

Comparison of PCV10, PCV13, PCV15, PCV20 and PPSV23 vaccine coverage of invasive *Streptococcus pneumoniae* isolate serotypes in Canada: the SAVE study, 2011–20

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Background: As pneumococci evolve under vaccine, antimicrobial and other selective pressures, it is important to track isolates covered by established (PCV10, PCV13 and PPSV23) and new (PCV15 and PCV20) vaccine formulations.

Objectives: To compare invasive pneumococcal disease (IPD) isolates from serotypes covered by PCV10, PCV13, PCV15, PCV20 and PPSV23, collected in Canada from 2011 to 2020, by demographic category and antimicrobial resistance phenotype.

Methods: IPD isolates from the SAVE study were initially collected by members of the Canadian Public Health Laboratory Network (CPHLN) as part of a collaboration between the Canadian Antimicrobial Resistance Alliance (CARA) and the Public Health Agency of Canada (PHAC). Serotypes were determined by quellung reaction, and antimicrobial susceptibility testing was performed using the CLSI broth microdilution method.

Results: A total of 14 138 invasive isolates were collected from 2011 to 2020, with 30.7% of isolates covered by the PCV13 vaccine, 43.6% of isolates covered by the PCV15 vaccine (including 12.9% non-PCV13 serotypes 22F and 33F), and 62.6% of isolates covered by the PCV20 vaccine (including 19.0% non-PCV15 serotypes 8, 10A, 11A, 12F and 15B/C). Non-PCV20 serotypes 2, 9N, 17F and 20, but not 6A (present in PPSV23) represented 8.8% of all IPD isolates. Higher-valency vaccine formulations covered significantly more isolates by age, sex, region and resistance phenotype including MDR isolates. Coverage of XDR isolates did not significantly differ between vaccine formulations.

Conclusions: When compared with PCV13 and PCV15, PCV20 covered significantly more IPD isolates stratified by patient age, region, sex, individual antimicrobial resistance phenotypes and MDR phenotype.

Introduction

Pneumococcal vaccines have proven effective in preventing severe pneumonia and invasive pneumococcal disease (IPD), especially in those most at risk (i.e. children <2 years of age and adults >65 years of age), and have reduced the usage of antimicrobials.¹ Since 1983, in Canada and in many other countries, the 23-valent polysaccharide vaccine (PPSV23, Pneumovax[®]) has been used to vaccinate adults and children >2 years of age. However, polysaccharide vaccines suffer from limitations, including poor suitability for use in infants and a humoral response of relatively short

duration, primarily because polysaccharide vaccines stimulate B cells to become short-lived antibody-producing plasma cells.²

In 2000, the first pneumococcal conjugated vaccine (PCV7, Prevnar[®]) was introduced. It provided stronger and more long-lasting protection than polysaccharide vaccines via stimulation of prolonged memory T helper cells. PCV7 covered 7 of the 23 serotypes contained in PPSV23, including serotypes 4, 6B, 9V, 14, 18C, 19F and 23F.³ PCV10 (Synflorix[®]), a formulation protecting against the PCV7 serotypes and an additional three serotypes (3, 6A and 19A) became available in 2009. It is still used in many countries although a newer 13-valent Prevnar[®] formulation

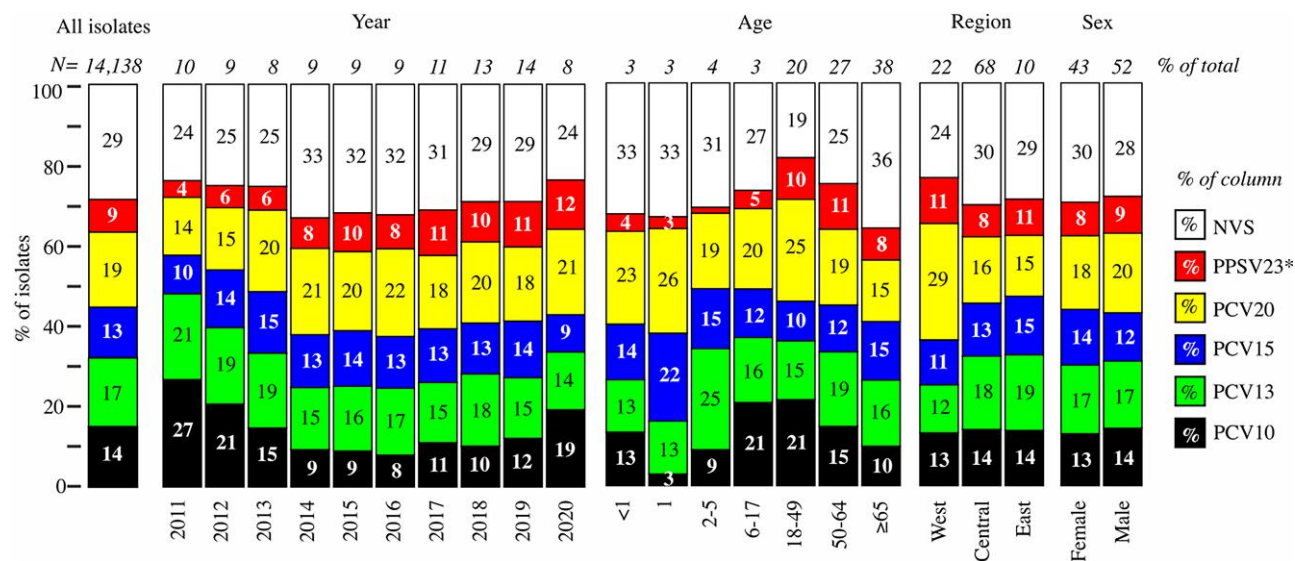


Figure 1. Coverage of SAVED isolates by PCV10, PCV13, PCV15, PCV20 and PPSV23 serotypes over time, by age group, region and biological sex. *For visual clarity of stacked bars, PPSV23 coverage includes a small number of serotype 6A isolates, which are covered by the other formulations, but not covered by PPSV23. PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine. Isolates with missing values for age ($n=245$; 1.7%) and sex ($n=663$; 4.7%) are not shown. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

(PCV13) is also available. PCV10 and PCV13 have now largely replaced the 7-valent formulation.⁴ PCV13 includes one serotype (6A) that is not included in the PPSV23 formulation, although 6B coverage provided by earlier vaccines has been reported to provide some cross-protection against 6A.⁵

Until recently, in the USA and Canada, PCV13 was the recommended vaccine for routine infant immunization as well as for persons aged >65 years and individuals aged 18 to 64 years with specific risk factors.⁶ Fifteen-valent (PCV15, Vaxneuvance[®]) and 20-valent (PCV20, Prevnar[®]-20) conjugate vaccine formulations have recently been developed and approved for use in the USA and Canada.^{7,8} In 2021, the US Advisory Committee on Immunization Practices (ACIP) recommended the use of PCV15 (followed by PPSV23) or PCV20 in PCV-naïve adults aged ≥65 years or ≥18 years with certain underlying conditions.⁷ Canada's National Advisory Committee on Immunization (NACI) made a preferential recommendation of a single dose of PCV20, reserving PCV15 (followed by PPSV23) only when PCV20 is not available for individuals in three patient groups: ≥65 years old, 50–64 years old with risk factors and ≥18 years old with immunocompromising conditions.⁷

Understanding the current distribution and dynamics of serotypes contained in existing vaccine formulations will help to predict the effects of newly introduced formulations on the additional serotypes included. Therefore, the purpose of this study was to compare the number and proportion of IPD isolates collected in Canada from 2011 to 2020 belonging to serotypes covered by PCV10, PCV13, PCV15, PCV20 and PPSV23 vaccine formulations.

Materials and methods

Bacterial isolates

The Canadian Antimicrobial Resistance Alliance (CARA), in collaboration with the Public Health Agency of Canada—National Microbiology

Laboratory (PHAC-NML), received *Streptococcus pneumoniae* isolates from sterile sites, initially collected by Canadian public health laboratories affiliated to the Canadian Public Health Laboratory Network (CPHLN), and forwarded to PHAC-NML. After permission was received from submitting CPHLN sites by PHAC-NML (as detailed in the Acknowledgements section), the *S. pneumoniae* isolates were forwarded to CARA for testing, as previously described.⁹

Serotyping

Serotyping was performed using the quellung reaction with pool/group/type/factor commercial antisera (SSI Diagnostica; Statens Serum Institute, Copenhagen, Denmark), as previously described.⁹

Antimicrobial susceptibility testing

Antimicrobial susceptibility testing was performed using custom-designed, broth microdilution panels produced in-house using CLSI standard methods, including quality control, as previously described.^{9,10} Isolates were classified as susceptible, intermediate and resistant according to CLSI breakpoints for seven antimicrobials: chloramphenicol, clindamycin, clarithromycin, doxycycline, levofloxacin, penicillin and trimethoprim/sulfamethoxazole. Non-susceptible (NS) isolates were defined as a combination of intermediate and resistant phenotypes. MDR was defined as being resistant to three or more antimicrobial classes and XDR isolates defined as being resistant to five or more antimicrobial classes. Penicillin resistance was defined as MIC ≥ 2 mg/L.⁹

Statistical analysis

Figures were generated using custom Python and R scripts. Sphere plots were generated with the matplotlib package, where sphere size is proportional to total isolates and colour indicates number of isolates relative to totals of each age group or antimicrobial non-susceptibility phenotype. Dark red signifies the top of the group range while dark blue signifies the bottom of the group range. Statistically significant differences ($P < 0.05$) in vaccine coverage of isolates by demographic category and coverage of MDR by PCV13 versus PCV15 and PCV15 versus PCV20 was

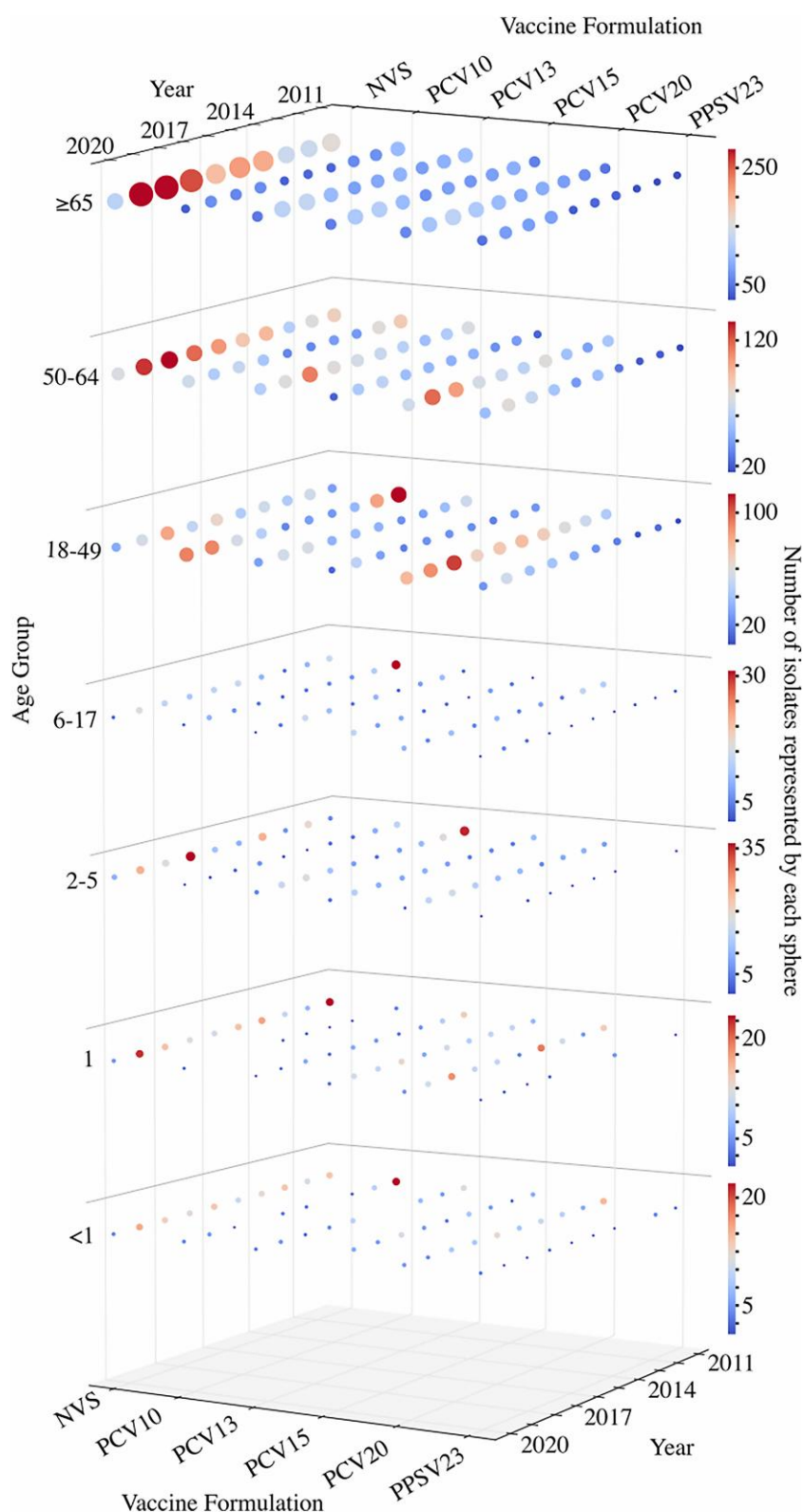


Figure 2. Comparison of time series for PCV10-, PCV13-, PCV15-, PCV20- and PPSV23-unique serotypes, by age group [$n = 13\,893$, isolates with missing age information ($n = 245$) not shown]. Each sphere (size and shade) represents the number of isolates for each combination of vaccine formulation, age group and year. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

Table 1. Proportion of invasive *S. pneumoniae* isolates with PCV13, PCV15 or PCV20 serotypes by age, geographic region and biological sex

Category (n)	Proportion of isolates with vaccine serotype, n (%)			P value	
	PCV13	PCV15	PCV20	PCV13 versus PCV15	PCV15 versus PCV20
All <i>S. pneumoniae</i> (14 138)	4334 (30.7)	6155 (43.5)	8844 (62.6)	<0.0001	<0.0001
Age group (years) (n) ^a					
0 to <1 (369)	97 (26.3)	148 (40.1)	233 (63.1)	<0.0001	<0.0001
1 to <2 (412)	66 (16.0)	156 (37.9)	263 (63.8)	<0.0001	<0.0001
2 to <6 (550)	187 (34.0)	269 (48.9)	372 (67.6)	<0.0001	<0.0001
6 to <18 (397)	146 (36.8)	194 (48.9)	273 (68.8)	0.0007	<0.0001
18 to <50 (2845)	1023 (36.0)	1303 (45.8)	2022 (71.1)	<0.0001	<0.0001
50 to <65 (3884)	1291 (33.2)	1742 (44.9)	2473 (63.6)	<0.0001	<0.0001
≥65 (5436)	1426 (26.2)	2215 (40.7)	3047 (56.1)	<0.0001	<0.0001
Region ^b					
Western (3045)	763 (25.1)	1102 (36.2)	1983 (65.1)	<0.0001	<0.0001
Central (9626)	3094 (32.1)	4363 (45.3)	5949 (61.8)	<0.0001	<0.0001
Eastern (1467)	477 (32.5)	690 (47.0)	912 (62.2)	<0.0001	<0.0001
Biological sex ^a					
Female (6107)	1830 (30.0)	2673 (43.8)	3792 (62.1)	<0.0001	<0.0001
Male (7368)	2279 (30.9)	3162 (42.9)	4618 (62.7)	<0.0001	<0.0001

^aMissing values for age (n=245; 1.7%) and biological sex (n=663; 4.7%) not shown.

^bWestern Canada includes Saskatchewan and Manitoba; Central Canada includes Ontario and Quebec; Eastern Canada includes Newfoundland and Labrador, Nova Scotia, Prince Edward Island and New Brunswick.

Table 2. Proportion of invasive *S. pneumoniae* isolates with PCV13, PCV15 or PCV20 serotypes by antimicrobial resistance phenotype

Category (n)	Proportion of isolates with vaccine serotype, n (%)			P value	
	PCV13	PCV15	PCV20	PCV13 versus PCV15	PCV15 versus PCV20
All <i>S. pneumoniae</i> (14 138)	4334 (30.7)	6155 (43.5)	8844 (62.6)	<0.0001	<0.0001
Clarithromycin-NS (3352)	955 (28.5)	1831 (54.6)	2516 (75.1)	<0.0001	<0.0001
Doxycycline-NS (1407)	634 (45.1)	705 (50.1)	822 (58.4)	0.0082	<0.0001
Penicillin-NS ^a (1558)	516 (33.1)	527 (33.8)	596 (38.3)	—	0.0362
SXT-NS (1808)	537 (29.7)	968 (53.5)	1266 (70.0)	<0.0001	<0.0001
MDR (902)	433 (48.0)	481 (53.3)	537 (59.5)	0.0268	0.0176
XDR (215)	188 (87.4)	192 (89.3)	204 (91.2)	—	—

MDR and XDR defined as resistance to three or more and five or more antimicrobial classes, respectively. —, not significant; SXT, trimethoprim/sulfamethoxazole.

^aOral penicillin V breakpoints (NS, MIC ≥0.12 mg/L).

determined using the two-tailed Fisher's exact test (α=0.05), using custom scripts in R.

Results

A total of 14,138 invasive isolates of *S. pneumoniae* were collected as part of the SAVE study from 2011 to 2020. Patient age and gender were available for most isolates, with 245 missing values for age (1.7%) and 663 missing values for gender (4.7%). Overall, isolates with serotypes covered by PCV10 and PCV13 vaccine formulations made up 14% and 31% of isolates, respectively (Figure 1). As depicted in Figure 1, isolates with serotypes covered by PCV10 and PCV13 vaccine formulations varied

by study year, age group and geographic region, but not biological sex. Overall, isolates with serotypes covered by PCV15 and PCV20 vaccine formulations made up 43.5% and 62.6% of isolates, respectively (Figure 1), which also varied by study year, age group and geographic region, but not biological sex. Overall, isolates with serotypes covered by PPSV23 represented 72% of all isolates, with the proportion of PPSV23-unique serotypes increasing over time (Figure 1). In addition, non-vaccine serotypes (NVSs) appeared to increase in prevalence over time except in 2020 (Figure 1).

For those aged 65 years and older, the number of isolates with serotypes covered by vaccine formulations was consistent over time, with an increase in the number of isolates with NVS,

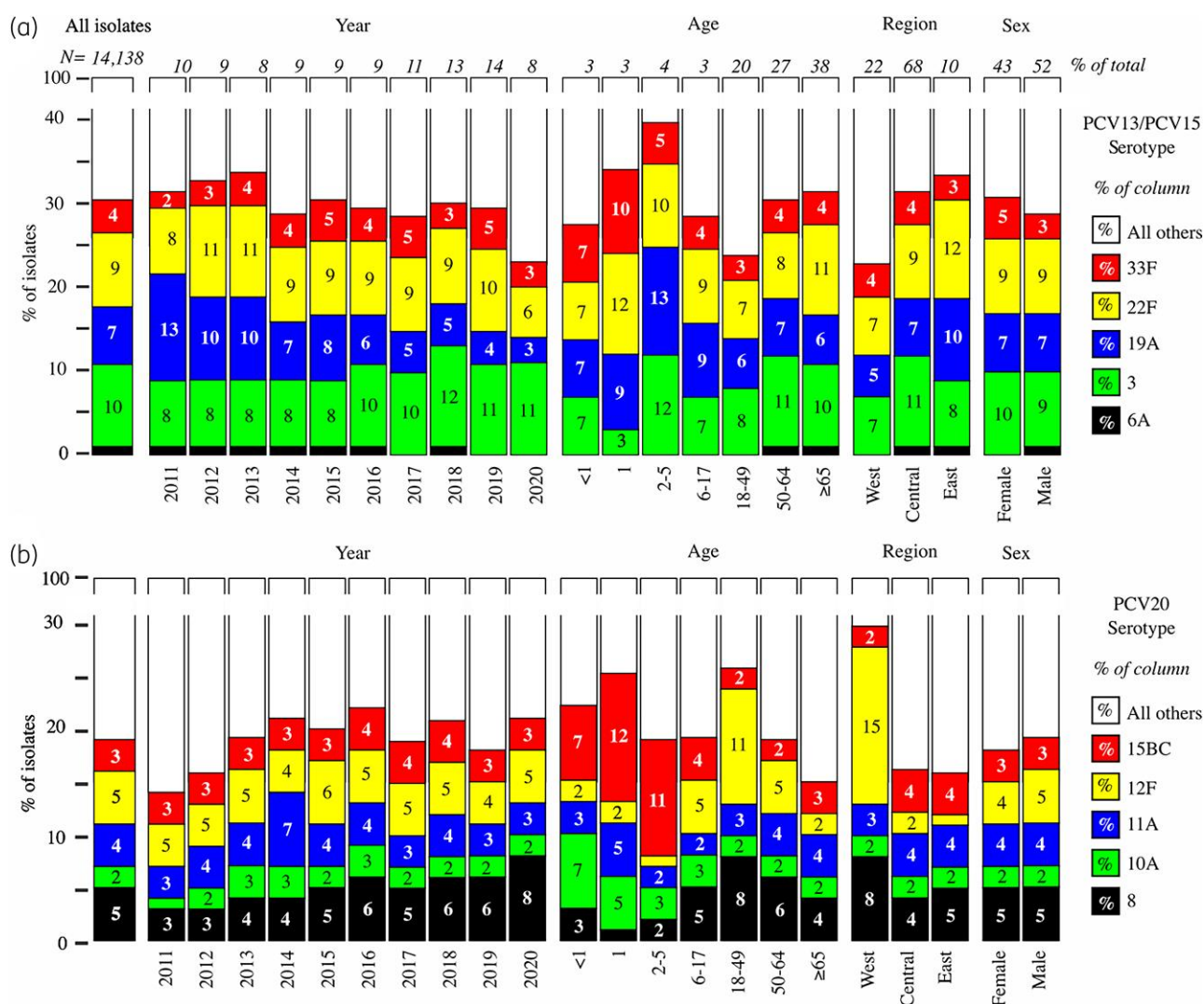


Figure 3. Coverage of SAVE isolates by specific PCV13, PCV15 and PCV20 serotypes over time, by age group, region and sex. (a) Coverage by PCV13 serotypes 3, 6A and 19A, and PCV15 serotypes 22F and 33F. (b) Coverage by PCV20 serotypes 8, 10A, 11A, 12F and 15BC. PCV, pneumococcal conjugate vaccine. Isolates with missing values for age ($n=245$; 1.7%) and sex ($n=663$; 4.7%) are not shown. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

especially during 2017 to 2019 (Figure 2). A similar increase in NVS isolates was observed in those aged 50–64 years, along with a modest increase in isolates with PCV20 serotypes in 2018–19. For those aged 18–49 years, isolates with PCV13 and PCV20 serotypes also increased in 2018–20. For younger age groups (<1, 1, 2–5 and 6–17 years), a small number of isolates from all vaccine coverage groups were observed during the study time period, with little variation over time. No isolates from PCV10 serotypes were found in those aged 1 year between 2017 and 2019, with a small number observed in 2020, even though fewer isolates were submitted that year (Figure 2).

PCV15 and PCV20 provided significantly greater coverage of IPD isolates than PCV10 and PCV13 in both males and females, all age groups, all geographic regions (Table 1) and in antimicrobial-resistant phenotypes, including MDR phenotypes (Table 2). Non-PCV13 serotypes 22F and 33F (in PCV15) represented 12.9% of all IPD serotypes, while non-PCV15 serotypes

8, 10A, 11A, 12F and 15B/C (in PCV20) represented 19.0% of all IPD serotypes (Table 1, Figure 1, Figure 3a and b). Non-PCV20 serotypes 2, 9N, 17F and 20 (but not 6A, which is not covered by PPSV23) represented 8.8% of all IPD serotypes (Figure 1). While higher-valency vaccine formulations covered significantly more isolates across demographic categories, serotype coverage of XDR isolates did not significantly differ between PCV13, PCV15 and PCV20 (Table 2). When considering the serotypes that make up each additional vaccine formulation (3, 6A and 19A in PCV13; 22F and 33F in PCV15; and 8, 10A, 11A, 12F and 15BC in PCV20), most have remained at similar proportions in each year of the study with some exceptions (Figure 3a and b). Serotype 19A (PCV13) isolates have decreased in proportion relative to total isolates each year, from 13% in 2011 to 3% in 2020 (Figure 3a), while serotype 8 (PCV20) isolates have increased in proportion over time, from 3% in 2011 to 8% in 2020 (Figure 3b).

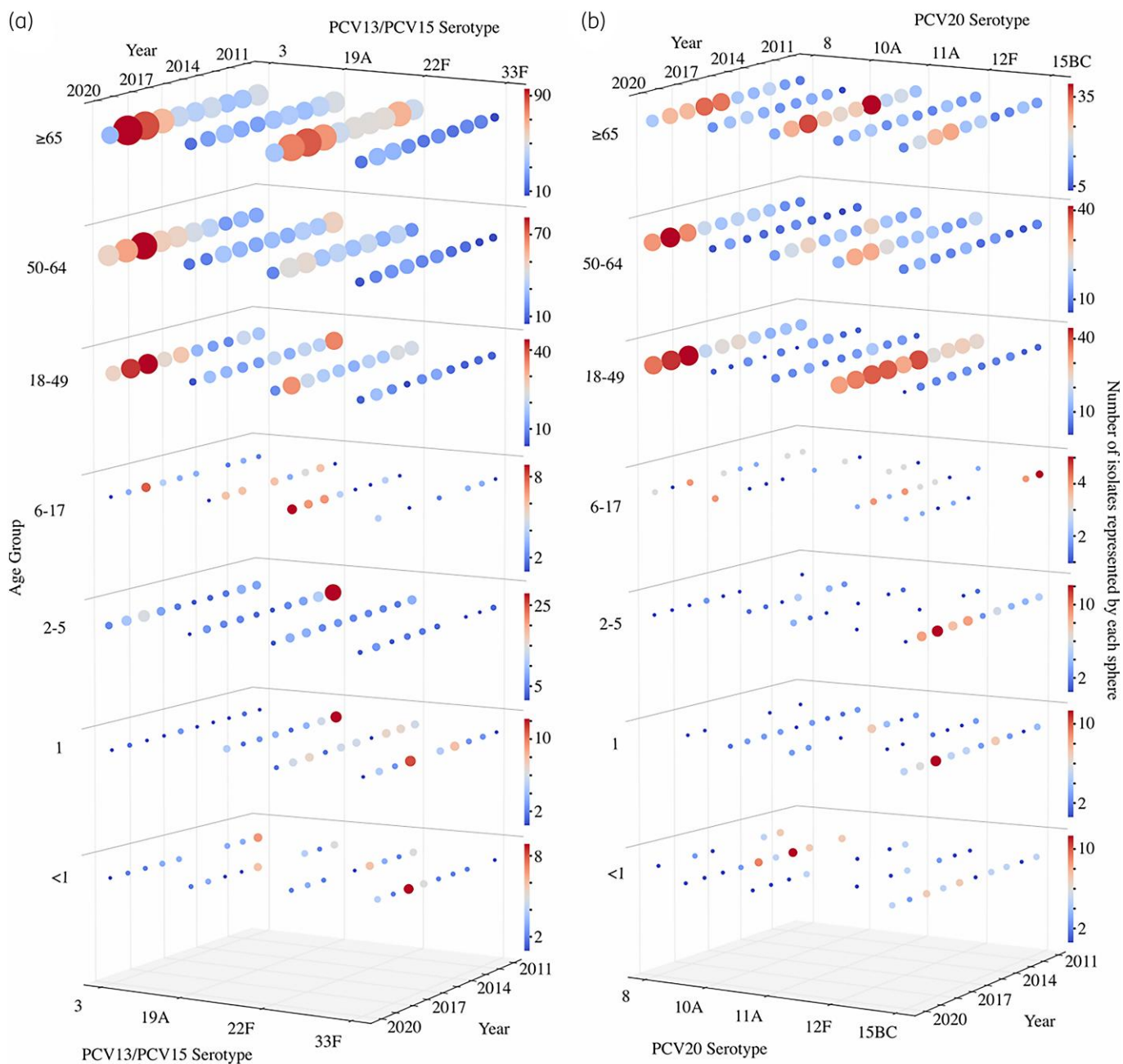


Figure 4. Comparison of time series for specific PCV13, PCV15 and PCV20 serotypes, by age group [$n=13\,893$, isolates with missing age information ($n=245$) not shown]. Each sphere (size and shade) represents the number of isolates for each combination of serotype, age group and year. This figure appears in colour in the online version of *JAC* and in black and white in the print version of *JAC*.

PCV13 serotype 19A and PCV15 serotype 33F isolates made up a higher proportion of isolates in younger age groups (Figure 3a), as did PCV20 serotype 10A and 15B/C isolates (Figure 3b). PCV20 serotypes 8 and 12F isolates made up the highest proportion of isolates from patients aged 18–49 years (Figure 3b). Patients aged 1 year had the lowest proportion of isolates with PCV13 serotype 3 (3%, compared with 7%–12% for other age groups) and PCV20 serotype 8 (1%, compared with 2%–8% for other

age groups). The proportion of isolates with any PCV13 or PCV15 serotype was lower in western Canada compared with central and eastern Canada (Figure 3a), while PCV20 serotypes 8 and 12F were higher in western Canada (Figure 3a). Isolates with PCV13 serotype 3 have increased over time in those aged 65 years and older, as well as in those aged 50–64 and 18–49 years, while serotype 19A has decreased marginally in both age groups (Figure 4a). PCV15 serotype 22F isolates

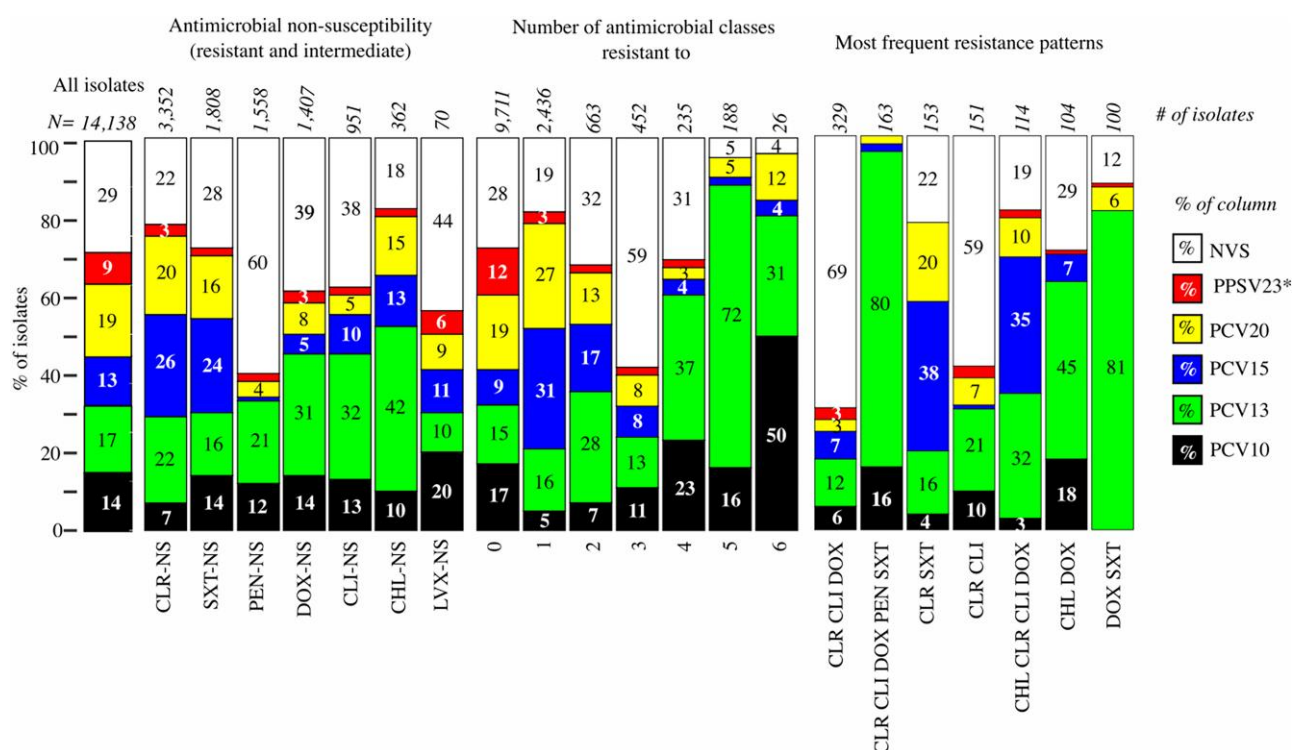


Figure 5. Coverage of antimicrobial-NS, resistant and multiresistant SAVE isolates by PCV10, PCV13, PCV15, PCV20 and PPSV23 serotypes. *For visual clarity of stacked bars, PPSV23 coverage includes a small number of serotype 6B isolates, which are covered by the other formulations, but not covered by PPSV23. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC. PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine, CLR, clarithromycin; DOX, doxycycline; PEN, penicillin; SXT, trimethoprim/sulfamethoxazole; CLI, clindamycin; CHL, chloramphenicol; LVX, levofloxacin.

have also increased in those aged 65 years and older and to a lesser extent in those aged 50–64 years (Figure 4a). Increases in isolates with PCV20 serotypes 8, 11A and 15B/C were seen in those aged 65 years and older, while serotype 8 and serotype 12F isolates both increased among those aged 50–64 years and especially among those aged 18–49 years (Figure 4a).

In younger age groups, isolate numbers were smaller and fewer trends over time were observed. In patients aged 1 year and 2–5 years, PCV13 serotype 19A isolates were infrequent following the decreases observed between 2011 and 2013 (Figure 4a). An increase in PCV15 serotype 22F isolates among those aged 6–17 years was seen from 2017 to 2019, although no 22F isolates were detected in this age group in 2020 (Figure 4a). For PCV20, an increase in serotype 15B/C was observed in patients aged 2–5 years from 2016 to 2019, with a smaller number of isolates observed in 2020 (Figure 4b).

Clarithromycin- and trimethoprim/sulfamethoxazole-NS isolates commonly belonged to PCV15- and PCV20-unique serotypes (Figure 5). Among NVS isolates, the most common NS phenotype was penicillin-NS (60% of isolates), followed by levofloxacin-NS (44%) (Figure 5). Isolates that were NS to doxycycline, clindamycin or chloramphenicol had the highest proportion belonging to PCV13-unique serotypes (31%–42%), while levofloxacin-NS isolates had the highest proportion belonging to PCV10 serotypes, at 20% (Figure 5).

Compared with antimicrobial-susceptible isolates, isolates resistant to a single antimicrobial class were represented in higher

proportions of PCV15-unique (31% versus 9% of non-resistant isolates) and PCV20-unique (27% versus 19%) serotypes, while isolates resistant to three classes of antimicrobials had the highest proportion of NVSs (59%) (Figure 5). Isolates resistant to two classes of antimicrobials also had a higher proportion of PCV13-unique serotypes relative to susceptible isolates (28% versus 15%). Isolates resistant to four, five or six classes of antimicrobials consisted of higher proportions of PCV10 (16%–50%) and PCV13-unique (31%–72%) serotypes. Those resistant to five or six classes of antimicrobials had the lowest representation of NVS (4%–5%) and none belonged to serotypes unique to PPSV23 (Figure 5).

The majority of PCV13-unique isolates resistant to five antimicrobial classes, and with the second most commonly observed resistance pattern (clarithromycin, clindamycin, doxycycline, penicillin and trimethoprim/sulfamethoxazole) (Figure 5), belonged to serotype 19A, which has declined in numbers in all age groups over the study period (Figure 4a).

NVSs accounted for the highest proportion (69%) of the isolates with the most commonly observed resistance pattern (resistance to clarithromycin, clindamycin and doxycycline) (Figure 5). Isolates with dual resistance to clarithromycin and trimethoprim/sulfamethoxazole had higher proportions that belonged to PCV15- (38%) and PCV20-unique (20%) serotypes, while isolates with dual resistance to clarithromycin and clindamycin had only small proportions of PCV15-/PCV20-unique serotypes (<8% for both formulations) and a high proportion of NVS isolates (59%) (Figure 5). A high proportion of isolates resistant to chloramphenicol,

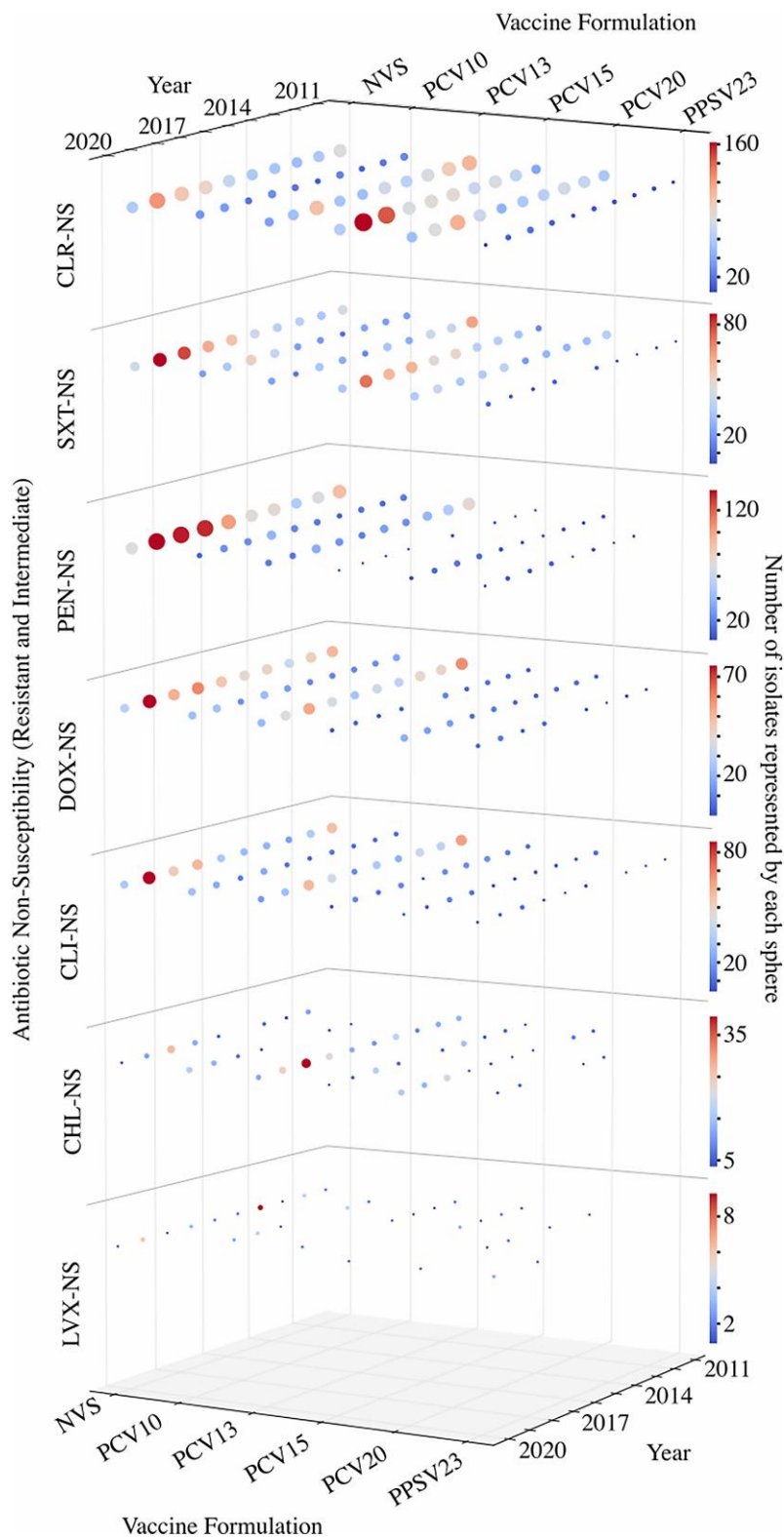


Figure 6. Comparison of time series for PCV10, PCV13, PCV15, PCV20 and PPSV23 serotypes, by antimicrobial non-susceptibility (including intermediate and resistant phenotypes). Each sphere (size and shade) represents the number of isolates for each combination of vaccine formulation, resistance phenotype and year. This figure appears in colour in the online version of JAC and in black and white in the print version of JAC.

clarithromycin, clindamycin and doxycycline also belonged to PCV15-unique serotypes (35%). Isolates with dual resistance to doxycycline and chloramphenicol or doxycycline and trimethoprim/sulfamethoxazole had high proportions that belonged to PCV13-unique serotypes (45% and 81% respectively) (Figure 5).

The number of antimicrobial-NS isolates with NVs increased in the 2017–19 period, particularly for penicillin-NS isolates, but also for clarithromycin-, trimethoprim/sulfamethoxazole-, doxycycline- or clindamycin-NS isolates (Figure 6). Over the same period, the number of NS isolates with PCV15-unique serotypes also increased, particularly for clarithromycin but also for trimethoprim/sulfamethoxazole (Figure 6). NS isolates with PCV13-unique serotypes followed a similar time series pattern for clarithromycin, doxycycline and clindamycin non-susceptibility, with higher numbers in 2011, reductions over the 2012–17 period and an increase in 2018. This was the most frequently observed resistance pattern among isolates resistant to two or more antimicrobials (Figure 5). A significantly higher proportion of clarithromycin-, doxycycline- and trimethoprim/sulfamethoxazole-NS and MDR IPD isolates in Canada were serotypes unique to PCV15 and PCV20 compared with PCV13-unique serotypes (Figure 5, Table 2).

Discussion

This comparative study highlights the dynamics of IPD isolate serotypes in Canada over 10 years, and their coverage by well-established vaccines and new vaccine formulations that target non-vaccine serotypes of increasing concern. The introduction of conjugate vaccine formulations has greatly reduced the incidence of disease caused by vaccine serotypes in many countries, particularly in the very young, accompanied by a rise in the incidence of disease caused by NVs in older age groups.^{10–13} This divergence may limit the long-term herd effects of childhood vaccination programmes as a strategy to protect the elderly.¹⁴ It is critical to understand the spread and evolution of pneumococcal vaccine serotypes as vaccine formulations with expanded coverage become available in North America, Europe and across the world.

The global reduction in IPD since the introduction of conjugated vaccines, particularly in young children, is an example of successful public investment in prevention of illness and antimicrobial resistance.¹⁵ Inevitably, reduction of the major IPD-causing serotypes subsequent to introduction of vaccines has been accompanied by an increase in NVs such as 19A causing severe disease.^{16,17} Our national results are consistent with recently published multi-site data from the USA, where a similar decrease in PCV13 (including PCV10) serotypes and an increase in PCV15-, PCV20- and PPSV23-unique serotypes was observed in the period from 2009 to 2017.¹⁸

Many pathogen and host factors predispose to severe *S. pneumoniae* infections and progression to invasive disease, with specific serotypes such as PCV13 serotypes 3 and 19A associated with severe outcomes such as septic shock, respiratory failure and higher mortality.^{2,19,20} Serotype is one of the main predictors of *S. pneumoniae* infection severity; however, the impact of vaccine formulations on serotype distribution through expansion of NVs and/or capsular switching has been highly variable around the world.¹⁷ For example, direct and indirect protection by PCV13 against infection by serotype 3 has been limited,^{14,15,21} with rising rates of infections with serotype 3 observed globally. In the

SAVE study, serotype 3 infections occurred in all age groups but increased in adults, particularly in the oldest age groups (those 50 years and older) (Figure 4a), indicating a lack of direct or indirect protection of older adults against this PCV13 serotype in the time period covered by this study.

In the UK, PCV20 serotypes 8 and 12F and PPSV23 serotype 9N demonstrated the greatest increase in the post-PCV13 era,¹² consistent with our data. Also consistent with our report, recent surveillance data from Canada demonstrated increases in PCV10 serotype 4, PCV13 serotype 3, and PCV20 serotypes 8 and 12F.²² Our group has previously shown that PCV15 serotypes 22F and 33F isolates were of increasing concern in the period from 2011 to 2018,^{23,24} a trend that the current study confirmed, with increases of 22F isolates in older children and adults (6–17, 18–49, 50–64 and ≥65 years) and increases in 33F isolates, especially in those aged 65 years and older (Figure 4a).

Vaccination with lower-valent formulations such as PCV7 or PCV10 has been shown to offer some protection against serotypes of concern that were not included in these formulations. For example, initial protection against serotype 19A by PCV7 and PCV10 was demonstrated in several locations around the world; however, the use of PCV7 and PCV10 was followed by an increase in frequency of MDR serotype 19A infections.²⁵ After widespread introduction of the PCV13 formulation, which includes serotype 19A, many jurisdictions demonstrated a reduction in both nasopharyngeal carriage and invasive disease caused by serotype 19A.^{18,25} In the SAVE study, the number and proportion of isolates belonging to serotype 19A fell from highs observed in several age groups in 2011 and remained low throughout the current study period (Figure 4a).

Diversification of serotypes causing IPD worldwide may reduce the utility of increasing vaccine valency as a strategy to improve future formulations,¹⁶ therefore, alternative approaches are required as serotype evolution continues. A vaccine providing universal protection against all serotypes would circumvent the problem of shifting patterns of serotype predominance and serotype switching due to the effects of vaccination and antimicrobial use. Several candidate targets are under investigation.²⁶

A limitation of this study is the lack of representation of Western Canada's two largest provinces, Alberta and British Columbia, mitigating any conclusions drawn from regional comparisons including Western Canada. As well, a lower total of isolates collected in 2020 relative to earlier years is likely explained by disruptions experienced due to COVID-19, and not a true drop in incidence.

In summary, new higher-valency conjugated vaccines PCV15 and PCV20 provided significantly greater coverage of IPD than PCV10 and PCV13 across all demographic categories, and various antimicrobial resistance phenotypes including MDR serotypes. From 2011 to 2020, the SAVE study showed that PCV15 vaccine coverage was 43.5%, PCV20 coverage was 62.6% and PPSV23 coverage was 71.3%. Individual vaccine coverage varied depending on the year tested, patient age, geographic location and antimicrobial resistance phenotype.

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Transparency declarations

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Disclaimer

The opinions expressed in this paper are those of the authors, and do not necessarily represent those of Merck Canada Inc. or Pfizer Canada Inc.

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