Trends in serotypes causing invasive pneumococcal disease in Canadian adults, 2000-2009

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Abstract (Updated)

Background:
Since 1993, the Canadian Bacterial Surveillance Network (CBSN) has comprised microbiology laboratories that submit *Streptococcus pneumoniae* (SPN) isolates to a central lab for serotyping and susceptibility testing. Routine paediatric PCV7 was introduced in Canadian provinces between 2002 and 2005.

Methods:
Labs submit one SPN isolate per adult IPD case for serotyping and susceptibility testing (CLSI standards).

Results:
From 2000 to 2009, 6747 SPN isolates from adult (≥15 years) IPD cases were submitted from 186 microbiology labs in all 10 provinces (blood: 6222, CSF: 169, pleural fluid: 140, other: 216). During this time, the percent of IPD due to serotypes in PCV7 decreased significantly (56% to 18%), while the percent of serotypes not in PCV7, but in PCV13, increased (18% to 43%), as did the percent due to non-conjugate vaccine (NPCV13) serotypes (26% to 40%). The majority of the increase in PCV13 serotypes was due to 19A (1% to 15%) and 7F (4% to 13%).

In 2009, serotypes 19A, 7F and 3 were the most common in adult IPD, representing 15%, 13 % and 10% of isolates. The most common NPCV13 serotypes were 22F (6%), 23A (4%), and 9N (3%). Between 2007 and 2009, 19A and 3 were the most common serotypes from blood (11%, 9%) and CSF (13%, 11%); 22F was most common from pleural fluid (12%); and 3, 6A and 16F from other sterile sites (11%, 10%, 10%). Isolates from pleural fluid were least likely to be covered by PCV13 (33% vs 60% for blood).

From 2000 to 2009, resistance to at least one antibiotic class increased from 22% to 32% and multidrug resistance (R to ≥3 classes) increased from 1% to 6%. From 2007 to 2009, RSPN were more likely to be covered by PCV13 than non-R isolates (RSPN: 65% due to PCV13; non-RSPN: 56% PCV13; MDR: 87% due to STs in PCV13); serotypes 33A, 15A, 33F, 6B, 9V, and 19A were most likely to be RSPN (77%, 69%, 67%, 64%, 56%, 55%).

Table 1. Serotype** distribution of SPN isolates from adult IPD cases, Canada, 2000 to 2009.

	Serotype	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
PCV13 (%)	4	11.1	11.6	8.0	8.2	10.5	10.5	9.4	6.7	5.9	5.5
PCV10 (%)	6B	7.5	8.1	6.2	7.5	7.1	6.8	5.3	3.5	3.0	1.8
PCV7 (%)	9V	6.0	7.0	8.0	7.8	6.7	6.7	7.2	5.9	3.9	2.0
	14	15.7	16.6	13.2	12.2	10.2	7.3	7.0	5.8	3.7	2.5
	18C	4.5	3.9	3.7	4.3	3.3	2.9	3.4	2.9	0.8	1.5
	19F	4.1	3.6	5.7	5.8	4.8	3.9	4.0	3.6	3.7	3.2
	23F	7.0	6.3	9.0	4.5	5.1	4.4	2.2	2.9	1.0	1.0
	1	1.2	0.8	1.6	1.9	1.4	0.8	0.3	0.3	0.3	0.0
	5	0.2	0.2	0.1	0.0	0.0	1.0	4.1	2.9	0.4	0.5
	7F	4.1	4.5	2.6	3.0	3.1	3.1	2.5	4.5	8.3	12.7
	3	7.0	6.4	9.2	8.3	9.5	7.5	9.1	8.3	9.5	9.8
	6A	4.3	3.0	4.0	4.3	4.3	5.4	5.0	7.0	5.3	4.8
	19A	1.3	0.9	1.9	2.4	2.4	3.7	4.6	6.7	10.2	14.7
NPCV13 serotypes with >50 isolates (05-09) (%)	8	2.2	2.2	1.2	1.9	2.6	1.9	2.4	3.2	3.6	2.3
	9N	2.6	2.7	1.7	2.4	2.3	2.8	3.4	3.2	3.0	3.0
	10A	0.3	0.8	1.0	0.8	1.3	1.7	1.5	0.8	1.0	1.7
	11A	2.2	3.6	3.0	2.2	1.9	3.5	2.2	2.4	2.5	2.8
	12F	2.1	1.6	1.4	3.7	4.1	4.2	3.8	3.3	2.9	1.3
	15A	0.3	0.6	1.0	0.5	0.6	0.7	0.9	1.1	1.5	2.5
	15B	0.7	0.3	0.6	1.3	1.0	1.4	0.9	0.6	1.5	0.8
	16F	1.3	1.3	1.4	0.6	1.1	1.1	1.0	2.0	1.4	1.3
	22F	4.7	6.6	6.2	5.4	6.7	6.2	7.2	7.4	6.6	6.2
	23A	0.9	1.1	0.6	1.3	1.4	1.4	1.6	2.1	3.6	3.5
	33A	0.4	0.9	0.6	1.0	1.0	1.8	1.2	2.1	3.9	2.5
	34	0.9	0.3	0.4	0.8	0.6	0.7	0.7	0.5	1.7	0.8
	35B	0.9	0.8	0.7	1.8	0.7	1.9	1.8	1.7	1.8	1.8
	35F	0.6	0.5	0.6	0.8	0.9	0.6	0.4	0.9	1.8	0.8

**Includes serotypes covered by the PCV13 vaccine or representing >0.7% (50) isolates from 2000 to 2009.

Methods

- Since 1993, CBSN has collected all SPN sterile site isolates from participating Canadian hospitals and private microbiology labs. In total, 186 labs have participated with 42 labs submitting for the entire period.
- Only one isolate per patient episode is included.
- Isolates are shipped to the central lab at Mount Sinai Hospital where they are confirmed as SPN and frozen. For this report, broth microdilution susceptibility testing is interpreted using EUCAST standards. Serotype is determined using latex pneumococcal antisera (Statens Serum Institute) and Quellung reaction as required.

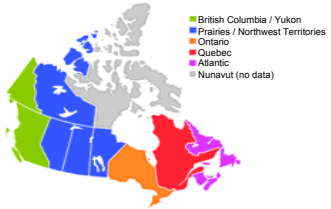

Figure 1. Canadian regions in the Canadian Bacterial Surveillance Network.

Results

From 2000 to 2009, 6747 SPN isolates from sterile sites of adult (≥15 years) patients were submitted including 6222 from blood cultures, 169 from CSF, 140 from pleural fluid, 49 from synovial fluid, 33 from peritoneal fluid, 27 from abscesses and 107 from other sterile sites. Susceptibility testing and serotyping was done on 6742 (99.9%) isolates. Isolates from older adults (>65 years) comprised 45% of the collection. Sixty-one percent of isolates were from Ontario, 6% from Quebec, 10% from the Atlantic provinces, 18% from the Prairies/Northwest Territories and 6% from British Columbia/Yukon.

In 2009, the most common serotypes in adult IPD were 19A, 7F and 3. The most common NPCV13 serotypes (serotypes not covered by the PCV13 vaccine), were 22F, 23A, and 9N.

From 2000 to 2009, the proportion of PCV7 serotypes decreased (56% to 17%) while the proportion of isolates included in PCV13, but not PCV7, increased (18% to 42%). IPD isolates due to NPCV13 serotypes increased from 26% to 40%.

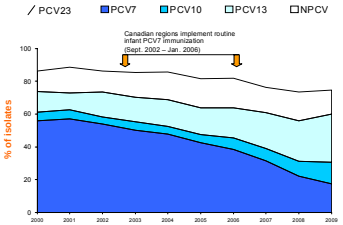

Figure 2. Percent of isolates of serotypes in the PCV7, PCV10, PCV13, and PPV23 vaccines; Canadian isolates collected from adult sterile sites, 2000-2009.
*Vaccines include serotypes of lower valent vaccines except PPV23's exclusion of 6A.

Results (con't)

The increased proportion of serotypes in PCV10, but not PCV7, is due to the increase in the percentage of 7F. The majority of the increase in the proportion of serotypes in PCV13, but not PCV10, is due to an increase in the percentage of 19A.

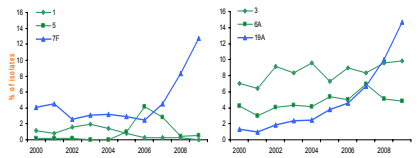

Figure 3: Percent of adult sterile site isolates of serotypes included in the PCV13, but not PCV7 vaccine, from across Canada, 2000 to 2009.

The increased proportion of NPCV13 serotypes was distributed across many serotypes. Serotypes 33A, 23A and 15A have the greatest proportional increases (Figure 4); however, of the 50 different NPCV13 serotypes, only serotype 22F comprised > 5% of isolates.

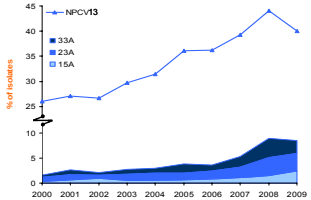

Figure 4. Percent of isolates of serotypes not included in PCV13 (NPCV13) and serotypes 15A, 23A and 33A; Canadian isolates from adult sterile sites, 2000 to 2009.

Serotypes 3 and 19A were the most common in blood and CSF. Serotype 22F was most common in pleural fluid and serotypes 3, 6A and 16F were most common from other sterile sites. CSF isolates were significantly more likely to be 23A than isolates from blood. Isolates from pleural fluid were significantly more likely to be of serotypes 31 and 15B.

Table 2. Percent by site for serotypes representing ≥3% of isolates from blood, CSF, pleural fluid or other sterile site, 2007-2009. Orange rows highlight significant differences between sites ($\alpha \leq 0.05$, Fisher's exact, between all sites).

		Blood	CSF	Pleural Fluid	Other Sterile Site
	Total number of isolates	1585	49	29	62
Serotype (%)	3	9.2	11.3	5.9	11.0
	4	6.5	1.9	2.9	0.0
	6A	5.6	3.8	5.9	9.6
	6B	2.8	3.8	2.9	2.7
	7F	8.9	1.9	0.0	2.7
	8	3.3	0.0	0.0	1.4
	9N	3.2	0.0	2.9	2.7
	9V	4.1	5.7	0.0	2.7
	10A	1.0	5.7	0.0	0.0
	11A	2.6	3.8	5.9	0.0
	12F	2.5	5.7	5.9	1.4
	14	4.3	1.9	0.0	1.4
	15A	1.6	1.9	5.9	1.4
	15B	0.9	3.8	5.9	0.0
	16F	1.3	0.0	0.0	9.6
	18C	1.5	3.8	5.9	2.7
	19A	10.6	13.2	2.9	6.9
	19F	3.3	5.7	2.9	8.2
	22F	6.8	1.9	11.8	6.9
	23A	2.7	7.6	5.9	6.9
	23B	1.2	5.7	0.0	2.7
	31	0.4	0.0	8.8	0.0
	33A	2.8	3.8	2.9	4.1

Results (con't)

Isolates of serotype 19A identified between 2007 and 2009 were five times more likely to be non-susceptible to penicillin than other serotypes (57% vs 11%), about twice as likely to be resistant to erythromycin (42% vs 20%), and four-times more likely to be non-susceptible to ceftriaxone (14% vs 4%). Serotypes 15A and 33A were also associated with antimicrobial resistance (69% and 63% erythromycin resistance, 16% and 65% trimethoprim-sulfamethoxazole resistance, 69% and 0% penicillin non-susceptibility, respectively). In contrast, serotypes 7F and 3 were rarely resistant to antibiotics.

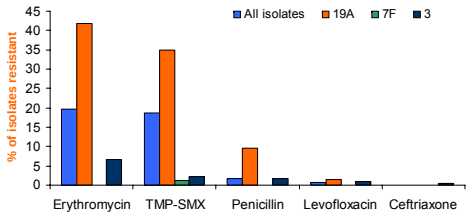

Figure 5: Percent of adult sterile site isolates by serotype resistant to trimethoprim-sulfamethoxazole, erythromycin, ceftriaxone, and amoxicillin and multidrug resistant Canadian isolates, 2000-2009. Includes serotypes representing ≥10% of 2009 isolates (non-mening/non-pneu resistance breakpoints: penicillin>2mg/L).

Conclusions

- Following the implementation of PCV7, the proportion of isolates causing IPD in adults due to serotypes in PCV7 has decreased,
- The increased proportion of serotypes covered by PCV13, but not PCV7, is primarily due to serotypes 7F and 19A.
- IPD due to serotypes not included in conjugate vaccines was due to 50 different serotypes with only serotype 22F comprising more than 5% of any isolates between 2000 and 2009.
- The serotype distribution of bacteremia, meningitis, and empyema in adults differs in our population.
- Among serotypes that are increasing in frequency, serotypes 19A, 15A and 33A are most likely to be antimicrobial resistant.

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