Vaccines to Prevent Respiratory Tract Infections in Adults: What’s new?

Natasha Press
Division of Infectious Diseases, UBC
May 23, 2015.

Conflict of Interest

• Pfizer is paying me an honorarium
• Pfizer makes Prevnar (PCV-13)
• I will be discussing PCV-13 in this lecture, and will be using some slides provided to me by Pfizer
• This represents a conflict of interest
• However, I am under no obligation to anyone for the information that I provide to you, and my research has been done independently
Objectives

1. Appreciate the burden of influenza and pneumococcal disease and their associated risk factors
2. Understand and explain the differences between available vaccine options
3. Translate the latest NACI guidelines into clinical practice from a pharmacist perspective.

Case

53 year old woman
RFR: 3 day history of productive cough, chest pain with coughing, fever
Previously well
Case

- On examination:
  - Looks uncomfortable
  - Temp 38.4°C, HR 110, BP 120/70 RR 22
  - Resp exam: bronchial breath sounds RLL

Case

- CXR:

Radiopaedia.org
Case

- Diagnosis:
  - Community-acquired pneumonia (CAP) affecting the right lower lobe

Treatment

- What’s the pathogen?
- No testing in outpatient setting
- In inpatient setting:
  - Usually we never find out
  - Sputum and blood cultures helpful when positive
Epidemiology of CAP

- Many possible pathogens
  - *Streptococcus pneumoniae* **
  - Respiratory viruses e.g. influenza, paraflu, RSV, metapneumovirus
  - *Staphylococcus aureus*
  - “atypical” pathogens (mycoplasma, legionella, chlamydophila) = 15% of CAP

Treatment

- Most likely bacteria causing CAP:
  - *Streptococcus pneumoniae*
Our local resistance rates

S. Pneumoniae Non-Susceptibility

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Outpatient (no comorbidity)</th>
<th>Inpatient (not ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>penicillin</td>
<td>17.2%</td>
<td></td>
</tr>
<tr>
<td>tetracycline</td>
<td>20.2%</td>
<td></td>
</tr>
<tr>
<td>erythromycin</td>
<td>33.7%</td>
<td>&lt;2%</td>
</tr>
<tr>
<td>moxifloxacin</td>
<td>&lt;2%</td>
<td></td>
</tr>
<tr>
<td>ceftriaxone</td>
<td>&lt;2%</td>
<td></td>
</tr>
</tbody>
</table>

www.bccdc.ca (2012)

Treatment recommendations from guidelines

<table>
<thead>
<tr>
<th>IDSA/ATS (2007)</th>
<th>Outpatient (no comorbidity)</th>
<th>Inpatient (not ICU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Macrolide or doxycycline</td>
<td>Macrolide or doxycycline</td>
<td>Flouroquinolone or beta-lactam PLUS macrolide</td>
</tr>
<tr>
<td>IDSA/ATS (2007)</td>
<td>Macrolide or doxycycline</td>
<td>Flouroquinolone or beta-lactam PLUS macrolide</td>
</tr>
</tbody>
</table>

| BTS (2009) | Amoxicillin or doxycycline or clarithromycin | Amox PLUS clarithromycin or flouroquinolone |

| Bugs&Drugs (2012) | Doxycycline +/-amoxicillin | Ceftriaxone PLUS doxycycline/azithro or flouroquinolone |
Back to the case

- Prevention:
- Smoking cessation
- Vaccinations: pneumococcus and influenza

Invasive Pneumococcal Disease (IPD) vs. Non-invasive Pneumococcal Disease

IPD is an infection of the blood stream and subsequent infection of secondary sites.

Non-invasive remains in the respiratory tract.
Age (≥65 years) is the greatest risk factor for pneumococcal disease in adults


Pneumonia is the most common presentation of PD among adults aged ≥65 years

Epidemiology of CAP

- 8th most common cause of death in Canada
- Risk increases with age
- Many predisposing conditions

Risk Factors for Invasive Pneumococcal Disease

<table>
<thead>
<tr>
<th>Adults &gt; 65 years</th>
<th>Persons with alcoholism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smokers</td>
<td>Asthma</td>
</tr>
<tr>
<td>Cardiac or pulmonary disease</td>
<td>Chronic renal disease</td>
</tr>
<tr>
<td>Immunosuppressive therapy*</td>
<td>Malignant neoplasms</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>Illicit drug use</td>
</tr>
<tr>
<td>HIV infection</td>
<td>Homelessness</td>
</tr>
<tr>
<td>Asplenia</td>
<td>Stem cell transplant</td>
</tr>
<tr>
<td>Sickle cell disease</td>
<td>Congenital immunodeficiency</td>
</tr>
<tr>
<td>Solid organ or islet transplant</td>
<td></td>
</tr>
</tbody>
</table>

*Patients with inflammatory and/or rheumatic diseases where DMARDS (biologic or traditional) are also indicated: e.g. ankylosing spondylitis, inflammatory bowel disease, psoriasis, etc.
How to reduce pneumococcal disease in older adults?

- Vaccines:
  - Pneumovax – 23-valent (PPV-23)
  - Prevnar – 13-valent (PCV-13)

Pneumococcal Vaccines - Canada

Vaccines:

- **PPSV23** = Pneumovax23® (licensed 1983)
  - Pneumococcal polysaccharide vaccine, 23 serotypes

- **PCV7** = Prevnar® (7 serotypes; licensed 2001 for infants & children < 5 yrs)

- **PCV13** = Prevnar13® (licensed 2010 infants; 2012 for >50; 2014 for all ages)
  - Pneumococcal protein conjugate vaccine, 13 serotypes

<table>
<thead>
<tr>
<th>PCV13</th>
<th>1</th>
<th>3</th>
<th>4</th>
<th>5B</th>
<th>7F</th>
<th>9V</th>
<th>14</th>
<th>18C</th>
<th>19A</th>
<th>19F</th>
<th>23F</th>
<th>6A</th>
<th>11A</th>
<th>12F</th>
<th>15B</th>
<th>17F</th>
<th>20</th>
<th>22F</th>
<th>33F</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
</tbody>
</table>

- IPD = invasive pneumococcal disease
  - meningitis, bacteremia, sepsis, bacteremic pneumonia, any sterile site

12 serotypes in common
6A unique to PCV13

PPV-23

- PPV-23 (pneumovax) protects against IPD
  - OR 0.26, 95% CI 0.14-0.45
- PPV-23 protects against vaccine-strain CAP
  - OR 0.46, 95% CI 0.25-0.84
- PPV-23 no effect on all-cause CAP or all-cause mortality
- PPV-23 less effective in higher-risk populations (e.g. elderly, chronic disease)

Cochrane Database Syst Rev. 2013;1:CD000422

---

**Characteristics of Different Vaccine Types**

**Conjugate vs. Polysaccharide**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Conjugate PCV13</th>
<th>Polysaccharide PPSV23</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell response</td>
<td>✔</td>
<td>--</td>
</tr>
<tr>
<td><strong>Strong immune response</strong></td>
<td>✔</td>
<td>--</td>
</tr>
<tr>
<td>IgG &gt; IgM</td>
<td></td>
<td>IgM mostly</td>
</tr>
<tr>
<td>Induces immune memory</td>
<td>✔</td>
<td>--</td>
</tr>
<tr>
<td><strong>Provides herd effect</strong></td>
<td>✔</td>
<td>--</td>
</tr>
<tr>
<td>(reduces transmission to unimmunized)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Hypo-responsive effect on re-immunization</strong></td>
<td>--</td>
<td>✔</td>
</tr>
<tr>
<td>(blunting)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NACI recommendations for high-risk adults:
PPV23

Current recommendations are that PPV23 should be given to persons at high risk of IPD:\(^1\)

- All those 65 years of age or older

---


---

S. pneumoniae disproportionately affects those at the extremes of age

**Incidence of IPD and Associated Mortality Rates (USA, 2010)**

![Graph showing incidence of IPD and associated mortality rates](image)

IPD = invasive pneumococcal disease, and includes meningitis, bacteremia, and pneumonia when accompanied by bacteremia.

For children: PCV
Pneumococcal conjugate vaccine

- Children:
  - 2002: PCV-7 authorized for use in Canada
  - 2010: PCV-13 replaced PCV-7

Invasive pneumococcal Diseases (IPD)
- Reportable to the BCCDC

![Figure 1. IPD Incidence by age, British Columbia, 2002-2010](image)

IPD in older adults

- PCV-7 ➔ 80% decrease in invasive pneumococcal disease (IPD) caused by vaccine-serotypes
- But, IPD caused by non-vaccine serotypes increased = replacement strains
Herd Immunity

- PCV decreases carriage in the nasopharynx
- Decreases transmission of vaccine strains
- → Herd immunity

- That’s why most IPD in older adults was NOT due to PCV-7 strains
- IPD in older adults due to replacement serotypes

Lessons learned

- 1. PCV-7 decreased IPD in young children
- 2. Not much change in IPD in older adults >64 years
- 3. IPD due to replacement strains
  (some are covered by PCV-13 e.g. 19A, 3)
- 4. 25% of IPD in adults >65, and 10% of CAP are caused by PCV-13 serotypes potentially preventable

NACI recommendations for adults

<table>
<thead>
<tr>
<th>Risk Group</th>
<th>PCV13 Recommended</th>
<th>PPSV23 Recommended</th>
<th>PPSV23 Revaccination at 5-yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults with hematopoietic stem cell transplants (HSCT)</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Adults with HIV</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Adults with immunosuppressive conditions including:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asplenia (anatomical or functional)</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Sickle cell disease or other hemoglobinopathies</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Congenital immunodeficiencies</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Immunosuppressive therapy†</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Malignant neoplasms including leukemia and lymphoma</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Solid organ or islet cell transplant (candidate or recipient)</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

PHAC: National Advisory Committee on Immunization (NACI). Statement on the Use of Conjugate Pneumococcal Vaccine – 13 valent in Adults (PHAC-C-13)
Sequential Use of PCV13 & PPSV23

Either: Patient has not received any pneumococcal vaccine

- PCV13 - PPSV23 - PPSV23
  > 8 wks interval  > 5 yrs interval

Or: Patient has received PPSV23 previously

- Date of last PPSV23 - PCV13 - PPSV23
  > 1 yr interval

As of Sept 2014


Approvals & Recommendations for PCV-13

U.S.
- FDA (Food and Drug Administration) approves (2011)
- ACIP (Advisory Committee on Immunization Practices) recommends (2014)

Canada
- Health Canada approves
- NACI (National Advisory Committee on Immunizations) recommends (2013)
Community-Acquired Pneumonia Immunization Trial in Adults — CAPiTA

March 19, 2015

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Polysaccharide Conjugate Vaccine against Pneumococcal Pneumonia in Adults

M.J.M. Bonten, S.M. Huijts, M. Bolkenbaas, C. Webber, S. Patterson, S. Gault, C.H. van Werkhoven, A.M.M. van Deursen, E.A.M. Sanders, T.J.M. Verheij,

CAPiTA is the largest blinded prospective adult vaccine study conducted to-date (~84,500 subjects)

CAPiTA TRIAL

45% efficacy (CI 14-65%) vaccine-type CAP

75% efficacy (CI 41-91% vaccine-type IPD

No effect on all-cause CAP (p=0.11)

No effect on all-cause mortality

Adults > 65 (n=84,496)

PCV-13

Placebo (no PPV-23)

### NACI: PCV-13 in adults

<table>
<thead>
<tr>
<th>All ages with co-morbidities:</th>
<th>All Adults</th>
<th>≥ 65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immuno-competent</td>
<td>Immuno-compromised</td>
<td>Social/Lifestyle</td>
</tr>
<tr>
<td>• Chronic heart disease</td>
<td>• HIV infection</td>
<td>• Residents of long term care facilities</td>
</tr>
<tr>
<td>• Chronic lung disease</td>
<td>• Immune deficiencies</td>
<td>• Homelessness</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
<td>• Transplant patients</td>
<td>• Alcoholism</td>
</tr>
<tr>
<td>• Chronic liver disease</td>
<td>• Stem cell</td>
<td>• Smokers</td>
</tr>
<tr>
<td>• Chronic kidney disease</td>
<td>• Solid organ</td>
<td>• illicit drug use</td>
</tr>
<tr>
<td>• CSF leaks</td>
<td>• Immune suppression due to disease or treatment</td>
<td></td>
</tr>
<tr>
<td>• Cochlear implants</td>
<td>• Malignancies, including leukemia and lymphoma</td>
<td></td>
</tr>
<tr>
<td>• Chronic neurologic conditions that may impair clearance of oral secretions</td>
<td>• Asplenia, sickle cell, hemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td><strong>KIDS ONLY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma (requiring medical care in past 12m)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Free in BC

<table>
<thead>
<tr>
<th>All ages with co-morbidities:</th>
<th>All Adults</th>
<th>≥ 65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immuno-competent</td>
<td>Immuno-compromised</td>
<td>Social/Lifestyle</td>
</tr>
<tr>
<td>• Chronic heart disease</td>
<td>• HIV infection</td>
<td>• Residents of long term care facilities</td>
</tr>
<tr>
<td>• Chronic lung disease</td>
<td>• Immune deficiencies</td>
<td>• Homelessness</td>
</tr>
<tr>
<td>• Diabetes mellitus</td>
<td>• Transplant patients</td>
<td>• Alcoholism</td>
</tr>
<tr>
<td>• Chronic liver disease</td>
<td>• Stem cell</td>
<td>• Smokers</td>
</tr>
<tr>
<td>• Chronic kidney disease</td>
<td>• Solid organ</td>
<td>• illicit drug use</td>
</tr>
<tr>
<td>• CSF leaks</td>
<td>• Immune suppression due to disease or treatment</td>
<td></td>
</tr>
<tr>
<td>• Cochlear implants</td>
<td>• Malignancies, including leukemia and lymphoma</td>
<td></td>
</tr>
<tr>
<td>• Chronic neurologic conditions that may impair clearance of oral secretions</td>
<td>• Asplenia, sickle cell, hemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td><strong>KIDS ONLY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma (requiring medical care in past 12m)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

KIDS ONLY
U.S.: It’s not just guns and health care

<table>
<thead>
<tr>
<th>All ages with co-morbidities:</th>
<th>All Adults</th>
<th>≥ 65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immuno-competent</td>
<td>Immuno-compromised</td>
<td>Social/Lifestyle</td>
</tr>
<tr>
<td>Chronic heart disease</td>
<td>HIV infection</td>
<td>Residents of long term care facilities</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>Immune deficiencies</td>
<td>Homelessness</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Transplant patients</td>
<td>Alcoholism</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>- Stem cell</td>
<td>Smokers</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>- Solid organ</td>
<td>Illicit drug use</td>
</tr>
<tr>
<td>CSF leaks</td>
<td>Immune suppression due to disease or treatment</td>
<td></td>
</tr>
<tr>
<td>Cochlear implants</td>
<td>Malignancies, including leukemia and lymphoma</td>
<td></td>
</tr>
<tr>
<td>Chronic neurologic conditions that may impair clearance of oral secretions</td>
<td>Asplenia, sickle cell, hemoglobinopathies</td>
<td></td>
</tr>
<tr>
<td>Asthma (requiring medical care in past 12m)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. MMWR Sept. 19, 2014/63 (37):822-825

U.S. recommends PCV-13 for adults >65 years old

- Probablistic model:
  - If you add PCV-13 to PPV-23 for adults > 65 years old
  - And you take into account:
    - Herd immunity from children
    - 60% of adults have received PPV-23

U.S. recommends PCV-13 for adults >65 years old

- Expected benefit of adding PCV-13:
  - IPD: ↓ 160 cases
  - CAP: ↓ 4500 cases
- Recommendation: Give PCV-13 then 6-12 months later, give PPV-23
- Reassess this recommendation in 2018


2018 – what the future holds

- Does PCV-13 in older adults add benefit to herd immunity?
- Does PCV-13 in older adults lead to decreases in all-cause pneumonia, all-cause mortality?
- Does PCV-13 add additional benefit to PPV-23?
Lessons learned

- NACI recommending PCV-13 and PPV-23 for adults with immunosuppression
- Still recommending PPV-23 alone for age > 65 and chronic conditions
- This may change as epidemiological data on herd immunity emerges
- All at-risk adults should receive immunization

Influenza

- Serious illness and death highest in older adults
- 90% of influenza-associated deaths occur in adults > 60 years old
- Influenza can lead to secondary bacterial pneumonia
Influenza vaccine

- Influenza vaccine 50% effective in older adults
- Vaccine effectiveness lower in older adults
- What about using a higher-dose of vaccine in older adults?
• Adults > 65 years old
• Randomized control trial (n= 32,000)
• Standard dose vaccine vs. High-dose vaccine (4x)

• Results: who got sick with the flu?
  • 228 with high-dose vaccine
  • 301 with standard-dose vaccine
• Relative efficacy of 24.2%
• Similar to an increased vaccine efficacy of 50% ➢ 62%
Which vaccine to use?

- **8 trivalent**
  - 7 inactivated
    - 5 IM, no adjuvant (*Agriflu, Fluviral, Fluzone, Influvac, Vaxigrip*)
    - 1 IM, adjuvant (*Fluad*) (for age >65)
    - 1 intradermal (Intanza)
    - 1 live attenuated (*FluMist*) for ages 2-17

- **2 quadrivalent** (Flulaval, Fluzone)

- **Quadrivalent FluMist** (publically funded ages 2-17)

Live attenuated influenza vaccine (LAIV)

- LAIV has a shorter shelf-life (≈4 months)
- Live attenuated so if you take oseltamavir, it will interfere with immune response
- Not for immunocompromised
- Not for pregnant
- Not for egg allergy
- Not for severe asthma
NACI recommendations

• Offer flu vaccine to all adults
• (everyone > 6 months!)
• For adults > 65 years: any of the inactivated formulations
• No specific recommendations on high-dose formulations (watch for it next flu season 2015-16)

NACI recommendations

• High-risk groups are same as IPD
• Additional risk groups:
  • Pregnant woman are included
  • Morbid obesity
  • Aboriginal Peoples
  • Long-term care facilities
  • Transmission issues: grandkids, health care, poultry farm
Why don’t people get the flu shot?

- Even healthy people need a flu vaccine
- The flu vaccine is safe
- Side effects to the vaccine are mild
  - With IM shot: achy, sore arm
  - With nasal spray: stuffy nose, sore throat
- Flu can be serious with complications. Even if you get well quickly, your contacts might not be so lucky
- Don’t wait until flu hits. It takes 2 weeks to build an antibody response
Why don’t people get the flu shot?

- Flu vaccines can’t give you the flu
- If you don’t like shots, use the nasal spray (ages 2-49, live vaccine)
- Even if you got one last year, you need a flu shot every year
- Even though this year was a mismatch, it was still 20% effective, which is a lot better than nothing!
- Egg allergy – inactivated vaccines ok (NOT live intranasal)

Objectives

- 1. Appreciate the burden of influenza and pneumococcal disease and their associated risk factors
  - 8th most common cause of death
  - (1 in 50 deaths in Canada due to flu/CAP)
  - Risk factors: Age++, chronic conditions, immunosuppression, social
Objectives

- 2. Understand and explain the differences between available vaccine options
  - PCV-13 decreases vaccine-strain IPD by 75%
  - PCV-13 decreases vaccine-strain CAP by 45%
  - PCV-13 leads to herd immunity by \( \downarrow \) nasopharyngeal carriage

- PPV-23 may have similar efficacy in younger adults
- PPV-23 loses efficacy in older adults, immunosuppressed
- PPV-23 has broader immunity (23 vs 13 serotypes)

Objectives

- 2. Understand and explain the differences between available vaccine options
  - Both PCV-13 and PPV-23 are necessary:
    - If no previous vaccine: PCV-13 first – 8 weeks – PPV-23
    - If already had PPV-23: wait a year, then PCV-13
    - Revaccinate with PPV-23 after 5 years
    - No booster for PCV-13
Objectives

- 3. Translate the latest NACI guidelines into clinical practice from a pharmacist perspective.
- Can give flu and pneumococcal shots at the same time
- NACI recommendations for PCV-13
- “Good” evidence: HSCT, HIV, kids with asthma
- “Fair” evidence: immunosuppression
- “Insufficient” evidence: >65 years old (pre-CAPITA) ➔ stay tuned!

Conclusion – looking ahead

- Things to watch out for:
- NACI statements based on:
  - Preventing pneumococcal disease in older adults: CAPITA trial – how will it affect recommendations?
  - Preventing influenza in older adults: Higher-dose influenza vaccine?