A Straight Shot: Update on Adult Vaccination Recommendations

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Disclosure

The program chair and presenters for this continuing education activity have reported no relevant financial relationships, except:

- **Christopher McCoy** - Allergan: Board Member/Advisory Panel; The Medicines Company: Board Member/Advisory Panel; Theravance Biopharma: Board Member/Advisory Panel; Zavante: Grant/Research Support
Objectives

At the conclusion of the lecture, the audience should be able to:

- Discuss the latest updates in vaccine recommendations from the Advisory Committee on Immunization Practices (ACIP) and/or the Center for Diseases Control (CDC) for select adult infections.

- Evaluate the literature supporting the changes in vaccine selection recommendations for adults.

- Given a patient scenario, determine the appropriate vaccine from the newer products available.
Quick Epidemiologic Facts

- **Pneumococcal disease**:  
  - 29,100 cases 2014 – 3,250 deaths  
  - Peak ages are over 50 years and ≤ 1 year

- **Influenza**:  
  - 625K influenza like illness patient care visits 2015-16  
  - Lower rates compared to the previous 2 seasons, peaked in Spring  
  - Predominant strain A (H1N1)  
  - Average number of hospitalizations (2014)= 226,000 annually  
  - >60% in adults over 24 years
Quick Epidemiologic Facts

- **Meningococcus:**
  - >14,000 cases annually 2013 – 2014
  - Incidence historically low however overall case-fatality rate 10%-15%, long term sequelae in 10-20%
  - >64% in adults
  - Outbreaks: 2016 in NJ, 2015 SoCal and Chicago

- **Varicella Zoster Virus (adult):**
  - 1 million cases annually
  - Lifetime risk is 30%: Risk increases with age over 50
  - Reactivation event in adults (aka Shingles)

CDC. MMWR 2013. 61: 719 – 32.
Process for Updating Vaccine Recommendations

- Annual meeting February, ACIP and CDC data review
  - Unpublished data provided by vaccine manufacturer
  - Published data and data from scientific meetings
  - Published epidemiologic data

- Important review topics
  - Immunogenicity including antibody kinetics
  - Efficacy in preventing disease and durability of response
  - Post-marketing dose selection
  - Comparative schedules for effectiveness
  - Response in special populations
  - Outbreak data and adverse events
2016 Vaccine Updates

- Interval change for pneumococcal vaccine
  - 13-valent pneumococcal conjugate vaccine (PCV13) followed by 23-valent pneumococcal polysaccharide vaccine (PPSV23)
    - From "6 to 12 months" to "at least 1 year" adults aged ≥65

- Expand receipt of serogroup B meningococcal (MenB) to persons ≥10 years at high risk

- Nine-valent human papillomavirus (HPV) vaccine (9vHPV) added as preferred

*References:
  - MMWR 2015;64[34]:944–947;
  - MMWR 2015;64[22]:608–612;
  - MMWR 2015;64[11]:300–304*
2016 Influenza Updates

- Live Activated Influenza Vaccine (LAIV4) should not be used

- Inactivated trivalent (IIV3) and quadrivalent (IIV4) are equivalent, no studies of comparative effectiveness

- Multiple brands of IIV3 and IIV4 are available, no preference

- Opting out due to egg allergy restricted, administer egg free for severe hx, recombinant (RIV3: Flublok®), observe all others

Groshkopf *MMWR* 2016;65:1–54
**Figure 1. Recommended immunization schedule for adults aged 19 years or older, by vaccine and age group**

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
<th>19-21 years</th>
<th>22-26 years</th>
<th>27-49 years</th>
<th>50-59 years</th>
<th>60-64 years</th>
<th>≥ 65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)</td>
<td>Substitute Tdap for Td once, then Td booster every 10 yrs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella</td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Female</td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV) Male</td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)</td>
<td>1 or 2 doses depending on indication</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td>1 dose</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal 23-valent polysaccharide (PPSV23)</td>
<td>1 or 2 doses depending on indication</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>2 or 3 doses depending on vaccine</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>3 doses</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Meningococcal 4-valent conjugate (MenACWY) or polysaccharide (MPSV4)</td>
<td>1 or more doses depending on indication</td>
<td></td>
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</tr>
<tr>
<td>Meningococcal B (MenB)</td>
<td>2 or 3 doses depending on vaccine</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae type b (Hib)</td>
<td>1 or 3 doses depending on indication</td>
<td></td>
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</tr>
</tbody>
</table>

*Covered by the Vaccine Injury Compensation Program

**Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster

**Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)

**No recommendation
Figure 2. Vaccines that might be indicated for adults aged 19 years or older based on medical and other indications

<table>
<thead>
<tr>
<th>VACCINE ▼</th>
<th>INDICATION ➤</th>
<th>Pregnancy</th>
<th>Immuno-compromising conditions (excluding HIV infection)</th>
<th>HIV infection CD4+ count (cells/µL)</th>
<th>Men who have sex with men (MSM)</th>
<th>Kidney failure, end-stage renal disease, on hemodialysis</th>
<th>Heart disease, chronic lung disease, chronic alcoholism</th>
<th>Asplenia and persistent complement component deficiencies</th>
<th>Chronic liver disease</th>
<th>Diabetes</th>
<th>Healthcare personnel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td></td>
<td></td>
<td>1 dose annually</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)</td>
<td>1 dose each pregnancy</td>
<td></td>
<td>Substitute Tdap for Td once, then Td booster every 10 yrs</td>
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<tr>
<td>Varicella</td>
<td></td>
<td></td>
<td>Contraindicated</td>
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</tr>
<tr>
<td>Human papillomavirus (HPV) Female</td>
<td>3 doses through age 26 yrs</td>
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<td>Zoster</td>
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<td></td>
<td>Contraindicated</td>
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<td>Messies, mumps, rubella (MMR)</td>
<td>Contraindicated</td>
<td></td>
<td>1 or 2 doses depending on indication</td>
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<td></td>
</tr>
<tr>
<td>Pneumococcal 13-valent conjugate (PCV13)</td>
<td>1 dose</td>
<td></td>
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</tr>
<tr>
<td>Pneumococcal polysaccharide (PPSV23)</td>
<td>1, 2, or 3 doses depending on indication</td>
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<td>Hepatitis A</td>
<td>2 or 3 doses depending on vaccine</td>
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<tr>
<td>Hepatitis B</td>
<td>3 doses</td>
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<tr>
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</tr>
<tr>
<td><em>Haemophilus influenzae</em> type b (Hib)</td>
<td>3 doses post-HSCT recipients only</td>
<td></td>
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</tr>
</tbody>
</table>

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Recommended for all persons who meet the age requirement, lack documentation of vaccination, or lack evidence of past infection; zoster vaccine is recommended regardless of past episode of zoster

Recommended for persons with a risk factor (medical, occupational, lifestyle, or other indication)

No recommendation

Contraindicated

Recommended for healthcare personnel
Immunization Rates Among Adults

Herpes Zoster, age >65

Tetanus with pertussis, age >65

Tetanus with pertussis, age 19-64

Pneumococcal, age ≥65

Pneumococcal, age 19-64 at high risk

CDC MMWR 2016; 65; 1: 34-49
## Immunization Rates: Influenza

<table>
<thead>
<tr>
<th>Group</th>
<th>2011-12 (%)</th>
<th>2012-13 (%)</th>
<th>2013-14 (%)</th>
<th>2014-15 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons ≥ 18 yrs</td>
<td>38.8</td>
<td>41.5</td>
<td>42.2</td>
<td>43.6</td>
</tr>
<tr>
<td>Persons 18-49 yrs, all</td>
<td>28.6</td>
<td>31.1</td>
<td>32.3</td>
<td>33.5</td>
</tr>
<tr>
<td>Persons 18-49 yrs, high risk</td>
<td>36.8</td>
<td>39.8</td>
<td>38.7</td>
<td>39.3</td>
</tr>
<tr>
<td>Persons 50-64 yrs</td>
<td>42.7</td>
<td>45.1</td>
<td>45.3</td>
<td>47.0</td>
</tr>
<tr>
<td>Persons ≥ 65 yrs</td>
<td>64.9</td>
<td>66.2</td>
<td>65.0</td>
<td>66.7</td>
</tr>
<tr>
<td>Health Care Workers</td>
<td>62.4</td>
<td>62.5</td>
<td>62.9</td>
<td>64.3</td>
</tr>
</tbody>
</table>

**Healthy People 2020 target = 70%**

CDC. National Flu Survey, MMWR 62 ;1-29  
CDC: MMWR 2016 ; 65 :10-12
Pneumococcal Vaccine
Pneumococcal Vaccine Timeline

- 1977: 14-valent polysaccharide vaccine (PPSV14)
- 1983: 23-valent polysaccharide vaccine (PPSV23)
- 2000: 7-valent polysaccharide conjugate vaccine (PCV7)
- 2010: 13-valent polysaccharide conjugate vaccine (PCV13)
# PPSV23 vs. PCV13

<table>
<thead>
<tr>
<th></th>
<th>PPSV23</th>
<th>PCV13</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Induction of antibody response</strong></td>
<td>T cell-independent (infants unable to process)</td>
<td>T cell-dependent (infant compatible)</td>
</tr>
<tr>
<td><strong>Serotype titer response</strong></td>
<td>Lower Ab titer</td>
<td>Increase in Ab titer (4x) greater with improved memory</td>
</tr>
<tr>
<td></td>
<td>Shorter memory time</td>
<td></td>
</tr>
<tr>
<td><strong>Serotypes covered</strong></td>
<td>1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F, 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F</td>
<td>1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F</td>
</tr>
<tr>
<td><strong>Protection in infants/elderly</strong></td>
<td>Poor response</td>
<td>Good response</td>
</tr>
</tbody>
</table>

CDC: MMWR 2010;59:258-61
# PPSV23 vs. PCV13

<table>
<thead>
<tr>
<th>Adults 65y or older</th>
<th>Adults 19-64y</th>
<th>Adults 19-64y</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPSV23 and PCV13</td>
<td>PPSV23 only</td>
<td>PPSV23 and PCV13</td>
</tr>
<tr>
<td>Administer dose of <strong>PCV13</strong> first</td>
<td>Chronic conditions:</td>
<td>o Functional or anatomic asplenia</td>
</tr>
<tr>
<td>WAIT 1 YEAR</td>
<td>o Asthma</td>
<td>o Cochlear implants</td>
</tr>
<tr>
<td>Administer dose</td>
<td>o Diabetes</td>
<td>o Cerebrospinal fluid leaks</td>
</tr>
<tr>
<td><strong>PPSV23</strong></td>
<td>o Heart disease</td>
<td>o Lymphoma, Leukemia, Hodgkin’s disease</td>
</tr>
<tr>
<td></td>
<td>o Alcoholism</td>
<td>o Solid organ transplant</td>
</tr>
<tr>
<td></td>
<td>o Liver disease</td>
<td>o HIV infection</td>
</tr>
<tr>
<td>If you accidentally give <strong>PPSV23</strong> first</td>
<td>Habits/Environment</td>
<td>o Chronic renal failure</td>
</tr>
<tr>
<td>WAIT 1 YEAR</td>
<td>o Cigarette smoking</td>
<td>o Nephrotic syndrome</td>
</tr>
<tr>
<td>Administer dose</td>
<td>o Nursing home or long term care facility dweller</td>
<td>o Long term immunosuppressive therapy</td>
</tr>
<tr>
<td><strong>PCV13</strong></td>
<td>Vaccinate every <strong>5 years</strong> until 65 years</td>
<td>o Multiple myeloma</td>
</tr>
<tr>
<td></td>
<td><strong>5 years</strong></td>
<td>Vaccinate PPSV23 every <strong>5 years</strong> until 65 years</td>
</tr>
<tr>
<td></td>
<td>until 65 years</td>
<td>Wait <strong>1 year</strong> if PCV13 given prior</td>
</tr>
</tbody>
</table>

If you accidentally give **PPSV23** first, wait **1 year** if PCV13 given prior.

*CDC/ACIP MMWR: 2015 64(34);944-47*
### PCV13 in Adults

**Community-Acquired Pneumonia Immunization Trial in Adults (CAPITA)**

<table>
<thead>
<tr>
<th>Objective</th>
<th>To evaluate PCV13 for the prevention of vaccine-type invasive and noninvasive CAP in adults ≥65 years</th>
</tr>
</thead>
</table>
| Inclusion Criteria | • Netherlands  
• September 08 – January 10 |
| Design and Enrollment | • N=84,492 randomized to PCV13 or placebo 1:1  
• Followed for incidence of invasive pneumococcal disease (IPD) or pneumonia |
| Results | • Efficacy (decrease) in vaccine-type invasive pneumococcal disease (IPD) 75.0% (CI 41.4 to 90.8) p<0.001  
• Efficacy (decrease) in vaccine-type non-bacteremic pneumonia: 45.0% (CI 14.2 to 65.3) p<0.007 |

MA is a 56-year-old female admitted to your hospital for a urinary tract infection with a past medical history of T2DM for 7 years. When asked about her vaccination status, MA reports that she has not received any vaccinations for several years. When viewing the medical record, the pneumococcal vaccine sheet is blank.

Based on her history, which vaccine should she receive as an inpatient, after her fever abates and she is clinically stable?

A. Neither vaccine as she is under 65 years
B. PCV13 today, followed by PPSV23 in 6-12 months
C. PCV13 only
D. PPSV23 only
MA is a 56-year-old female admitted to your hospital for a urinary tract infection with a past medical history of T2DM for 7 years. When asked about her vaccination status, MA reports that she has not received any vaccinations for several years. When viewing the medical record, the pneumococcal vaccine sheet is blank.

Based on her history, which vaccine should she receive as an inpatient, after her fever abates and she is clinically stable?

- **A**: Neither vaccine as she is under 65 years
- **B**: PCV13 today, followed by PPSV23 in 6-12 months
- **C**: PCV13 only
- **D**: PPSV23 only
Influenza Vaccine
Selected Strains: 2016-17

- Trivalent vaccines containing:
  - A/California/7/2009 (H1N1)
  - A/Hong Kong/4801/2014 (H3N2)
  - B/Brisbane/60/2008 (Victoria lineage)

- Quadrivalent vaccines containing additional
  - B/Phuket/3073/2013 (Yamagata lineage)
Name that Viral Strain

A / California / 7 / 2009 (H1N1)

Typing
- Ground Zero
- Strain number

Subtype
- Hemagglutinin
- Neuraminidase

Year of pandemic
# TIV vs. LAIV

<table>
<thead>
<tr>
<th></th>
<th>TIV (Trivalent Inactivated Vaccine)</th>
<th>LAIV (Live Attenuated Influenza Vaccine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indicated population</td>
<td>&gt; 6 months</td>
<td>2-49 years of age</td>
</tr>
<tr>
<td>Content of vaccine</td>
<td>Trivalent (15 μg of each strain)</td>
<td>Trivalent (15 μg of each strain)</td>
</tr>
<tr>
<td>Production</td>
<td>Chicken egg except FLUBLOK™</td>
<td>Chicken egg</td>
</tr>
<tr>
<td>Virus state</td>
<td>Inactivated</td>
<td>Cold-adapted</td>
</tr>
<tr>
<td>Route of administration</td>
<td>Intramuscular</td>
<td>Intranasal</td>
</tr>
<tr>
<td>Contraindication</td>
<td>Severe allergy to vaccine or vaccine components, history of Guillain Barre Syndrome (GBS), acute illness</td>
<td>Immunocompromise, children &lt; 5 and history of recurrent wheezing, children/adolescents receiving ASA, pregnancy, severe egg allergy, GBS</td>
</tr>
</tbody>
</table>
TIV vs. LAIV – Metaanalysis

LAIV more efficacious
- Children, 6 months–18 year
  - Ashkenazi
  - Belshe
  - Fleming
  - Piedra/Halloran*

- Adults, 17–49 year
  - Ohmit 2006
  - Ohmit 2008
  - Monto
  - Wang, all*
  - Wang, recently unvaccinated*
  - Eick, recruits*
  - Eick, non-recruits*
  - Treanor†

TIV more efficacious
- Adults, > 60 year
  - Forrest

Incidence rate ratio

Ambrose et al. Influenza and Other Respiratory Viruses, 2010: 5, 67–7
## TIV vs. LAIV

### Comparative Trial for Prevention of Influenza

<table>
<thead>
<tr>
<th>Objective</th>
<th>To evaluate whether vaccinating children and adolescents with LAIV provides better community protection than IIV</th>
</tr>
</thead>
</table>
| Inclusion Criteria | ages 36 mo-15 years: Canada  
 | October 2012 and May 2015 over 3 flu seasons |
| Design and Enrollment | N=4611 randomized to LAIV or TIV randomized by colony cluster randomized blinded trial |
| Outcome measured | Confirmed influenza A or B virus infection |
| Results | Hazard ratio comparing LAIV with IIV for influenza A or B virus was 1.03 (95% CI, 0.85 to 1.24) |
# TIV vs. LAIV

## US Flu Vaccine Effectiveness

<table>
<thead>
<tr>
<th>Objective</th>
<th>To evaluate the effectiveness of LAIV vs. IIV in children and adolescents during the 2015-16 season</th>
</tr>
</thead>
</table>
| Inclusion Criteria | Nov 2, 2015–Apr 15, 2016  
Children 2-17 years of age with confirmed flu |
| Design and Enrollment | N=2286 observational trial |
| Outcome measured | Confirmed influenza A or B virus infection |
| Results | LAIV higher OR for confirmed infection 2.63 (95% CI, 2.59-4.37) |
# Influenza Vaccines 2016-17

<table>
<thead>
<tr>
<th>Approved Age</th>
<th>IIV3 Standard dose (Trivalent)</th>
<th>IIV3 High dose (Trivalent)</th>
<th>IIV4 (Quadrivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;6 months</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>&gt;65 years</td>
<td></td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Route</th>
<th>IIV3 Standard dose (Trivalent)</th>
<th>IIV3 High dose (Trivalent)</th>
<th>IIV4 (Quadrivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IM/Intradermal</td>
<td>IM/Intradermal</td>
<td>IM</td>
<td>IM</td>
</tr>
<tr>
<td>0.5ml/0.1ml</td>
<td>0.5ml</td>
<td>0.5ml</td>
<td>0.5ml</td>
</tr>
<tr>
<td>(9 mcg each strain)</td>
<td>(60 mcg each strain)</td>
<td>(9 mcg each strain)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Contain Thimerosal?</th>
<th>IIV3 Standard dose (Trivalent)</th>
<th>IIV3 High dose (Trivalent)</th>
<th>IIV4 (Quadrivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Product dependent</td>
<td>No Product dependent</td>
<td>No Product dependent</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Egg derived</th>
<th>IIV3 Standard dose (Trivalent)</th>
<th>IIV3 High dose (Trivalent)</th>
<th>IIV4 (Quadrivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not all (Flublok™)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>
# High Dose – Effectiveness

## Comparative Effectiveness of High-Dose versus Standard Dose Influenza Vaccines in US Residents

<table>
<thead>
<tr>
<th>Objective</th>
<th>To establish whether high-dose (60mcg) vaccine was more effective for prevention of influenza-related visits and hospital admissions vs standard dose</th>
</tr>
</thead>
</table>
| Inclusion Criteria | US Medicare beneficiaries 2012-13  
Medically stable persons $\geq$65 years of age living in the community |
| Design and Enrollment | N=2,545,275 observational trial retrospective cohort  
Data from billing codes |
| Outcome measured | Positive influenza test followed by neuraminidase prescription  
Hospital or Emergency Department visits coded for influenza |
| Results | High dose was associated with 22% (95% CI 15–29) fewer positive influenza tests requiring treatment and 22% (95% CI 16–27%) fewer hospital or Emergency Department visits |

ACIP Recommendations –Influenza

- Everyone annually –aged 6 months or older
- Special effort to vaccinate patients at increased risk of complications and their close contacts:
  - Immunocompromised
  - Medical comorbidities including: Asthma/ COPD/ Diabetes/ Cardiovascular Disease/CKD
  - Age greater than 65 years or under 2 years
  - Pregnant women
  - Healthcare workers

WH is a 69 year old female with asthma. Of the following flu vaccines, which is the preferred influenza vaccine for this patient?

A. IIV3, Standard Dose
B. IIV4, Standard Dose
C. IIV3, High Dose
D. LAIV3, Standard Dose
E. A, B, or C
WH is a 69 year old female with asthma. Of the following flu vaccines, which is the preferred influenza vaccine for this patient?

- A. IIV3, Standard Dose
- B. IIV4, Standard Dose
- C. IIV3, High Dose
- D. LAIV3, Standard Dose
- E. A, B, or C
Meningococcal Vaccines
## N. meningitidis Serogroups

<table>
<thead>
<tr>
<th>Serogroup: Polysaccharide capsule</th>
<th>Characteristics</th>
</tr>
</thead>
</table>
| A                                | - Leading cause of epidemic meningitis worldwide  
                                   | - Most prevalent in Africa and China |
| B                                | - Europe and Americas, not previously covered by vaccine  
                                   | - Recent highly publicized outbreaks |
| C                                | - Europe and North America  
                                   | - Multiple outbreaks |
| Y                                | - Unusual presentation, pneumonia  
                                   | - Increasing prevalence in the US, affecting all age groups |
| W-135                            | - Infrequent and unusual infection: arthritis-pericarditis  
                                   | - Younger age groups with high case fatality rate |

# Meningococcal ACWY Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
<th>Approved age range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menomune™ (MPSV4)</td>
<td>Polysaccharide</td>
<td>≥2 years (single dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 doses asplenia/HIV/comp def</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 doses asplenia/HIV/comp def</td>
</tr>
<tr>
<td>Menactra™ (MenACWY-D)</td>
<td>Conjugate</td>
<td>9 to 23 mos. (2-dose series)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 to 55 years (single dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 doses asplenia/HIV/comp def</td>
</tr>
<tr>
<td>Menveo™ (MenACWY-CRM)</td>
<td>Conjugate</td>
<td>9 to 23 mos. (2-dose series)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 to 55 years (single dose)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 doses asplenia/HIV/comp def</td>
</tr>
</tbody>
</table>
# Meningococcal B Vaccines

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Type</th>
<th>Approved age range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trumenba™ (MenB-FHbp)</td>
<td>Factor H Binding Protein Bivalent recombinant lipoprotein</td>
<td>10-25 years at increased risk (3 dose series)</td>
</tr>
<tr>
<td>Bexsero™ (MenB-4C)</td>
<td>(Neisserial adhesion A [NadA], factor H binding protein [FHbp] fusion protein, and neisserial heparin binding antigen [NHBA] fusion protein)</td>
<td>10-25 years at increased risk (2 dose series)</td>
</tr>
</tbody>
</table>
ACWY Vaccine Shortages

- Both Menveo and Menactra have been intermittently in shortage

- Many providers have been caught in a position of giving immunization with Menveo or Menactra, to be told that the vaccine wasn’t available for their next patient or follow up dose

- In 2006, CDC recommended that Menactra (MCV4) be preferentially given to patients at highest risk and that young children getting their last booster receive Menomune (MPSV4)

Cohn et.al. MMWR 2013;62(2):10-11
ACIP Recommendations – ACWY vaccine

- ACIP recommends vaccine for patients aged ≥2 months at increased risk and for all adolescents aged 11-18 years

- **2 doses** of MenACWY ≥2 months apart to 1.) adults with functional asplenia or 2.) persistent complement deficiencies and HIV-infected persons of any age

- **Single dose:**
  - First-year college students aged ≤ 21 years living in residence halls if they have not received dose on or after 16th birthday
  - Microbiologists exposed to *Neisseria meningitidis*
  - Persons at risk during outbreak from a vaccine serogroup
  - Persons who travel to/live in countries where meningococcal disease is hyperendemic or epidemic

Cohn et.al. MMWR 2013;62(2):10-11
Meningococcal Outbreaks

- Generally rare, historic low (0.2/100K) with vaccines, but occurrences are highly publicized

- Serogroup B meningococcal disease clusters/outbreaks on college campuses
  - Princeton: 1400 fold increase; 7,500 administered vaccine
  - UCSB: 200 fold increase; 20,000 administered vaccine

- Surveillance in HIV positive: 10x the incidence in NYC 2000-2011

- Threshold for vaccination for serogroup B outbreaks in institutional settings
  - 2 cases in population <5,000 persons
  - 3 cases in population ≥5,000 persons

# Newer MenB Vaccines

- Accelerated approval in the US based on pre-published data for safety and immunogenicity

<table>
<thead>
<tr>
<th></th>
<th>Bexsero (MenB-4C)</th>
<th>Trumenba (MenB-FHbp)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Doses (interval)</strong></td>
<td>2 (0, 6 months)</td>
<td>3 (0, 2, 6 months)</td>
</tr>
<tr>
<td><strong>No. of patients</strong></td>
<td>N= 1509 active/ 498 control</td>
<td>N= 1982 active/ 501 control</td>
</tr>
<tr>
<td><strong>Patient age</strong></td>
<td>11-18 yr</td>
<td>11-18 yr</td>
</tr>
<tr>
<td><strong>Concomitant vaccine</strong></td>
<td>No studies</td>
<td>4vHPV, MenACWY, Tdap and Tdap/IPV</td>
</tr>
<tr>
<td><strong>Immunogenicity</strong></td>
<td>88% (CI = 82%–93%)</td>
<td>80% (CI = 82%–84%)</td>
</tr>
<tr>
<td><strong>Long term immunity</strong></td>
<td>24 month: 25% waning</td>
<td>48 month: 30% waning</td>
</tr>
</tbody>
</table>

ACIP 2016 Recommendations

- Serogroup B meningococcal vaccine series should be administered to persons aged ≥10 years at increased risk for meningococcal disease
  - Persistent complement deficiency
  - Anatomic or functional asplenia
  - Risk in a serogroup B meningococcal disease outbreak
  - Certain microbiologists
  - Persons receiving eculizumab (Soliris®)

- Continuing discussions about the potential for broader immunization in HIV positive patients
Case 3

FT a 53yo M s/p splenectomy after trauma arriving to clinic for vaccinations against capsular organisms. Which meningococcal serotype vaccine is most appropriate?

- A Serotype B
- B Serotypes ACWY
- C None – only for HIV positive patients
- D Both A and B
Case 3

FT a 53yo M s/p splenectomy after trauma arriving to clinic for vaccinations against capsular organisms. Which meningococcal serotype vaccine is most appropriate?

- A Serotype B
- B Serotypes ACWY
- C None – only for HIV positive patients
- D Both A and B
Pertussis Vaccine
Epidemiology

Bordetella Pertussis associated with respiratory illness (Whooping Cough) affecting up to 200,000 per year in the early 20th century

- **1940’s**: Whole cell vaccine introduced
- **1970’s**: Pertussis cases reported to CDC fall to an all time low in the US: 1000 cases
- **1990’s**: Acellular Pertussis vaccine replaces whole cell vaccine
- **2004**: Pertussis rates rise to an all time high of ~26,000 cases
- **2005**: Booster vaccine (Tdap) introduced for adults and children to make up for waning immunity and vaccine refusal

Outbreak Analysis

- **California epidemic 2010**
  - 9,154 cases, 52% of cases were adults exposed to sick children

- **Full recognition of the limitations of DTaP and Tdap in terms of long term immunity recognized**

- **2011: ACIP expands booster recommendations: Pregnant women and adults**

- **In 2015, 18,166 cases in the US, 22.2% in patients over age 19**
  - Subset of patients 6 mo - 6 yrs with available immunization data
    - 45% unknown or unvaccinated
    - 49% are fully immunized

CDC. MMWR 2016; 64(52) 1-2.
## ACIP Recommendations

### Age of patient/vaccine status

<table>
<thead>
<tr>
<th>Age of patient/vaccine status</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 weeks to 6 yrs</td>
<td>Use DTaP to complete the primary series</td>
</tr>
<tr>
<td>7 to 10 yrs not fully vaccinated against pertussis</td>
<td>One dose of Tdap</td>
</tr>
<tr>
<td>11-64 yrs No record of TdaP</td>
<td>One dose of Tdap, then one dose of Td every 10 years</td>
</tr>
<tr>
<td>&gt;65 yrs No record of TdaP</td>
<td>One dose of Tdap, then one dose of Td every 10 years</td>
</tr>
</tbody>
</table>

### Population/vaccine status

<table>
<thead>
<tr>
<th>Population/vaccine status</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Care Providers No record of TdaP</td>
<td>One dose of Tdap</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>One dose of Tdap at 27-36 wks</td>
</tr>
</tbody>
</table>

Tdap in Pregnancy

- Pregnant women due for tetanus booster:
  - >10 years since previous Td → Tdap one dose

- Wound management for pregnant women:
  - If ≥5 years since the previous Td booster → Tdap one dose

- Pregnant women (all):
  - Tdap should be administered for all pregnancies between 27 to 36 wks

# Pertussis Vaccines

Excluding the combination agents with polio, hepatitis, *H. influenzae*, etc.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Brand(s)</th>
<th>Approved age range/doses</th>
</tr>
</thead>
</table>
| **Diphtheria & Tetanus Toxoids & Acellular Pertussis (DTaP)** | Tripedia™, Infanrix™, Daptacel™ | ≥2 mo - 6 yrs (5 doses)  
1) 2 months  
2) 4 months  
3) 6 months  
4) 15 - 18 months  
5) 4 - 6 years |
| **Tetanus, Diphtheria and Acellular Pertussis (Tdap)** | Adacel™, Boostrix™   | 7 yrs to late adulthood (single dose)     |
DM, a 37 yo F who is 7 months pregnant, arrives at clinic for her influenza vaccine. She received the Tdap vaccine prior to her previous pregnancy 3 years ago. According to current recommendations, should she receive the Tdap vaccine?

A. Yes, Tdap should be administered irrespective of prior history
B. No, Tdap is contraindicated during pregnancy
C. No, it’s too late in her pregnancy (>4 months)
D. No, Tdap is a once per lifetime dose as an adult
DM, a 37 yo F who is 7 months pregnant, arrives at clinic for her influenza vaccine. She received the Tdap vaccine prior to her previous pregnancy 3 years ago. According to current recommendations, should she receive the Tdap vaccine?

A. Yes, Tdap should be administered irrespective of prior history
B. No, Tdap is contraindicated during pregnancy
C. No, it’s too late in her pregnancy (>4 months)
D. No, Tdap is a once per lifetime dose as an adult
Varicella Zoster
Epidemiology Varicella

- Reactivation of latent virus in immunocompromised adults (any age) or immunocompetent adults (over age 50)

- Manifestation as a dermatominal vesicular rash primarily but can cause more invasive disease

- If non-invasive, most serious complication is painful post-herpetic neuralgia (PHN)

- Incidence: 2 to 4.6 per 1000 person years but increases to 10 to 12.8 at age 80 years
ACIP Recommendations –Zoster

- 2006: vaccinate adults > 60 years
- 2011: vaccinate adults > 50 years
  - Drug shortages ensued, waning immunity at older ages
- Updated recommendation to adults >60 years again
- Not recommended for immunocompromised patients, high potency live vaccine
  - Exceptions, patients with well controlled HIV, patients about to undergo chemotherapy, patients about to receive immunomodulatory therapy

Hales CM et.al. MMWR 2014; 63; 33: 729-31.
## Varicella Vaccines

<table>
<thead>
<tr>
<th>Brand(s)</th>
<th>Type</th>
<th>Potency</th>
<th>Indication</th>
<th>Approved age range</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zostavax™</td>
<td>Live Attenuated</td>
<td>19,400 PFU</td>
<td>Prevention of reactivation</td>
<td>≥50 years* (single dose) Recommended over age 60</td>
<td>allergy to vaccine, immunocompromise**, pregnancy</td>
</tr>
<tr>
<td>Varivax™</td>
<td>Inactivated</td>
<td>1,350 PFU</td>
<td>Prevention of primary infection</td>
<td>1: 12 - 15 months</td>
<td>allergy to vaccine, acute infection, pregnancy</td>
</tr>
<tr>
<td>Proquad™</td>
<td></td>
<td></td>
<td></td>
<td>2: 4 through 6 yrs (2 doses)***</td>
<td></td>
</tr>
</tbody>
</table>

PFU=plaque forming unit

*can consider for younger patients with chronic renal failure, diabetes mellitus, rheumatoid arthritis, and chronic pulmonary disease

**immunocompromise definition: HIV CD4<200, cancer on chemotherapy, transplant or other requiring immunosuppressants, high dose prolonged steroids

***can also immunize after age 13 if patient has never had chicken pox or immunization
**Zostavax – Efficacy**

### Shingles Prevention Study: Prevention of Infection and Post-Herpetic Neuralgia (PHN) in Older Adults

<table>
<thead>
<tr>
<th><strong>Objective</strong></th>
<th>To compare the incidence of zoster and PHN in a high risk older population vaccinated with active vaccine versus placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion Criteria</strong></td>
<td>healthy adults aged ≥60 years who had a history of varicella or at least 30 years of residence in the US</td>
</tr>
<tr>
<td><strong>Design and Enrollment</strong></td>
<td>Phase 3: double-blind randomized, placebo-controlled trial N=38,456, 3 year observation period post injection</td>
</tr>
<tr>
<td><strong>Outcome measured</strong></td>
<td>Confirmed zoster infection by PCR or viral culture, if positive, severity of infection and incidence of PHN for 182 days after infection</td>
</tr>
</tbody>
</table>
| **Results** | Reduction in risk for developing zoster by 51.3% vaccine vs. placebo (95% CI = 44.2–57.6; p<0.001)  
Reduction in rate of PHN by 66.5% vaccine vs. placebo (95% CI = 47.5–79.2; p<0.001) |

It’s November and LB is a 56-year-old male admitted to the hospital for pneumonia, he has a past medical history of chronic renal failure for 7 years. When asked about his vaccination status, LB reports that he has not received any vaccination for several years.
Based on his history, which vaccine should he receive as an inpatient, after fever has subsided and he is clinically stable?

- Inactivated quadrivalent influenza vaccine
- PCV13 today, followed by PPSV23 12 months later
- Zostavax
- Meningococcal B vaccine
- A and B
Case 5

Based on his history, which vaccine should he receive as an inpatient, after fever has subsided and he is clinically stable?

- Inactivated quadrivalent influenza vaccine
- PCV13 today, followed by PPSV23 12 months later
- Zostavax
- Meningococcal B vaccine
- A and B
ISMP – Top Three Vaccine Errors

- Inappropriate schedule – Wrong age, wrong timing between doses
- Storage errors – Expired vaccine administered, incorrect storage of vaccine
- Wrong vaccine administered

Common Wrong Vaccine Mix-ups

- Varicella primary vaccine vs. Herpes-zoster “booster”
- Diphtheria, tetanus and pertussis (DTaP) vs. Tetanus, diphtheria and pertussis (Tdap)
- Pneumococcal conjugate vs. Pneumococcal polysaccharide
- Hepatitis A vs. Hepatitis B

CDC. Immunization Safety Office. May 2015
Key Takeaways

- **Key Takeaway #1**
  - Have handy references available, alphabet soup can get confusing for all: MenHBFp, DTaP, Tdap, MenCV

- **Key Takeaway #2**
  - Review the ACIP recommendations annually (Feb) and keep schedule handy to include exempt patients

- **Key Takeaway #3**
  - Help identify patients at risk and work towards more universal immunization