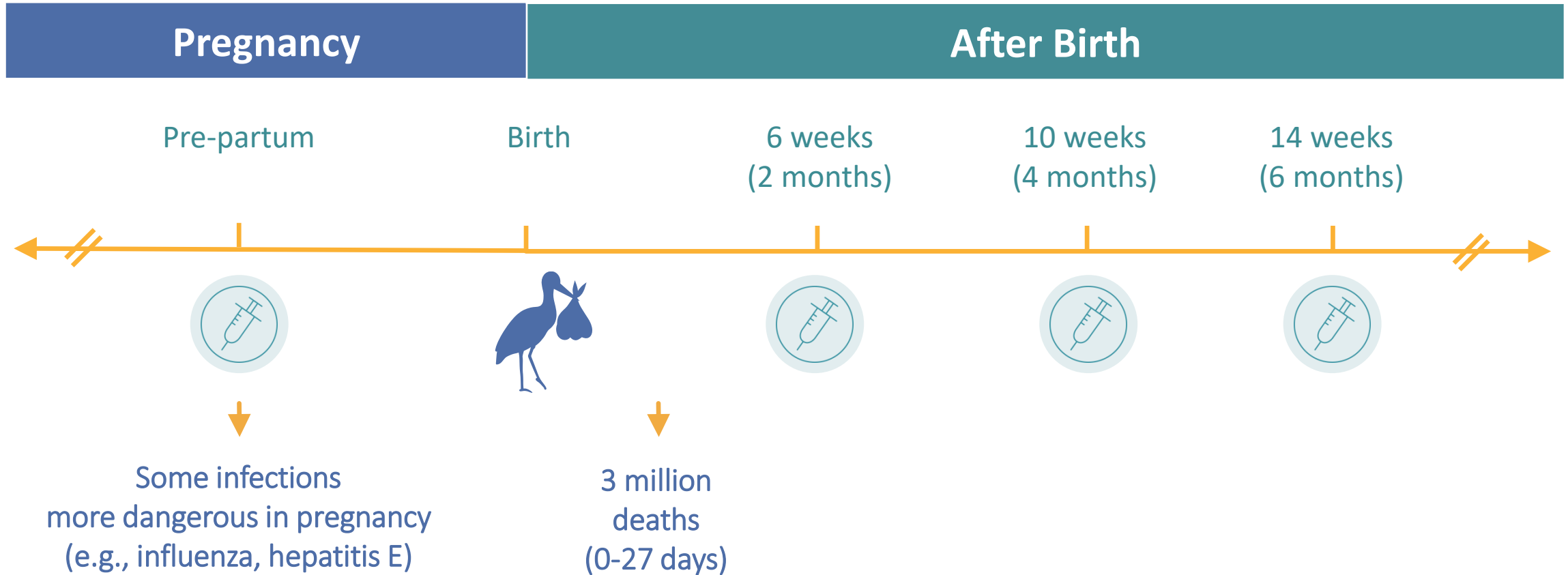
**2.5**  
million

children under age 5 died  
of vaccine-preventable diseases.

In 2013, only

**750,000**  
died.

# Role of Maternal Immunization in Protecting Neonates



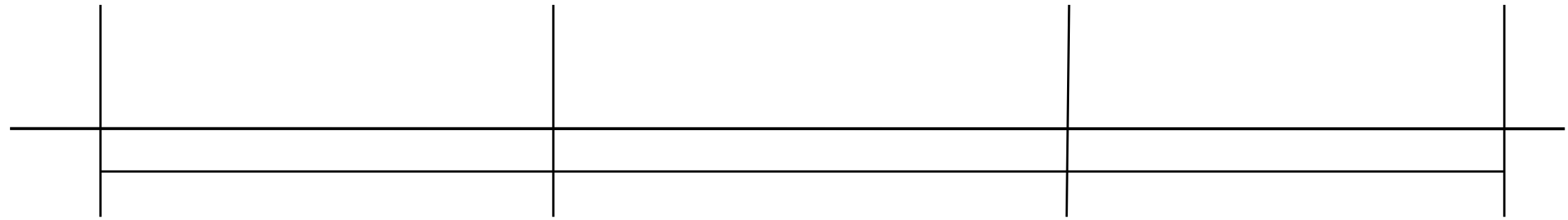


Group B Streptococcus  
Respiratory syncytial virus  
Cytomegalovirus (CMV)

Hepatitis E  
Pneumococcus  
Rotavirus\*

Meningococcus  
Hepatitis A  
Hepatitis B

Tetanus  
Influenza\*\*  
Pertussis\*\*



Vaccine in development that could be used by pregnant women

Vaccine licensed; not routinely recommended for pregnant women

Vaccine licensed; can be given to pregnant women but not routinely recommended

Vaccine licensed; routinely recommended for pregnant women

\* Live vaccine contraindicated for use in pregnancy; inactivated vaccine has been developed but is not currently recommended for use

\*\* Recommended for routine vaccination of pregnant women in some high-income countries including United States

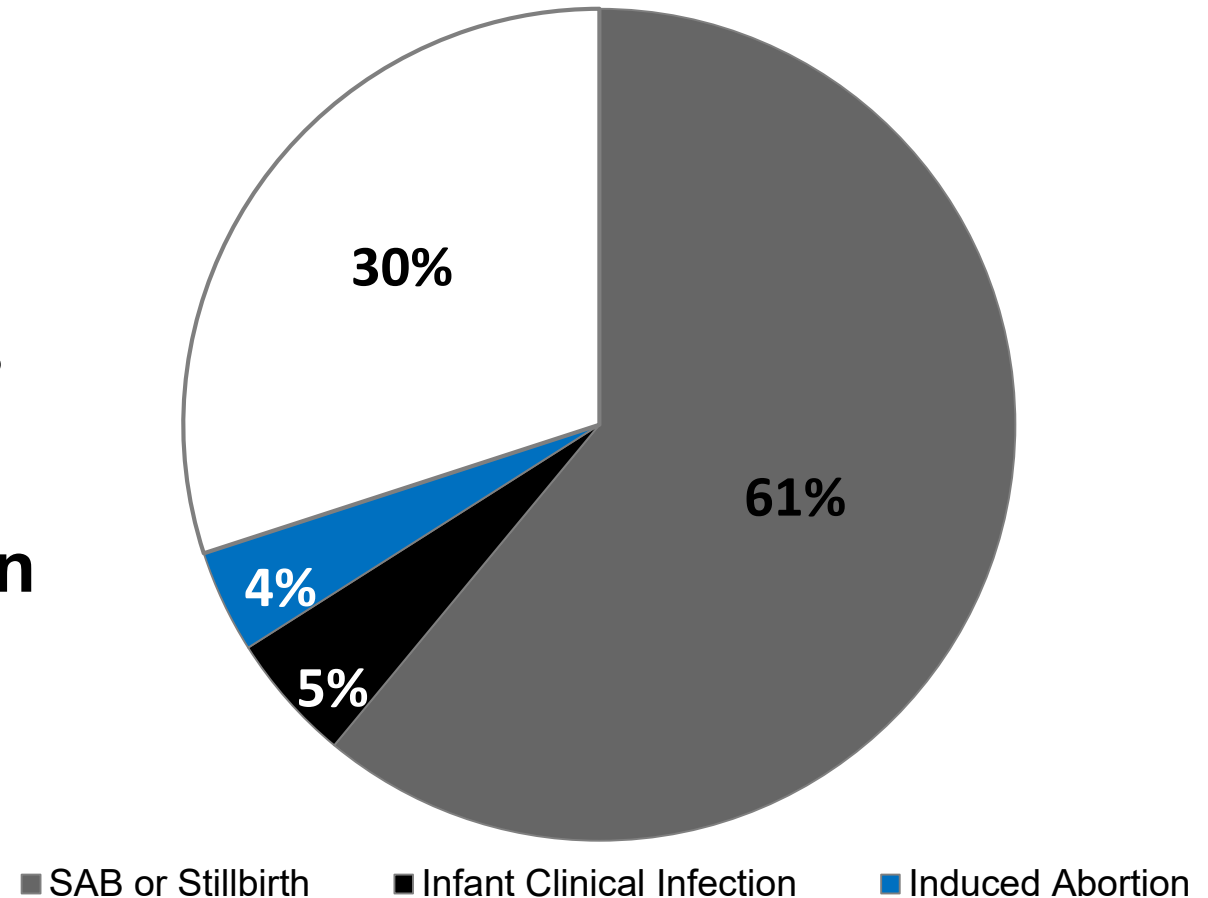
# **Group B Streptococcus (GBS) Vaccine**

# Invasive Group B Streptococcus Disease in Infants

- ❑ **Early-onset Group B Streptococcus (EOGBS) occurs before age 7 days**
  - sepsis (80%-95%)
  - pneumonia (10%-15%)
  - meningitis (5%-10%)
  
- ❑ **Late-onset GBS (LOGBS) occurs in infants aged 7 to 89 days old**
  - Meningitis more frequent (21%–35%)
    - » 30% of infants have permanent complications (e.g., hearing loss, developmental delay)

# Pregnancy Outcomes Among Women with Invasive GBS

- **Active, population-based surveillance in 10 U.S. states**
- **Identified 409 invasive GBS infections in pregnant women**

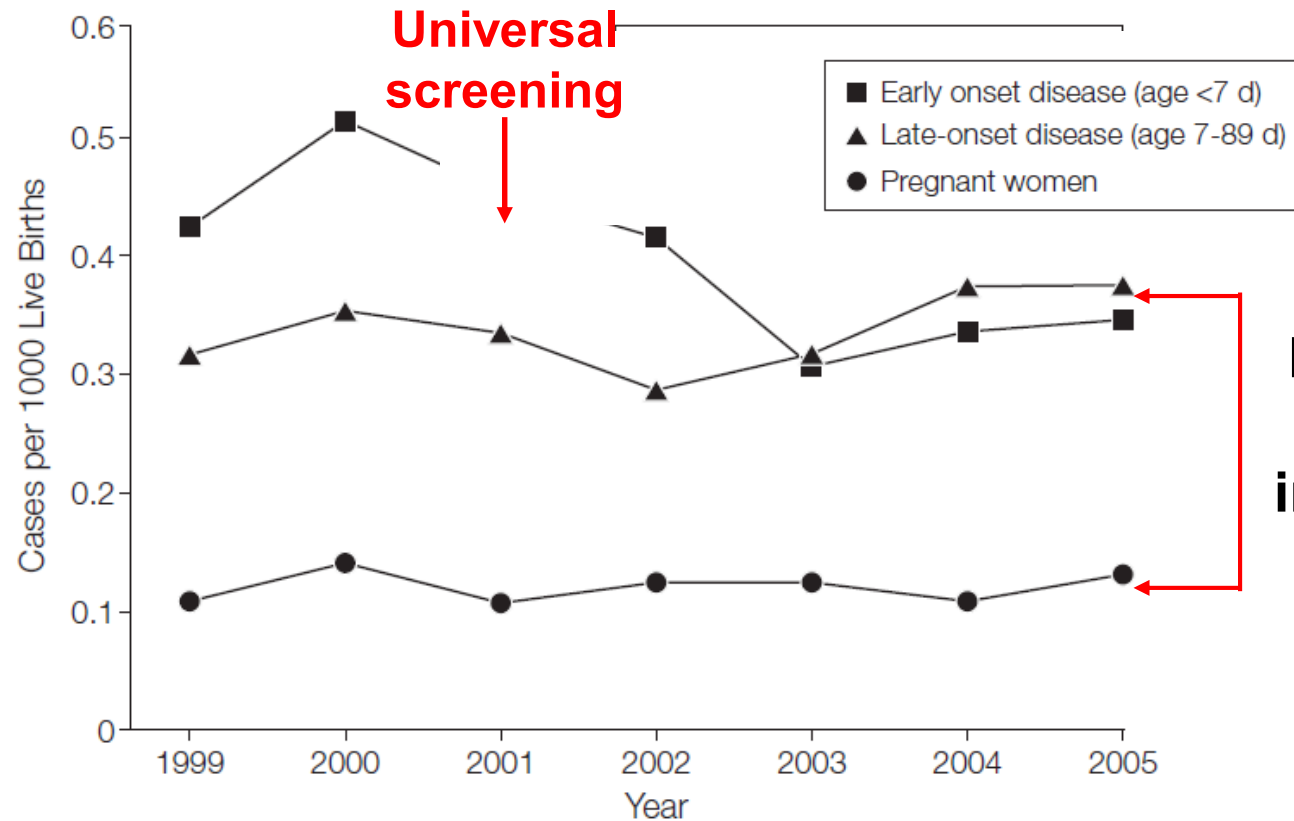


Phares CR, Lynfield R, Farley MM et al. JAMA. 2008 May 7;299(17):2056-65.

GBS: Group B Streptococcus  
SAB: spontaneous abortion

# Epidemiology of GBS Infection in Pregnant Women in Select U.S. Areas

**Figure 2.** Incidence of Invasive Group B Streptococcal Disease Among Infants (<90 Days) and Pregnant Women in Select US Areas, 1999-2005



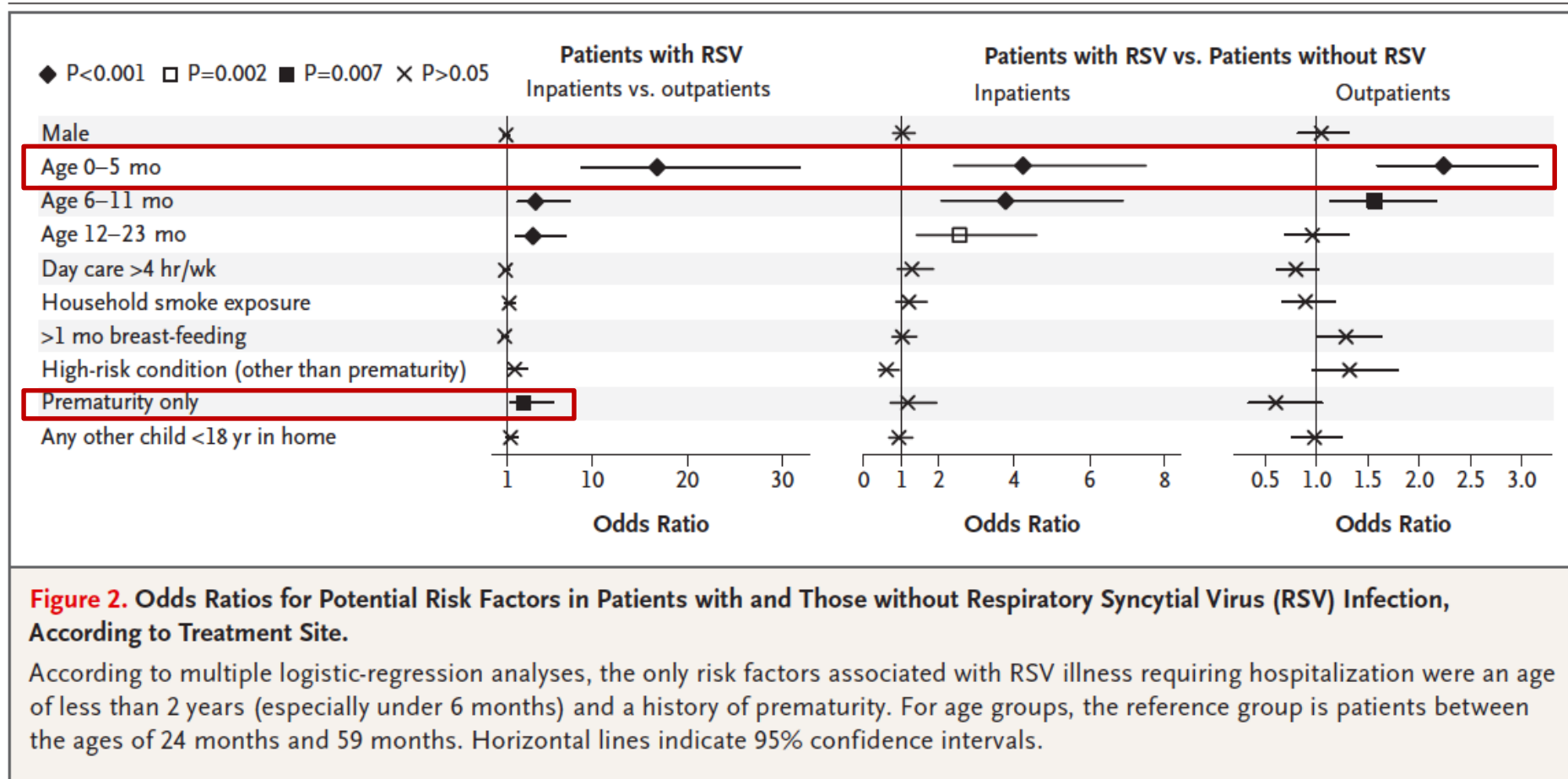
**No decrease in late-onset disease in infants, or disease in pregnancy**

# GBS Vaccine Progress

- ❑ **Trivalent Type Ia, Ib and III vaccine to prevent GBS infection (Novartis®)**
- ❑ **Purified capsular polysaccharide conjugated to CRM197**  
(nontoxic version of diphtheria toxin, used to make polysaccharides more immunogenic)
- ❑ **Phase I and II trials**
  - Phase I: small groups of people receive the trial vaccine
  - Phase II: vaccine is given to people who have characteristics similar to those for whom the new vaccine is intended

# **Respiratory Syncytial Virus (RSV) Vaccine**

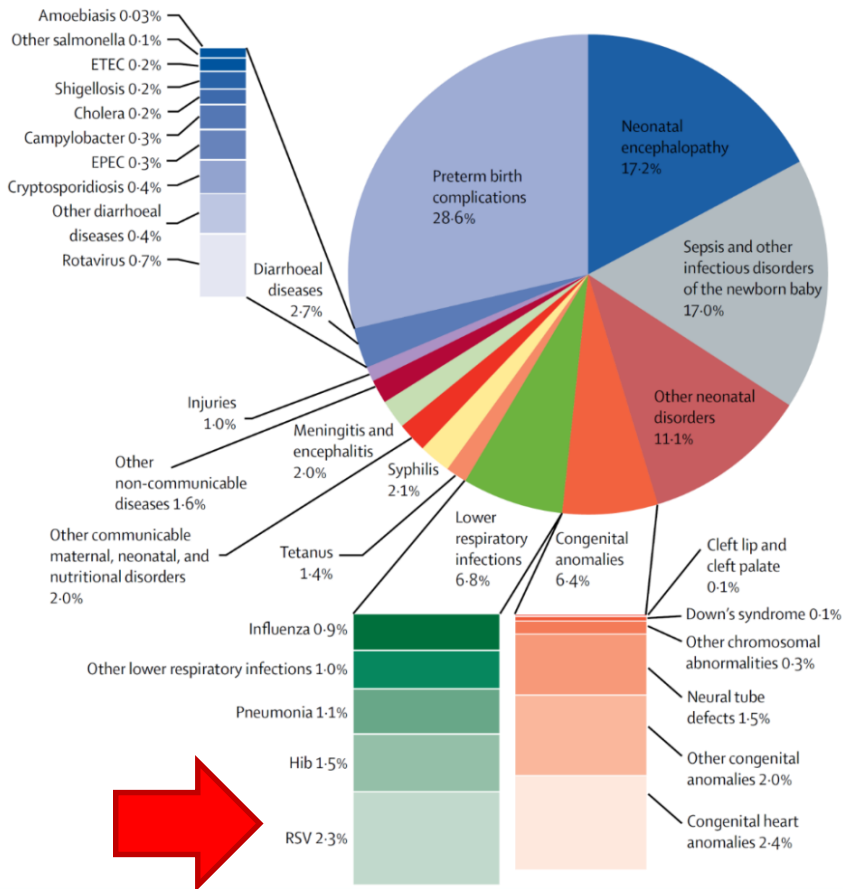
# Infants Under 6 Months and Premature Infants at High Risk for Hospitalization Due to RSV



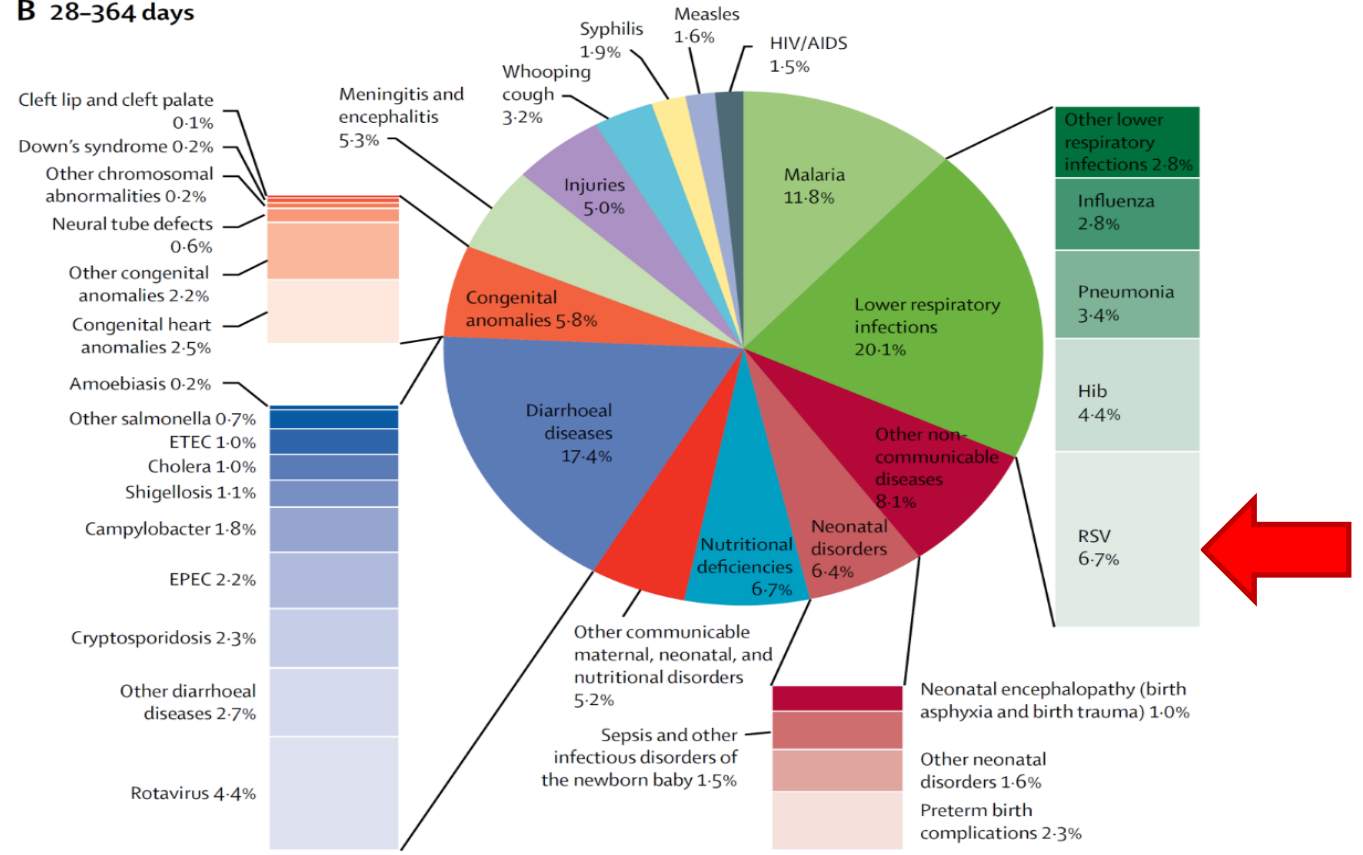


# Large Numbers of Global Neonatal and Infant Deaths Due to RSV, 2010

**A 0-27 days**

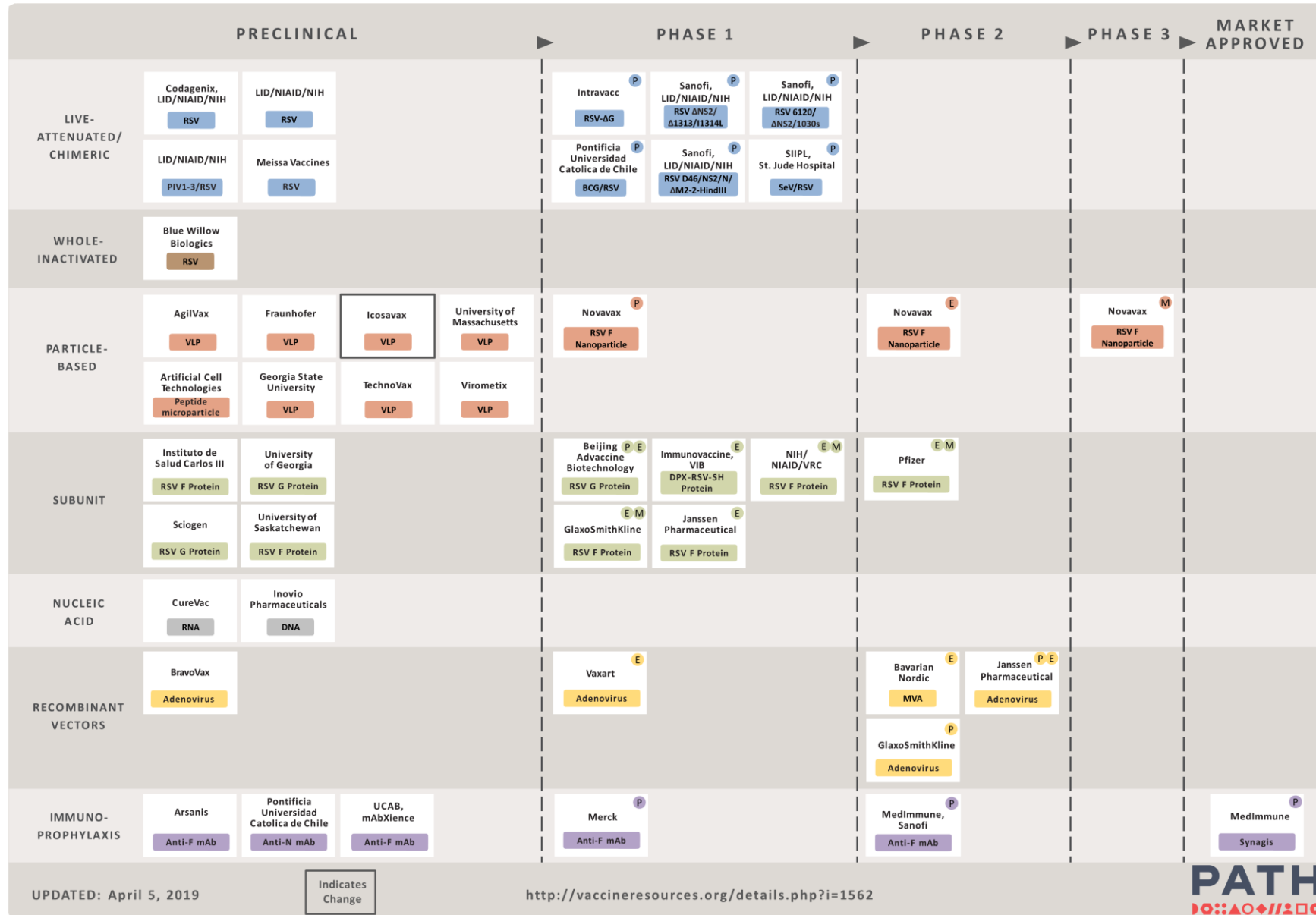


**B 28-364 days**



# RSV Vaccine and mAb Snapshot

TARGET INDICATION: P = PEDIATRIC M = MATERNAL E = ELDERLY



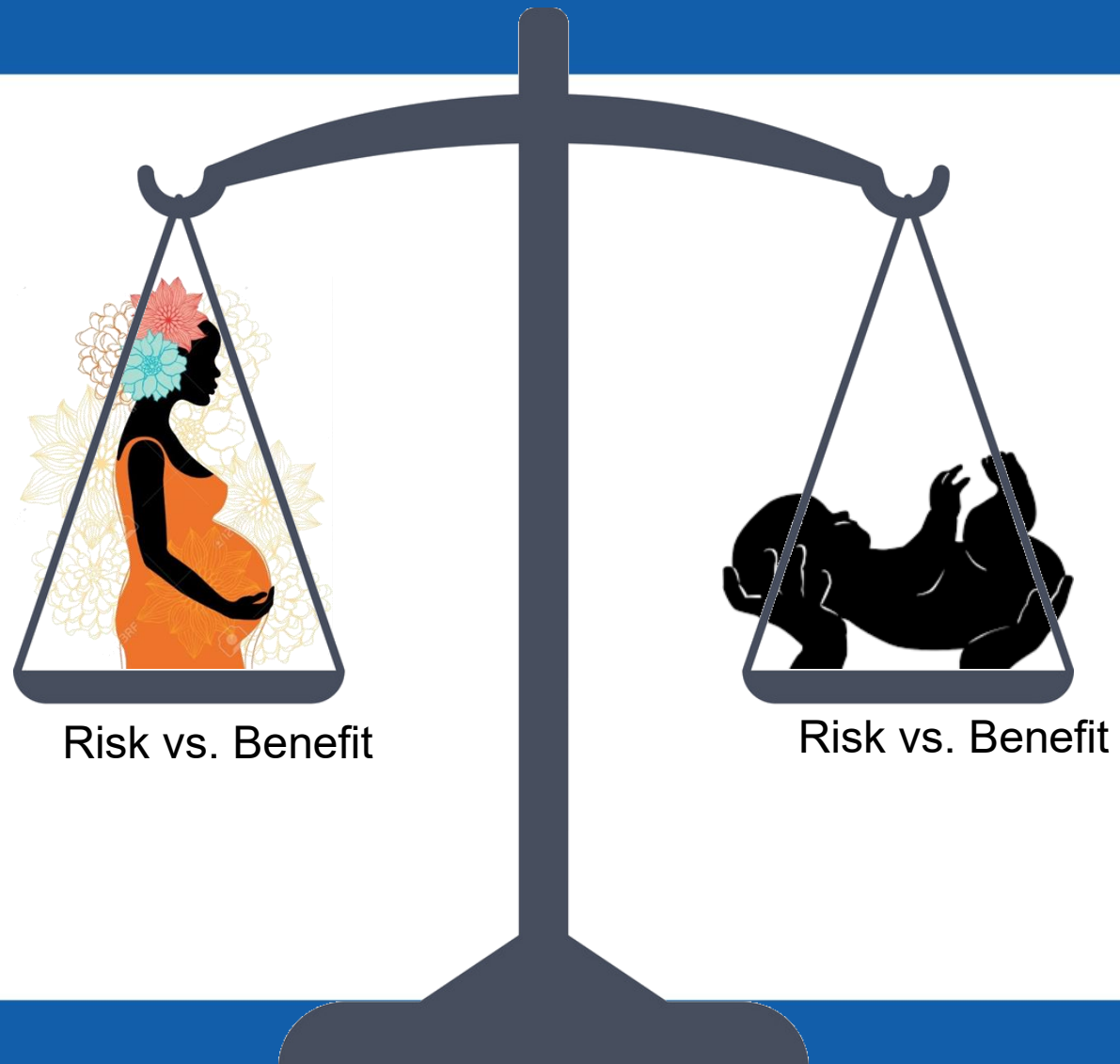
UPDATED: April 5, 2019

Indicates Change

<http://vaccineresources.org/details.php?i=1562>



# **Ethics of Maternal Vaccination**



Risk vs. Benefit

Risk vs. Benefit

ETHICS

# *Ethics of maternal vaccination*

Involvement of women is critical in establishing guidelines

By **A. T. Chamberlain,<sup>1</sup> J. V. Lavery,<sup>1</sup>**

**A. White,<sup>2</sup> S. B. Omer<sup>1</sup>**

**“...legitimacy of a mother’s interests in the welfare of her fetus/infant ...”**

# Characteristics of an Interests-based Approach



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Mother's self-determination  
front and center



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Inclusion of women in  
decision-making

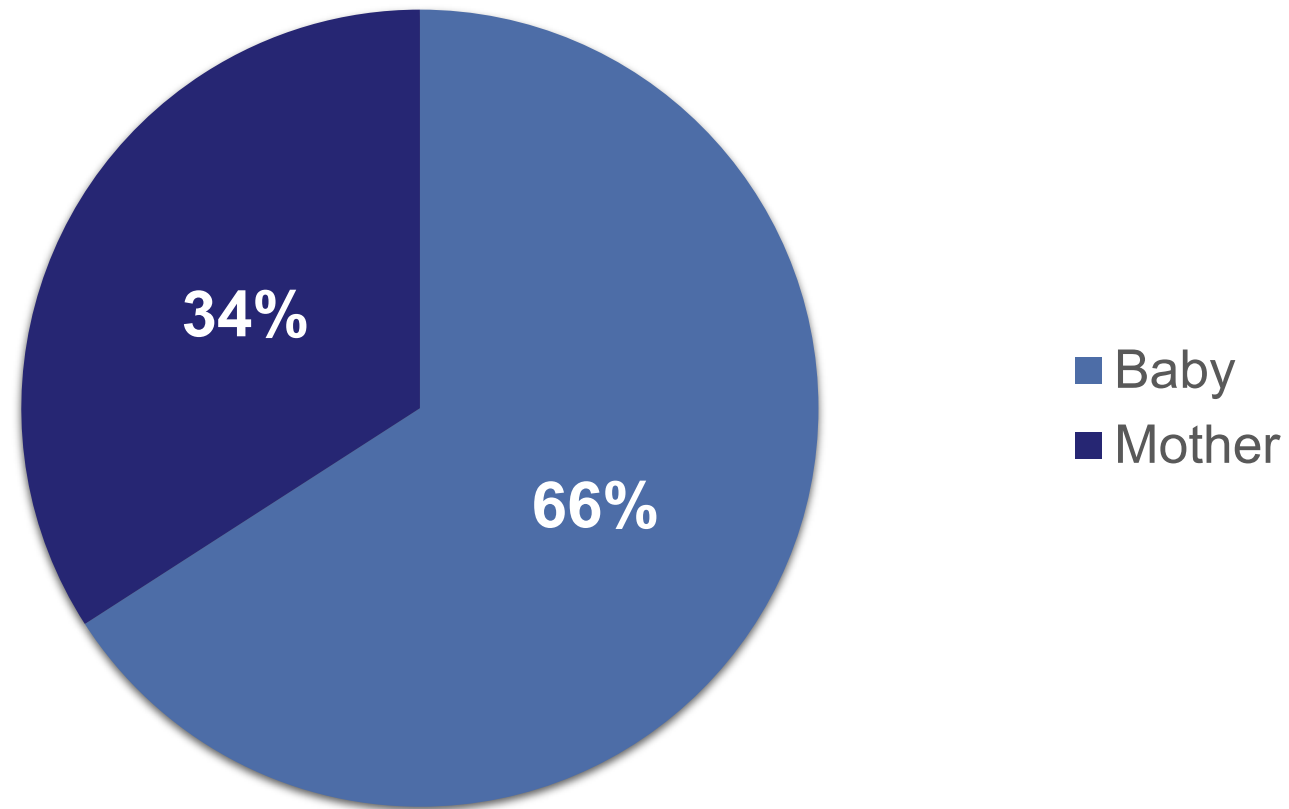


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Limits options for  
mandatory maternal  
immunization

# Priorities when Vaccinating Among 601 Pregnant Kenyan Women

When deciding to get a vaccine, whose benefit do you prioritize first (the mother or the baby)?



# Overall Summary and Conclusions

- **Maternal vaccinations are important for protecting pregnant women and their babies.**
- **With the support of professional organizations and local immunization champions, vaccination coverage of pregnant women has improved over the course of the past decade, but there is a long way to go.**
- **As new vaccines for pregnant women are being developed, continuous improvement in vaccination coverage can prevent more disease.**

