Pneumococcal Vaccines – New Vaccines and New Schedules

Dr. Jim Kellner

Pediatric Infectious Diseases, Alberta Children's Hospital

Professor, Department of Pediatrics, University of Calgary

Jim.Kellner@ahs.ca

I would like to acknowledge and pay tribute to the traditional territories of the peoples of Treaty 7 located in the heart of Southern Alberta, which include the Blackfoot Confederacy (comprised of the Siksika, the Piikani, and the Kainai First Nations), the Tsuut'ina First Nation, and the Stoney Nakoda (including Chiniki, Bearspaw, and Goodstoney First Nations). The City of Calgary is also home to the Métis Nation of Alberta (Districts 5 and 6).

Disclosure of Conflict of Interest

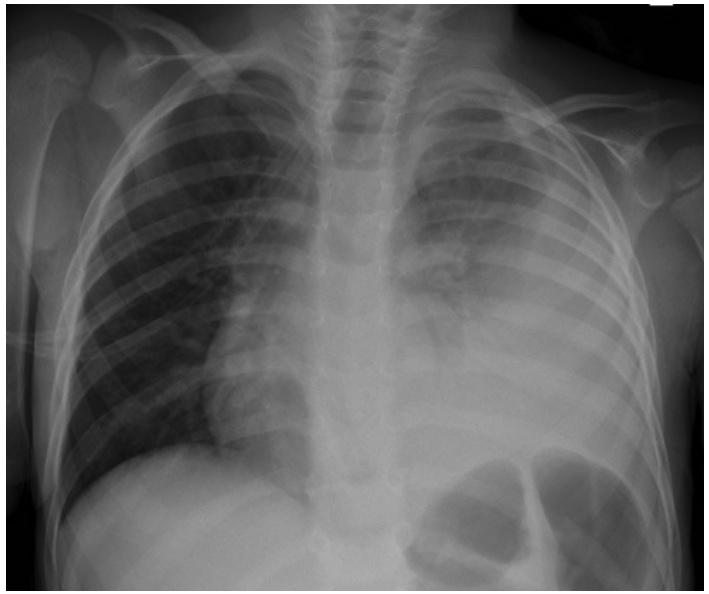
- I have/had a relationship (financial or otherwise) with for-profit or not-for-profit organizations (past 2 years)

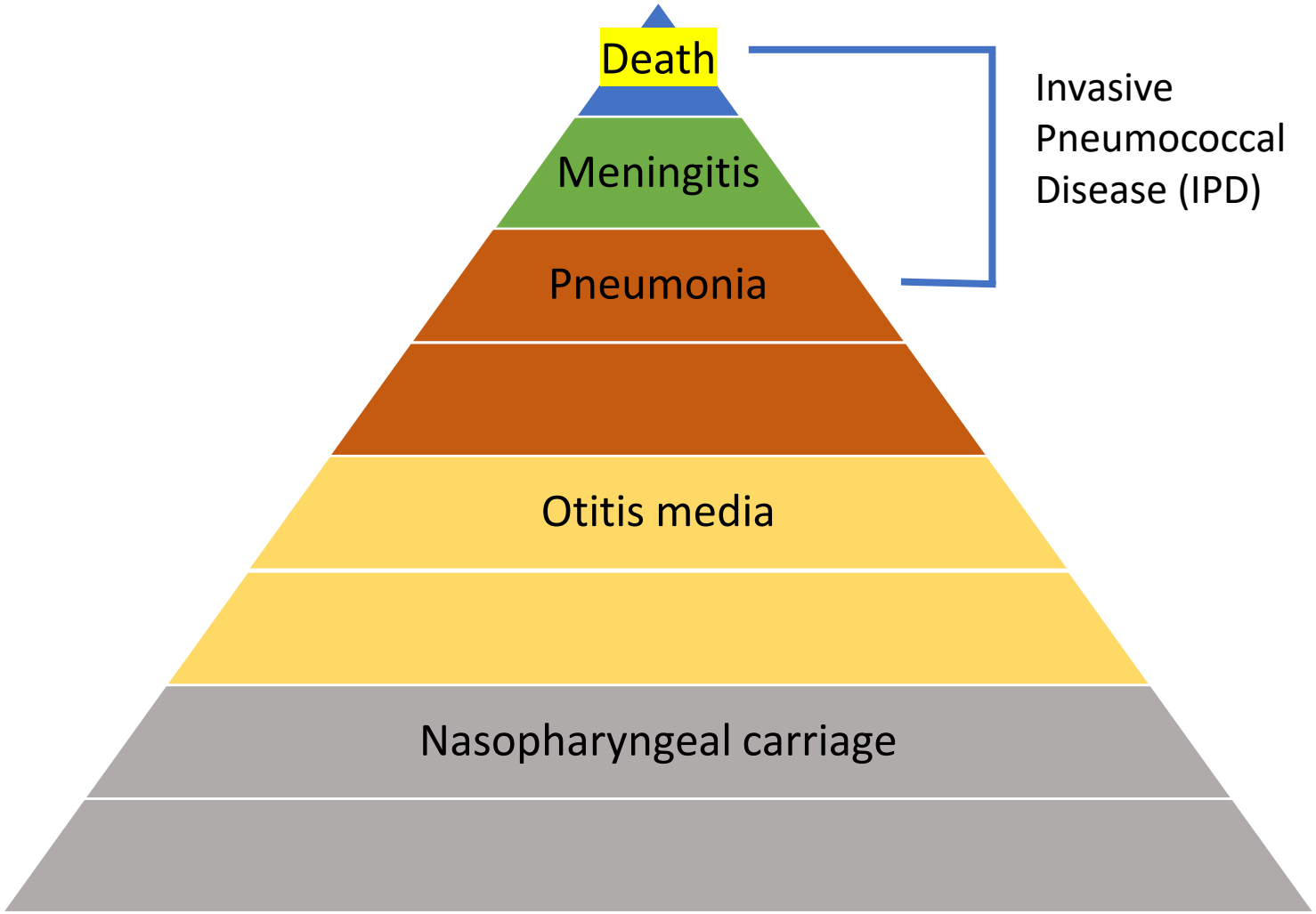
Nature of Relationships (last 2 years)	Name of for-profit or not-for-profit organization	Description of relationships
Funded grants, research, or clinical trials	Pfizer, Merck, Moderna, GSK	Local investigator on contract vaccine clinical trials (Merck, GSK, Moderna) and investigator-initiated grant for epidemiology study (Pfizer). All funds paid to U of Calgary with no payments to investigator.
All other relationships	NACI Pneumococcal Vaccine Working Group	Member
	Alberta Advisory Committee on Immunizations	Member

Objectives

- Describe current trends in serious pneumococcal disease across Canada
- Describe the new PCV15 and PCV20 vaccines
- Describe the updated NACI recommendations for pneumococcal vaccines at all ages

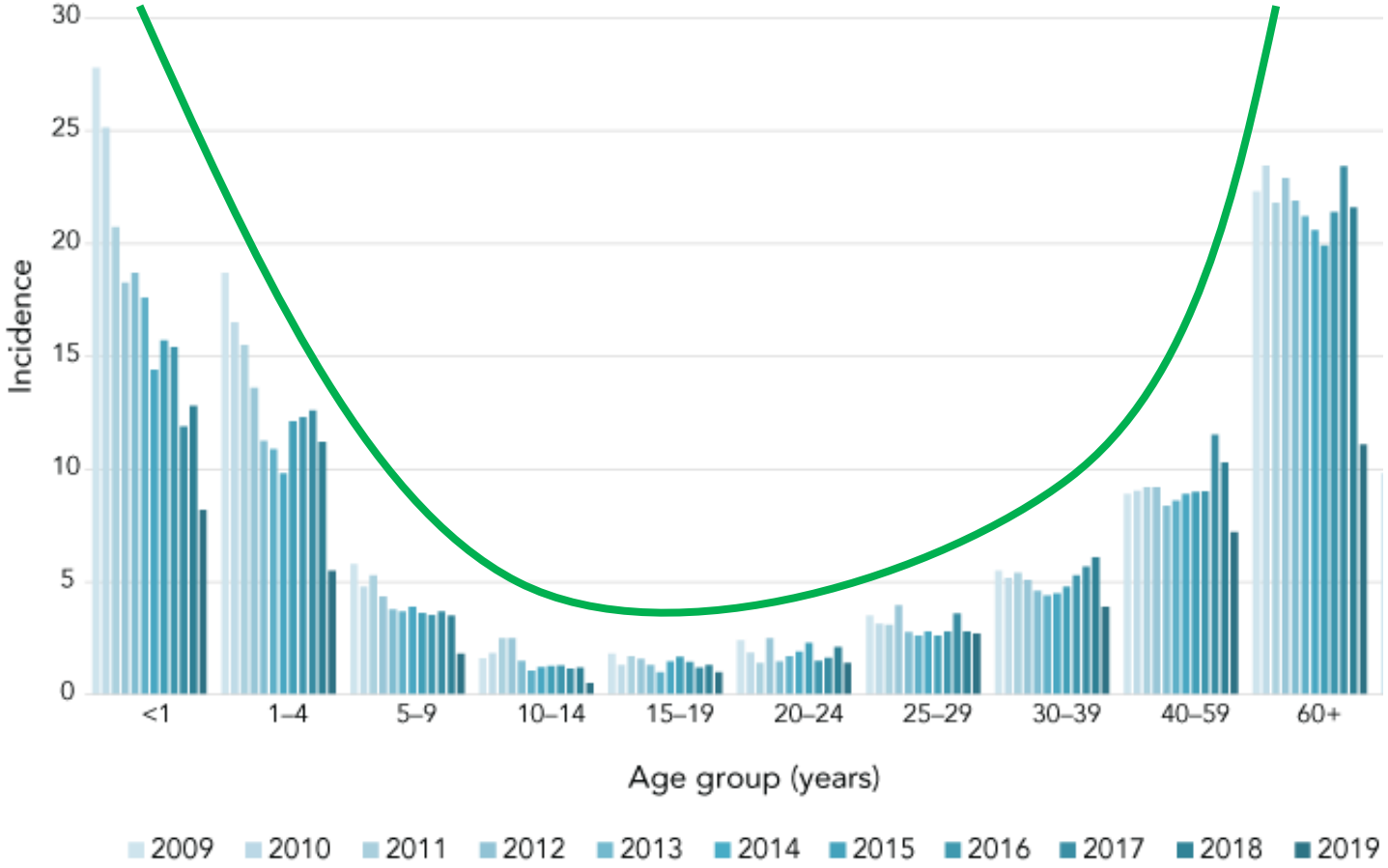
Pneumococcal Disease Burden





IPD Incidence in Canada by Age Group 2010–2020

Cases/100,000/
yr/age group



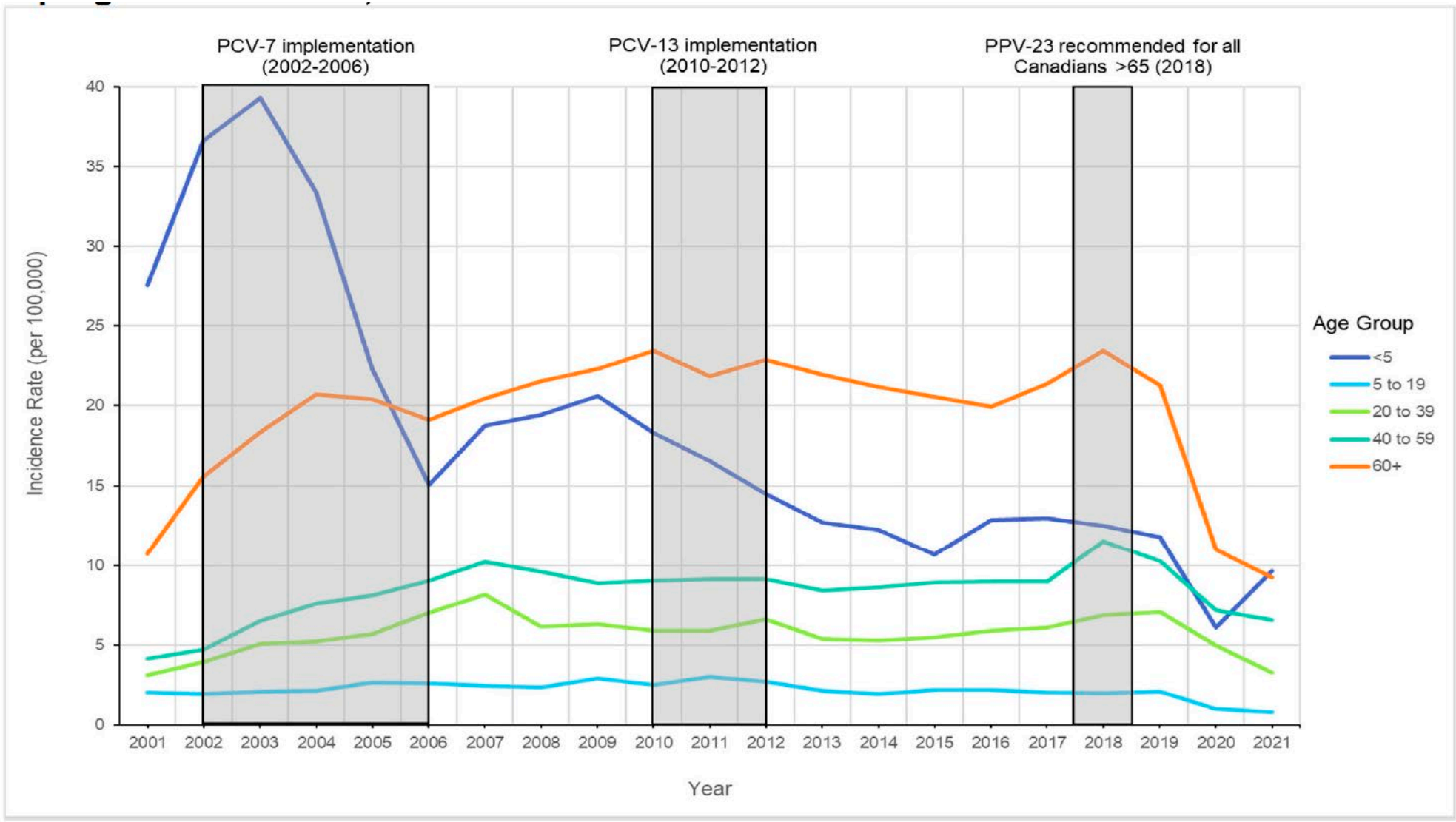
30-Day Mortality
Calgary

<2y	**0%**
2-4y	**4%**
5-15y	**3%**
16-64y	**10%**
65-84y	**13%**
85+y	**25%**

CASPER 2012-2022

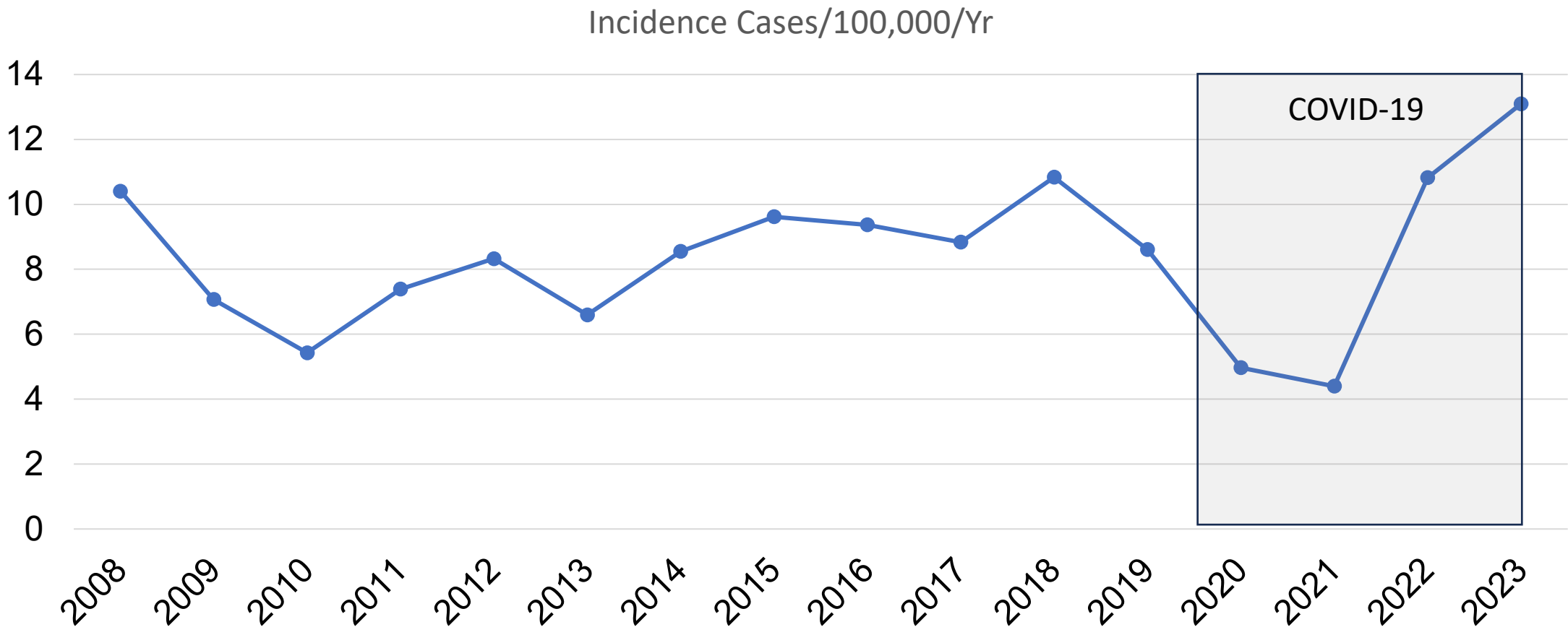
National Microbiology Lab Surveillance: Golden et al. CCDR 2022

IPD Incidence in **Canada** by Age Group 2001-2021



NACI Statement – Awaiting Link

IPD Incidence in **Calgary**, All Ages 2008-2023



CASPER (Calgary *S. pneumoniae* Epidemiology Research) Study to be presented at 13th ISPPD Mar 2024

Who is at risk for pneumococcal disease?

Health & Other Factors with High Risk of IPD

Non-Immunocompromising

- Chronic cerebrospinal fluid (CSF) leak
- Chronic neurologic condition that may impair clearance of oral secretions
- Cochlear implants
- Chronic heart disease
- Diabetes mellitus
- Chronic kidney disease*
- Chronic liver disease, including cirrhosis*
- Chronic lung disease, including asthma requiring medical care in the preceding 12 months

***Highest Risk**

Immunocompromising

- Sickle cell disease, congenital or acquired asplenia, or splenic dysfunction*
- Congenital immunodeficiencies*
- Immunocompromising therapy (steroids, chemotherapy, radiation therapy, and post-organ transplant therapy)*
- HIV*
- Hematopoietic stem cell transplant (recipient)*
- Malignant neoplasms*
- Nephrotic syndrome*
- Solid organ or islet transplant*

Other Factors – Behaviours, Living Conditions

- Smoking, alcoholism, illicit drug use, unhoused
- Communities with sustained high IPD rates

Canadian Immunization Guide 2016 and New NACI Statement

How well are pneumococcal vaccine programs working?

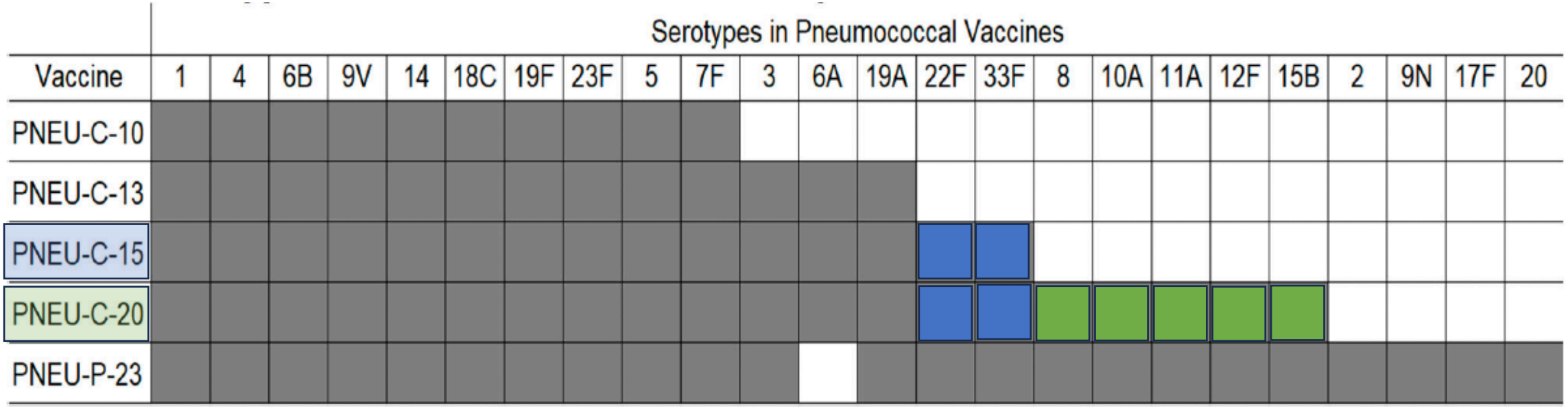
Successes and Gaps with Pneumococcal Vaccines

- Successes
  - PCVs have very high direct effectiveness against vaccine serotypes and good indirect (herd) benefit), but offset by serotype replacement with non-vaccine serotypes
  - PS vaccines have some benefit to prevent IPD but less certain benefit against pneumonia and duration of benefit is limited
  - Young children are very well protected, all other ages less so
- Gaps
  - Uptake of current vaccines low, especially in adults
    - Children: 84% have 3-4 doses by age 2 y (2019)
    - At risk young/middle-aged adults: 26% have 1 dose
    - Adults ≥65 y: 55% have 1 dose (2020)
  - New vaccines will be “chasing serotypes” one way or another for the foreseeable future, with no universal vaccine on the horizon

Canadian Immunization Guide 2016 Canada 2025 Vaccine Coverage Goals

New approaches to pneumococcal vaccine development

Serotypes in Current and New Pneumococcal Vaccines



Adapted from NACI Statement – Awaiting Link

Updated NACI Recommendations in 2023 & 2024

Pneumococcal Vaccine Recommendations Canada

PCV13 (13-valent protein-polysaccharide conjugate vaccine)

- **Healthy infants: 3-dose (2, 4, 12 mos)** or 4-dose (2, 4, 6, 12 mos)
- **High risk infants: 4-dose**
- High risk children 1-17 yrs: 1-2 doses
- High risk adults: 1 dose ≥ 1 year after PPSV23 (but usually before PPSV23)
  - HSCT recipients: 3 doses starting 3-9 months after HSCT

PPSV23 (23-valent plain polysaccharide vaccine)s

- High risk children (>2 yrs) & adults: 1 dose & 1 booster >5 yrs after prior dose
- **Adults ≥65 yrs: 1 dose**
- Adults with high-risk lifestyle factors (smoking, alcoholism, illicit drug use, persons experiencing homelessness): 1 dose

Canadian Immunization Guide 2016

Pneumococcal Vaccine Recommendations Canada

NACI Statement Feb 2023 – **PCV15 & PCV20 in Adults**

- **PCV20** should be offered to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are ≥65 yrs, or who are 50 – 65 yrs living with risk factors placing them at higher risk of pneumococcal disease, or who are 18 – 49 yrs living with immunocompromising conditions. (***Strong NACI recommendation***).

- **PCV15 followed by PPSV23** may be offered as an alternative to PNEU-C-20 to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are ≥65 yrs, or who are 50 – 64 yrs living with risk factors placing them at higher risk of pneumococcal disease, or who are 18 – 64 yrs of age living with immunocompromising conditions. (***Discretionary NACI recommendation***).

NACI Statement 2023-02-24

Pneumococcal Vaccine Recommendations Canada

NACI Statement Feb 2023 – **PCV15 & PCV20 in Adults**

- PCV20 should be offered to adults ≥65 yrs who have been immunized previously with PPSV23 alone, or PCV13 and PPSV3 in series, if it has been at least 5 years from the last dose of any previous pneumococcal vaccine. *(Strong NACI recommendation)*

- PCV20 may be offered to adults ≥65 yrs who have been immunized previously with PCV13 alone, if it has been ≥1 year from the last dose of PCV13 *(Discretionary NACI recommendation)*

- PCV20 should be offered to adults 18 years old or older who received a **hematopoietic stem cell transplant** (HSCT). A primary series of 3 doses of PCV20 starting 3 to 9 months after transplant should be administered 4+ weeks apart, followed by booster dose 12 to 18 months post-transplant (6 to 12 months after the last dose of PCV20). (*Strong NACI recommendation)* Timing should be determined in consultation with the recipient's transplant specialist.

NACI Statement 2023-02-24

Pneumococcal Vaccine Recommendations Canada

NACI Statement Late 2023 – **PCV15 and PCV20 in Children <18 y**

- Either **Pneu-C-15 (PCV15) <u>or</u> Pneu-C-20 (PCV20)** should be the current product of choice for children <5 y/o for routine immunization programs. (***Strong NACI recommendation***)
  - 3-dose or 4-dose schedule (2, 4, (6), 12-15 mos)

- 4-dose PCV20 recommended for children at increased risk of IPD
  - Including finishing primary series started with PCV13 or PCV15
  - (*Strong NACI recommendation*)

NACI Statement – Awaiting Link

Pneumococcal Vaccine Recommendations Canada

NACI Statement Late 2023 – **PCV15 and PCV20 in Children <18 y**

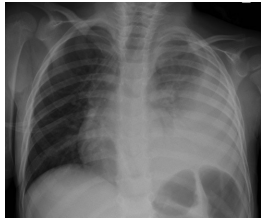
- One catch-up (additional) dose PCV20 for children with have **medical risk factors** and who have completed recommended schedule with PCV13 or PCV15, (*Strong NACI recommendation*)

- One catch-up (additional) dose PCV20 for children with **environmental or living conditions** that result in increased risk for IPD and who have completed recommended schedule with PCV13 or PCV15, (*Strong NACI recommendation*)

- PCV20 should be offered to children who received a hematopoietic **stem cell transplant** (HSCT). A primary series of 3 doses of PCV20 starting 3 to 9 months after transplant should be administered 4+ weeks apart, followed by booster dose 12 to 18 months post-transplant (6 to 12 months after the last dose of PCV20). (*Strong NACI recommendation)* Timing should be determined in consultation with the recipient's transplant specialist.

NACI Statement – Awaiting Link

Conclusions



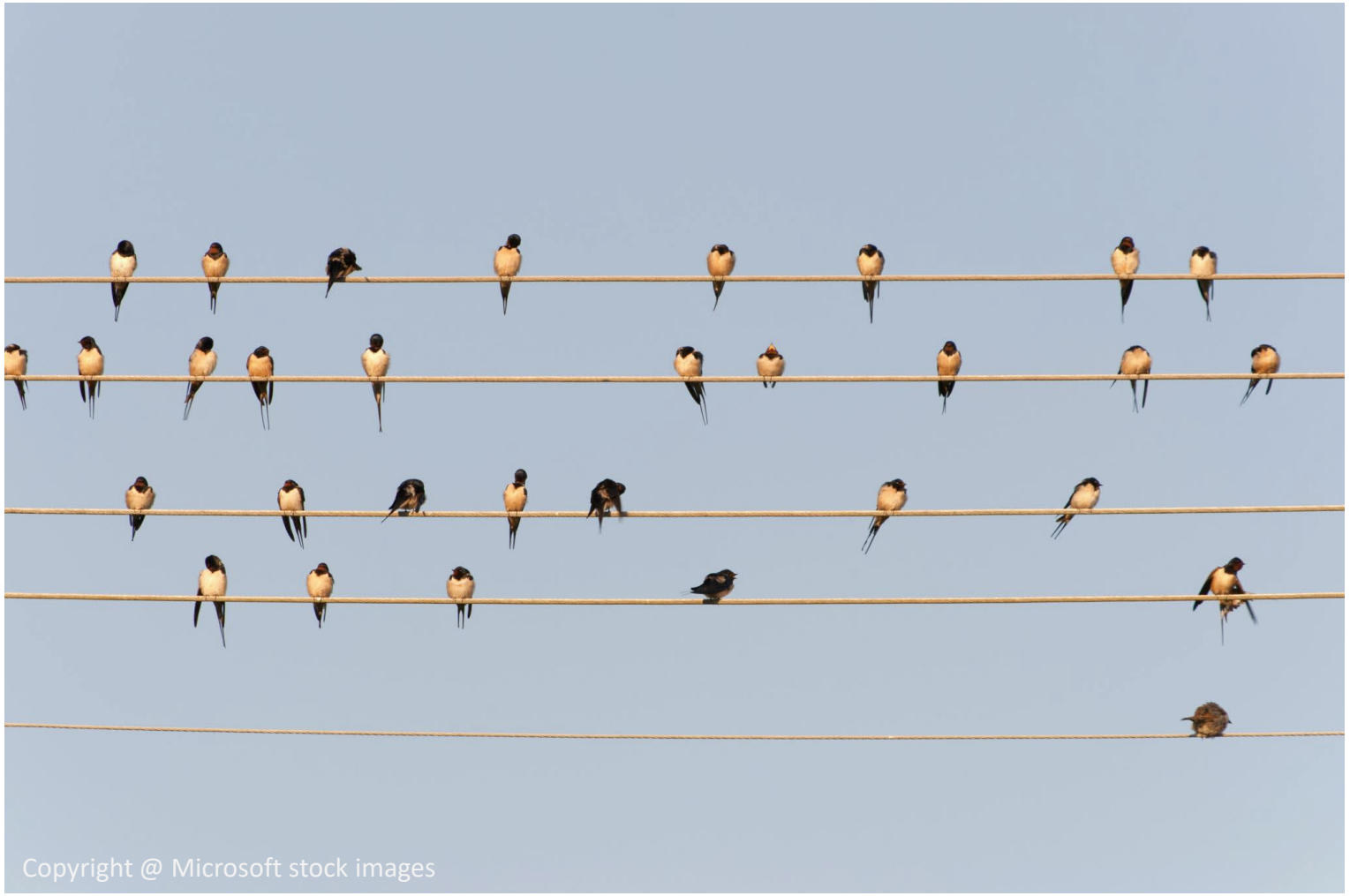
- Pneumococcal infections still cause high disease burden globally, especially in children and older adults, and in those with specific health conditions and other risk factors.

- Polyvalent polysaccharide vaccines (plain and protein-conjugate) are highly effective globally against vaccine-serotype infections but their benefits are partially offset by serotype replacement.

- 2 expanded-valency PCVs (PCV15, PCV20) now approved and recommended for use in Canada.

- Higher valency PCVs may/will soon replace PPSV23.

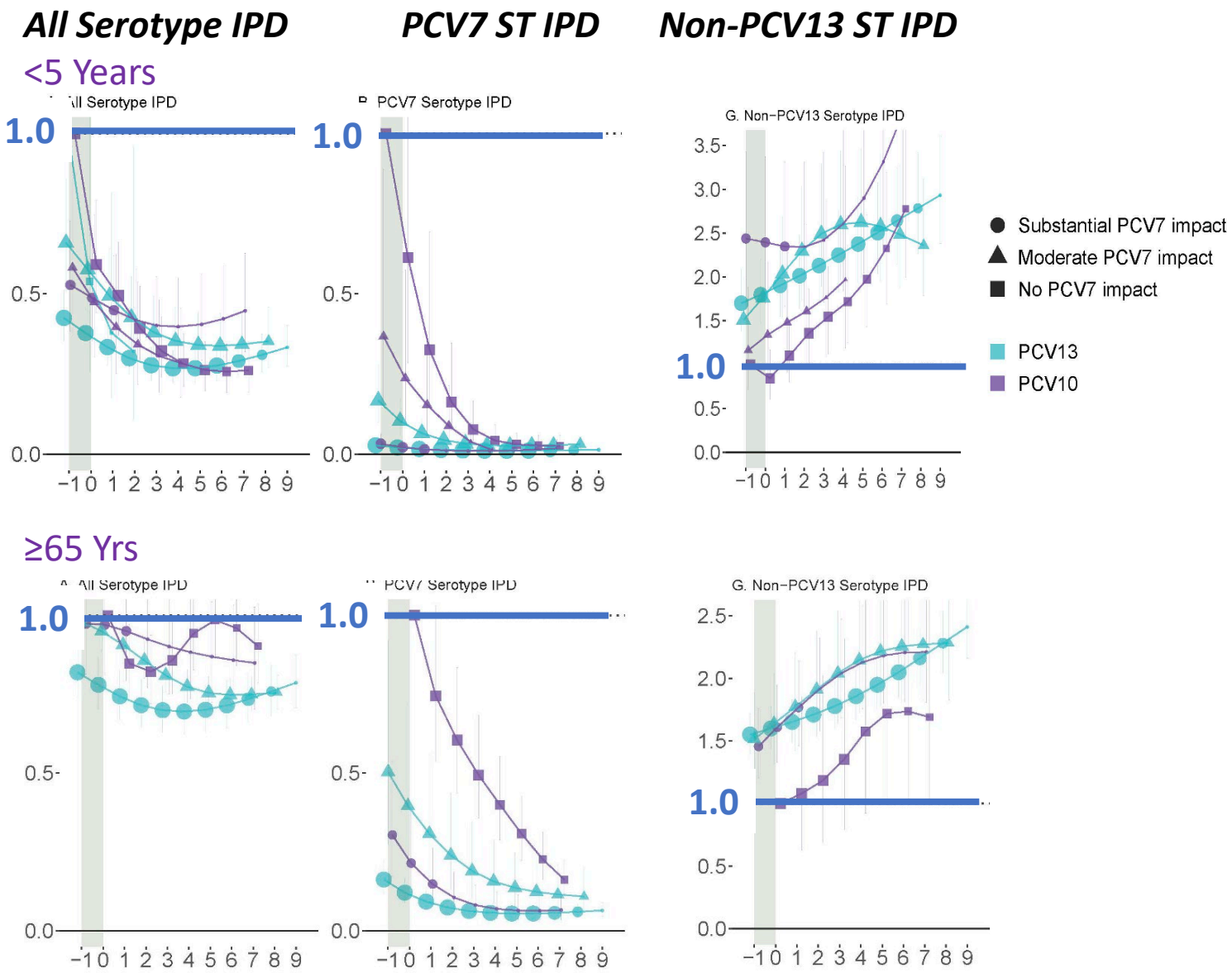
Additional Slides for Q & A



Impact of Serotype – Specific Pneumococcal Vaccines

- **PSERENADE** – WHO, BMGF, JHU initiative
- >525,000 IPD cases from 47 surveillance sites in 30 countries in all WHO regions, pre- and post-PCV10/PCV13 x up to 9 years
- Excellent direct effect to prevent vaccine-ST IPD in vaccine recipients
- Good to excellent indirect (herd) effect in non-vaccine recipients
- Serotype replacement with non-vaccine serotypes has, and will, limit long term benefit of serotype-specific vaccines

Incidence Rate Ratio (IRR) up to 9 years after PCV10/13



From Bennett et al (Kellner JD co-author). ISPPD 2022, Toronto

Approaches to Polyvalent Conjugate Pneumococcal Vaccines

- Capsular polysaccharide from multiple prevalent pediatric serotypes conjugated to protein antigen (e.g., CRM197, from diphtheria)
  - Focus on prevalent pediatric serotypes from >100 known serotypes - **PCV7/10/13**
- *Current and new approaches*
  - Increased number of serotypes including those prevalent in adult disease
    - **PCV15, PCV20**
  - New polysaccharide-protein complex with pneumococcal virulence proteins
    - **PCV24 (AFX3772), PCV30**
  - Choosing serotypes: focus on “residual” serotypes prevalent in adults, with fewer pediatric serotypes
    - **PCV21 (V116)**
  - Work on universal protein vaccines continues

Strength of NACI Recommendations

Recommendation(s) based on factors not isolated to strength of evidence (e.g., consider public health need)	Strong	Discretionary
Wording	"should/should not be offered"	"may/may not be offered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), **or** Known/Anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages are closely balanced with known/anticipated disadvantages, **or** uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present.	A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

NACI Statement 2023-03-21