U.S. Adult Vaccine Program Update: The Evolving Landscape

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Objectives

• Discuss current status of adult vaccination in U.S.
• Review how the ACA might affect the adult immunization program
• Describe new ACIP recommendations
  – High dose influenza
  – Tdap
  – Herpes Zoster
  – HPV
  – hepatitis B
• Communicate new developments in preventing pneumococcal disease
• Understand when Hepatitis B immune titers should be checked after vaccination
Background

• Vaccination is one of the greatest public health achievements of the 20th century
• ACIP routinely recommends 11 vaccines for adults
• In an average year, 95% of the 20,000-50,000 Americans who die as a result of a vaccine preventable illness are adults*
• Adult vaccination rates remain low

* Depends on the severity of the annual influenza
## Current state of affairs

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended group</th>
<th>2008 % vaccinated</th>
<th>Healthy People 2020 Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonal Influenza</td>
<td>Noninstitutionalized adults 18-64*</td>
<td>25</td>
<td>80</td>
</tr>
<tr>
<td></td>
<td>Noninstitutionalized high risk adults 18-64</td>
<td>39</td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>≥ 65</td>
<td>67</td>
<td>90</td>
</tr>
<tr>
<td>Healthcare personnel*</td>
<td></td>
<td>45</td>
<td>90</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>Noninstitutionalized high risk adults 18-64</td>
<td>17</td>
<td>60</td>
</tr>
<tr>
<td></td>
<td>Noninstitutionalized adults ≥ 65</td>
<td>60</td>
<td>90</td>
</tr>
<tr>
<td>Herpes Zoster</td>
<td>≥ 60*</td>
<td>7</td>
<td>30</td>
</tr>
</tbody>
</table>

*new objective

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Recommended Subgroup</th>
<th>Percent vaccinated in 2009</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seasonal influenza</td>
<td>Age 50-64&lt;br&gt;Age &gt;65&lt;br&gt;Healthcare personnel&lt;br&gt;High risk ≥ 18&lt;br&gt;Age 18 and older w/ Asthma&lt;br&gt;Chronic lung disease&lt;br&gt;Diabetes&lt;br&gt;Heart disease</td>
<td>52.9&lt;br&gt;65.6&lt;br&gt;40.1&lt;br&gt;55.2&lt;br&gt;44.8&lt;br&gt;70.9&lt;br&gt;66.0&lt;br&gt;69.5</td>
</tr>
<tr>
<td>Td/Tdap</td>
<td>19-49</td>
<td>63.1</td>
</tr>
<tr>
<td>Tdap</td>
<td>19-64</td>
<td>6.6</td>
</tr>
<tr>
<td>HPV</td>
<td>Women up to 26</td>
<td>17.1</td>
</tr>
<tr>
<td>HZ</td>
<td>≥ 60</td>
<td>10.0</td>
</tr>
<tr>
<td>Pneumovax</td>
<td>19-64 years, high risk ≥ 65</td>
<td>60.6&lt;br&gt;17.5</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>Adults 10-49 at risk</td>
<td>9.8</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>18-49 at risk</td>
<td>41.8</td>
</tr>
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<td>Age &gt;65</td>
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</tr>
<tr>
<td></td>
<td>Healthcare personnel</td>
<td>40.1</td>
</tr>
<tr>
<td></td>
<td>High risk ≥ 18</td>
<td>55.2</td>
</tr>
<tr>
<td></td>
<td>Age 18 and older w/ Achastma</td>
<td>44.8</td>
</tr>
<tr>
<td></td>
<td>Chronic lung disease</td>
<td>70.9</td>
</tr>
<tr>
<td></td>
<td>Diabetes</td>
<td>66.0</td>
</tr>
<tr>
<td></td>
<td>Heart disease</td>
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Affordable Care Act (ACA) and Vaccines

• Re-authorization of Section 317 of the Public Health Service Act
• Authorization of state immunization programs to use state funds to purchase vaccines for adults using the federal purchase price
• Authorization of a CDC-funded demonstration program where states can receive federal grants to improve the provision of recommended immunizations to all groups
ACA and Vaccines

• Charged the General Accountability Office to study and report to Congress about Medicare beneficiary access to recommended vaccines under Medicare Part D
• Initiatives to improve communication regarding the ground implementation of ACIP recommendations in clinics and communities
• Mandates insurance companies pay for adult vaccinations with no patient co-payments
Recommended adult immunization schedule, by vaccine and age group-2011

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>AGE GROUP</th>
<th>19–26 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(^1,)*</td>
<td>1 dose annually</td>
<td>Substitute 1-time dose of Tdap for Td booster; then boost with Td every 10 years</td>
<td></td>
<td></td>
<td></td>
<td>Td booster every 10 years</td>
</tr>
<tr>
<td>Tetanus, diphtheria, pertussis (Td/Tdap)(^2,)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Varicella(^3,)*</td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human papillomavirus (HPV)(^4,)*</td>
<td>2 doses (females)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zoster(^5)</td>
<td>1 dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles, mumps, rubella (MMR)(^6,)*</td>
<td>1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumococcal (polysaccharide)(^7,)*</td>
<td>1 or 2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningococcal(^8,)*</td>
<td>1 or more doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis A(^9,)*</td>
<td>2 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B(^10,)*</td>
<td>3 doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Covered by the Vaccine Injury Compensation Program

For all persons in this category who meet the age requirements and who lack evidence of immunity (e.g., lack documentation of vaccination or have no evidence of previous infection)

Recommended if some other risk factor is present (e.g., based on medical, occupational, lifestyle, or other indications)

No recommendation

Vaccines that might be indicated for adults based on medical and other indications-2011

Vaccines that might be indicated for adults based on medical and other indications-2011

Case presentation

• Your colleague’s parents, Mr. and Mrs. R, approach you about whether they should receive the high dose influenza vaccine this year. They are both in their 70s and without significant medical problems. What would you advise them?
Influenza in persons aged ≥ 65 years

• ≥ 65 are at greatest risk for hospitalization/death from seasonal influenza

• Rates of hospitalization and death due to seasonal influenza in elderly individuals have increased in past 2 decades despite increased vaccine coverage

• ≥ 65 respond with lower antibody titers to influenza hemagglutinin

http://www.cdc.gov/mmwr/pdf/wk/mm5916.pdf
Efficacy and effectiveness of current influenza vaccines

• Systematic review and meta-analysis
• Studies were required to use RT-PCR or culture to confirm influenza
• Pooled efficacy 59% (95%CI 51-67) in 18-65y
• No trials met inclusion criteria for ≥65y
• Vaccine effectiveness variable by season
• New vaccines are needed

Osterholm et el. The Lancet Infectious Diseases. Published online Oct. 26, 2011
• New vaccine with higher titers of antigen (180μg vs. 45μg) licensed by FDA in December 2009

• $25 (double the price of regular dose influenza inactivated vaccine)
Falsey et al.

- Multicenter, randomized, double-blind controlled trial
- 3876 “healthy” subjects ≥ 65 at 30 centers in U.S.
- Fall 2006
- Excluded: allergy to eggs, h/o GBS, immunodeficiency or receipt of immunosuppressive tx, active neoplastic dx
- 99% of participants completed follow-up
- Primary outcomes
  - Lot-to-lot consistency of the vaccine
  - Immunogenicity by antibody titers measured by hemagglutination inhibition
- Secondary outcomes
  - Adverse effects

Falsey et al. JID. 2009: 200;172-179.
The ratio of the HAI GMTs for HD vaccine recipients and SD vaccine recipients was assessed for all vaccine strains; superiority was demonstrated if the lower limit of the 95% confidence interval for the ratio was >1.5, and noninferiority was defined as an HAI GMT ratio value >0.67.

<table>
<thead>
<tr>
<th>Response by antigen</th>
<th>HAI GMT ratio for HD and SD vaccine, (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>1.7 (1.6-1.8)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>1.8 (1.7-2.0)</td>
</tr>
<tr>
<td>B</td>
<td>1.3 (1.2-1.4)</td>
</tr>
</tbody>
</table>
### Immunogenicity—Falsey et al.

<table>
<thead>
<tr>
<th>Response by antigen</th>
<th>Percentage difference in rate of seroconversion between HD and SD, (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/H1N1</td>
<td>25.4 (22.4-28.5)</td>
</tr>
<tr>
<td>A/H3N2</td>
<td>18.4 (15.1-21.7)</td>
</tr>
<tr>
<td>B</td>
<td>11.8 (8.6-15.0)</td>
</tr>
</tbody>
</table>

Superiority was demonstrated if the lower limit of the 95% confidence interval for the difference in seroconversion rates (i.e., HD vaccine minus SD vaccine) was >10%, and noninferiority was shown if the lower limit of the 95% confidence interval was >-10%.
Local and systemic symptoms reported by recipients of high-dose influenza vaccine (A) and standard-dose influenza vaccine (B) during the 7 days after vaccination.
Comparison of high-dose (HD) and standard-dose (SD) influenza vaccine with respect to solicited systemic symptoms during the 7 days after vaccination.

<table>
<thead>
<tr>
<th>Reaction</th>
<th>HD vaccine recipients, % (95% CI)</th>
<th>SD vaccine recipients, % (95% CI)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic reaction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>34.3 (32.5–36.2)</td>
<td>29.4 (26.9–32.0)</td>
<td>1.2 (1.1–1.3)</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>10.7 (9.5–11.9)</td>
<td>7.1 (5.7–8.6)</td>
<td>1.5 (1.2–1.9)</td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>3.6 (2.9–4.4)</td>
<td>2.3 (1.5–3.3)</td>
<td>1.6 (1.0–2.4)</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>1.1 (0.9–1.6)</td>
<td>0.3 (0.1–0.9)</td>
<td>3.6 (1.3–10.1)</td>
</tr>
<tr>
<td>Headache</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>16.8 (15.3–18.3)</td>
<td>14.4 (12.5–16.5)</td>
<td>1.2 (1.0–1.4)</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>4.2 (3.4–5.0)</td>
<td>2.8 (1.9–3.8)</td>
<td>1.5 (1.0–2.1)</td>
</tr>
<tr>
<td>Malaise</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>18.0 (16.5–19.5)</td>
<td>14.0 (12.1–16.0)</td>
<td>1.3 (1.1–1.5)</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>6.3 (5.4–7.3)</td>
<td>4.2 (3.2–5.5)</td>
<td>1.5 (1.1–2.0)</td>
</tr>
<tr>
<td>Myalgia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>21.4 (19.8–23.0)</td>
<td>18.3 (16.2–20.5)</td>
<td>1.2 (1.0–1.4)</td>
</tr>
<tr>
<td>Moderate or severe</td>
<td>5.8 (5.0–6.8)</td>
<td>3.4 (2.5–4.6)</td>
<td>1.7 (1.2–2.4)</td>
</tr>
</tbody>
</table>

**NOTE.** There were 2573 individuals in the HD group and 1260 individuals in the SD group. CI, confidence interval; RR, relative risk.

* n values are the number of subjects used for the safety analysis (i.e., the counts of subjects as actually vaccinated rather than as randomized; see figure 1A).

Comparison of high-dose (HD) and standard-dose (SD) influenza vaccine with respect to solicited systemic symptoms during the 7 days after vaccination.

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<tr>
<td>Systemic reaction</td>
<td>n = 2572</td>
<td>n = 1260</td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>34.3 (32.5–36.2)</td>
<td>29.4 (26.9–32.0)</td>
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<td>1.5 (1.2–1.9)</td>
</tr>
<tr>
<td>Fever</td>
<td>n = 2569</td>
<td>n = 1258</td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>3.6 (2.9–4.4)</td>
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<tr>
<td>Malaise</td>
<td>n = 2570</td>
<td>n = 1259</td>
<td></td>
</tr>
<tr>
<td>Any</td>
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Adverse events-Falsey et al.

• The rate of unsolicited adverse events within 28 days was comparable between the 2 groups

• During the 6 month follow-up, events were reported less commonly by HD group
  – 2 events were determined to be related to vaccination
    • 1 Exacerbation of Crohn’s
    • 1 Myasthenia Gravis
Limitations

• Lacks clinical efficacy data
• Industry sponsored
• Only healthy subjects
Recommendation for Mr. and Mrs. R

• No strong indication to receive the HD vaccine at this point
  – No efficacy data available
  – More adverse effects
  – Twice the cost of SD vaccine

• ACIP has not expressed a preference for Fluzone High-Dose for use in persons ≥65 years

• More efficacy data should be available in 2012
Case presentation

• Mr. and Mrs. R are the proud grandparents of a 1 month old grandson. They both received a Td booster less than a year ago, but are curious if they should receive the new Tdap vaccine. What would you recommend?
Pertussis in U.S.

• In 2010, 27,550 cases of pertussis were reported
  – Many cases go unreported
• Several outbreaks across U.S. in 2010
  • CA 9,143 cases and 10 infant deaths
  • MI 1564 cases
  • OH 964 cases in Columbus and Franklin counties
• Pertussis is one of the least well controlled diseases that is preventable by a vaccine

http://www.cdc.gov/pertussis/outbreaks.html accessed 11/15/11
Tdap

- Tetanus toxoid, reduced diptheria toxoid and acellular pertussis vaccine
- Two licensed in the U.S. since June 2005
  - Boostrix, GlaxoSmithKline
    - Originally licensed for 10-18
    - In 2008 expanded age indication to 19-64
  - Adacel, Sanofi Pasteur (11-64)
Tdap-Immunogenicity

- October 2010, ACIP reviewed unpublished data from trial for Boostrix (N=1,104) and Adacel (N=1,170) on immunogenicity and safety of Tdap in ≥ 65
  - Both vaccines showed immune responses to diptheria and tetanus toxoids noninferior to Td
  - Boostrix-immune responses to pertussis antigens (pertussis toxin (PT), filamentous hemagglutinin (FHA), and pertactin (PRN) were non-inferior to those observed following 3-dose primary pertussis series
  - Adacel-immune responses to PT, FHA, PRN + Fimbriae occurred

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6001a4.htm
Tdap-safety

• Both vaccines
  • Frequency and severity of adverse events in persons ≥ 65 were comparable to those < 65
  • No increase in reactions compared to those who received Td
  • No serious adverse events

• Vaccine Adverse Event Reporting System (VAERS) 2005-2010
  – 243 reports regarding ≥ 65 out of 10,981 total
    • 232 (96%) reports were not serious
    • 37% of reports were local reactions
    • 11 serious events including 2 deaths

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6001a4.htm
ACIP recommendation and FDA Approval

• October 2010 ACIP recommended Tdap for ≥ 65 (replaces a single decennial Td booster dose)
• Tdap can be administered regardless of the interval since the last tetanus or diptheria toxoid containing vaccine
• July 2011 FDA approves expanded age indication for Boostrix
• Adacel not FDA approved in this age group, but CDC states either Tdap product may be used in persons ≥ 65

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6001a4.htm
http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6037a3.htm
Recommendation for Mr. and Mrs. R

- No efficacy data
- Tdap almost 3x the cost of Td ($26.53 vs. $9.66)
- ACIP recommendation holds a lot of weight
- Tdap offers pertussis protection
- Recommend that the grandparents get Tdap vaccination
Case Presentation

• A 52 year-old female is interested in having the herpes zoster vaccine as she remembers a relative having a severe bout of shingles. Her past medical history is notable for rheumatoid arthritis for which she takes low dose prednisone. She was wondering about her candidacy for a “shingles shot.”
Herpes Zoster (HZ)

- 90% of Americans have had chickenpox as children placing them at risk of HZ
- Affects up to 1 million in the U.S.
- Incidence of HZ and its complications increase with aging resulting in incidence of 10 per 1,000 in persons >75
- People >50 more likely affected postherpetic neuralgia (PHN), most common complication of HZ
HZ vaccine

- Most data comes from the Shingles Prevention Study (SPS) which only evaluated individuals ≥60
- HZ incidence
  - RRR 51.3% (CI-44.2-57.6%)
  - 11.12 per 1000 cases in unvaccinated vs. 5.4 per 1000 cases in the vaccinated
  - NNT=59
- Has been recommended for ≥ 60 for 5 years

HZ vaccine for 50-59 year olds

- In March 2011, FDA approved HZ vaccine in adults aged 50 through 59
- Unpublished double blind, placebo controlled RCT of 22,439 subjects
- U.S. and 4 other countries
- Efficacy outcome
  - HZ incidence RRR 69% (95%CI 54.1-80)
  - 1.99 per 1000 person-years in vaccinated group vs. 6.57 per 1000 person-years in placebo group
  - NNT=163
- HZ vaccine group reported more adverse effects (72.8 % vs. 41%) primarily due to injection site reactions and headache

ACIP Decision

• June 2011, ACIP declined to recommend the HZ vaccine for adults aged 50-59
  – Lack of secure supply
  – Cost-effectiveness is less attractive in this age group

http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6044a5.htm
Contraindications to HZ vaccine

• Allergy to component of vaccine
  – Neomycin or gelatin
• Immunocompromised
  – High dose corticosteroid (>20mg prednisone/d)
  – Azathioprine (>3.0mg/kg/d)
  – Methotrexate (≥0.4mg/kg/wk)
  – Immune modulator/mediator therapy
• Pregnancy

Recommendation

• She could receive it. She might have to pay out of pocket for it.

• No data are available regarding the effectiveness of HZ vaccine in adults who become immunosuppressed subsequent to vaccination
Question

For which of the following individuals is the HPV vaccine currently recommended by the ACIP?

a) 27 y.o. female with no history of prior sexual activity
b) 18 y.o. male with no history of prior sexual activity
c) 24 y.o. sexually active female who has not been vaccinated previously
d) All of the above
HPV Vaccines

- Two vaccines now licensed
  - Gardasil/Merck product
    - Licensed in June 2006
    - Effective against 4 HPV virus types
      - 6, 11 (responsible for 90% of genital warts)
      - 16, 18 (associated with 70% of cervical cancers)
  - Cervarix/GlaxoSmithKline product
    - Licensed in October 2009
    - Effective against 2 HPV virus types
      - 16, 18
- 3 shot series- 0, 1-2, and 6 months
HPV recommendations

• March 2007
  – Routine vaccination of girls 11 to 12 (FDA approved to start series at age 9)
  – “Catch-up” vaccination for unvaccinated girls and women aged 13 to 26

• October 2009
  – HPV4 was licensed for use in males 9-26, but ACIP only permissively recommended

• October 2011 (Awaiting approval by CDC and HHS)
  – Routine vaccination of males aged 11 to 12 (FDA approved to start series at age 9)
  – “Catch-up” vaccination for unvaccinated males aged 13 to 21
  – Routine recommendation of immunocompromised males aged 22 to 26 who did not get full series of vaccinations when they were younger
  – Routine recommendation for MSM aged 22-26
  – Permissive recommendation for all other males aged 22-26
Question

• For which of the following individuals is the Human Papilloma Virus (HPV) vaccine currently recommended by the Advisory Committee on Immunization Practices?

  a) 27 y.o. female with no history of prior sexual activity
  b) 18 y.o. male with no history of prior sexual activity
  c) 24 y.o. sexually active female who has not been vaccinated previously
  d) All of the above
Hepatitis B

- Outbreaks of hepatitis B among patients with diabetes
- Analysis of data from more than 91,000 individuals in
  - CDC’s Emerging Infection Program
  - Behavioral Risk Factor Surveillance Survey
Adjusted Odds* of Acute Hepatitis B Among Persons with Diabetes: Multivariate Analyses

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (no “Other HBV risk factor” present)</td>
<td>1.89 (1.40-2.57)</td>
</tr>
<tr>
<td>Diabetes (&quot;Other HBV risk factor&quot; present)</td>
<td>1.10 (0.57-2.11)</td>
</tr>
</tbody>
</table>

*Adjusted for age, gender, race, ethnicity

Adjusted Odds* of Acute Hepatitis B Among Persons with Diabetes** by Age: Multivariate Analyses

<table>
<thead>
<tr>
<th>Age</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>23-59</td>
<td>2.09 (1.48-2.95)</td>
</tr>
<tr>
<td>≥ 60</td>
<td>1.45 (0.79-2.68)</td>
</tr>
</tbody>
</table>

* Adjusted for age, gender, race, ethnicity
** and no “Other Hepatitis B risk factor”

## Cost-effectiveness of Vaccinating Adults with Diabetes*

<table>
<thead>
<tr>
<th>Age at Vaccination</th>
<th>Number vaccinated with 10% uptake</th>
<th>Cost per QALY saved</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-59</td>
<td>528,047</td>
<td>$75,094</td>
</tr>
<tr>
<td>≥ 60</td>
<td>774,394</td>
<td>$2,760,753</td>
</tr>
<tr>
<td>≥ 20</td>
<td>1,302,441</td>
<td>$196,557</td>
</tr>
</tbody>
</table>

*Assumes private practice price

The Source of Infection
New ACIP recommendation October 2011

• Hepatitis B vaccination should be given to previously unvaccinated adults with diabetes who are younger than 60 years of age
Pneumococcal Disease

- Burden of disease in U.S.
  - 29,500 cases of IPD annually
  - 502,600 cases of nonbacteremic pneumonia

- Costs related to above disease is $5.5 billion (indirect and direct costs)

- Majority of disease is associated with 25 serotypes
Pneumococcal Vaccines

• 23-valent PPSV licensed in U.S. in 1983
  – Controversy in literature about strength of efficacy data supporting use of this vaccine

• PPSV do not induce an effective immune response in children < 2 therefore conjugate pneumococcal vaccines were developed

• PCV7 was approved by the FDA in 2000
Associations with Introduction of Pneumococcal Conjugate Vaccine

• Major reduction in invasive disease caused by vaccine serotypes in vaccinated children
• Reduction in other diseases (e.g. otitis media) attributable to pneumococcus
• Reduced rate of colonization by vaccine serotypes in vaccinated children
• Reduced rate of infection and colonization by antibiotic resistant strains
• Reduction in disease caused by vaccine serotypes in nonvaccinated persons of all ages
• Increased prevalence of colonization and disease caused by nonvaccine strains
PCV13

- March 2010 ACIP recommended transitioning from PCV7 to PCV13 for children
- Randomized, placebo-controlled trial titled Community Acquired Pneumonia Immunization Trial in Adults (CAPITA) has been initiated in the Netherlands
  - 85,000 subjects ≥ 65
  - Study does not contain a PPSV23 arm
Possible Future Developments in Use of Pneumococcal Vaccines in Adults

1. Current recommendations will remain
2. PCV13 will replace PPSV23 as the vaccine recommended for use in adults
3. PCV13 and PPSV23 will be used in some combined regimen in adults
I don't remember all this fuss when we were being vaccinated for polio!

It was sugar coated then!
Hepatitis B Vaccine Recommendations

• Behavioral
  – MSM
  – Seeking treatment for STD
  – More than 1 sex partner in last 6 months
  – Current or recent IVDU

• Occupational
  – Healthcare or public-safety workers

• Medical
  – ESRD, chronic liver disease, HIV

• Other
  – Household contacts and sex partners of individuals w/ HBV
  – Clients and staff of institutions for persons with developmental disabilities
  – Travel to countries with intermediate or high prevalence of HBV infection
Hepatitis B Vaccine Recommendations

• **Behavioral**
  – MSM
  – Seeking treatment for STD
  – More than 1 sex partner in last 6 months
  – Current or recent IVDU

• **Occupational**
  – Healthcare or public-safety workers

• **Medical**
  – ESRD, chronic liver disease, HIV

• **Other**
  – Household contacts and sex or needle sharing partners of individuals w/ HBV
  – Clients and staff of institutions for persons with developmental disabilities
  – Travel to countries with intermediate or high prevalence of HBV infection

*Would also check antibody titers in other immunocompromised persons*
Hepatitis B Vaccine Formulations

• Recombivax HB® (Merck)
  - 5 mcg/0.5 mL (pediatric)
  - 10 mcg/1 mL (adult)
  - 40 mcg/1 mL (dialysis)

• Engerix-B® (GSK)
  - 10 mcg/0.5 mL (pediatric)
  - 20 mcg/1 mL (adult)
Concluding Remarks

• Vaccinations represent opportunity for medical progress and are underutilized
• The ACA might provide opportunity to improve vaccination rates
• Several changes to the U.S. Vaccine program have occurred in the past 5 years and there are more to come
Falsey et al.

- No difference between the groups that received different lots of HD vaccine or between the HD group and SD group with respect to age, race, sex or underlying dx.
- Pre-vaccination hemagglutination (HAI) geometric mean titers (GMT) were similar between the standard dose (SD) and high dose (HD) groups.
Keitel et al.

- Randomized trial (not controlled)
- 202 ambulatory, medically stable, ≥ 65 in Houston
- Fall 2002
- 97.5% white, 41% women, median age 72.5
- 100% follow-up

Primary outcomes

- Assess immunogenicity (hemagglutination inhibition (HAI) and neutralizing antibody 1 mo after immunization
- Assess reactogenicity

# Geometric Mean Serum HAI and Neutralizing Antibody Responses Before and 1 Month After Immunization


<table>
<thead>
<tr>
<th>Dose, μg</th>
<th>Participants</th>
<th>Before HAI</th>
<th>After HAI</th>
<th>Before Neutralizing</th>
<th>After Neutralizing</th>
<th>Before HAI</th>
<th>After HAI</th>
<th>Before Neutralizing</th>
<th>After Neutralizing</th>
<th>Before HAI</th>
<th>After HAI</th>
<th>Before Neutralizing</th>
<th>After Neutralizing</th>
<th>Before HAI</th>
<th>After HAI</th>
<th>Before Neutralizing</th>
<th>After Neutralizing</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>50</td>
<td>20 (18-25)</td>
<td>23 (19-29)</td>
<td>15 (11-21)</td>
<td>12 (8-16)</td>
<td>11 (8-14)</td>
<td>10 (8-13)</td>
<td>62 (45-87)</td>
<td>59 (41-85)</td>
<td>8 (6-10)</td>
<td>14 (11-18)</td>
<td>57 (44-72)</td>
<td>129 (95-176)</td>
<td>8 (6-11)</td>
<td>10 (14-25)</td>
<td>60 (41-88)</td>
<td>152 (111-208)</td>
</tr>
<tr>
<td>15</td>
<td>51</td>
<td>20 (18-25)</td>
<td>23 (19-29)</td>
<td>14 (11-19)</td>
<td>28 (21-57)</td>
<td>45 (31-65)</td>
<td>96 (63-116)</td>
<td>52 (34-80)</td>
<td>101 (70-146)</td>
<td>8 (6-10)</td>
<td>14 (11-18)</td>
<td>57 (44-72)</td>
<td>129 (95-176)</td>
<td>8 (6-11)</td>
<td>10 (14-25)</td>
<td>60 (41-88)</td>
<td>152 (111-208)</td>
</tr>
<tr>
<td>30</td>
<td>51</td>
<td>20 (18-27)</td>
<td>60 (39-66)</td>
<td>15 (11-20)</td>
<td>25 (26-47)</td>
<td>39 (29-62)</td>
<td>91 (69-120)</td>
<td>45 (31-65)</td>
<td>106 (76-146)</td>
<td>8 (6-11)</td>
<td>10 (14-25)</td>
<td>60 (41-88)</td>
<td>152 (111-208)</td>
<td>8 (6-11)</td>
<td>10 (14-25)</td>
<td>60 (41-88)</td>
<td>152 (111-208)</td>
</tr>
<tr>
<td>60</td>
<td>50</td>
<td>22 (18-27)</td>
<td>61 (48-76)</td>
<td>19 (13-28)</td>
<td>50 (30-66)</td>
<td>53 (37-71)</td>
<td>125 (97-160)</td>
<td>58 (39-80)</td>
<td>180 (144-225)</td>
<td>9 (7-13)</td>
<td>24 (8-32)</td>
<td>64 (44-93)</td>
<td>199 (141-262)</td>
<td>9 (7-13)</td>
<td>24 (8-32)</td>
<td>64 (44-93)</td>
<td>199 (141-262)</td>
</tr>
</tbody>
</table>

**Abbreviations:** CI, confidence interval; HAI, hemagglutination inhibition.

*We tested for differences among the doses in the geometric mean titers before immunization using analysis of variance. None of these differences were statistically significant. Differences among doses after immunization were analyzed using linear regression models (Table 5).*

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Percentage of participants with a serum hemagglutination inhibition antibody titer of 32 or greater after immunization for each vaccine dose group

Percentage of participants with 4-fold or greater increases in serum antibody titers after immunization for each vaccine dose group

![Graph showing percentage of participants with 4-fold or greater increases in serum antibody titers for different influenza strains and dose groups.]

Percentage of participants reporting injection site reactions during the week after immunization for each vaccine dose group


Copyright restrictions may apply.
Conclusions

• Increasing dosage of antigens induced an increase in serum antibody
Limitations

- Lacks clinical efficacy data
- Small sample size
- Only healthy subjects
- Safety and immunogenicity of repeated vaccination with high-dose vaccines not known
Couch et al.

- Multi-site, phase II, randomized, double-blind stratified study
- Comparing SD to HD 2004-2005 Sanofi-Pasteur inactivated influenza vaccine
- 414 “healthy” subjects ≥ 65 from Baylor, Univ. of Iowa, St. Louis Univ., Cincinnati Children’s and Univ. of Maryland
- April 2005?
- 98% white
- 100% completed follow-up

Primary outcomes
- Proportion of subjects in the SD and HD vaccine groups who developed a 4-fold increase in antibody titer
- GMT attained by each group
- Proportion who attain HAI titers ≥ 1:32, ≥ 1:64, and ≥ 1:128

Secondary outcomes
- Frequency and severity of solicited local and systemic reactions
- Proportion of reactions that were moderate or severe
- Occurrence and nature of unsolicited reactions

• Mean age of enrollees 73-74
• No differences in gender, race/ethnicity/age between HD and SD groups
Adverse event

- Reaction reports were more common HD group, but reactogenicity was “mostly mild and well tolerated.”
- 1 oculo-respiratory syndrome
• Serum antibody responses to HD vaccine were significantly greater than those for SD vaccine
  – Regardless of prior vaccination status
  – For all antigens in the vaccine (A/H1N1, A/H3N2, B)
  – By both antibody assays
SPS-Efficacy outcomes

• BOI
  – 61.1% (CI-51.1-69.1%)

• HZ incidence
  – 51.3% (CI-44.2-57.6%)
  – 11.12 per 1000 cases in unvaccinated vs. 5.4 per 1000 cases in the vaccinated
  – NNT=59

• PHN incidence
  – 66.5% (CI-47.5-79.2)
  – 1.38 per 1000 cases in unvaccinated vs. 0.46 per 1000 in the vaccinated
  – NNT=364
Recommended adult immunization schedule, by vaccine and age group-2009

http://www.cdc.gov/vaccines/recs/schedules/adult-schedule.htm#past
I don't remember all this fuss when we were being vaccinated for polio!

It was sugar coated then!