



# Invasive pneumococcal disease surveillance in Canada, 2020

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## Abstract

**Background:** Invasive pneumococcal disease (IPD), which is caused by *Streptococcus pneumoniae*, has been a nationally notifiable disease in Canada since 2000. The use of conjugate vaccines has markedly decreased the incidence of IPD in Canada; however, the distribution of serotypes has shifted in favour of non-vaccine types. This report summarizes the demographics, serotypes and antimicrobial resistance of IPD infections in Canada in 2020.

**Methods:** The Public Health Agency of Canada's National Microbiology Laboratory (Winnipeg, Manitoba) collaborates with provincial and territorial public health laboratories to conduct national surveillance of IPD. A total of 2,108 IPD isolates were reported in 2020. Serotyping was performed by Quellung reaction and antimicrobial susceptibilities were determined in collaboration with the University of Manitoba/Canadian Antimicrobial Resistance Alliance. Population-based IPD incidence rates were obtained through the Canadian Notifiable Disease Surveillance System.

**Results:** Overall incidence of IPD in Canada decreased significantly from 11.5 (95% confidence interval [CI]: 10.1–13.1) to 6.0 (95% CI: 5.0–7.2), and from 10.0 (95% CI: 9.7–10.3) to 5.9 (95% CI: 5.7–6.2) cases per 100,000 from 2019 to 2020; in those younger than five years and those five years and older, respectively. The most common serotypes overall were 4 (11.2%, n=237), 3 (10.9%, n=229) and 8 (7.2%, n=151). From 2016 to 2020, serotypes with increasing trends ( $p < 0.05$ ) included 4 (6.4%–11.2%), 3 (9.5%–10.9%), 8 (5.2%–7.2%) and 12F (3.6%–5.7%). The overall prevalence of PCV13 serotypes increased over the same period (30.3%–34.9%,  $p < 0.05$ ). Antimicrobial resistance rates in 2020 included 23.0% clarithromycin and 9.9% penicillin (IV meningitis breakpoints). Multidrug-resistant IPD has significantly increased since 2016 (4.2%–9.5%,  $p < 0.05$ ).

**Conclusion:** Though the incidence of IPD decreased in 2020 in comparison to previous years across all age groups, disease due to PCV13 serotypes 3 and 4, as well as non-PCV13 serotypes such as 8 and 12F, increased in prevalence. Continued surveillance of IPD is imperative to monitor shifts in serotype distribution and antimicrobial resistance.

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**Keywords:** invasive pneumococcal disease, IPD, Canada, *Streptococcus pneumoniae*, PCV13, pneumococcus, serotype, surveillance, antimicrobial resistance

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## Introduction

Invasive pneumococcal disease (IPD) causes severe infections such as meningitis and bacteraemia, with children and the elderly being at greatest risk for infection (1). Of the approximately 100 distinct pneumococcal serotypes currently recognized, the majority of disease worldwide is caused by only a few serotypes (1,2). Vaccination has proven effective in reducing the incidence of IPD. A 7-valent pneumococcal conjugate vaccine (PCV7), consisting of serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, was introduced in all Canadian provincial and territorial vaccination programs between 2002 and 2006 (3). Though PCV7 use led to a dramatic decrease in incidence of disease caused by the constituent serotypes (3–5), a subsequent increase in non-PCV7 serotype infections occurred, including serotypes 7F and 19A (3,6). In 2009, a 10-valent pneumococcal conjugate vaccine (PCV10) program (consisting of all PCV7 serotypes plus serotypes 1, 5 and 7F) was implemented in Québec, Ontario, Yukon and Newfoundland and Labrador. The 13-valent pneumococcal conjugate vaccine (PCV13, consisting of all PCV10 serotypes plus serotypes 3, 6A and 19A) was recommended for use in Canada in 2010 and introduced by all provinces and territories during 2010 and 2011, though specific immunization schedules vary by jurisdiction (5,7,8). In 2018, Québec replaced PCV13 with PCV10 for paediatric IPD immunization; subsequently Québec introduced a mixed schedule in late 2020: two doses of PCV10 (two and four months of age); and one dose of PCV13 (one year old). A 23-valent pneumococcal polysaccharide vaccine (PPV23 which includes all PCV13 serotypes except 6A, plus serotypes 2, 8, 9N, 10A, 11A, 12F, 15B/C, 17F, 20, 22F and 33F) has been available for use in Canada since 1989, particularly in older adults and children over two years of age at high risk of IPD (7,9).

Surveillance of the distribution of *Streptococcus pneumoniae* serotypes is important to monitor serotype replacement and inform future vaccine composition. Several higher valency pneumococcal conjugate vaccines (PCVs) are in development. These incorporate emerging serotypes, including PCV15 (consisting of all PCV13 serotypes plus serotypes 22F and 33F) and PCV20 (all PCV15 serotypes plus serotypes 8, 10A, 11A, 12F and 15BC) (10,11). The objective of this annual surveillance report is to provide a summary of the serotypes and antimicrobial resistance associated with IPD in Canada in 2020.

## Methods

### Surveillance program

Surveillance of IPD in Canada consists of a passive laboratory-based system where all invasive isolates from all provincial/territorial public health laboratories are serotyped by the National Microbiology Laboratory (NML), Winnipeg; the *Laboratoire de santé publique du Québec* (LSPQ); or the Provincial Laboratory for Public Health, Edmonton, Alberta (ProvLab Alberta). In 2019, surveillance of IPD in Québec was expanded to all invasive strains. A total of 2,108 IPD isolates were reported in 2020, including 1,408 submitted to NML by provincial and territorial public health laboratories; as well as data for 426 and 274 IPD isolates serotyped by LSPQ and ProvLab Alberta, respectively (Table 1). Sterile clinical isolation sites include blood, cerebrospinal fluid, peritoneal, pericardial or joint fluid, internal body sites and deep tissue including surgical or biopsy samples. Although *S. pneumoniae* isolated from the pleural cavity does not currently meet the national case definition for invasive disease, these isolates are included for the analyses in this report as *S. pneumoniae* isolated from pleural fluid is widely considered as invasive in other jurisdictions (3).

**Table 1: Number of invasive *Streptococcus pneumoniae* isolates submitted by province in 2020**

Province	Age groups (years)						Not given	Total
	Younger than 2	2–4	5–14	15–49	50–64	65 or older		
British Columbia <sup>a</sup>	2	3	6	88	115	74	1	289
Alberta	7	3	0	115	80	68	1	274
Saskatchewan	3	2	1	41	41	21	2	111
Manitoba	6	3	2	79	48	29	0	167
Ontario	26	13	8	150	229	246	4	676
Québec	38	14	9	71	117	225	1	475 <sup>b</sup>
Atlantic <sup>c</sup>	0	0	2	14	21	51	6	94
Northern <sup>d</sup>	0	0	1	9	8	4	0	22
Total	82	38	29	567	659	718	15	2,108

<sup>a</sup> Includes isolates from the Yukon

<sup>b</sup> Québec provincial surveillance program expanded in 2019

<sup>c</sup> Includes isolates from New Brunswick, Prince Edward Island, Nova Scotia and Newfoundland and Labrador

<sup>d</sup> Includes isolates from Northwest Territories and Nunavut



Preliminary population-based incidence of disease data for 2020 were obtained through the Canadian Notifiable Disease Surveillance System (CNDSS). Population data for incidence rates were obtained from Statistics Canada's July 1<sup>st</sup> annual population estimates.

## Isolate testing

All IPD isolates were screened using bile solubility and optochin disc susceptibility (Oxoid) (12). Serotyping of IPD at NML, LSPQ and ProvLab Alberta was performed by the Quellung reaction using pool, group, type and factor commercial antisera (SSI Diagnostica; Statens Serum Institute, Copenhagen, Denmark) (13). Isolates for which a Quellung reaction was not observed were confirmed as *S. pneumoniae* by *rpoB* gene sequencing (14,15). For this study serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (16,17).

In 2011, the NML began a collaboration with the University of Manitoba/Canadian Antimicrobial Resistance Alliance to provide antimicrobial susceptibility testing for *S. pneumoniae* isolates submitted to NML. All IPD isolates (n=1,022) submitted to NML for serotyping by the provincial public health laboratories of Saskatchewan, Manitoba, Ontario, Québec, Nova Scotia, Prince Edward Island, Newfoundland and Labrador and six of seven health regions in New Brunswick were included in the study. Tested antimicrobials included penicillin, amoxicillin/clavulanate, ceftriaxone, chloramphenicol, clarithromycin, clindamycin, doxycycline, imipenem, meropenem, levofloxacin, trimethoprim/sulfamethoxazole, linezolid and vancomycin. Minimum inhibitory concentrations were determined by the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method using 96-well custom designed microtitre plates prepared by Canadian Antimicrobial Resistance Alliance (18). Minimum inhibitory concentration interpretive standards were defined according to CLSI breakpoints (19). Multidrug resistance (MDR) was defined as resistance to three or more classes of antimicrobials. Antimicrobial susceptibility testing results from other laboratories are not included in this report.

## Data analysis

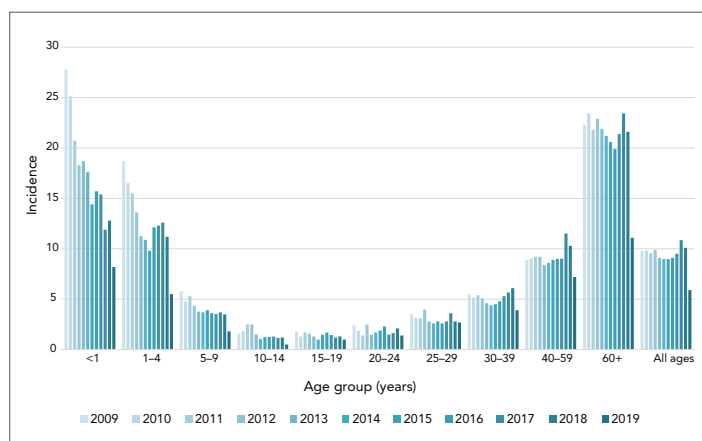
Data submitted with bacterial isolates included patient age, sex, clinical source, province and date of collection. Multiple isolates with the same serotype and collected from the same patient within 14 days were counted once with the most invasive isolation site assigned. Meningitis related isolates were regarded as most invasive, followed by blood and then other sterile sites. The laboratory data were aggregated by age into younger than two, 2–4, 5–14, 15–49 and 50–64 years and 65 years and older age groups and regionally into Western (British Columbia, Alberta, Saskatchewan, Manitoba), Central (Ontario and Québec), Eastern (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador) and Northern

(Yukon Territories, Northwest Territories and Nunavut) regions of Canada. Statistical significance of trends was assessed using the Cochran-Armitage test for trend, with a *p*-value of <0.05 considered significant.

## Results

Prior to 2020, the overall IPD incidence rates in Canada have remained stable since 2009. In 2020 the national incidence rate was 5.9 cases per 100,000 population (95% CI: 5.7–6.2); this was a significant decrease compared to 10.1 cases per 100,000 population in 2019 (95% CI: 9.8–10.4) (**Figure 1; Supplemental material Table S1**). Though IPD incidence declined across all age groups from 2019 to 2020, the largest absolute decline in incidence was seen in seniors aged 60 years and older. It remained around 20 cases per 100,000 population between 2009 and 2019 but declined from 21.6 cases per 100,000 population in 2019 (95% CI: 20.6–22.6) to 11.1 cases per 100,000 population in 2020 (95% CI: 10.4–11.8).

**Figure 1: Annual incidence of invasive pneumococcal disease cases per 100,000 population in Canada by age group, 2010–2020**



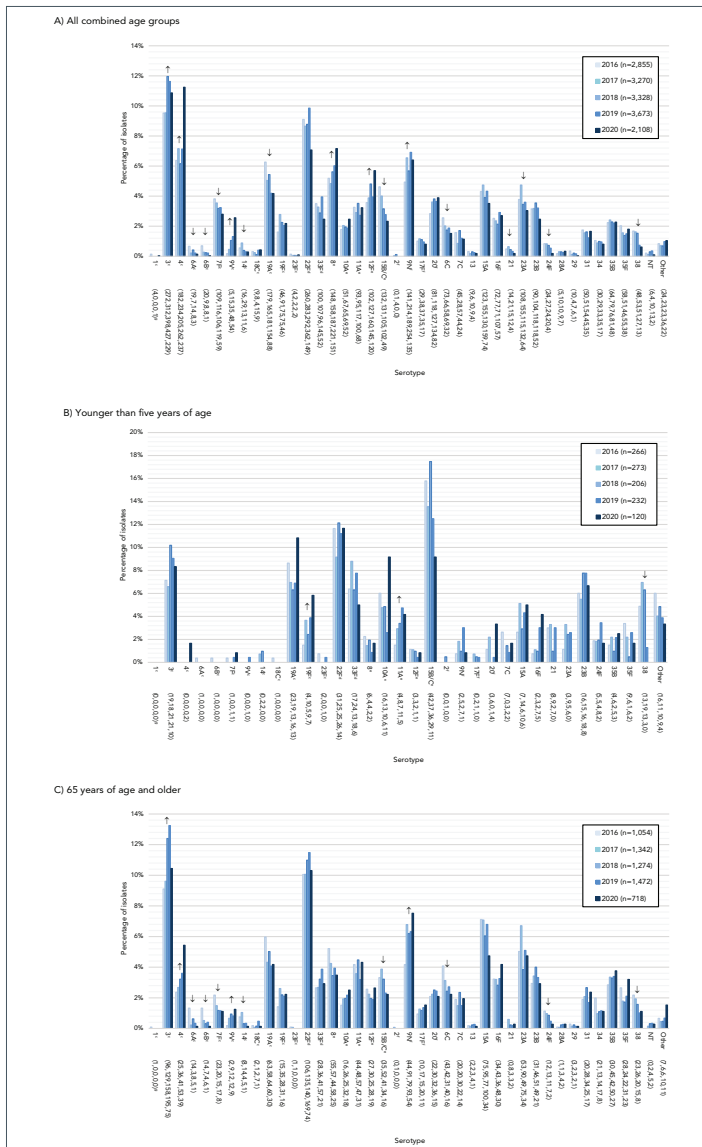
Of the 2,108 IPD isolates serotyped in 2020, 2,098 had patient ages. Infants younger than two years of age accounted for 3.9% (n=82), toddlers aged 2–4 years for 1.8% (n=38), children aged 5–14 years for 1.4% (n=29), adults aged 15–49 years for 26.9% (n=567), older adults aged 50–64 years for 31.3% (n=659) and seniors aged 65 years and older for 34.1% (n=718). Sex information was specified for 2,066 isolates of which 58.2% (n=1,203) were from male patients. Blood was the most frequent clinical isolation site accounting for 92.3% (n=1,945) of all isolates collected in 2020. Additional information on serotypes by specimen source can be found in **Figures S1 to S4**.

The most commonly collected serotypes overall in 2020 were 4 (11.2%, n=237), 3 (10.9%, n=229), 8 (7.2%, n=151),



22F (7.1%, n=149), 9N (6.4%, n=135) and 12F (5.7%, n=120). Serotypes that demonstrated significant increasing trends in prevalence from 2016 to 2020 (Figure 2; A) include PCV13 serotypes 4 (6.4%–11.2%, p<0.001), 3 (9.5%–10.9%, p=0.004) and 9V (0.2%–2.6%, p<0.001), as well as PPV23 serotype 9N (4.9%–6.4%, p=0.02) and PCV20/PPV23 serotypes 8 (5.2%–7.2%, p<0.001) and 12F (3.6%–5.7%, p=0.002). Vaccine serotypes that significantly decreased in prevalence from 2016 to 2020 include 6A, 6B, 7F, 14, 15B/C and 19A (p≤0.04).

Figure 2: Invasive Streptococcus pneumoniae serotype prevalence trends by age, 2016–2020<sup>a,b</sup>



<sup>a</sup> For serotypes with an overall (2016–2020) N≥30: up or down arrows indicate statistically significant trends toward increasing or decreasing prevalence for the 2016–2020 timespan, using the chi-squared test for trend. Serotypes with no arrow either did not demonstrate a statistically significant trend or did not have an overall N≥30. Trends for more detailed age groups can be found in the Supplemental material as Figures S5 to S9  
<sup>b</sup> Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them in vivo during infection, making it difficult to precisely differentiate between the two types (16,17)  
<sup>c</sup> Component of PCV13  
<sup>d</sup> Component of PCV15  
<sup>e</sup> Component of PCV20  
<sup>f</sup> Component of PPV23  
<sup>g</sup> Number of isolates for 2016, 2017, 2018, 2019 and 2020 respectively

The most common serotypes in children younger than two years of age during 2020 included 19A, 15B/C and 22F, all at 12.2% (n=10), while the most common for children 2–4 years old were serotypes 3 (15.8%, n=6), 10A (13.2%, n=5) and 22F (10.5%, n=4). Serotypes 3 (17.2%, n=5), 8 (13.8%, n=4) and 10A (13.8%, n=4) were the most common in those 5–14 years old. Serotype 4 was the most prevalent serotype in those 15–49 years old (20.8%, n=118) followed by serotypes 8 (11.1%, n=63) and 12F (10.9%, n=62). Serotypes 3 (12.6%, n=83) and 4 (11.4%, n=75) were the most common in those 50–64 years old, while serotypes 3 (10.4%, n=75) and 22F (10.3%, n=74) were dominant in adults over 65 years of age (Figure S10 and Figure S11).

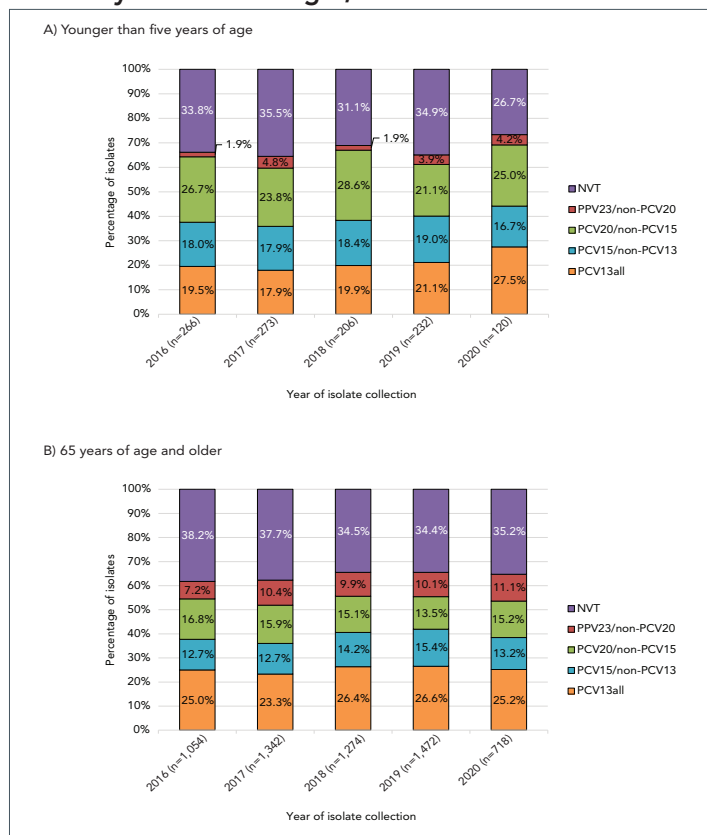
From 2016 to 2020 in children younger than five years of age, significant increases of serotypes 19F (1.5%–5.8%, p=0.04) and 11A (1.5–4.2%, p=0.04) were observed (Figure 2; B). The proportion of serotype 4 isolates increased significantly in adults 15–49 years of age (14.6%–20.8%, p<0.05) (Figure S8) and those 65 years of age and older (2.4%–5.4%, p<0.001) (Figure 2; C). Significant increases of serotype 8 were noted for adults 15–49 years (7.6%–11.1%, p=0.02) and 50–64 years (4.2%–8.6%, p<0.001) (Figure S10 and Figure S11). The 15–49 years of age group saw a significant increase of serotype 12F (6.5%–10.9%, p=0.02), while the 65 years and older age group also demonstrated increases of serotypes 3 (9.1%–10.4%, p=0.007) and 9N (4.2%–7.5%, p=0.02). The PCV13 vaccine serotype 9V increased significantly in all adult age groups (p≤0.01), whereas previously common vaccine serotypes 19A and 7F decreased significantly from 2016 to 2020 in the 50–64 years (7.7%–3.8%, p<0.001) and 65 years and older (2.2%–1.1%, p=0.03) groups, respectively.

Serotypes prevalent in Western Canada during 2020 included 4 (18.2%, n=153), 12F (9.2%, n=77), 3 (8.6%, n=72) and 8 (8.2%, n=69). In Central regions, serotype 3 continued to be the most prevalent (13.0%, n=150), followed by 22F (8.0%, n=92) and 9N (6.8%, n=78). Serotypes 9N (10.6%, n=10) and 22F (10.6%, n=10) were predominant in Eastern Canada. Northern Canada had very few isolates overall, but 63.6% (n=14) were serotype 4 (Figures S12 to S16).

Serotypes belonging to the currently recommended PCV13 formulation have significantly increased in prevalence overall from 2016 to 2020 (30.3%–34.9%, p=0.0034). There were no significant changes in prevalence in child age groups (Figure 3; A). However an increase from 38.7% to 46.9% was observed in the 15–49 years age group (p=0.02). Proportions of PCV15-specific and PCV20-specific serotypes have not significantly changed from 2016 to 2020 among the age groups. The proportion of PPV23 unique serotypes increased in the older than or 65 years age group (7.2%–11.1%, p=0.02) (Figure 3; B) and the number of non-vaccine serotypes (NVTs) overall has decreased from 2016 to 2020 (29.9%–23.6%, p<0.001) (Figures S17 to S21 and Tables S2 to S7).



**Figure 3: Invasive *Streptococcus pneumoniae* serotype trends by vaccine and age<sup>a</sup>, 2016–2020**



Abbreviation: NVT, non-vaccine serotype  
<sup>a</sup> Vaccine serotypes include PCV13 (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F, 18C, 23F); PCV15 (all PCV13 plus 22F and 33F); PCV20 (all PCV15 plus 8, 10A, 11A, 12F, 15B/C) and PPV23 (PCV20 serotypes except 6A, plus 2, 9N, 17F, 20); NVT=all serotypes not included in PCV13, PCV15, PCV20 and PPV23. Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (16,17). Trends for more detailed age groups can be found in the Supplemental material as Figures S17 to S21 and Tables S2 to S7

Antimicrobial susceptibility testing was performed on 1,022 *S. pneumoniae* isolates collected in 2020 (Table 2, Figure S22). The highest rate of resistance during 2020 was observed for clarithromycin at 23.0% (n=235); a decrease from 25.0% (n=453) reported in 2019, though the decrease from 2016 to 2020 was not statistically significant. Penicillin resistance decreased over the 2016 to 2020 timespan, from 12.2% (n=136) to 9.9% (n=101) ( $p=0.003$ ). Other antimicrobial resistance rates for 2020 included doxycycline at 11.4% (n=117), trimethoprim-sulfamethoxazole at 11.1% (n=113), clindamycin at 7.0% (n=72) and chloramphenicol at 4.1% (n=42). All isolates were susceptible to linezolid and vancomycin. Resistance rates for specific serotypes in 2020 are listed in Table 3.

Multidrug resistant IPD increased from 4.2% (n=47) of the isolates tested in 2016 to 9.5% (n=97) in 2020 ( $p<0.001$ ) (Figure 4, Table S8). Of the serotypes where 10 or more isolates were collected in 2020, the highest rates of MDR were identified in 15A (66.7%, n=18), 19A (34.3%, n=12), 19F (27.3%, n=6) and 12F (25.9%, n=14) (Table 3, Figure S23). The most common MDR pattern for serotypes 15A and 19F was macrolide-clindamycin-tetracycline (n=16 and n=13, respectively). Multidrug resistant serotype 19A isolates were most commonly resistant to five antimicrobial classes ( $\beta$ -lactam, macrolide, clindamycin, tetracycline and trimethoprim/sulfamethoxazole; n=9), while the most common MDR pattern for serotype 12F was tetracycline-trimethoprim/sulfamethoxazole-chloramphenicol (n=13) (Table S9).

**Table 2: Proportion of antimicrobial resistant<sup>a</sup> invasive *Streptococcus pneumoniae* isolates by year, 2016–2020**

Antimicrobial	Year									
	2016		2017		2018		2019		2020	
	%	n	%	n	%	n	%	n	%	n
AMC	0.1%	1	0.4%	5	1.2%	22	0.4%	7	1.4%	14
PEN	12.2%	136	15.0%	169	11.2%	199	10.7%	194	9.9%	101
AXO	0.4%	4	0.7%	8	0.7%	13	0.2%	4	0.4%	4
IMI	0.3%	3	1.3%	15	1.4%	25	0.2%	4	1.2%	12
MER	0.7%	8	1.6%	18	2.0%	36	0.9%	17	2.0%	20
LEV	0.3%	3	0.4%	5	0.3%	5	0.6%	10	0.1%	1
CLA	21.5%	240	25.8%	291	25.9%	462	25.0%	453	23.0%	235
CLI	4.2%	47	7.9%	89	6.8%	122	7.3%	133	7.0%	72
CHL	1.2%	13	2.0%	23	5.6%	100	3.1%	57	4.1%	42
DOX	8.5%	95	10.7%	121	8.5%	151	10.5%	191	11.4%	117
SXT	8.8%	98	10.6%	120	7.7%	137	9.5%	172	11.1%	113
Total tested	-	1,114	-	1,130	-	1,784	-	1,815	-	1,022

Abbreviations: AMC, amoxicillin/clavulanic acid; AXO, ceftriaxone using the parenteral meningitis interpretive standard; CHL, chloramphenicol; CLA, clarithromycin; CLI, clindamycin; DOX, doxycycline; IMI, imipenem; LEV, levofloxacin; MER, meropenem; PEN, penicillin using the parenteral meningitis CLSI interpretive standard; SXT, trimethoprim/sulfamethoxazole; -, not applicable  
<sup>a</sup> All isolates were susceptible to linezolid and vancomycin

Table 3: Percentage of antimicrobial resistance and multidrug resistance of invasive *Streptococcus pneumoniae* serotypes collected in 2020

Serotype	Percent resistance <sup>a</sup>										
	PEN	AXO	IMI	MER	LEV	CLA	CLI	CHL	DOX	SXT	MDR
3 <sup>b</sup> (n=112)	-	-	-	-	-	8.9	3.6	8.9	10.7	3.6	3.6
4 <sup>b</sup> (n=133)	0.8	-	-	-	-	14.3	10.5	10.5	13.5	0.75	11.3
6A <sup>b</sup> (n=2)	100	-	-	-	-	100	-	-	-	-	-
7F <sup>b</sup> (n=24)	-	-	-	-	-	-	-	-	-	-	-
9V <sup>b</sup> (n=7)	14.3	-	-	-	-	14.3	-	-	14.3	14.3	14.3
14 <sup>b</sup> (n=5)	60.0	-	20.0	20.0	-	100	80.0	20.0	20.0	80.0	80.0
18C <sup>b</sup> (n=9)	11.1	-	-	-	-	11.1	-	-	11.1	11.1	11.1
19A <sup>b</sup> (n=35)	37.1	5.7	25.7	28.6	-	60.0	31.4	-	34.3	34.3	34.3
19F <sup>b</sup> (n=22)	18.2	4.5	4.5	9.1	-	27.3	22.7	-	27.3	13.6	27.3
23F <sup>b</sup> (n=1)	-	-	-	-	-	-	-	-	-	-	-
22F <sup>c</sup> (n=64)	1.6	1.6	1.6	1.6	-	50.0	3.1	1.6	4.7	6.3	4.7
33F <sup>c</sup> (n=32)	-	-	-	-	-	84.4	6.3	-	9.4	71.9	6.3
8 <sup>d</sup> (n=85)	1.2	-	-	-	-	-	-	-	-	1.2	-
10A <sup>d</sup> (n=22)	-	-	-	-	-	22.7	-	-	-	-	-
11A <sup>d</sup> (n=33)	6.1	-	-	-	-	39.4	3.0	-	3.0	9.1	3.0
12F <sup>d</sup> (n=54)	1.9	-	-	-	-	51.9	1.9	25.9	35.2	35.2	25.9
15B/C <sup>d,e</sup> (n=27)	3.7	-	-	-	-	14.8	-	-	3.7	3.7	-
9N <sup>f</sup> (n=71)	2.8	-	-	-	-	2.8	1.4	-	4.2	2.8	2.8
17F <sup>f</sup> (n=10)	-	-	-	-	-	-	-	-	-	-	-
20 <sup>f</sup> (n=45)	-	-	-	-	-	4.4	2.2	-	6.7	6.7	2.2
6C (n=16)	12.5	-	-	-	-	25.0	-	-	-	18.8	-
7C (n=14)	7.1	-	-	-	-	-	-	7.1	7.1	57.1	7.1
9A (n=2)	-	-	-	-	-	-	-	-	-	-	-
9L (n=1)	-	-	-	-	-	-	-	-	-	-	-
10B (n=1)	-	-	-	-	-	-	-	-	-	-	-
13 (n=3)	-	-	-	-	-	100	33.3	-	66.7	66.7	66.7
15A (n=27)	74.1	-	-	3.7	-	77.8	66.7	-	77.8	3.7	66.7
16F (n=25)	-	-	-	-	-	-	-	-	-	-	-
21 (n=2)	-	-	-	-	-	-	-	-	-	-	-
23A (n=28)	42.9	-	-	-	-	32.1	17.9	-	17.9	3.6	14.3
23B (n=21)	57.1	-	-	-	-	-	-	-	-	14.3	-
24F (n=1)	-	-	-	-	-	-	-	-	-	100	-
28A (n=4)	-	-	-	-	-	-	-	25.0	25.0	-	-
29 (n=1)	-	-	-	-	-	-	-	-	-	-	-
31 (n=19)	5.3	-	-	-	-	10.5	5.3	-	-	-	-
34 (n=12)	-	-	-	-	-	8.3	8.3	-	8.3	41.7	8.3
35B (n=28)	64.3	-	-	17.9	3.6	53.6	-	-	3.6	17.9	14.3
35D (n=2)	50	-	-	-	-	50	-	-	-	50	-
35F (n=15)	-	-	-	-	-	-	-	-	-	-	-
38 (n=5)	-	-	-	-	-	-	-	-	-	-	-
45 (n=1)	100	-	-	-	-	100	-	-	100	100	100
NT (n=1)	-	-	-	-	-	-	-	-	-	-	-
All (n=1,022)	9.9	0.4	1.2	2.0	0.1	23.0	7.0	4.1	11.4	11.1	9.5

Abbreviations: AXO, ceftriaxone using the parenteral meningitis interpretive standard; CHL, chloramphenicol; CLA, clarithromycin; CLI, clindamycin; DOX, doxycycline; IMI, imipenem; LEV, levofloxacin; MER, meropenem; PEN, penicillin using the parenteral meningitis CLSI interpretive standard; SXT, trimethoprim/sulfamethoxazole

<sup>a</sup> "-" denotes no resistance (0%) to the antimicrobial

<sup>b</sup> Component of PCV13

<sup>c</sup> Component of PCV15

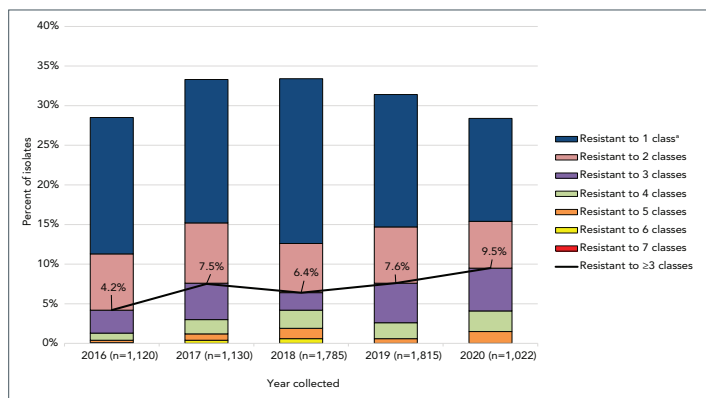
<sup>d</sup> Component of PCV20

<sup>e</sup> Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (16,17)

<sup>f</sup> Component of PPV23



**Figure 4: Annual trend of multidrug resistance of invasive *Streptococcus pneumoniae*, 2016–2020**



\* Antimicrobial classes include:  $\beta$ -lactams (amoxicillin/clavulanic acid, penicillin using meningitis breakpoints, ceftriaxone using meningitis breakpoints, imipenem and meropenem); macrolides (clarithromycin); fluoroquinolones (levofloxacin); tetracyclines (doxycycline); folate pathway inhibitors (trimethoprim-sulfamethoxazole); phenicols (chloramphenicol); lincosamides (clindamycin); oxazolidinones (linezolid)

## Discussion

In 2020, the national incidence rate of IPD in Canada was 5.9 cases per 100,000 population; this was a dramatic decrease in the incidence of IPD in comparison with previous years. After the first case of coronavirus disease 2019 (COVID-19) was recorded in Canada in late January 2020, the first national intervention strategies to prevent the spread of the virus were announced in March/April 2020, including border closures, isolation requirements, masking and work-from-home recommendations. Closures of schools, non-essential businesses and recreational activities followed at the discretion of provincial and territorial governments (20). Like severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), *S. pneumoniae* is transmitted via respiratory droplets; the same measures put in place to prevent the spread of COVID-19 likely also prevented significant transmission of *S. pneumoniae*, possibly accounting for the reduction of IPD cases. The Invasive Respiratory Infection Surveillance Initiative studied the incidence of respiratory-transmitted pathogens associated with invasive disease in the early months of the COVID-19 pandemic; 26 countries submitted data for IPD (21). The study noted that there was a marked decrease in IPD among all participating countries due to containment measures, though the stringency of said measures varied by country. The Invasive Respiratory Infection Surveillance Initiative also estimated that social changes caused by the pandemic resulted in an initial 38% decrease in the incidence of IPD, followed by an additional 13% average weekly reduction up to the end of May 2020 when the study concluded (21). Canada has gone through periods of both increased mobility and restrictive containment measures due to the various pandemic waves; therefore, it is expected that decreased IPD incidence will continue in the near future.

The PCV13 serotypes 3 and 4 continued to be significant sources of IPD in Canada during 2020. Serotype 3 was the second most common serotype collected in 2020 and continued to be a substantial cause of IPD in all age groups. Studies have noted poor immunogenicity of PCV13 against serotype 3, possibly due to the abundant capsule polysaccharide produced during growth that ultimately overwhelms any PCV13-generated protective response (22,23). Early immunogenicity studies of the PCV15 formulation have noted a superior immune response to serotype 3 in comparison to PCV13, though it is currently unclear if this will translate to increased clinical effectiveness (24). Some real-world effectiveness data should be available in the near future; as of late 2021, the United States Advisory Committee on Immunization Practices now recommends using PCV15 (or PCV20) in PCV-naïve adults 65 years or older, or older than 18 years with certain underlying conditions (25). If PCV15 is administered, the Advisory Committee on Immunization Practices recommends that it be followed by PPSV23 (25).

PCV13 serotype 4 overtook serotype 3 as the most predominant IPD serotype in 2020. Serotype 4 has been associated with IPD outbreaks in vulnerable groups of adults and is regionally biased in Western regions of Canada. A study of serotype 4 associated with shipyard outbreaks in Northern Europe found an emergent sequence type (ST801) to be responsible for disease across different countries, though there was significant diversity (26). Another study of serotype 4 in Alberta, Canada observed that this serotype was overrepresented in adults experiencing homelessness and those using illicit drugs. This study also noted genetic diversity within serotype 4, including an emergent sequence type (ST244) associated with the outbreak (27). Similarly, ST244 was found to be responsible for outbreaks of serotype 4 IPD in adults experiencing homelessness in the United States (28). Few serotype 4 isolates were identified in paediatric age groups (n=2) in 2020, where there is also wide uptake of PCV13 (29). According to the 2019 childhood National Immunization Coverage Survey, uptake for pneumococcal conjugate vaccines was 84.4% among those younger than two years of age (29).

Despite the COVID-19 pandemic topping the list of health crises in 2020, antimicrobial resistant pathogens still remain an imminent threat and a significant source of morbidity and mortality worldwide. In general, our surveillance of IPD isolates collected in 2020 noted relatively low rates of antimicrobial resistance. The only resistance rate of concern was that for clarithromycin (23.0%), which has been relatively stable since 2016. Of note is the decrease in penicillin resistance during the same period, which can be speculatively attributed to the PCV13-driven decrease in the overall prevalence of high penicillin-resistant and MDR serotype 19A, a finding observed in other countries such as Portugal (30). In contrast, serotype 19F has been included in all PCV formulations to date. However it has been increasing in prevalence in children younger than five years



of age since 2016 (5.8% of isolates in 2020). This will be crucial to monitor going forward, as a steady increase of a common MDR serotype could have a significant impact on patient outcomes in the future.

## Strengths and limitations

Caution should be exercised when interpreting the data presented in this report. Only a subset of laboratory isolates from each province may have been submitted for testing; therefore, this report does not reflect the true incidence or rates of disease in Canada. The representativeness of the proportions of isolates submitted to the NML for testing as compared to information submitted to [CNDSS](#) are presented in **Table S10**. Not all provinces and territories report line list data to CNDSS; therefore, only aggregated data were available at the national level. For this reason, CNDSS and NML laboratory data are presented differently in terms of age grouping. Age groups are consistent with literature and current immunization recommendations.

## Conclusion

Although the incidence of IPD in Canada decreased significantly in 2020, likely in part due to the intervention strategies used to contain the SARS-CoV-2 virus, several PCV13 vaccine serotypes have increased in prevalence: serotypes 3 and 4 in adult age groups, and 19F in children younger than five years of age. Continued surveillance of IPD serotypes and antimicrobial resistance in Canada is important to monitor existing trends, identify new trends, and assess the effect of the COVID-19 pandemic on the pneumococcal serotype distribution in Canada.

## Authors' statement

ARG — Formal analysis, data curation, visualization, writing—original draft, review and editing of final version  
AG — Formal analysis, validation, investigation, data curation, visualization, writing—review and editing  
WHBD — Formal analysis, validation, investigation, data curation, visualization, writing—review and editing  
BL — Resources, methodology, writing—review and editing  
AM — Resources, methodology, writing—review and editing  
GJT — Resources, methodology, writing—review and editing  
GGZ — Resources, methodology, writing—review and editing  
JVK — Resources, methodology, writing—review and editing  
LH — Resources, methodology, writing—review and editing  
JM — Resources, methodology, writing—review and editing  
PVC — Resources, methodology, writing—review and editing  
HS — Resources, methodology, writing—review and editing  
DH — Resources, methodology, writing—review and editing  
GZ — Resources, methodology, writing—review and editing  
KM — Resources, methodology, writing—review and editing  
LS — Resources, methodology, writing—review and editing  
LS — Resources, methodology, writing—review and editing  
AYL — Writing—review and editing  
MRM — Methodology, writing—review and editing  
IM — Conceptualization, validation, methodology, supervision, project administration, writing—review and editing

## Competing interests

None.

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## Supplementary material

These documents can be accessed on the [Supplemental material](#) file.

Table S1: Annual incidence of invasive pneumococcal disease cases per 100,000 population in Canada by age group, 2010–2020

Figure S1: Clinical isolation site of invasive *Streptococcus pneumoniae* isolates collected in 2020, by age

Figure S2: Percentage of invasive *Streptococcus pneumoniae* isolates from blood in 2020, by serotype

Figure S3: Percentage of invasive *Streptococcus pneumoniae* isolates from cerebrospinal fluid in 2020, by serotype

Figure S4: Percentage of invasive *Streptococcus pneumoniae* isolates from other sterile sites in 2020, by serotype

Figure S5: Prevalence of invasive *Streptococcus pneumoniae* serotypes in those younger than two years old, 2016–2020

Figure S6: Prevalence of invasive *Streptococcus pneumoniae* serotypes in those 2–4 years old, 2016–2020

Figure S7: Prevalence of invasive *Streptococcus pneumoniae* serotypes in those 5–14 years old, 2016–2020

Figure S8: Prevalence of invasive *Streptococcus pneumoniae* serotypes in those 15–49 years old, 2016–2020

Figure S9: Prevalence of invasive *Streptococcus pneumoniae* serotypes in those 50–64 years old, 2016–2020

Figure S10: Prevalence of invasive *Streptococcus pneumoniae* serotypes isolated in 2020 for those younger than two, 2–4 and 5–14 years old

Figure S11: Prevalence of invasive *Streptococcus pneumoniae* serotypes isolated in 2020 for those 15–49 and 50–64 years and 65 years and older

Figure S12: Number of invasive *Streptococcus pneumoniae* isolates collected in 2020, by region and serotype





Figure S13: Prevalence of the ten most common invasive *Streptococcus pneumoniae* serotypes collected from Western Canada in 2020

Figure S14: Prevalence of the ten most common invasive *Streptococcus pneumoniae* serotypes collected from Central Canada in 2020

Figure S15: Prevalence of the ten most common invasive *Streptococcus pneumoniae* serotypes collected from Eastern Canada in 2020

Figure S16: Prevalence of invasive *Streptococcus pneumoniae* serotypes collected from Northern Canada, 2020

Figure S17: Proportion of invasive pneumococcal disease isolates by vaccine for those younger than two years old, 2016–2020

Figure S18: Proportion of invasive pneumococcal disease isolates by vaccine for those 2–4 years old, 2016–2020

Figure S19: Proportion of invasive pneumococcal disease isolates by vaccine for those 5–14 years old, 2016–2020

Figure S20: Proportion of invasive pneumococcal disease isolates by vaccine for those 15–49 years old, 2016–2020

Figure S21: Proportion of invasive pneumococcal disease isolates by vaccine for those 50–64 years old, 2016–2020

Table S2: Proportion of vaccine serotypes for those younger than two years old, 2016–2020

Table S3: Proportion of vaccine serotypes for those 2–4 years old, 2016–2020

Table S4: Proportion of vaccine serotypes for those 5–14 years old, 2016–2020

Table S5: Proportion of vaccine serotypes for those 15–49 years old, 2016–2020

Table S6: Proportion of vaccine serotypes for those 50–64 years old, 2016–2020

Table S7: Proportion of vaccine serotypes for those 65 years and older, 2016–2020

Figure S22: Antimicrobial resistance trends of invasive *Streptococcus pneumoniae* isolates, 2016–2020

Figure S23: Invasive *Streptococcus pneumoniae* serotypes by resistance to different antimicrobial classes, 2020

Table S8: Multidrug resistance of invasive *Streptococcus pneumoniae* isolates, 2016–2020

Table S9: Multidrug resistance profiles of invasive *Streptococcus pneumoniae* serotypes in 2020

Table S10: Number of invasive *Streptococcus pneumoniae* isolates serotyped by the National Microbiology Laboratory (NML) in comparison to the total number of cases reported to Canadian Notifiable Diseases Surveillance System (CNDSS), 2020

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