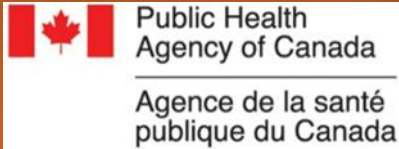




PCV21 (V116) Vaccine Coverage of Invasive and Respiratory *Streptococcus pneumoniae* in Canada: CANWARD Study

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Introduction

Streptococcus pneumoniae is an important pathogen worldwide as it is a common cause of respiratory infections, including community-acquired pneumonia and acute otitis media, and the causative agent of invasive pneumococcal disease (IPD). The introduction of the first pneumococcal conjugate vaccine, Prevnar®, a 7-valent pneumococcal vaccine (PCV7), into routine infant immunization programs in the early 2000s resulted in significant reductions of IPD. A 13-valent pneumococcal conjugate vaccine, Prevnar®13 (PCV13), replaced PCV7 in routine infant immunization programs largely in response to the significant rise in the incidence of serotype 19A, which was frequently MDR. Vaccine formulations with increased serotype coverage were subsequently developed: VAXNEUVANCE™, a 15-valent pneumococcal conjugate vaccine (PCV15) and PREVNAR20™, a 20-valent pneumococcal conjugate vaccine (PCV20). In 2024, CAPVAXIVE®, a 21-valent conjugate vaccine (PCV21) with different serotype coverage from the sequentially developed previous conjugate vaccines was approved. Currently, PCV15 and PCV20 are recommended for children and PCV20 and PCV21 are recommended for adults in Canada. The objective of this analysis was to assess the vaccine coverage provided by PCV21 for *S. pneumoniae* in Canada.

Materials and Methods

Bacterial isolates

Between January 2007 and December 2023, 3111 *S. pneumoniae* isolates from blood and respiratory cultures were collected as part of the CANWARD surveillance program.

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using the reference CLSI broth microdilution method with custom-designed, in-house prepared, 96-well microtitre panels. MICs were interpreted using CLSI MIC breakpoints. MDR was defined as resistance to three or more antimicrobial agents selected as antimicrobial class markers [penicillin (MIC, ≥2 µg/mL), clarithromycin, clindamycin, doxycycline, levofloxacin, trimethoprim/sulfamethoxazole and vancomycin]. 2939 isolates had complete antimicrobial susceptibility testing profiles for the MDR analysis.

Serotyping

Isolates collected from 2007 to 2022 were serotyped by the Quellung reaction, with pool, group, type and factor commercial antisera (SSI Diagnostica; Statens Serum Institut, Copenhagen, Denmark). From late 2022 onwards, *S. pneumoniae* were sequenced using the Illumina platform and serotypes were identified directly from whole genome data using the WADE pipeline (<https://github.com/phac-nml/wade>). Isolates that were non-typeable (NT) by WGS were confirmed by Quellung reaction. Serotypes 15B and 15C were grouped as 15B/C due to the reported reversible switching between serotypes.

Statistical analysis

Differences in the proportion of isolates included in PCV21 compared to PCV15, PCV20 and PPSV23 by antimicrobial resistance pattern and patient demographics were assessed for significance (P≤0.05) using a two-tailed Fisher’s exact test.

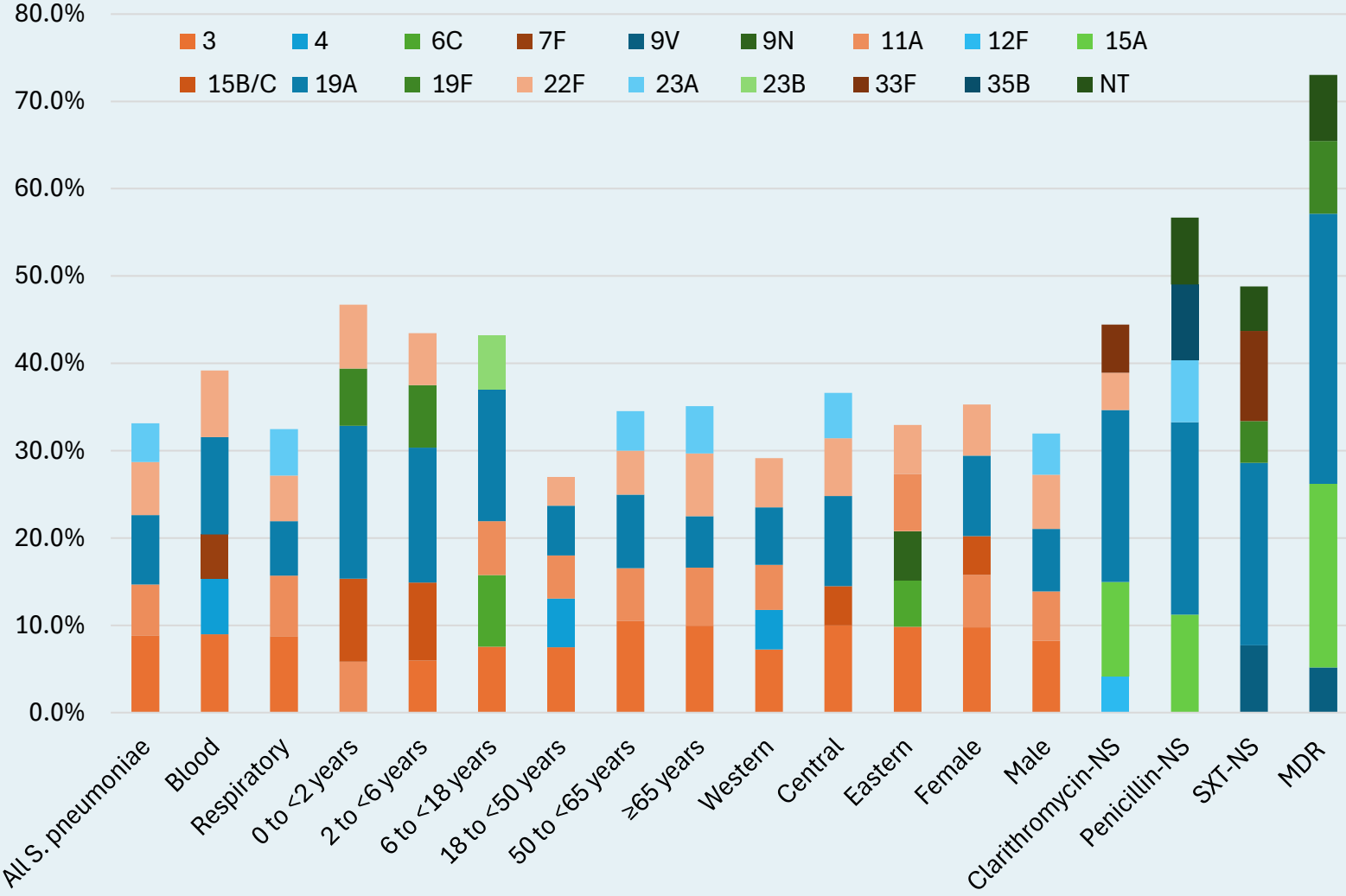


Figure 1. The 5 most common serotypes by demographic and antimicrobial resistance category.

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Results

Table 1. Proportion of *S. pneumoniae* isolates with serotypes included in PCV21 and comparator vaccines by age, geographic region, biological sex, and antimicrobial resistance phenotype. a) All *S. pneumoniae* CANWARD isolates b) Blood culture isolates c) Respiratory isolates

a)	Category (n)	Proportion of isolates with vaccine serotype, n (%)				P-value		
		PCV21	PCV15	PCV20	PPSV23	PCV21 vs PCV15	PCV21 vs PCV20	PCV21 vs PPSV23
	All <i>S. pneumoniae</i> (3111)	2324 (70.7)	1372 (44.1)	1861 (59.8)	2012 (64.7)	<0.0001	<0.0001	<0.0001
	Age group (years)							
	0 to <2 (137)	107 (78.1)	59 (43.1)	86 (62.8)	90 (65.7)	<0.0001	0.008	0.03
	2 to <6 (168)	128 (76.2)	82 (48.8)	108 (64.3)	107 (63.7)	<0.0001	0.02	0.02
	6 to <18 (146)	114 (78.1)	73 (50.0)	96 (65.8)	99 (67.8)	<0.0001	0.03	-
	18 to <50 (789)	558 (70.7)	347 (44.0)	490 (62.1)	548 (69.5)	<0.0001	0.0003	-
	50 to <65 (817)	615 (75.3)	364 (44.6)	482 (59.0)	524 (64.1)	<0.0001	<0.0001	<0.0001
	≥65 (1054)	802 (76.1)	447(42.4)	599 (56.8)	644 (61.1)	<0.0001	<0.0001	<0.0001
	Region ^a							
	Western (1260)	897 (71.2)	533 (42.3)	759 (60.2)	836 (66.3)	<0.0001	<0.0001	0.01
	Central (1423)	1115 (78.4)	668 (46.9)	876 (61.6)	920 (64.7)	<0.0001	<0.0001	<0.0001
	Eastern (428)	312 (72.9)	171 (40.0)	226 (52.8)	256 (59.8)	<0.0001	<0.0001	<0.0001
	Biological sex							
	Female (1261)	938 (74.4)	578 (45.8)	770 (61.1)	830 (65.8)	<0.0001	<0.0001	<0.0001
	Male (1850)	1386 (74.9)	794 (42.9)	1091 (59.0)	1182 (63.9)	<0.0001	<0.0001	<0.0001
	Antimicrobial resistance							
	Clarithromycin-NS (655)	497 (75.9)	335 (51.1)	434 (66.3)	420 (64.1)	<0.0001	0.0002	<0.0001
	Penicillin ^b -NS (508)	353 (69.5)	258 (50.8)	276 (54.3)	250 (49.2)	<0.0001	<0.0001	<0.0001
	SXT-NS (455)	270 (59.3)	290 (63.7)	330 (72.5)	322 (70.8)	-	<0.0001*	0.0004*
	MDR (252)	168 (66.7)	141 (56.0)	148 (58.7)	154 (61.1)	0.02	-	-
b)	Category (n)	Proportion of isolates with vaccine serotype, n (%)				P-value		
		PCV21	PCV15	PCV20	PPSV23	PCV21 vs PCV15	PCV21 vs PCV20	PCV21 vs PPSV23
	All <i>S. pneumoniae</i> - blood (1103)	847 (76.8)	602 (54.6)	790 (71.6)	858 (77.8)	<0.0001	0.006	-
	Age group (years)							
	0 to <2 (69)	58 (84.1)	33 (47.8)	47 (68.1)	51 (73.9)	<0.0001	0.04	-
	2 to <6 (71)	59 (83.1)	48 (67.6)	59 (83.1)	59 (83.1)	-	-	-
	6 to <18 (51)	39 (76.5)	35 (68.6)	42 (82.4)	42 (82.4)	-	-	-
	18 to <50 (287)	206 (71.8)	155 (54.0)	220 (76.7)	248 (86.4)	<0.0001	-	<0.0001*
	50 to <65 (274)	201 (73.4)	148 (54.0)	194 (70.8)	205 (74.8)	<0.0001	-	-
	≥65 (351)	284 (80.9)	183 (52.1)	228 (65.0)	253 (72.1)	<0.0001	<0.0001	0.007
	Region ^a							
	Western (459)	312 (68.0)	245 (53.4)	343 (74.7)	373 (81.3)	<0.0001	0.03*	<0.0001*
	Central (553)	465 (84.1)	311 (56.2)	396 (71.6)	423 (76.5)	<0.0001	<0.0001	0.002
	Eastern (91)	70 (76.9)	46 (50.5)	51 (56.0)	62 (68.1)	0.0004	0.005	-
	Biological sex							
	Female (491)	378 (77.0)	271 (55.2)	351 (71.5)	382 (77.8)	<0.0001	-	-
	Male (612)	469 (76.6)	331 (54.1)	439 (71.7)	476 (77.8)	<0.0001	-	-
	Antimicrobial resistance							
	Clarithromycin-NS (206)	171 (83.0)	122 (59.2)	162 (78.6)	159 (77.2)	<0.0001	-	-
	Penicillin ^b -NS (123)	91 (74.0)	84 (68.3)	85 (69.1)	77 (62.6)	-	-	-
	SXT-NS (143)	94 (65.7)	108 (75.5)	120 (83.9)	118 (82.5)	-	0.0006*	0.002*
	MDR (60)	46 (76.7)	39 (65.0)	42 (70.0)	43 (71.7)	-	-	-
c)	Category (n)	Proportion of isolates with vaccine serotype, n (%)				P-value		
		PCV21	PCV15	PCV20	PPSV23	PCV21 vs PCV15	PCV21 vs PCV20	PCV21 vs PPSV23
	All <i>S. pneumoniae</i> - respiratory (2008)	1477 (73.6)	770 (38.3)	1071 (53.3)	1154 (57.5)	<0.0001	<0.0001	<0.0001
	Age group (years)							
	0 to <2 (68)	49 (72.1)	26 (38.2)	39 (57.4)	39 (57.4)	0.0001	-	-
	2 to <6 (97)	69 (71.1)	34 (35.1)	49 (50.5)	48 (49.5)	<0.0001	0.005	0.003
	6 to <18 (95)	75 (78.9)	38 (40.0)	54 (56.8)	57 (60.0)	<0.0001	0.002	0.007
	18 to <50 (502)	352 (70.1)	192 (38.2)	270 (53.8)	300 (59.8)	<0.0001	<0.0001	0.0007
	50 to <65 (543)	414 (76.2)	216 (39.8)	288 (53.0)	319 (58.7)	<0.0001	<0.0001	<0.0001
	≥65 (703)	518 (73.7)	264 (37.6)	371 (52.8)	391 (55.6)	<0.0001	<0.0001	<0.0001
	Region ^a							
	Western (801)	585 (73.0)	288 (36.0)	416 (51.9)	463 (57.8)	<0.0001	<0.0001	<0.0001
	Central (870)	650 (74.7)	357 (41.0)	480 (55.2)	497 (57.1)	<0.0001	<0.0001	<0.0001
	Eastern (337)	242 (71.8)	125 (37.1)	175 (51.9)	194 (57.6)	<0.0001	<0.0001	0.0001
	Biological sex							
	Female (770)	560 (72.7)	307 (39.9)	419 (54.4)	448 (58.2)	<0.0001	<0.0001	<0.0001
	Male (1238)	917 (74.1)	463 (37.4)	652 (52.7)	706 (57.0)	<0.0001	<0.0001	<0.0001
	Antimicrobial resistance							
	Clarithromycin-NS (449)	326 (72.6)	213 (47.4)	272 (60.6)	261 (58.1)	<0.0001	0.0002	<0.0001
	Penicillin ^b -NS (385)	262 (68.1)	174 (45.2)	191 (49.6)	173 (44.9)	<0.0001	<0.0001	<0.0001
	SXT-NS (312)	176 (56.4)	182 (58.3)	210 (67.3)	204 (65.4)	-	0.006*	0.03*
	MDR (192)	122 (63.5)	102 (53.1)	106 (55.2)	111 (57.8)	0.05	-	-

^a, Western: BC/AB/SK/MB, Central: ON/QC, Eastern: NS/NB; ^b, oral penicillin breakpoints; NS, non-susceptible; -, non-significant; *, comparator vaccine demonstrated statistical significance versus PCV21

Conclusions

- Against both all *S. pneumoniae* (blood and respiratory) and respiratory *S. pneumoniae*, PCV21 provided significantly higher coverage compared with all other vaccines across most categories (age group, region, biological sex and antimicrobial resistance).
- Significantly less coverage by PCV21 compared to the other vaccines was only observed with PCV20 for trimethoprim-sulfamethoxazole non-susceptible isolates overall and blood isolates from the western region as well as PPSV23 for trimethoprim-sulfamethoxazole non-susceptible isolates overall and blood isolates from individuals aged 18 - <50 years and from the western region.
- The serotypes unique to PCV21 that were most commonly isolated in this study were: 23A, 15A, 9N, 23B and 35B, representing 4.4%, 3.7%, 3.5%, 3.3% and 3.0% of isolates overall, respectively.
- Of the MDR isolates, 19A and 15A were the predominant serotypes representing 31.0% and 21.0% of the isolates. While the inclusion of 15A in PCV21 provided significant coverage of MDR isolates, comparisons to the other vaccines generally resulted in non-statistically significant results due to other less commonly isolated MDR serotypes, including 19F (8.3%), 9V (5.2%), 23F (2.8%) and 14 (2.4%).