

# Updated Recommendations for Pneumococcal Immunization in Adults, Including the Use of a 21-valent Pneumococcal Conjugate Vaccine

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# Key Highlights

- In Ontario, children from 6 weeks to under 5 years of age, individuals 5 to 64 years of age with certain medical or non-medical conditions who are at increased risk of invasive pneumococcal disease (IPD), and adults 65 years of age and older who have not received all publicly funded pneumococcal vaccines are eligible for pneumococcal immunization programs.
- As of June 2024, Ontario transitioned to the 15-valent pneumococcal conjugate vaccine (PCV15) for the routine pediatric pneumococcal immunization program and the 20-valent pneumococcal conjugate vaccine (PCV20) for the high-risk and routine older adult programs.
- In May 2025, the Ontario Immunization Advisory Committee (OIAC) updated its recommendation for the adult pneumococcal immunization programs. These updated recommendations come after Health Canada authorized a new 21-valent pneumococcal conjugate vaccine (PCV21) and the National Advisory Committee on Immunization (NACI) released updated guidance on PCV21.
- Based on scientific and programmatic considerations and assuming Ontario will maintain the current eligibility for the adult pneumococcal immunization programs, the OIAC recommends:
  - The use of PCV21 for all adults  $\geq$ 65 years of age.
  - The continued use of PCV20 for eligible adults 18 to 64 years of age at increased risk of IPD (i.e., no change to the current high-risk program).
- The OIAC additionally recommends that the Ministry of Health continue to monitor the serotype distribution and burden of disease in these populations to inform whether OIAC needs to revise these recommendations in the future and align its eligibility for the high-risk program with the risk factors defined within the <u>Canadian Immunization Guide chapter on pneumococcal vaccines</u>.<sup>1</sup>

## Overview

The OIAC previously reviewed the use of pneumococcal vaccines in adults following the authorization of PCV20 its statement released in September 2023, <u>Recommendation: New Health Canada Authorized</u> <u>Pneumococcal Conjugate Vaccines for Adults Aged  $\geq$ 18 Years</u>.<sup>2</sup> In this statement, the OIAC recommended PCV20 for the adult pneumococcal immunization programs. In June 2024, Ontario implemented PCV20 for both the routine older adult (all adults  $\geq$ 65 years of age) and high-risk (children and adults 6 weeks to 64 years of age at increased risk of IPD) programs.<sup>3</sup> Currently, only individuals who have not received all publicly funded pneumococcal immunization program from PCV13 to PCV15.

On July 15, 2024, Health Canada authorized PCV21 for adults ≥18 years of age. In November 2024, NACI released, <u>Recommendations on the use of pneumococcal vaccines in adults, including PNEU-C-21.</u><sup>4</sup> In their statement, NACI recommends that adult pneumococcal immunization programs should include at least one of PCV20 or PCV21 for all adults ≥65 years of age and adults 18 to 64 years of age who are at increased risk of IPD. They advise that provinces and territories should consider local epidemiology and programmatic factors when deciding between these two products.

To inform its programmatic decision for Ontario, the Ministry of Health requested that the OIAC provide an updated recommendation on whether to continue using PCV20 or transition to PCV21 for the routine older adult and high-risk adult pneumococcal immunization programs. The committee met on February 12 and April 9, 2025, to review and discuss the evidence on the burden of disease, immunogenicity and safety, equity, ethics, feasibility and acceptability (EEFA) considerations, and cost-effectiveness.

In an electronic vote held from April 16 to May 6, 2025, almost all OIAC voting members supported transitioning to PCV21 for the routine older adult program for all adults ≥65 years of age. Additionally, most members supported the ongoing use of PCV20 for the high-risk program for adults 18 to 64 years of age at increased risk of IPD. Some members acknowledged that select high-risk groups may benefit from PCV21 but did not reach a consensus on which high-risk groups, if any, should be offered PCV21 given uncertainty in the serotype distribution following the recent changes to Ontario's pneumococcal immunization programs, shifting local epidemiology, and implementation concerns around program complexity. The OIAC will update these recommendations as needed based on ongoing monitoring of the serotype distribution and burden of disease in these populations.

#### Recommendations

- 1. The OIAC recommends PCV21 for all adults ≥65 years of age.
- 2. The OIAC continues to recommend PCV20 for eligible adults 18 to 64 years of age at increased risk of IPD, except for hematopoietic stem cell transplant (HSCT) recipients. As stated in the updated NACI guidelines, HSCT recipients should receive both PCV20 and PCV21 according to a 4-dose schedule after consultation with the transplant specialist.<sup>4</sup>

# Background

*Streptococcus pneumoniae* is a common cause of bacterial respiratory tract infections and a leading cause of community-acquired pneumonia.<sup>5</sup> S. pneumoniae can also cause IPD, including sepsis, bacteremic pneumonia, bacteremia, and meningitis.<sup>6</sup> Older adults and individuals with certain medical conditions or risk factors are at increased risk of morbidity and mortality due to pneumococcal disease.<sup>6</sup> As of 2023, national survey data shows that uptake of pneumococcal vaccines for these populations was only 42% in Ontario.<sup>7</sup>

On May 9, 2022, Health Canada authorized PCV20 (PREVNAR20<sup>™</sup>, Pfizer) for the prevention of pneumonia and IPD caused by 20 different *S. pneumoniae* serotypes in adults ≥18 years of age; this indication was later expanded to children 6 weeks to 17 years of age.<sup>8</sup> On July 15, 2024, Health Canada authorized PCV21 (CAPVAXIVE<sup>®</sup>, Merck) for the prevention of IPD caused by 21 different *S. pneumoniae* serotypes in adults ≥18 years of age.<sup>9</sup> PCV21 is not authorized for use in children <18 years of age. Compared with PCV20, PCV21 contains 10 unique serotypes, one cross-reactive serotype and 10 shared serotypes (Figure 1).



#### Figure 1: Serotype Coverage in Currently Authorized Pneumococcal Vaccines

PCV20 contains 9 unique, non-cross-reactive serotypes (vs. PCV21)

PCV20 and PCV21 contain 10 shared serotypes PCV21 contains 10 unique, non-cross-reactive serotypes (vs. PCV20)

PPV=pneumococcal polysaccharide vaccine; PCV=pneumococcal conjugate vaccine

\* Serotypes 15B/C are considered cross-reactive due to reversible switching between serotypes during infection.

+ Serotype 6A provides cross-protection against serotype 6C.

**‡** PCV21 contains serotype 20A.

## Changes to Ontario's Pneumococcal Immunization Program

Ontario has two publicly funded pneumococcal immunization programs for adults: 1) a routine program for all adults  $\geq$ 65 years of age and 2) a high-risk program for adults 18 to 64 years of age who are at increased risk of IPD due to certain medical or non-medical conditions. Starting in June 2024, Ontario transitioned to PCV15 for the routine pediatric program and PCV20 for the routine older adult and pediatric and adult high-risk programs (<u>Table 1</u>). Since then, all adults  $\geq$ 65 years of age and adults 18 to 64 years of age at increased risk of IPD who have not received all publicly funded pneumococcal vaccines have been eligible for PCV20 according to appropriate age and risk criteria.<sup>3</sup>

#### Table 1: Current Eligibility for the Pneumococcal Immunization Program in Ontario

Age Group	Program	Eligibility <sup>*</sup>
Children 6 weeks to 4 years of age	Routine	PCV15 (up to 3 doses)
Children 6 weeks to 4 years of age	High-risk	PCV20 (up to 4 doses)
Children and adults 5 to 64 years of age	High-risk	PCV20 (1 dose) $^{\dagger}$
Adults ≥65 years of age	Routine	PCV20 (1 dose) $^{\dagger}$

HSCT=hematopoietic stem cell transplant; PCV=pneumococcal conjugate vaccine

\* Only individuals who have not previously completed or received all publicly funded pneumococcal vaccines are currently eligible for PCV15 or PCV20.

<sup>+</sup> HSCT recipients are eligible to receive 4 doses of PCV20.

## Updated NACI Recommendations

In November 2024, NACI updated its recommendations for pneumococcal vaccination in adults, recommending that all adults ≥65 years of age and adults 18 to 64 years of age at increased risk of IPD should receive one dose of either PCV20 or PCV21 (<u>Table 2</u>).<sup>4</sup> This recommendation applies to vaccine-naïve adults, those with an unknown vaccination history, and adults previously immunized with PCV13, PCV15 and/or the 23-valent pneumococcal polysaccharide vaccine (PPV23).

## Table 2: Summary of Updated NACI Recommendations for Adult Pneumococcal Vaccination<sup>4</sup>

Group	Recommendation	Strength of Recommendation
Adults ≥65 years of age	PCV20 or PCV21 (1 dose)	Strong
Adults 18 to 64 years of age at increased risk of IPD <sup>*</sup>	PCV20 or PCV21 (1 dose)	Strong
Adults ≥18 years of age who received a HSCT after consultation with the transplant specialist	PCV20 and PCV21 (4 doses total) $^{\dagger}$	Strong

HSCT=hematopoietic stem cell transplant; IPD=invasive pneumococcal disease; NACI=National Advisory Committee on Immunization; PCV=pneumococcal conjugate vaccine

\* Risk factors for IPD include certain medical conditions and social, behavioural, and environmental factors, as defined in the updated Canadian Immunization Guide chapter on pneumococcal vaccines (2025).<sup>1</sup>

<sup>+</sup> For HSCT recipients, NACI recommends that a primary series of 3 doses starting 3 to 9 months after transplant should be administered at least 4 weeks apart, followed by a booster dose 12 to 18 months post-transplant (6 to 12 months after the last dose). To broaden the serotype coverage, the higher valency vaccine that was not given as part of the primary series can be offered as the booster dose (i.e., 3 doses of PCV20 + 1 dose of PCV21, or 3 doses of PCV21 + 1 dose of PCV20).

# **Evidence Summary and Considerations**

The OIAC considered the evidence on product choice (PCV20 or PCV21) for: 1) the routine older adult program for all adults  $\geq$ 65 years of age and 2) the high-risk program for adults 18 to 64 years of age who are at increased risk of IPD. For the high-risk program, individuals at increased risk of IPD included those with certain medical conditions and/or social, behavioural, and environmental risk factors, as defined in the <u>Canadian Immunization Guide chapter on pneumococcal vaccines</u> (updated in May 2025).<sup>1</sup> To inform its recommendation, the OIAC reviewed and discussed evidence on scientific (i.e., burden of disease, vaccine characteristics) and programmatic (i.e., EEFA considerations, cost-effectiveness) factors.

The following factors were influential in its decision to recommend PCV21 for all adults ≥65 years of age and PCV20 for adults 18 to 64 years of age who are at increased risk of IPD:

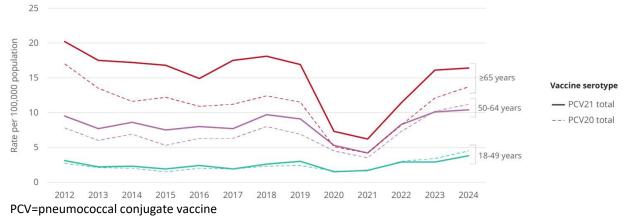
- Burden of disease: Based on recent IPD epidemiology in Ontario, serotypes contained within PCV21 cause a greater burden of disease in older adults ≥65 years of age and individuals who are immunocompromised due to disease or therapy. Conversely, serotypes contained within PCV20 cause a greater burden of disease in adults 18 to 64 years of age, particularly in adults with non-immunocompromising medical conditions and those who are unhoused/underhoused. Following the COVID-19 pandemic, the epidemiology of IPD in Ontario has shifted toward more PCV20-unique serotypes across all age groups but especially in younger adults. Ongoing monitoring will be required to determine if this trend continues following the introduction of PCV15 and PCV20 for the routine and high-risk pediatric pneumococcal immunization programs, respectively.
- Vaccine characteristics: PCV20 contains nine non-cross-reactive serotypes not included in PCV21, while PCV21 contains 10 non-cross-reactive serotypes not included in PCV20. In immunogenicity trials, PCV21 was considered non-inferior to PCV20 for shared serotypes in adults ≥50 years of age, with similar safety profiles.<sup>10,11</sup>
- EEFA considerations: OIAC members noted that using three different vaccine products (PCV15, PCV20 and PCV21) may make it more difficult for immunization providers to assess program eligibility, order and store vaccines, and manage the immunization schedule, potentially impacting vaccine acceptability and uptake. However, most members felt that this increased complexity could be potentially mitigated if the Ministry of Health adopts an age-based program eligibility for PCV21. Members recommended that Ontario transition to PCV21 for all adults ≥65 year of age, while continuing to use PCV20 for all eligible children and adults 6 weeks to 64 years of age at increased risk of IPD, rather than select high-risk groups, since PCV20 is currently being used for the pediatric high-risk program in Ontario and PCV21 is not authorized for children. This recommendation would also allow for broader serotype coverage if individuals at increased risk of IPD who are vaccinated with PCV20 become eligible for PCV21 once they reach age 65. A minority of members preferred a single-product option for the adult immunization programs (i.e., either PCV20 or PCV21 for both adult populations with PCV15 continuing to be used for the routine pediatric program and PCV20 continuing to be used for the high-risk pediatric program) citing implementation concerns.
- Cost effectiveness: In NACI's cost-utility analysis, PCV21 was consistently found to be the optimal strategy in older adults ≥65 years of age regardless of assumptions around indirect effects and vaccine price.<sup>4,12</sup> Conversely, the cost-effectiveness of PCV21 relative to PCV20 in younger adults was highly dependent on the serotype distribution and assumptions around indirect effects, vaccine price, and relative risk of IPD. The most recent 2024 serotype distribution data in Ontario shows a greater burden of disease due to PCV20-unique serotypes in younger adults, notably in those 50 to 64 years of age, compared with the 2022 national data used to inform NACI's modelling, which would likely favour PCV20 as a more cost-effective option in this age group.

## IPD Epidemiology and Burden of Disease in Ontario

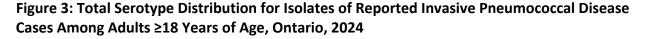
OIAC members reviewed epidemiological data on reported IPD cases in Ontario from 2012 to 2024 using data from the Integrated Public Health Information System (iPHIS). These provincial surveillance data were supplemented with active surveillance data from the Toronto Invasive Bacterial Diseases Network (TIBDN) on IPD incidence in populations at increased risk of IPD in the Toronto and Peel regions (guest presenter: Dr. Allison McGeer, University of Toronto).

Confirmed IPD case rates in Ontario declined during the peak of the COVID-19 pandemic (2020–2021) but have since returned to pre-pandemic levels in most age groups. Adults  $\geq$ 65 years of age, particularly those  $\geq$ 85 years of age, experience the highest burden of IPD (Figure 2). In this age group, serotypes contained within PCV21 cause a greater burden of disease compared with those contained within PCV20. Since the COVID-19 pandemic, the opposite has been true for younger adults: serotypes contained within PCV20 cause a greater burden of disease than those contained within PCV21. In 2024, the absolute difference in the proportion of IPD cases caused by PCV21 versus PCV20 serotypes was –12.6% in adults 18 to 49 years of age, –5.8% in adults 50 to 64 years of age, and +12.7% in adults  $\geq$ 65 years of age (Figure 3).

Figure 2: Confirmed Invasive Pneumococcal Disease Case Rate Due to Serotypes Contained within PCV20 or PCV21 by Age Group, Ontario, 2012 to 2024



Data source: iPHIS (data extracted on March 26, 2025); excludes isolates with missing serotype information.





PCV=pneumococcal conjugate vaccine

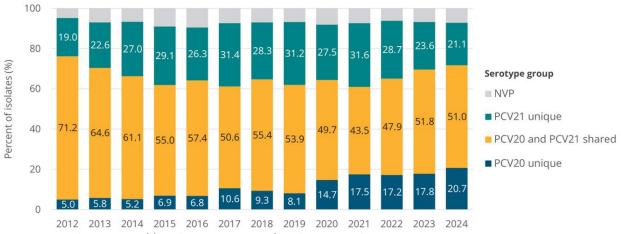
Absolute difference ( $\Delta$ ) calculated as % of isolates due to PCV21-unique serotypes minus % of isolates due to PCV20-unique serotypes.

Data source: iPHIS (data extracted on March 26, 2025); excludes isolates with missing serotype information.

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These overall age-related trends are consistent with data from the TIBDN stratified by age and risk group. Based on unpublished TIBDN data from 2022 to 2024, PCV21 serotypes were more common than PCV20 serotypes in older adults  $\geq$ 65 years of age (absolute difference=+20.6%) and adults 18 to 64 years of age with immunocompromising conditions (+13.6%). Conversely, PCV20 serotypes were more common than PCV21 serotypes in adults 18 to 64 years of age who had no underlying illness (-4.7%) or non-immunocompromising conditions (-7.6%) and in those experiencing homelessness (-13.9%).

Following the COVID-19 pandemic, the epidemiology of IPD has shifted toward more PCV20-unique serotypes over time (Figure 4). Among all adults ≥18 years of age, the absolute difference between PCV21 versus PCV20 serotypes decreased from +20.9% during the pre-pandemic period (2015–2019) to +12.5% during the pandemic-affected period (2020–2022) to +2.9% during the post-pandemic period (2023–2024). This trend was most pronounced among younger adults 18 to 49 years of age but was also apparent among middle-aged adults 50 to 64 years of age and older adults ≥65 years of age.

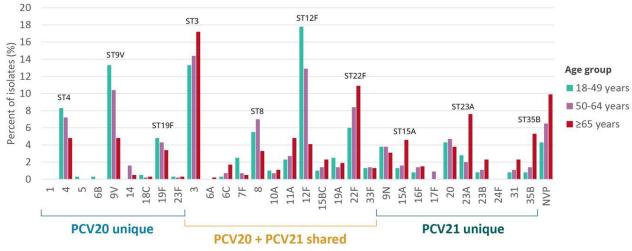


# Figure 4: Serotype Group Distribution for Isolates of Reported Invasive Pneumococcal Disease Cases Among Adults ≥18 Years of Age, Ontario, 2012 to 2024

NVP=not vaccine preventable; PCV=pneumococcal conjugate vaccine Data source: iPHIS (data extracted on March 26, 2025); excludes isolates with missing serotype information.

These age-related differences in the serotype distribution were driven by a greater detection of PCV20unique serotypes (e.g., 4 and 9V) in younger adults, largely associated with IPD outbreaks among people experiencing homelessness,<sup>13</sup> and a greater detection of PCV21-unique serotypes (e.g., 15A, 16F, 23A and 23B) in older adults (Figure 5). Older adults were also more likely to have IPD caused by serotypes that were not vaccine preventable. Across all age groups, PCV20/PCV21-shared serotype 3 was among the most frequent serotype detected among IPD isolates in Ontario. Older adults  $\geq$ 65 years of age, in particular, may experience reduced protection against community-acquired pneumonia due to serotype 3 based on vaccine efficacy studies using the older PCV13 vaccine.<sup>14,15</sup>

#### Figure 5: Serotype Distribution for Isolates of Reported Invasive Pneumococcal Disease Cases Among Adults ≥18 Years of Age, Ontario, 2024



NVP=not vaccine preventable; PCV=pneumococcal conjugate vaccine; ST=serotype Data source: iPHIS (data extracted on March 26, 2025); excludes isolates with missing serotype information.

## Immunogenicity and Safety

OIAC members reviewed immunogenicity evidence that was relevant to the current policy question from two industry-sponsored, pivotal phase III trials.<sup>10,11</sup> A more detailed summary of immunogenicity and safety evidence can be found in the recent NACI statement on PCV21 (2024).<sup>4</sup>

In one trial (V116-003), vaccine-naïve adults ≥50 years of age were randomized to receive either PCV20 or PCV21.<sup>10</sup> In vaccine-naïve adults, PCV21 met the pre-specified non-inferior criteria for all 10 shared serotypes compared with PCV20 but had statistically lower immune responses for shared serotypes 6A, 10A, 19A and 22F at one month post-immunization. Conversely, PCV20 had statistically lower immune responses for shared serotypes 3, 8, 11A and 33F compared with PCV21. The clinical significance of these statistical differences in immunogenicity is unknown in the absence of efficacy/effectiveness data. PCV21 met the pre-defined superiority criteria for 10 out of 11 PCV21-unique serotypes; superiority was not achieved for serotype 15C due to cross-reactivity with serotype 15B contained in PCV20. Immune responses for the 10 PCV20-unique serotypes were not reported.

In the other trial (V116-006), vaccine-experienced adults ≥50 years of age were randomized to receive PCV21 or PCV15 (if previously vaccinated with PPV23), PCV21 or PPV23 (if previously vaccinated with PCV13) or PCV21 only (if previously vaccinated with PCV13/15 and PPV23 or PCV15 alone).<sup>11</sup> In vaccine-experienced adults, PCV21 elicited comparable immune responses to PCV15- or PPV23-shared serotypes and higher immune responses to PCV21-unique serotypes at one-month post-vaccination.

In terms of safety, OIAC members reviewed pooled PCV21 safety data from approximately 6,000 individuals presented to NACI.<sup>4</sup> As with other PCVs, PCV21 was safe and well-tolerated with a similar frequency of adverse events (e.g., injection site pain, fatigue, headache) to comparator vaccines and with severe events occurring in less than 1% of study participants.<sup>4,10</sup>

## **Cost Effectiveness**

OIAC members reviewed two sources of cost-effectiveness data from NACI: 1) a systematic review of PCV21 cost-effectiveness studies in adults; and 2) a cost-utility analysis of PCV21 in Canadian adults (guest presenter: Dr. Ashleigh Tuite, Public Health Agency of Canada).<sup>12,16</sup> A more detailed summary of economic evidence can be found in the recent NACI statement on PCV21 (2024).<sup>4</sup>

### NACI Systematic Review of PCV21 Cost Effectiveness in Adults

NACI's systematic review included five cost-effectiveness studies.<sup>17-21</sup> Four studies were conducted in the United States and one in the Netherlands; none were conducted in Canada. One was industry-sponsored by Merck, the manufacturer of PCV21. All five studies used static cohort models, presented the societal perspective, and included indirect effects from pediatric pneumococcal immunization programs in primary or sensitivity analyses. Except for the study from the Netherlands, which assumed price parity, all four U.S. studies assumed a higher vaccine price for PCV21 than PCV20 (relative difference=+10–33%).

In all five studies, where serotypes contained in PCV21 accounted for more IPD cases than PCV20, PCV21 was generally more cost-effective than PCV20 at a threshold of \$50,000 per quality-adjusted life year (QALY) in adults  $\geq$ 65 years of age and adults 18 to 49 years of age with specific risk conditions.

### NACI Cost-Utility Analysis of PCV21 in Adults

In addition to the systematic review, NACI conducted a cost-utility analysis using a static cohort model to estimate sequential incremental cost-effectiveness ratios (ICERs) (measured in 2023 Canadian dollars per QALY).<sup>12</sup> Their model included three age cohorts: 1) all adults ≥65 years of age (vaccination at 65 years of age), 2) adults 50 to 64 years of age with additional risk factors for IPD (vaccination at 50 years of age), and 3) adults 18 to 49 years of age with additional risk factors for IPD (vaccination at 33 years of age, corresponding to the midpoint of the age group). Risk factors for IPD included immunocompromising conditions, other chronic medical conditions, and being unhoused. NACI used risk multipliers based on assumed relative risks of pneumococcal disease and mortality to estimate the impact of vaccination in these populations; they did not have data on serotype distribution by risk factor to inform their models.

In their primary analysis, NACI used Canadian list prices (\$109.91/dose for PCV20 and \$129.90/dose for PCV21, relative difference=18%) but varied vaccine price in a two-way sensitivity analysis. Their primary analysis assumed no indirect effects from pediatric vaccination. In sensitivity analyses, they included indirect effects due to pediatric PCV15 or PCV20 programs (50% reduction in pneumococcal disease due to vaccine serotypes) and serotype replacement (100% replacement) over a period of five years.

NACI used Canada-wide IPD data from two time periods (2015–2019 and 2022) in separate models to account for shifts in the serotype distribution during the COVID-19 pandemic. OIAC members focused on results using the 2022 data, as this distribution was more reflective of the current IPD epidemiology in Ontario. Although NACI does not use an explicit cost-effectiveness threshold, optimal strategies are summarized below based on a \$50,000/QALY threshold for the health system perspective (Table 3). Findings did not substantially differ using different thresholds or the societal perspective.

	Optimal Strategy (ICER for PCV21, $(QALY)^{\dagger}$		
Population	No Indirect Effects	Indirect Effects from PCV15	Indirect Effects from PCV20
All adults ≥65 years of age	PCV21 (dominant)	PCV21 (dominant)	PCV21 (dominant)
Adults 50–64 years of age who are unhoused	<b>PCV20</b> (\$74,501)	PCV21 (dominant)	PCV21 (dominant)
Adults 50–64 years of age who are immunocompromised	<b>PCV20</b> (\$341,785)	<b>PCV21</b> (\$13,149)	PCV21 (dominant)
Adults 50–64 years of age with other chronic medical conditions	<b>PCV20</b> (\$1,225,461)	<b>PCV20</b> (\$101,313)	<b>PCV21</b> (\$6,496)
Adults 18–49 years of age who are unhoused	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)
Adults 18–49 years of age who are immunocompromised	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)
Adults 18–49 years of age with other chronic medical conditions	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)	PCV20 (dominated by PCV20)

ICER=incremental cost-effectiveness ratio; QALY=quality-adjusted life year

\* NACI results are summarized based on the 2022 serotype distribution data using a health system perspective at a cost-effectiveness threshold of \$50,000/QALY.

<sup>+</sup> PCV21 is considered the optimal strategy when the ICER for PCV21 is dominant (i.e., more effective and cost saving) compared with PCV20 or is less than \$50,000/QALY; PCV20 is considered the optimal strategy when the ICER for PCV21 is dominated by PCV20 or is greater than \$50,000/QALY.

Overall, NACI found that the choice of the optimal vaccine strategy is highly dependent on serotype distribution. In adults ≥65 years of age, where serotypes contained in PCV21 accounted for more IPD cases than PCV20 in 2022, PCV21 was the dominant strategy (i.e., more effective and less costly) compared with PCV20 regardless of assumptions around indirect effects and vaccine price.

In adults 50 to 64 years of age with risk factors for IPD, where serotypes contained in PCV21 and PCV20 accounted for similar proportions of IPD cases, PCV20 was the optimal strategy (i.e., ICER for PCV21 greater than \$50,000/QALY) when no indirect effects were assumed, while PCV21 was generally the dominant or optimal strategy (i.e., ICER for PCV21 less than \$50,000/QALY) when indirect effects from PCV15 or PCV20 were assumed. Findings in adults 50 to 64 years of age were sensitive to assumptions around vaccine price, with PCV20 favoured when the price of PCV21 increased and *vice versa*.

In adults 18 to 49 years of age with risk factors for IPD, where serotypes contained in PCV20 accounted for more IPD cases than PCV21, PCV20 was the dominant strategy compared with PCV21 or no vaccination regardless of assumptions around indirect effects and vaccine price.

#### Comparison with 2024 Ontario Epidemiology Data

The most recent 2024 iPHIS data in Ontario showed a reduced burden of disease due to PCV21 (vs. PCV20) serotypes in adults 50 to 64 years of age compared with the 2022 national data used to inform NACI's modelling where the proportions were more similar in this age group (-5.8% Ontario vs. -0.1% NACI). Differences in serotype distribution were also noted in younger adults 18 to 49 years of age (-12.6% vs. -14.2%) and older adults  $\geq 65$  years of age (+12.7% vs. +21.2%).

The impact of these serotype differences on NACI's cost-effectiveness models is unknown. In particular, the findings in adults 50 to 64 years of age should be interpreted with caution as model inputs may not reflect the current Ontario context. Furthermore, 2022–2024 TIBDN data show a greater burden of PCV21 serotypes in adults who are immunocompromised and a greater burden of PCV20 serotypes in adults with underlying illness who are not immunocompromised and those experiencing homelessness in Ontario. The NACI models did not account for these risk group-specific serotype distributions. However, as the optimal strategy in NACI's modelling was highly dependent on serotype distribution, these trends would likely favour PCV21 for the former but PCV20 for the latter risk groups.

# **Additional Considerations**

- Given the shifting IPD epidemiology and recent programmatic changes in Ontario, the OIAC suggests that these recommendations be reviewed in five to 10 years. Ongoing surveillance will be required to monitor the serotype distribution and burden of disease in adults, including potential indirect effects and serotype replacement following PCV15 and PCV20 implementation for the pediatric immunization programs, as well as to determine the long-term effectiveness of pneumococcal conjugate vaccines and need for booster doses.
- Although out of scope for this discussion on adult pneumococcal immunization programs, the OIAC reinforces its recommendation of PCV20 for the routine pediatric program.<sup>22</sup> If the Ministry of Health adopts the OIAC's recommendations, pneumococcal immunization program delivery would be simplified with only two products (PCV20 for the routine pediatric and high-risk programs and PCV21 for the routine older adult program) available in Ontario.
- The OIAC encourages the Ministry of Health to align its eligibility for the high-risk pneumococcal immunization program with the risk factors defined within the <u>Canadian Immunization Guide</u> <u>chapter on pneumococcal vaccines</u>.<sup>1</sup> In particular, individuals with asthma requiring medical care in the preceding 12 months and those with certain social, behavioural, and environmental risk factors, including those who are unhoused/underhoused, live in communities or settings experiencing sustained high IPD rates, smoke or use substances (i.e., alcohol misuse, cocaine use and injection drug use), are not currently eligible for pneumococcal immunization under Ontario's publicly funded schedule.<sup>3</sup> The OIAC previously recommended PCV20 for adults 18 to 64 year of age who are unhoused/underhoused and adults 50 to 64 years of age within these other risk groups.<sup>2</sup> The more recent NACI guidelines (2024) extend these high-risk recommendations to all age groups.<sup>4</sup> The OIAC did not re-review the risk groups who would benefit from publicly funded pneumococcal vaccination and instead defer to its previous recommendation and the updated NACI guidelines.
- The OIAC further encourages the Ministry of Health to implement targeted strategies to promote pneumococcal immunization and improve vaccine uptake for adults ≥65 years of age and individuals at increased risk of IPD given that immunization coverage for pneumococcal vaccine remains below national targets.<sup>7</sup>
- The OIAC continues to recommend that Ontario develop and implement a comprehensive electronic immunization registry to provide real-time, individual-level immunization data to facilitate program monitoring, evaluation and research.<sup>23</sup>

# References

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# About the Ontario Immunization Advisory Committee

The Ontario Immunization Advisory Committee (OIAC) was established in August 2021 at the request of the Chief Medical Officer of Health. The Committee provides scientific and technical advice to Public Health Ontario on vaccines and immunization matters, including program implementation in Ontario, priority populations, clinical guidance, and vaccine safety and effectiveness.

OIAC's work focuses 'on publicly funded vaccines and immunization programs in Ontario, and those under consideration for new programming. The OIAC provides advice by applying scientific knowledge and the best available evidence, in addition to feasibility, acceptability and other implementation considerations.

For more information about the OIAC and its members contact secretariat@oahpp.ca.

## About Public Health Ontario

Public Health Ontario is an agency of the Government of Ontario dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world. For more information about PHO, visit <u>publichealthontario.ca</u>.

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OIAC members with real or perceived conflicts of interest abstained from discussion and decisions related to these recommendations.

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