

# Maternal Immunization: Past, present and future

Kevin A. Ault, MD

University of Kansas School of Medicine

Kansas City KS

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# Conflicts of Interest Etc

- I have no conflicts of interest with this talk.
- Use of vaccines during pregnancy are “off label” use as defined by the FDA
- I will discuss potential future vaccines which are not FDA approved



# Maternal Immunization

- Influenza and pregnancy ‘back story’
- Influenza vaccine during pregnancy – safety and efficacy
- Pertussis vaccine during pregnancy
- Vaccine Uptake
- Future directions – RSV, GBS, etc.

# Plague, war and revolution in 1918

“Shut your eyes,” said  
Miss Tanner.

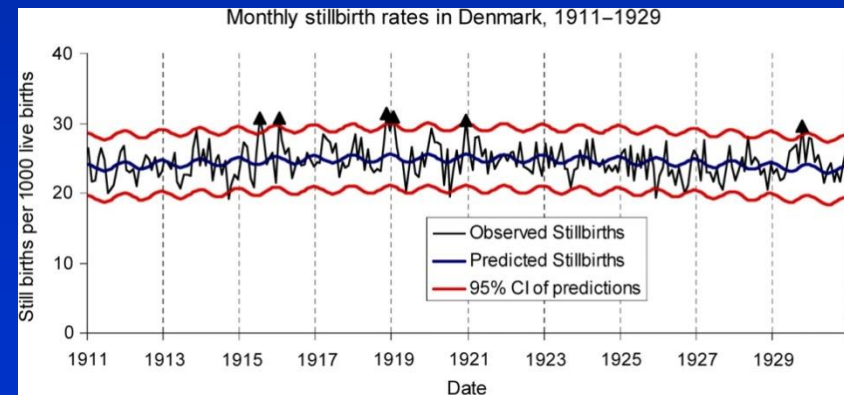
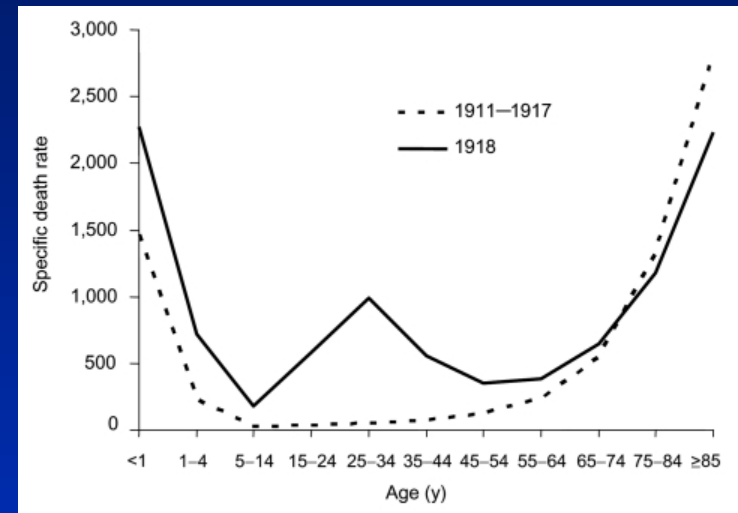
“Oh no,” said Miranda,  
“for then I see worse  
things...”

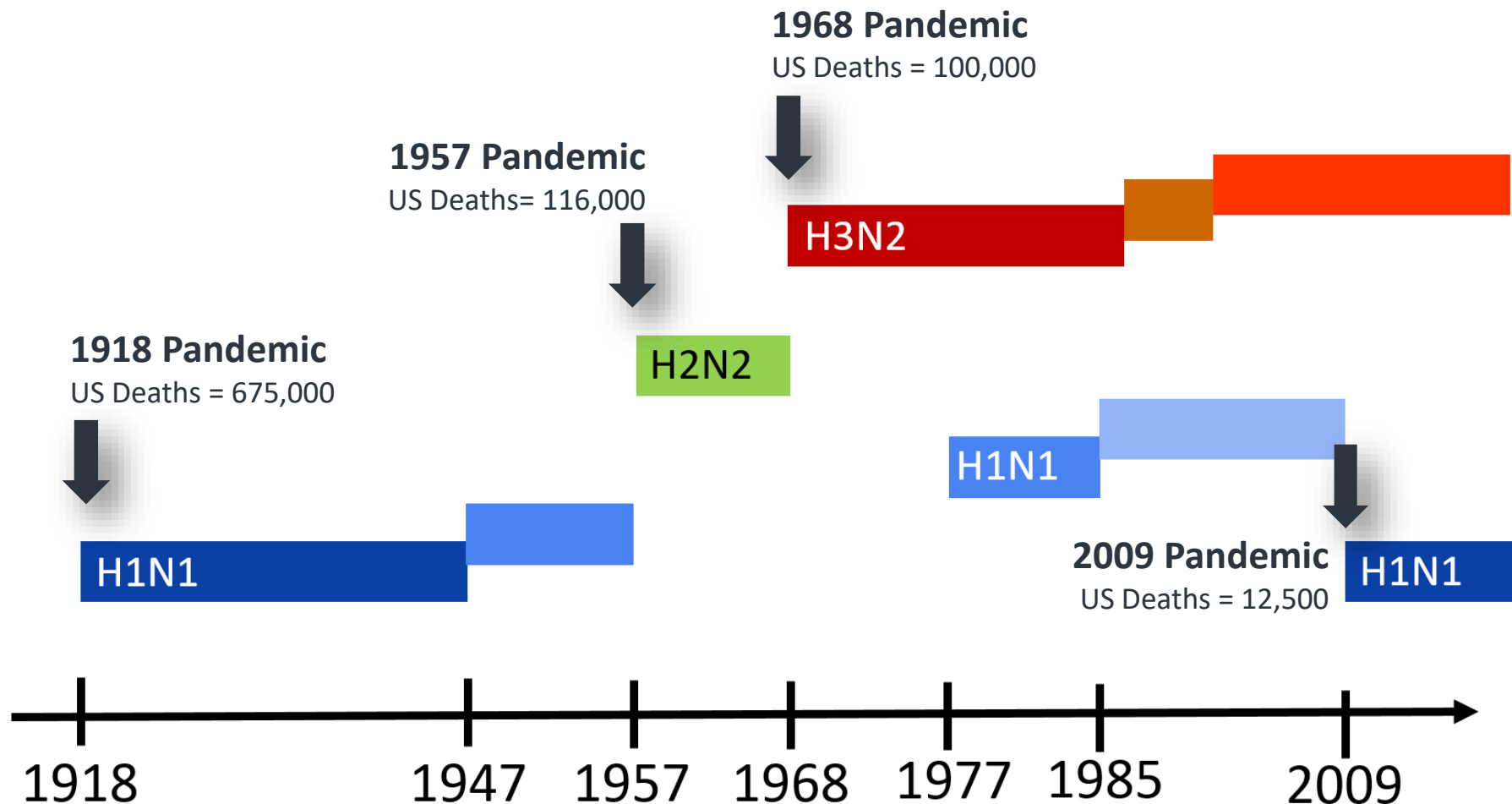
— Katherine Anne Porter in *Pale  
Horse, Pale Rider* (1939)



# Morbidity and Mortality of Influenza during Pregnancy

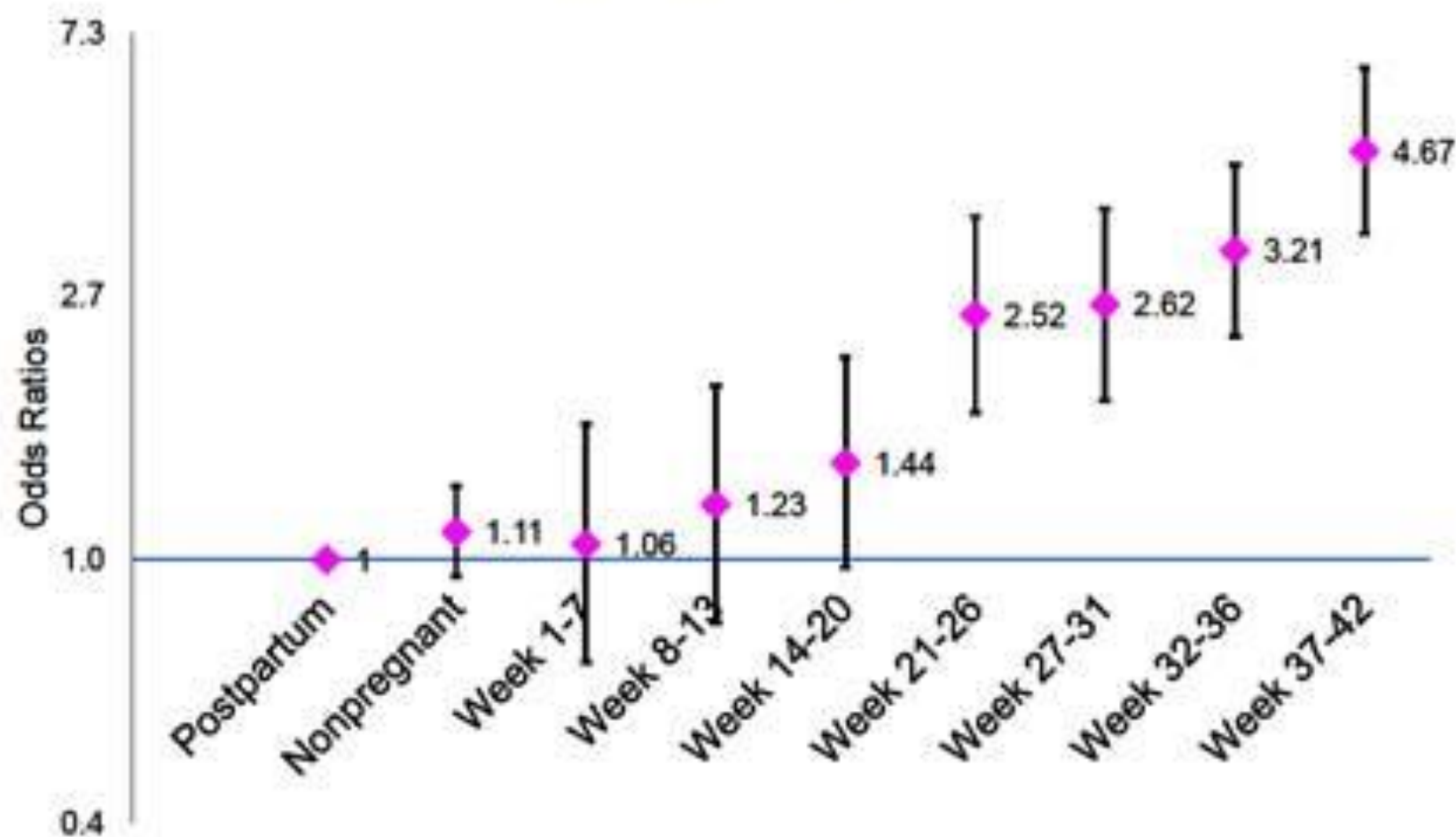
- “Cytokine storm”
- 1918 cases series – 50% mortality with pneumonia, 52% pregnancy complication
- “Highly predisposed to and fatally afflicted by this malady”
- 2009 pandemic with six fold increase mortality





# Odds Ratios of Cardiopulmonary Events by Pregnancy Status

## Tennessee Medicaid Program 1974-1993



Data Source: Neuzil et al, AJE, 1998



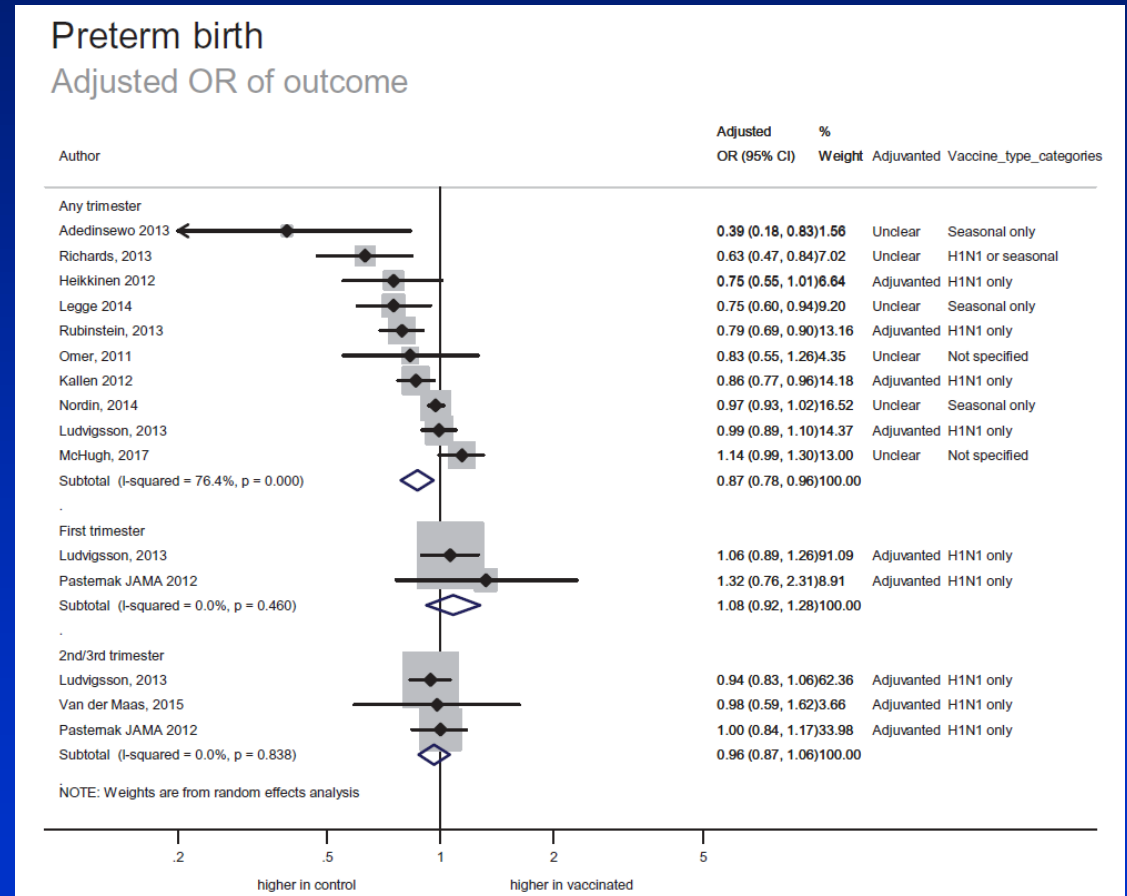
## Efficacy of influenza vaccine in pregnant women

- PREVENT Trial – Five sites in 4 countries over multiple flu seasons
- 19, 450 pregnant women hospitalized for respiratory or febrile illness
- Influenza vaccine was 40 % effective against hospitalization



# Pregnancy outcomes for maternal immunization - Influenza

- Decreases in preterm birth, stillbirth, low birth weight
- No increase in anomalies



# Health outcomes of young children born to mothers who received influenza vaccination

- Approximately 100,000 Canadian children born during 2009 pandemic, 30 % maternal vaccination rate
- Follow for five years - associations were found with respiratory infections, otitis media, any infectious diseases, neoplasms, sensory disorders, health services use, pediatric complex chronic conditions, or mortality.
- Similar to a another recent Dutch study

# History of Pertussis and Pertussis Vaccines

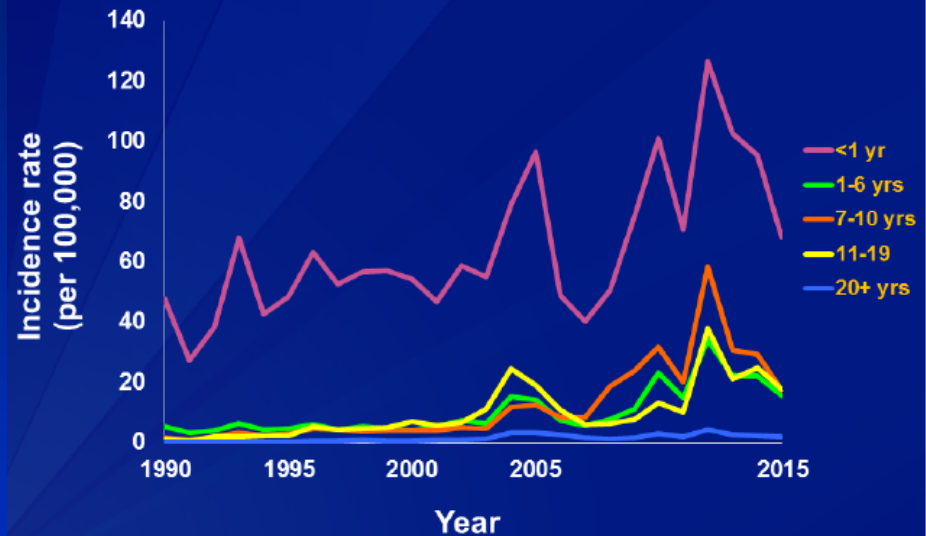
Reported NNDSS pertussis cases: 1922-2016



SOURCE: CDC, National Notifiable Diseases Surveillance System and Supplemental Pertussis Surveillance System and 1922-1949, passive reports to the Public Health Service

1

Reported pertussis incidence by age group: 1990-2015




2

Similar to influenza, mortality concentrated in youngest ages group

# Pertussis Vaccination during pregnancy

- “dramatic and persistent increase in pertussis disease” lead to pregnancy recommendation
- Should be given every pregnancy at 27-36 weeks gestation
- Goal – prevention of newborn morbidity and mortality



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

## COMMITTEE OPINION

Number 566 • June 2013  
Reaffirmed 2016

(Replaces No. 521, March 2012)

**Committee on Obstetric Practice**  
*This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The information should not be construed as dictating an exclusive course of treatment or procedure to be followed.*

### Update on Immunization and Pregnancy: Tetanus, Diphtheria, and Pertussis Vaccination

**ABSTRACT:** In the face of dramatic and persistent increases in pertussis disease in the United States, the Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices has updated its guidelines for the use of the tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine (Tdap) for pregnant women. The new guidance was issued based on an imperative to minimize the significant burden of pertussis disease in vulnerable newborns, the reassuring safety data on the use of Tdap in adults, and the evolving immunogenicity data that demonstrate considerable waning of immunity after immunization. The revised Advisory Committee on Immunization Practices guidelines recommend that health care personnel administer a dose of Tdap during each pregnancy, irrespective of the patient's prior history of receiving Tdap. To maximize the maternal antibody response and passive antibody transfer and levels in the newborn, optimal timing for Tdap administration is between 27 weeks and 36 weeks of gestation, although Tdap may be given at any time during pregnancy. However, there may be compelling reasons to vaccinate earlier in pregnancy. There is no evidence of adverse fetal effects from vaccinating pregnant women with an inactivated virus or bacterial vaccines or toxoids, and a growing body of robust data demonstrates safety of such use. For women who previously have not received Tdap, if Tdap was not administered during pregnancy it should be administered immediately postpartum to the mother in order to reduce the risk of transmission to the newborn. Additionally, other family members and planned direct caregivers also should receive Tdap as previously recommended (sustained efforts at cocooning). Given the rapid evolution of data surrounding this topic, immunization guidelines are likely to change over time and the American College of Obstetricians and Gynecologists will continue to issue updates accordingly.

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The overwhelming majority of morbidity and mortality attributable to pertussis infection occurs in infants who are less than or equal to 3 months of age (1). Infants do not begin their own vaccine series against pertussis (with the diphtheria, tetanus and acellular pertussis vaccine [DTaP]) until 2 months of age (2). This situation leaves a window of significant vulnerability for newborns, many of whom appear to contract serious pertussis infections from family members and caregivers, including the mother (3). Starting in 2006, the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention (CDC) recommended an approach to combat neonatal pertussis infection referred to as “cocooning” (4). This approach essentially consisted of a recommendation to administer Tdap to all women in the immediate postpartum period and all other family members and caregivers who had not previously received the vaccine in order to provide a protective cocoon of immunity around the newborn. This approach has proved challenging and insufficient when used alone at preventing neonatal pertussis infections for a variety of reasons. Importantly, cocooning leaves vulnerable infants without any endogenous protective antibody until they begin their own vaccine series at 2 months of age. Thus, they are solely dependent on the immunity of those around them for pertussis protection in the critical first 2–3 months of life.

In June of 2011, the ACIP considered this situation and issued a new recommendation that pregnant women who had not previously received a dose of Tdap should

# Safety and efficacy of Pertussis Vaccine during Pregnancy

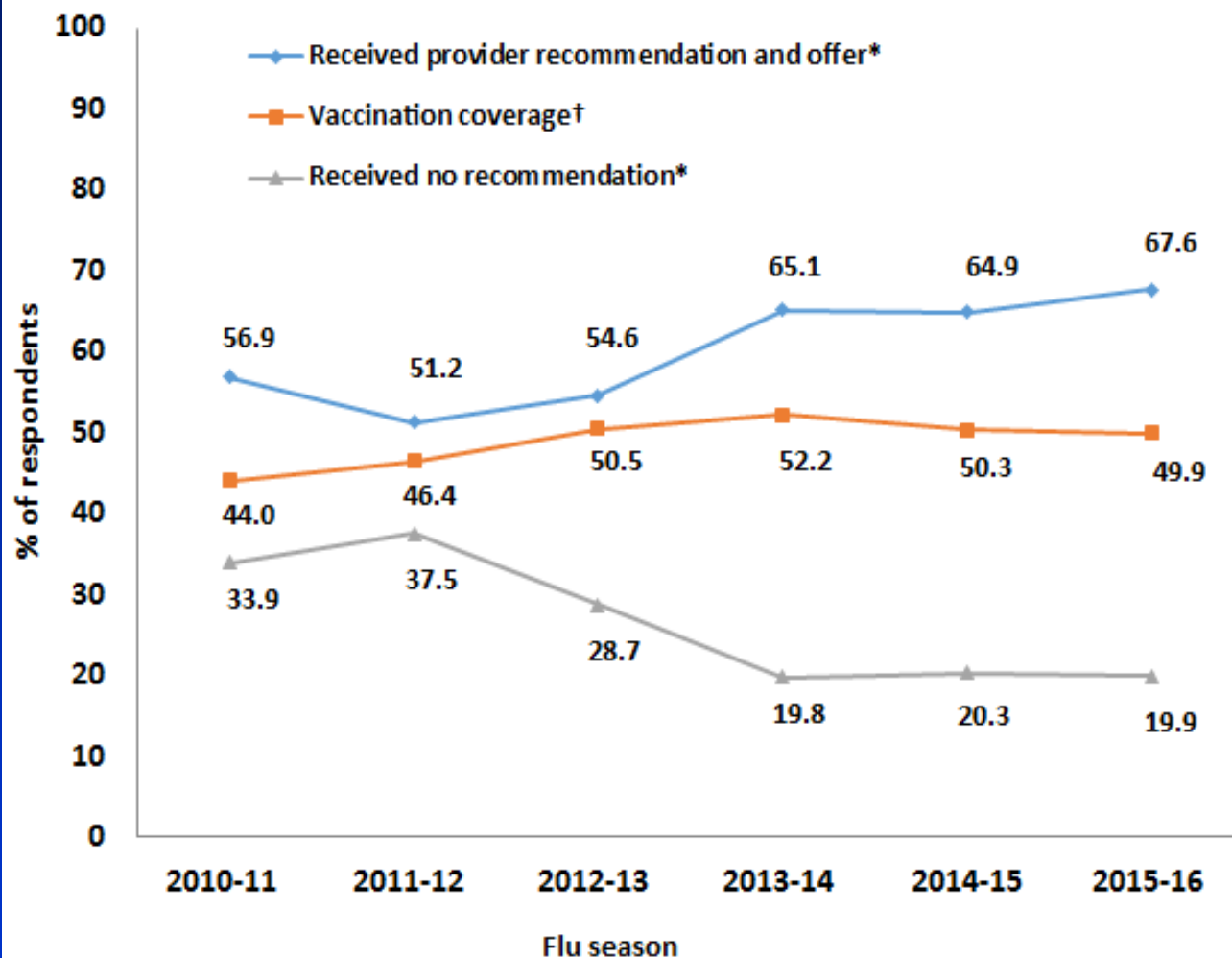
- A meta analysis of 21 studies of pertussis vaccination during pregnancy showed no increases in stillbirth, preterm birth, neonatal death and congenital anomalies
- 90 % effective against newborn hospitalization for pertussis
- 80 % effective against ICU admission for pertussis

<b>Vaccine*</b>	<b>Indicated During Every Pregnancy</b>	<b>May Be Given During Pregnancy in Certain Populations</b>	<b>Contraindicated During Pregnancy</b>	<b>Can Be Initiated Postpartum or When Breastfeeding or Both</b>
Inactivated influenza	X <sup>†,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>†</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>

**Figure 1. Trend of flu vaccination coverage before and during pregnancy and prevalence of provider recommendation / offer or no recommendation for vaccination among women pregnant anytime October through January, Internet panel survey, United States, 2010-11 through 2015-2016 flu seasons**





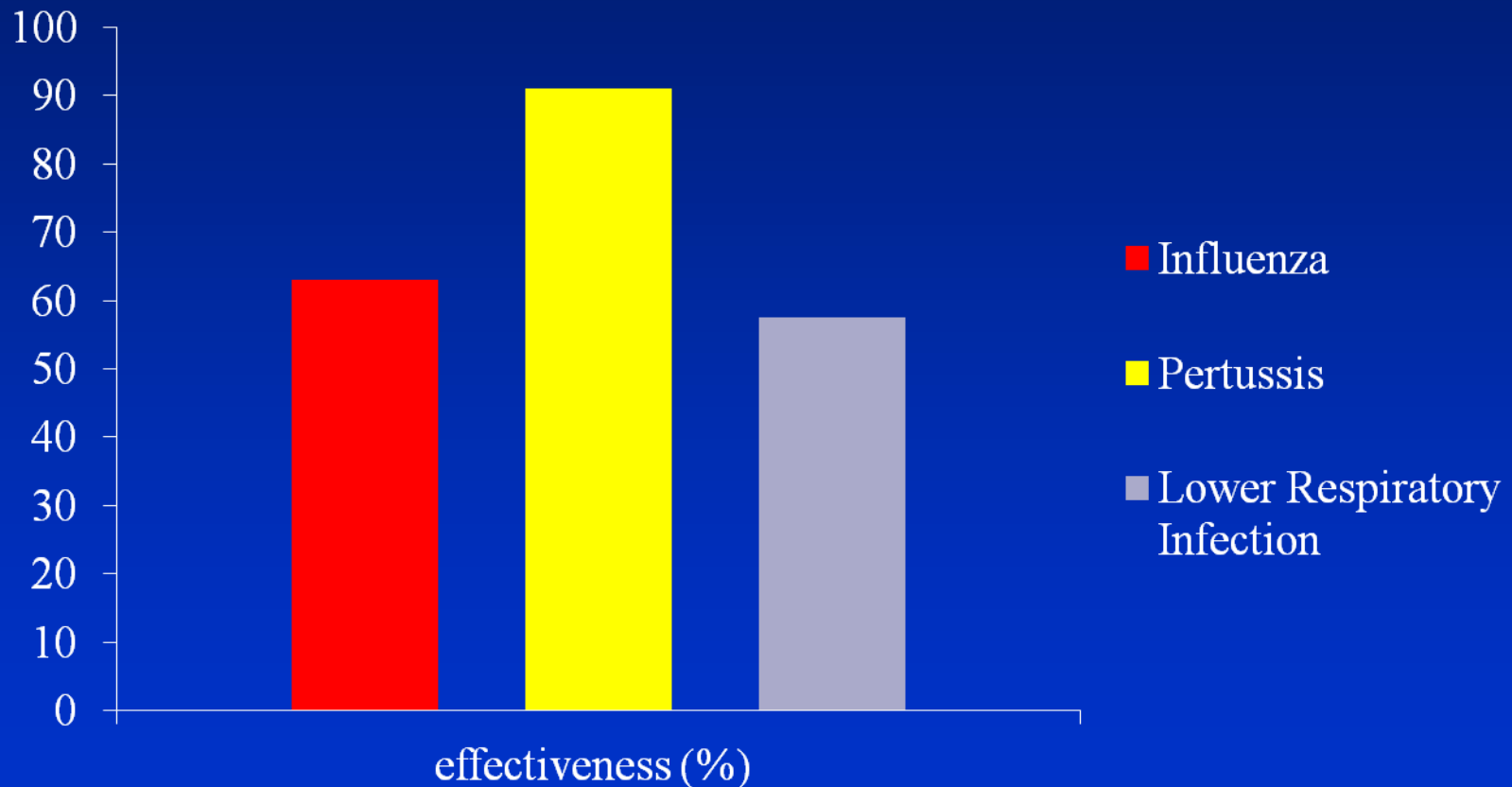
# How to increase uptake?

- Provider recommendation
- Ease of access – during prenatal care
- Standing orders
- Provider assessment and feedback
- Education for patients via video, text, ACOG packets

## Future Targets for Maternal Immunization

- Group B Streptococcus – 1/1000 live births, cause of severe newborn infections, protein conjugate vaccine, serological markers
- RSV – 3 million hospitalizations, peaking at age 2-3 months, conjugate vaccine, common infection = smaller clinical trial

# Effectiveness of Maternal Immunization to prevent Neonatal Infection



# “Thank you ever so much”

## Any questions?



Kevin A. Ault, MD  
Department of Obstetrics and Gynecology  
3901 Rainbow Blvd  
University of Kansas Medical Center  
Kansas City KS USA 66160  
[kault2@kumc.edu](mailto:kault2@kumc.edu) or Twitter @kevinault