

# Vaccine Updates

**William Atkinson, MD, MPH\***  
**Missouri Immunization Training**  
**November 19, 2014**

**\*Representing the Immunization Action  
Coalition, Saint Paul, MN**



# Disclosures

- **William Atkinson has no financial conflict or interest with the manufacturer of any product named during this presentation**
- **The speaker will discuss the use of Tdap vaccine in a manner not approved by the Food and Drug Administration (FDA) but recommended by ACIP**
- **The speaker will briefly discuss 2 vaccines not currently licensed by the FDA**

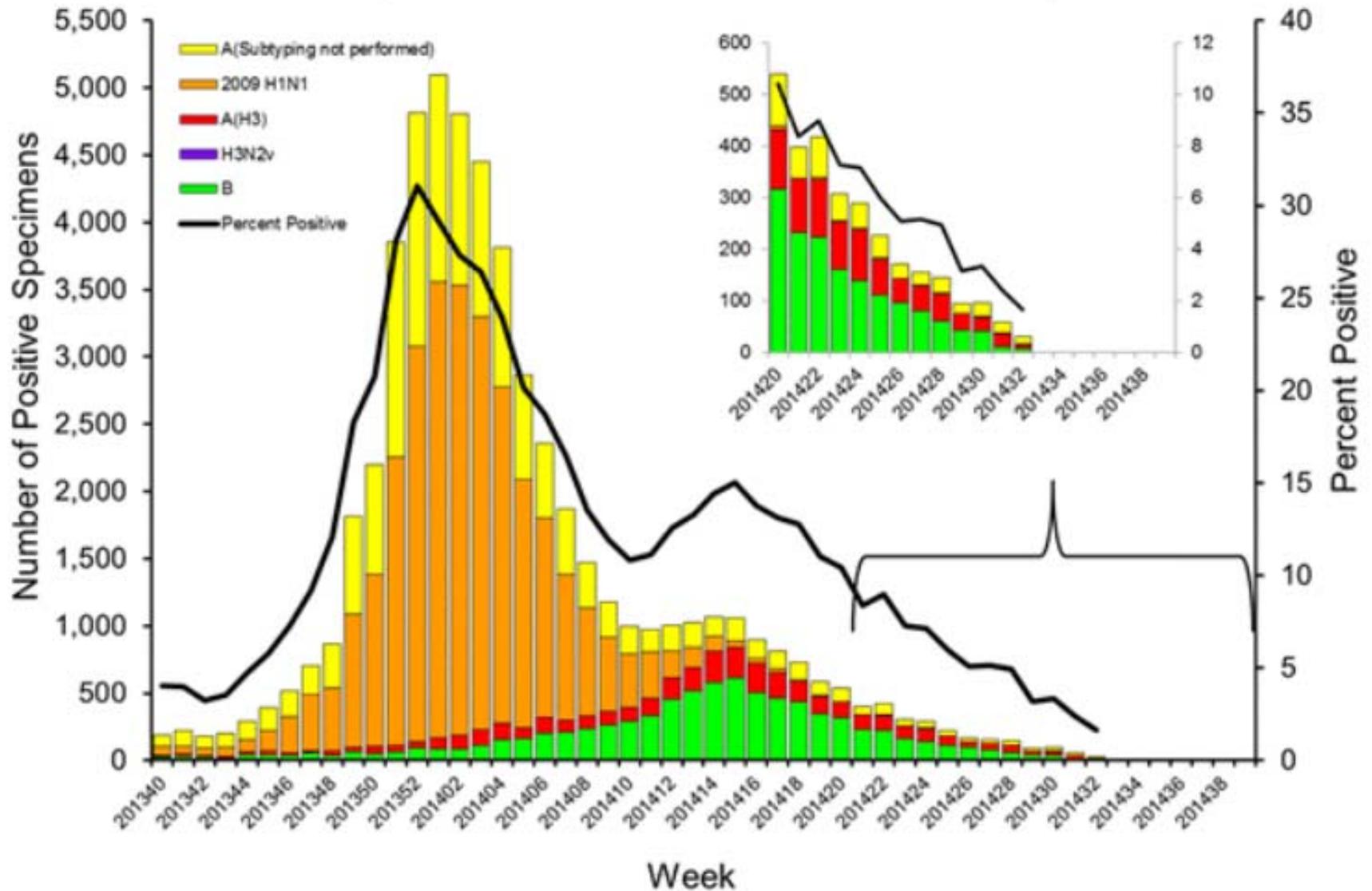
# What's New?

- **Influenza vaccines**
- **Pneumococcal conjugate vaccine for adults**
- **Tdap (not so new but important)**
- **Meningococcal serogroup B vaccines**
- **Human Papillomavirus (HPV) vaccines (also not so new but very important)**

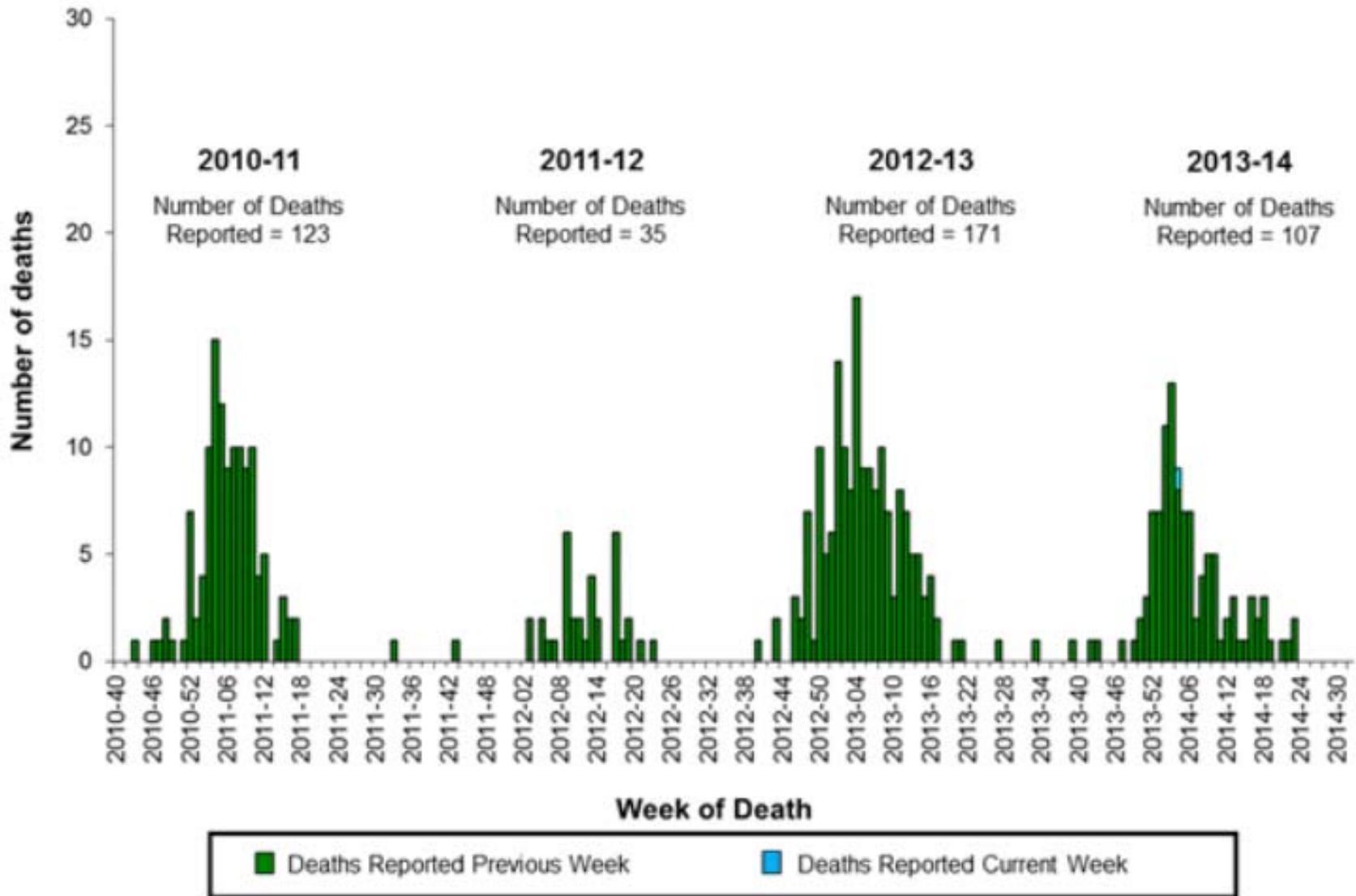
# Advisory Committee on Immunization Practices (ACIP)

- Composed of 15 experts in clinical medicine and public health who are not government employees
- Ex-officio (FDA, NIH, CMS, etc) and liaison (AAP, AAFP, ASTHO, Pharma, etc) members (non-voting)
- Provide guidance on the use of vaccines and other biologic products to the Department of Health and Human Resources, CDC, and the U.S. Public Health Service

# Influenza Positive Tests Reported to CDC by U.S. WHO/NREVSS Collaborating Laboratories, National Summary, 2013-14



## Number of Influenza-Associated Pediatric Deaths by Week of Death: 2010-11 season to present



# **Influenza Vaccines Available in 2014-15**

- **Quadrivalent live attenuated (LAIV4)**
- **Quadrivalent inactivated (IIV4), standard dose**
- **Trivalent inactivated (IIV3), standard dose**
- **Trivalent inactivated (IIV3), intradermal dose**
- **Trivalent inactivated (IIV3), standard dose, cell culture-based**
- **Trivalent inactivated (IIV3), high dose**
- **Trivalent inactivated, recombinant (RIV3)**

# Quadrivalent Influenza Vaccines

- **Two lineages (“families”) of influenza B viruses: Victoria and Yamagata**
  - immunization against virus from one lineage provides only limited cross-protection against viruses in the other
- **Trivalent vaccines contain only one B virus**
- **Predominant lineage is difficult to predict in advance of the season**
- **Quadrivalent vaccines contain one virus from each B lineage as well as 2 influenza A viruses (H1N1, H3N2)**

*MMWR* 2013;62(RR-7)

# Live Attenuated Influenza Vaccine (LAIV) for Children

- **Two randomized studies have been conducted in young children that compare the benefits provided by the LAIV and IIV**
  - **one study was conducted in children 6 to 59 months of age and the other was conducted in children 6 to 71 months of age**
- **Both studies indicated that LAIV provided about 50% better protection than IIV in young children**

# **LAIV Preference, 2014-2015**

- **When immediately available, LAIV should be used for healthy children aged 2 through 8 years who have no contraindications or precautions**
- **If LAIV is not immediately available, IIV should be used**
- **Vaccination should not be delayed to procure LAIV**

# Influenza Vaccine Effectiveness

- **Studies conducted by CDC and MedImmune during the 2013-2014 influenza season found good efficacy against influenza B but little or no efficacy against influenza A H1N1**
- **MedImmune found efficacy lower for lots shipped in late summer – possible temperature effect on vaccine**
- **No change in ACIP recommendation for LAIV**

# Choice of Influenza Vaccine

- Where more than one type of vaccine is appropriate and available, ACIP has no preferential recommendation for use of any influenza vaccine product over another
  - quadrivalent vs trivalent
  - high-dose vs standard dose (for people age 65 years and older)
  - IIV vs LAIV except in children ages 2 through 8 years

# Choice of Influenza Vaccine

- Where more than one type of vaccine is appropriate and available, ACIP has no preferential recommendation for use of any influenza vaccine product over another
  - **quadrivalent** vs trivalent
  - **high-dose** vs standard dose (for people age 65 years and older)
  - IIV vs LAIV except in children ages 2 through 8 years

# Afluria Administered by PharmaJet Device

- Randomized trial of PharmaJet vs. standard IM injection
- Immunogenicity and safety
  - no difference in titer or seroprotection rates
  - more local reactions with PharmaJet
  - no difference in systemic Aes
- Approved by FDA in August 2014

## Components

### Reusable hardware:

- Injector
- Reset Station



### Disposables:

- Syringe
- Filling/Vial Adapter



### Simple, Robust Design Injector Unique features:

- Durable
- Double safety feature
- Tested for 20,000 cycles



# Pneumococcal Conjugate Vaccine (PCV13) and Adults

- FDA approved PCV13 for use among adults 50 years of age and older in December 2011
- Immunogenicity of PCV13 was found to be non-inferior to PPSV23
- ACIP recommended 1 dose of PCV13 for adults at high risk of invasive pneumococcal disease\* in October 2012

\*immunocompromised, functional or anatomic asplenia, cochlear implant, CSF leak

# CAPITA trial

- **Community-Acquired Pneumonia Immunization Trial in Adults**
- Intended to determine if PCV13 was effective in reducing the risk of a first episode of CAP among persons 65 years and older
- Double-blind, placebo controlled
- ~85,000 persons 65 years or older in the Netherlands

Pfizer data presented to ACIP, June 25, 2014

# CAPITA trial

- **46% efficacy against vaccine-type CAP**
- **75% efficacy against vaccine-type invasive pneumococcal disease**
- **More effective in persons younger than age 75**
- **35% of recipients reported local AE (mostly pain)**

Pfizer data presented to ACIP, June 25, 2014

# Pneumococcal Conjugate Vaccine (PCV13) and Adults

- On August 13, 2014 ACIP convened a special remote session to discuss PCV13 recommendations
- ACIP voted to recommend that
  - both PCV13 and PPSV23 should be routinely administered in series to all adults age 65 years and older
  - recommendations for routine PCV13 use among adults age 65 and older years will be reevaluated in 2018 and revised as needed
- Published in *MMWR* on September 19, 2014

# **Pneumococcal Vaccines for Persons Age 65 Years and Older**

- **One lifetime dose of PCV13 for adults**
- **PCV13 and PPSV23 should NOT be administered at the same visit**
- **Administer PCV13 before PPSV23, whenever possible**
- **PCV13 should be administered to those who have already received PPSV23**

**BOX. Sequential administration and recommended intervals for PCV13 and PPSV23 for adults aged  $\geq 65$  years — Advisory Committee on Immunization Practices, United States**

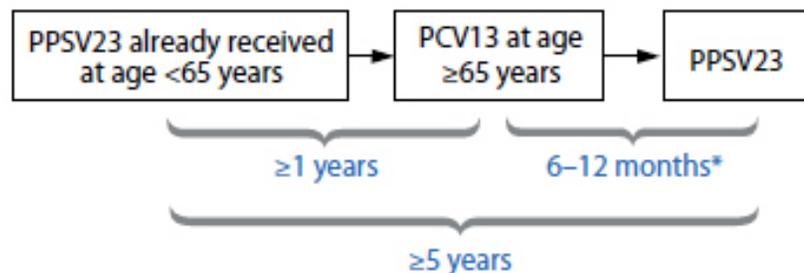
*Pneumococcal vaccine-naïve persons aged  $\geq 65$  years*



*Persons who previously received PPSV23 at age  $\geq 65$  years*



*Persons who previously received PPSV23 before age 65 years who are now aged  $\geq 65$  years*



**Abbreviations:** PCV13 = 13-valent pneumococcal conjugate vaccine; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

\*Minimum interval between sequential administration of PCV13 and PPSV23 is 8 weeks; PPSV23 can be given later than 6-12 months after PCV13 if this window is missed.

MMWR 2014;63(No 37):825

## Recommendations for PCV13 and PPSV23 in Pneumococcal Vaccine-Naïve Adults

- For high-risk adults (asplenia, immunocompromised, etc)
  - single dose of PCV13
  - dose of PPSV23 at least **8 weeks** later
- For persons 65 years or older who are not at high risk
  - single dose of PCV13
  - dose of PPSV23 **6 to 12 months** later
- Minimum interval for all groups is 8 weeks

# PPSV23 at 65 Years or Age

- **Recommendations for PPSV23 have not changed**
- **All adults are eligible for a dose of PPSV23 at 65 years of age regardless of previous pneumococcal vaccination**
- **Maximum of 3 lifetime doses of PPSV23**
- **Adults vaccinated with PPSV23 at/after age 65 require no further doses of PPSV23**

# **Pneumococcal Vaccines for Persons Age 65 Years and Older**

- **Currently Medicare will reimburse for only 1 dose of pneumococcal vaccine**
- **Will reimburse for either PCV13 OR PPSV23 but not both**
- **Persons who have already been reimbursed for PPSV23 may be denied payment for PCV13**
- **CMS is working to change this rule**

TABLE. Medical conditions or other indications for administration of 13-valent pneumococcal conjugate vaccine (PCV13), and indications for 23-valent pneumococcal polysaccharide vaccine (PPSV23) administration and revaccination for adults ~~aged  $\geq 19$  years,\*~~ by risk group — Advisory Committee on Immunization Practices, United States, 2012

19-64 years

Risk group	Underlying medical condition	PCV13	PPSV23	
		Recommended	Recommended	Revaccination 5 yrs after first dose
Immunocompetent persons	Chronic heart disease <sup>†</sup>		✓	
	Chronic lung disease <sup>§</sup>		✓	
	Diabetes mellitus		✓	
	Cerebrospinal fluid leak	✓	✓	
	Cochlear implant	✓	✓	
	Alcoholism		✓	
	Chronic liver disease, cirrhosis		✓	
	Cigarette smoking		✓	
Persons with functional or anatomic asplenia	Sickle cell disease/other hemaglobinopathy	✓	✓	✓
	Congenital or acquired asplenia	✓	✓	✓
Immunocompromised persons	Congenital or acquired immunodeficiency <sup>¶</sup>	✓	✓	✓
	Human immunodeficiency virus infection	✓	✓	✓
	Chronic renal failure	✓	✓	✓
	Nephrotic syndrome	✓	✓	✓
	Leukemia	✓	✓	✓
	Lymphoma	✓	✓	✓
	Hodgkin disease	✓	✓	✓
	Generalized malignancy	✓	✓	✓
	Iatrogenic immunosuppression**	✓	✓	✓
	Solid organ transplant	✓	✓	✓
	Multiple myeloma	✓	✓	✓

\* All adults aged  $\geq 65$  years should receive a dose of PPSV23, regardless of previous history of vaccination with pneumococcal vaccine.

<sup>†</sup> Including congestive heart failure and cardiomyopathies, excluding hypertension.

<sup>§</sup> Including chronic obstructive pulmonary disease, emphysema, and asthma.

<sup>¶</sup> Includes B- (humoral) or T-lymphocyte deficiency, complement deficiencies (particularly C1, C2, C3, and C4 deficiencies), and phagocytic disorders (excluding chronic granulomatous disease).

\*\* Diseases requiring treatment with immunosuppressive drugs, including long-term systemic corticosteroids and radiation therapy.

# Pertussis in the U.S. – 2013

- 28,639 reported cases (559 from Missouri)
- Highest incidence among adolescents age 11-19 years (29/100,000) and adults age 20 years and older (21/100,000)
- 9 deaths reported – all among infants less than 3 months of age)

# Tdap Recommendations

- Routinely recommended at 11 or 12 years of age
- Catch up 13 through 18 years who have not been vaccinated with Tdap
- Administer Tdap to ALL unvaccinated adults 19 years and older including adults 65 years of age and older\*

\*Off-label recommendation for Adacel. *MMWR* 2011; 60 (No. 1):13-5

# Tdap and Pregnant Women

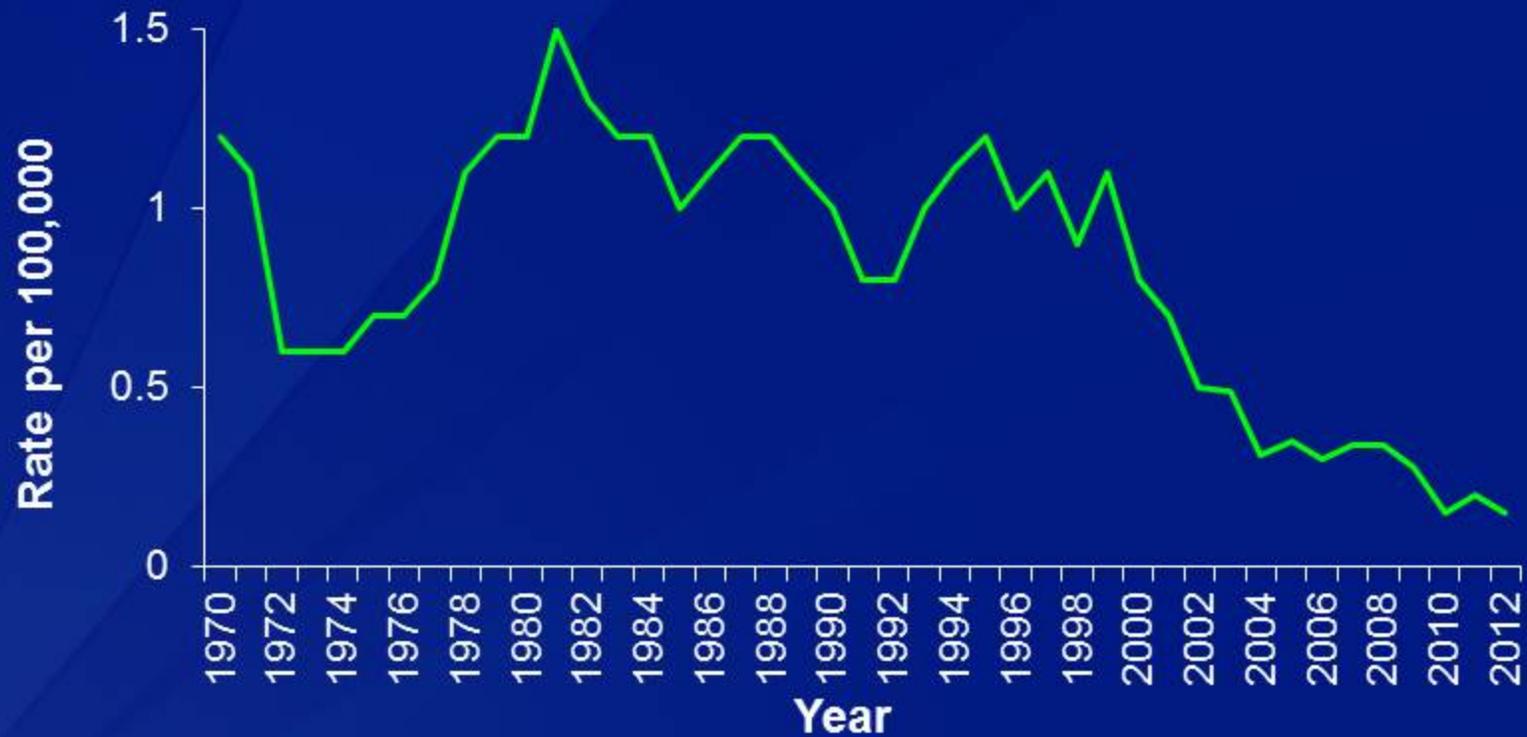
- Administer a dose of Tdap vaccine to during each pregnancy irrespective of the woman's prior history of receiving Tdap\*
- To maximize passive transfer of antibody to the fetus optimum timing of Tdap is between 27 and 36 weeks gestation
- Tdap may be administered earlier in pregnancy if necessary (e.g. wound management)

\*Off-label recommendation. *MMWR* 2013;62( (No.7): 131-135

# Tdap Revaccination

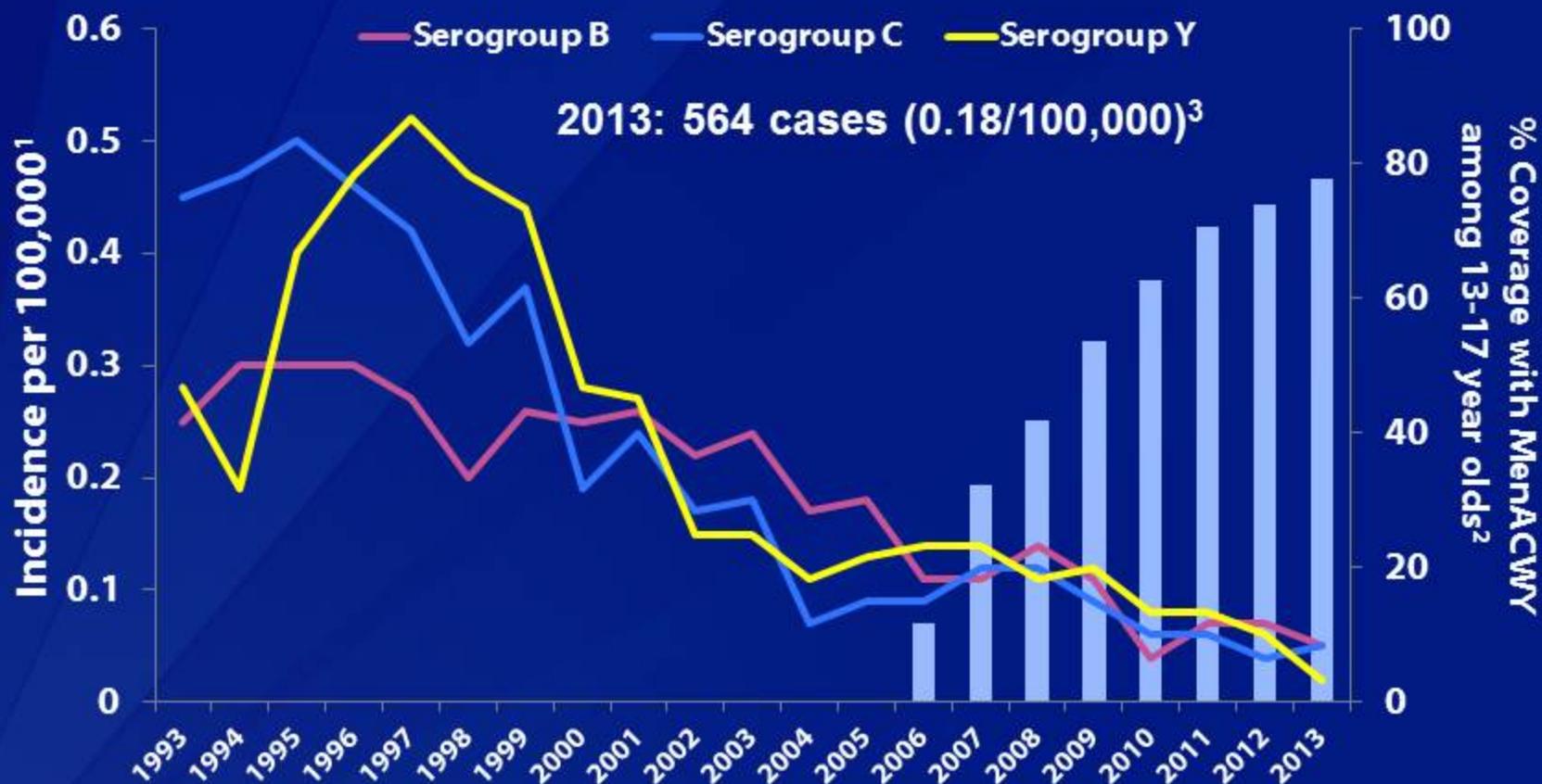
- Revaccination with Tdap applies **ONLY** to pregnant women
- Does **NOT** apply to family members or other contacts
- ACIP does not currently recommend Tdap revaccination for HCP
- Focus on current Tdap program
  - improve adult Tdap coverage, including HCP (31% in 2012)
  - vaccination of pregnant women

## Meningococcal Disease Incidence, United States, 1970-2012



1970-1996 NNDSS data, 1997-2012 ABCs data estimated to U.S. population

## Meningococcal Incidence in All Ages by Serogroup and Adolescent MenACWY Vaccine Coverage, 1993-2013

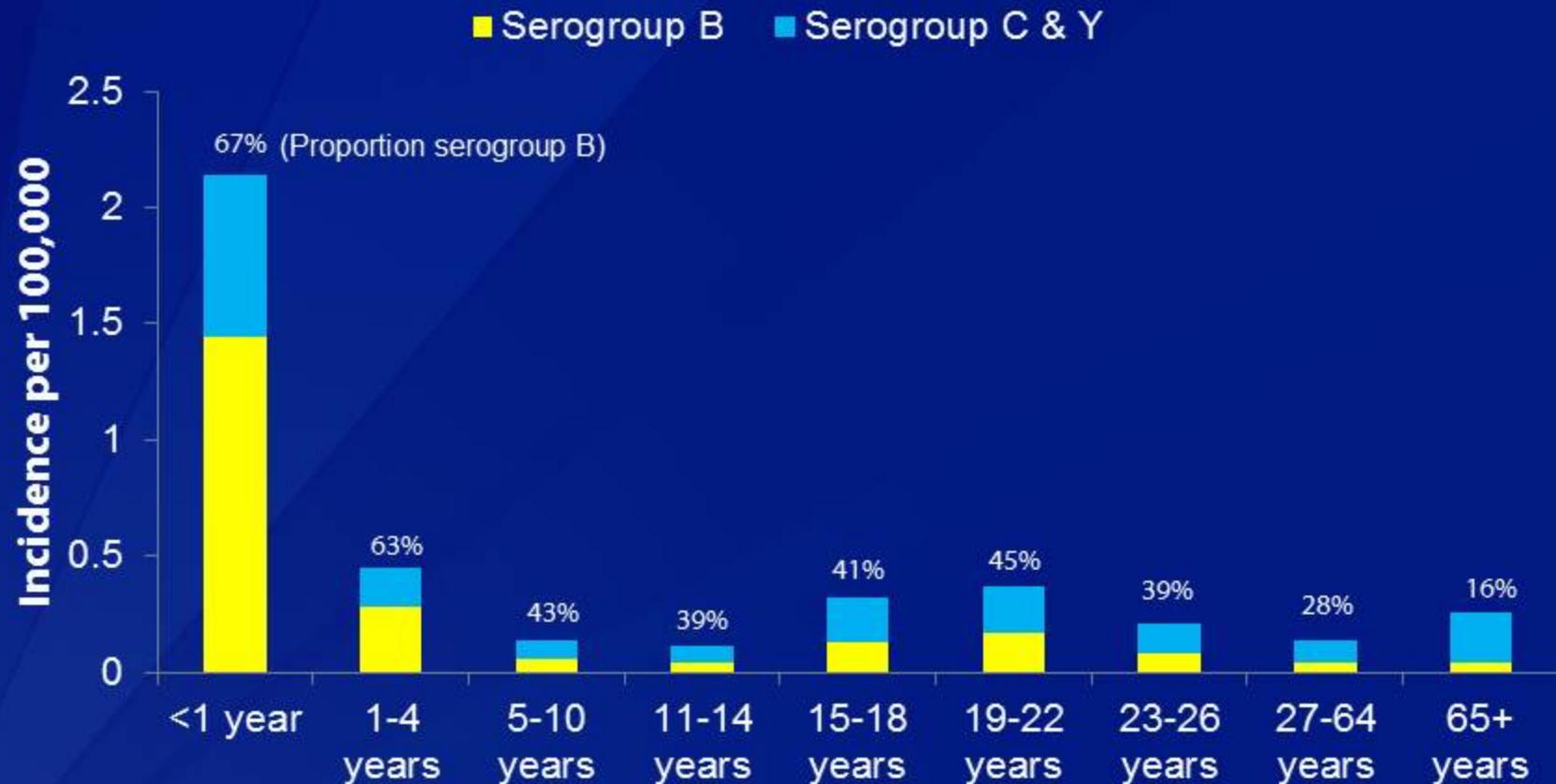


<sup>1</sup>Source: ABCs cases from 1993-2013 estimated to the U.S. population with 18% correction for under reporting

<sup>2</sup>National Immunization Survey – Teen; 2006-2013

<sup>3</sup>NNDSS 2013 final case count

## Meningococcal Incidence by Serogroup\* and Age-Group, 2005-2012



\*NNDSS data with additional serogroup data from ABCs and state health departments.  
Unknown serogroup (23%) and other serogroups (8%) excluded

# Groups at Increased Risk for Meningococcal B Disease

- **High-risk medical conditions:**
  - **persistent complement component deficiencies**
  - **functional or anatomic asplenia**
- **Certain microbiologists**
- **Populations at risk during an outbreak**

# Outbreaks of Meningococcal Disease

- Meningococcal outbreaks are rare, historically causing ~2-3% of US cases
- Five serogroup B meningococcal disease clusters/outbreaks on college campuses
  - Princeton: 1,400 fold increased risk; 5,800 recommended vaccine
  - UCSB: 200 fold increased risk; 20,000 recommended vaccine

# Meningococcus Serogroup B (MenB)

- **MenB capsular polysaccharide is poorly immunogenic and structurally similar to certain proteins in human tissue**
  - **concern (unproven) about auto-immunity created by using MenB capsular polysaccharide in a vaccine**
- **Vaccine research has focused on surface proteins**
- **However, MenB strains are highly diverse with more than 8,000 genetically different B strains identified**

# Meningococcal Serogroup B Vaccines

- rLP2086 bivalent vaccine (Trumenba, Pfizer)
  - 2 fHbp (factor H-binding protein) subvariants (B/v1 and A/v2-3)
- 4CMenB (Bexsero, Novartis)
  - Single subvariant of fHbp (B/v1)
  - NadA (Neisserial adhesin A)
  - NhbA (Neisserial heparin binding antigen)
  - Outer membrane vesicles of the New Zealand epidemic strain (OMV - NZ)

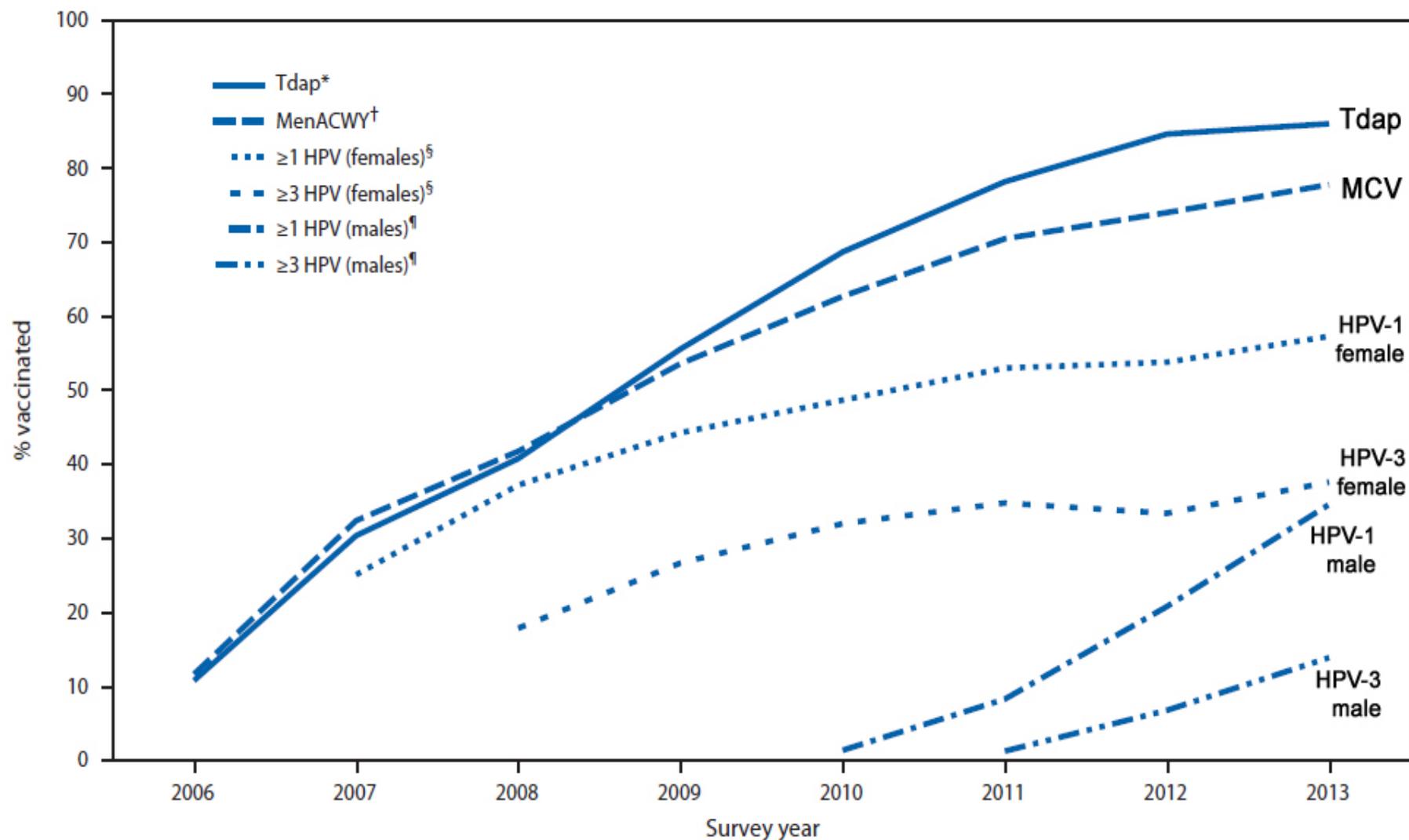
# **rLP2086 Bivalent Vaccine (Trumenba, Pfizer)**

- **Licensed by FDA on October 29, 2014**
- **Licensure based on serologic response to vaccination**
- **Approved for 10 through 25 years of age**
- **3 dose series (0, 2, 6 months)**
- **Intramuscular**

# ACIP Recommendations for Meningococcal B Vaccine

- ACIP has not yet made recommendations for use of meningococcal B vaccine
- Recommendations will probably include persons with
  - persistent complement component deficiencies
  - anatomic or functional asplenia
  - risk in a serogroup B meningococcal disease outbreak
  - certain microbiologists
- A recommendation to vaccinate the general population is unlikely

# National Immunization Survey – Teen, 2006-2013



# HPV Vaccine Coverage Among 13-17 Year-Olds, 2013

	US	MO
• <b>Females</b>		
– one or more doses	57%	46%
– full series	38%	29%
• <b>Males</b>		
– one or more doses	35%	21%
– full series	4%	NA

# Why HPV Vaccine Coverage Is Important

- For each year coverage remains at 30% instead of achieving 80%, 4,400 future cervical cancer cases and 1,400 cervical cancer deaths will occur

# Top 5 Reasons for Not Receiving HPV Vaccine – NIS-Teen, 2013

Parents of girls		
Reason	%	(95% CI)
Lack of knowledge	15.5	(13.0–18.5)
Not needed or necessary	14.7	(12.5–17.3)
Safety concern/Side effects	14.2	(11.8–16.8)
Not recommended	13.0	(10.8–15.5)
Not sexually active	11.3	(9.1–13.9)

Parents of boys		
Reason	%	(95% CI)
Not recommended	22.8	(20.6–25.0)
Not needed or necessary	17.9	(15.9–20.1)
Lack of knowledge	15.5	(13.7–17.6)
Not sexually active	7.7	(6.4–9.2)
Safety concern/Side effects	6.9	(5.6–8.5)

MMWR 2014;63(29):625-33

# Practical Approaches to Improve HPV Vaccination Rates In Your Practice

- **Provide an unequivocal recommendation for the vaccine!**
- **Remind parents that the full series is 3 doses over 6 months**
- **Check vaccination status of all patients at every visit and vaccinate at every opportunity**
- **Incorporate patient reminder systems such as telephone calls, texts, postcards, or letters**

# HPV Vaccination Resources for Providers

CDC Home  
 Centers for Disease Control and Prevention  
CDC 24/7: Saving Lives. Protecting People.™

A-Z Index [A](#) [B](#) [C](#) [D](#) [E](#) [F](#) [G](#) [H](#) [I](#) [J](#) [K](#) [L](#) [M](#) [N](#) [O](#) [P](#) [Q](#) [R](#) [S](#) [T](#) [U](#) [V](#) [W](#) [X](#) [Y](#) [Z](#) <#>

## Preteen and Teen Vaccines

Vaccines Home  
**V**accines & **I**mmunizations

[Vaccines Home](#) > [Specific Groups](#) > [Preteen and Teen Home](#) > [For HCPs](#)

[Email page link](#)  
[Print page](#)

### HPV Vaccine Resources for Healthcare Professionals



**HPV YOU ARE THE KEY TO CANCER PREVENTION**

#### HPV Vaccine is Cancer Prevention

**Overview** | Tools for Your Practice | Handouts to Give to Patients & Parents

- HPV is so common that almost everyone will be infected with HPV at some point in their lives; however most people will never know they have been infected.
- HPV exposure can occur with any type of intimate sexual contact.
- In the U.S., HPV causes about 17,000 cancers in women, and about 9,000 cancers in men each year.

Low HPV vaccination rates are leaving another generation of

#### Resource Spotlight



[www.cdc.gov/vaccines/YouAreTheKey](http://www.cdc.gov/vaccines/YouAreTheKey)

You're  
not  
opening  
the door  
to sex.

You're  
closing  
the  
door to  
cancer.

HPV vaccine is  
cancer prevention.

Talk to your child's doctor about  
vaccinating your 11-12 year old  
against HPV.

[www.cdc.gov/vaccines/teens](http://www.cdc.gov/vaccines/teens)

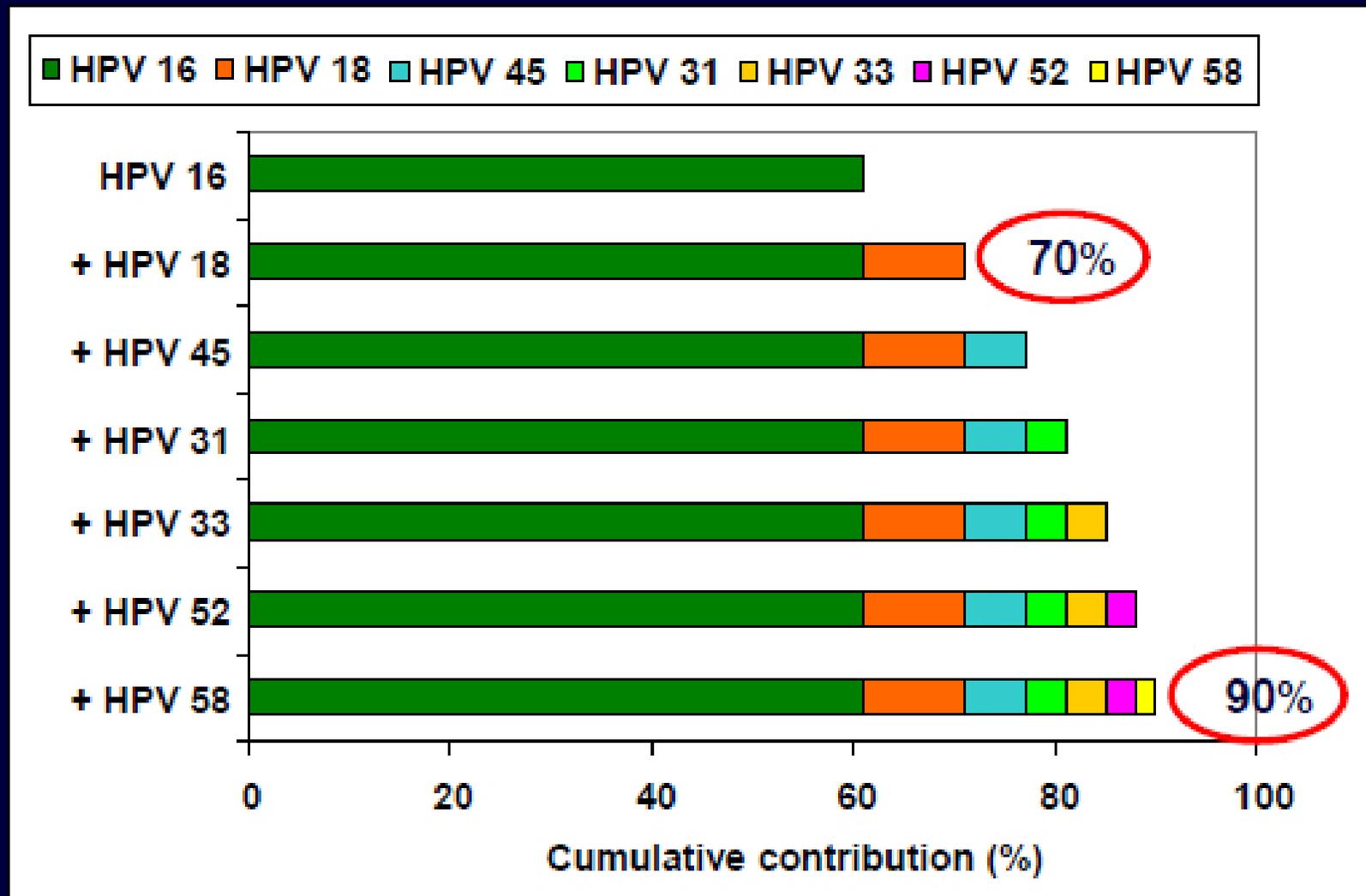


U.S. Department of  
Health and Human Services  
Centers for Disease  
Control and Prevention



Distributed by:

# Relative Contribution of HPV Types in 9vHPV Vaccine to Cervical Cancers Worldwide



Among HPV-positive cervical cancers; based on de Sanjose et al. *Lancet Oncol.* 11:1048-56 (2010); Serrano et al. *Infect Agent Cancer* 7:38 (2012)

# 9-Valent HPV Vaccine

- **Expected to be licensed by FDA before the end of 2014**
- **Application is for females 9 through 26 years and males 9 through 15 years**
- **Both HPV4 and HPV9 will be available for up to 24 months after licensure**

# HPV9 ACIP Recommendations

- Will likely be the same as the current recommendations for HPV4 (female 9 through 26, male 9 through 21, permissive through 26)
- Guidance on “mixed” schedules and revaccination?
- Vote at February 2015 meeting

# Thank You

