

National Laboratory Surveillance of Invasive Streptococcal Disease in Canada

Annual Summary 2017

**Streptococcus and STI Unit
Bacterial Pathogens Division
National Microbiology Laboratory
Public Health Agency of Canada**

**Vaccine Preventable Diseases
Centre for Immunization and Respiratory Infectious Diseases
Public Health Agency of Canada**

**Provincial and Territorial Public Health Microbiology
Laboratories**

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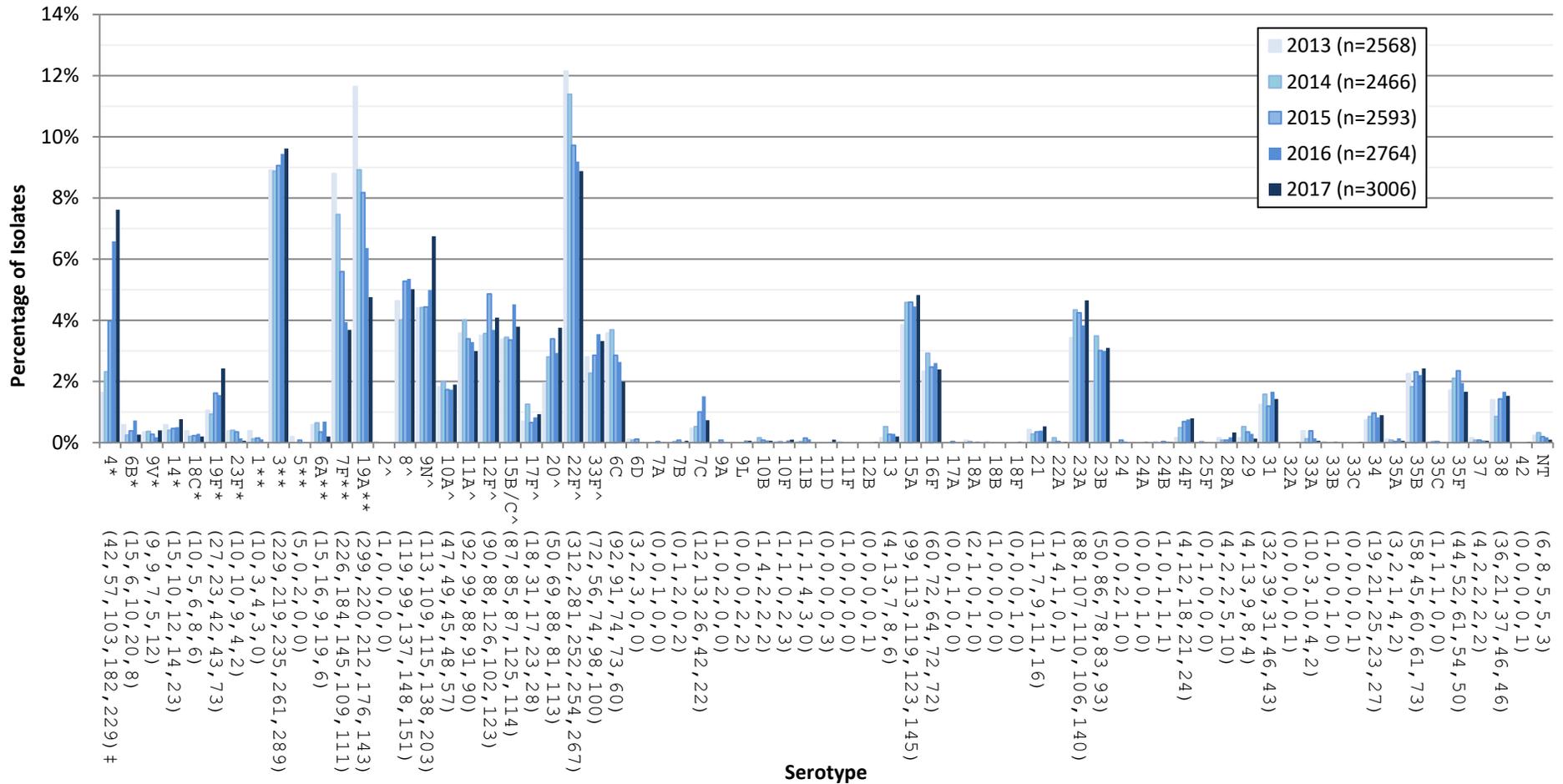
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EXECUTIVE SUMMARY

- ***Streptococcus pneumoniae***: 3,006 isolates causing invasive pneumococcal disease (IPD) were characterized in 2017.
- In 2017, incidence of IPD declined in children under <1 year of age to 14.9 cases per 100,000 population; and in seniors ≥60 years increased to 21.1 cases per 100,000 population. The overall crude incidence rate has remained stable averaging 9.4 cases per 100,000 population since 2009.
- PCV7 serotypes remained relatively unchanged overall in 2017 accounting for 12% of IPD. Increases were seen in serotypes 4 and 19F.
- PCV13 (not including PCV7) serotypes accounted for 18% of overall IPD, continuing an overall decline from 36% in 2012. However, rates of serotype 3 remain fairly consistent in all age groups. Continued declines of PCV7 and PCV13 serotypes in seniors ≥65 years of age, as well as lower case rates in this age group, indicate indirect reduction of disease most likely through herd immunity effects.
- Overall levels of PPV23 and non-vaccine serotypes (NVT) have remained relatively unchanged in 2017 at 42% and 29%, respectively. Increases were seen in serotype 9N in ≥50 year olds.
- **Predominant serotypes** in 2017 were serotype 3 (10%), 22F (9%), 4 (8%), 9N (7%) and 8 (5%). 33F was the most prevalent serotype in <2 year olds accounting for 16% followed closely by 15B/C at 15%. For 2–4 year olds 22F remains predominant with 12%. An increase of serotype 4 in adults was associated with Western regions; 23B was predominant in 2–14 year olds, and 15A was associated with the <65 year old age group in 2017 (Figure A).
- **Antimicrobial susceptibility**: Testing of 1,129 isolates indicated levels of resistance were again relatively stable during 2017 with the following resistance rates: clarithromycin (26%), penicillin (15%), chloramphenicol (15%), doxycycline (11%), clindamycin (8%), trimethoprim/sulfamethoxazole (7%), meropenem (1.6%), and imipenem (0.1%). Serotypes 6A/C, 19A/F, 23A/F, 15A, 9V, 14 and 35B generally had the highest rates of antimicrobial resistance. **Multi-drug resistance** increased from 6% in 2016 to 10% in 2017. The highest rates of multi-drug resistance were seen in serotypes 15A (65%) and 19F (31%) (Figure B).
- ***S. pyogenes* (Group A *Streptococcus*)**: 2,473 isolates causing invasive disease were characterized for *emm* type.
- Overall incidence of invasive disease has increased from 4.0 to 6.7 cases per 100,000 population from 2009 to 2017.
- Despite a decline since 2013, *emm1* continues to be most predominant among all combined age groups and regions (18%) (Figure C). Regional increases of *emm12* in the East (15%), *emm74* in Central (14%) and *emm49* (5%) in the West have been noted.
- **Antimicrobial susceptibility**: Antimicrobial resistance of *S. pyogenes* is relatively low, however small increases were seen in 2017 with chloramphenicol non-susceptibility at 5%, erythromycin resistance at 10%; and clindamycin resistance at 7%.
- ***S. agalactiae* (Group B *Streptococcus*)**: There were 229 invasive Group B *Streptococcus* submitted to NML during 2017, of which 7 isolates were from early onset cases (infants ≤7 days old) and 8 were from late onset cases (infants 8 – 31 days old). Annual incidence of invasive disease per 100,000 population has fluctuated from a low in 2009 (27.6) to a high in 2014 (38.7), the incidence rate in 2017 was 30.6.
- **Serotypes** Ia (22%), IV (19%) and III and V (17% each) were most predominant.

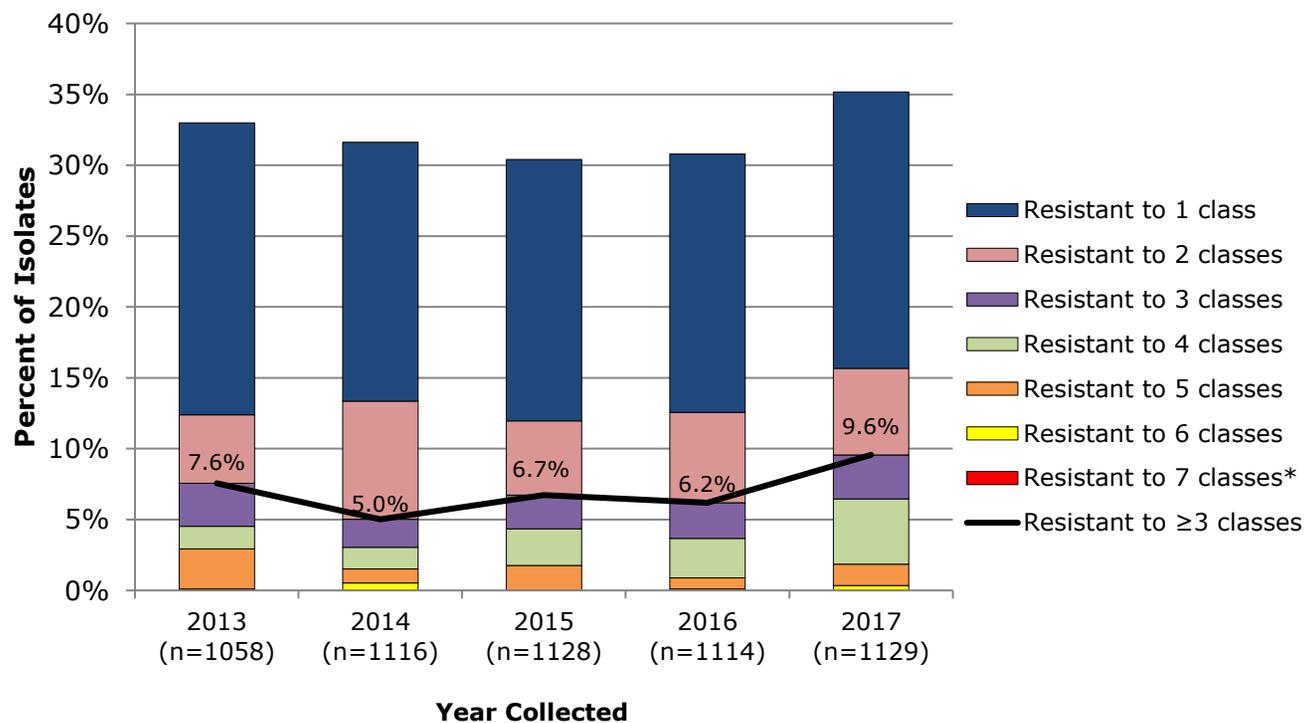
- **Antimicrobial susceptibility:** Resistance to erythromycin increased to 58% while clindamycin resistance increased to 45%.

Figure A. Invasive *S. pneumoniae* serotypes in all ages



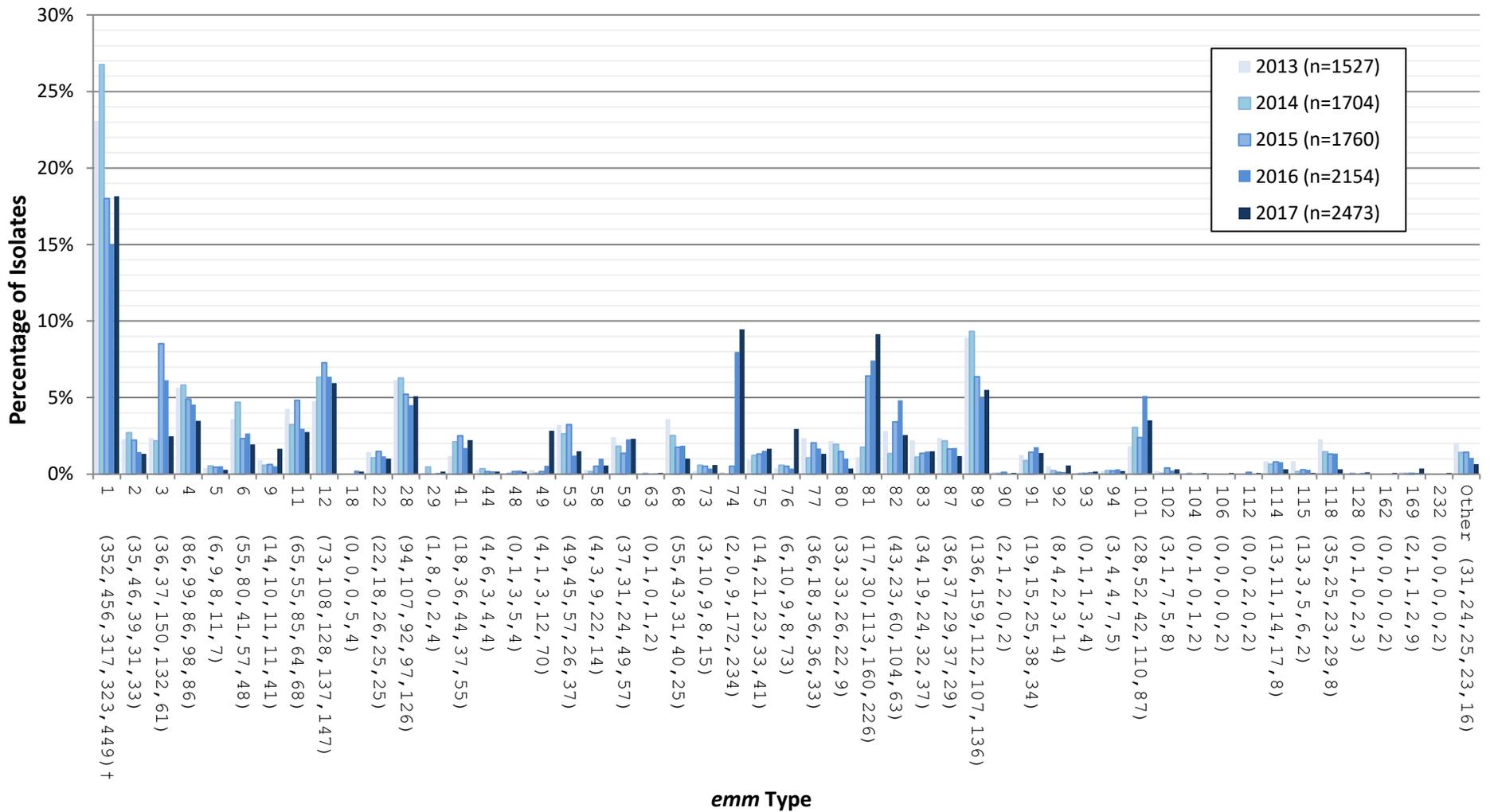
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure B. Annual trend of multi-drug resistance of *S. pneumoniae*



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

Figure C. Invasive *S. pyogenes* emm types



+Number of isolates from 2013, 2014, 2015, 2016 and 2017, respectively.

INTRODUCTION

On April 1, 2010 the National Microbiology Laboratory (NML), Winnipeg began offering surveillance, reference diagnostics and outbreak support on invasive *Streptococcus pneumoniae* (pneumococcus), *Streptococcus pyogenes* (Group A *Streptococcus*, iGAS), and *Streptococcus agalactiae* (Group B *Streptococcus*, GBS). The Streptococcus and STI Unit also participates in a number of international, national and regional surveillance programs.

This report is intended to present the current distribution of serotypes of *S. pneumoniae*, *emm* types of *S. pyogenes*, and serotypes of *S. agalactiae* isolated from sterile sites that are forwarded from Canadian provincial and territorial public health laboratories, regional health units and reference centres to the NML. To broaden the representativeness of the data presented, the aggregated counts also include *S. pneumoniae* serotype data submitted by Laboratoire de santé publique du Québec (LSPQ), Toronto Invasive Bacterial Diseases Network (TIBDN), and the Alberta Provincial Laboratory for Public Health (ProvLab Alberta), organizations that perform their own serotyping.

Invasive pneumococcal disease (IPD, *S. pneumoniae*): IPD causes severe infections such as meningitis and bacteraemia [Marchessault, 2002; Schuchat, 1997] with children and the elderly being at greatest risk for infection [Robinson, 2001; Scott, 1996]. Of the 92 distinct pneumococcal serotypes currently recognized, the majority of disease worldwide is caused by only a few serotypes.

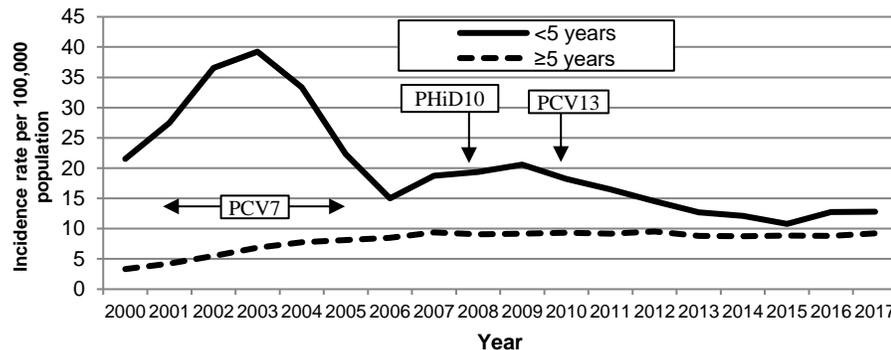
A 7-valent pneumococcal conjugate vaccine (**PCV7**), consisting of serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F, was introduced in all provincial and territorial vaccination programs between 2002 and 2006 [Bettinger, 2010]. This led to a dramatic decrease in incidence of disease and in the constituent serotypes in children [Bettinger, 2010;

Bjornson, 2007; Bruce, 2008; Demczuk, 2012; Deng, 2013; DeWals, 2012; Kellner, 2008; Kellner, 2009; Lim, 2013; Lovgren, 1998; McIntosh, 2011; NACI, 2010; Shahidi, 2008; Tyrrell, 2009; Weinberger, 2011;]

(Figure 1). After the

introduction of vaccination programs, paediatric IPD increased due to serotype replacement among pneumococcal infections with increases in non-PCV7 serotype infections, such as serotypes 7F and 19A [Kellner, 2009; Tyrrell, 2009]. In 2009, a 10-valent Pneumococcal conjugate vaccine (non-typelable Haemophilus influenza (NTHi) protein D, diphtheria or tetanus toxoid conjugates) adsorbed (Synflorix®), (**PHiD10**); consisting of all the PCV7 serotypes plus serotypes 1, 5 and 7F; was used in Québec, Ontario, Yukon and Newfoundland and Labrador. The 13-valent pneumococcal conjugate vaccine (**PCV13**); consisting of all PHiD10 serotypes plus serotypes 3, 6A and 19A; was recommended for use in Canada in 2010 [National Advisory Committee on Immunization (NACI), 2010] and introduced by all provinces and territories between mid-2010 and mid-2011. Immunization schedules vary by jurisdiction, however

Figure 1. Annual incidence of IPD in Canada, 2000-2017



National Advisory Committee on Immunization (NACI) / Public Health Agency of Canada (PHAC) recommendations have been published [NACI, 2010; Public Health Agency of Canada (PHAC), 2017a]. The 23-valent pneumococcal polysaccharide vaccine (**PPV23**) is indicated for those over the age of 2 years with high risk of IPD and is also recommended for older adults. PPV23 is not effective in children under the age of 2 years due to a poor T-cell-independent antibody response in immature immune systems [Merck & Co. Inc.]. Surveillance of the distribution of *S. pneumoniae* serotypes is important to inform vaccine composition and monitor for possible serotype replacement [Demczuk, 2013].

Invasive Group A Streptococcus (GAS, *S. pyogenes*) is responsible for a wide range of disease including bacteraemia, toxic shock syndrome, and skin and soft tissue infections, of which necrotizing fasciitis is most notorious [Cunningham, 2000]. Surveillance of strains is important to monitor increasing virulence patterns associated with this organism [Schwartz, 1990; Siljander, 2010]. Overcrowded and disadvantaged populations have been reported to be at particular risk of disease [Teatero, 2018; Hammond-Collins, 2018]. The M protein, encoded by the *emm* gene, is an important virulence factor and an epidemiological marker used to characterize *S. pyogenes* isolates.

Group B Streptococcus (GBS, *S. agalactiae*) GBS is commonly associated with neo-natal disease where the highest infection risk is during childbirth. In order to decrease the risk of infection in neonates, women are swabbed late in pregnancy and if positive for GBS, they are offered prophylactic antibiotics to decrease the risk of transmission of GBS to their infants. Group B Streptococcal disease is only nationally notifiable in newborns, however, isolates submitted to NML include those that meet the case definition, as well as sterile site isolates from all age groups, since GBS is an increasing health concern among adults causing septicemia, meningitis, pneumonia, bone, joint and tissue infections. At risk adults groups include those with underlying medical conditions, pregnant women and those residing in extended health care facilities [Lamangni, 2013].

METHODS

A total of 3,006 invasive *S. pneumoniae*, 2,473 invasive *S. pyogenes* and 229 *S. agalactiae* isolates are included in this report for 2017. The data include test results for isolates submitted to the NML by provincial and territorial public health laboratories and data provided by jurisdictions including 399 IPD isolates serotyped by Laboratoire de santé publique du Québec, 429 IPD and 390 iGAS by the Alberta Provincial Laboratory for Public Health and 341 IPD by the Toronto Invasive Bacterial Diseases Network. Invasive GAS isolates from all provinces and territories (except Alberta) are submitted to the NML, and invasive GBS isolates are only routinely submitted by Saskatchewan, Manitoba, Newfoundland and Labrador and the Northern Territories for testing.

Data submitted with bacterial isolates included patient age, gender, clinical source 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 <2, 2-4, 5-14, 15-49, 50-64 and ≥65 year old 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. Caution should be exercised when interpreting the data presented in this report as the overall interpretation of the results is limited to only

isolates available for testing. A subset of laboratory isolates within each province may be submitted for testing and therefore this report does not reflect true incidence or rates of disease in Canada. The representativeness of the proportions of isolates submitted to the NML for testing as compared to the Canadian Notifiable Disease Surveillance System (CNDSS) [PHAC, 2017b] are presented in the Appendix. Validated disease incidence data for 2017 was obtained through CNDSS using population data obtained from Statistics Canada July 1st annual population estimates. The population of provinces and territories for whom case data were not available were excluded from the denominator. Not all provinces and territories report line list data to CNDSS and therefore only aggregated data are available at the national level. Therefore, CNDSS data and NML laboratory data were presented differently in terms of age grouping and are consistent with literature and current immunization recommendations.

All IPD isolates were screened by bile solubility and optochin (Oxoid) analyses and GAS/GBS isolates were confirmed using PYR (Pyrrolidonyl- α -naphthylamide) reaction and susceptibility to bacitracin (Oxoid) [Spellerberg, 2007] at NML. Sterile clinical isolation sites include blood, cerebrospinal fluid or other nervous tissue (CSF), peritoneal fluid, pericardial fluid, joint fluid, internal body sites and muscle including surgical or biopsy samples and aspirates. Although pleural fluid (empyema) does not currently meet the national case definition for invasive disease, these isolates are included in this report as they are widely considered as invasive in other jurisdictions [Bettinger, 2010]. Additionally for *S. pyogenes*, any isolation site was tested if a case of toxic shock syndrome or necrotizing fasciitis was associated with the infection [Canadian Communicable Disease Report, 2009; Minnesota Department of Health].

National case definitions for IPD, GAS and GBS can be found at the following:

<https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2009-35/definitions-communicable-diseases-national-surveillance.html>

Serotyping of IPD at NML is performed by observing the Quellung reaction using pool, group, type and factor commercial antisera (SSI Diagnostica; Statens Serum Institute, Copenhagen, Denmark) [Austrian, 1976; Lovgren, 1998]. Isolates for which a Quellung reaction is not observed are confirmed by *rpoB* gene sequencing [Drancourt, 2004; Clinical Laboratory Standards Institute (CLSI) MM18, 2018].

In 2011, the NML began a collaboration with the University of Manitoba – Health Sciences Centre - Canadian Antimicrobial Resistance Alliance (CARA) to provide antimicrobial susceptibility testing (AST) for *S. pneumoniae* isolates submitted to the NML. All sterile-site IPD isolates (n=1,129) submitted to the NML by 8 participating jurisdictions (Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, Prince Edward Island, New Brunswick, Newfoundland and Labrador) are included in the study. A panel of 18 antimicrobials are tested, including: penicillin, amoxicillin/clavulanate, cefuroxime, ceftriaxone, clarithromycin, ertapenem, meropenem, clindamycin, vancomycin, ciprofloxacin, levofloxacin, moxifloxacin, linezolid, tigecycline, trimethoprim/sulfamethoxazole and doxycycline. MICs of these antimicrobials are determined by the CLSI broth microdilution method using 96-well custom designed microtitre plates [CLSI M07, 2018]. MIC interpretive standards were defined according to CLSI breakpoints [CLSI M100, 2019] for all antibiotics except ciprofloxacin for which EUCAST interpretive breakpoints were used [EUCAST, 2015]. Antimicrobial susceptibilities for GAS (n=2,328) and GBS (n=227) were determined at NML using Kirby-Bauer Disc diffusion for chloramphenicol (CHL, 30 μ g), erythromycin (ERY, 15 μ g), clindamycin (CLI, 2 μ g), penicillin (PEN, 10 μ g), ceftriaxone (CRO, 30 μ g) and vancomycin (VAN, 30 μ g) according to CLSI guidelines [CLSI M02, 2018].

The *emm* types were determined for all invasive Group A *Streptococcus* isolates submitted to the NML. Isolates were characterized using the *emm* sequencing CDC protocol available at:

<http://www.cdc.gov/streplab/M-ProteinGene-typing.html>. The *emm* sequences obtained are compared with the CDC (Atlanta) data bank and results reported to the type level if possible

Serotypes of Group B *Streptococcus* were determined using commercial latex agglutinating antisera (SSI Diagnostica; Statens Serum Institute, Copenhagen, Denmark).

RESULTS AND DISCUSSION

Streptococcus pneumoniae

Based on 2017 data from CNDSS, the overall IPD incidence rate in Canada increased slightly from 9.0 cases per 100,000 population in 2016 to 9.4 cases per 100,000 in 2017. (Figure 1, Table 1) Since 2009, IPD incidence rates have remained fairly stable over time. IPD incidence rates remained similar or slightly decreased in all age groups in 2017 compared to 2016, except among 30-39 year olds and among seniors (60+ years) where slight increases were observed.

Figure 2. Annual incidence of IPD cases in Canada by age group, 2009–2017

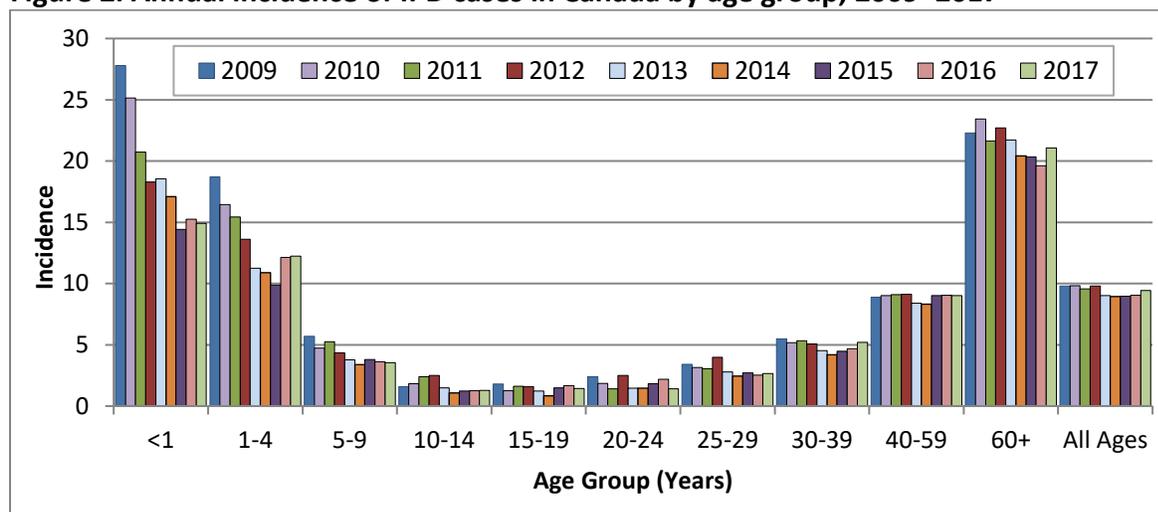


Table 1. Annual incidence of IPD cases in Canada by age group, 2009–2017

Year	Age Group (Years)										All Ages
	<1	1-4	5-9	10-14	15-19	20-24	25-29	30-39	40-59	60+	
2009	27.8	18.7	5.7	1.6	1.8	2.4	3.4	5.5	8.9	22.3	9.8
2010	25.1	16.4	4.7	1.8	1.2	1.9	3.1	5.2	9.0	23.4	9.8
2011	20.7	15.5	5.2	2.4	1.6	1.4	3.1	5.4	9.2	21.8	9.6
2012	18.3	13.6	4.3	2.5	1.6	2.5	4.0	5.1	9.2	22.8	9.8
2013	18.7	11.2	3.8	1.5	1.2	1.5	2.8	4.5	8.4	21.9	9.1
2014	17.3	11.0	3.4	1.1	1.0	1.5	2.5	4.2	8.3	20.4	8.9
2015	14.4	9.8	3.9	1.2	1.5	1.8	2.7	4.4	9.0	20.4	9.0
2016	15.5	12.1	3.6	1.3	1.7	2.2	2.5	4.7	9.1	19.8	9.1
2017	14.9	12.2	3.5	1.3	1.4	1.4	2.7	5.2	9.0	21.1	9.4

Distribution of *Streptococcus pneumoniae* serotypes

Of the 3,006 IPD isolates serotyped in 2017, 2,999 had patient ages and infants <2 years of age accounted for 4.2% (n=125), toddlers aged 2-4 years for 3.1% (n=94), children aged 5-14 years for 2.5% (n=75), adults aged 15-49 years for 20.9% (n=628), adults aged 50-64 years for 27.9% (n=839) and seniors aged ≥65 years for 41.2% (n=1238). Of the 3,256 isolates with gender information specified 56.9% (n=1,852) were from male patients.

The overall most prevalent serotype in 2017 was serotype 3, increasing from 8.9% (n=229) to 9.6% (n=289) since 2013. From 2013 to 2017, serotype 22F continued to predominate, declining from 12.1% (n=312) to 8.9% (n=267); and serotype 4 has increased dramatically from 1.6% (n=42) to 7.6% (n=229). Serotype 9N accounted for 6.8% (n=203) of the isolates in 2017, an increase from 4.4% (n=115) in 2015, and serotype 15A has remained relatively constant since 2014 representing 4.8% (n=145) in 2017.

Blood was the most frequent clinical isolation site accounting for 92.3% (n=2,775) of all isolates. Serotype 3 was prevalent in all clinical sources representing 9.3% (n=257) of all blood, 10.4% (n=8) of CSF, 22.5% (n=16) of pleural fluid and 9.6% (n=8) of other sterile isolation site isolates. Serotype 22F and 4 were also prevalent among blood isolates with 9.3% (n=259) and 7.9% (n=220) respectively. Among CSF isolates serotypes 23B and 23C predominated, each accounting for 13% (n=10).

Serotypes associated with **Western Canada** during 2017 included serotypes 4 (12.2%, n=157), 3 (7.8%, n=100), 7F (6.1%, n=79), 8 (7.1%, n=92), 12F (7.8%, n=101), 20 (6.9%, n=89) and 22F (6.1%, n=79). In **Central** regions, serotype 3 was most prevalent (12.0%, n=180), followed by 22F (10.8%, n=162), 9N (7.1% (n=107) and 15A (6.9%, n=103); and serotypes 22F (12.1%, n=25), 9N (11.1%, n=23) and 23A (7.2%, n=15) were predominant in **Eastern Canada**. **Northern Canada** had very small sample numbers overall with 40.0% (n=4) being 9N.

In 2017 among the **<2 year olds** the most predominant serotypes included 33F (16%, n=20) and 15B/C (15.2%, n=19). Common in the **2 – 4 year olds** were serotypes 22F (11.7%, n=11), 38 (10.6%, n=10), 3 (9.6%, n=9), 19A (8.5%, n=8) and 15B/C (8.5%, n=8) and serotypes 23B (13.3%, n=10), 3 (9.3%, n=7), 19A (8.0%, n=6), 22F (8.0%, n=6) and 15B/C (6.7%, n=5) in **5 – 14 year olds**. Serotype 4 was the most prevalent serotype in **15 – 49 year olds** (17.2%, n=108), serotype 3 in **50 – 64 year olds** (10.7%, n=90), and serotype 22F in those **65 years of age** and older (10.3%, n=128).

Serotype 3: There has been a steady overall increase of serotype 3 from 2013 (8.9%, n=229) to 2017 (9.6%, n=289). In infants <2 years of age serotype 3 has remained relatively constant since 2015 to now account for 5.6% (n=7) of the isolates in 2017. In the 2–4 year olds, serotype 3 has steadily declined between 2013–2016 from 10.5% (n=8) to 6.7% (n=6), however increased in 2017 to 9.6% (n=9). Small declines during 2016 – 2017 were observed among 5–14 year olds from 12.2% (n=10) to 9.3% (n=7), in 15–49 year olds from 11.3% (n=58) to 8.3% (n=52) and in 50 – 64 year olds from 11.3% (n=86) to 10.7% (n=90). In the ≥65 year old age group serotype 3 increased from 8.8% (n=91) to 9.9% (n=123).

Serotype 22F: Continued declines in the relative proportion of serotype 22F isolates have been seen in most age groups with decreases between 2013 – 2017 in <2 year old isolates from 16.3% (n=22) to 8.8% (n=11), from 11.9% (n=8) to 8.0% (n=6) in the 5 – 14 year old, from 10.6% (n=57) to 6.2% (n=39) in the 15 – 49 year olds, from 11.7% (n=80) to 8.6% (n=72) in those aged 50 – 64 years, and from 13.0% (n=134) to

10.3% (n=128) in seniors ≥65 years of age. Proportions of 22F in the 2 – 4 year olds remained relatively constant after the 5 year period at around 11% (n=8 to 11), peaking in 2015 at 14.0%(n=9).

Serotype 4: Increases of serotype 4 can be attributed to a pneumococcal outbreak among the homeless population in Western Canada. Large increases from 2013 to 2017 have been seen in the 15 – 49 year old age group from 3.5% (n=19) to 17.2% (n=108), in 50 – 64 year olds from 1.4% (n=10) to 10.1% (n=85) and in the <65 year old group a slight increase from 1.1% (n=12) to 2.8% (n=35).

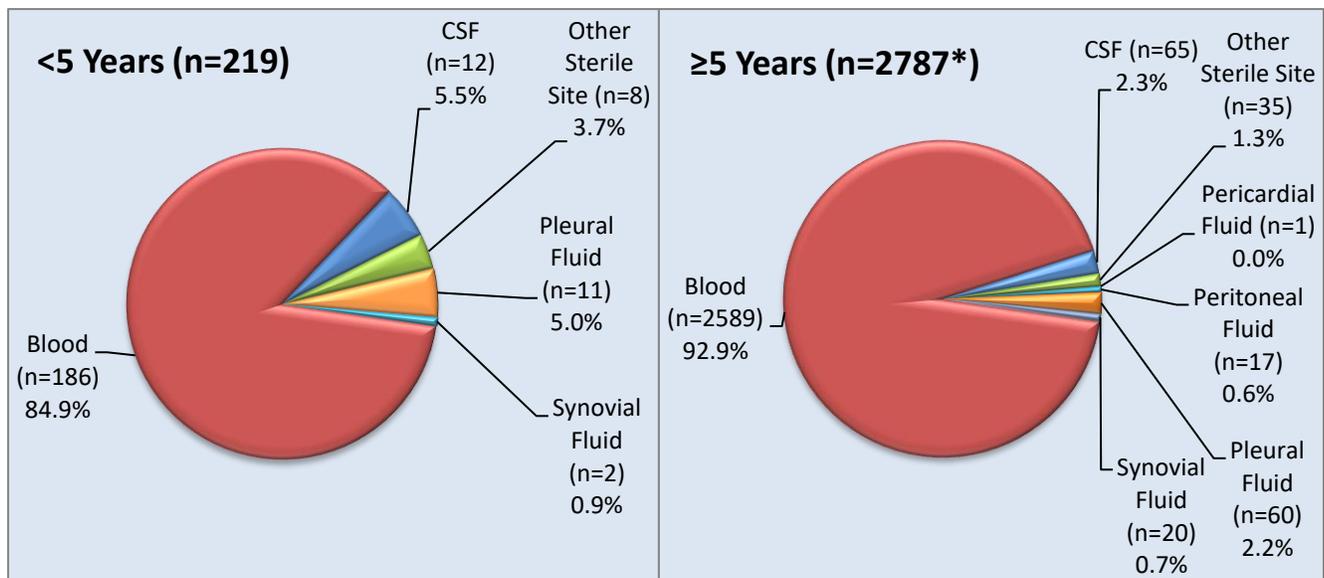
Serotype 19A: After a continued decrease in <2 year olds from 11.9% (n=16) in 2013 to 4.7% (n=6) in 2015, serotype 19A increased in 2016 to account for 9.0% (n=13) of isolates then decreased again in 2017 to 4.8% (n=6). Overall declines have been seen from 2013 to 2017 in 2 – 4 year olds from 22.4% (n=17) to 8.5% (n=8), in the 5 – 14 year olds from 26.9 % (n=18) to 8.0 % (n=6), the 15 – 49 year olds from 9.4% (n=51) to 4.8% (n=30), the 50 – 64 year olds from 11.8% (n=82) to 4.6% (n=39), and in ≥65 year olds from 11.0% (n=114) to 4.4% (n=54).

Serotype 7F: In 2017 there were no isolations of serotype 7F in children under 5 years of age. In all other age groups declines from 2013 to 2017 have continued with 7F decreasing in the 5 – 14 year olds from 10.4% (n=7) to 4.0% (n=3), the 15 – 49 year olds from 15.4% (n=83) to 8.4% (n=53), the 50 – 64 year olds from 8.7% (n=60) to 4.3% (n=36), and in the ≥65 year old age group from 6.9% (n=71) to 1.5% (n=19).

Other Serotypes: Serotype **33F** was the most prevalent among <2 year olds at 16.0% (n=20) followed closely by serotype **15B/C** accounting for 15.2% (n=19) of isolates. Serotype **38** was predominant in 2 – 4 year olds in 2017 representing 10.6% (n=10). In the 5 – 14 year old age group serotype **23B** is the most prevalent serotype, increasing from 5.3% (n=3) in 2013 to 13.3% (n=10) in 2017. Serotype **9N** was associated with the 50 - 64 year old age group increasing from 5.8% (n=40) in 2013 to 8.1% (n=68) in 2017 and in the ≥65 year old age group increasing from 4.4% (n=45) to 6.9% (n=75) over the 5 year period. **15A** was also associated with the <65 year olds in 2017 with 7.4% (n=91) of the total.

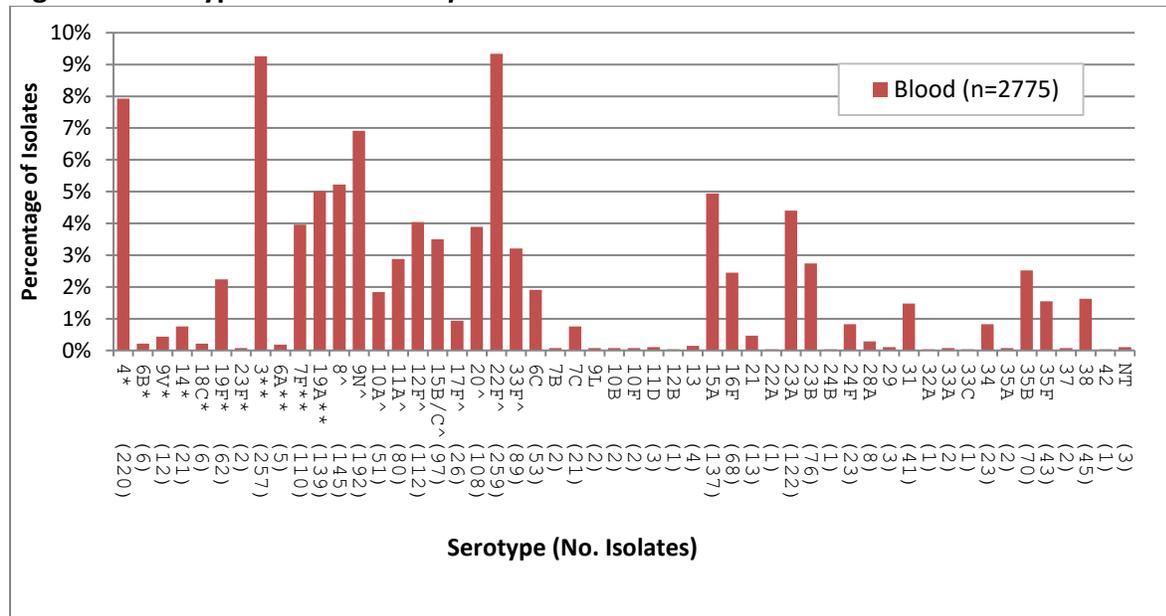
Table 2. Number of invasive *S. pneumoniae* in 2017

Province	Age Groups (Years)						Not Given	Total
	< 2	2 – 4	5 – 14	15 – 49	50 – 64	≥ 65		
British Columbia	5	4	16	160	168	183	1	537
Alberta	21	13	8	127	137	122	1	429
Saskatchewan	7	3	2	30	37	52	0	131
Manitoba	13	9	0	62	45	62	1	192
Ontario	42	42	31	171	299	515	1	1101
Quebec	32	16	9	48	91	201	2	399
New Brunswick	2	4	4	9	17	29	0	65
Nova Scotia	1	2	0	10	25	48	1	87
Prince Edward Island	0	0	2	4	6	9	0	21
Newfoundland and Labrador	2	1	3	2	9	17	0	34
Yukon	0	0	0	1	2	0	0	3
Northwest Territories	0	0	0	4	3	0	0	7
Grand Total	125	94	75	628	839	1238	7	3006

Figure 3. Clinical isolation sites in 2017

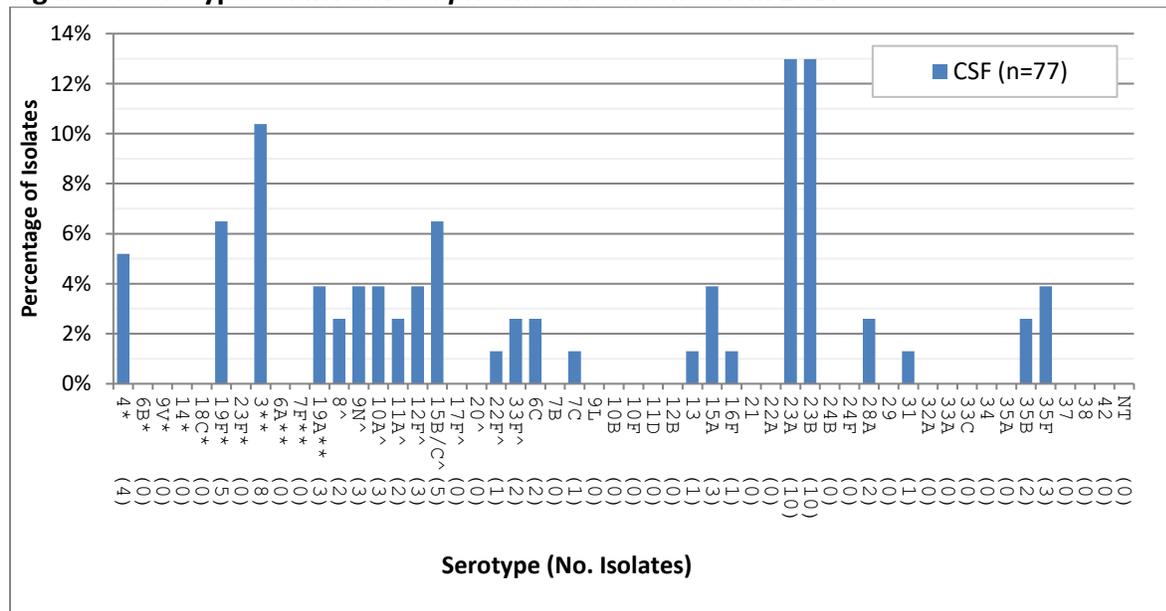
*Includes 7 isolates with age not available. Other sterile sites for children under 5 years of age include 5 deep tissue and fluid, 1 vitreous humor, 1 lymph node, and 1 unknown clinical source; and the 5 year or older age group include 31 deep tissue, abscess or fluid, 1 vitreous humor, and 1 unknown clinical source.

Figure 4. Serotypes of invasive *S. pneumoniae* from blood in 2017



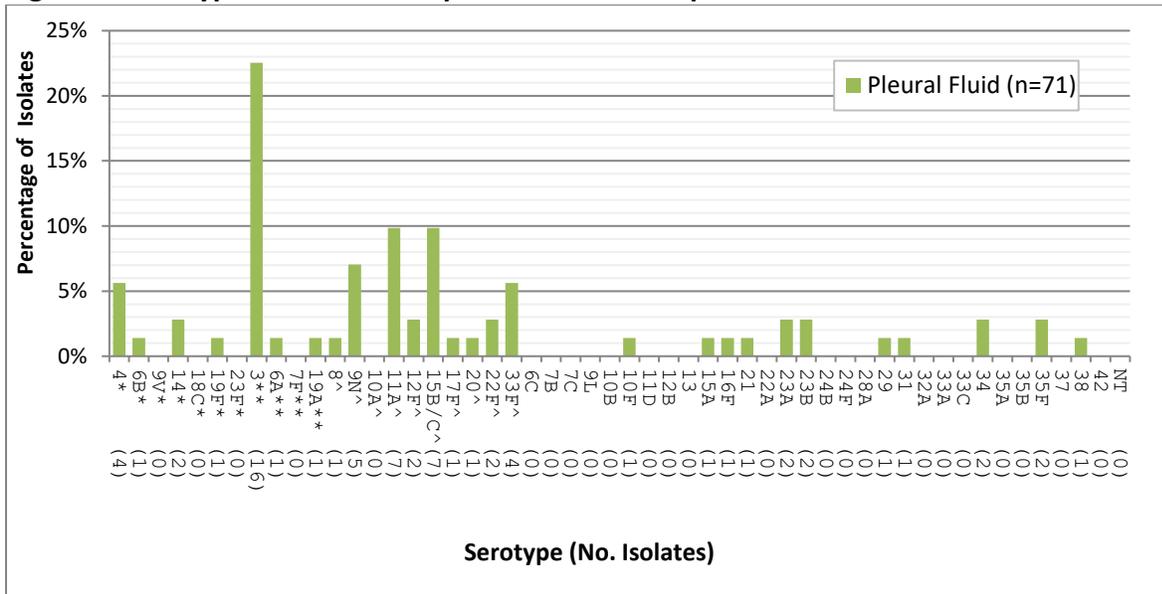
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23.

Figure 5. Serotypes of invasive *S. pneumoniae* from CSF in 2017



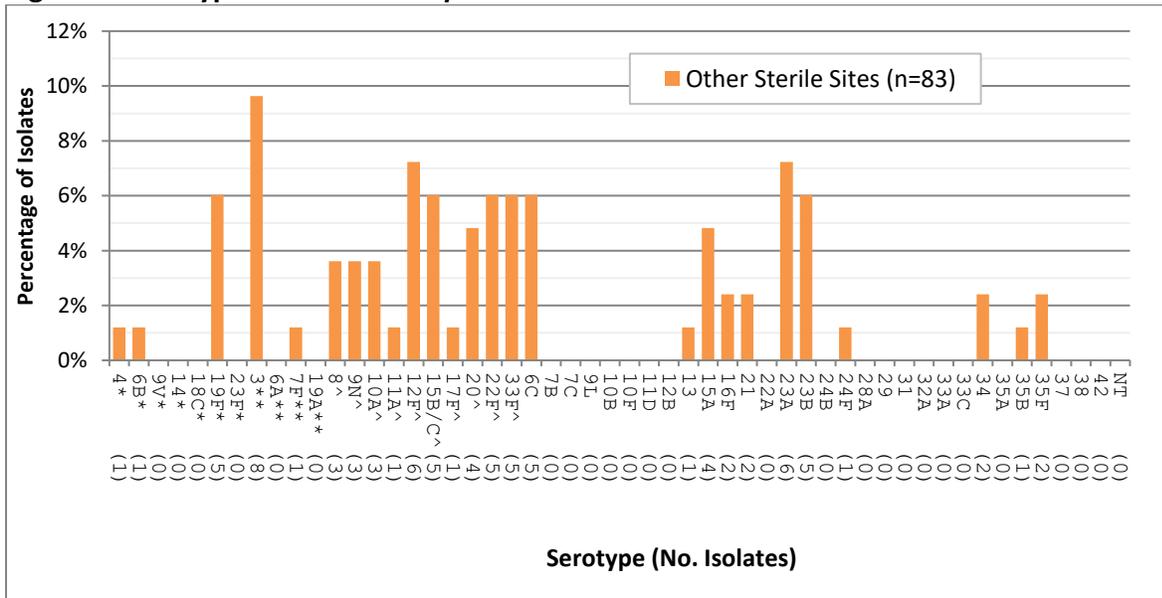
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23.

Figure 6. Serotypes of invasive *S. pneumoniae* from pleural fluid in 2017



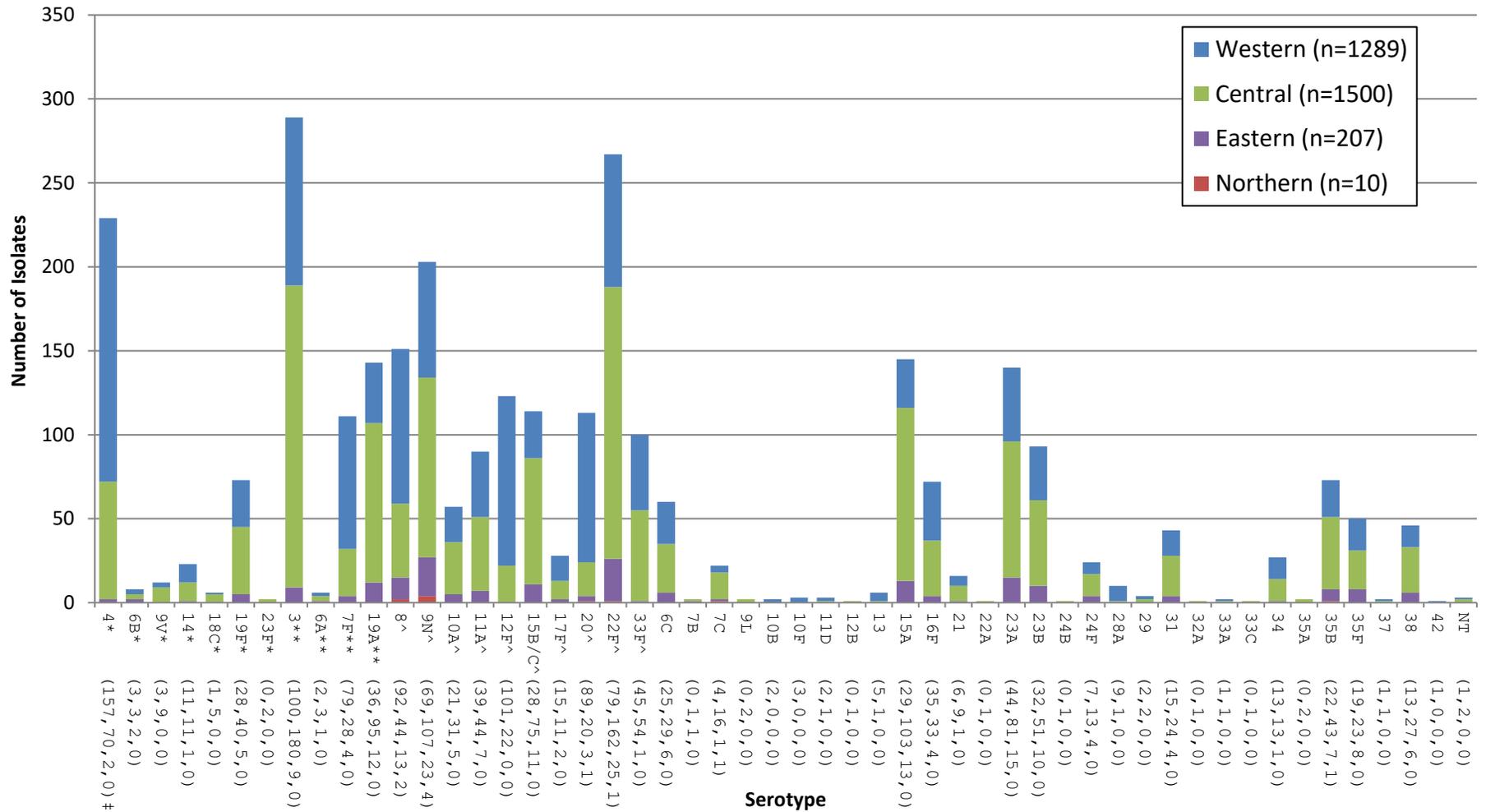
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23.

Figure 7. Serotypes of invasive *S. pneumoniae* from other sterile sites in 2017



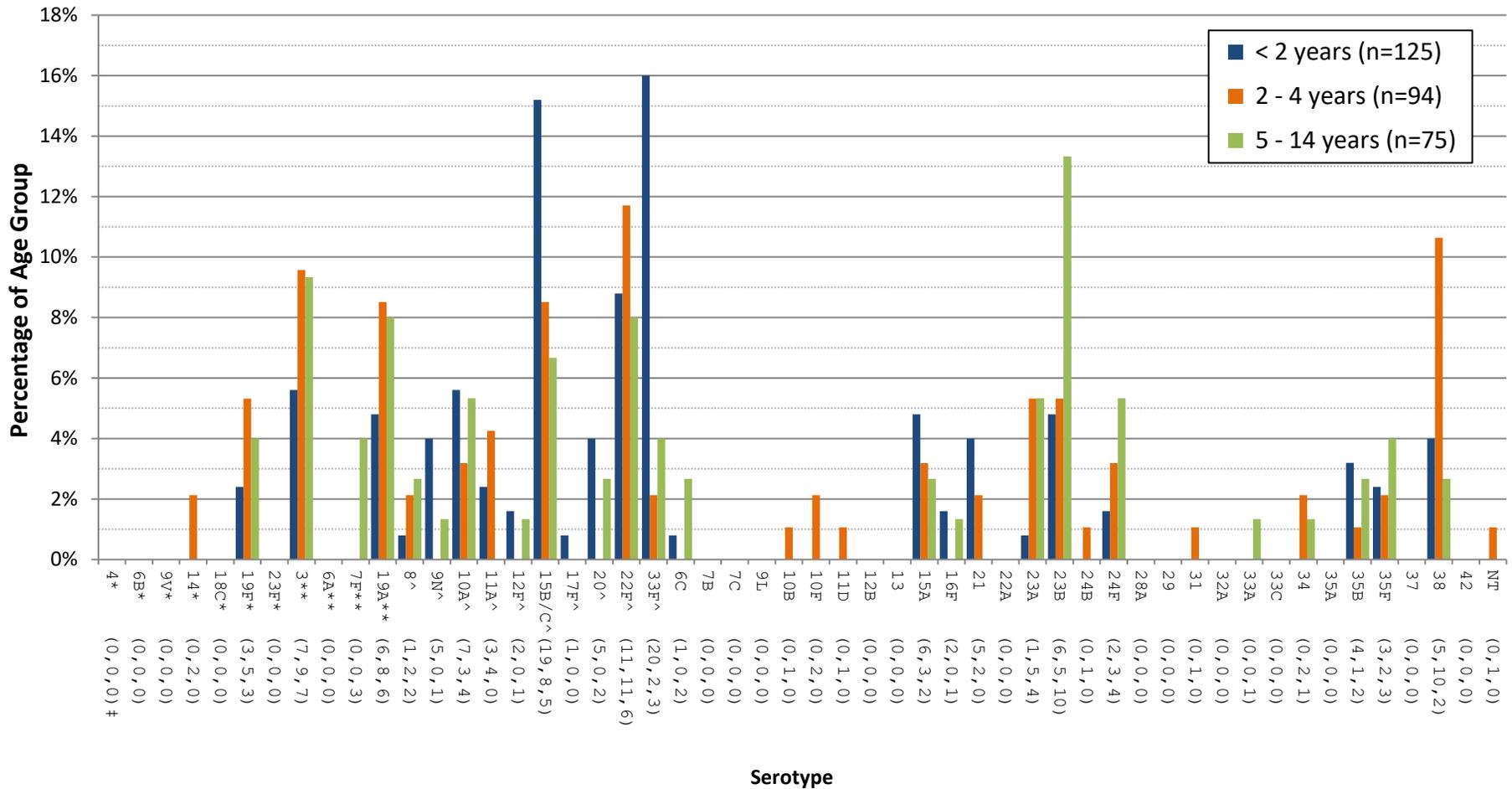
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23. Other sterile sites include: 1 pericardial fluid, 17 peritoneal fluid, 22 synovial fluid, 43 from deep tissue, biopsy or surgical samples.

Figure 8. Regional Distribution of Invasive *S. pneumoniae* serotypes in 2017



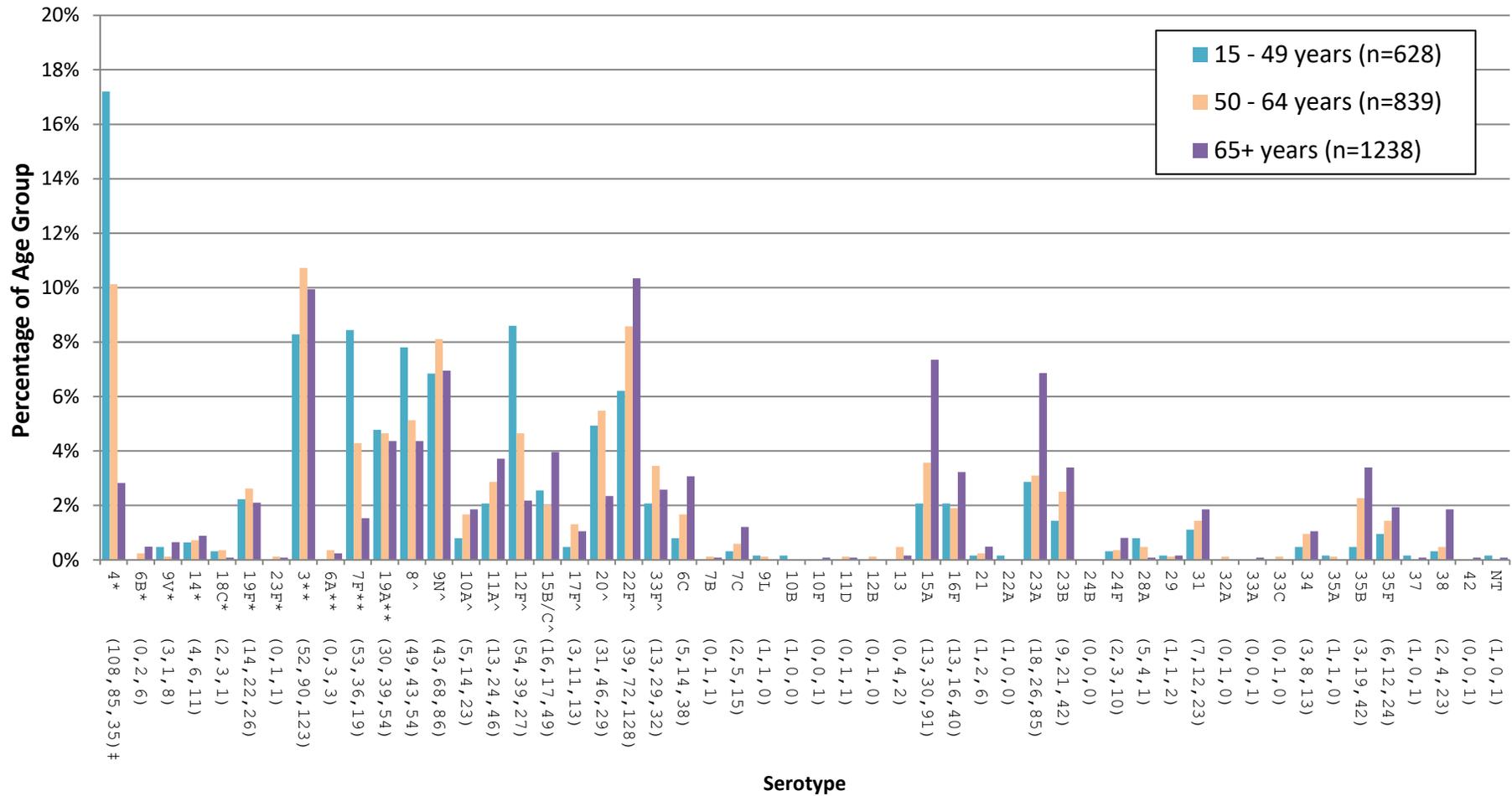
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡Number of isolates from Western, Central, Eastern and Northern Canada, respectively.

Figure 9. Invasive *S. pneumoniae* serotypes isolated in 2017: <2, 2-4 and 5-14 year old age groups



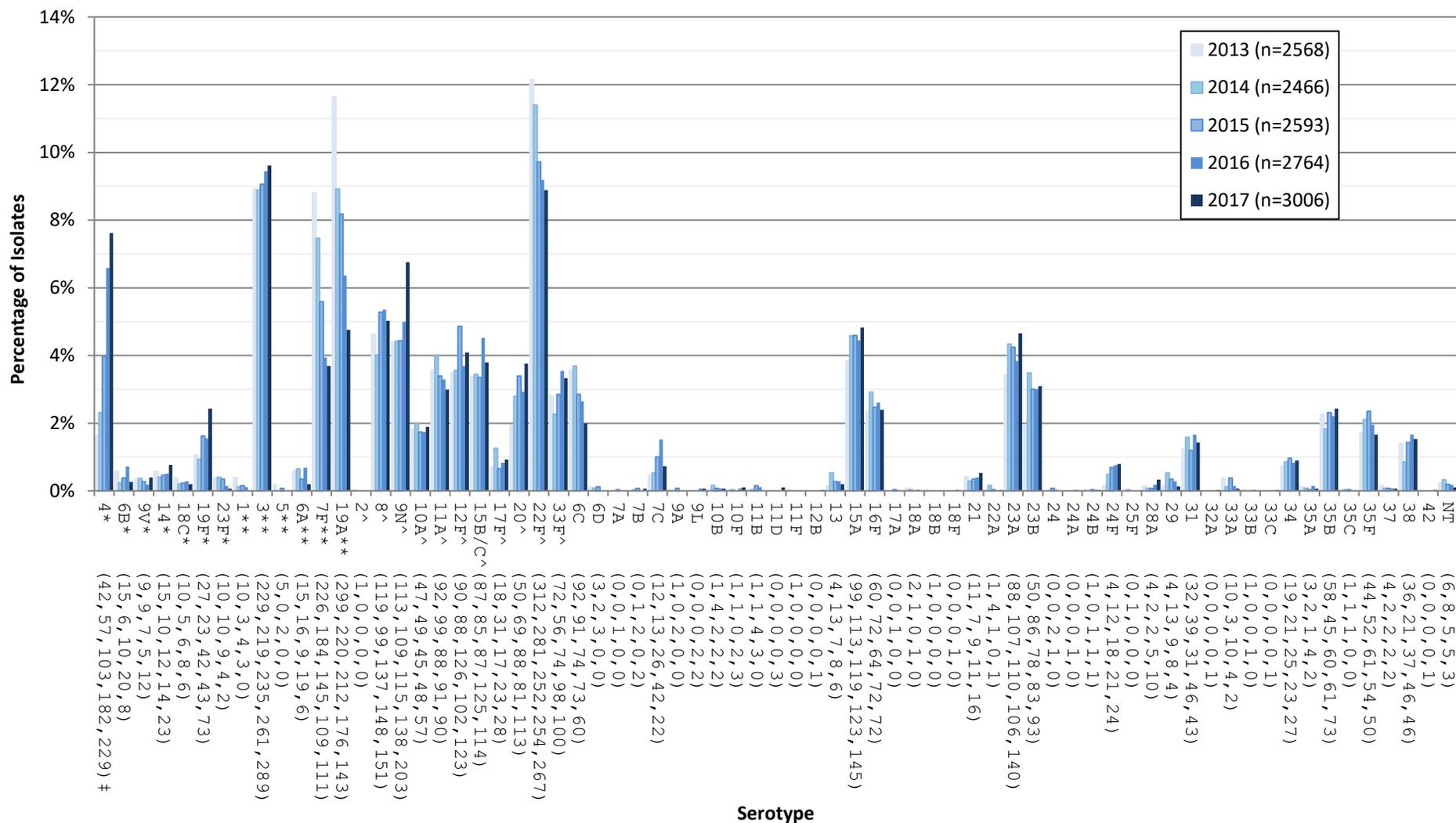
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡Number of isolates from <2, 2-4, 5-14 year olds, respectively.

Figure 10. Invasive *S. pneumoniae* serotypes isolated in 2017: 15-49, 50-64, and ≥65 year old age groups



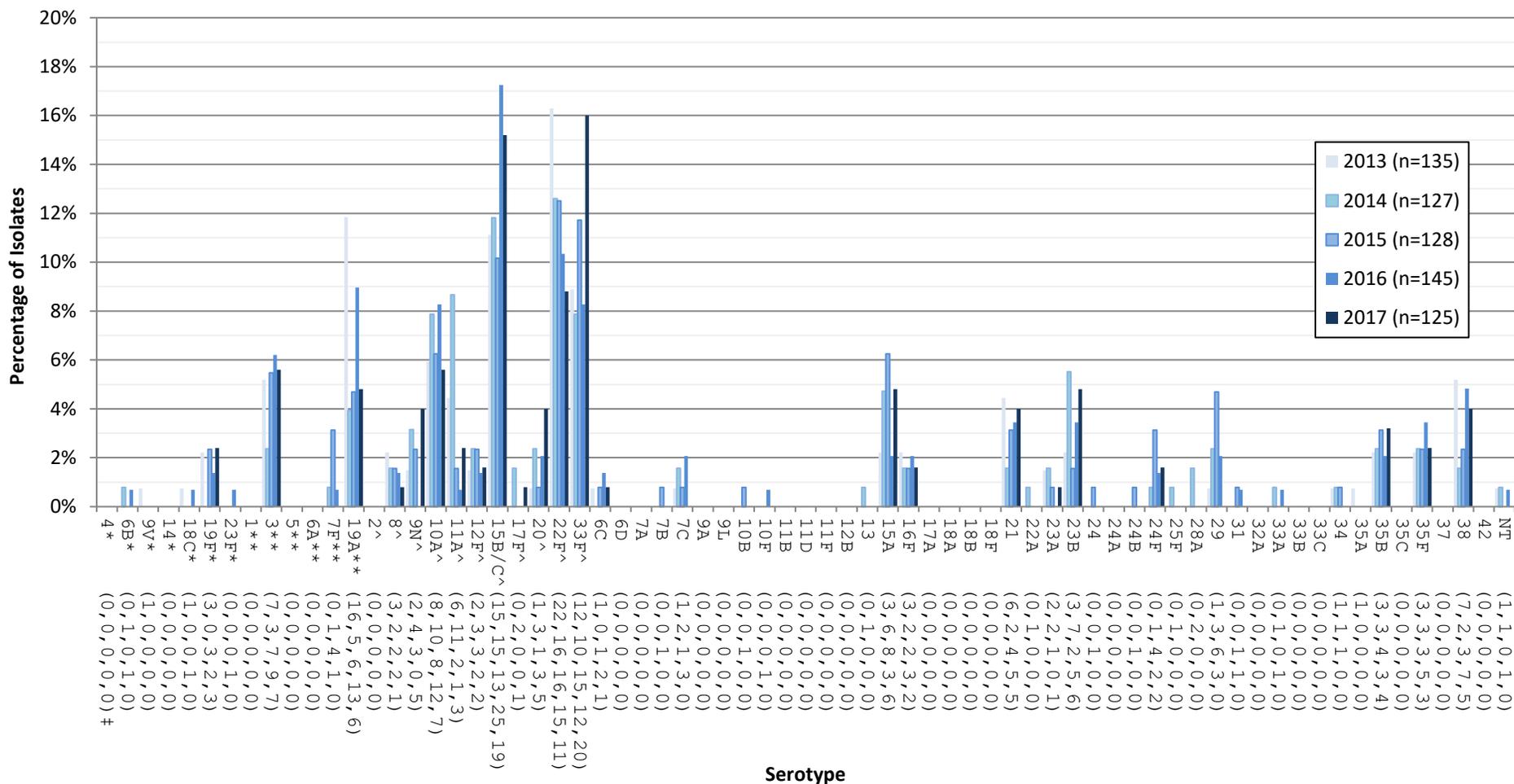
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23. ‡Number of isolates from 15-49, 50-64, ≥65 year olds, respectively.

Figure 11. Invasive *S. pneumoniae* serotypes in all combined age group



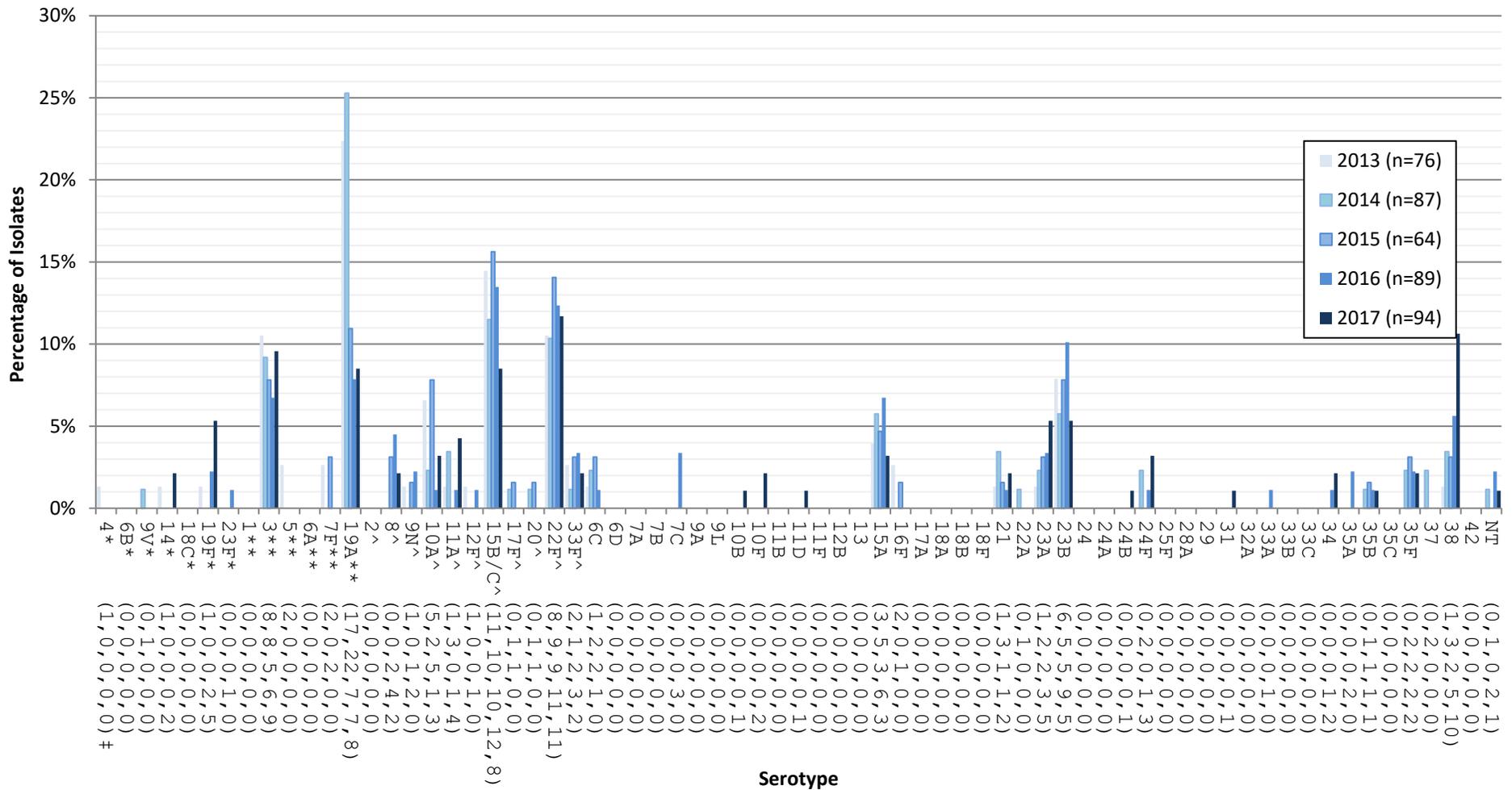
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure 12. Invasive *S. pneumoniae* serotypes in <2 year olds



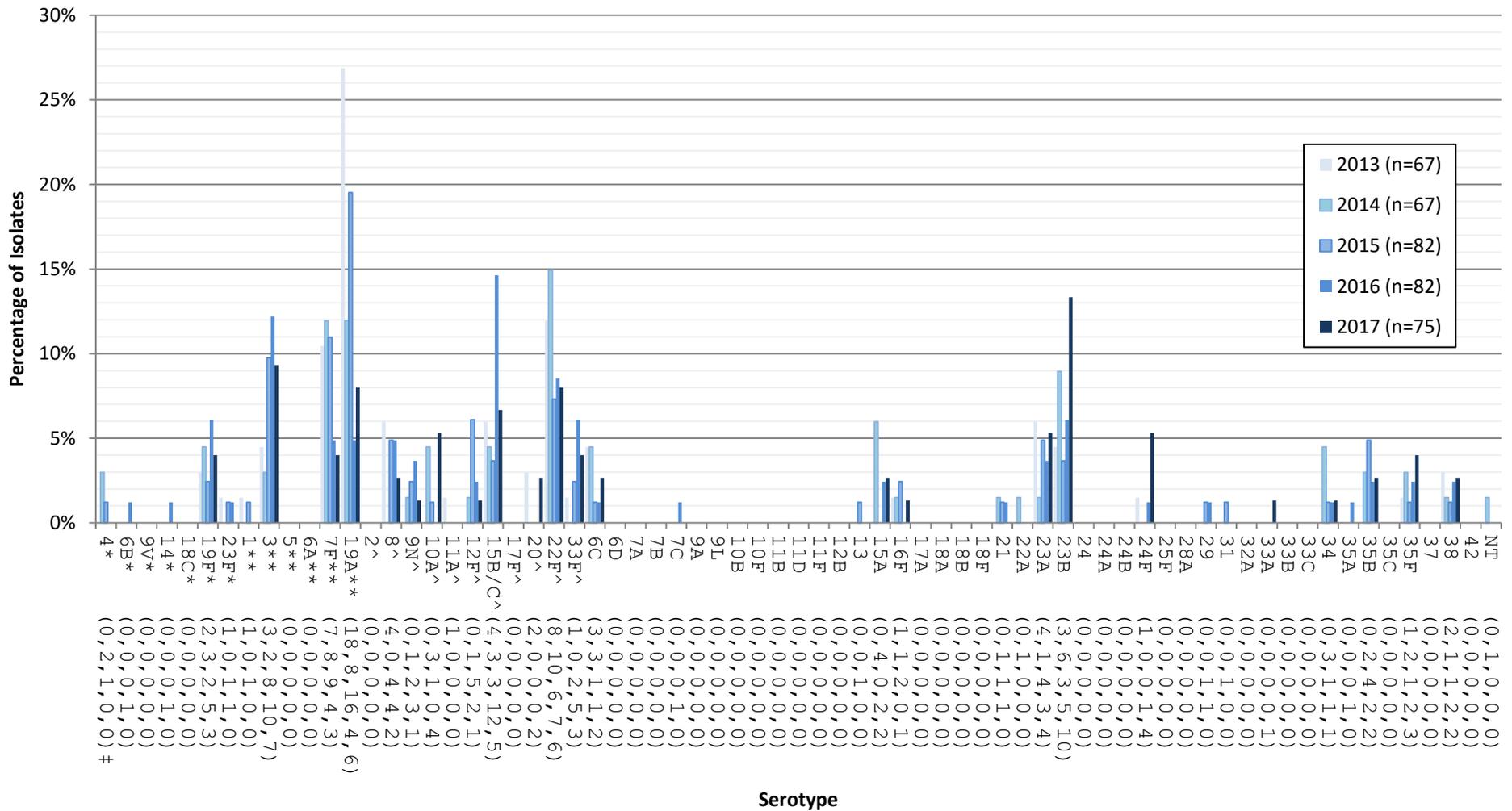
* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure 13. Invasive *S. pneumoniae* serotypes in 2-4 year olds



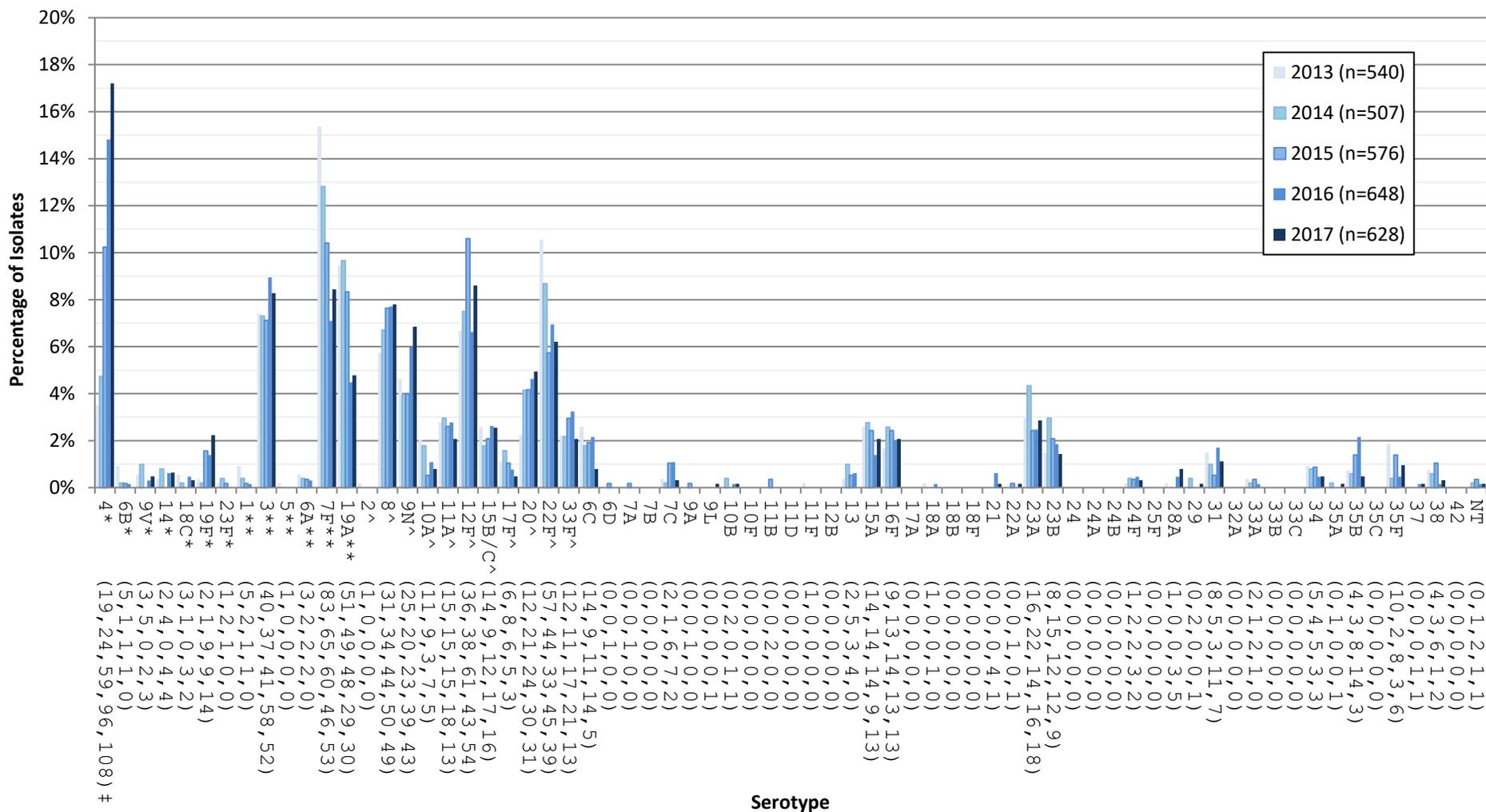
* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure 14. Invasive *S. pneumoniae* serotypes in 5-14 year olds



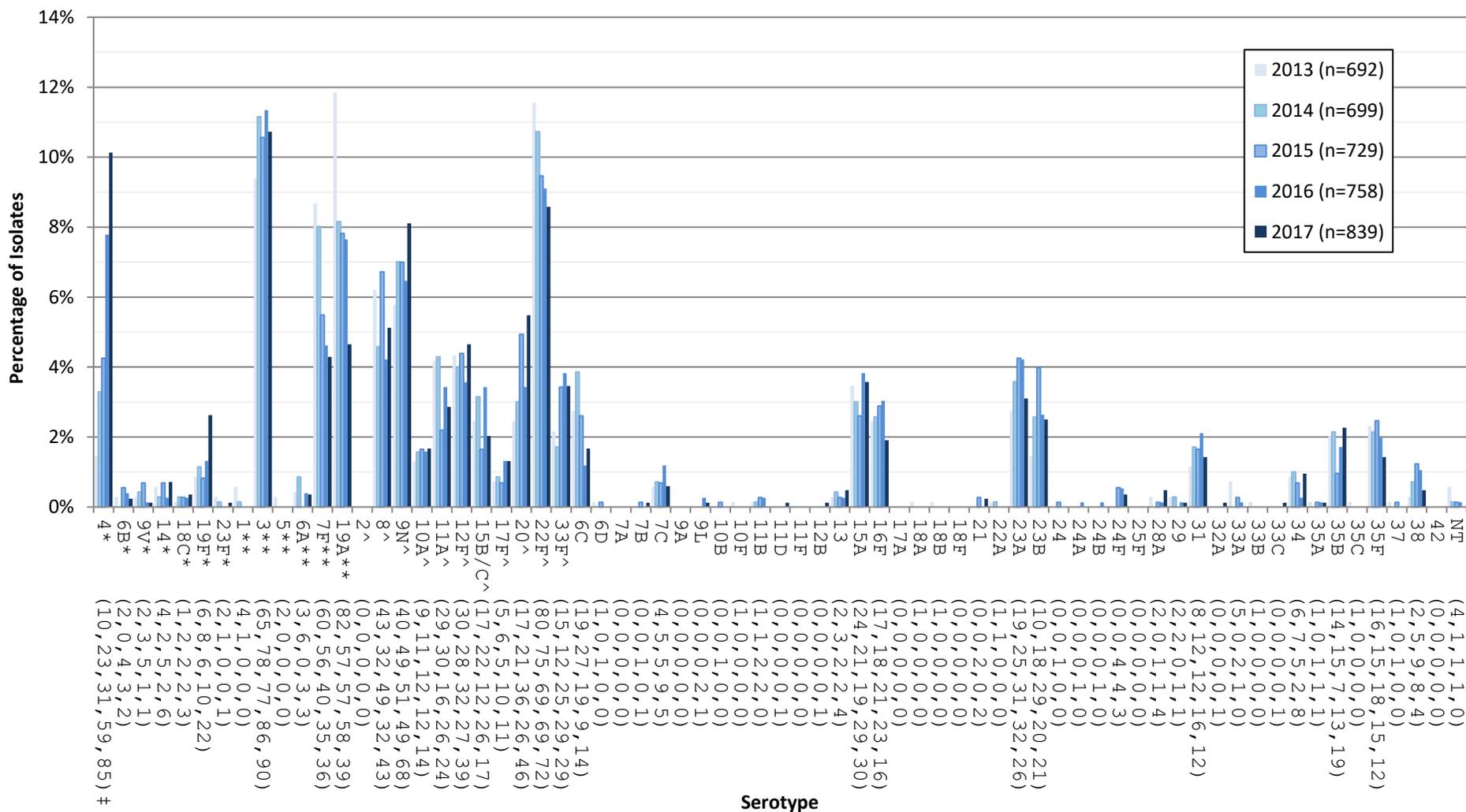
* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure 15. Invasive *S. pneumoniae* serotypes in 15-49 year olds



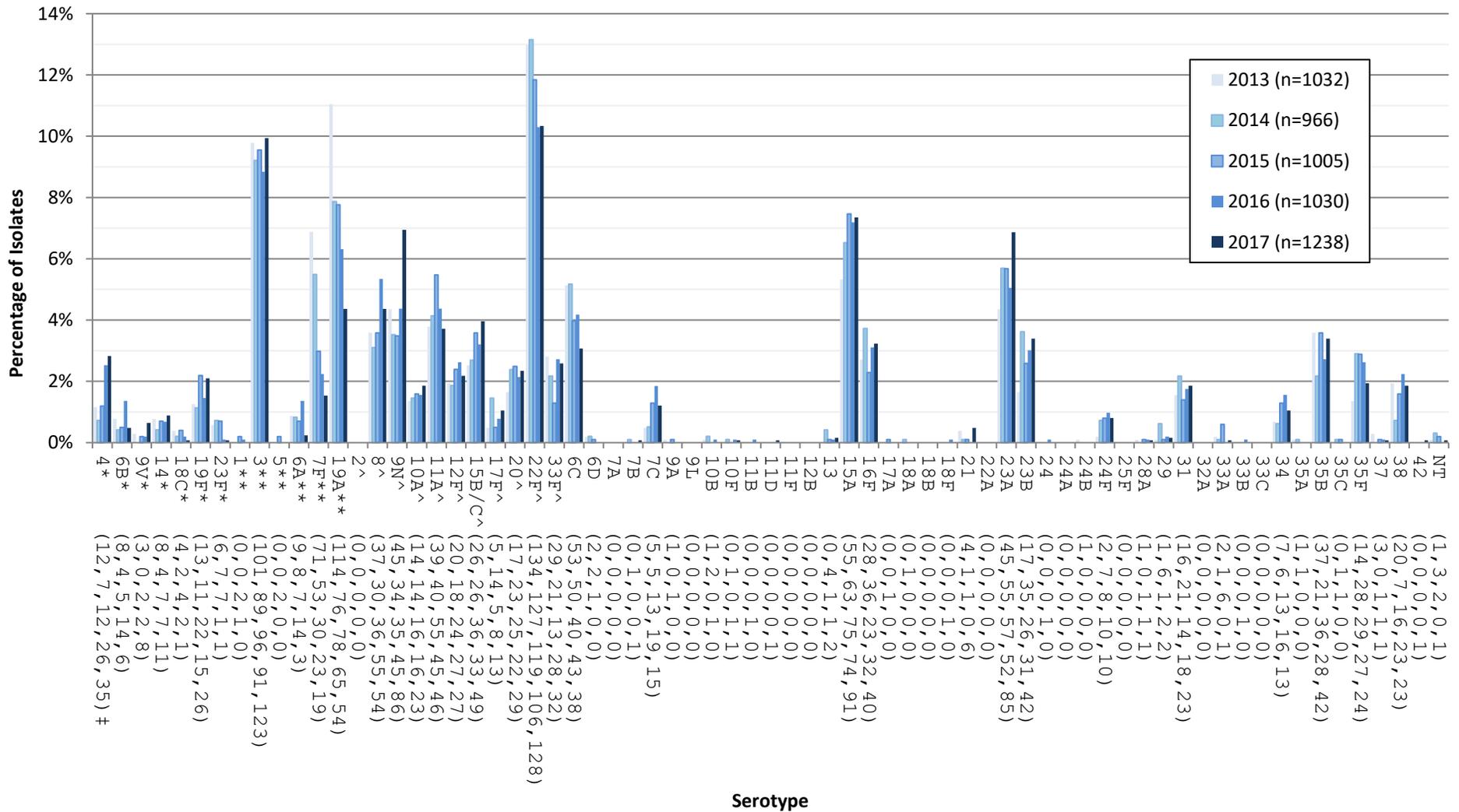
* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; † Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Figure 16. Invasive *S. pneumoniae* serotypes in 50-64 year olds



* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 17. Invasive *S. pneumoniae* serotypes in ≥65 year olds



* Component of PCV7; ** Component of PCV13; ^ Component of PPV23; † Number of isolates for 2013, 2014, 2015, 2016 and 2017 respectively.

Pneumococcal Vaccine Serotypes

PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F) continue to represent a small number of isolates in the <15 year old age groups during 2017 with only 3 isolates in the <2 year olds, 7 isolates from 2 – 4 year olds, and 3 isolates in the 5-14 year old age group. Increases in the older age groups may be attributed to increases of serotype 4 among homeless population in Western Canada. Large increases from 2013 to 2017 have been seen in the 15 – 49 year olds from 6.5% (n=35) to 20.9% (n=131); and in the 50 - 64 year olds from 3.9% (n=27) to 14.3% (n=120).

Proportions of PCV13-specific serotypes (1, 3, 5, 6A, 7F and 19A) have decreased across all age groups from 2013 to 2017, the largest decreases are seen in the 2-4 year olds from 38.2% (n=29) to 18.1% (n=17) and the 5-14 year olds from 43.3% (n=29) to 21.3% (n=16). Among <2 year olds, levels increased from 7.1% (n=9) in 2014 to 15.9% (n=23) in 2016 mainly attributable to resurgences of serotypes 3 and 19A; and then decreased once again in 2017 to 10.4% (n=13). Overall in all age groups combined, PCV13-specific serotypes have continued a general decline and now represent 18.3% (n=549) of isolates in 2017.

The proportion of isolates representing PPV23 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F) have remained relatively unchanged in all groups in 2017, representing 31.9% (n=30) of 2 – 4 year olds, 32.0% (n=24) of 5 – 14 year olds, 42.4% (n=266) of 15 – 49 year olds, 43.3% (n=363) of 50 – 64 year olds and 39.3% (n=487) of those ≥65 years old. A 10% increase was seen in the <2 year olds from 49.7% (n=72) in 2016 to 59.2% (n=74) of isolates in 2017.

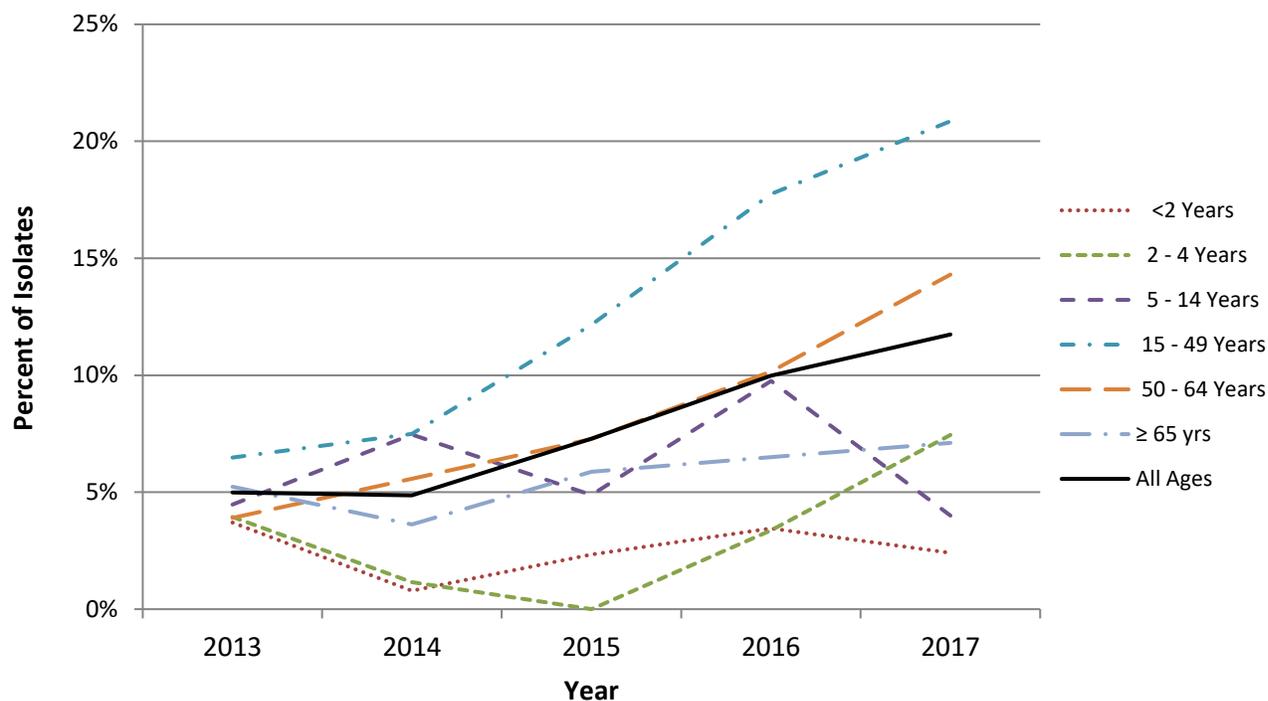
After a general increase of non-vaccine serotypes (NVT) during 2013 – 2014 among all age groups, levels have remained relatively unchanged from 2016 – 2017 in all age groups except for an increase in the 5 – 14 year olds from 28.0% (n=23) in 2016 to 42.7% (n=32) 2017 mostly attributable to increases in 23B and 24F. Proportions of NVTs during 2017 in the other age groups have remained relatively stable at 2016 levels with 28.0% (n=35) in <2 year olds, 42.6% (n=40) in 2 – 4 year olds, 15.3% (n=96) in 15 – 49 year olds, 22.4% (n=188) in 50 – 64 year olds and 37.5% (n=464) in ≥65 year olds.

According to the 2017 childhood National Immunization Coverage Survey, vaccine uptake for pneumococcal vaccine was 81.4% among those less than 2 years of age [PHAC, 2019].

Table 3. Pneumococcal Vaccine Serotypes 2017

Vaccine*	Age Group						
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	All Ages**
PCV7	2.4%(3)***	7.4%(7)	4.0%(3)	20.9%(131)	14.3%(120)	7.1%(88)	11.7%(353)
PCV13	10.4%(13)	18.1%(17)	21.3%(16)	21.5%(135)	20.0%(168)	16.1%(199)	18.3%(549)
PCV13 All	12.8%(16)	25.5%(24)	25.3%(19)	42.4%(266)	34.3%(288)	23.2%(287)	30.0%(902)
PPV23	59.2%(74)	31.9%(30)	32.0%(24)	42.4%(266)	43.3%(363)	39.3%(487)	41.5%(1246)
PPV23 All	72.0%(90)	57.4%(54)	57.3%(43)	84.7%(532)	77.2%(648)	62.3%(771)	71.3%(2142)
NVT	28.0%(35)	42.6%(40)	42.7%(32)	15.3%(96)	22.4%(188)	37.5%(464)	28.5%(858)
Total	(125)	(94)	(75)	(628)	(839)	(1238)	(3006)

*PCV7 includes serotypes 4, 6B, 9V, 14, 18C, 19F and 23F. PCV13 serotypes include 1, 5, 7F, 3, 6A, and 19A; and PCV13 All serotypes include all PCV7 and PCV13 serotypes. PPV23 serotypes include 2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F and 33F and PPV23 All includes all PCV7, PCV13 (except 6A) and PPV23 serotypes. NVT includes all other non-vaccine serotypes. ** Includes isolates for which an age was not available: PCV7 = 1, PCV13 = 1, PPV23 = 2 and NVT = 3. *** Percentage of isolates (number of isolates).

Figure 18. Trends of PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F)**Table 4. PCV7 serotypes by age group**

Year	Age Group						All Ages**
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	
2013	3.7% (5)*	3.9% (3)	4.5% (3)	6.5% (35)	3.9% (27)	5.2% (54)	5.0% (128)
2014	0.8% (1)	1.1% (1)	7.5% (5)	7.5% (38)	5.6% (39)	3.6% (35)	4.9% (120)
2015	2.3% (3)	0.0% (0)	4.9% (4)	12.2% (70)	7.3% (53)	5.9% (59)	7.3% (189)
2016	3.4% (5)	3.4% (3)	9.8% (8)	17.7% (115)	10.2% (77)	6.5% (67)	10.0% (276)
2017	2.4% (3)	7.4% (7)	4.0% (3)	20.9% (131)	14.3% (120)	7.1% (88)	11.7% (353)

* Percentage of isolates (number of isolates). ** Includes isolates for which an age was not available.

Figure 19. Trends of PCV13 serotypes (1, 5, 7F, 3, 6A, 19A)

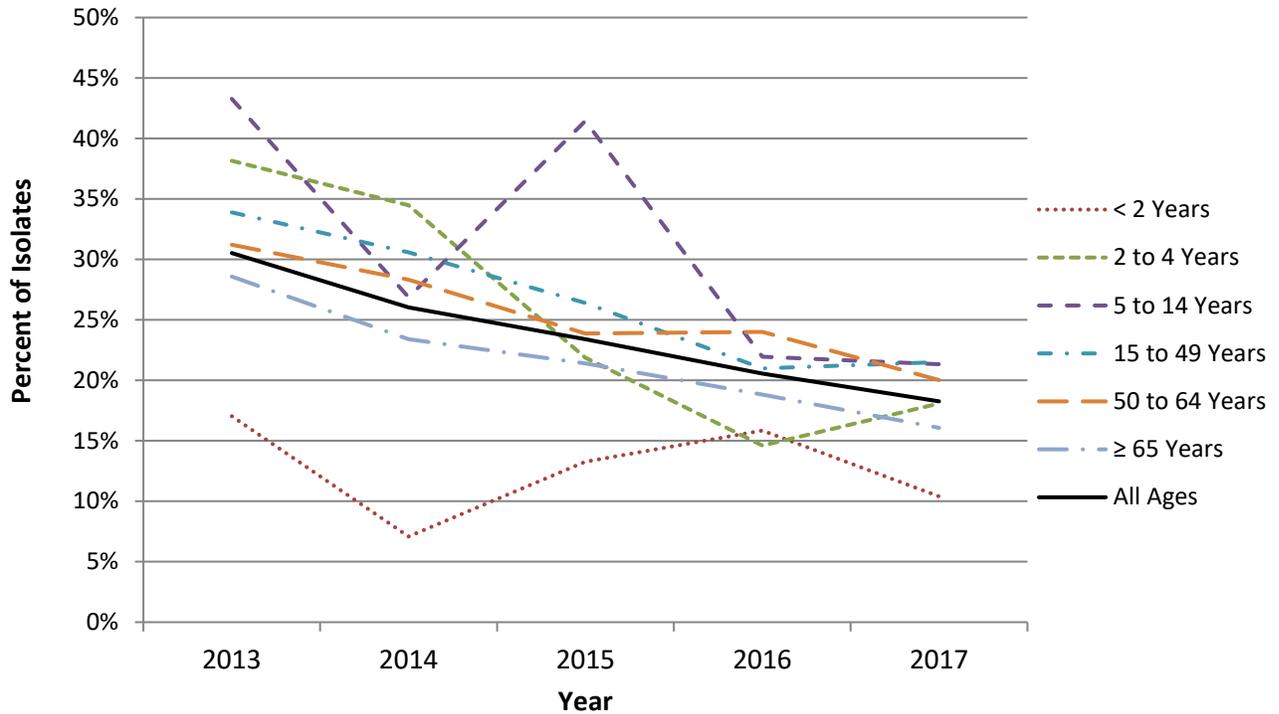
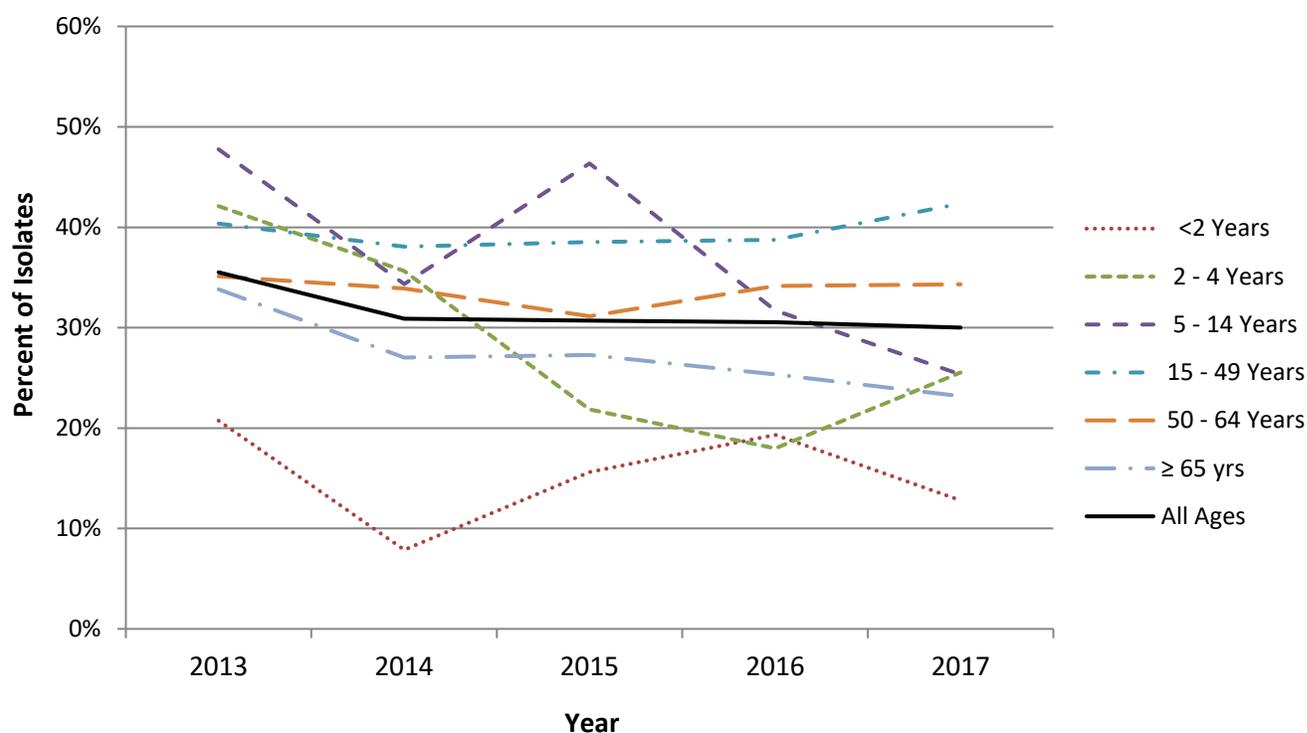


Table 5. PCV13 serotypes by age group

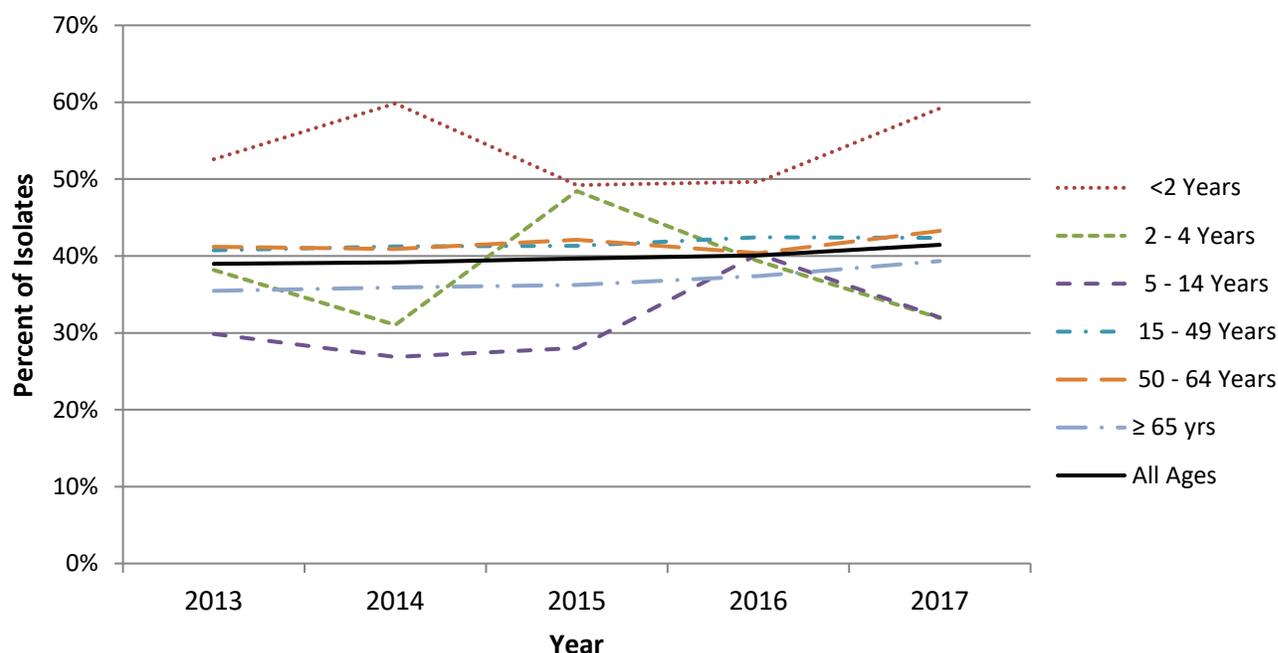
Year	Age Group						
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	All Ages**
2013	17.0% (23)*	38.2% (29)	43.3% (29)	33.9% (183)	31.2% (216)	28.6% (295)	30.5% (784)
2014	7.1% (9)	34.5% (30)	26.9% (18)	30.6% (155)	28.3% (198)	23.4% (226)	26.0% (642)
2015	13.3% (17)	21.9% (14)	41.5% (34)	26.4% (152)	23.9% (174)	21.4% (215)	23.4% (607)
2016	15.9% (23)	14.6% (13)	22.0% (18)	21.0% (136)	24.0% (182)	18.8% (194)	20.5% (568)
2017	10.4% (13)	18.1% (17)	21.3% (16)	21.5% (135)	20.0% (168)	16.1% (199)	18.3% (549)

* Percentage of isolates (number of isolates). ** Includes isolates for which an age was not available.

Figure 20. Trends of all PCV13 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F; and 1, 5, 7F, 3, 6A, 19A)**Table 6. Combined PCV7 and PCV13 serotypes by age group**

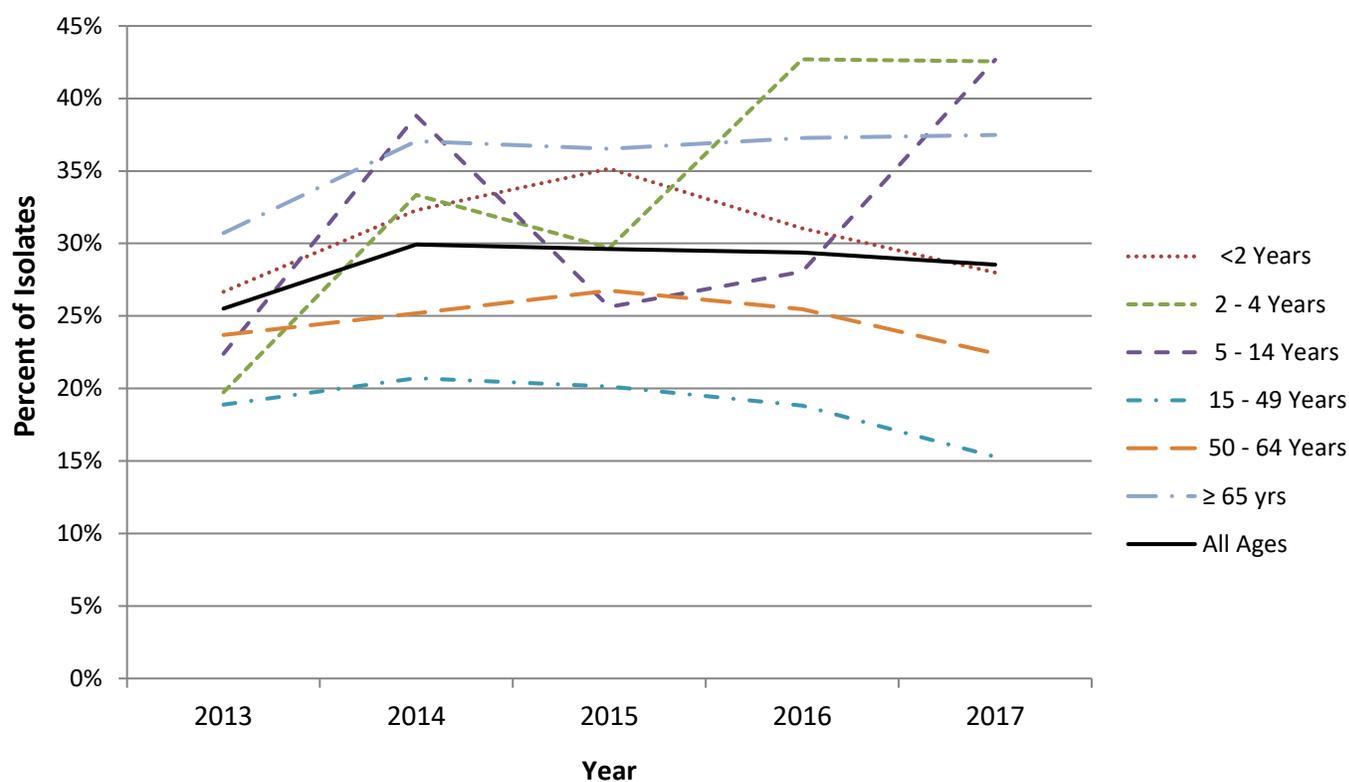
Year	Age Group						
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	All Ages**
2013	20.7% (28)*	42.1% (32)	47.8% (32)	40.4% (218)	35.1% (243)	33.8% (349)	35.5% (912)
2014	7.9% (10)	35.6% (31)	34.3% (23)	38.1% (193)	33.9% (237)	27.0% (261)	30.9% (762)
2015	15.6% (20)	21.9% (14)	46.3% (38)	38.5% (222)	31.1% (227)	27.3% (274)	30.7% (796)
2016	19.3% (28)	18.0% (16)	31.7% (26)	38.7% (251)	34.2% (259)	25.3% (261)	30.5% (844)
2017	12.8% (16)	25.5% (24)	25.3% (19)	42.4% (266)	34.3% (288)	23.2% (287)	30.0% (902)

* Percentage of isolates (number of isolates). ** Includes isolates for which an age was not available.

Figure 21. Trends of PPV23 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F)**Table 7. PPV23 serotypes by age group**

Year	Age Group						
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	All Ages**
2013	52.6% (71)*	38.2% (29)	29.9% (20)	40.7% (220)	41.2% (285)	35.5% (366)	39.0% (1001)
2014	59.8% (76)	31.0% (27)	26.9% (18)	41.2% (209)	40.9% (286)	35.9% (347)	39.2% (966)
2015	49.2% (63)	48.4% (31)	28.0% (23)	41.3% (238)	42.1% (307)	36.2% (364)	39.7% (1029)
2016	49.7% (72)	39.3% (35)	40.2% (33)	42.4% (275)	40.4% (306)	37.4% (385)	40.1% (1108)
2017	59.2% (74)	31.9% (30)	32.0% (24)	42.4% (266)	43.3% (363)	39.3% (487)	41.5% (1246)

* Percentage of isolates (number of isolates). ** Includes isolates for which an age was not available.

Figure 22. Trends of non-vaccine serotypes (NVT)**Table 8. Non-vaccine serotype (NVT) isolates**

Year	Age Group						
	<2 years	2-4 years	5-14 years	15-49 years	50-64 years	≥65 years	All Ages**
2013	26.7% (36)*	19.7% (15)	22.4% (15)	18.9% (102)	23.7% (164)	30.7% (317)	25.5% (655)
2014	32.3% (41)	33.3% (29)	38.8% (26)	20.7% (105)	25.2% (176)	37.1% (358)	29.9% (738)
2015	35.2% (45)	29.7% (19)	25.6% (21)	20.1% (116)	26.7% (195)	36.5% (367)	29.6% (768)
2016	31.0% (45)	42.7% (38)	28.0% (23)	18.8% (122)	25.5% (193)	37.3% (384)	29.4% (812)
2017	28.0% (35)	42.6% (40)	42.7% (32)	15.3% (96)	22.4% (188)	37.5% (464)	28.5% (858)

* Percentage of isolates (number of isolates). ** Includes isolates for which an age was not available.

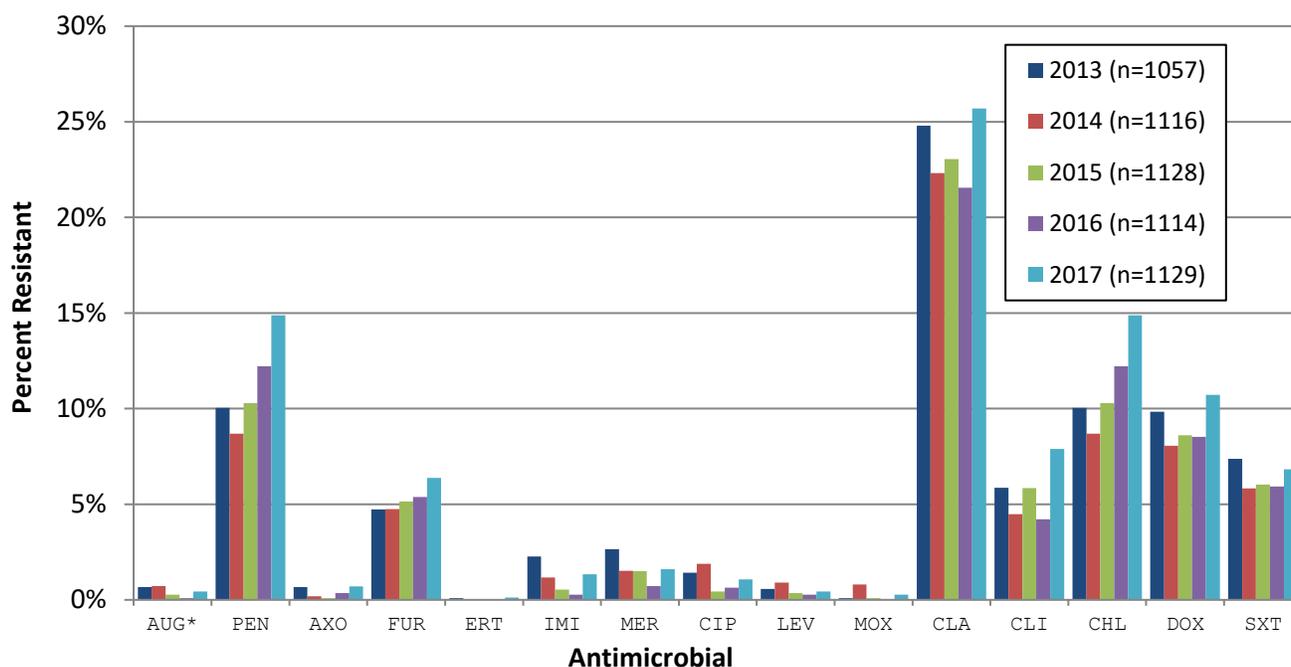
Antimicrobial Resistance of S. pneumoniae

Antimicrobial susceptibility testing was performed on 1,129 *S. pneumoniae* isolates collected in 2017 that were submitted to the NML from 8 participating jurisdictions (Saskatchewan, Manitoba, Ontario, Québec, Nova Scotia, Prince Edward Island, New Brunswick and Newfoundland and Labrador).

Antimicrobial resistance rates among invasive *S. pneumoniae* in Canada have increased slightly in 2017. The highest rate of resistance during 2017 was observed for clarithromycin at 25.7% (n=290), a small increase from 24.8% (n=262) in 2013. Penicillin resistance (using meningitis breakpoints) was identified in 14.9% (n=168), doxycycline in 10.7% (n=121), trimethoprim-sulfamethoxazole in 6.8% (n=77), and clindamycin in 7.9% (n=89) of the isolates tested. All isolates were susceptible to daptomycin, linezolid, tigecycline and vancomycin.

Serotypes 19F, 6C, 19A, 15A, 23A, 23B and 35B generally had the highest rates of antimicrobial resistance. **Clarithromycin** resistance was associated with serotypes 33F (73.2%, n=41), 15A (73.0%, n=27), 12F (63.9%, n=39), 19A (61.0%, n=36), 22F (30.7%, n=31), 23A (31.5%, n=17), 35B (36.7%, n=11) and 6C (31.6%, n=6). High rates of **penicillin** resistance were predominant in serotypes 15A (67.6%, n=25), 35B (63.3%, n=19), 23A (42.6%, n=23), 23B (33.3%, n=13), 19F (33%, n=18) and 19A (30.5%, n=18). **Cefuroxime** resistance was associated with serotypes 35B (56.7%, n=17) and 19F (29.2%, n=14). A relatively high proportion of isolate with **clindamycin** resistance was seen in serotypes 15A (62.2%, n=23), 19F (29.2%, n=14) and 19A (28.8%, n=17). **Doxycycline** resistance in serotypes 15A (64.9%, n=24), 23A (37.0%, n=20) and 19F (33.3%, n=16). Resistance to **trimethoprim-sulfamethoxazole** was mainly associated with serotype 7C and 11A isolates (77.8%, n=7; and 25.0%, n=10; respectively).

Multidrug resistance (MDR) to 3 or more classes of antimicrobials among *S. pneumoniae* increased from 6.2% (n=76) of the isolates tested in 2016 to 9.6% (n=108) in 2017. The highest rates of MDR were seen in serotype 15A with 64.9% (n=15) and 19F with 31.3% (n=15) resistant to 3 or more antimicrobial classes. The major MDR pattern among serotype 15A and 19F isolates was β -lactam-macrolide-clindamycin-tetracycline (n=19 and n=6, respectively).

Figure 23. Antimicrobial resistance of *S. pneumoniae* isolates**Table 9. Antimicrobial resistant *S. pneumoniae* isolates**

Antimicrobial	Year				
	2013	2014	2015	2016	2017
Amoxicillin/Clavulanic Acid	0.7% (7)**	0.7% (8)	0.3% (3)	0.1% (1)	0.4% (5)
Penicillin	10.0% (106)	8.7% (97)	10.3% (116)	12.2% (136)	14.9% (168)
Ceftriaxone	0.7% (7)	0.2% (2)	0.1% (1)	0.4% (4)	0.7% (8)
Cefuroxime	4.7% (50)	4.7% (53)	5.1% (58)	5.4% (60)	6.4% (72)
Ertapenem	0.1% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.1% (1)
Imipenem	2.3% (24)	1.2% (13)	0.5% (6)	0.3% (3)	1.3% (15)
Meropenem	2.6% (28)	1.5% (17)	1.5% (17)	0.7% (8)	1.6% (18)
Ciprofloxacin	1.4% (15)	1.9% (21)	0.4% (5)	0.6% (7)	1.1% (12)
Levofloxacin	0.6% (6)	0.9% (10)	0.4% (4)	0.3% (3)	0.4% (5)
Moxifloxacin	0.1% (1)	0.8% (9)	0.1% (1)	0.0% (0)	0.3% (3)
Clarithromycin	24.8% (262)	22.3% (249)	23.0% (260)	21.5% (240)	25.7% (290)
Clindamycin	5.9% (62)	4.5% (50)	5.9% (66)	4.2% (47)	7.9% (89)
Chloramphenicol	10.0% (106)	8.7% (97)	10.3% (116)	12.2% (136)	14.9% (168)
Doxycycline	9.8% (104)	8.1% (90)	8.6% (97)	8.5% (95)	10.7% (121)
Trimethprim/Sulfamethoxazole	7.4% (78)	5.8% (65)	6.0% (68)	5.9% (66)	6.8% (77)
Total Tested	(1057)	(1116)	(1128)	(1114)	(1129)

*AUG = amoxicillin/clavulanic acid; PEN = penicillin using the parenteral meningitis CLSI interpretive standard; LEV = levofloxacin; MOX = moxifloxacin; AXO = ceftriaxone using the parenteral meningitis interpretive standard; FUR = cefuroxime using the parenteral interpretive standard; ETP = ertapenem; IMI = imipenem; MER = meropenem; CIP = ciprofloxacin; CLA = clarithromycin; CLI = clindamycin; CHL = chloramphenicol; DOX = doxycycline; SXT = trimethoprim/sulfamethoxazole. Non susceptibility was not observed for daptomycin (no interpretative standard), linezolid, tigecycline (no interpretative standard), or vancomycin. EUCAST[EUCAST, 2017] interpretative breakpoints were used for CIP, all other according to CLSI[CLSI, 2017]. ** Percentage of isolates (number of isolates).

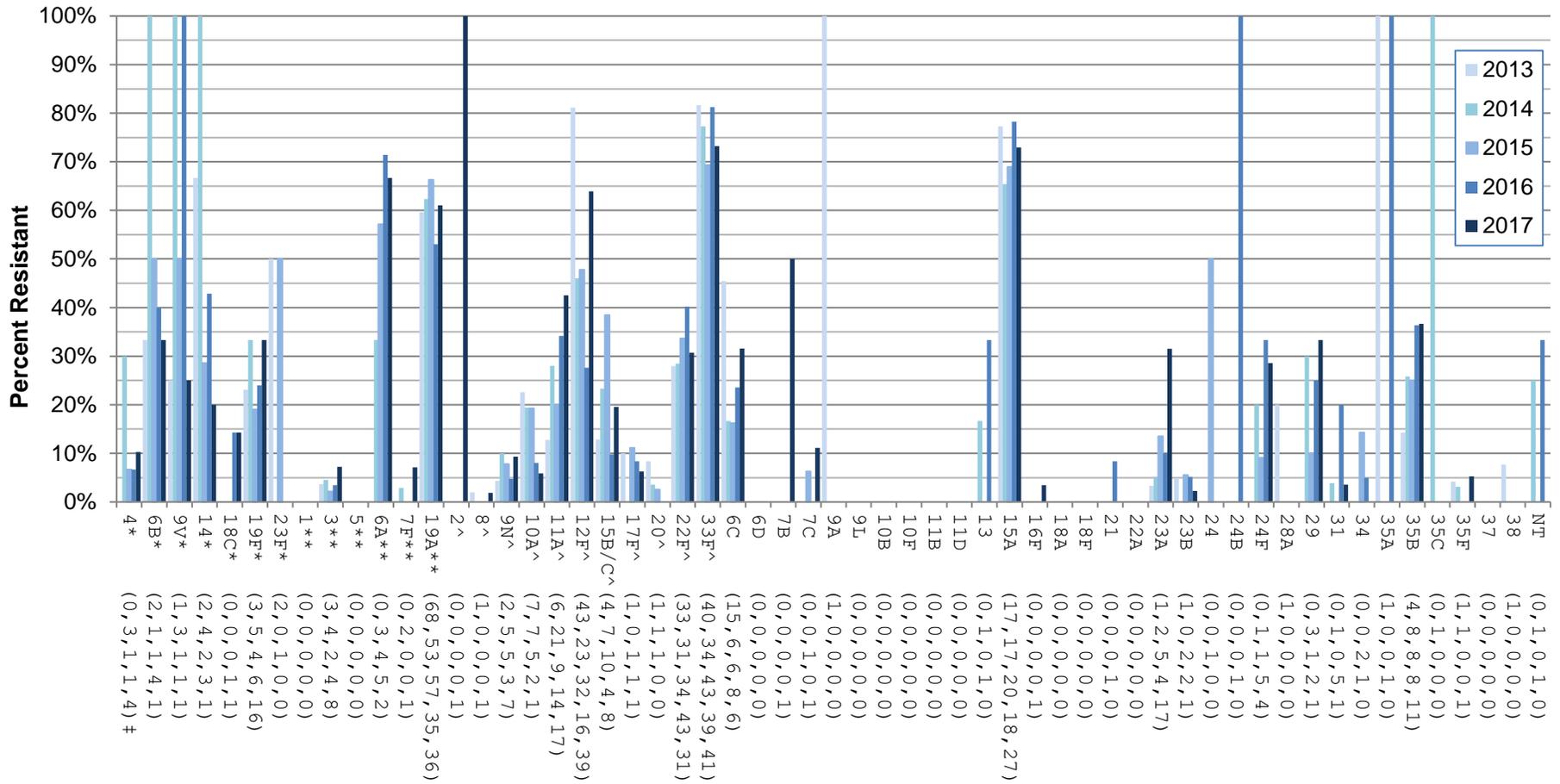
Table 10. Percentage Antimicrobial resistance[†] of *S. pneumoniae* serotypes, 2017

Serotype	PEN	AXO	FUR	ERT	IMI	MER	CIP	LEV	MOX	CLA	CLI	CHL	DOX	SXT
4* (n=39)	2.6	-	-	-	-	-	-	-	-	10.3	-	2.6	-	2.6
6B* (n=3)	-	-	-	-	-	-	-	-	-	33.3	-	-	33.3	-
9V* (n=4)	100.0	-	100.0	-	-	-	-	-	-	25.0	-	100.0	-	100.0
14* (n=5)	80.0	-	80.0	-	-	-	-	-	-	20.0	-	80.0	40.0	80.0
18C* (n=7)	-	-	-	-	-	-	-	-	-	14.3	14.3	-	14.3	14.3
19F* (n=48)	33.3	8.3	29.2	-	14.6	6.3	4.2	4.2	4.2	33.3	29.2	33.3	33.3	18.8
23F* (n=2)	50.0	-	50.0	-	-	-	50.0	50.0	-	-	-	50.0	-	50.0
3** (n=111)	2.7	-	0.9	-	-	-	-	-	-	7.2	5.4	2.7	15.3	2.7
6A** (n=3)	100.0	33.3	33.3	-	-	33.3	-	-	-	66.7	-	100.0	33.3	33.3
7F** (n=14)	-	-	-	-	-	-	-	-	-	7.1	-	-	-	-
19A** (n=59)	30.5	3.4	13.6	-	10.2	6.8	1.7	-	-	61.0	28.8	30.5	23.7	18.6
2^ (n=1)	100.0	-	-	-	-	-	-	-	-	100.0	-	100.0	100.0	-
8^ (n=54)	-	-	-	-	-	-	-	-	-	1.9	1.9	-	3.7	-
9N^ (n=75)	6.7	-	1.3	-	-	-	1.3	-	-	9.3	1.3	6.7	2.7	1.3
10A^ (n=17)	-	-	-	-	-	-	-	-	-	5.9	-	-	-	5.9
11A^ (n=40)	17.5	2.5	5.0	-	-	-	2.5	-	-	42.5	5.0	17.5	5.0	25.0
12F^ (n=61)	-	-	-	-	-	-	-	-	-	63.9	-	-	-	-
15B/C^ (n=41)	12.2	-	2.4	-	-	-	-	-	-	19.5	2.4	12.2	9.8	4.9
17F^ (n=16)	-	-	-	-	-	-	6.3	-	-	6.3	-	-	-	-
20^ (n=39)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
22F^ (n=101)	1.0	-	-	-	-	-	-	-	-	30.7	5.0	1.0	1.0	-
33F^ (n=56)	-	-	-	-	-	-	-	-	-	73.2	5.4	-	5.4	16.1
6C (n=19)	26.3	-	21.1	-	-	5.3	-	-	-	31.6	-	26.3	-	21.1
7B (n=2)	50.0	-	-	-	-	-	-	-	-	50.0	-	50.0	100.0	100.0
7C (n=9)	-	-	-	-	-	-	-	-	-	11.1	11.1	-	11.1	77.8
9L (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
10F (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
11D (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
15A (n=37)	67.6	-	24.3	-	-	-	2.7	2.7	2.7	73.0	62.2	67.6	64.9	-
16F (n=29)	3.4	-	-	-	-	-	3.4	3.4	-	3.4	3.4	3.4	3.4	-
21 (n=9)	11.1	-	-	-	-	-	-	-	-	-	-	11.1	-	-
22A (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
23A (n=54)	42.6	-	1.9	-	1.9	-	1.9	-	-	31.5	20.4	42.6	37.0	-
23B (n=44)	38.6	-	-	-	-	-	-	-	-	2.3	-	38.6	-	2.3
24B (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
24F (n=14)	21.4	-	-	-	-	-	-	-	-	28.6	7.1	21.4	28.6	14.3
28A (n=2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
29 (n=3)	100.0	-	100.0	-	-	-	-	-	-	33.3	-	100.0	-	-
31 (n=28)	-	-	-	-	-	-	-	-	-	3.6	-	-	-	-
34 (n=13)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35B (n=30)	63.3	-	56.7	4.2	3.3	30.0	6.7	-	-	36.7	-	63.3	3.3	10.0
35F (n=19)	-	-	-	-	-	-	-	-	-	5.3	5.3	-	5.3	-
37 (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
38 (n=12)	8.3	-	8.3	-	-	-	-	-	-	-	-	8.3	-	-
NT (n=3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
All (n=1129)	14.9	0.7	6.4	0.1	1.3	1.6	1.1	0.4	0.3	25.7	7.9	14.9	10.7	6.8

[†]Percentage of serotype total interpreted as resistant to the antimicrobial agent; “-” denotes no resistance (0%) to the antimicrobial. PEN = penicillin using the parenteral meningitis CLSI interpretive standard; AXOm = ceftriaxone using the parenteral meningitis interpretive standard; FUR = cefuroxime using the parenteral interpretive standard; ERT = ertapenem; IMI = imipenem; MER = meropenem; CIP=ciprofloxacin; LEV = levofloxacin; MOX = moxifloxacin; CLA = clarithromycin;; CLI = clindamycin; CHL = chloramphenicol; DOX = doxycycline; SXT = trimethoprim/sulfamethoxazole.

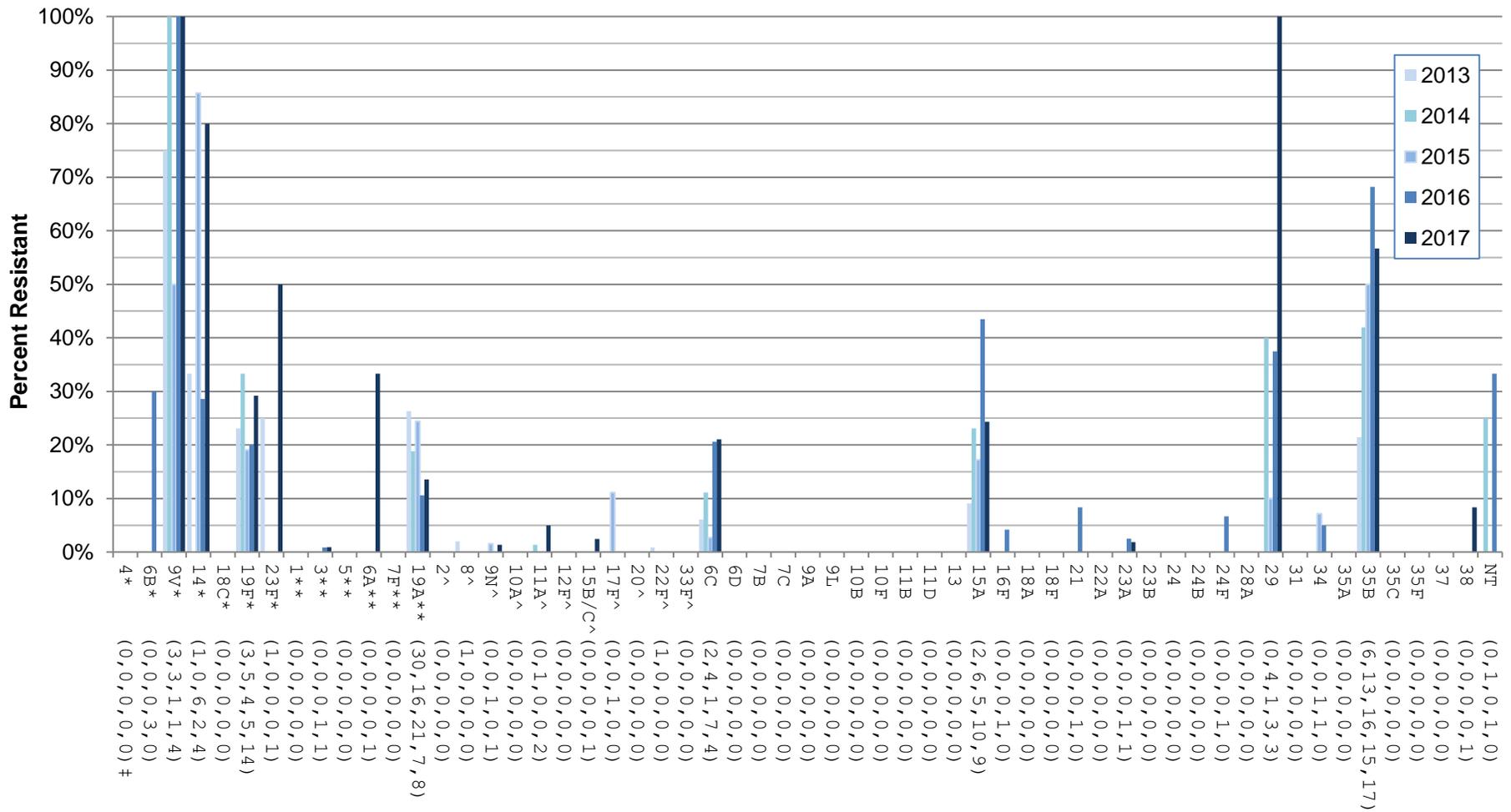
Non susceptibility was not observed for daptomycin (no interpretative standard), linezolid, tigecycline (no interpretative standard), or vancomycin. EUCAST[EUCAST, 2015] interpretative breakpoints were used for CIP, all other according to CLSI[CLSI, 2017]. * represent PCV7 serotypes, ** represent PCV13 serotypes, and ^ represent PPV23.

Figure 24. Clarithromycin resistance of *S. pneumoniae* serotypes



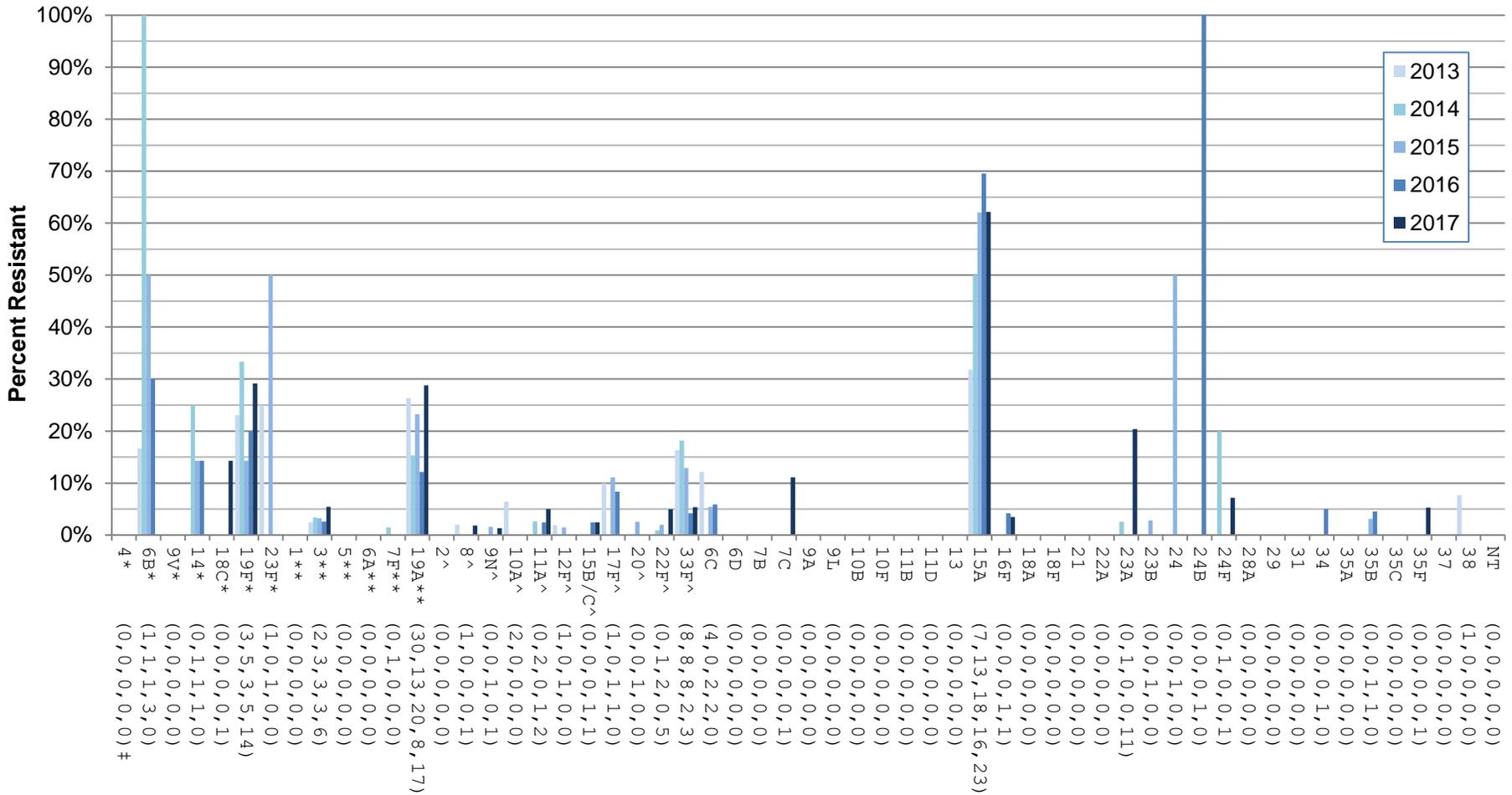
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 25. Cefuroxime resistance of *S. pneumoniae* serotypes



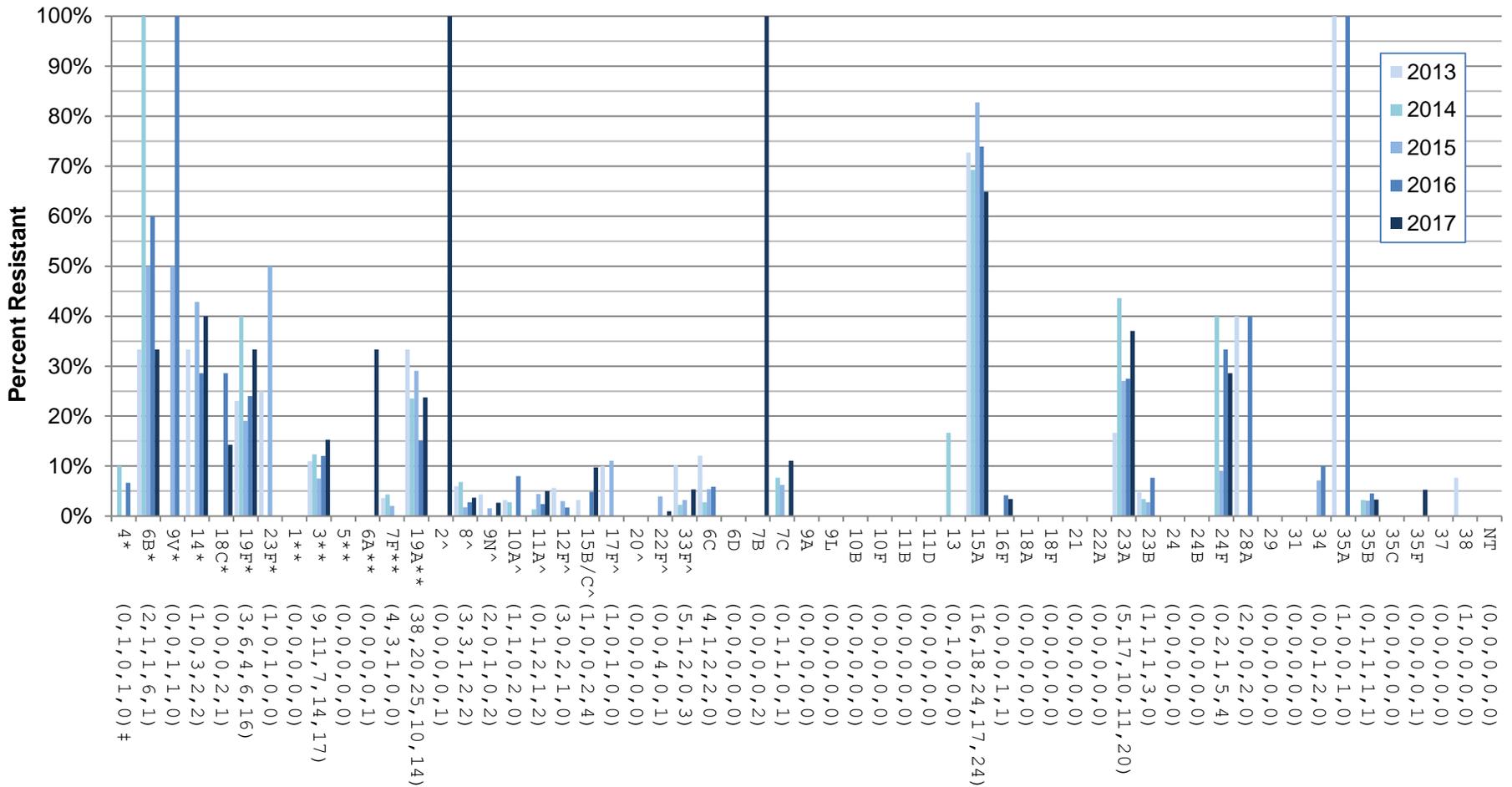
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 26. Clindamycin resistance of *S. pneumoniae* serotypes



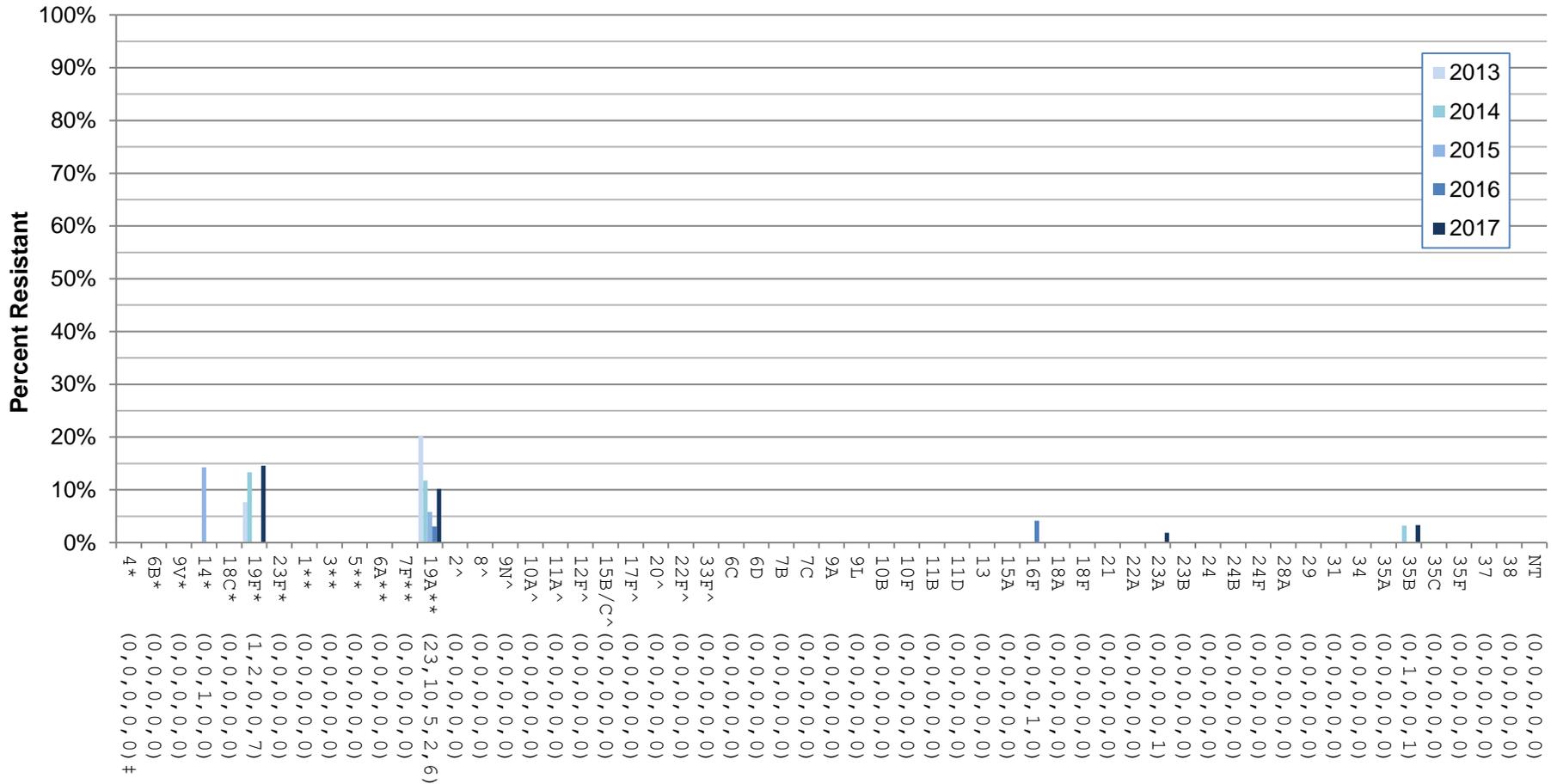
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 27. Doxycycline resistance of *S. pneumoniae* serotypes



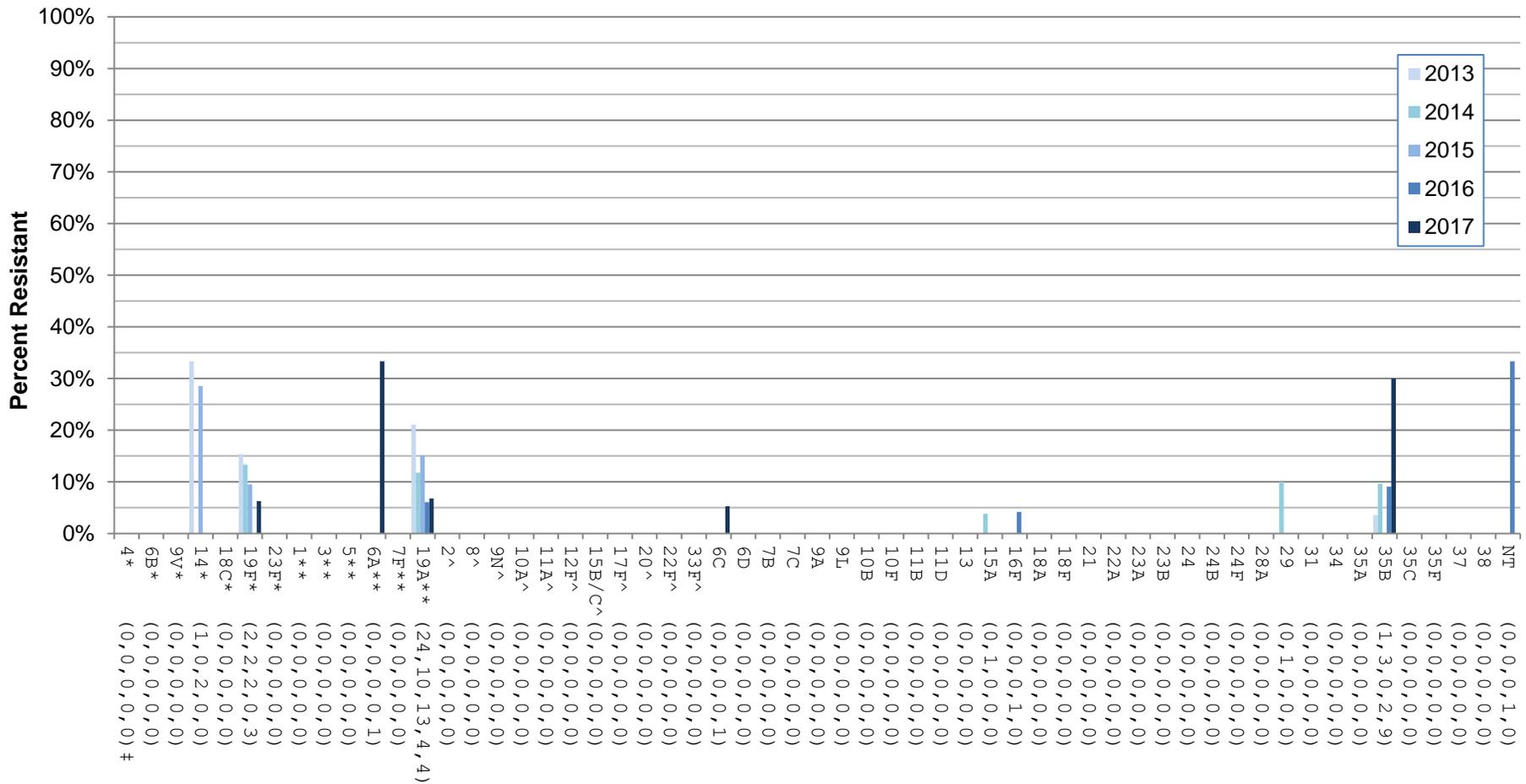
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 28. Imipenem resistance of *S. pneumoniae* serotypes



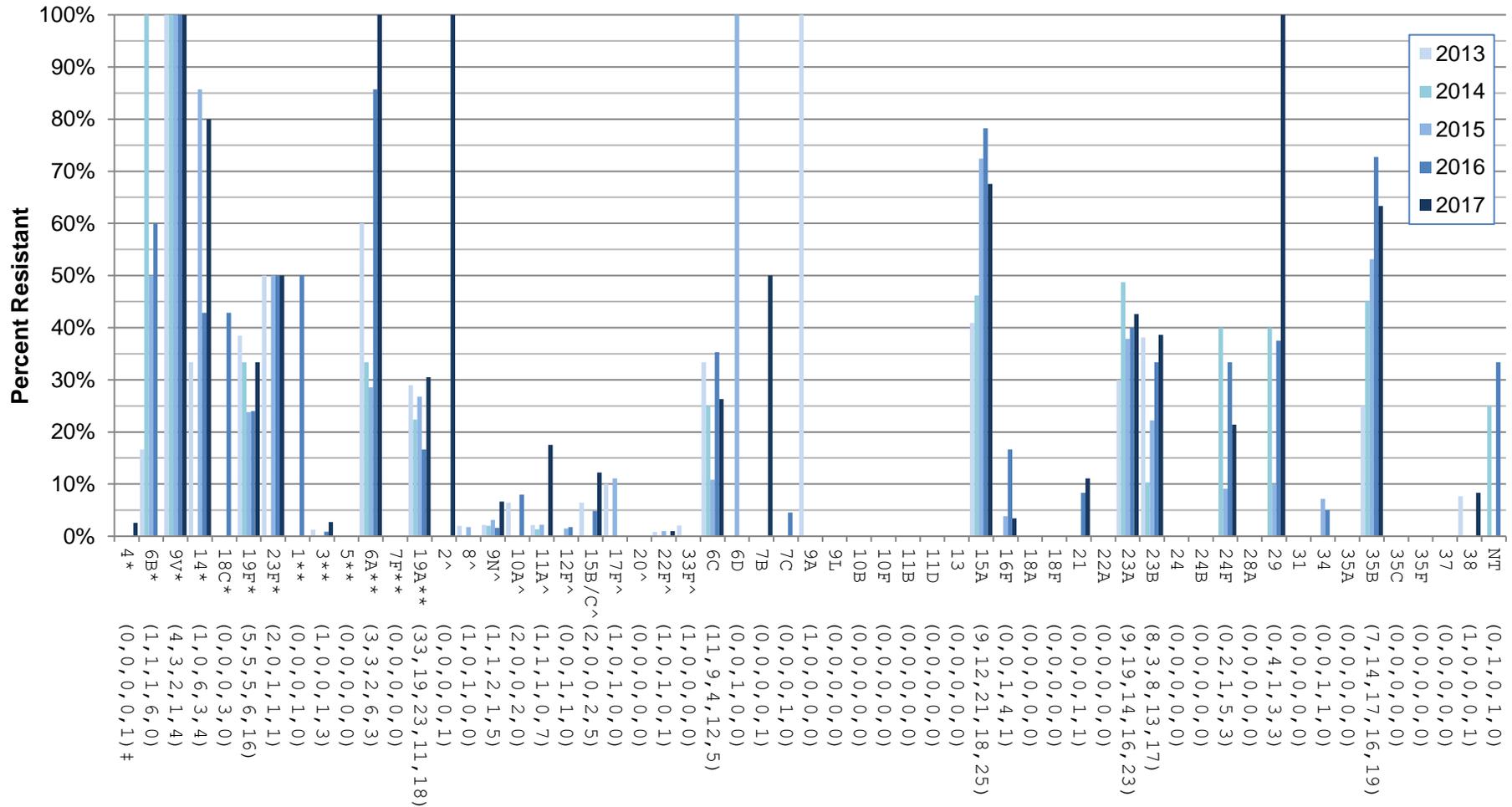
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 29. Meropenem resistance of *S. pneumoniae* serotypes



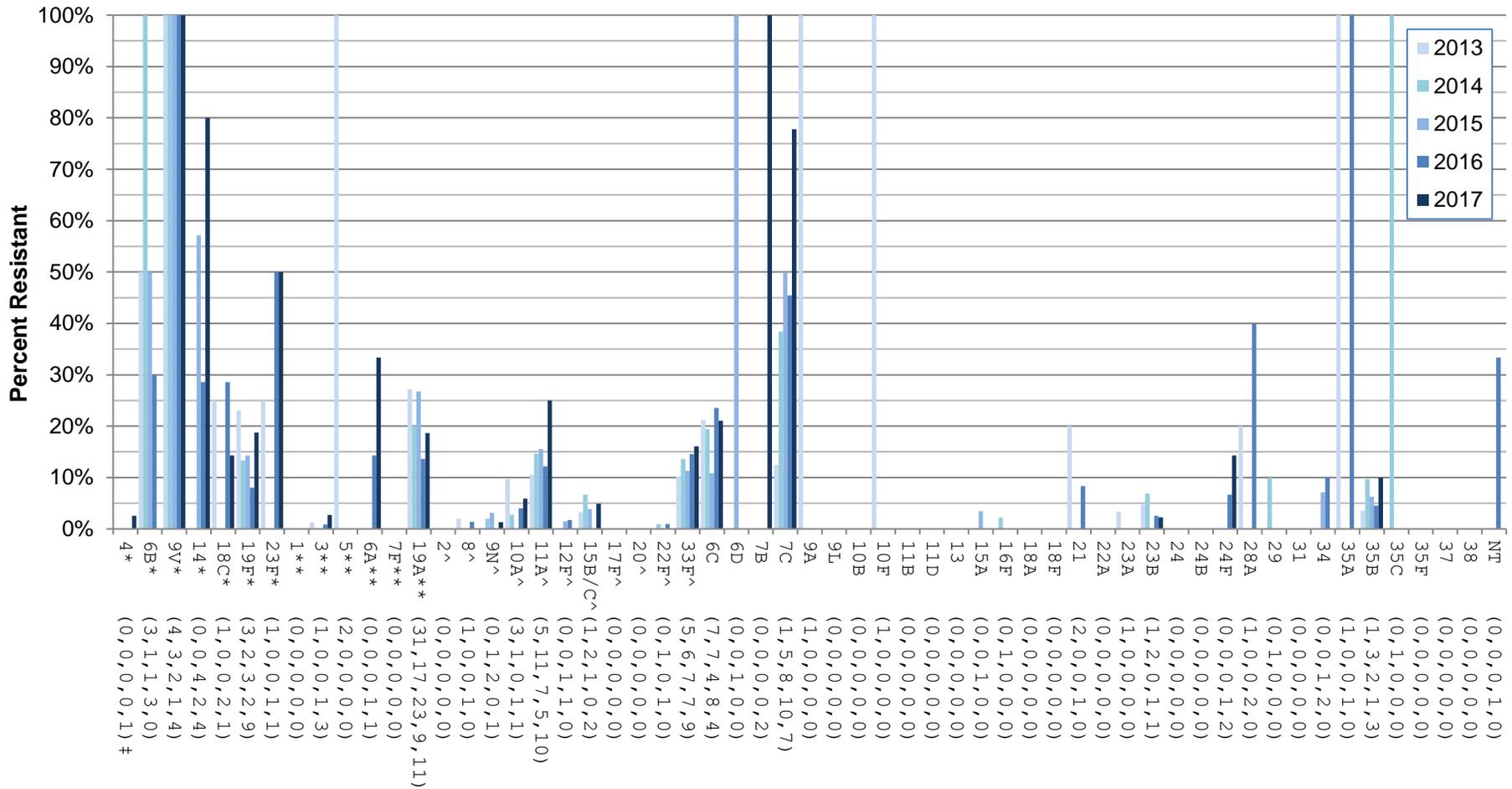
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 30. Penicillin resistance of *S. pneumoniae* serotypes

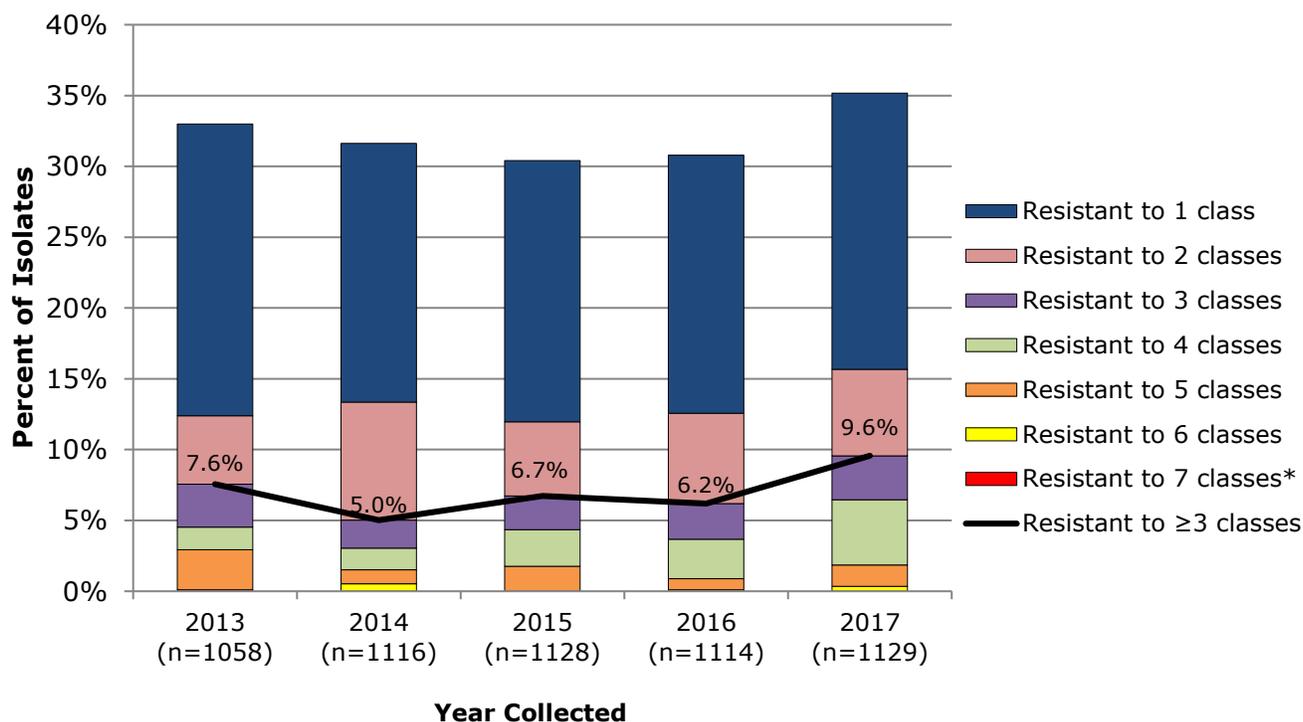


*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 31. Trimethoprim/Sulfamethoxazole resistance of *S. pneumoniae* serotypes



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of resistant isolates for 2013, 2014, 2015, 2016 and 2017, respectively.

Figure 32. Annual trend of multi-drug resistance of *S. pneumoniae*

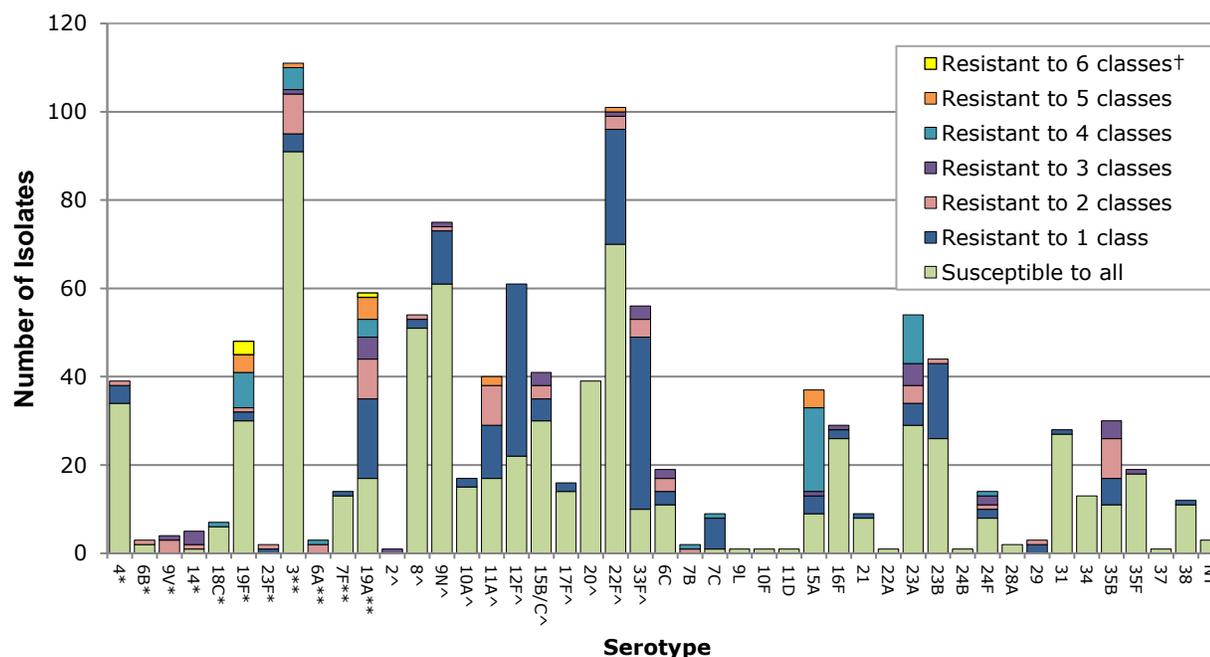
*Antimicrobial classes include: β -lactams (amoxicillin/clavulanic acid, penicillin using meningitis breakpoints, ceftriaxone using meningitis breakpoints, cefuroxime using parenteral breakpoint, ertapenem, imipenem and meropenem); macrolides (clarithromycin); fluoroquinolones (levofloxacin and moxifloxacin);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

Table 11: Multi-drug resistance of *S. pneumoniae*

Year	Number of Antimicrobial Classes Resistant							
	1	2	3	4	5	6	7	≥ 3
2013	20.6%(218)*	4.8%(51)	3.0%(32)	1.6%(17)	2.8%(30)	0.0%(0)	0.1%(1)	7.6%(80)
2014	18.3%(204)	8.3%(93)	2.0%(22)	1.5%(17)	1.0%(11)	0.5%(6)	0.0%(0)	5.0%(56)
2015	18.4%(208)	5.2%(59)	2.4%(27)	2.6%(29)	1.8%(20)	0.0%(0)	0.0%(0)	6.7%(76)
2016	18.2%(203)	6.4%(71)	2.5%(28)	2.8%(31)	0.8%(9)	0.1%(1)	0.0%(0)	6.2%(69)
2017	19.5%(220)	6.1%(69)	3.1%(35)	4.6%(52)	1.5%(17)	0.4%(4)	0.0%(0)	9.6%(108)

* Percentage of isolates (number of isolates).

Figure 33. Multi-drug resistance of *S. pneumoniae* serotypes in 2017



†Antimicrobial classes include: β-lactams (amoxicillin/clavulanic acid, penicillin using meningitis breakpoints, ceftriaxone using meningitis breakpoints, cefuroxime using parenteral breakpoint, ertapenem, imipenem and meropenem); macrolides (clarithromycin); fluoroquinolones (levofloxacin and moxifloxacin); tetracyclines (doxycycline); folate pathway inhibitors (trimethoprim-sulfamethoxazole); phenicols (chloramphenicol); lincosamides (clindamycin); oxazolidinones (linezolid). *Component of PCV7; ** Component of PCV13; ^ Component of PPV23

Table 12. Multi-drug resistant profiles of *S. pneumoniae* serotypes in 2017

Serotype	BLA+	BLA-FQN	BLA-MAC	BLA-MAC-CLI-SXT	BLA-MAC-CLI-TET	BLA-MAC-CLI-TET-CHL	BLA-MAC-CLI-TET-SXT	BLA-MAC-CLI-TET-SXT-CHL	BLA-MAC-FQN-CLI-TET	BLA-MAC-FQN-CLI-TET-SXT	BLA-MAC-SXT	BLA-MAC-TET	BLA-MAC-TET-CHL	BLA-MAC-TET-SXT	BLA-SXT	BLA-TET	BLA-TET-SXT	CHL	FQN	MAC	MAC-CLI	MAC-CLI-CHL	MAC-CLI-TET	MAC-CLI-TET-CHL	MAC-CLI-TET-SXT	MAC-FQN	MAC-SXT	MAC-TET	MAC-TET-SXT	SXT	TET	TET-CHL	TET-SXT
4*														1					4														
6B*																											1						
9V*										1				3																			
14*										1			1			2																	
18C*																								1									
19F*				1	6		4	1		2			1	1						1					1					1			
23F*														1					1												1		
3**							1							1		1				2				5						2	8		
6A**			1									1	1																				
7F**																				1													
19A**	3		1		2		5			1	2		1		1	2				15	7		1	1									
2^												1																					
8^																						1									2		
9N^	4													1					1	6			1						1				
10A^																				1									1				
11A^							2							5			1			11					1	3			1				
12F^																				39													
15B/C^											2		1	1	1				5	1													
17F^																			1	1													
20^																																	
22F^					1															26	3	1											
33F^																				34		3					4			5			
6C	1		1							2			1						2							1							
7B												1																				1	
7C																								1						7			
9L																																	
10F																																	
11D																																	
15A	1				19	3		1			1									3													
16F	1																		1				1										
21	1																																
22A																																	
23A	3				11						5			4					1	1													
23B	16												1							1													
24B																																	
24F					1						1			1						1								1	1				
28A																																	
29	2		1																														
31																				1													
34																																	
35B	6	2	7								3	1																					
35F																							1										
37																																	
38	1																																
NT																																	
All	39	2	11	1	39	4	12	1	1	3	9	11	1	3	16	9	6	1	5	155	12	1	7	7	1	1	8	1	1	15	5	8	1

+Antimicrobial classes: BLA= β -lactams (amoxicillin/clavulanic acid, penicillin and ceftriaxone (meningitis breakpoints), cefuroxime (parenteral breakpoint),ertapenem, imipenem and meropenem); MAC=macrolides (clarithromycin); FQN=fluoroquinolones (levofloxacin and moxifloxacin); TET=tetracyclines (doxycycline); SXT=folate pathway inhibitors (trimethoprim-sulfamethoxazole); CLI=lincosamides (clindamycin); CHL=phenicols (chloramphenicol). *Component of PCV7; ** Component of PCV13; ^ Component of PPV23

Invasive *Streptococcus pyogenes* (Group A Streptococcus, iGAS)

The overall incidence of disease from iGAS in Canada as reported to the CNDSS has continued to increase in 2017 to 6.7 cases per 100,000 population, an increase from 4.0 cases per 100,000 population in 2009. In 2017 the highest average annual incidence of invasive disease was in seniors ≥ 60 years old with 9.3 cases followed by infants <1 year of age with 8.3 cases, and lowest rate was seen among the 10-14 and 15-19 age groups with 1.8 cases per 100,000 population each.

Figure 34. Annual incidence of invasive *S. pyogenes* cases

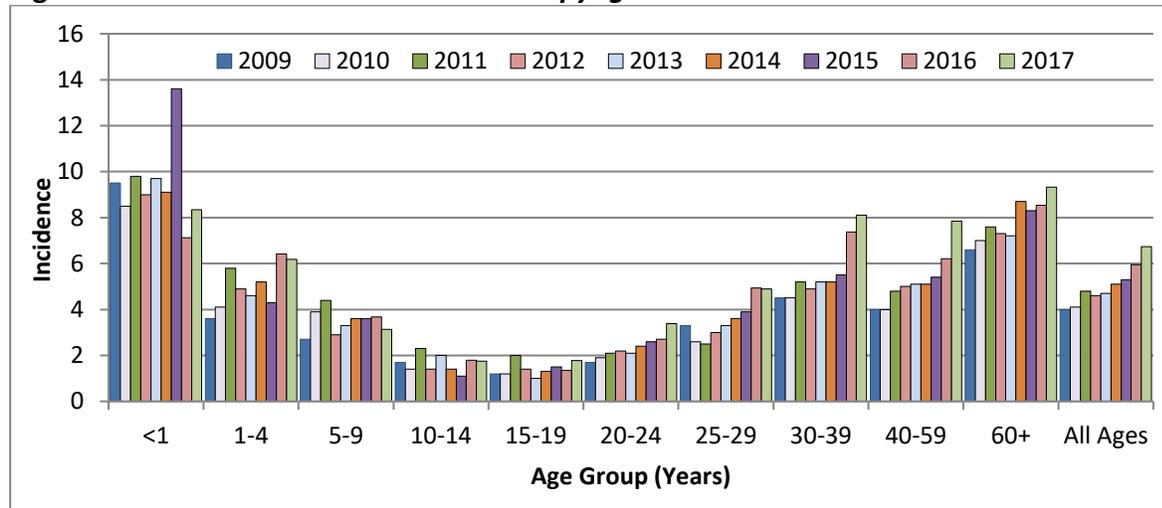


Table 13. Annual incidence rates of invasive *S. pyogenes*

Year	Age Group (Years)										
	<1	1-4	5-9	10-14	15-19	20-24	25-29	30-39	40-59	60+	All Ages
2009	9.5*	3.6	2.7	1.7	1.2	1.7	3.3	4.5	4.0	6.6	4.0
2010	8.5	4.1	3.9	1.4	1.2	1.9	2.6	4.5	4.0	7.0	4.1
2011	9.8	5.8	4.3	2.3	2.0	2.1	2.5	5.2	4.7	7.5	4.8
2012	9.0	4.9	2.9	1.5	1.4	2.2	3.0	4.9	5.0	7.4	4.7
2013	9.7	4.6	3.3	2.0	1.0	2.2	3.3	5.2	5.1	7.2	4.7
2014	8.4	5.1	3.5	1.3	1.2	2.2	3.5	4.9	4.7	8.2	5.1
2015	13.8	4.4	3.6	1.1	1.5	2.6	3.9	5.5	5.4	8.3	5.3
2016	7.2	6.4	3.7	1.8	1.4	2.7	5.0	7.4	6.2	8.6	6.0
2017	8.3	6.2	3.1	1.8	1.8	3.4	4.9	8.1	7.8	9.3	6.7

* Cases per 100,000 population

Of the 2,473 invasive *Streptococcus pyogenes* isolates tested by *emm* typing, 8.4% (n=208) were isolated from children <15 years of age and 2,253 (91.1%) were from adults ≥15 years of age. Isolates from male patients represented 55.2% (n=1364) of the isolates for which gender information was available.

There were no major differences observed in the relative proportions of clinical isolation sites between adults and children except for more pleural fluid isolations sites were observed among pediatric isolates (7.4%, n=16) than in the adults (1.8%, n=40). There was a similar distribution of *emm* types among each of the major clinical isolation sites. The predominant type from blood was *emm1* with 19.4% (n=338). Synovial fluid and other sterile sites shared the majority of their strains between *emm1* (9.2%, n=16; 16.4%, n=95), *emm74* (13.9%, n=24; 14.5%, n=83) and *emm81* (9.8%, n=17; 9.5%, n=54) respectively.

In Western regions *emm1* (15.5%, n=182) and *emm81* (12.0%, n=141) were predominant; in Central regions *emm1* (20.8%, n=252) and *emm74* (15.3%, n=170) were predominant; and in Eastern Canada *emm* types *emm1* (17.7%, n=14), *emm12* (15.2%, n=12), *emm89* (12.7%, n=10), and *emm4* (11.4%, n=9) were predominant.

Although *emm1* continues to be most prevalent in Canada, it has decreased from 23.1% (n=352) in 2013 to 18.2% (n=449) in 2017. *Emm89* continues to decline from 8.9% (n=136) in 2013 to 5.5% (n=136) in 2017. Large increases from 2013 to 2017 were observed for *emm74* from 0.1% (n=2) in 2013 to 9.5% (n=234) and *emm81* from 1.1% (n=17) to 9.1% (n=226).

Table 14. Number of invasive *S. pyogenes* (GAS) isolates by province

Province	Age Group (Years)						Not Given	Total
	< 2	2 – 4	5 – 14	15 – 49	50 – 64	≥ 65		
British Columbia	5	8	13	152	100	76	1	355
Alberta	5	5	14	186	81	91	8	390
Saskatchewan	9	1	6	91	39	36		182
Manitoba	14	5	9	105	61	55		249
Ontario	15	25	28	306	180	215	3	772
Québec	14	9	16	195	93	111		438
New Brunswick	1		1	14	11	9		36
Prince Edward Island				4	4	3		11
Nova Scotia		1	2	7	9	8		27
Newfoundland and Labrador			1	1	1	2		5
Yukon					1	1		2
Northwest Territories	1			1	1	2		5
Nunavut					1			1
Canada	64	54	90	1062	582	609	12	2473

Figure 35a. Clinical isolation sites of *S. pyogenes* from children <15 years of age in 2017 (n=217)

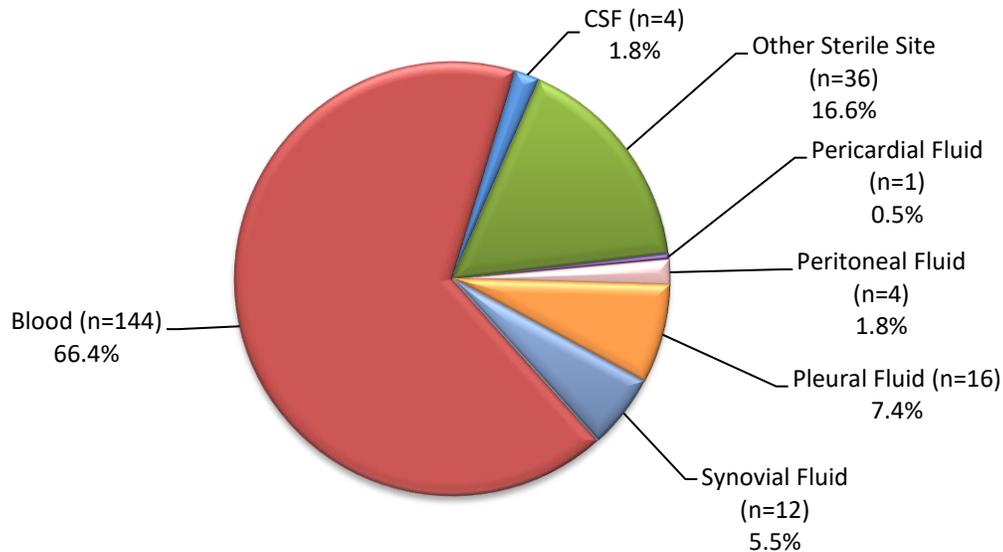
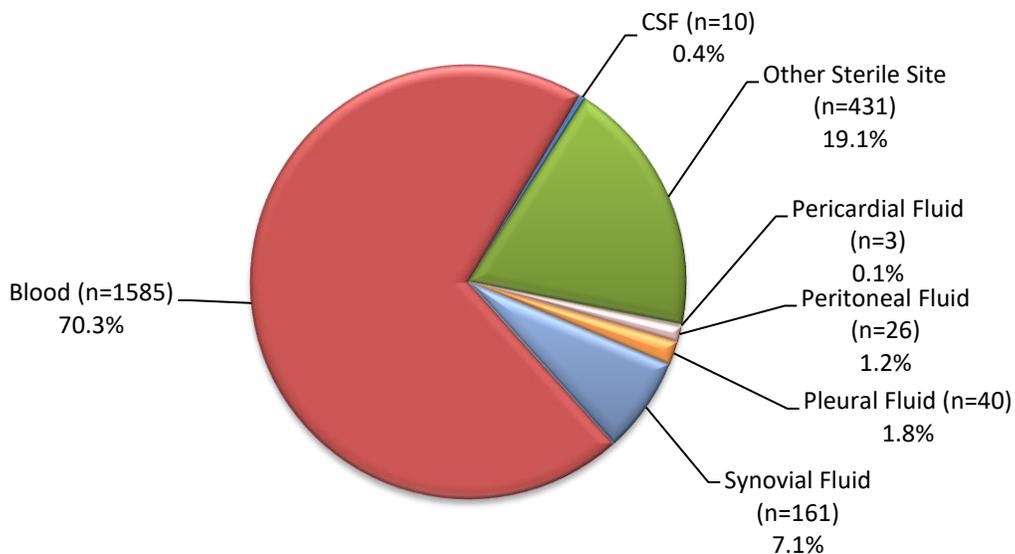


Figure 35b. Clinical isolation sites of *S. pyogenes* from adults ≥15 years in 2017 (n=2256*)



Other sterile sites include: deep tissue, biopsy and surgical samples, bone, mastoid and any clinical sources associated with necrotizing fasciitis or toxic shock syndrome. *Includes 12 isolates with no age available.

Figure 36a. Invasive *S. pyogenes* emm types from blood

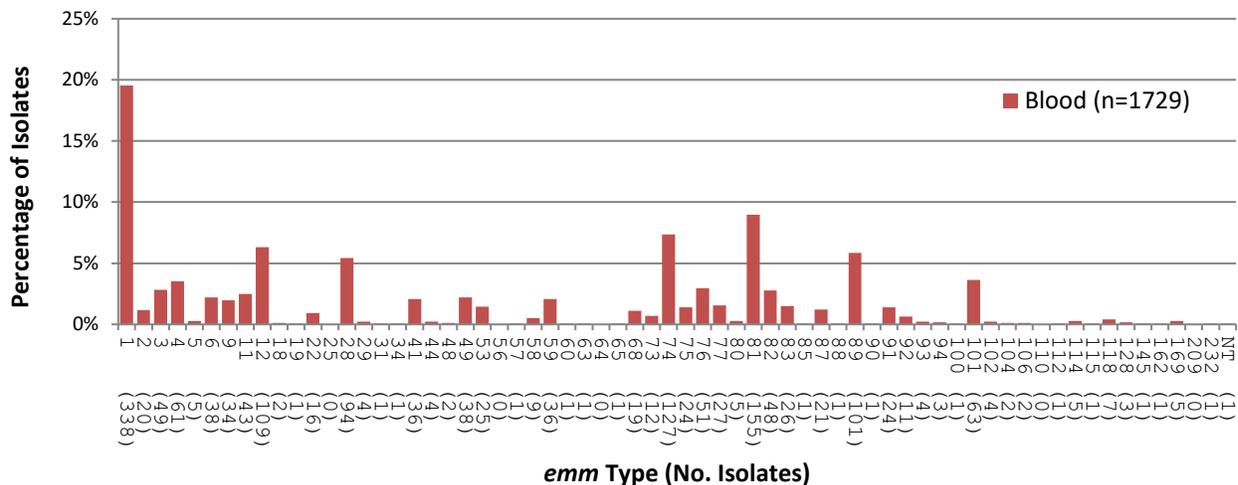


Figure 36b. Invasive *S. pyogenes* emm types from synovial fluid

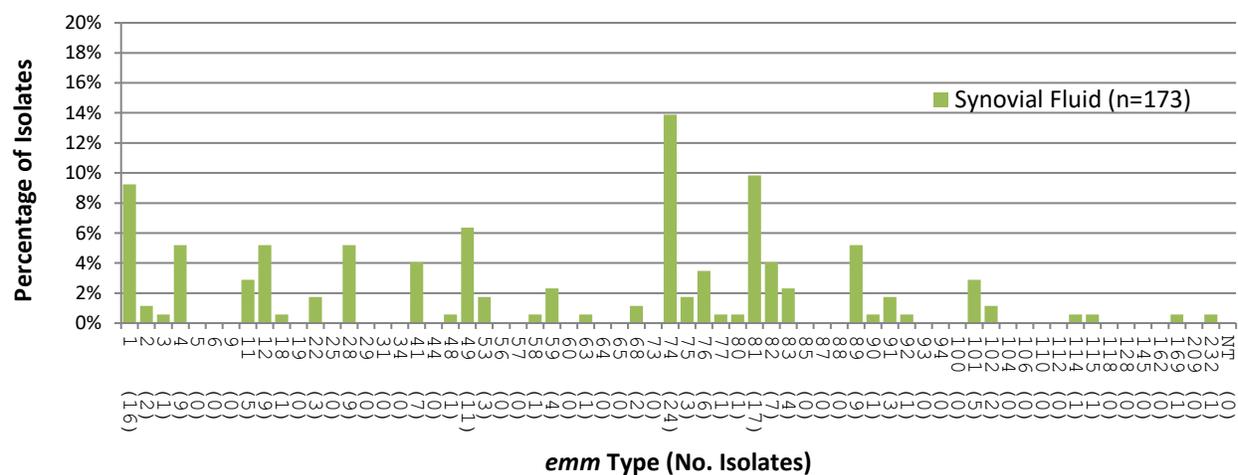
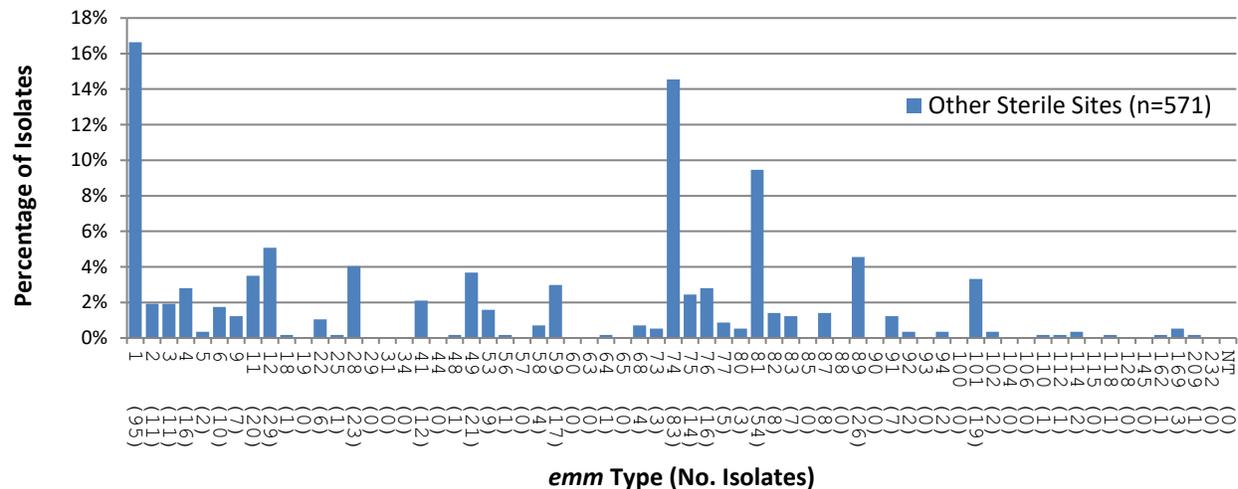
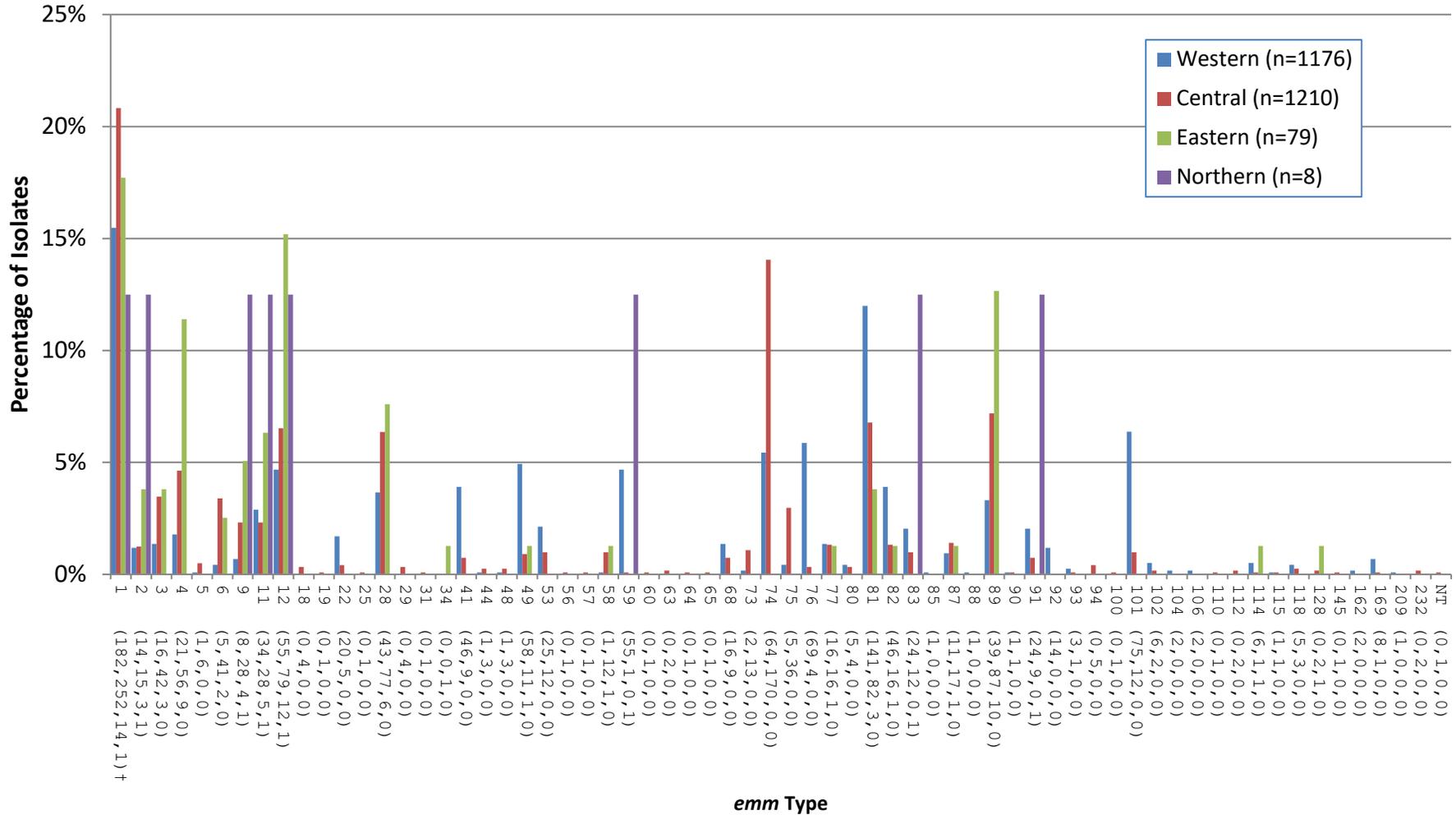


Figure 36c. Invasive *S. pyogenes* emm types from other clinical sources



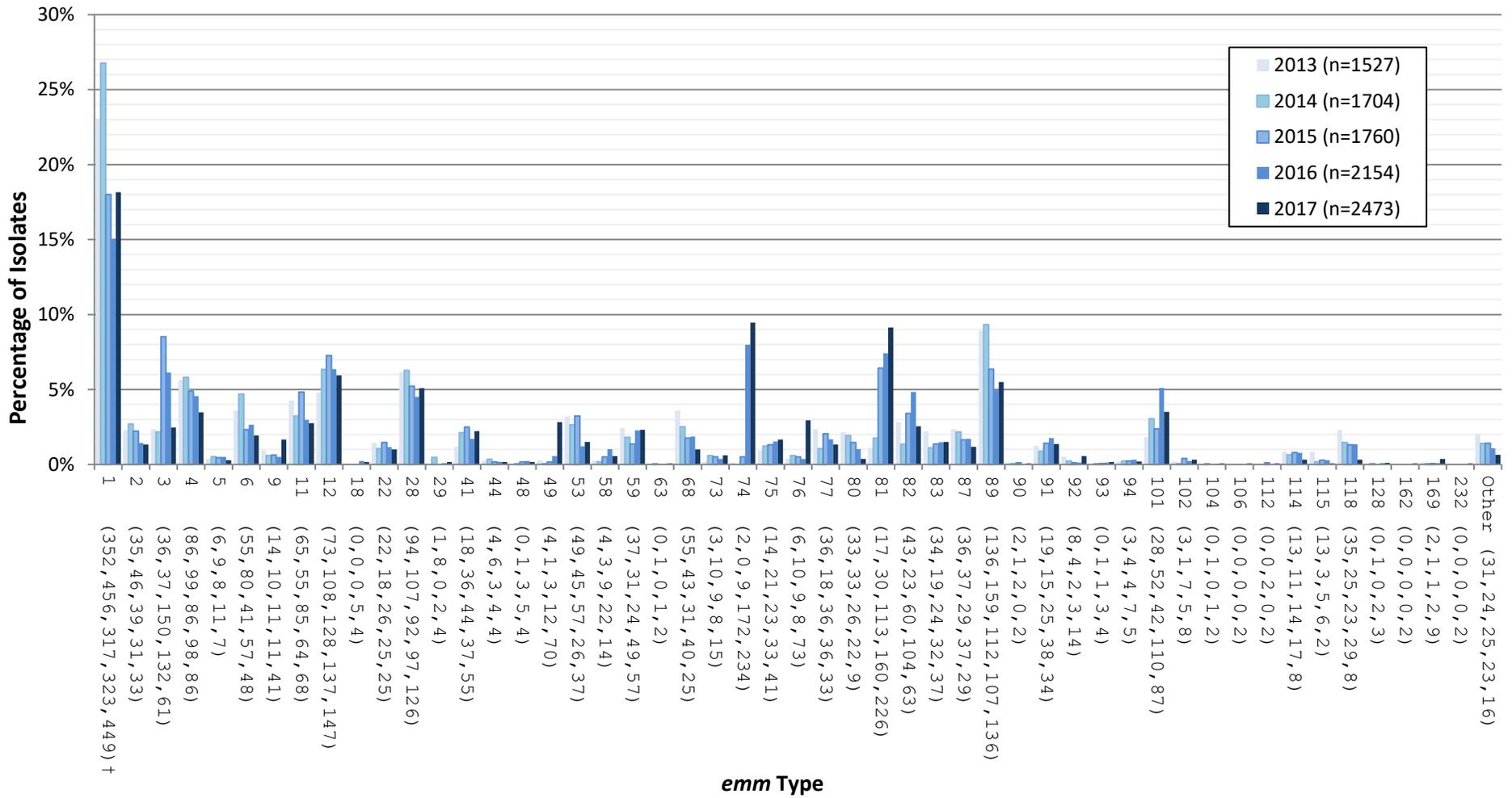
Other sterile sites include: CSF, pericardial fluid, peritoneal fluid, deep tissue, biopsy and surgical samples, bone, mastoid and any clinical sources associated with necrotizing fasciitis or toxic shock.

Figure 37. Regional distribution of Invasive *S. pyogenes* emm types



† Number of isolates in the Western, Central, Eastern and Northern regions of Canada, respectively.

Figure 38. Invasive *S. pyogenes* emm types



+Number of isolates from 2013, 2014, 2015, 2016 and 2017, respectively.

Antimicrobial Resistance of *Streptococcus pyogenes*

Antimicrobial resistance among Group A *Streptococcus* isolates continued to increase in 2017. **Erythromycin** resistance increased from 8.8% (n=156) in 2016 to 10.3% (n=239) in 2017 and resistance to **clindamycin** from 3.9% (n=69) in 2016 to 7.2% (n=167) in 2017. **Chloramphenicol** non-susceptible isolates remained consistent at 4.7% (n=83) in 2016 to 4.8% (n=112) in 2017. Relatively high macrolide (erythromycin) resistance was observed among *emm92* (100.0%, n=15), *emm58* (88.2%, n=15), *emm9* (79.1%, n=34), *emm11* (76.0%, n=19) and *emm101* (70.9%, n=39). There was no resistance observed to penicillin or vancomycin.

Figure 39. Antimicrobial resistance of invasive *S. pyogenes*

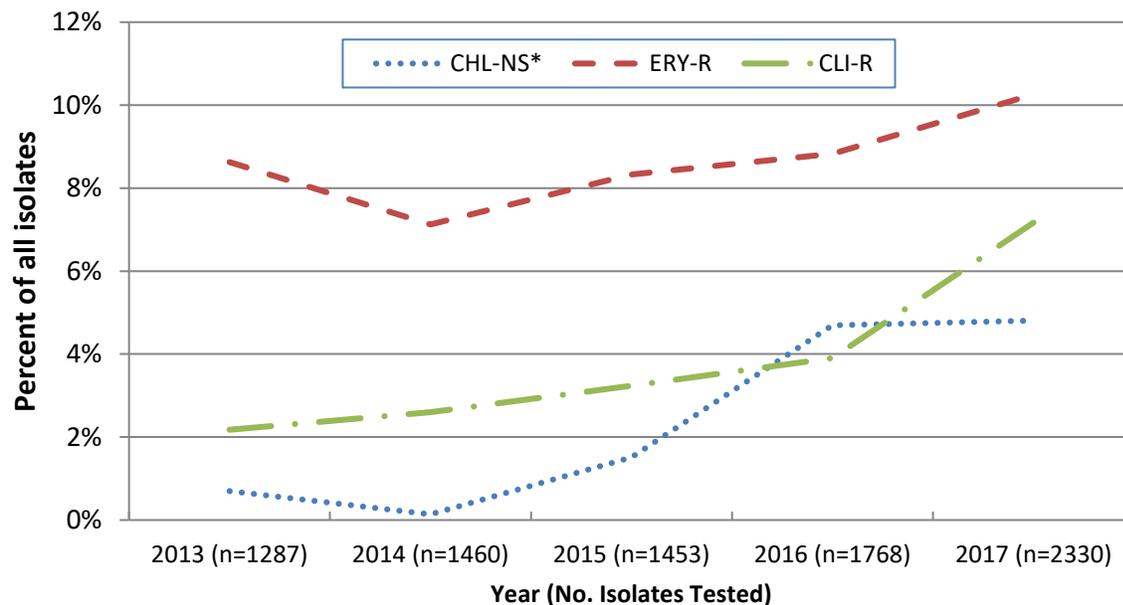
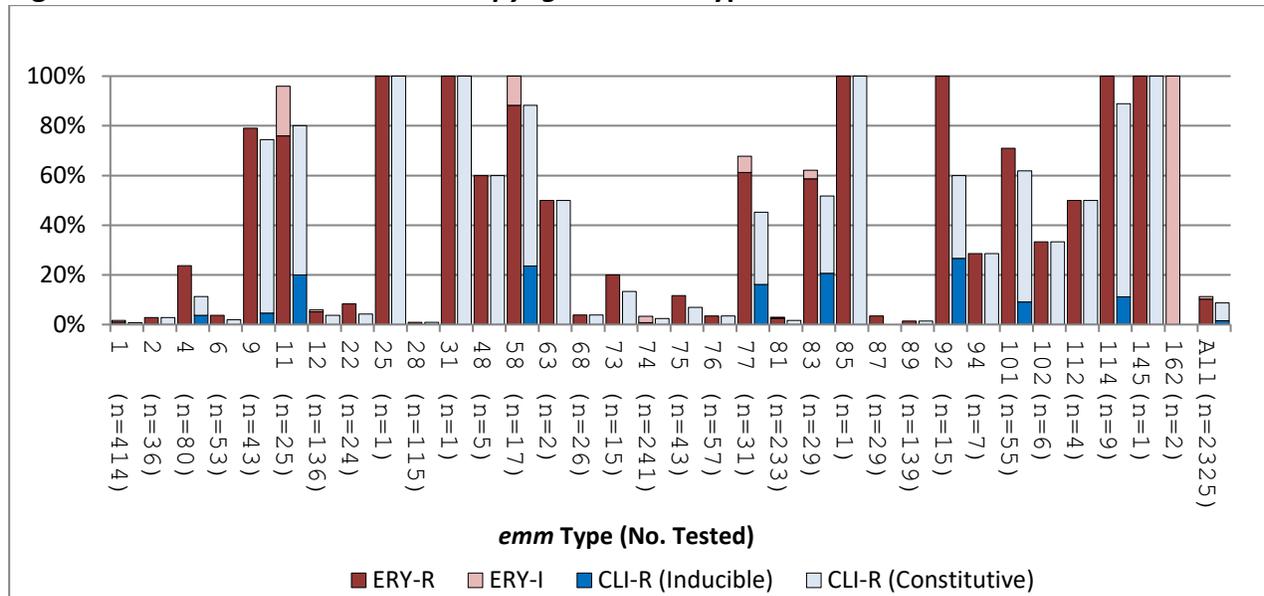


Table 15. Antimicrobial resistance of invasive *S. pyogenes* isolates

Antimicrobial	Year				
	2013	2014	2015	2016	2017
CHL-NS*	0.7% (9)	0.1% (2)	1.5% (22)	4.7% (83)	4.8% (112)
ERY-R	8.6% (111)	7.1% (104)	8.3% (121)	8.8% (156)	10.3% (239)
CLI-R	2.2% (28)	2.6% (38)	3.2% (47)	3.9% (69)	7.2% (167)
No. Tested	(1287)	(1460)	(1453)	(1768)	(2330)

*CHL-NS = Chloramphenicol not-susceptible (resistant or intermediate); ERY-R = Erythromycin resistant; CLI-R = constitutively clindamycin resistant.

Figure 40. Macrolide resistance of *S. pyogenes emm* types

*ERY-R = erythromycin resistant; ERY-I = erythromycin intermediately resistant; CLI-R = clindamycin resistant (constitutive or inducible).

Table 16. Macrolide resistance of *S. pyogenes emm* types

<i>Emm</i> (Tested)	ERY-R		ERY-I		CLI-R (Constitutive)		CLI-R (Inducible)	
1 (n=414)	1.0%	(4)	0.7%	(3)	0.7%	(3)	0.0%	(0)
2 (n=36)	2.8%	(1)	0.0%	(0)	2.8%	(1)	0.0%	(0)
4 (n=80)	23.8%	(19)	0.0%	(0)	7.5%	(6)	3.8%	(3)
6 (n=53)	3.8%	(2)	0.0%	(0)	1.9%	(1)	0.0%	(0)
9 (n=43)	79.1%	(34)	0.0%	(0)	69.8%	(30)	4.7%	(2)
11 (n=25)	76.0%	(19)	20.0%	(5)	60.0%	(15)	20.0%	(5)
12 (n=136)	5.1%	(7)	0.7%	(1)	3.7%	(5)	0.0%	(0)
22 (n=24)	8.3%	(2)	0.0%	(0)	4.2%	(1)	0.0%	(0)
25 (n=1)	100.0%	(1)	0.0%	(0)	100.0%	(1)	0.0%	(0)
28 (n=115)	0.9%	(1)	0.0%	(0)	0.9%	(1)	0.0%	(0)
31 (n=1)	100.0%	(1)	0.0%	(0)	100.0%	(1)	0.0%	(0)
48 (n=5)	60.0%	(3)	0.0%	(0)	60.0%	(3)	0.0%	(0)
58 (n=17)	88.2%	(15)	11.8%	(2)	64.7%	(11)	23.5%	(4)
63 (n=2)	50.0%	(1)	0.0%	(0)	50.0%	(1)	0.0%	(0)
68 (n=26)	3.8%	(1)	0.0%	(0)	3.8%	(1)	0.0%	(0)
73 (n=15)	20.0%	(3)	0.0%	(0)	13.3%	(2)	0.0%	(0)
74 (n=241)	0.8%	(2)	2.5%	(6)	2.5%	(6)	0.0%	(0)
75 (n=43)	11.6%	(5)	0.0%	(0)	7.0%	(3)	0.0%	(0)
76 (n=57)	3.5%	(2)	0.0%	(0)	3.5%	(2)	0.0%	(0)
77 (n=31)	61.3%	(19)	6.5%	(2)	29.0%	(9)	16.1%	(5)
81 (n=233)	2.6%	(6)	0.4%	(1)	1.7%	(4)	0.0%	(0)
83 (n=29)	58.6%	(17)	3.4%	(1)	31.0%	(9)	20.7%	(6)
85 (n=1)	100.0%	(1)	0.0%	(0)	100.0%	(1)	0.0%	(0)
87 (n=29)	3.4%	(1)	0.0%	(0)	0.0%	(0)	0.0%	(0)
89 (n=139)	1.4%	(2)	0.0%	(0)	1.4%	(2)	0.0%	(0)
92 (n=15)	100.0%	(15)	0.0%	(0)	33.3%	(5)	26.7%	(4)
94 (n=7)	28.6%	(2)	0.0%	(0)	28.6%	(2)	0.0%	(0)
101 (n=55)	70.9%	(39)	0.0%	(0)	52.7%	(29)	9.1%	(5)
102 (n=6)	33.3%	(2)	0.0%	(0)	33.3%	(2)	0.0%	(0)
112 (n=4)	50.0%	(2)	0.0%	(0)	50.0%	(2)	0.0%	(0)
114 (n=9)	100.0%	(9)	0.0%	(0)	77.8%	(7)	11.1%	(1)
145 (n=1)	100.0%	(1)	0.0%	(0)	100.0%	(1)	0.0%	(0)
162 (n=2)	0.0%	(0)	100.0%	(2)	0.0%	(0)	0.0%	(0)
All (n=2325)	10.3%	(239)	1.0%	(23)	7.2%	(167)	1.5%	(35)

*ERY-R = erythromycin resistant; ERY-I = erythromycin intermediately resistant; CLI-R = clindamycin resistant (constitutive or inducible).

Invasive *Streptococcus agalactiae* (Group B Streptococcus)

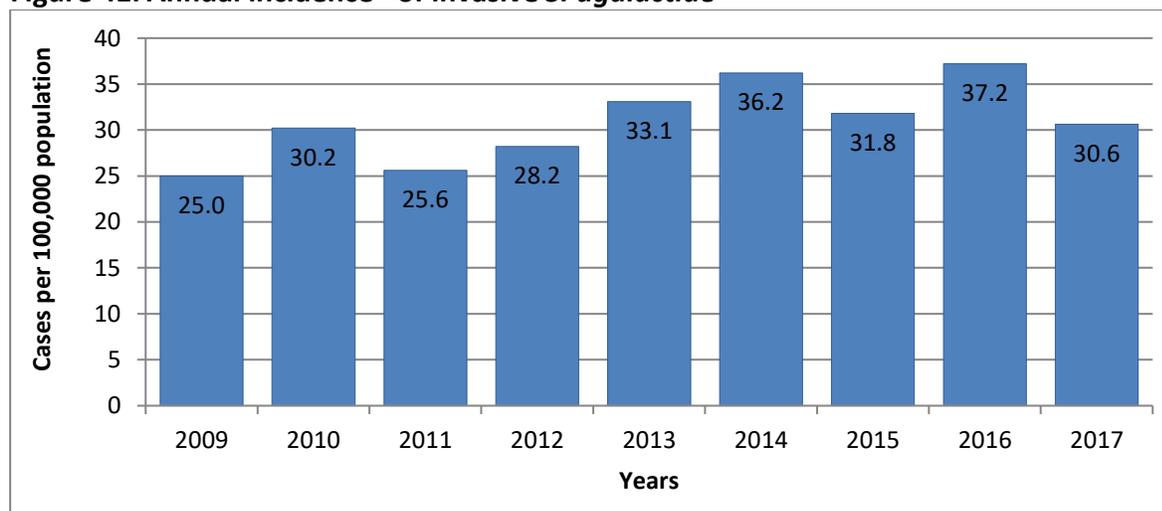
The incidence of disease within newborns less than one year of age as reported to the CNDSS has steadily increased from 25.0 to 36.2 cases per 100,000 population from 2009 to 2014, and has subsequently declined to 30.6 in 2017.

Of the 229 *Streptococcus agalactiae* isolates tested at the NML during 2017, 3.1% (n=7) were early onset isolates from infants <8 days old; 3.5% (n=8) were late onset from infants 8-31 days old; 7.9% (n=18) were from children 1 month to 14 years old; 52.8% (n=121) were from adults 15-64 years old; and 32.3% (n=74) were from seniors ≥65 years of age. Isolates from male patients accounted for 59.1% (n=143) of the isolates for which gender information was available (n=242).

Serotype III was most prevalent among infant and child age groups (60.0%, n=9; and 61.1%, n=11; respectively), whereas serotype IV was most prevalent in adults (25.6%, n=31) and 1a most prevalent in seniors (29.7%, n=22).

Overall the proportion of serotypes has remained similar to 2016 with the exception of serotype V which increased from 11.8% (n=27) in 2016 to 17.0% (n=39) in 2017.

Figure 41. Annual incidence* of invasive *S. agalactiae*

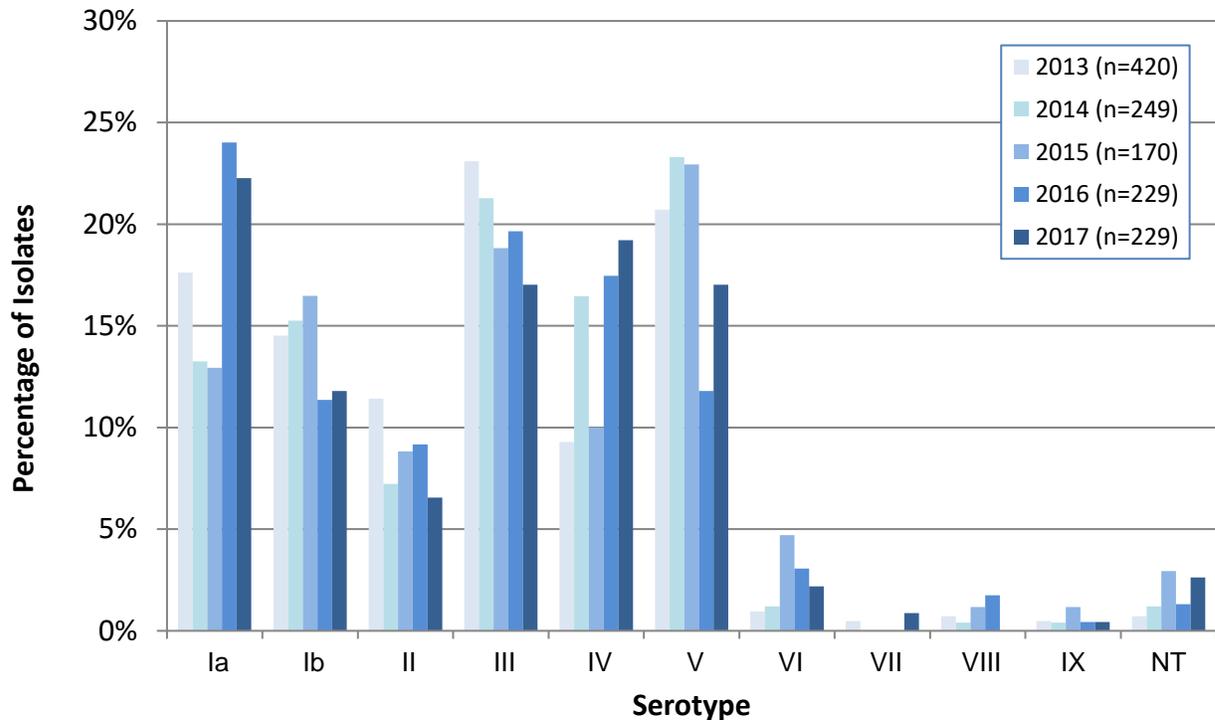


*Incidence per 100,000 population. Case data from 2009 to 2017 was obtained from CNDSS. Case data doesn't include Alberta (2009-2010), Manitoba (2009-2014) and Québec (2009-2016). CNDSS only collects data on Group B *Streptococcus* in newborns < 1 year of age.

Table 17. Invasive *S. agalactiae* serotypes by age group in 2017

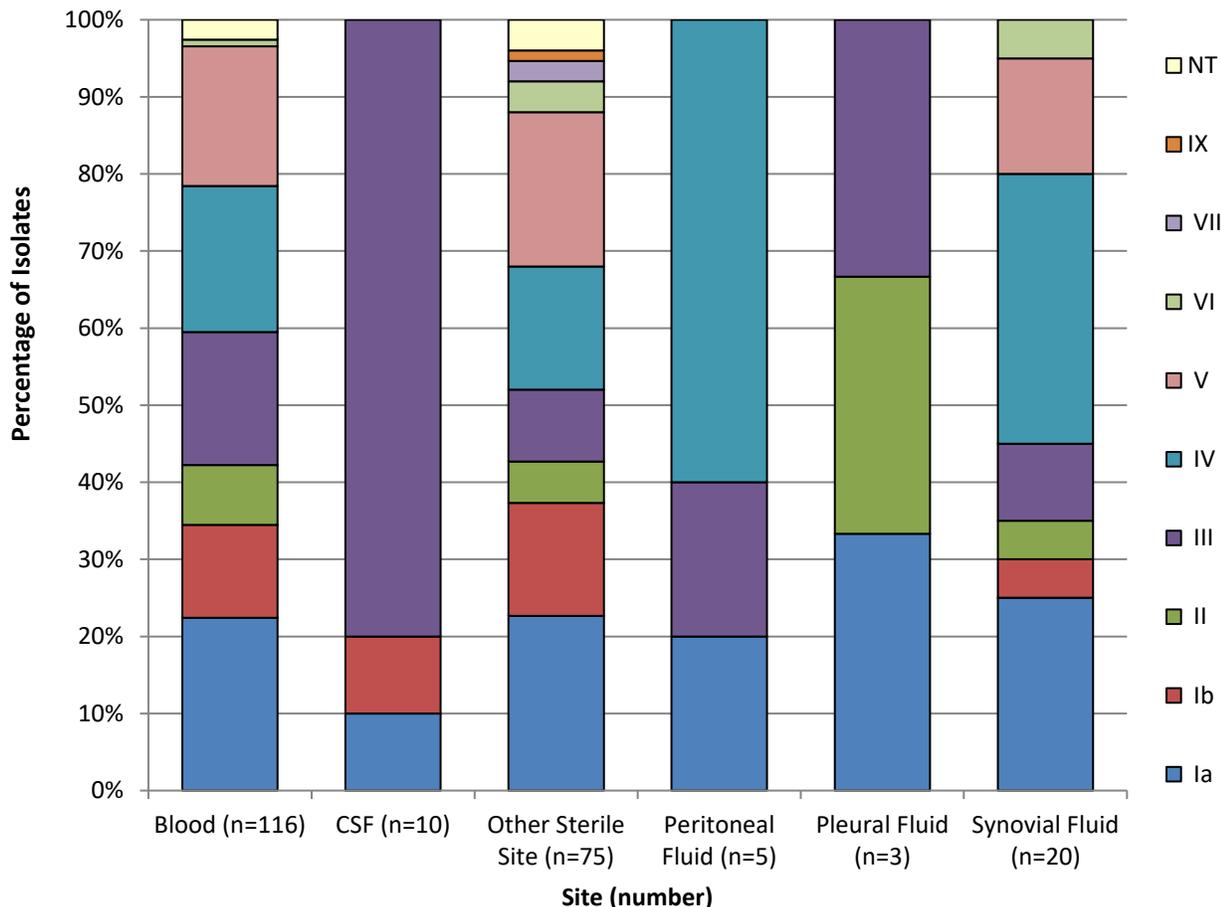
Serotype	Age Group*					Total
	Infant Early Onset	Infant Late Onset	Child	Adult	Senior	
la	0.0%	0.0%	16.7%(3)	21.5%(26)	29.7%(22)	22.3%(51)
lb	0.0%	25.0%(2)	0.0%	10.7%(13)	16.2%(12)	11.8%(27)
II	0.0%	0.0%	0.0%	6.6%(8)	9.5%(7)	6.6%(15)
III	42.9%(3)	75.0%(6)	61.1%(11)	10.7%(13)	8.1%(6)	17.0%(39)
IV	28.6%(2)	0.0%	11.1%(2)	25.6%(31)	10.8%(8)	19.2%(44)†
V	14.3%(1)	0.0%	11.1%(2)	17.4%(21)	20.3%(15)	17.0%(39)
VI	0.0%	0.0%	0.0%	3.3%(4)	1.4%(1)	2.2%(5)
VII	0.0%	0.0%	0.0%	1.7%(2)	0.0%	0.9%(2)
IX	0.0%	0.0%	0.0%	0.8%(1)	0.0%	0.4%(1)
NT	14.3%(1)	0.0%	0.0%	1.7%(2)	4.1%(3)	2.6%(6)
Total	(7)	(8)	(18)	(121)	(74)	(229)†

*Infant Early Onset ≤ 7 days, Infant Late Onset = 8-30 days, Child = 1 month-14 years, Adult = 15-64 years, Senior ≥ 65 years, NT = Non-typeable. **Percentage of age group isolates (number of isolates). † Age for 1 isolate was not available.

Figure 42. Invasive *S. agalactiae* serotypesTable 18. Invasive *S. agalactiae* serotypes

Serotype	Year				
	2013	2014	2015	2016	2017
Ia	17.6% (74)	13.3% (33)	12.9% (22)	24.0% (55)	22.3% (51)
Ib	14.5% (61)	15.3% (38)	16.5% (28)	11.4% (26)	11.8% (27)
II	11.4% (48)	7.2% (18)	8.8% (15)	9.2% (21)	6.6% (15)
III	23.1% (97)	21.3% (53)	18.8% (32)	19.7% (45)	17.0% (39)
IV	9.3% (39)	16.5% (41)	10.0% (17)	17.5% (40)	19.2% (44)
V	20.7% (87)	23.3% (58)	22.9% (39)	11.8% (27)	17.0% (39)
VI	1.0% (4)	1.2% (3)	4.7% (8)	3.1% (7)	2.2% (5)
VII	0.5% (2)	0.0% (0)	0.0% (0)	0.0% (0)	0.9% (2)
VIII	0.7% (3)	0.4% (1)	1.2% (2)	1.7% (4)	0.0% (0)
IX	0.5% (2)	0.4% (1)	1.2% (2)	0.4% (1)	0.4% (1)
NT	0.7% (3)	1.2% (3)	2.9% (5)	1.3% (3)	2.6% (6)
Total	(420)	(249)	(170)	(229)	(229)

*Percentage of age group isolates (number of isolates)

Figure 43. Invasive *S. agalactiae* serotypes by clinical isolation site**Table 19. Invasive *S. agalactiae* isolates by clinical isolation site**

	Clinical Isolation Site						
	Blood	CSF	Other Sterile Site	Peritoneal Fluid	Pleural Fluid	Synovial Fluid	Total
Ia	22.4%(26)	10.0%(1)	22.7%(17)	20.0%(1)	33.3% (1)	25.0%(5)	22.3%(51)
Ib	12.1%(14)	10.0%(1)	14.7%(11)	0.0%(0)	0.0% (0)	5.0%(1)	11.8%(27)
II	7.8%(9)	0.0%(0)	5.3%(4)	0.0%(0)	33.3% (1)	5.0%(1)	6.6%(15)
III	17.2%(20)	80.0%(8)	9.3%(7)	20.0%(1)	33.3% (1)	10.0%(2)	17.0%(39)
IV	19.0%(22)	0.0%(0)	16.0%(12)	60.0%(3)	0.0% (0)	35.0%(7)	19.2%(44)
V	18.1%(21)	0.0%(0)	20.0%(15)	0.0%(0)	0.0% (0)	15.0%(3)	17.0%(39)
VI	0.9%(1)	0.0%(0)	4.0%(3)	0.0%(0)	0.0% (0)	5.0%(1)	2.2%(5)
VII	0.0%(0)	0.0%(0)	2.7%(2)	0.0%(0)	0.0% (0)	0.0%(0)	0.9%(2)
IX	0.0%(0)	0.0%(0)	1.3%(1)	0.0%(0)	0.0% (0)	0.0%(0)	0.4%(1)
NT	2.6%(3)	0.0%(0)	4.0%(3)	0.0%(0)	0.0% (0)	0.0%(0)	2.6%(6)
Total	(116)	(10)	(75)	(5)	(3)	(20)	(229)

*Percentage of age group isolates (number of isolates)

Antimicrobial Resistance of *Streptococcus agalactiae*

Of the 227 invasive *S. agalactiae* isolates tested for antimicrobial resistance by the disc diffusion method in 2017, the proportion of isolates resistant to **erythromycin** increased slightly from 56.8% (n=129) to 58.1% (n=132) from 2016 to 2017, while **clindamycin** resistance has increased more dramatically from 35.7% (n=81) in 2016 to 44.9% (n=102) in 2017. Three isolates were resistant to chloramphenicol during 2017.

Relatively high macrolide (erythromycin) resistance was observed among serotypes IV (84.1%, n=37), II (78.6%, n=11), Ib (77.8%, n=21) and V (53.8%, n=14). High resistance to clindamycin was seen in serotype IV (86.4%, n=38) and Ib (77.8%, n=21).

Figure 44. Antimicrobial resistance of invasive *S. agalactiae*

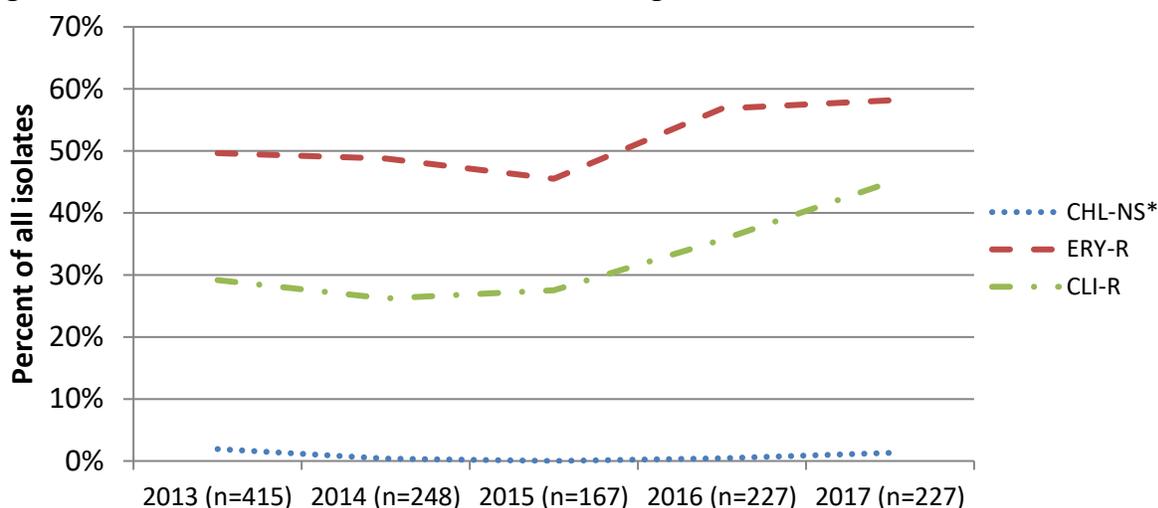
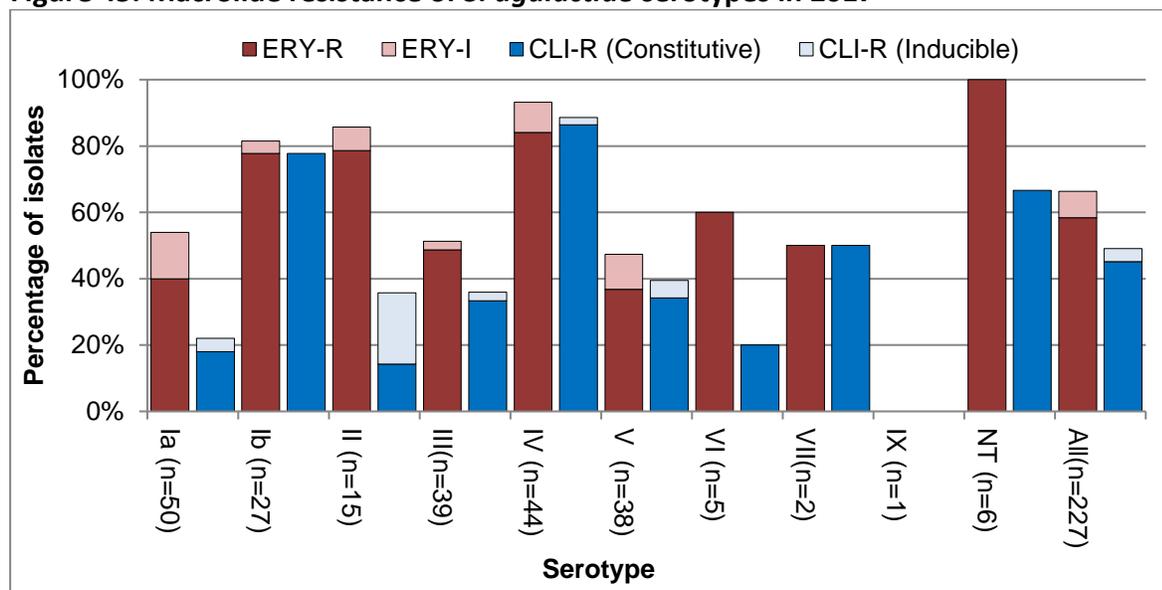


Table 20. Antimicrobial resistance of invasive *S. agalactiae*

Antimicrobial	Year				
	2013	2014	2015	2016	2017
CHL-NS*	1.9% (8)	0.4% (1)	0.0% (0)	0.4% (1)	1.3% (3)
ERY-R	49.6% (206)	48.8% (121)	45.5% (76)	56.8% (129)	58.1% (132)
CLI-R	29.2% (121)	26.2% (65)	27.5% (46)	35.7% (81)	44.9% (102)
Total Tested	(415)	(248)	(167)	(227)	(227)

*CHL-NS = Chloramphenicol non susceptible (resistant or intermediate); ERY-R = Erythromycin resistant; CLI-R = constitutively clindamycin resistant. ** Percent resistant (number of isolates).

Figure 45. Macrolide resistance of *S. agalactiae* serotypes in 2017

*ERY-R = erythromycin resistant; ERY-I = erythromycin intermediately resistant; CLI-R = clindamycin resistant (constitutive or inducible).

Table 21. Macrolide resistance of *S. agalactiae* serotypes

Serotype (Tested)	ERY-R	ERY-I	CLI-R (Constitutive)	CLI-R (Inducible)
Ia (n=50)	40.0% (20)	14.0% (7)	18.0% (9)	4.0% (2)
Ib (n=27)	77.8% (21)	3.7% (1)	77.8% (21)	0.0% (0)
II (n=15)	78.6% (11)	7.1% (1)	14.3% (2)	21.4% (3)
III (n=39)	48.7% (19)	2.6% (1)	33.3% (13)	2.6% (1)
IV (n=44)	84.1% (37)	9.1% (4)	86.4% (38)	2.3% (1)
V (n=38)	36.8% (14)	10.5% (4)	34.2% (13)	5.3% (2)
VI (n=5)	60.0% (3)	0.0% (0)	20.0% (1)	0.0% (0)
VII (n=2)	50.0% (1)	0.0% (0)	50.0% (1)	0.0% (0)
IX (n=1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
NT (n=6)	100.0% (6)	0.0% (0)	66.7% (4)	0.0% (0)
All (n=227)	58.4% (132)	8.0% (18)	45.1% (102)	4.0% (9)

CONCLUSIONS

In 2017, IPD caused by PCV7 serotypes of *S. pneumoniae* in Canada remains low and sustained overall decreases of PCV13 serotypes have been observed. Together with continued declines in the incidence of disease in both child and senior age groups provide evidence of the effectiveness of the childhood PCV vaccination programs in Canada in reducing the burden of disease directly in children, as well as indirectly through herd immunity effects in seniors. Further surveillance is critical to identify potential threats in the future such as increases of non-vaccine replacement serotypes such as serotypes 15A, 23A, 23B and 35B; and the increase of some non PCV serotypes such as 33F in children <2 years of age. Close monitoring of serotype levels can also alert health authorities to sudden increases of disease in various at risk populations. Despite the success of the PCV vaccination programs in lowering disease attributed to the component serotypes, little change has been observed in the levels of serotype 3, raising concerns of the virulence and the effectiveness of the current vaccine against this serotype. The continued monitoring of the relative frequency of serotypes circulating in Canada will help inform and guide the evaluation and development of vaccines which will lower the total burden of disease.

Antimicrobial resistance among isolates of *S. pneumoniae* generally increased in 2017, concern of serotype-specific increases of resistant serotypes 15A and 35B are warranted.

The incidence of disease attributed to **invasive *S. pyogenes*** has continued to increase in most age groups from 2013 to 2017. Dominant strains in Canada tended to be regionally distributed with the exception of *emm1* which is dominant country wide. *Emm81 and emm49* are prevalent in Western Canada; *emm74 and emm89* in Central Canada; and *emm4, emm12, and emm89* predominant in Eastern Canada. **Antimicrobial resistance** in Group A *Streptococcus* has increased again in 2017. Although overall resistance is low and Group A Streptococcal disease is readily treated with penicillin, due to the severity, high risk of infection and heightened public awareness of Group A *Streptococci*, the continued monitoring and surveillance of circulating strains and antimicrobial resistance levels are important to help identify outbreaks of disease and to inform and guide public health interventions.

S. agalactiae serotypes Ia, IV followed by V and III were the predominate strains in Canada during 2017. Macrolide resistance has been relatively high among Group B *Streptococci* and an increase of macrolide resistance has been observed in 2016 and 2017 after being relatively stable in previous years. Although Group B *Streptococci* generally causes severe outcomes in neonatal groups, there is an increasing burden of disease among adults. Monitoring shifts in the distribution of serotypes, levels of antimicrobial resistance as well as collecting additional enhanced epidemiological information, is important to help identify potential risk factors, spread of invasive strains, and to raise awareness of future prevention and treatment options.

APPENDIX

Table A. Proportion of invasive *S. pneumoniae* cases serotyped in Canada, 2017

Age group	Total number of isolates serotyped*	Total number of illnesses reported to CNDSS**	Percent serotyped
<5 years	208	251	82.9%
5 – 39 years	434	494	87.9%
40 – 59 years	765	910	84.1%
≥60 years	1,521	1,822	83.5%
All Ages	2,935	3,477	84.4%

* All Ages total includes 7 isolates with no patient age. Total does not include isolates from pleural fluid. ** Data from Canadian Notifiable Diseases Surveillance System, PHAC.

Table B. Proportion of invasive *S. pyogenes* cases typed in Canada, 2017

Age group	Total number of isolates tested*	Total number of illnesses reported to CNDSS**	Percent serotyped
<5 years	106	130	81.5%
5 – 39 years	756	757	99.9%
40 – 59 years	774	791	97.9%
≥60 years	769	807	95.3%
All Ages	2,417	2,486	97.2%

* All Ages total includes 13 isolates with no patient age. Total does not include isolates from pleural fluid. **Canadian Notifiable Diseases Surveillance System, PHAC.

REFERENCES

- Austrian R. The Quellung reaction, a neglected microbiological technique. 1976. Mt. Sinai J. Med. 43:699–709.
- Bettinger JA, Scheifele DA, Kellner JD, et al. 2010. The effect of routine vaccination on invasive pneumococcal infections in Canadian children, Immunization Monitoring Program, Active 2000–2007. *Vaccine* 28:2130–2136.
- Bjornson G, Scheifele DW, Bettinger J, et al. 2007. Effectiveness of Pneumococcal Conjugate Vaccine in Greater Vancouver, Canada: 2004-2005. *Ped. Inf. Dis. J.* 26(6):540-542.
- Bruce, MG, Deeks SL, Zulz T, et al. 2008. International Circumpolar Surveillance System for Invasive Pneumococcal Disease, 1999-2005. *Emerging Infect. Dis.* 14(1):25-33.
- Case Definitions for Communicable Diseases under National Surveillance - 2009. 2009. CCDR: 35s2. Available: <https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2009-35/definitions-communicable-diseases-national-surveillance.html>
- CLSI. *Interpretive Criteria for Identification of Bacteria and Fungi by Targeted DNA Sequencing*. 2nd CLSI guideline MM18. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
- CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically*. 11th ed. CLSI standard M07. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
- CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Wayne, PA: Clinical and Laboratory Standards Institute; 2018.
- CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 29th ed. CLSI supplement M100. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
- Cunningham MW. 2000 (July). Pathogenesis of Group A Streptococcal Infections. *Clin. Micro. Rev.* 470-511.
- Demczuk WHB, Martin I, Griffith A, et al. 2012. Serotype distribution of *invasive Streptococcus pneumoniae* in Canada during the introduction of the 13-valent pneumococcal conjugate vaccine, 2010. *Can. J. Microbiol.* 58:1008-1017.
- Demczuk WHB, Martin I, Griffith A, et al. 2013. Serotype distribution of *invasive Streptococcus pneumoniae* in Canada after the introduction of the 13-valent pneumococcal conjugate vaccine, 2010-2012. *Can. J. Microbiol.* 59:778-788.
- Deng X, Church D, Vanderkooi OG, et al. 2013. *Streptococcus pneumoniae* infection: a Canadian perspective. *Expert Rev. Anti Infect. Ther.* 11(8):781-791.
- De Wals P, Lefebvre B, Defay F, et al. 2012. Invasive pneumococcal diseases in birth cohorts vaccinated with PCV-7 and/or PHiD-CV in the province of Quebec, Canada. *Vaccine* 30:6416-6420.
- Drancourt M, Roux V, Fournier PE, Raoult D. 2004 (February). *rpoB* gene sequence-based identification of aerobic gram-positive cocci of the genera *Streptococcus*, *Enterococcus*, *Gemella*, *Abiotrophia* and *Granulicatella*. *J. Clin. Micro.* 42(2):497-504.

European Committee on Antimicrobial Susceptibility Testing (EUCAST). 2015. Clinical Breakpoint Table. Version 5.0. Available: http://www.eucast.org/clinical_breakpoints/

Hammond-Collins K, Strauss B, Barnes K, et al. 2018. Group A Streptococcus Outbreak in a Canadian Armed Forces Training Facility. *Military Medicine*, 00, 0/01 :1.

Kellner, JD, Scheifele, D, Vanderkooi, OG, et al. 2008. Effects of Routine Infant Vaccination with the 7-Valent Pneumococcal Conjugate Vaccine on Nasopharyngeal Colonization with *Streptococcus pneumoniae* in Children in Calgary, Canada. *The Ped. Infect. Dis. Journal*. 27(6):526-532.

Kellner, JD, Vanderkooi OG, MacDonald J, Church DL, Tyrrell GJ, Scheifele DW. 2009 (July). Changing epidemiology of invasive pneumococcal disease in Canada, 1998-2007: update from the Calgary-area *Streptococcus pneumoniae* research (CASPER) study. *Clin Infect Dis*. 49(2):205-12.

Lamangni, TL, Keshishian C, Efstratiou A, et al. 2013. Emerging Trends in the Epidemiology of Invasive Group B Streptococcal Disease in England and Wales, 1991 – 2010. *Clin Inf Dis* 2013;57(5):682-8.

Lim, GH, Wormsbecker, AE, McGeer A, et al. 2013. Have changing pneumococcal vaccination programmes impacted disease in Ontario? *Vaccine* 31:2680-2685.

Lovgren M, Spika JS, Talbot JA. 1998. Invasive *Streptococcus pneumoniae* infections: serotype distribution and antimicrobial resistance in Canada, 1992-1995. *Can.Med.Assoc.J*. 158(3):327-331.

Marchessault V, editor. 2002. Canadian Immunization Guide. 6th ed. Ottawa: Canadian Medical Association.

Merck & Co. Inc., Whitehouse Station, NJ 08889, USA. Pneumovax[®] 23 (Pneumococcal vaccine polyvalent).

McIntosh ED, Reinert RR. 2011 (Jan). Global prevailing and emerging pediatric pneumococcal serotypes. *Expert Rev Vaccines*. 10(1):109-29.

Minnesota Department of Health, Infectious Disease Epidemiology, Prevention and Control Division. Available: <http://www.helath.state.nm.us/divs/idepc/dtopics/invbacterial/sterile.html>

National Advisory Committee on Immunization (NACI). 2010 (November). An Advisory Committee Statement (ACS), Update on the Use of Conjugate Pneumococcal Vaccines in Childhood. *CCDR* 36(ACS-12):1-21.

Public Health Agency of Canada. 2015. Childhood National Immunization Coverage Survey, 2017 [online]. <https://www150.statcan.gc.ca/n1/daily-quotidien/190326/t001d-eng.htm>

Public Health Agency of Canada. 2017. Canada's Provincial and Territorial Routine (and catch-up) Vaccination Programs for Infants and Children (as of September 2017) [online]. Available from <https://www.canada.ca/en/public-health/services/provincial-territorial-immunization-information/provincial-territorial-routine-vaccination-programs-infants-children.html> [Accessed 2017-11-17].

Public Health Agency of Canada. 2017. Notifiable Diseases On-Line. <http://dsol-smed.phac-aspc.gc.ca/dsol-smed/ndis/charts.php?c=pl> Accessed: April 2019.

Robinson KA, Baughman W, Rothrock G, Barrett NL, Pass M, Lexau C, et al. 2001 (April). Epidemiology of invasive *Streptococcus pneumoniae* infections in the United States, 1995–1998: opportunities for prevention in the conjugate vaccine era. *JAMA*. 285(13):1729–35.

Schuchat A, Robinson K, Wenger JD, Harrison LH, Farley M, Reingold AL, et al. 1997.

Bacterial meningitis in the United States in 1995. Active Surveillance Team. *N Engl J Med*;337(October (14)):970–6.

Schwartz B, Facklam RR, Breiman RF. 1990. Changing epidemiology of group A streptococcal infection in the USA. *Lancet* 336:1167-1171.

Scott JA, Hall AJ, Dagan R, Dixon JM, Eykyn SJ, Fenoll A, et al. 1996 (June). Serogroup-specific epidemiology of *Streptococcus pneumoniae*: associations with age, sex, and geography in 7,000 episodes of invasive disease. *Clin Infect Dis*. 22(6):973–81.

Shahidi N, Dhaliwa J, Tyrrell G, et al. 2008. Trends in incidence of invasive pneumococcal disease following introduction of the universal infant immunization program in British Columbia, 2001 – 2006. *BC Medical Journal* 50(1):18-21.

Siljander T, Lyytikäinen O, Vähäkuopus S, et al. 2010. Epidemiology, outcome and *emm* types of invasive group A streptococcal infections in Finland. *Eur J Clin Microbiol Infect Dis*; 29:1229-1235.

Spellerberg B, Brandt C. *Streptococcus*. In: Murray PR, Baron EL, Jorgensen JH, Landry ML, Pfaller MA. editors. 2007. *Manual of Clinical Microbiology*. 9th ed. Washington: American Society for Microbiology; p. 412-429.

Teatero S, McGeer A, Tyrrell GJ, et al. 2018. Canada-Wide Epidemic of emm74 Group A Streptococcus Invasive Disease. *Open Forum Infectious Disease*; DOI: 10.1093/ofid/ofy085.

Tyrrell GJ, Lovgren M, Chui N, et al. 2009. Serotypes and antimicrobial susceptibilities of invasive *Streptococcus pneumoniae* pre- and post-seven valent pneumococcal conjugate vaccine introduction in Alberta, Canada 2000-2006. *Vaccine*; 27:3553-3560.

Weinberger DM, Malley R, Lipsitch M. 2011 (April). Serotype replacement in disease after pneumococcal vaccination. *The Lancet*, Available online ISSN 0140-6736, DOI: 10.1016/S0140-6736(10)62225-8. (<http://www.sciencedirect.com/science/article/B6T1B-52M217X-4/2/f3141605bd8e55b78bbc1df8f2dd8677>)