# New pneumococcal vaccines under review in Canada

Kyla Hildebrand MD, FRCPC, MScCH

BC Immunization Forum

March 2, 2022

# BC Immunization Forum 2022
# 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**

- **<u>Potential for conflict(s) of interest</u>:**
  - 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 Pneumoccocal 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
- Immunecompromised 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 used 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

Vadlamudi NK et al. 2020, PLoS ONE 15(9): e0239848.

# BC Data

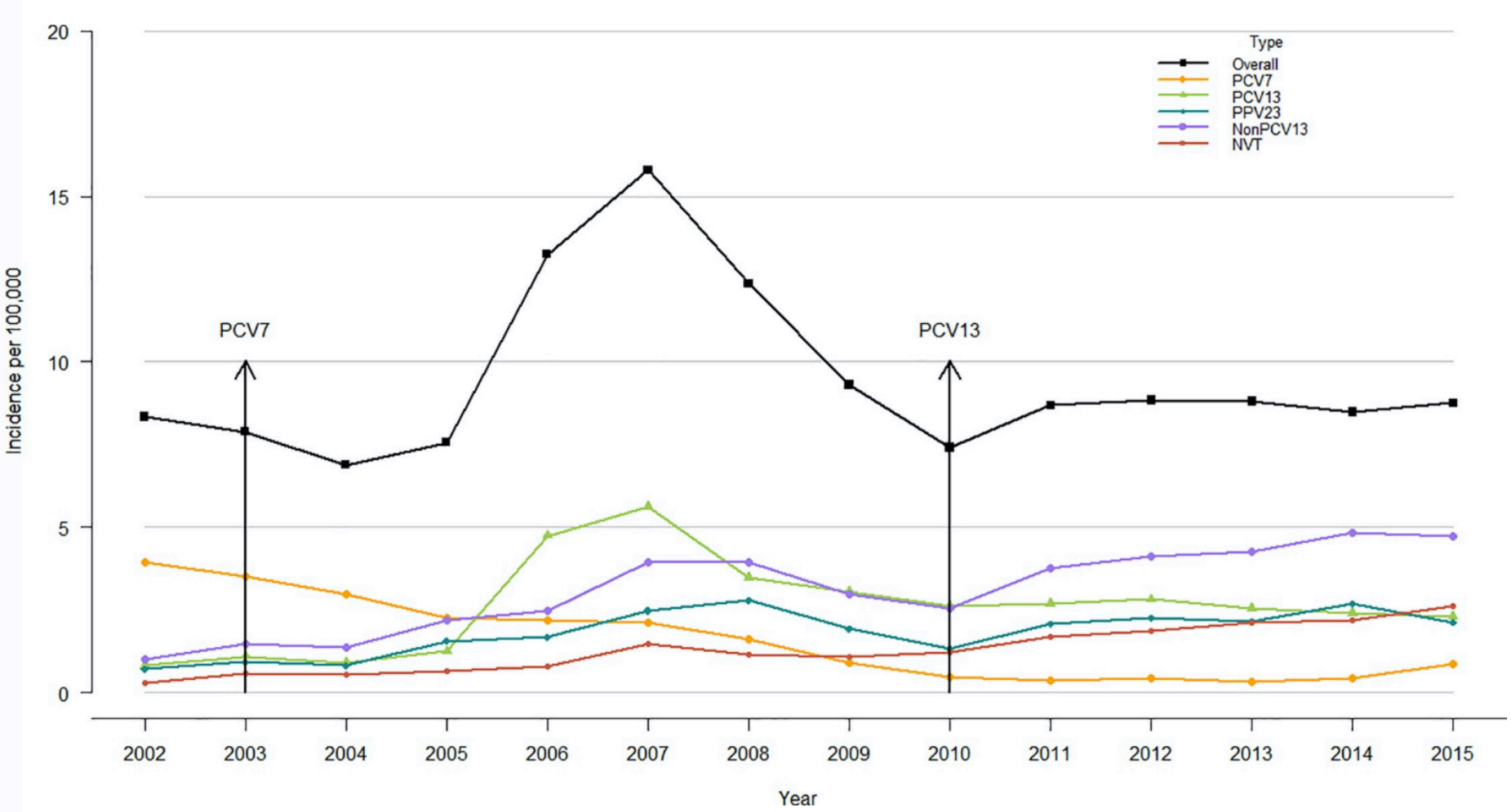



**Fig 1. Invasive pneumococcal disease incidence from 2002 to 2015.** Overall = laboratory and hospitalization data. PCV7 = serotypes in the 7- valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. PPV23 = additional 11 serotypes not 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

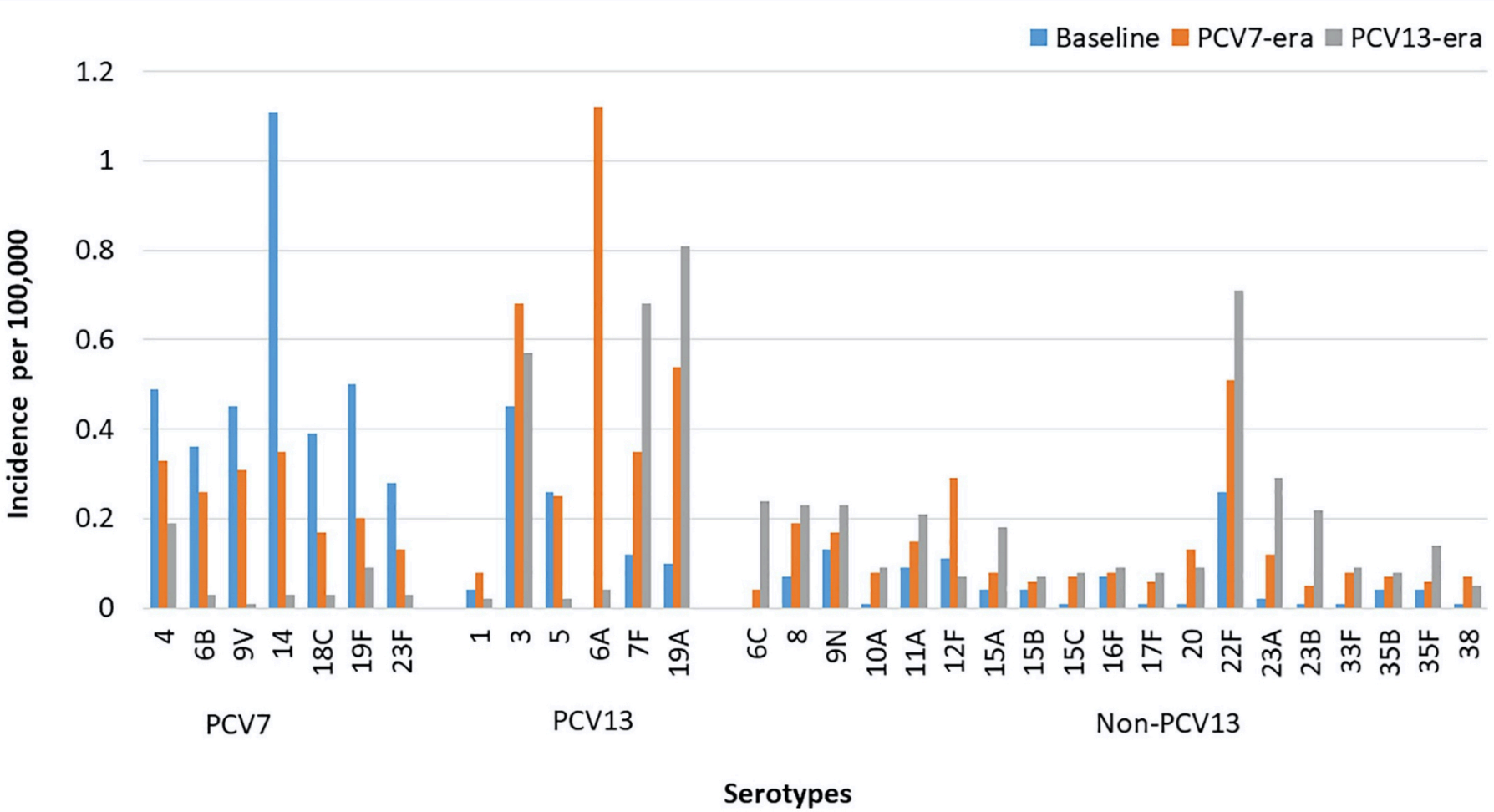



**Fig 3. Incidence of invasive pneumococcal disease by serotypes in British Columbia from 2002–2015.** PCV7 = serotypes in the 7- valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. Non-PCV13 = serotypes not included in the conjugate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

https://doi.org/10.1371/journal.pone.0239848.g003

# IPD by serotype in BC 2002-2015

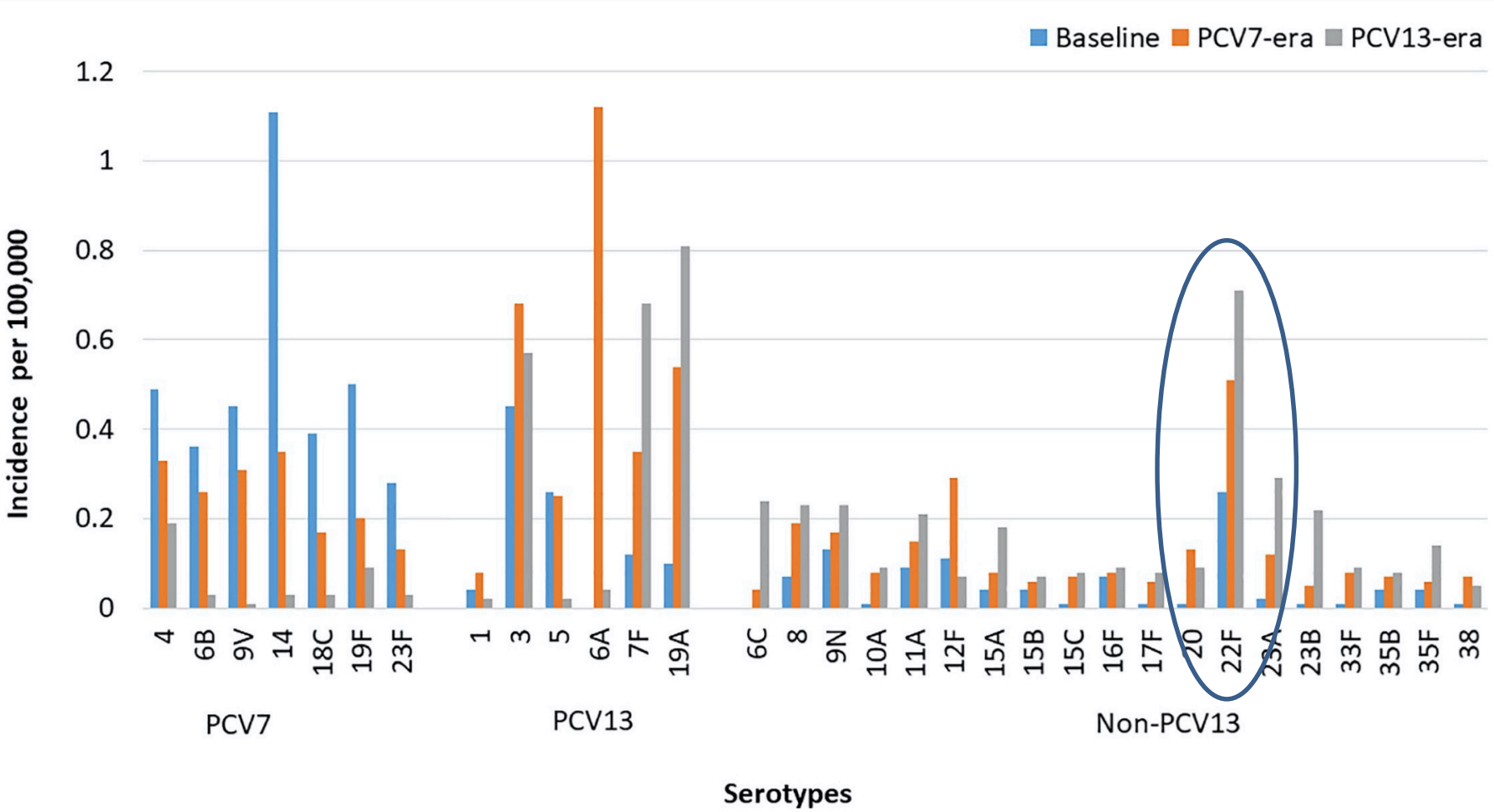
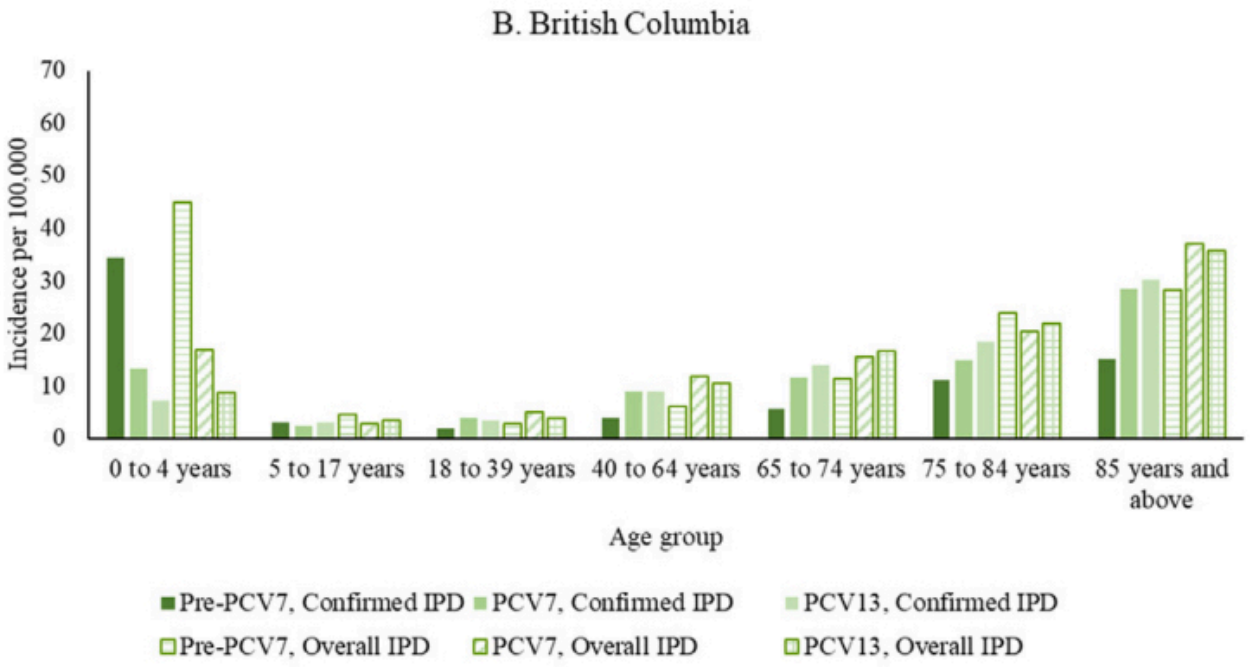



**Fig 3. Incidence of invasive pneumococcal disease by serotypes in British Columbia from 2002–2015.** PCV7 = serotypes in the 7- valent pneumococcal conjugate vaccine. PCV13 = additional six serotypes in the PCV13 vaccines not in PCV7 vaccine serotype. Non-PCV13 = serotypes not included in the conjugate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

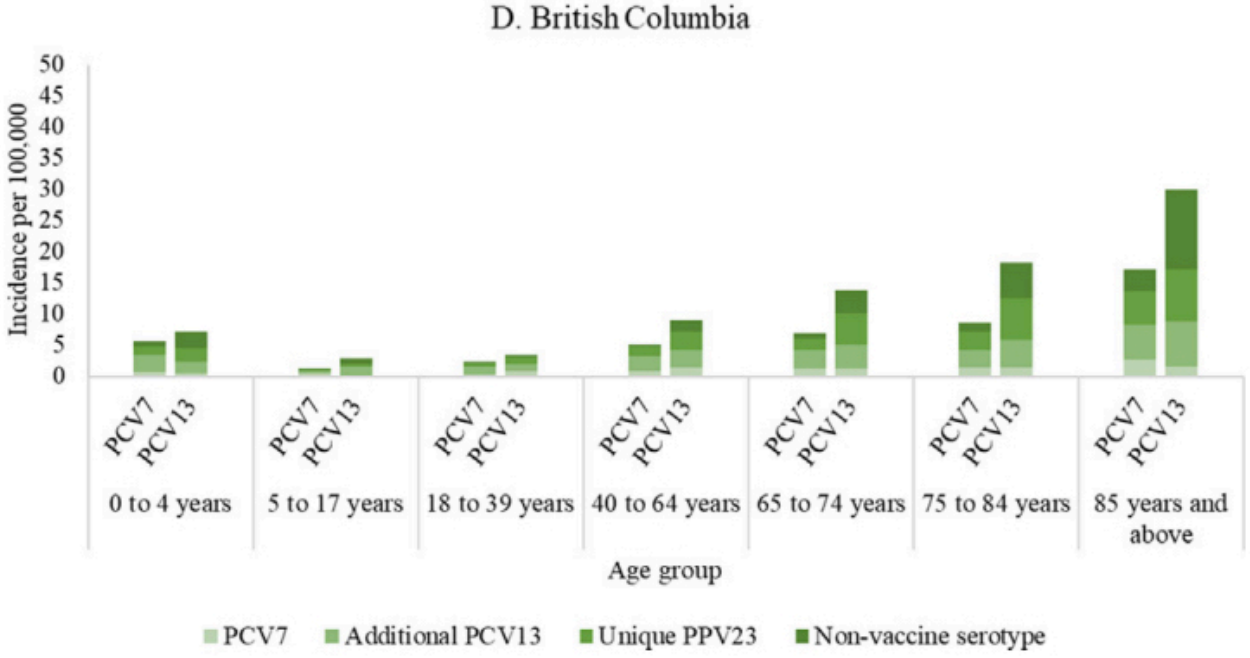
https://doi.org/10.1371/journal.pone.0239848.g003

# Population-based incidence of invasive pneumococcal disease in children and adults in Ontario and British Columbia, 2002–2018: A Canadian Immunization Research Network (CIRN) study

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 [p,q], Frank Rudzicz [j,r,s,t], Shaza Fadel [a,b], Fawziah Marra [u,*]

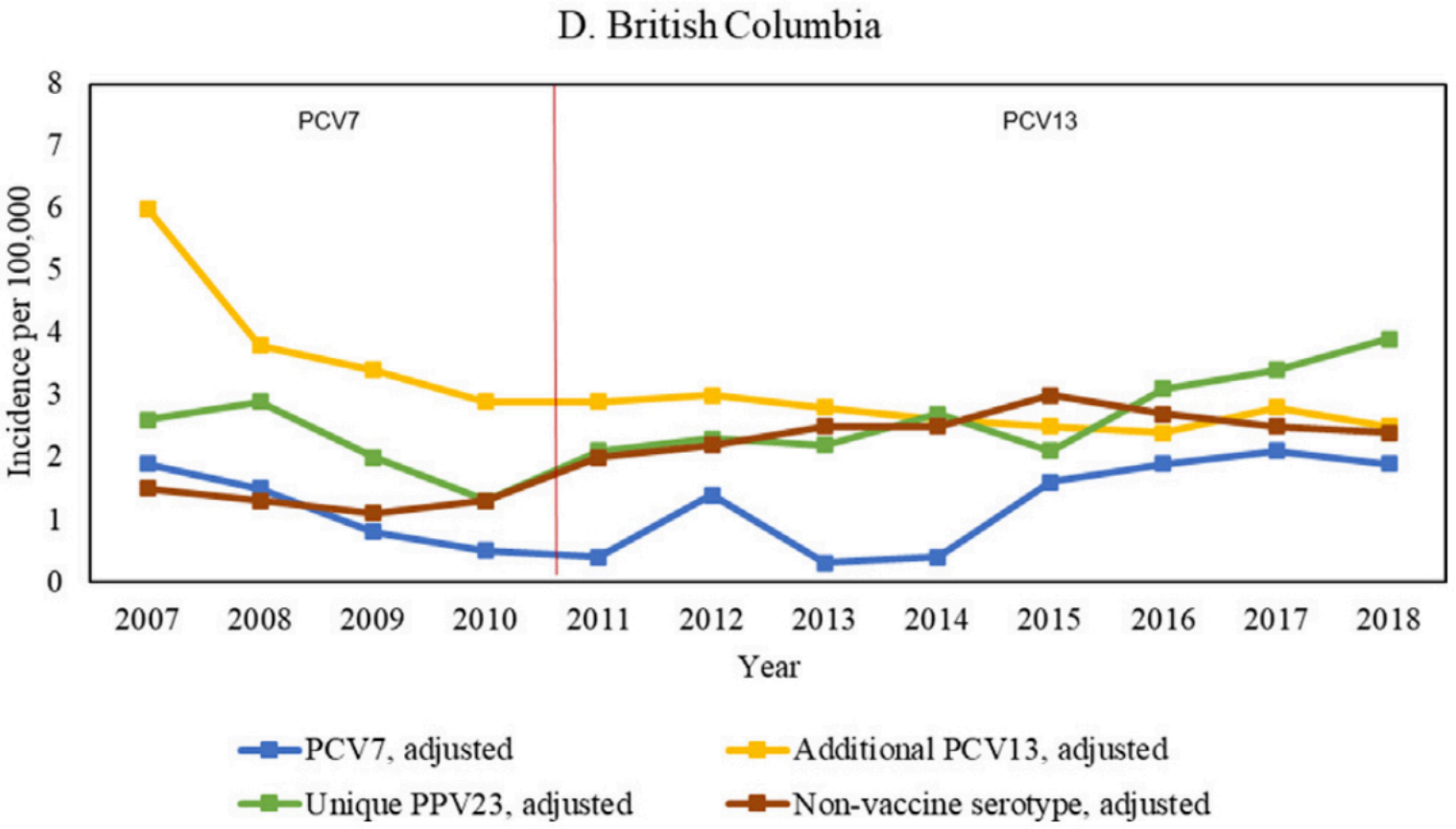



Burden of IPD remains high despite 8 years of a national pediatric PCV13 program




Increase incidence of IPD due to serotypes 3, 19A, 7F, 22F

# CIRN study data



# Incidence rate of IPD

- CIRN data from 2018 surveillance:
  - 10.5 per 100,000 in Ontario
  - 12 per 100,000 in BC

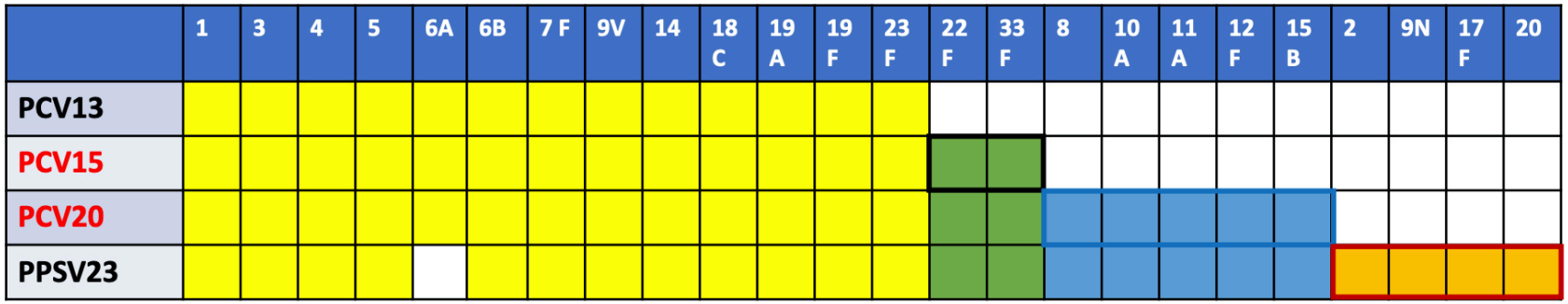
# New pneumococcal conjugate vaccines

- 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


PCV13: 13-valent pneumococcal conjugate vaccine
PPSV23: 23-valent pneumococcal polysaccharide vaccine

# Serotypes Contained in Current and New Pneumococcal Vaccines




- **PCV15 non-PCV13**: includes serotypes **22F and 33F**
- **PCV20 non-PCV13**: includes serotypes **22F, 33F, 8, 10A, 11A, 12F, and 15B**
- **PPSV23 non-PCV20**: includes serotypes **2, 9N, 17F, and 20**

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 71 / No. 4
January 28, 2022

# 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

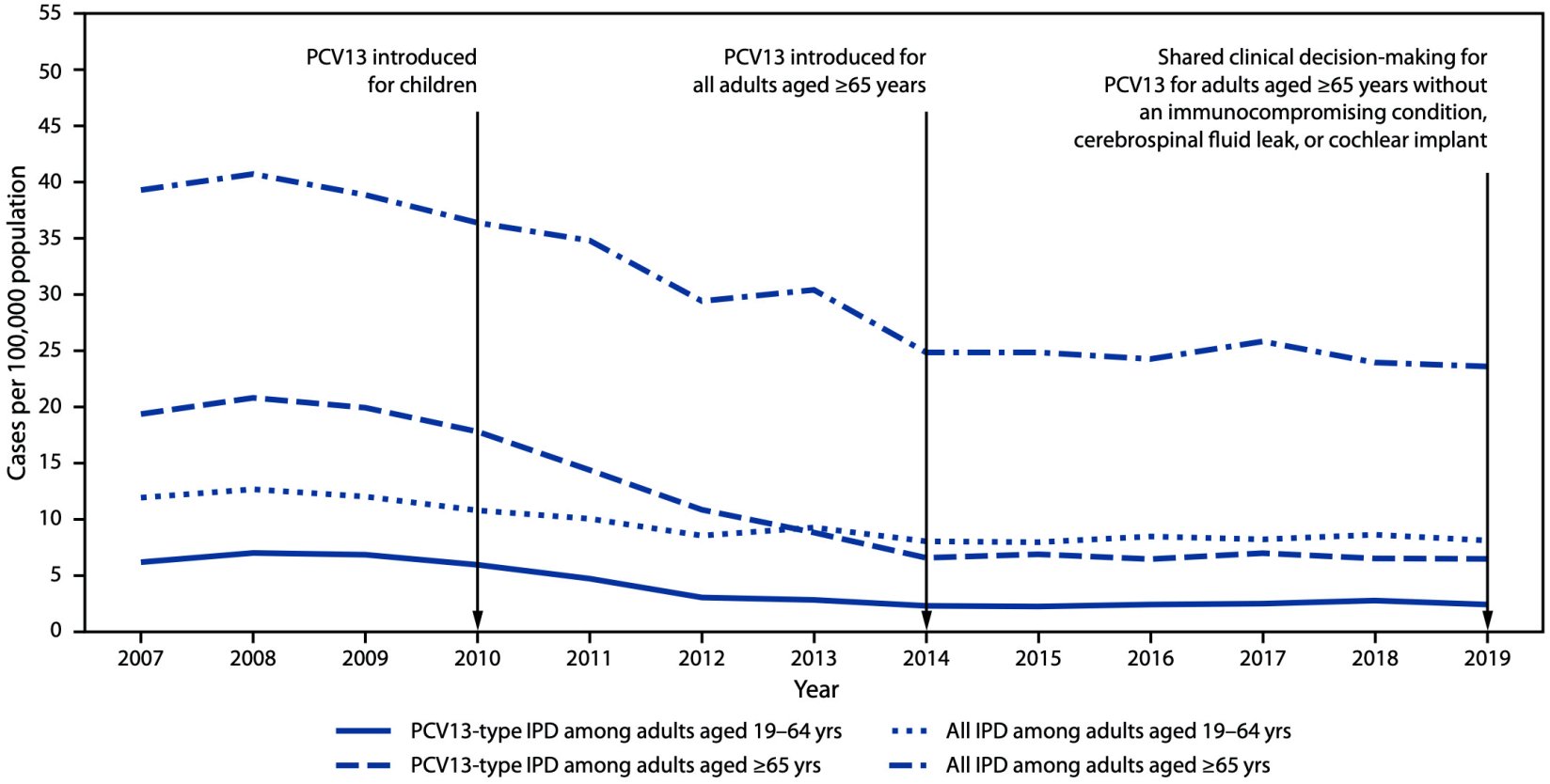
Miwako Kobayashi, MD[1]; Jennifer L. Farrar, MPH[1]; Ryan Gierke, MPH[1]; Amadea Britton, MD[1,2]; Lana Childs, MPH[3]; Andrew J. Leidner, PhD[1]; Doug Campos-Outcalt, MD[4]; Rebecca L. Morgan, PhD[5]; Sarah S. Long, MD[6]; H. Keipp Talbot, MD[7]; Katherine A. Poehling, MD[8]; Tamara Pilishvili, PhD[1]

# 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)

# US data

**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†**



# 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 immunecompromised, 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

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

*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