An Advisory Committee Statement (ACS)

National Advisory Committee on Immunization (NACI)

Recommendations on the use of pneumococcal vaccines in adults, including PNEU-C-21: Supplemental clinical evidence synthesis

PROTECTING AND EMPOWERING CANADIANS TO IMPROVE THEIR HEALTH

Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

—Public Health Agency of Canada

Également disponible en français sous le titre :

Recommandations sur l'utilisation des vaccins antipneumococciques chez l'adulte, y compris le PNEU-C-21 : Synthèse des preuves cliniques supplémentaires

To obtain additional information, please contact:

Public Health Agency of Canada 130 Colonnade Rd
A.L 6501H
Ottawa, ON K1A 0K9 Toll free: 1-844-280-5020
Fax: 613-941-5366
TTY: 1-800-465-7735
E-mail: publications-publications@hc-sc.gc.ca

Publication date: November 15, 2024

Cat.: HP40-373/2024-2E-PDF ISBN: 978-0-660-74240-3 Pub.: 240600

Preamble

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

This document contains supplemental information for the NACI guidance on **Recommendations on the use of pneumococcal vaccines in adults, including PNEU-C-21.** A summary of the clinical trials is provided in Table 6 of NACI statement.

Table S-1. Summary of evidence from studies [1] [2] [3] comparing Pneu-C-21 and Pneu-P-23

Measured outcome	Vaccine naïve adults	Previously vaccinated adults ≥50 years of age
Immunogenicity		
Opsonophagocytic activity (OPA) geometric mean titer (GMT)	OPA GMTs for the common serotypes shared between Pneu-C-21 and Pneu-P-23 were comparable. For the 9 unique serotypes to Pneu-C-21, OPA GMTs were higher in the Pneu-C-21 group compared to the Pneu-P-23 group.	Immune responses were overall comparable between intervention groups (Pneu-C-21 or Pneu-P-23) for common serotypes; OPA GMT point estimates following Pneu-C-21 administration were higher for some serotypes and lower for others. In adults previously immunized with Pneu-C-13, Pneu-P-23 or Pneu-C-13+Pneu-P-23, Pneu-C-21 was immunogenic for all 21 serotypes contained in the vaccine in all age groups (as assessed by serotype-specific OPA GMTs at 30 days postvaccination).
% with ≥4-fold rise in OPA responses	The proportions of participants with a ≥4-fold rise in OPA responses were generally comparable in the intervention groups for the common serotypes. The proportion of participants with a ≥4-fold rise in OPA responses was higher in the Pneu-C-21 group for the serotypes unique to Pneu-C-21.	In adults previously immunized with Pneu-C-13, Pneu-P-23 or Pneu-C-13+Pneu-P-23, Pneu-C-21 was immunogenic for all 21 serotypes contained in the vaccine (as assessed by the proportions of participants with a ≥4-fold rise in serotype-specific OPA responses)
Safety		
Vaccine-related serious adverse events (SAEs)	No vaccine-related SAEs were observed in either group.	No vaccine-related SAEs were observed in either group.
Total SAEs	18 to 49 years of age Pneu-C-21: 14/1,646 Pneu-P-23: 6/571 ≥50 years of age Pneu-C-21: 4/254 Pneu-P-23: 3/254	Cohort 2; participants who previously received PCV13 >1 year prior to study enrollment: Pneu-C-21: 2/174 Pneu-P-23: 3/85
Death	No vaccine-related deaths were observed.	No vaccine-related deaths were observed.

Table S-2. GRADE evidence summary of safety of Pneu-C-21 (V116) compared to Pneu-C-20 in vaccine naïve adults ≥ 65 years of age

Outcome	Summary of findings					
	Number of studies, study design	Pneu-C-21	Pneu-C-20	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	1 RCT (V116-003)	N=0/590	N=0/590	No vaccine-related SAEs were observed in either group.	Moderate*	There is probably little to no difference between vaccines in the occurrence of vaccine-related SAEs.
Total SAEs	1 RCT (V116-003)	N=11/590	N=16/590	Relative effects: Peto OR 0.68 (95% CI: 0.32 to 1.47) Absolute effects: 9 fewer per 1,000 (from 18 fewer to 12 more)	Moderate*	There is probably little to no difference between vaccines in the occurrence of SAEs.
Death	1 RCT (V116-003)	N=2/590	N=2/590	Relative effects: Peto OR 1 (95% CI: 0.14 to 7.12) Absolute effects: 0 per 1,000 (from 3 fewer to 20 more) No deaths were determined to be related to study vaccine.	Moderate*	There is probably little to no difference between vaccines in the occurrence of deaths.

**Downrated for imprecision as did not meet the review information size (400 people with events or, for very few to no events, ≥4,000 sample size).*

Table S-3. GRADE evidence summary of safety of Pneu-C-21 compared to Pneu-C-20 in vaccine naïve adults ≥ 50 years of age with one or more medical risk factors for pneumococcal disease

Outcome	Summary of findings					
	Number of studies, study design	Pneu-C-21	Pneu-C-20	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	1 RCT (V116-003)	No risk: N=0/730	No risk: N=0/766	No vaccine-related SAEs were observed in either group.	Moderate*	There is probably little to no difference between vaccines in the occurrence of vaccine-related SAEs.
		Single risk factor: N=0/347	Single risk factor: N=0/328			
		2 or more risk factors: N=0/100	2 or more risk factors: N=0/81			
Total SAEs	1 RCT (V116-003)	No risk: N=10/730	No risk: N=13/766	Relative effects: Peto OR 0.81 (95% CI: 0.35 to 1.84) Absolute effects: 3 fewer per 1,000 (11 fewer to 14 more)	Moderate*	There is probably little to no difference between vaccines in the occurrence of SAEs.
		Single risk factor: N=3/347	Single risk factor: N=8/328	Relative effects: Peto OR 0.38 (95% CI: 0.11 to 1.23) Absolute effects: 15 fewer per 1,000 (22 fewer to 5 more)		
		2 or more risk factors: N=6/100	2 or more risk factors: N=3/81	Relative effects: Peto OR 1.62 (95% CI: 0.42 to 6.22) Absolute effects: 22 more per 1,000 (21 fewer more to 156 more)		
Death	1 RCT (V116-003)	No risk: N=2/730	No risk: N=1/766	Relative effects: Peto OR 2.05 (95% CI: 0.21 to 19.72)	Moderate*	

				Absolute effects: 1 more per 1,000 (1 fewer to 24 more)		No deaths determined to be related to study vaccine. There is probably little to no difference between vaccines in the occurrence of deaths.
		Single risk factor: N=1/347	Single risk factor: N=0/328	Relative effects: Peto OR 7.00 (95% CI: 0.14 to 353.12) Absolute effects: 0 more per 1,000		
		2 or more risk factors: N=1/100	2 or more risk factors: N=1/81	Relative effects: RR 1.62 (0.42 to 6.23) Absolute effects: 8 more per 1,000 (7 fewer to 60 more)		

**Downrated for imprecision as did not meet the review information size (400 people with events or, for very few to no events, ≥4,000 sample size).*

Table S-4. GRADE evidence summary of safety of Pneu-C-21 compared to Pneu-C-20 in vaccine naïve adults 18-64 years of age with no additional risk factors

Outcome	Summary of findings					
	Number of studies, study design	Pneu-C-21	Pneu-C-20	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	1 RCT (V116-003 Cohort 2)	N=0/787	N=0/685	No vaccine-related SAEs were observed in either group.	Moderate*	There is probably little to no difference between vaccines in the occurrence of vaccine-related SAEs.
Total SAEs	1 RCT (V116-003 Cohort 2)	N=9/787	N=11/685	Relative effects: Peto OR 0.71 (95% CI: 0.29 to 1.72) Absolute effects: 5 fewer per 1,000 (from 11 fewer to 11 more)	Moderate*	There is probably little to no difference between vaccines in the occurrence of SAEs.
Death	1 RCT (V116-003 Cohort 2)	N=2/787	N=0/685	Relative effects: Peto OR 6.50 (95% CI: 0.93 to 104.71) Absolute effects: 0 per 1,000 (0 to 0)	Moderate*	No deaths determined to be related to study vaccine.There is probably little to no difference between vaccines in the occurrence of deaths.

**Downrated for imprecision as did not meet the review information size (400 people with events or, for very few to no events, ≥4,000 sample size).*

Table S-5. Safety of Pneu-C-21 compared to Pneu-P-23 in vaccine naïve adults

Outcome	Summary of findings					
	Number of studies, study design	Pneu-C-21	Pneu-P-23	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	3 RCTs (V116-001; Haranaka et al.; V116-004)	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=0/254	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=0/254	No vaccine-related SAEs were reported across studies.	Not assessed	Across all 3 studies comparing Pneu-C-21 to Pneu-P-23, safety and reactogenicity was comparable between the products.
		Haranaka et al. N=0/51	Haranaka et al. N=0/51			
		V116-004 N=0/1,616	V116-004 N=0/541			
		Total = 0/1,921	Total = 0/846			
Total SAEs	3 RCTs (V116-001; Haranaka et al.; V116-004)	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=4/254	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=3/254	Relative effects: Peto OR 0.84 (95% CI: 0.37 to 1.93)Absolute effects: 3 fewer per 1,000 (8 fewer to 8 more)	Not assessed	SAEs occurred infrequently across studies and with similar proportions across intervention groups.
		Haranaka et al. N=0/51	Haranaka et al. N=0/51			
		V116-004 N=14/1,616	V116-004 N=6/541			

		Total = 18/1,870	Total = 9/795			
Death	3 RCTs (V116-001; Haranaka et al.; V116-004)	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=1/254	V116-001 18 to 49 years of age: N=0/30 ≥50 years of age: N=0/254	No deaths were related to the study vaccine.	Not assessed	No vaccine-related deaths were reported across studies.
		Haranaka et al. N=0/51	Haranaka et al. N=0/51			
		V116-004 N=0/1,616	V116-004 N=1/541			
		Total = 1/1,921	Total = 1/846			

Table S-6. Safety of Pneu-C-21 compared to Pneu-P-23 in previously vaccinated adults

Outcome	Summary of Findings					
	Number of studies, study design	Pneu-C-21	Pneu-P-23	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	1 RCT (V116-006 Cohort 2)	N=0/174	N=0/85	No vaccine-related SAEs were observed in either group.	Not assessed	In adults who received prior pneumococcal vaccines, Pneu-C-21 was well tolerated with a safety profile that was generally comparable to vaccination with Pneu-P-23.
Total SAEs	1 RCT (V116-006 Cohort 2)	N=2/174	N=3/85	The proportion of participants with SAEs was low (<4%) and generally comparable between intervention groups.	Not assessed	There is probably little to no difference between vaccines in the occurrence of SAEs.
Death	1 RCT (V116-006 Cohort 2)	N=0/174	N=0/85	No vaccine-related deaths were reported in any of the study groups.	Not assessed	There is probably little to no difference between vaccines in the occurrence of deaths.

Table S-7. Safety of Pneu-C-21 compared to Pneu-C-15 and Pneu-P-23 in adults living with HIV

Outcome	Summary of findings					
	Number of studies, study design	Pneu-C-21	Pneu-C-15 + Pneu-P-23	Impact – quantitative or narrative	Certainty of evidence	Comments/summary
Day 1 through duration of participation in study						
Vaccine-related SAEs	1 RCT (V116-007)	N=0/155	N=0/155	No vaccine-related serious adverse events were reported in either groups. Vaccine-related SAEs were comparable between the two intervention groups.	Not assessed	There is probably little to no difference between vaccines in the occurrence of vaccine-related SAEs.
Total SAEs	1 RCT (V116-007)	N=4/155	N=6/155	The proportions of participants with SAEs were low (<4%) and generally comparable in both intervention groups.	Not assessed	There is probably little to no difference between vaccines in the occurrence of SAEs.
Death	1 RCT (V116-007)	N=1/155	N=0/155	One death was reported for a participant who received Pneu-C-21. No additional information was provided.	Not assessed	There is probably little to no difference between vaccines in the occurrence of deaths.

Table S-8. GRADE evidence summary of immunogenicity of Pneu-C-21 compared to Pneu-C-20 in vaccine naïve adults ≥ 65 years of age

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-C-20			
30 days post vaccination						
OPA GMT (common serotypes)	1 RCT (V116-003)	Range N= 579-586 analysed across common serotypes	Range N= 575-585 analysed across common serotypes	Distribution of serotype-specific OPA titres was generally comparable between groups for common serotypes. This was also observed for age subgroups of individuals 65 to 74 years of age and individuals 75 years of age and older.	Moderate	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
OPA GMT (unique serotypes)	1 RCT (V116-003)	Range N= 579-586 analysed across unique serotypes	Range N= 575- 585 analysed across unique serotypes	Serotype-specific OPA titres numerically higher for most Pneu-C-21 unique serotypes. This was also observed for age subgroups of individuals 65 to 74 years of age and individuals 75 years of age and older.	Moderate	The distribution of serotype-specific OPA titres for unique serotypes is generally higher for Pneu-C-21.
≥4-fold rise in OPA responses for unique serotypes	1 RCT (V116-003)	N= 590 analysed across unique serotypes	N= 590 analysed across unique serotypes	The proportion of seroresponders was numerically higher against all unique serotypes for Pneu-C-21 compared to Pneu-C-20. However, the difference in the proportion of responders between Pneu-C-21 and Pneu-C-20 was lowest for serotype 15C. The difference in the proportion of seroresponders to Pneu-C-21 and Pneu-C-20 was comparable between individuals 65-74 years of age and individuals 75 years of age and older.	Moderate	N/A

Table S-9. GRADE evidence summary of immunogenicity of Pneu-C-21 compared to Pneu-C-20 in vaccine naïve adults ≥ 50 years of age with one or more medical risk factors for pneumococcal disease

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-C-20			
30 days post vaccination						
OPA GMT (common serotypes)	1 RCT (V116-003)	Range N= 435-440 analysed across common serotypes	Range N= 397-404 analysed across common serotypes	Distribution of serotype-specific OPA titres was generally comparable between groups for common serotypes.	Moderate*	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
OPA GMT (unique serotypes)	1 RCT (V116-003)	Range N= 411-441 analysed across unique serotypes	Range N= 385-404 analysed across unique serotypes	Serotype-specific OPA titres were significantly higher for nearly all Pneu-C-21 unique serotypes.	Moderate*	The distribution of serotype-specific OPA titres for unique serotypes is generally higher for Pneu-C-21.
≥4-fold rise in OPA responses for unique serotypes	1 RCT (V116-003)	N=447 analysed across unique serotypes	N=409 analysed across unique serotypes	Proportion of seroresponders was numerically higher against all unique serotypes for Pneu-C-21 compared to Pneu-C-20.	Moderate*	N/A

**Downrating for indirectness (immunogenicity used in absence of disease endpoints). There is absence on information on PCV-20 unique serotypes and uncertainty as to how these findings translate to vaccine effectivness against longer term clinical outcomes*

Table S-10. GRADE evidence summary of immunogenicity of Pneu-C-21 compared to Pneu-C-20 in vaccine naïve adults 18-49 years of age

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-C-20			
30 days post vaccination						
OPA GMT (common serotypes)	1 RCT (V116-003 Cohort 2)	N=200 analysed across common serotypes	N=100 analysed across common serotypes	Distribution of serotype-specific OPA titres was generally comparable between groups for common serotypes.	Moderate*	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
OPA GMT (unique serotypes)	1 RCT (V116-003 Cohort 2)	N=200 analysed across unique serotypes	N=100 analysed across unique serotypes	Serotype-specific OPA titres were significantly higher for Pneu-C-21 unique serotypes.	Moderate*	The distribution of serotype-specific OPA titres for unique serotypes is higher for Pneu-C-21.
≥4-fold rise in OPA responses for unique serotypes (data not available for common serotypes)	1 RCT (V116-003 Cohort 2)	N=200 analysed across unique serotypes	N=100 analysed across unique serotypes	The proportion of seroresponders was numerically higher against all unique serotypes for Pneu-C-21 compared to Pneu-C-20.	Moderate*	N/A

**Downrating for indirectness (immunogenicity used in absence of disease endpoints). There is absence on information on PCV-20 unique serotypes and uncertainty as to how these findings translate to VE against longer term clinical outcomes*

Table S-11. Immunogenicity of Pneu-C-21 compared to Pneu-P-23 in vaccine naïve adults

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-P-23			
30 days post vaccination						
OPA GMT (common serotypes)	3 RCTs (V116-001; Haranaka et al.; V116-004)	Haranaka et al.: 65 years of age and older: N=34	Haranaka et al.: 65 years of age and older: N=34	Across all 3 studies comparing Pneu-C-21 to Pneu-P-23, Pneu-C-21 was immunogenic for all 21 serotypes contained in the vaccine in all age groups (as assessed by serotype-specific OPA GMTs at 30 days postvaccination). OPA GMTs for the 12 common serotypes shared between Pneu-C-21 and Pneu-P-23 were comparable.	Not assessed	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
		V116-001: 18 to 49 years of age (2 cohorts, N=30 each): Range N=27 to 29 ≥50 years of age: N= 252	V116-001: 18 to 49 years of age: Range N=27 to 30 ≥50 years of age: N=254			
		V116-004 : Range N=1,573 to 1,593 analysed across serotypes (combined lots)	V116-004 : Range N= 530 to 537 analysed across serotypes			
OPA GMT (unique serotypes)	3 RCTs (V116-001; Haranaka et al.; V116-004)	Haranaka et al.: N=34	Haranaka et al.: N=34	For the 9 unique serotypes to Pneu-C-21, OPA GMTs were numerically higher in the Pneu-C-21 group compared to the Pneu-P-23 group.	Not assessed	The distribution of serotype-specific OPA titres for unique serotypes is generally higher for Pneu-C-21.

		V116-001: 18 to 49 years of age: Range N= 27 to 29 ≥50 years of age: N=252	V116-001: 18 to 49 years of age: Range N= 28 to 29 ≥50 years of age: N=254			
		V116-004: Range N= 1,520 to 1,583 (combined lots)	V116-004 : Range N= 512 to 537			
≥4-fold rise in OPA responses for unique serotypes	3 RCTs (V116-001; Haranaka et al.; V116-004)	Haranaka et al.: Outcome not assessed	Haranaka et al.: Outcome not assessed	The proportions of participants with a ≥4-fold rise in OPA responses from pre-vaccination to 30 days postvaccination were higher in the Pneu-C-21 group for the serotypes unique to Pneu-C-21.	Not assessed	N/A
		V116-001: 18 to 49 years of age: Range N= 27 to 29 ≥50 years of age: N= 252	V116-001: 18 to 49 years of age: Range N= 28 to 30 ≥50 years of age: N= 254			
		V116-004: Range N=950 to 1,360 (combined lots)	V116-004: Range N= 334 to 465			
≥4-fold rise in OPA responses for common serotypes	3 RCTs (V116-001; Haranaka et al.; V116-004)	Haranaka et al.: Outcome not assessed	Haranaka et al.: Outcome not assessed	The proportions of participants with a ≥4-fold rise in OPA responses from pre-vaccination to 30 days postvaccination were generally comparable in the Pneu-C-21 and Pneu-P-23 intervention groups for the common serotypes.	Not assessed	N/A
		V116-001: 18 to 49 years of age: Range N= 28 to 29 ≥50 years of age: N= 252	V116-001: 18 to 49 years of age: Range N= 27 to 30 ≥50 years of age: N= 254			

		V116-004: Range N=950 to 1,360 (combined lots)	V116-004: Range N= 334 to 465			

Table S-12. Immunogenicity of Pneu-C-21 compared to Pneu-P-23 in previously vaccinated adults

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-P-23			
30 days post vaccination						
OPA GMT (common serotypes)	1 RCT (V116-006 Cohort 2)	V116-006 Range: N=125-161 across common serotypes	V116-006 Range: N=58-75 across common serotypes	Immune responses were overall comparable between intervention groups (Pneu-C-21 or Pneu-P-23) for common serotypes; OPA GMT point estimates following Pneu-C-21 administration were higher for some serotypes and lower for others.	Not assessed	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
OPA GMT (unique serotypes)	1 RCT (V116-006)	V116-006 Range: N=134-160 across unique serotypes	V116-006 Range: N=60-76 across unique serotypes	In adults previously immunized with Pneu-C-13, Pneu-P-23 or Pneu-C-13+Pneu-P-23, Pneu-C-21 was immunogenic for all 21 serotypes contained in the vaccine in all age groups (as assessed by serotype-specific OPA GMTs at 30 days postvaccination).	Not assessed	N/A

≥4-fold rise in OPA responses for unique serotypes	1 RCT (V116-006 Cohort 2)	V116-006 Range: N=110-157 across unique serotypes	V116-006 Range: N=38-72 across unique serotypes	In adults previously immunized with Pneu-C-13, Pneu-P-23 or Pneu-C-13+Pneu-P-23, Pneu-C-21 was immunogenic for all 21 serotypes contained in the vaccine (as assessed by the proportions of participants with a ≥4- fold rise in serotype-specific OPA responses).	Not assessed	N/A

Table S-13. Immunogenicity of Pneu-C-21 + Placebo compared to Pneu-C-15 + Pneu-P-23 in adults living with HIV

Outcome	Summary of findings					
	Number of studies, study design	Number of study participants		Impact – quantitative or narrative	Certainty of evidence	Comments/summary
		Pneu-C-21	Pneu-C-15 + Pneu-P-23			
30 days post vaccination						
OPA GMT (common serotypes)	1 RCT (V116-007)	Range: N=123-137 across common serotypes	Range: N=123-130 across common serotypes	Pneu-C-21 elicited immune responses that were generally comparable to Pneu-C-15 + Pneu-P-23 for the common serotypes.	Not assessed	There is probably little to no difference between vaccines in the distribution of serotype-specific OPA titres for common serotypes.
OPA GMT (unique serotypes)	1 RCT (V116-007)	Range: N=127-137 across unique serotypes	Range: N=98-128 across unique serotypes	Pneu-C-21 elicited immune responses that was higher compared to Pneu-C-15 + Pneu-P-23 for the unique serotypes.	Not assessed	The distribution of serotype-specific OPA titres for unique serotypes is higher for Pneu-C-21.

Table S-14. GRADE certainty of evidence for NACI recommendations

GRADE certainty of evidence rating	Description
High	Very confident that the true effect lies close to that of the effect estimate.
Moderate	Moderately confident: the true effect is likely to be close to the effect estimate, but there is a possibility that it is substantially different.
Low	Limited confidence in the effect estimate: the true effect may be substantially different from the effect estimate.
Very low	Very little confidence in the effect estimate: true effect likely to be substantially different from the effect estimate.

ABBREVIATIONS

CI	Confidence interval
GMT	Geometric mean titer
NACI	National Advisory Committee on Immunization
OPA	Opsonophagocytic activity
OR	Odds ratio
Pneu-C-15	15-valent pneumococcal conjugate vaccine
Pneu-C-20	20-valent pneumococcal conjugate vaccine
Pneu-C-21	21-valent pneumococcal conjugate vaccine
Pneu-P-23	23-valent pneumococcal polysaccharide vaccine
PHAC	Public Health Agency of Canada
RR	Relative risk
SAE	Serious adverse event

REFERENCES

1. Merck Canada Inc. Personal communication. Merck clinical dossier submission for V116 (Capvaxive), 21-valent pneumococcal conjugate vaccine. 2023 Dec 8.

2. Haranaka M, Yono M, Kishino H, et al. Safety, tolerability, and immunogenicity of a 21- valent pneumococcal conjugate vaccine, V116, in Japanese healthy adults: A Phase I study. *Hum Vaccin Immunother.* 2023 Aug 1;19(2):2228162. http://doi.org/10.1080/21645515.2023.2228162.

3. Merck Canada Inc. Personal communication. Request for data on V116-007 received 2024 Apr 24.