# Immunization Update 2015

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**Kentucky Immunization Conference**
**Louisville, Kentucky**
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**Information in this presentation are valid as of September 9, 2015**

## Advisory Committee on Immunization Practices (ACIP)

- **The recommendations to be discussed are primarily those of the ACIP**
  - **composed of 15 experts in clinical medicine and public health who are not government employees**
  - **provides 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**

**www.cdc.gov/vaccines/acip/**

## ACIP Recommendations

- **Recommendations approved by the Committee are just the first step**
- **Recommendations do not become official policy until**
  - **approved by the CDC Director**
  - **published in *Morbidity and Mortality Weekly Report* (MMWR)**

## Influenza Summary – 2014-15 Season

- **"Moderately severe" season**
- **Peak during last week of December 2014**
- **Antigenically drifted A/H3N2 virus predominated early; influenza B predominated in February-May**
- **Highest hospitalization rate (323/100,000) among persons 65 years and older**
- **141 laboratory-confirmed pediatric deaths reported from 40 states**
  - **57% of deaths among children age 5 years or older**

***MMWR* 2015;64:583-90**

## Predominant Influenza Virus by Season

| Season | Early (Oct-Jan) | Late (Jan-May) |
|---|---|---|
| 2009-2010 | A/H1N1 | A/H1N1 |
| 2010-2011 | A/H3N2 | A/H1N1, B |
| 2011-2012 | A/H3N2 | B |
| 2012-2013 | A/H3N2 | B |
| 2013-2014 | A/H1N1 | B |
| 2014-2015 | A/H3N2 | B |

**www.cdc.gov/flu/weekly/fluactivitysurv.htm**

## Influenza Vaccine Virus Strains for 2015-16

- **Trivalent vaccines will contain:**
  - **an A/California/7/2009 (H1N1)-like virus**
  - **an A/Switzerland/9715293/2013* (H3N2)-like virus, and**
  - **a B/Phuket/3073/2013*-like virus (Yamagata lineage)**
- **Quadrivalent vaccines also contain:**
  - **a B/Brisbane/60/2008-like virus (Victoria lineage)**

***different from 2014-15 formulation. www.cdc.gov/flu/weekly/**

## New Influenza Vaccines for the 2015-2016 Season

- Afluria (trivalent, bioCSL) approved by FDA for intramuscular administration via the Stratis needle-free jet injector (PharmaJet, Inc)
- FluBlok (trivalent, Protein Sciences) expanded age range
- Fluzone Intradermal quadrivalent replaces Fluzone Intradermal trivalent
- Fluzone trivalent SDS 0.5 mL no longer available (only quadrivalent)

## 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

*MMWR* 2014;63:691-7

## Influenza Vaccine Effectiveness for 2014-15

- During November 10, 2014–January 2, 2015 overall vaccine effectiveness (VE) against laboratory-confirmed influenza associated with medically attended ARI was 23% (95% CI = 8%–36%)
- VE for 24% for persons 6 months-17 years, 14% for 50 years and older
- No apparent benefit of LAIV vs. IIV
- Low VE consistent with circulation of drifted influenza A H3N2 strain

*MMWR* 2014;63:691-7

## LAIV – No Preference, 2015-2016

- **During 2013-2014 neither LAIV nor IIV provided protection against H3N2**
- **Recommendation for 2015-2016 season:**
  - **for healthy children aged 2 through 8 years who have no contraindications or precautions either LAIV or IIV can be used**
  - **no preference for LAIV or IIV for any person aged 2 through 49 years for whom either vaccine is appropriate**

***MMWR* 2015;64(No 30):818-25**

## 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**
  - **IIV vs LAIV**

***MMWR* 2015;64(No 30):818-25**

## Influenza Vaccine Administration Errors

- **Clinicians should not administer Influenza vaccine (IIV and LAIV) to persons outside the licensed age range for the vaccine they are using**
- **If LAIV or IIV* is given outside the licensed age ranges it is not necessary to repeat the dose unless a 0.25 mL dose was administered to a person 3 years or older**

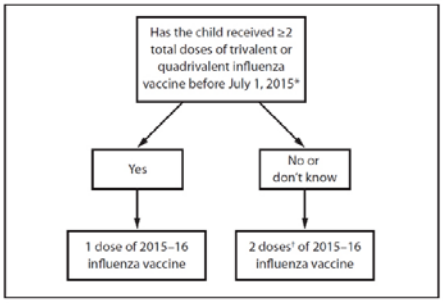
***except Fluzone Intradermal in some circumstances**

## Influenza Vaccine for Children 6 Months Through 8 Years

- Children 6 months through 8 years require 2 doses in first season they are vaccinated
- The recommendation for the number of doses recommended for children who previously received influenza vaccine has changed several times during the previous 10 years
- For 2015-2016 the algorithm has been simplified

*MMWR* 2015;64(No 30):818-25

**FIGURE 1. Influenza vaccine dosing algorithm for children aged 6 months through 8 years — Advisory Committee on Immunization Practices, United States, 2015–16 influenza season**



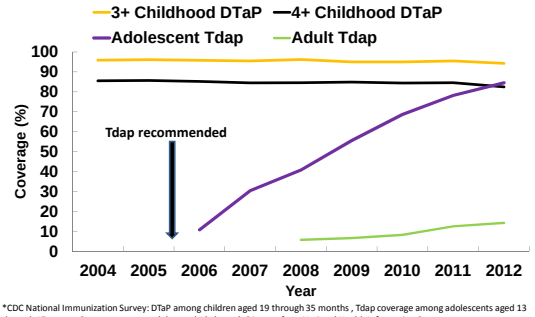

* The two doses need not have been received during the same season or consecutive seasons.
† Doses should be administered ≥4 weeks apart. *MMWR* 2015;64:818-25

## Pertussis in the United States

- 28,639 reported cases in 2013 (383 in KY)
- 28,660 provisional in 2014 (268 in KY)
- Highest incidence among infants (105/100,000), and adolescents age 7-10 years (30/100,000)
- 9 deaths reported – all among infants less than 3 months of age)

*MMWR* 2014;63(No. 32):702-15 and CDC unpublished data

## DTaP Coverage Among Children and Tdap Coverage Among Adolescents and Adults




*CDC National Immunization Survey: DTaP among children aged 19 through 35 months , Tdap coverage among adolescents aged 13 through 17 years . Coverage among adults aged 19 through 64 years from National Health Information Survey .

## 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. *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

*MMWR* 2013:62( (No.7): 131-135

## 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
- Recommendation for healthy adults deferred pending additional data

*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
- 84,496 persons 65 years or older in the Netherlands

*N Engl J Med* 2015;372;1114-23

## 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)

*N Engl J Med* 2015;372;1114-23

## Pneumococcal Conjugate Vaccine (PCV13) and Adults

- ACIP recommend that both PCV13 and PPSV23 should be routinely administered in series to all adults age 65 years and older

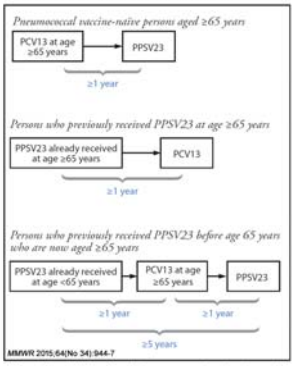
*MMWR* 2014;63(No. 37):822-5

## 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

*MMWR* 2014;63(No. 37):822-5

**BOX. Recommended intervals for sequential use of PCV13 and PPSV23 for immunocompetent adults aged ≥65 years — Advisory Committee on Immunization Practices, United States**




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

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

- **For high-risk adults (asplenia, immunocompromised, etc)**
  - **single dose of PCV13**
  - **dose of PPSV23 <u>at least 8 weeks later</u>**
- **For persons 65 years or older who are not at high risk**
  - **single dose of PCV13**
  - **dose of PPSV23 <u>at least 1 year later</u>**

## Pneumococcal Vaccine Minimum Intervals

- **The minimum interval between PCV13 and PPSV23 is 8 weeks**
- **The minimum interval between PPSV23 and PCV13 is 1 year**
- **The minimum interval between doses of PPSV23 is 5 years**
- **CDC does not recommend repeating a dose of PPSV23 or PCV13 if the minimum interval between doses is violated**

***MMWR* 2015;64(34):944-7**

TABLE. Summary of recommended intervals, by risk and age groups, for persons with indications to receive PCV13 and PPSV23 sequence — Advisory Committee on Immunization Practices, United States, September 2015

| Risk group/Underlying medical condition | Intervals for PCV13–PPSV23 sequence, by age group | | | | Intervals for PPSV23–PCV13 sequence, by age group | | | |
|---|---|---|---|---|---|---|---|---|
| | 24–71 months | 6–18 years | 19–64 years | ≥65 years | 24–71 months | 6–18 years | 19–64 years | ≥65 years |
| **No underlying chronic conditions** | NA | NA | NA | ≥1 year | NA | NA | NA | ≥1 year |
| **Immunocompetent persons**<br>Chronic heart disease<br>Chronic lung disease<br>Diabetes mellitus<br>Alcoholism*<br>Chronic liver disease, cirrhosis*<br>Cigarette smoking* | ≥8 weeks | NA | NA | ≥1 year | ≥8 weeks | NA | NA | ≥1 year |
| **Immunocompetent persons**<br>Cerebrospinal fluid leak<br>Cochlear implant | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥1 year | ≥1 year |
| **Persons with functional or anatomic asplenia**<br>Sickle cell disease/other hemoglobinopathy<br>Congenital or acquired asplenia | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥1 year | ≥1 year |
| **Immunocompromised persons**<br>Congenital or acquired immunodeficiency<br>Human immunodeficiency virus infection<br>Chronic renal failure<br>Nephrotic syndrome<br>Leukemia<br>Lymphoma<br>Hodgkin disease<br>Generalized malignancy<br>Iatrogenic immunosuppression<br>Solid organ transplant<br>Multiple myeloma* | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥8 weeks | ≥1 year | ≥1 year |

**Abbreviation:** NA = not applicable, sequential use of PCV13 and PPSV23 is not recommended for these age and risk groups.
* Underlying medical conditions that are not included in the recommendations for children aged <6 years.

***MMWR* 2015;64(34):944-7**

## Pneumococcal Vaccines and Medicare

- **Effective September 19, 2014 Medicare will cover**
  - **an initial pneumococcal vaccine to all Medicare beneficiaries who have never received the vaccine under Medicare Part B; and**
  - **a different, second pneumococcal vaccine <u>one year after the first vaccine</u> was administered (that is, 11 full months have passed following the month in which the last pneumococcal vaccine was administered)**

**www.cms.gov**

## 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**

## *Neisseria meningitidis*

- Aerobic gram-negative bacteria
- At least 13 serogroups based on characteristics of the polysaccharide capsule
- Most invasive disease caused by serogroups A, B, C, Y, and W-135
- Relative importance of serogroups depends on geographic location and other factors (e.g. age)
  - serogroups B, C and Y in the U.S.
  - serogroup A in Sub-Saharan Africa

## *Neisseria meningitidis* Epidemiology

- Incidence falling since 2000 (before licensure of MCV4)
- Incidence of all serogroups falling, including serogroup B which is not in MCV4
- 556 cases reported in 2013
- Of cases with known serogroup (n=258)
  - 55% ACWY (n=142), 38% B (n=99)
- Highest incidence among infants (2.1/100,000), more than half is serogroup B

CDC unpublished data

## 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
- NOT at increased risk: international travelers, first year college students

CDC unpublished data

## 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

National Notifiable Diseases Surveillance System

## Meningococcal Vaccines

- ACWY polysaccharide (Menomune)
  - available since 1978
  - not recommended except for certain persons age 56 years and older
- ACWY conjugate polysaccharide (Menactra, Menveo, MenHibrix)
  - available since 2005
  - routinely recommended for adolescents, international travelers and other high-risk persons
- B capsular protein (Trumenba, Bexero)
  - available since 2014
  - recommended only for certain high-risk persons

## Meningococcal 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 (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)

## Meningococcal Serogroup B Vaccines

- rLP2086 (Trumenba, Pfizer)
  - Licensed by FDA on October 29, 2014
  - Approved for 10 through 25 years of age
  - 3 dose series (0, 2, 6 months)
- 4CMenB (Bexsero, Novartis)
  - Licensed by FDA on January 23, 2015
  - Approved for 10 through 25 years of age
  - 2 dose series (0, 1 months)

## ACIP Recommendations for Meningococcal B Vaccine of High Risk Persons

- Certain persons 10 years of age or older* who are at increased risk for meningococcal disease should receive MenB vaccine
  - persistent complement component deficiency
  - anatomic or functional asplenia
  - risk in a serogroup B meningococcal disease outbreak
  - certain microbiologists
- MenB vaccines are included in VFC
- NOT routinely recommended for college students or international travelers

*off-label for persons 26 years and older
MMWR 2015;64:608-12

## ACIP Recommendations for Meningococcal B Vaccine

- On June 25, 2015 ACIP approved a Category B ("permissive") recommendation for MenB vaccine for persons not at increased risk*
- Allows for individual clinical decision-making
- Vaccines with a Category B recommendation are included in the VFC program and ACA insurance programs

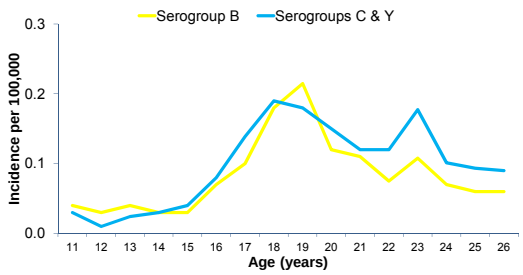
*unpublished as of September 9, 2015

## ACIP Recommendations for Meningococcal B Vaccine

- Recommendation wording will likely be something like:
  - "A serogroup B meningococcal (MenB) vaccine series *may* be administered to adolescents and young adults 16 thorough 23 years of age to provide short term protection against most strains of serogroup B meningococcal disease. The preferred age for MenB vaccination is 16 through 18 years of age."

*unpublished as of September 9, 2015

## Meningococcal Incidence in Adolescents and Young Adults by Serogroup, 2009–2013




Source: NNDSS data supplemented with additional serogroup data from ABCs and state health departments

## Average Annual Cases by Age Group and Serogroup, 2009–2013

| | Age Group | Cases[1] |
|---|---|---|
| Serogroup B | <5 years | 74–94 |
| | 11-24 years | 54–67 |
| | All ages | 203–260 |
| Serogroups C & Y | <5 years | 34–43 |
| | 11-24 years | 62–77 |
| | All ages | 307–393 |

Range in estimated cases: Low=NNDSS data supplemented with additional serogroup data from ABCs and state health departments, High= NNDSS data supplemented with additional serogroup data from ABCs and state health departments + proportion serogroup B or serogroup C & Y applied to cases with unknown serogroup.

## HPV Infection Is the Most Common Sexually Transmitted Disease in the United States

- Approximately 79 million Americans are currently infected
- 14 million new infections/year in the United States
  - about half of these new infections occur among persons 15-24 years of age
- Almost all sexually active men and women will be infected at some point in their lives
- Immunocompromised persons have higher rates of HPV acquisition and progression to disease

www.cdc.gov/std/hpv/default.htm

## Average Annual HPV-Attributable Cancers in the United States, 2006-2010

- 26,900 HPV-associated cancers diagnosed annually
  - 9,300 in men
  - 17,600 in women

| Site | Male | Female | Total Cancers |
|---|---|---|---|
| Cervix | 0 | 10,400 | 10,400 |
| Anus | 1,400 | 2,600 | 4,000 |
| Vagina | 0 | 600 | 600 |
| Oropharynx | 7,200 | 1,800 | 9,000 |
| Vulva | 0 | 2,200 | 2,200 |
| Penis | 700 | 0 | 700 |

Anal, oral, penile, and vulvar cancer rates are increasing

MMWR 2014;63(RR-5):1-3. Zandberg DP, et al. *CA Cancer J Clin*. 2013;63:57-81.

## HPV-Associated Cancers

| | 16,18 | 31,33,45,52,58 |
|---|---|---|
| Cervical | 66% | 15% |
| Vaginal | 55% | 18% |
| Vulvar | 49% | 14% |
| Anal (M) | 79% | 4% |
| Anal (F) | 80% | 11% |
| Penile | 48% | 9% |
| Oropharyng (M) | 63% | 4% |
| Oropharyng (F) | 51% | 9% |
| Overall | 64% | 10% |

www.cdc.gov/cancer/hpv/

## HPV Vaccines

| | 2vHPV (Cervarix, GSK) | 4vHPV (Gardisil, Merck) | 9vHPV (Gardisil 9, Merck) |
|---|---|---|---|
| Virus types | 16, 18 | 6, 11, 16, 18 | 6, 11, 16, 18, 31, 33, 45, 52, 59 |
| Adjuvant | Yes – aluminum hydroxide | Yes – aluminum hydroxyphosphate sulfate | Yes – aluminum hydroxyphosphate sulfate |
| Licensure | Females 9-25 yrs | Females 9-26 yrs Males 9-26 yrs | Females 9-26 yrs Males 9-15 yrs |
| Prevents | Cervical cancer and precancer | Cervical, vulvar, vaginal, and anal cancer and precancer, genital warts | Cervical, vulvar, vaginal, and anal cancer and precancer, genital warts |

www.fda.gov/BiologicsBloodVaccines/Vaccines/ApprovedProducts/ucm093833.htm

## 9-Valent HPV Vaccine

- 9vHPV licensed by FDA on December 10, 2014
- Approved for females 9 through 26 years and males 9 through 15 years
- Same schedule as 4vHPV
- Both 4vHPV and 9vHPV will be available for up to 24 months after licensure

## 9vHPV Clinical Trial - Efficacy

- The rate of high-grade cervical, vulvar, or vaginal disease related to HPV types 31, 33, 45, 52, and 58
  - 9vHPV group 0.1 per 1,000 person years
  - 4vHPV group 1.6 per 1,000 person years
- 9vHPV efficacy disease caused by the 5 additional strains was 96.7% (CI 81%-99.8%)

Joura et al. *NEJM* 2015;372:711-23

## 9vHPV Clinical Trial - Safety

- Local reactions (pain, swelling, etc)
  - 9vHPV recipients 91%
  - 4vHPV recipients 85%
- Systemic reactions (headache, fever, nausea, dizziness etc)
  - 9vHPV recipients 56%
  - 4vHPV recipients 55%
- No serious AEs were attributed to either vaccine

Joura et al. *NEJM* 2015;372:711-23

## 9vHPV ACIP Recommendations

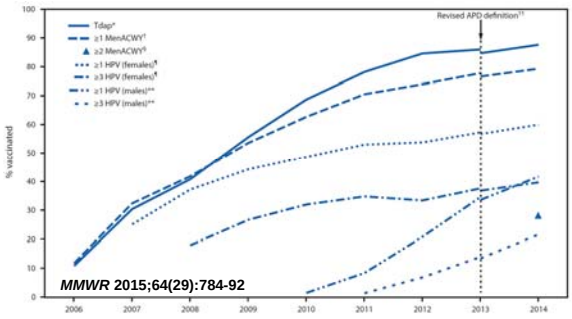
- Same as the current recommendations for 4vHPV
  - routine vaccination at 11 or 12 years of age
  - female 9 through 26, male 9 through 21, permissive through 26 (off-label for males 16 years and older)
- Any vaccine can be used to finish an incomplete series
- ACIP did not state a preference for one HPV vaccine over another

*MMWR* 2015;64(No.11):300-4

## 9vHPV ACIP Recommendations

- At their June 2015 meeting ACIP declined to make any recommendation regarding revaccination with 9vHPV for persons who already completed a series of 2vHPV or 4vHPV
- Clinicians are free to revaccinate with 9vHPV but VFC will not cover additional doses and insurance plans are unlikely to pay for these doses

## National Immunization Survey – Teen, 2006-2014




*MMWR* 2015;64(29):784-92

## HPV Vaccine Coverage Among 13-17 Year-Olds, 2014

| | US | KY |
|---|---|---|
| • Females | | |
| – one or more doses | 60% | 52% |
| – full series | 40% | 38% |
| • Males | | |
| – one or more doses | 42% | 24% |
| – full series | 22% | 13% |

***Tdap rate in Kentucky was 86%. *MMWR* 2015;64(29):784-92**

## 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

*Vaccine* 2011;29:8443-50

## 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
- Many practice resources at www.cdc.gov/vaccines/who/teens/for-hcp/hpv-resources.html

## Resources

- **CDC Vaccines and Immunization Website**
  - **www.cdc.gov/vaccines/**
- **Immunization Action Coalition**
  - **www.immunize.org**
- **Vaccine Education Center at the Children's Hospital of Philadelphia**
  - **www.chop.edu/service/vaccine-education-center/home.html**