New pneumococcal vaccines under review in Canada

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Presenter Disclosure

• Dr. Kyla Hildebrand

• Relationships with financial sponsors:
  – BC Society of Allergy and Clinical Immunology - honorarium
  – Canadian Society of Allergy and Clinical Immunology - honorarium
Disclosure of Financial Support

• This program has not received financial support or in-kind support from any organizations

• **Potential for conflict(s) of interest:**
  - None to declare
Mitigating Potential Bias

• Previous speaker honoraria were for topics unrelated to this presentation
• I will use only generic names
• Inform the audience if there is limited evidence for an assertion or recommendation
Current vaccines for pneumococcal disease

PCV13
• Implemented in 2003

PPV23
• Implemented in 2010
What do we aim to prevent with PC vaccines?

• Invasive Pneumococcal Disease (IPD)
  – Bacteremia
  – Sepsis
  – Meningitis

• Non-invasive Pneumococcal Disease
  – Community Acquired Pneumonia (CAP)
  – Otitis media
  – Sinusitis
Who is at risk for IPD?

- Adults ≥ 65 years
- Children < 2 years
- Immunocompromised individuals
- Chronic medical conditions
- Homelessness, crowded living conditions
Epidemiology Pre/Post past PC vaccines

- In 2010, BC introduced the PCV13 vaccine for the infant immunization program
- BC recommended the use of the PPV23 for adults ≥ 65 years and individuals over 2 y with underlying medical conditions
- Addition of the PCV13 vaccine resulted in decline of 19% IPD from PCV13 serotypes compared to PCV7 era
  - Benefits seen in < 2 years and adults between 18-49 y

Fig 1. **Invasive pneumococcal disease incidence from 2002 to 2015.** Overall = laboratory and hospitalization data. PCV7 = serotypes in the 7-valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. PPV23 = additional 11 serotypes not in the PCV13 vaccine. NVT = non-vaccine serotype. Non-PCV13 = serotypes not included in the conjugate vaccines (they consist of serotypes comprised of the additional 11 serotypes included in the 23-valent polysaccharide pneumococcal vaccine and NVT serotypes). While no changes were noted for overall IPD (p = 0.2138), significant changes occurred for PCV7, PCV13, PPV23, NVT, Non-PCV13 serotype IPD (p<0.0001).

https://doi.org/10.1371/journal.pone.0239848.g001
IPD by serotype in BC 2002-2015

![Graph showing incidence of invasive pneumococcal disease by serotypes in British Columbia from 2002-2015. PCV7 = serotypes in the 7-valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. Non-PCV13 = serotypes not included in the conjugate vaccines (they consist of serotypes comprised of the additional 11 serotypes included in the 23-valent polysaccharide pneumococcal vaccine and NVT serotypes).](https://doi.org/10.1371/journal.pone.0239848.g003)
**IPD by serotype in BC 2002-2015**

![Bar chart showing incidence of IPD by serotype in BC 2002-2015](https://doi.org/10.1371/journal.pone.0239848.g003)

**Fig 3. Incidence of invasive pneumococcal disease by serotypes in British Columbia from 2002–2015.** PCV7 = serotypes in the 7-valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. Non-PCV13 = serotypes not included in the conjugate vaccines (they consist of serotypes comprised of the additional 11 serotypes included in the 23-valent polysaccharide pneumococcal vaccine and NVT serotypes).

Sharifa Nasreen a,b, Jun Wang c,d, Jeffrey C. Kwong a,b,c,d,e,f, Natasha S. Crowcroft a,b, Manish Sadarangani g,h, Sarah E. Wilson a,b,c,d, Allison McGeer a,b,i,j,k, James D. Kellner l, Caroline Quach m, Shaun K. Morris n, Beate Sander c,d,k, Julianne V. Kus c,j, Monika Naus o,p, Linda Hoang n,q, Frank Rudzicz j,r,s,t, Shaza Fadel a,b, Fawziah Marra u,*
Burden of IPD remains high despite 8 years of a national pediatric PCV13 program.

Increase incidence of IPD due to serotypes 3, 19A, 7F, 22F.
CIRN study data

D. British Columbia

Incidence per 100,000

Year

PCV7

PCV13


PCV7, adjusted
Additional PCV13, adjusted
Unique PPV23, adjusted
Non-vaccine serotype, adjusted
Incidence rate of IPD

• CIRN data from 2018 surveillance:
  – 10.5 per 100,000 in Ontario
  – 12 per 100,000 in BC
New pneumococcal conjugate vaccines

- **PCV15**
  - Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F and 33F
  - Approved by US FDA July 2021

- **PCV20**
  - Serotypes Serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F, 33F, 8, 10A, 11A, 12F, 15B
  - Approved by US FDA June 2021
### Serotypes Contained in Current and New Pneumococcal Vaccines

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PCV13: 13-valent pneumococcal conjugate vaccine  
PPSV23: 23-valent pneumococcal polysaccharide vaccine
## Serotypes Contained in Current and New Pneumococcal Vaccines

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- **PCV15 non-PCV13**: includes serotypes **22F** and **33F**
- **PPSV23 non-PCV20**: includes serotypes **2**, **9N**, **17F**, and **20**
Use of 15-Valent Pneumococcal Conjugate Vaccine and 20-Valent Pneumococcal Conjugate Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

Miwako Kobayashi, MD; Jennifer L. Farrar, MPH; Ryan Gierke, MPH; Amadea Britton, MD; Lana Childs, MPH; Andrew J. Leidner, PhD; Doug Campos-Outcalt, MD; Rebecca L. Morgan, PhD; Sarah S. Long, MD; H. Keipp Talbot, MD; Katherine A. Pochling, MD; Tamara Pilishvili, PhD
Is there a need?

• Incidence of IPD in adults ≥ 65 y was 24 per 100,000 population
  – 27% = PCV13 strains
  – 15% = Additional serotypes unique to PCV15 (22F and 33F)
  – 27% = Additional serotypes unique to PCV20 (8, 10A, 11A, 12F, 15B, 22F, and 33F)
  – 35% = Additional serotypes unique to PPSV23 (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F and 33F)
FIGURE. Incidence of all invasive pneumococcal disease and 13-valent pneumococcal conjugate vaccine-type* invasive pneumococcal disease among adults aged ≥19 years, by invasive pneumococcal disease type and age group — United States, 2007–2019†

PCV13 introduced for children
PCV13 introduced for all adults aged ≥65 years
Shared clinical decision-making for PCV13 for adults aged ≥65 years without an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant

Cases per 100,000 population

Year


PCV13-type IPD among adults aged 19–64 yrs
PCV13-type IPD among adults aged ≥65 yrs
All IPD among adults aged 19–64 yrs
All IPD among adults aged ≥65 yrs
2021 ACIP Recommendations

• October 20, 2021: Advisory Committee on Immunizations Practices (ACIP) recommended the following:
  • For adults ≥ 65 years
  • Adults 19-64 y with certain underlying medical conditions or risk factors who have not previously received PC vaccine
    – PCV20 alone OR
    – PCV15 in series with PPSV23
• ACIP used an Evidence to Recommendation (EtR) framework using GRADE approach
Immunogenicity

PCV15

• Phase II/III RCTs evaluated immunogenicity of single dose of PCV15 compared with a dose of PCV13

• Study Population
  – Healthy adults ≥ 50 y
  – Adults 18-49 y who are Native American
  – Adults 18-49 y with ≥ 1 risk condition for PC disease
  – Adults ≥ 18 y with HIV infection

• Serotype-specific functional antibody responses measures 1 month after vaccination
  – One Phase III RCT of adults ≥ 50 y met non-inferiority criteria for the 13 shared serotypes and had a statistically significant greater response for serotype 3
  – PCV15 + PPV23 compared to PCV13 + PPV23: individuals who received PPV15 + PPV23 had higher OPA geographic-mean antibody titers (GMTs) for 9-13 of the shared serotypes and higher percentage of seroresponders for 5-11 of the shared serotypes
Immunogenicity

PCV20

- Phase II study among adults 60-64 y and two phase III RCTs among adults ≥18 y evaluated immunogenicity and safety of single dose of PCV20 compared with a dose of PCV13 and with PPV23
- Serotype-specific functional antibody responses measures 1 month after vaccination
  - Compared with PCV13 recipients: PVC20 recipients elicited responses that met non-inferiority criteria for the 13 shared serotypes, however had a lower GMTs and lower percentage of seroresponders to 12-13 of the shared serotypes
  - Compared with PPV23: PCV20 recipients had higher GMTs and higher percentage of seroresponders for 6 of 7 shared non-PCV13 serotypes.
Safety

PCV15
- 7 RCTS; 5,630 participants
- 1 study included 302 adults with H
- Common: Injections site pain, fatigue, myalgia
- Severe AEs within 6 months:
  - 2.5% of PCV15 recipients
  - 2.4% of PCV13 recipients
  - No SAE or deaths were considered related to vaccine

PCV20
- 6 trials; 4,552 participants
- Adverse events:
  - Common: Injections site pain, muscle pain, fatigue, headache, joint pain
  - Severe AEs within 6 months:
  - 1.5% of PCV20 recipients
  - 1.8% of placebo recipients
  - No SAE or deaths were considered related to vaccine
ACIP Dosing interval

• Interval between PCV15 and PPV23 is ≥ 1 year
• Minimum of 8 weeks among individuals with immunocompromised, cochlear implant or cerebral spinal fluid leak
• Adults with previous PPV23:
  – May receive PCV15 or PCV20 ≥ 1 year after last PPV23 dose
# Summary of WG Considerations: PCV20 Use Alone OR PCV15+PPSV23

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<thead>
<tr>
<th>Advantages of PCV20 Use Alone</th>
<th>Disadvantages of PCV20 Use Alone</th>
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<tbody>
<tr>
<td>• Acceptable and feasible to implement a single</td>
<td>• Clinical significance of lower immunogenicity vs. PCV13 unknown</td>
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<tr>
<td>vaccine option</td>
<td>• No data in immunocompromised adults</td>
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<td>• Cost-saving* in cost-effectiveness analyses</td>
<td>• Losing protection against PPSV23, non-PCV20 serotypes</td>
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<td>• Expected to provide better protection for the</td>
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<td>serotypes covered by PPSV23 alone</td>
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<table>
<thead>
<tr>
<th>Advantages of PCV15+PPSV23</th>
<th>Disadvantages of PCV15+PPSV23</th>
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<tr>
<td>• Provides broad serotype coverage</td>
<td>• Logistically more challenging to administer PCV15-PPSV23 vaccine</td>
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<tr>
<td>• Age-based use at age 65 was cost-saving*</td>
<td>series</td>
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<td>according to CDC’s cost-effectiveness analysis</td>
<td>• Need to know vaccination history to correctly complete series</td>
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<td>• Can result in lower serotype coverage if series not completed</td>
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*lower cost and better health outcome compared to current recommendations
Summary

• Evidence from BC data that PC vaccines work in preventing IPD
• Canadian data indicating that IPD remains high despite 8 years of a national pediatric PCV13 program
• Non-PCV13 serotypes causing IPD are on the rise, including 22F
• PCV15 and PCV20 are currently under review at Health Canada
Thank you