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Annual Summary 2013

Streptococcus and STI Unit
Bacteriology and Enteric Diseases Program
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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EXECUTIVE SUMMARY

- 2577 isolates of ***Streptococcus pneumoniae*** causing invasive pneumococcal disease (IPD) were characterized in 2013.
- Overall incidence of IPD in all combined age groups has remained relatively stable, at around 9.6 cases per 100 000 (range: 9.0 to 9.8) from 2009 to 2013. Incidence of IPD has declined in children under 5 years of age; however rates in the older age groups have remained relatively unchanged.
- In 2013, the highest incidence rates were observed in adults aged 60 years and over (21.7 cases per 100 000 population), infants aged less than 1 year (17.8 cases per 100 000 population), and children aged 1 to 4 years (11.2 cases per 100 000 population).
- **PCV7** serotypes (4, 6B, 9V, 14, 18C, 19F, 23F) have declined from 9.5% to 5.0% of all IPD isolates from 2010 to 2013.
- **PCV13** serotypes (1, 5, 3, 6A, 7F, 19A) have declined in all ages, with an overall decline from 45.5% in 2010 to 30.4% in 2013.
- **PPV23** serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F) have increased in all age groups, with an overall increase from 24.7% (n=670) to 37.6% (n=970) between 2010 and 2013.
- **Serotype 22F** was the most prevalent serotype in 2013, increasing from 6.7% to 12.1% between 2010 and 2013, respectively, in all age groups.
- **Serotype 19A** has continued to decline since 2010 from 19.0% to 11.6% in 2013. Reductions from 2012 levels have been observed in < 2 year olds from 20.7% to 11.6%; and in the 2 – 4 year olds from 23.6% to 18.7%.
- **Serotype 7F** has similarly decreased from 14.3% in 2010 to 8.8% in 2013, and none were reported from children < 2 years of age during 2013.
- **Serotype 3** has increased slightly overall since 2010 from 8.3% to 8.9% of the 2013 isolates, decreasing in <2 year olds from 8.6% to 5.4% since 2012, and increasing in the 5-14 year old age group from 2.9% to 5.1% since 2012.
- **Antimicrobial susceptibility** testing of 1,061 isolates indicated 24.8% were resistant to clarithromycin, 11.9% to penicillin, 9.9% to doxycycline, 5.9% to clindamycin, 7.4% to trimethoprim/sulfamethoxazole, 2.6% to meropenem, and 2.3% to imipenem. No resistance was seen to linezolid, tigecycline, or vancomycin.
- Increases of antimicrobial resistance have been observed to clarithromycin, trimethoprim/sulfamethoxazole, imipenem and meropenem.
- Multi-drug resistance to 3 or more classes of antimicrobials was observed in 7.5% of the isolates tested with the highest rates seen in serotypes 15A (50.0%) and 19A (28.9%).
- Of the 1294 invasive ***S. pyogenes*** **(Group A *Streptococcus*)** tested during 2013, *emm*1 continues to be most predominant accounting for 28.4% of isolates from those <15 years old and 23.7% of those ≥15 years old. *Emm*89 was the next most prevalent with 7.4% of isolates from children and 9.9% from adults.
- 0.6% of 1294 *S. pyogenes* isolates tested in 2013 where non-susceptible to chloramphenicol, 8.5% to erythromycin, and 2.3% to clindamycin. No resistance was seen to penicillin or vancomycin.
- 416 invasive ***S. agalactiae*** **(Group B *Streptococcus*)** were submitted to NML during 2013, with serotypes III (23.8%), V (19.7%) and Ia (17.8%) being most predominant.
- Increases of erythromycin resistance (48.8%) and clarithromycin (28.8%) have been observed in 2013 in Group B Streptococci.

INTRODUCTION

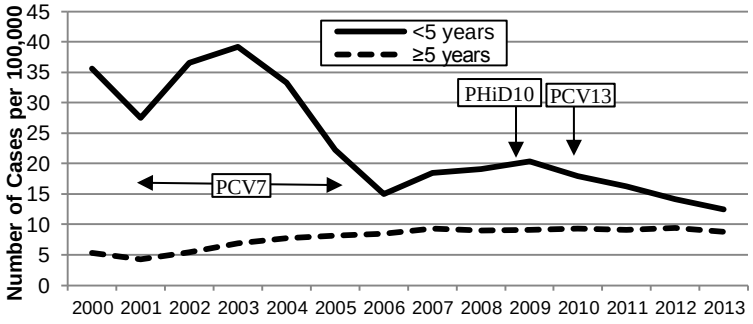
As of April 1, 2010, the National Microbiology Laboratory (NML), Winnipeg began offering surveillance, reference diagnostics and outbreak support on invasive *Streptococcus pneumoniae* (pneumococcus), *Streptococcus pyogenes* (Group A *Streptococcus*), and *Streptococcus agalactiae* (Group B *Streptococcus*). 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 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*) 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], that 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, *Haemophilus influenzae*, and Diptheria vaccine (**PHiD10)**; consisting of all the PCV7 serotypes plus serotypes 1, 5 and 7F; was used in Québec, Ontario 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 National Advisory Committee on Immunization (NACI) / Public Health Agency of Canada (PHAC) recommendations have been published [NACI , 2010; Public Health Agency of Canada (PHAC), 2013]. The 23-valent pneumococcal

Figure 1. Incidence of IPD in Canada, 2000-2013



polysaccharide vaccine (**PPV23)** vaccine is available for adults; however it is not effective in children 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, 2010, Demczuk 2013].

Invasive Group A *Streptococcus* (iGAS, *S. pyogenes*) is nationally notifiable and 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]. 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*) is commonly associated with neo-natal disease where the highest infection risk is during childbirth, and often treated prophylactically with antibiotics. Infant associated disease is nationally notifiable, however GBS is also is also 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 2577 invasive *S. pneumoniae,* 1294 invasive *S. pyogenes* and 420 *S. agalactiae* isolates are included in this report for 2013. Data for 2013 includes test results for isolates submitted to the NML by provincial and territorial public health laboratories and data provided by jurisdictions including: 531 IPD isolates serotyped by Laboratoire de santé publique du Québec , 342 by the Alberta Provincial Laboratory for Public Health and 310 by the Toronto Invasive Bacterial Diseases Network.

Data submitted with bacterial isolates included patient age, gender, clinical source and date of collection. Multiple isolates, with the same serotype, 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 data were aggregated by age into <2 year, 2-14 year, 15-49 year, 50-64 year and ≥65 year age groups; and regionally into Western (British Columbia, Alberta, Saskatchewan, Manitoba, Yukon Territories, Northwest Territories and Nunavut); Central (Ontario and Québec) and Eastern (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador) regions of Canada. Caution should be exercised when interpreting the data presented in this report as the overall interpretation of the results is difficult due to the limitations related to the isolates available for testing. Only 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. Submission of isolates to the NML is voluntary and not standardized across the country. Accordingly, aggregated national and regional summaries are presented in this report.

Validated surveillance data for 2009 to 2012 were obtained through the Canadian Notifiable Disease Surveillance System (CNDSS) [PHAC, 2014]. Population data were obtained from Statistics Canada July 1st annual population estimates, 2009 to 2013. The

population of provinces and territories for whom case data were not available were excluded from the denominator.

All IPD isolates were screened by bile solubility and optochin (Oxoid) analyses and iGAS/GBS isolates were confirmed using PYR (Pyrrolidonyl-α-naphthylamide) reaction and susceptibility to bacitracin (Oxoid) and trimethoprim/sulfamethoxazole susceptibility discs (BBL; 1.25/23.75 µg/ml) [Spellerberg, 2007]. Sterile clinical isolation sites include blood, cerebrospinal fluid or other nervous tissue (CSF), pleural fluid, peritoneal fluid, pericardial fluid, joint fluid, internal body sites and muscle including surgical or biopsy samples and aspirates. 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].

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), 2008] as well as PCR serotyping as outlined at: http://www.cdc.gov/ncidod/biotech/strep/pcr.htm .

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 called SAVE (*S. pneumoniae* Serotyping and Antimicrobial Susceptibility: Assessment for Vaccine Efficacy in Canada After the Introduction of PCV-13). All sterile-site isolates from any age group causing invasive pneumococcal disease submitted 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, 2011]. MIC interpretive standards were defined according to CLSI breakpoints (M100-S21, 2011) for all antibiotics except ciprofloxacin and doxycycline for which EUCAST interpretative breakpoints were used [EUCAST, 2012].

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/ncidod/biotech/strep/M-ProteinGene_typing.htm. The *emm* sequences obtained are compared with the CDC (Atlanta) data bank (www.cdc.gov/ncidod/biotech/strep/strepblast.htm) and results reported to the type level, not the subtype level (*emm*4.4 is reported as *emm*4). Antimicrobial susceptibilities were determined by Kirby-Bauer Disc diffusion for chloramphenicol (CHL, 30 µg), erythromycin (ERY, 15 µg), clindamycin (CLI, 2 µg), penicillin (PEN, 10 µg) and vancomycin (VAN, 30, µg) according to CLSI guidelines [Kellner, 2009].

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

RESULTS AND DISCUSSION

Streptococcus pneumoniae

Overall incidence of IPD in Canada has remained relatively stable over the previous 5 years. In 2013, the overall incidence of IPD was 9.0 cases per 100 000 population, with higher rates of disease still seen in infants <1 year of age (17.8 cases per 100 000 population), children 1 – 4 years of age (11.2 cases per 100 000 population) and in the 60+ age group (21.7 cases per 100 000 population) (Figure 2, Table 1). There has been a steady decline of illness in the < 1 year old age groups from 27.6 to 17.8 cases per 100 000 population, and in the 1 - 4 year olds from 18.7 to 11.2 cases per 100 000 between 2009 and 2013.

Figure 2. Incidence of IPD cases per 100 000 in Canada, 2009 – 2013

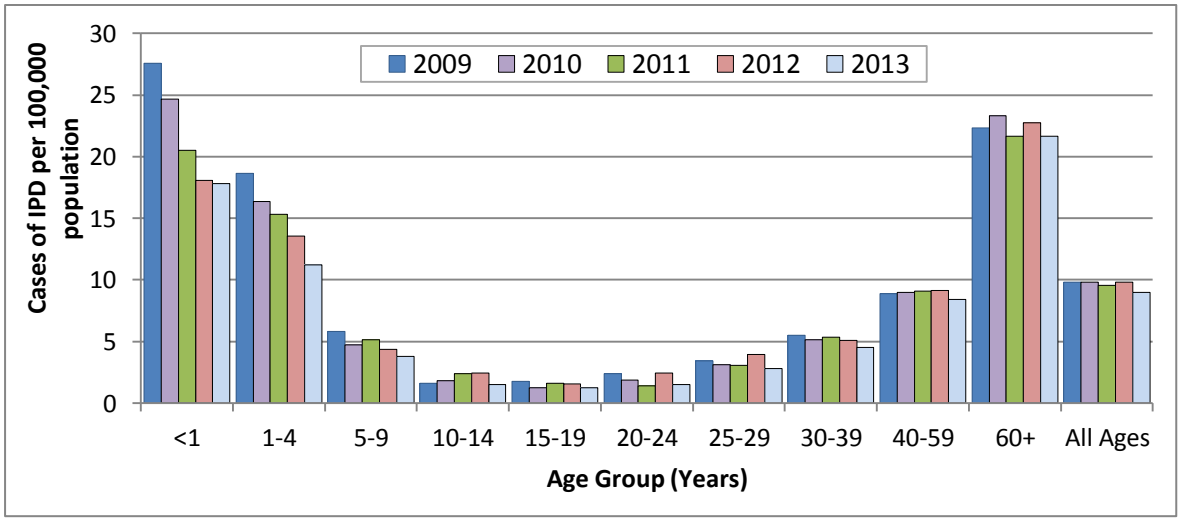


Table 1. Incidence of IPD cases per 100 000 in Canada, 2009 – 2013

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	27.6	18.7	5.8	1.6	1.8	2.4	3.5	5.5	8.9	22.3	9.8
2010	24.7	16.4	4.8	1.8	1.3	1.9	3.1	5.1	9	23.3	9.8
2011	20.5	15.3	5.2	2.4	1.6	1.4	3	5.4	9.1	21.6	9.6
2012	18.1	13.6	4.4	2.4	1.6	2.5	4	5.1	9.1	22.7	9.8
2013	17.8	11.2	3.8	1.5	1.2	1.5	2.8	4.5	8.4	21.7	9.0

Population data were obtained from Statistics Canada July 1st annual population estimates, 2009 to 2013. The population of provinces and territories for whom case data were not available were excluded from the denominator.

Distribution of *Streptococcus pneumoniae* Serotypes

Of the 2577 IPD isolates serotyped in 2013, children <2 years of age accounted for 5.0% (n=129), children aged 2 – 4 years for 2.9% (n=75), children aged 5 – 14 years for 3.0% (n=78), adults aged 15 – 49 years for 20.6% (n=532), adults aged 50 – 64 years for 26.5% (n=682), and seniors aged ≥65 years for 40.6% (n=1047) (Table 2). Blood was the most frequent clinical isolation site accounting for 92.1% (n=2373) of all isolates (Figure 3 and 4). Serotype 22F was evenly prevalent in all sources representing 10% to 12% of isolates from each clinical isolation source, whereas 7F represented a higher proportion of blood (8.9%, n=212) and pleural fluid isolates (11.7%, n=7) than CSF (5.2%, n=4) or other sterile clinical isolation sites (4.5%, n=3). Similarly, serotype 3 was more predominant in blood and pleural fluid representing 9.1% (n=216) and 11.7% (n=7) of the isolates, respectively. Of the 2542 isolates with gender information specified, 55% (n=1390) were from male patients.

The overall most predominant serotypes in 2013 were 22F (12.1%, n=311), 19A (11.6%, n=299), 3 (8.9%, n=229), and 7F (8.8%, n=226), together representing 41.3% (n=1065) of all IPD in Canada (Figure 4). Serotype 22F (a component of PPV23) increased since 2010, becoming the most predominant serotype overall in Canada in 2013. Serotypes 19A, 7F and 6A have continued a steady decline since 2010 with 19A decreasing from 19.0% (n=517) in 2010 to 11.6% (n=299) in 2013; 7F from 14.3% (n=389) to 8.8% (n=226); and 6A from 2.7% (n=72) to 0.6% (n=15). From 2010 to 2013 serotype 3 has increased slightly from 8.3% (n=225) to 8.9% (n=229), despite concurrent decreases in the other additional PCV13-associated serotypes (1, 5, 7F, 6A and 19A).

Serotype 22F: The largest increase in the relative proportion of 22F isolates was seen in the < 2 year olds increasing from 7.8% (n=9) in 2012 to 17.1% (n=22) in 2013. Increases from 7.6% (n=8) to 10.3% (n=8) in the 5 – 14 age group, and from 7.2% (n=44) to 10.7% (n=57) in the 15 – 49 year old age groups were also observed between 2012 and 2013, respectively. Serotype 22F has declined slightly in the 2 – 4 year olds from 12.2% (n=15) of the isolates in 2012 to 9.3% (n=7) in 2013, but still considerably elevated from 2010 levels of 2.7% (n=4). Levels of 22F in the 50 – 64 and ≥65 year olds have remained relatively constant since last year at 11.4% (n=78) and 12.9% (n=135), respectively (Figure 18).

Serotype 19A: Continued declines of 19A has been observed in 2013 among all age groups, except the 5 – 14 year olds where proportions have increased to 28.2% (n=22) in 2013 from 27.6% (n=29) in 2012, and more significantly from 12.7% (n=14) in 2010. Dramatic reductions from 2012 levels have been seen in <2 year olds from 20.7% (n=24) to 11.6% (n=15) and in the 2 – 4 year olds from 23.6% (n=29) to 18.7 (n=14). More modest declines were seen in the 15 – 49 year olds from 10.8% (n=66) in 2012 to 9.6% (n=51) in 2013; in the 50 – 64 year olds from 12.8% (n=89) to 12.0% (n=82); and the ≥65 year olds from 12.9% (n=135) to 10.9% (n=114) (Figure 15).

Serotype 7F: There were no serotype 7F isolates reported among the 129 isolates collected from children < 2 years of age during 2013, decreasing from representing 11.4% (n=21) in 2010. Between 2010 and 2013 serotype 7F has also decreased in the 2 – 4 year old age group from 9.5% (n=14) to 2.7% (n=2), the 5 – 14 year olds from 25.5% (n=28) to 9.0% (n=7), 15 – 49 year olds from 24.3% (n=142) to 15.6% (n=83), 50 – 64 year olds from 12.3% (n=85) to 8.7% (n=59), and in the ≥65 year olds from 9.9% (n=96) to 6.9% (n=72). Interestingly in the 5 – 14 year old age group, a concurrent decrease of 7F and increase of 19A has been observed, despite both being PCV13 serotypes (Figure 16).

Serotype 3: After increasing in the < 2 year olds from 6.5% (n=12) to 8.6% (n=10) of the isolates from 2010 to 2012, serotype 3 decreased in 2013 to 5.4% (n=7). Conversely in the 5 – 14 year old age group, serotype 3 declined from 7.3% (n=8) to 2.9% (n=3) from 2010 to 2012, then increased during 2013 to 5.1% (n=4). In the other age groups, serotype 3 has remained at relatively similar levels over the past few years at 9.3% (n=7) in the 2 – 4 year old, 7.5% (n=40) in the 15 – 49 year old, 9.5% (n=65) in the 50 – 64 year old, and 9.7% (n=101) in the ≥65 year old age groups during 2013 (Figure 17).

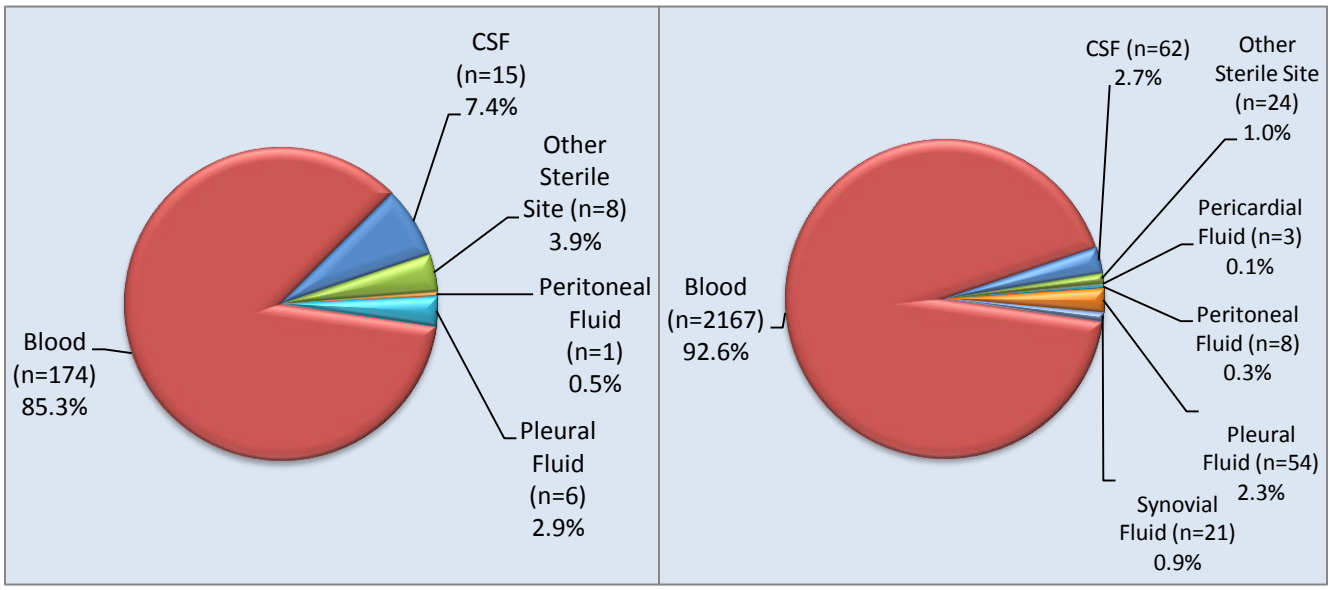
Other Serotypes: Although currently present in low numbers, the PPV23 serotype 15B has increased in <2 year olds from 1.6% (n=3) to 7.8% (n=10), and in 2 – 4 year olds from 3.4% (n=5) to 10.7% (n=8), from 2012 to 2013. Serotype 33F (PPV23) has also increased since 2012 in these age groups from 2.6% (n=3) to 8.5% (n=11) in the <2 year olds and from 1.6% (n=2) to 4.0% (n=3) in the 2 – 4 year olds. Serotype 21 increased in the < 2 year old age group from 1.7% (n=2) to 5.4% (n=7) from 2012 to 2013, and 23B continues to increase in the 2 – 4 year olds from 2.0% (n=3) to 9.0% (n=6).

Table 2. Number of invasive *S. pneumoniae* isolates from each province and territory, 2013

Province	< 2	2 – 4	5 – 14	15 – 49	50 – 64	≥ 65	Not Given	Total
British Columbia	9	8	20	74	83	135	-	**329**
Alberta	14	15	9	93	101	105	5	**342**
Saskatchewan	9	3	3	42	30	38	-	**125**
Manitoba	11	3	5	40	23	41	8	**131**
Ontario	37	27	26	155	244	418	16	**923**
Québec	42	14	11	93	152	219	-	**531**
New Brunswick	3	1	1	11	18	39	1	**74**
Nova Scotia	2	3	1	14	20	33	-	**73**
Prince Edward Island	-	-	-	5	2	5	3	**15**
Newfoundland and Labrador	-	1	2	1	4	11	1	**20**
Yukon Territories	-	-	-	-	2	1	-	**3**
Northwest Territories	-	-	-	3	3	2	-	**8**
Nunavut	2	-	-	1	-	-	-	**3**
Canada	**129**	**75**	**78**	**532**	**682**	**1047**	**34**	**2577**

Figure 3. Clinical isolation sites of *S. pneumoniae,* 2013

Figure3a Isolates from < 5years of age (N=204) Figure 3b Isolates from ≥5 years of age (N=2339)*



*NOTE: Age was not available for 34 isolates.

Figure 4. Distribution of invasive *S. pneumoniae* serotypes from blood, 2013

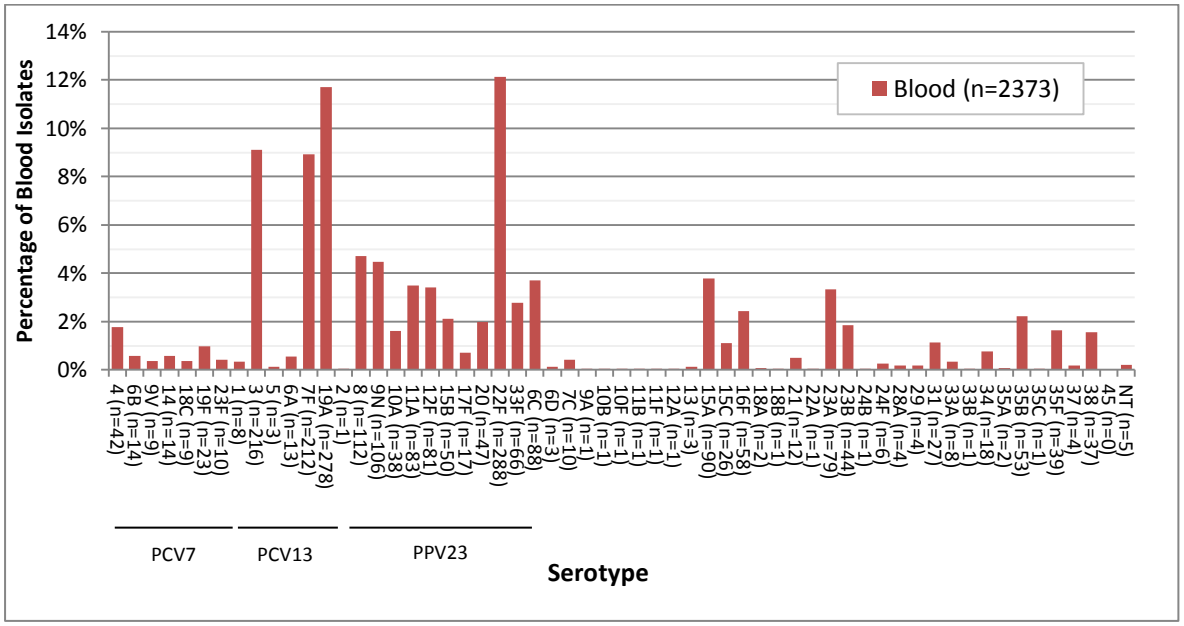


Figure 5. Distribution of invasive *S. pneumoniae* serotypes from CSF, 2013

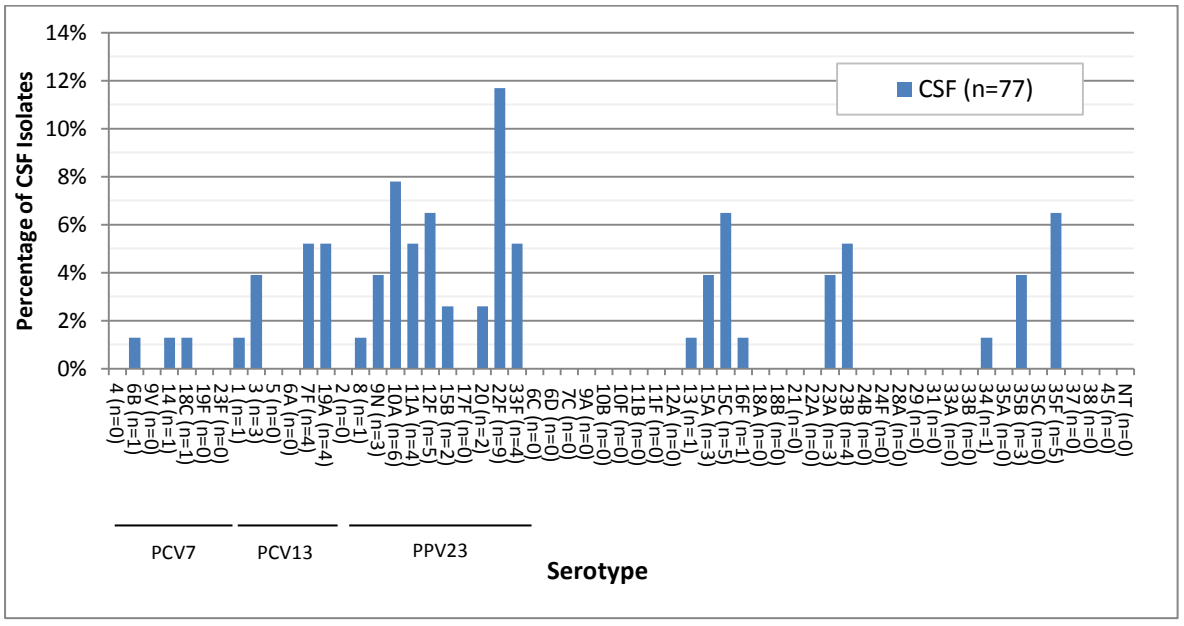


Figure 6. Distribution of invasive *S. pneumoniae* serotypes from pleural fluid, 2013

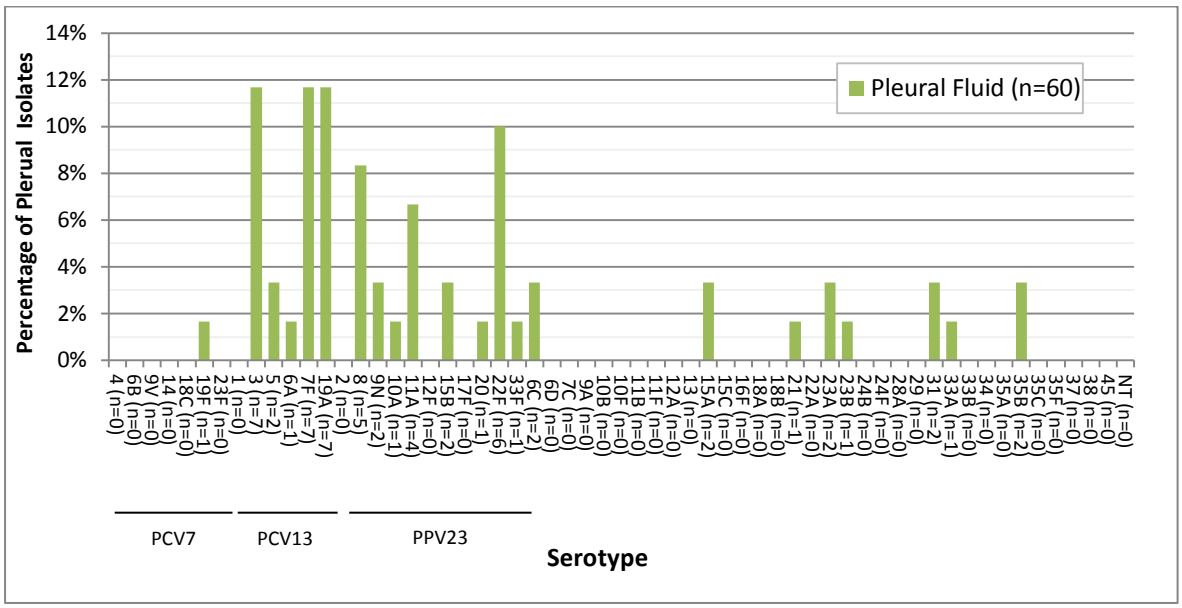
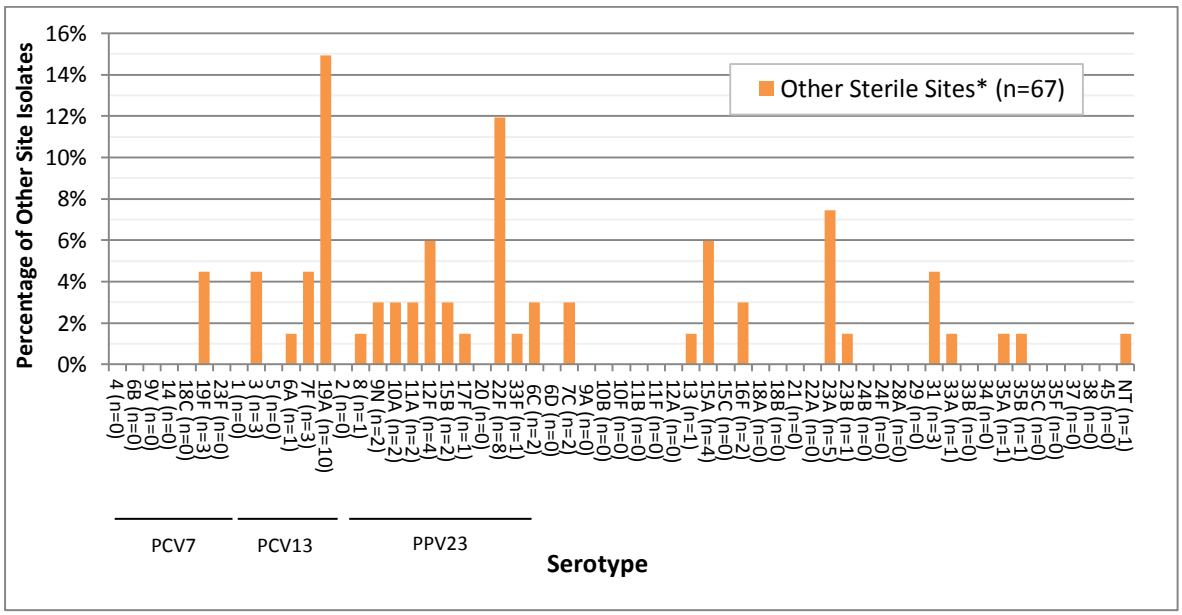
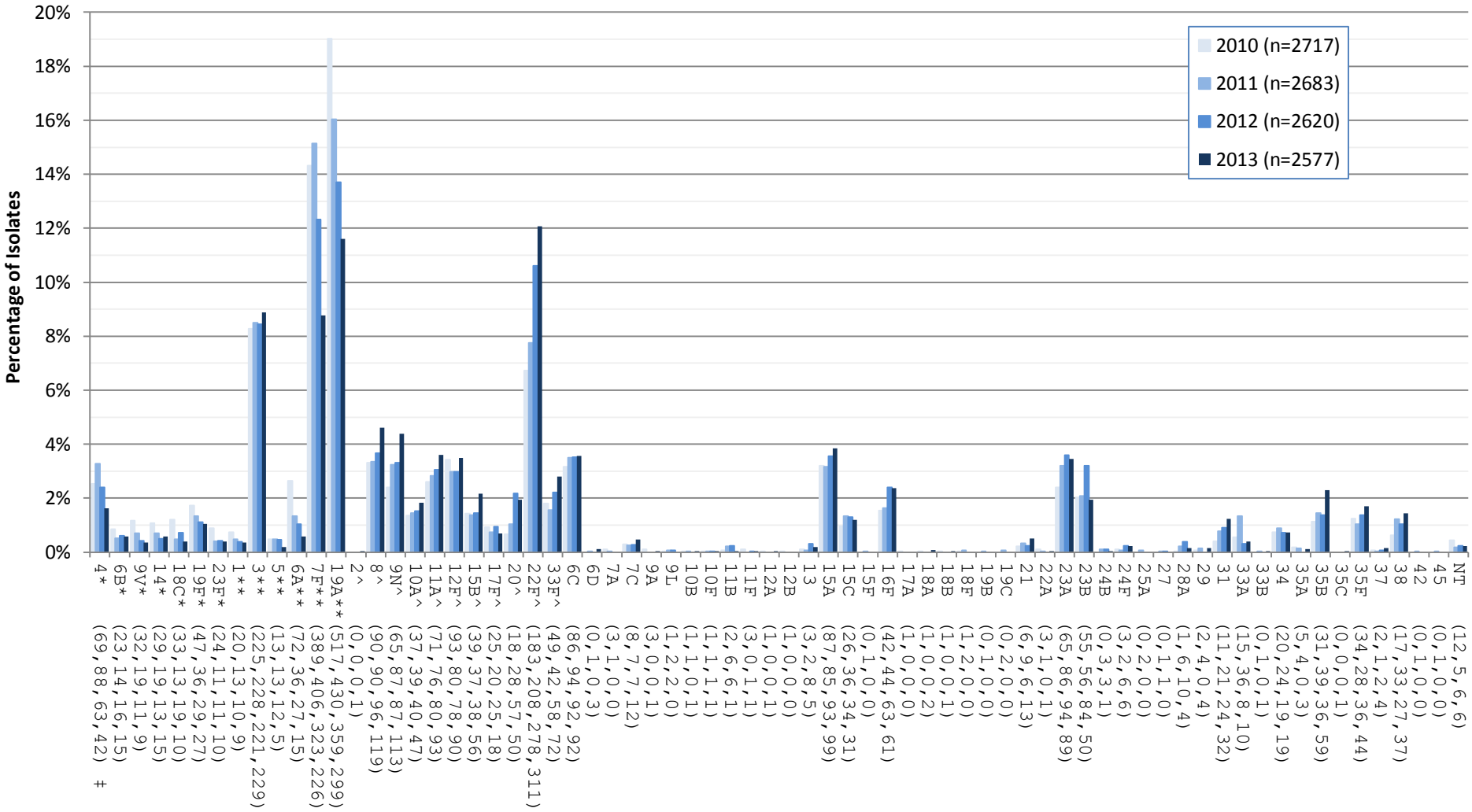


Figure 7. Distribution of invasive *S. pneumoniae* serotypes from other sterile sites, 2013



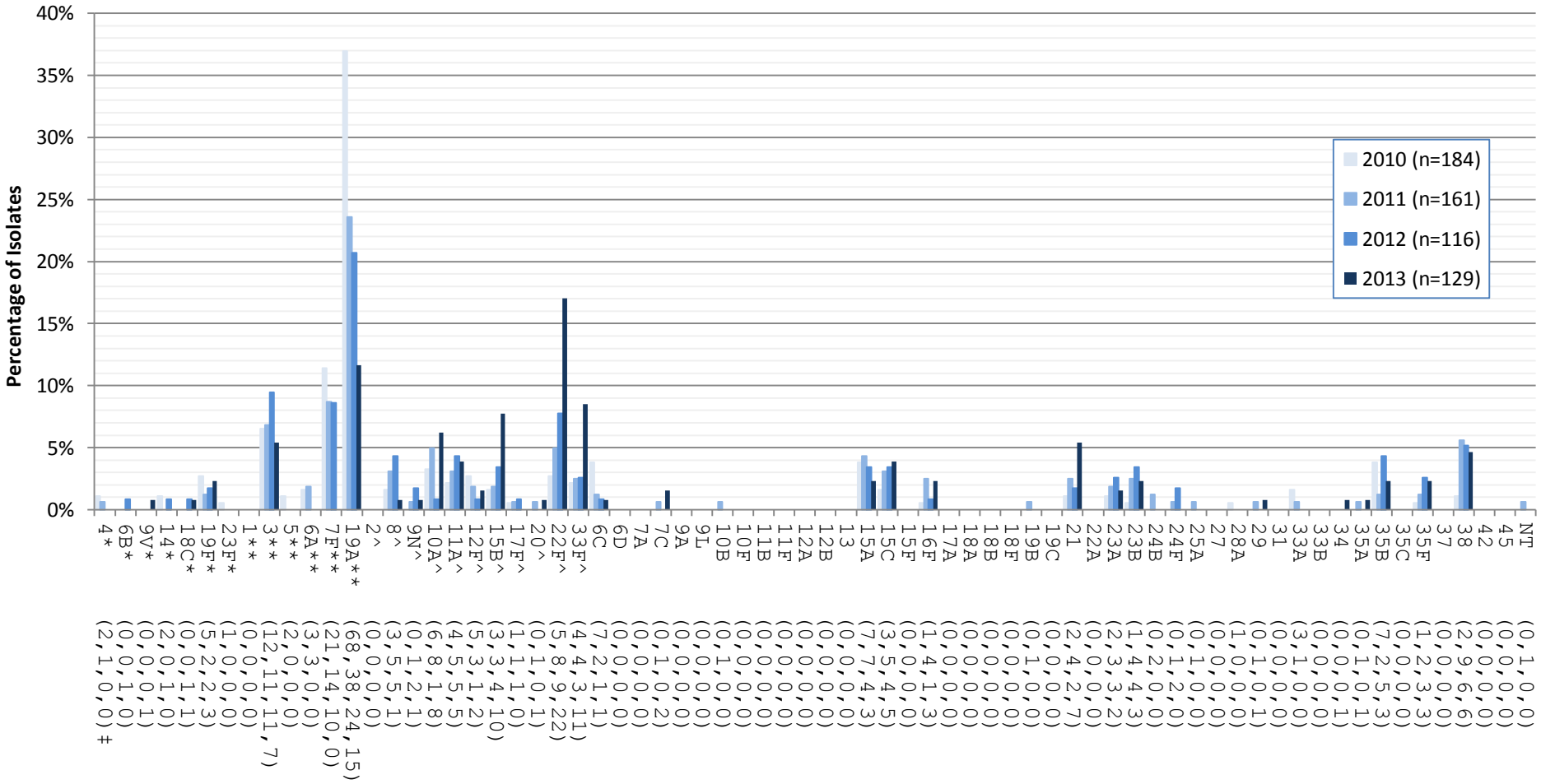
*Other Sterile Sites include: 4 pericardial fluid, 10 peritoneal fluid, 21 synovial fluid and 32 from sites such as deep tissue, biopsy and surgical samples.

Figure 8. Invasive *S. pneumoniae* serotypes in all combined age groups, 2010 – 2013



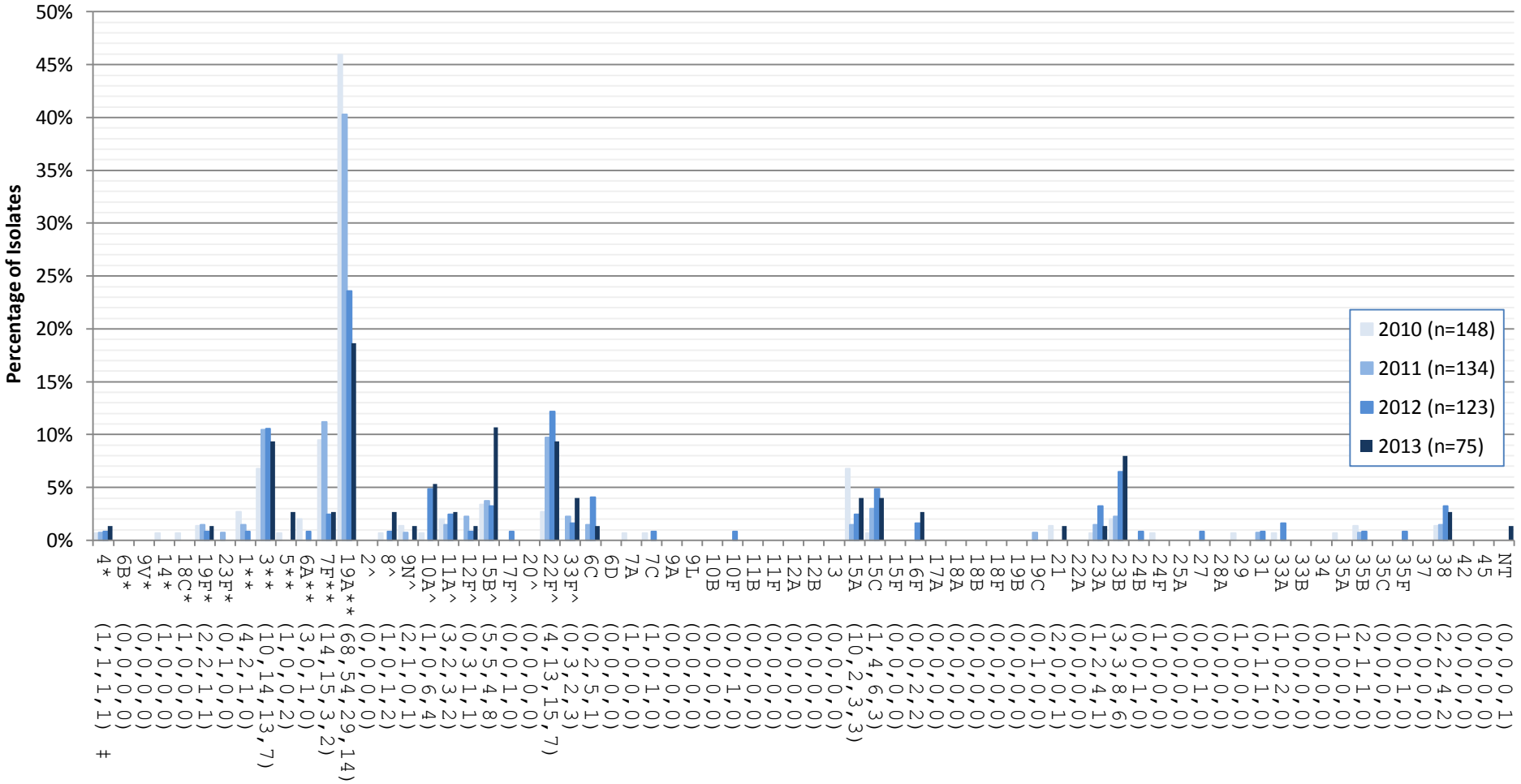
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 9. Invasive *S. pneumoniae* serotypes in < 2 year olds, 2010 – 2013



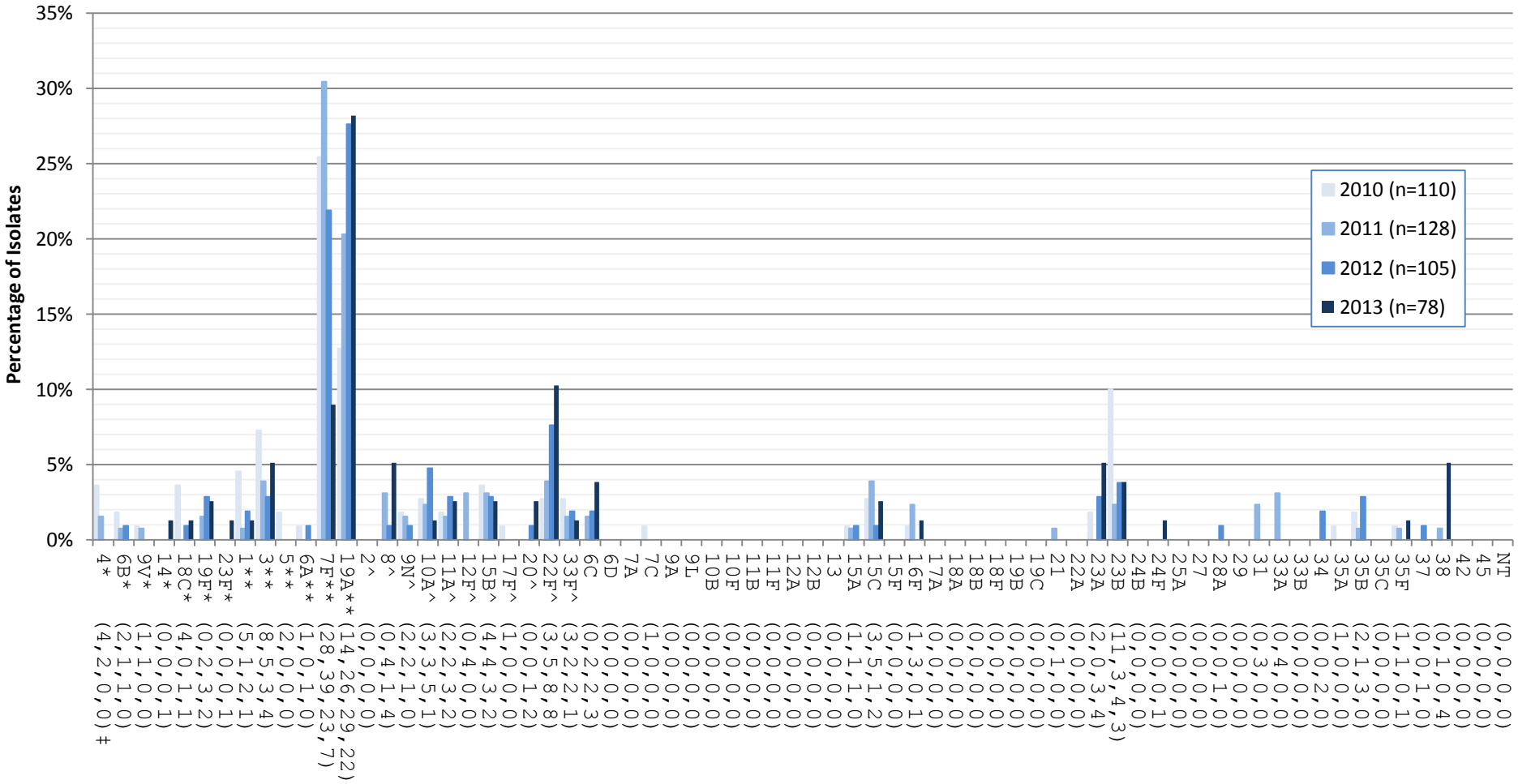
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 10. Invasive *S. pneumoniae* serotypes in 2 – 4 year olds, 2010 – 2013



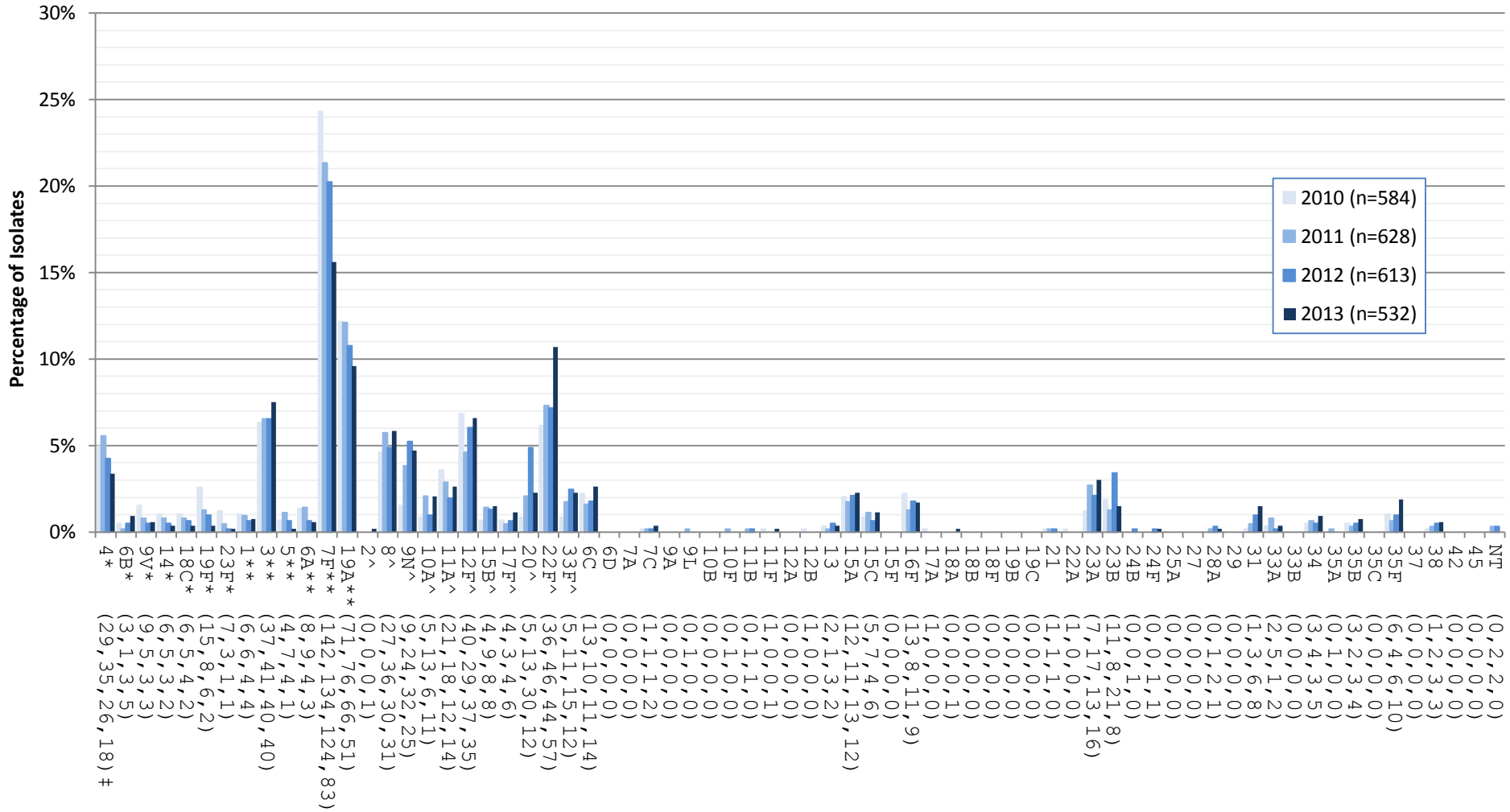
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 11. Invasive *S. pneumoniae* serotypes in 5 - 14 year olds, 2010 - 2013



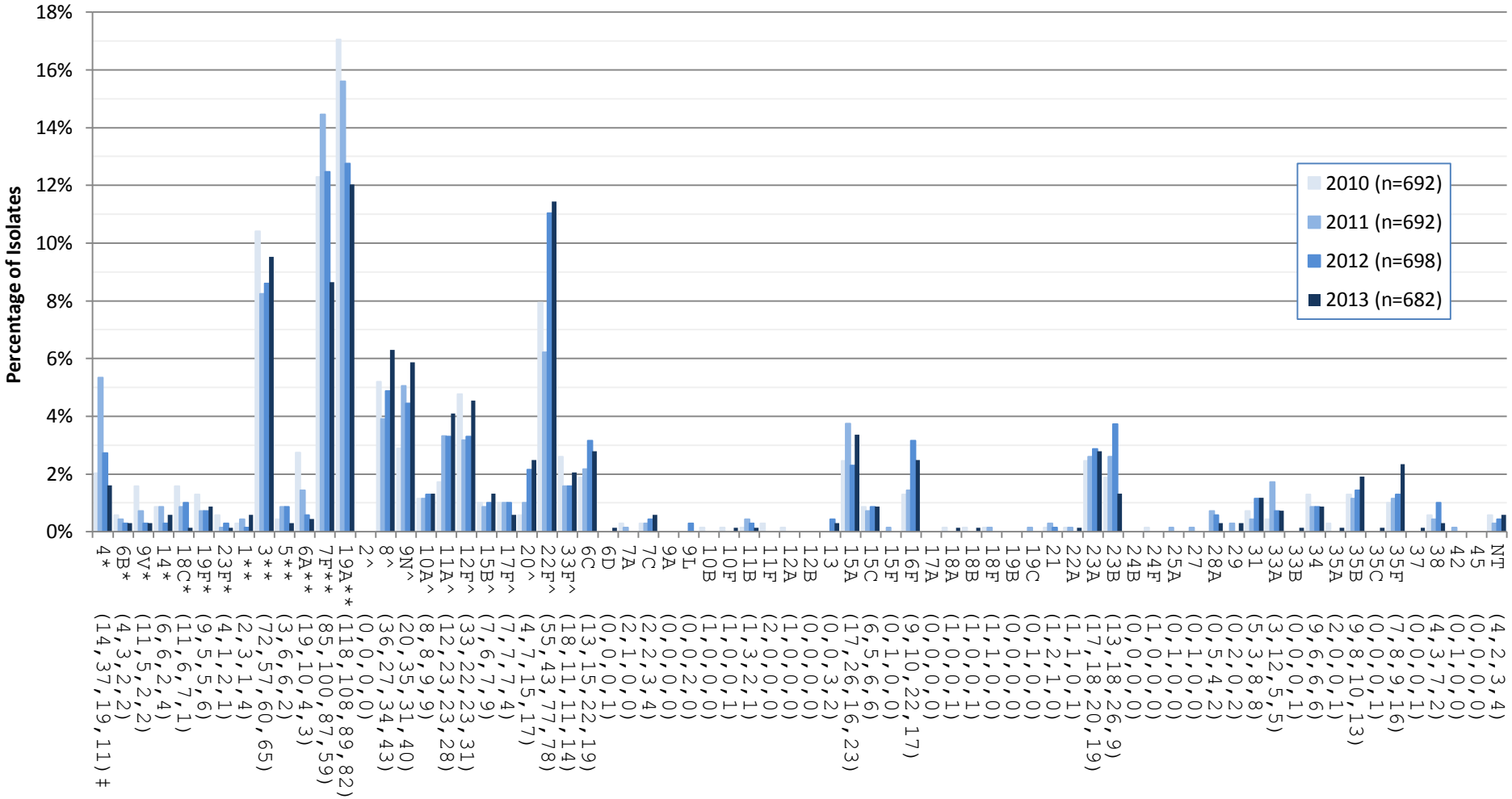
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 12. Invasive *S. pneumoniae* serotypes in 15 – 49 year olds, 2010 - 2013



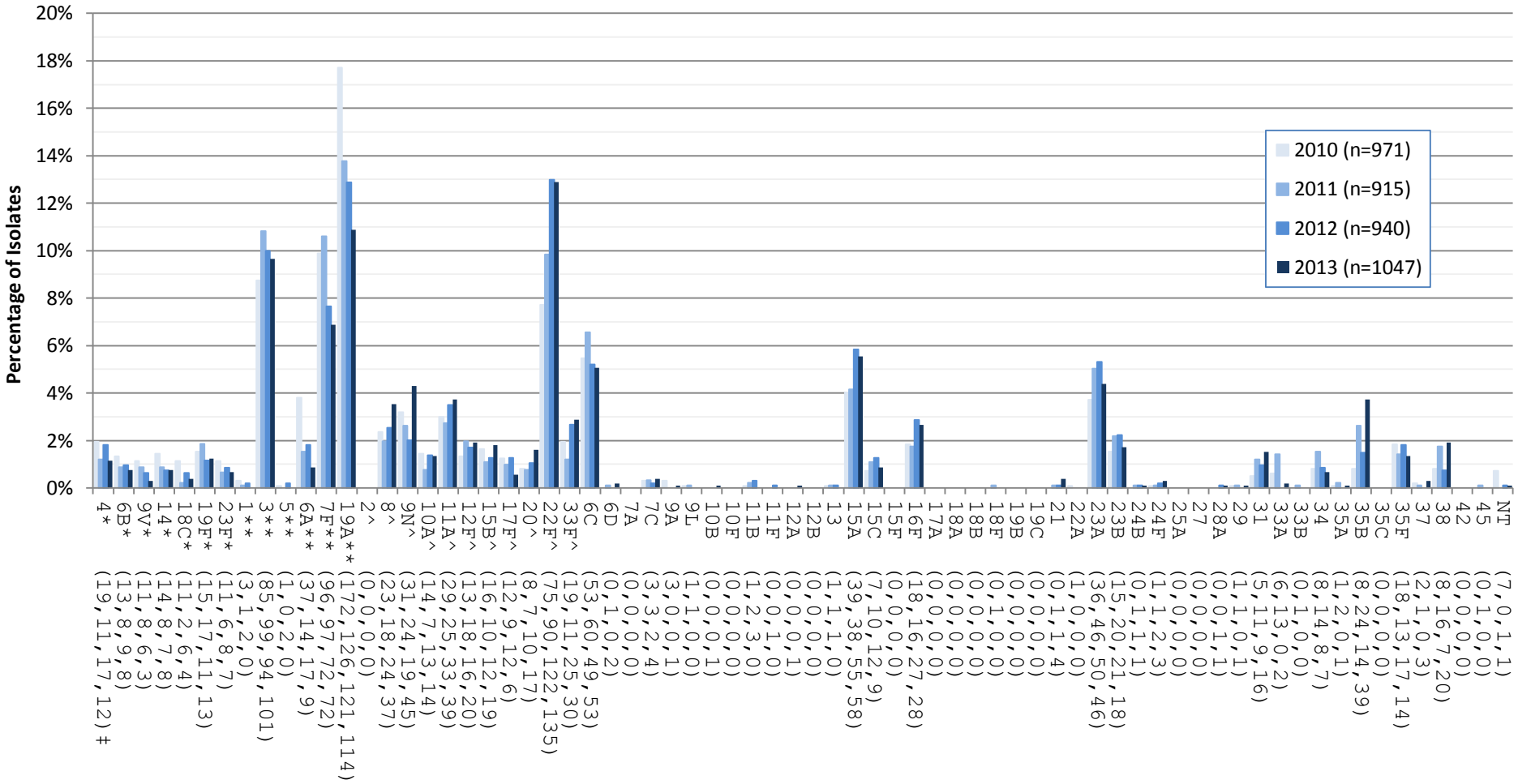
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 13. Invasive *S. pneumoniae* serotypes in 50 – 64 year olds, 2010 - 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively

Figure 14. Invasive *S. pneumoniae* serotypes in ≥ 65 year olds, 2010 - 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively

Figure 15. Serotype 19A by age

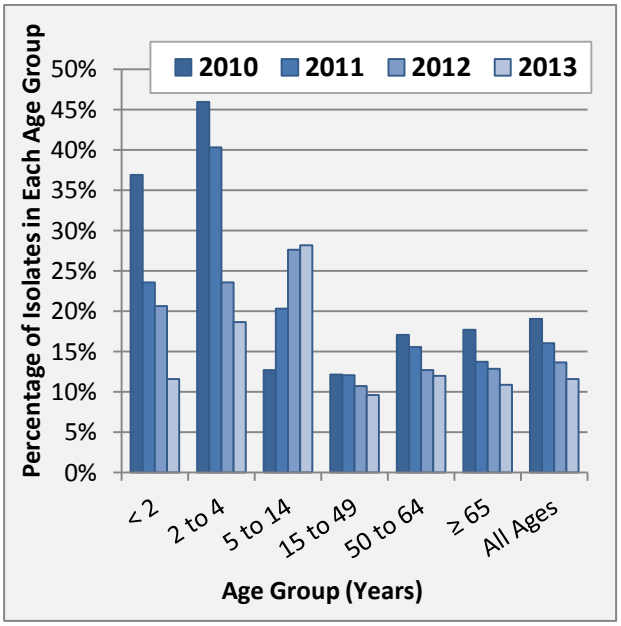


Figure 16. Serotype 7F by age

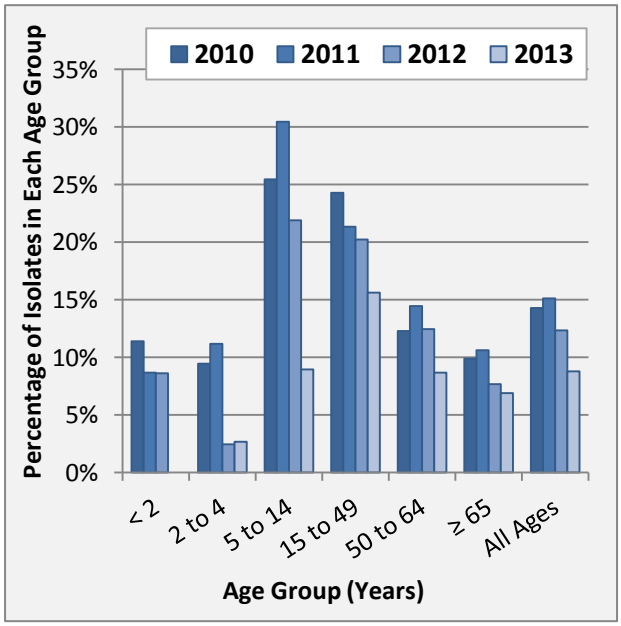


Figure 17. Serotype 3 by age

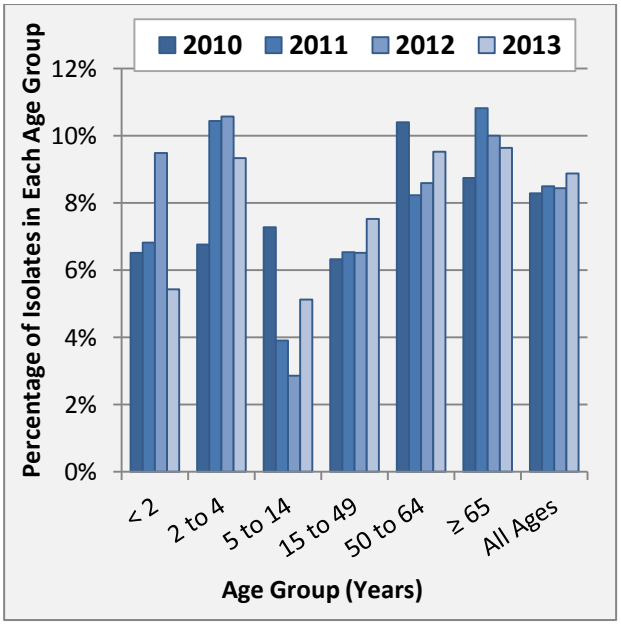
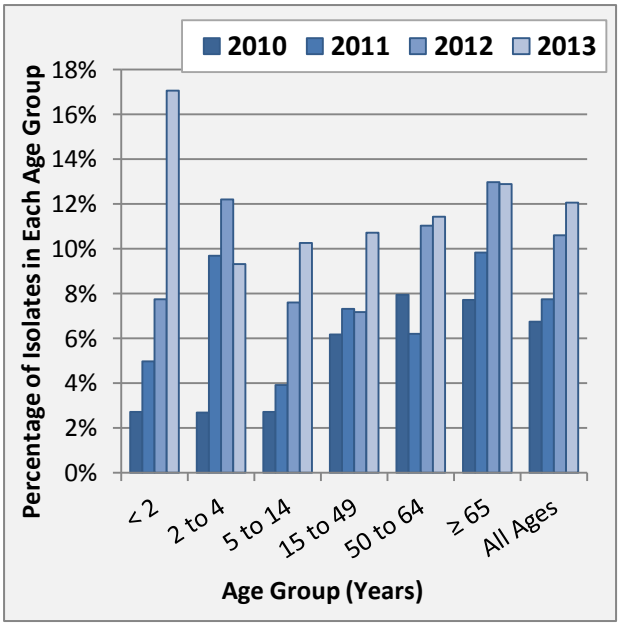


Figure 18. Serotype 22F by age



Regional Distribution of *S. pneumoniae* Serotypes

Serotype 19A was the most prevalent serotype in Western and Central regions in 2013 representing 8.2% (n=77) and 13.6% (n=197), whereas in Eastern regions 7F was most predominant with 15.4% (n=28). Serotype 7F was also prominent in Central Canada with 8.4% (n=122), but only represented 8.1% (n=76) of the Western isolates. Serotype 22F was evenly distributed among the regions with 11.5% (n=108), 12.8% (n=186), and 9.3% (n=17) of the Western, Central and Eastern regional totals, respectively. Serotype 3 was also relatively evenly distributed through the regions representing 8.7% (n=82) of Western, 9.0% (n=131) of Central, and 8.8% (n=16) of Eastern (Figure 19) Canadian isolates.

Among isolates from children <2 years of age (Figure 20), serotype 19A represented a higher proportion of Central region isolates (15.2%, n=12) than of Western isolates (4.4%, n=2). In Western Canada, serotype 33F represented a relatively high proportion of isolates in this age group (13.3%, n=6).

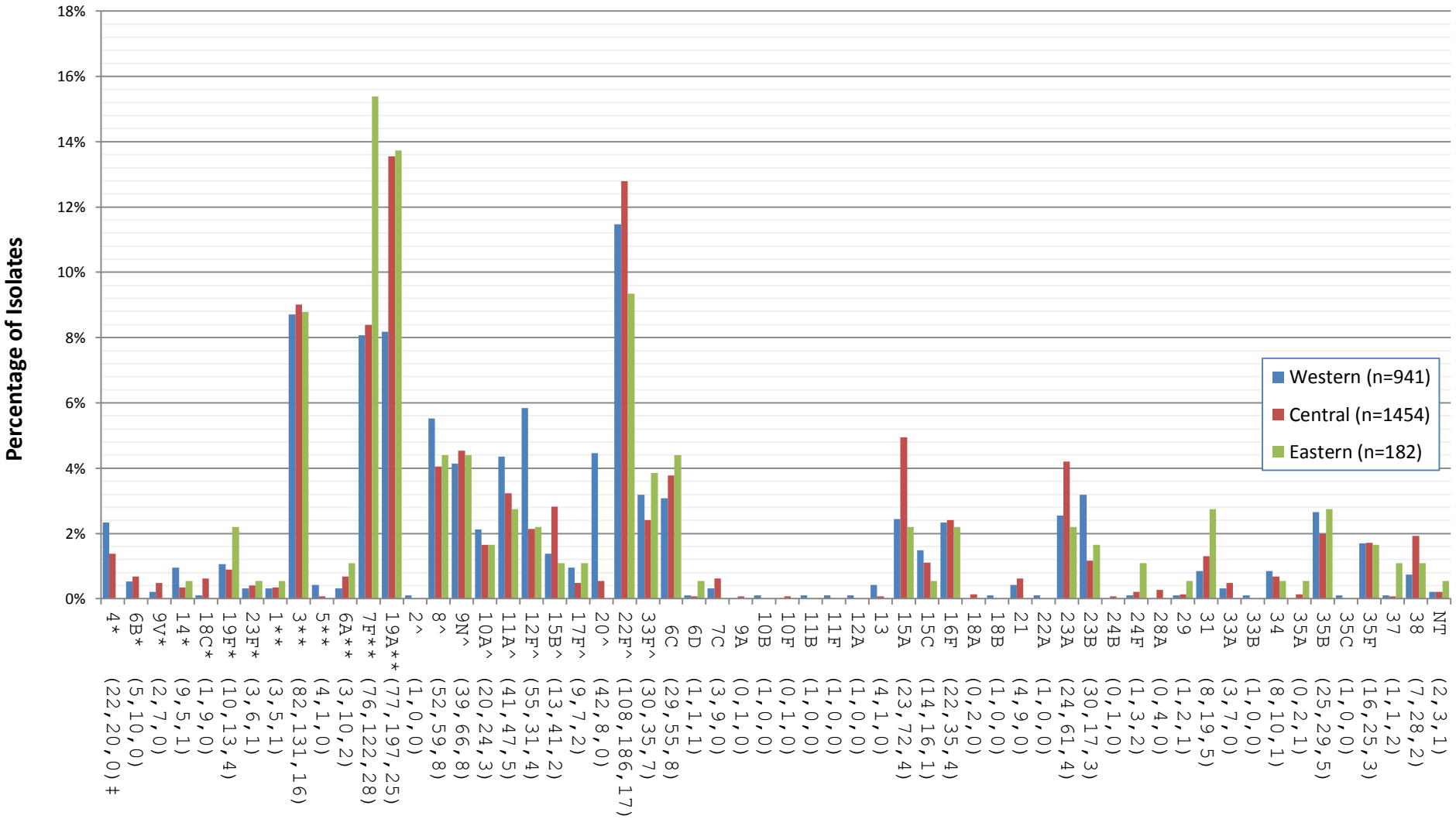
Among isolates from the 2 – 4 year old age group (Figure 21) serotype 19A is prominent in Central regions representing 22.0% (n=9) of the isolates. In the West serotypes 23B (13.8%, n=4), 33F (10.3%, n=3) and 15A (6.9%, n=2) are more prevalent than in other regions.

Serotypes of isolates from the 5 – 14 (Figure 22) and 15 – 49 (Figure 23) year old age groups were relatively evenly distributed regionally with slightly higher proportions of serotypes 3, 19A and 22F in Central Canada and in Western regions serotypes 8, 9N, 12F and 20 were slightly elevated.

In the 50 – 64 year old age group (Figure 24), serotype 19A and 7F were present in lower proportions in Western Canada (7.4%, n=18 and 6.2%, n=15; respectively) than in Central (14.9%, n=59 and 9.3%, n=37; respectively) and Eastern (11.4%, n=5 and 15.9%, n=7; respectively) regions. Serotype 3 was present at similar levels in Western (10.7%, n=26) and Central Canada (9.3%, n=37), and lower levels were seen in the East (4.6%, n=2). Similarly, 22F was evenly distributed in Western (12.0%, n=29) and Central regions (11.9%, n=47), and in lower proportions in Eastern Canada (4.6%, n=2). Other serotypes with greater relative prevalence include serotypes 12F, 20 and 23B in Western (7.4%, n=18; 6.2% n=15; and 2.5%, n=6; respectively); 15A and 23A in Central (4.8%, n=19; 3.5%, n=14; respectively); and 8, 33F, and 6C in Eastern regions (13.6%, n=6; 6.8%, n=3; and 6.8%, n=3; respectively).

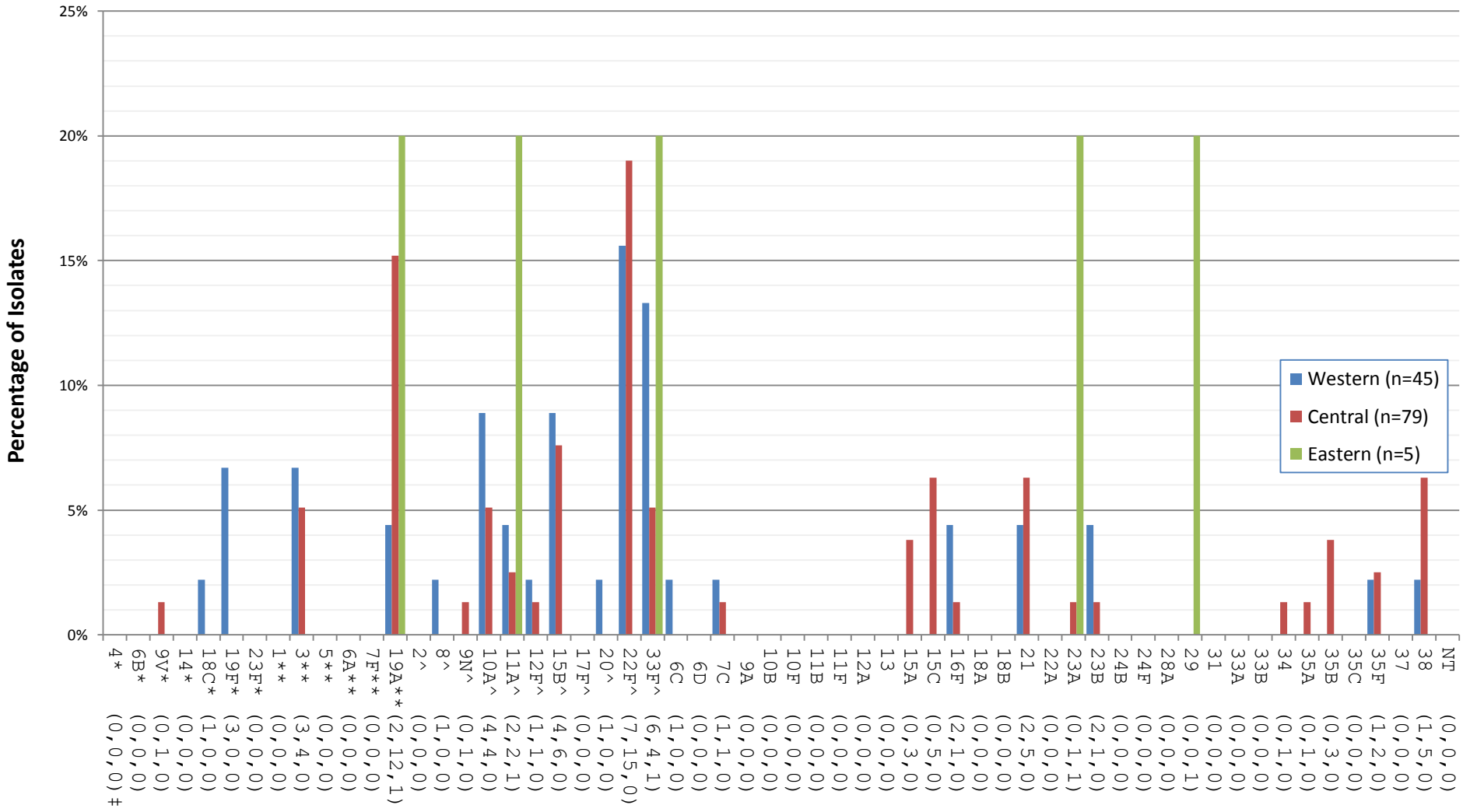
The regional distribution of serotypes in the senior age group of ≥ 65 years of age (Figure 25) reflects that of the 50 – 64 year olds. Serotypes 19A and 7F are lower in the West (8.4%, n=27; 5.9%, n=19; respectively) than in the East (14.8%, n=13; 11.6%, n=74; respectively) and Central Canada (11.6%, n=74; 7.1%, n=45; respectively). Serotypes 3 and 22F were evenly distributed across Canada in this age group at about 10% and 13%, respectively. Similar to the regional distribution of serotypes in the 50 – 64 year old age group, the West had elevated proportions of serotypes 12F, 20 and 23B (4.7%, n=15; 4.0%, n=13; and 3.1%, n=10; respectively); and in Central Canada proportions of 15A and 23A (6.9%, n=44; 5.2%, n=33; respectively) were elevated with respect to other regions.

Figure 19. Regional distribution of invasive *S. pneumoniae* serotypes in all combined age groups, 2013



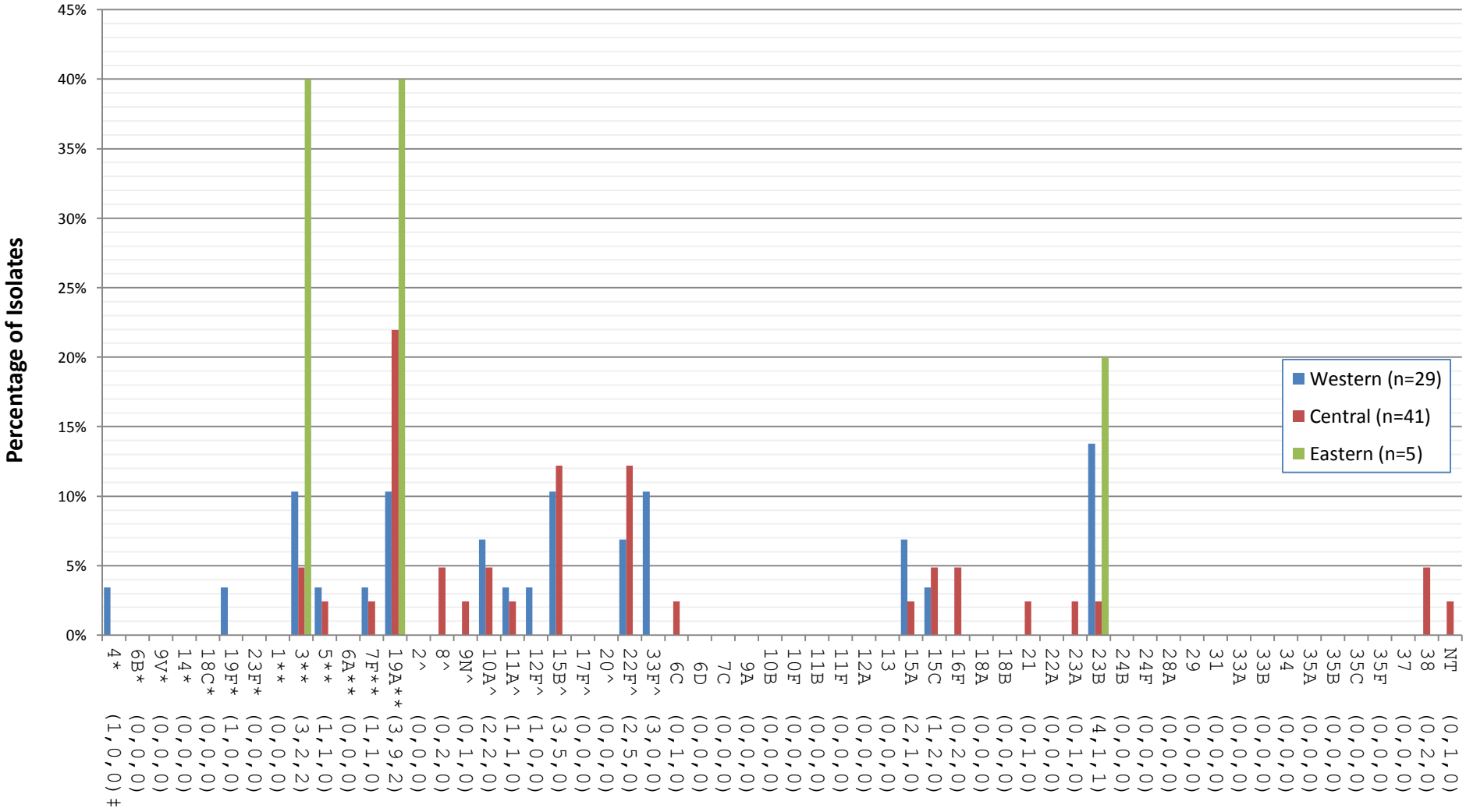
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 20. Regional distribution of invasive *S. pneumoniae* serotypes in <2 year olds, 2013



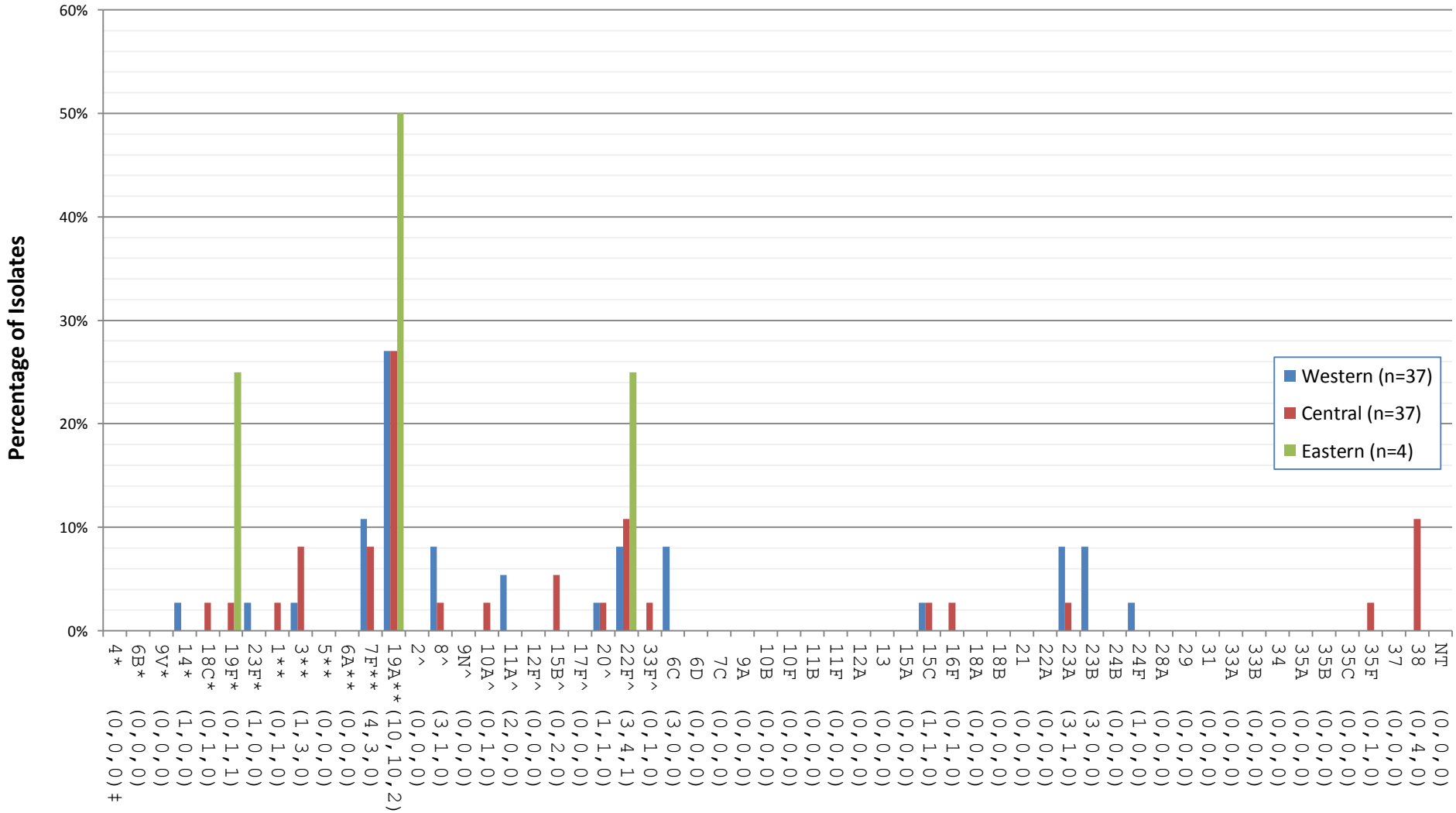
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 21. Regional distribution of invasive *S. pneumoniae* serotypes in 2 – 4 year olds, 2013



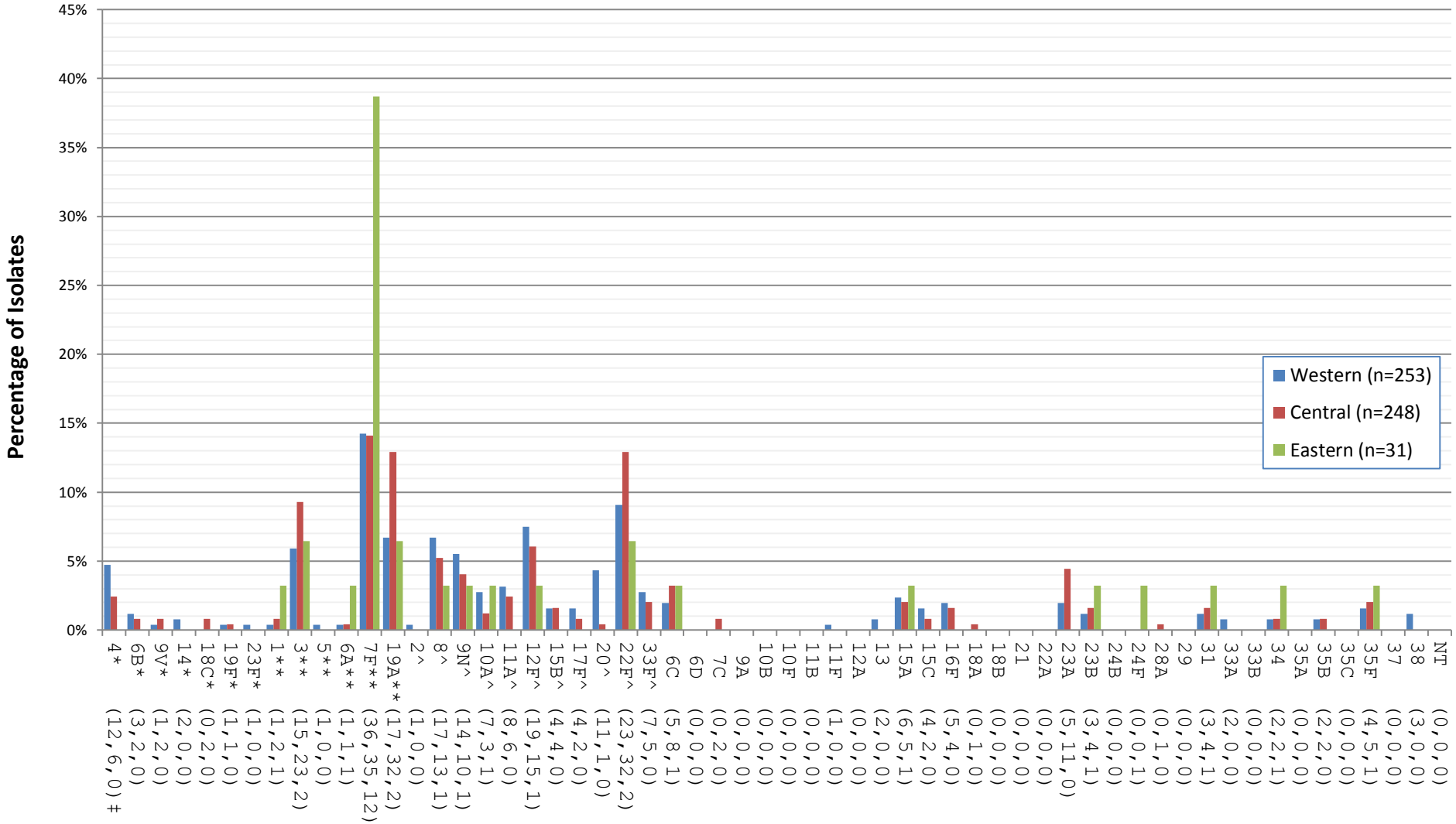
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 22. Regional distribution of invasive *S. pneumoniae* serotypes in 5 – 14 year olds, 2013



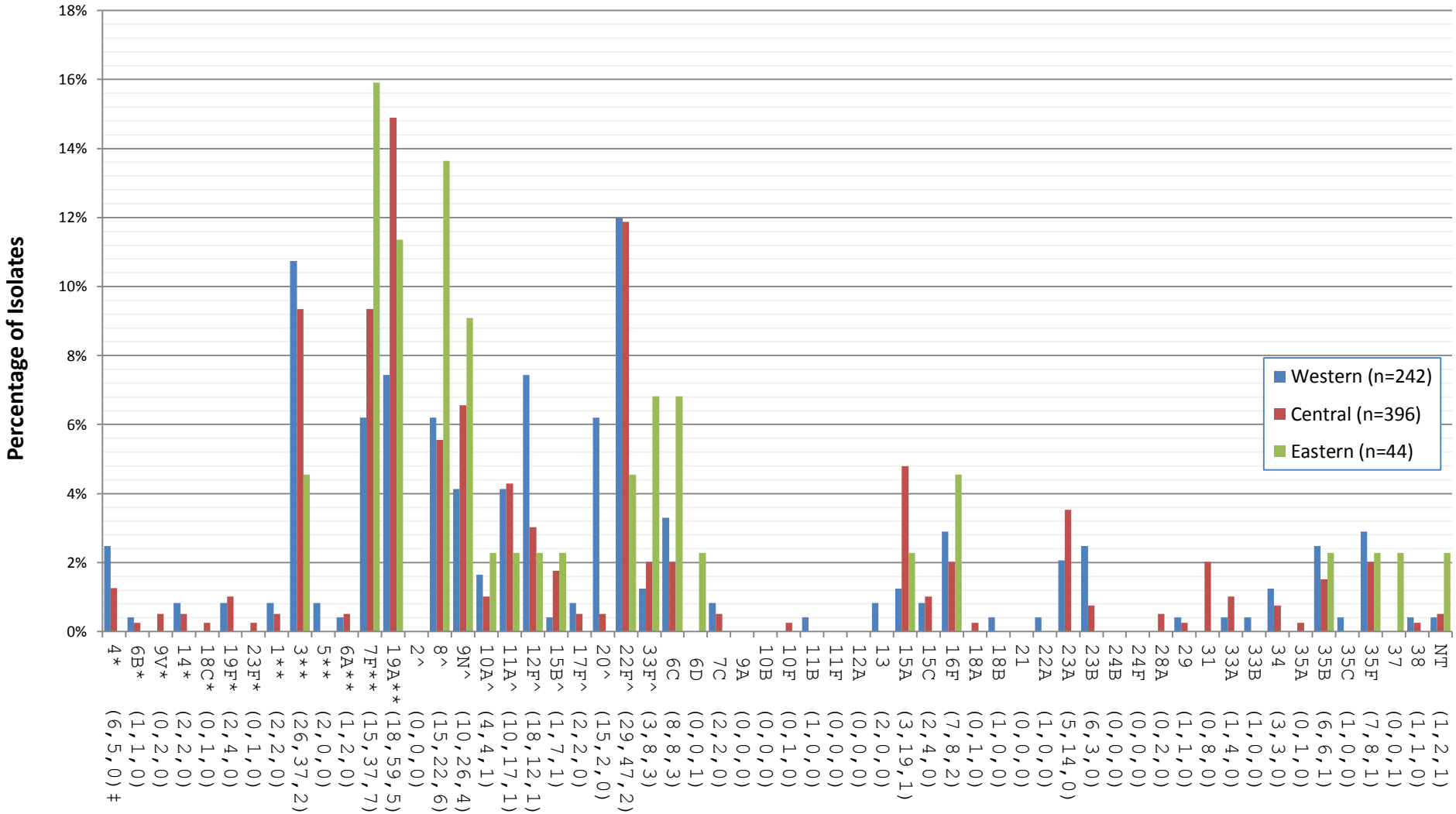
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 23. Regional distribution of invasive *S. pneumoniae* serotypes in 15 – 49 year olds, 2013



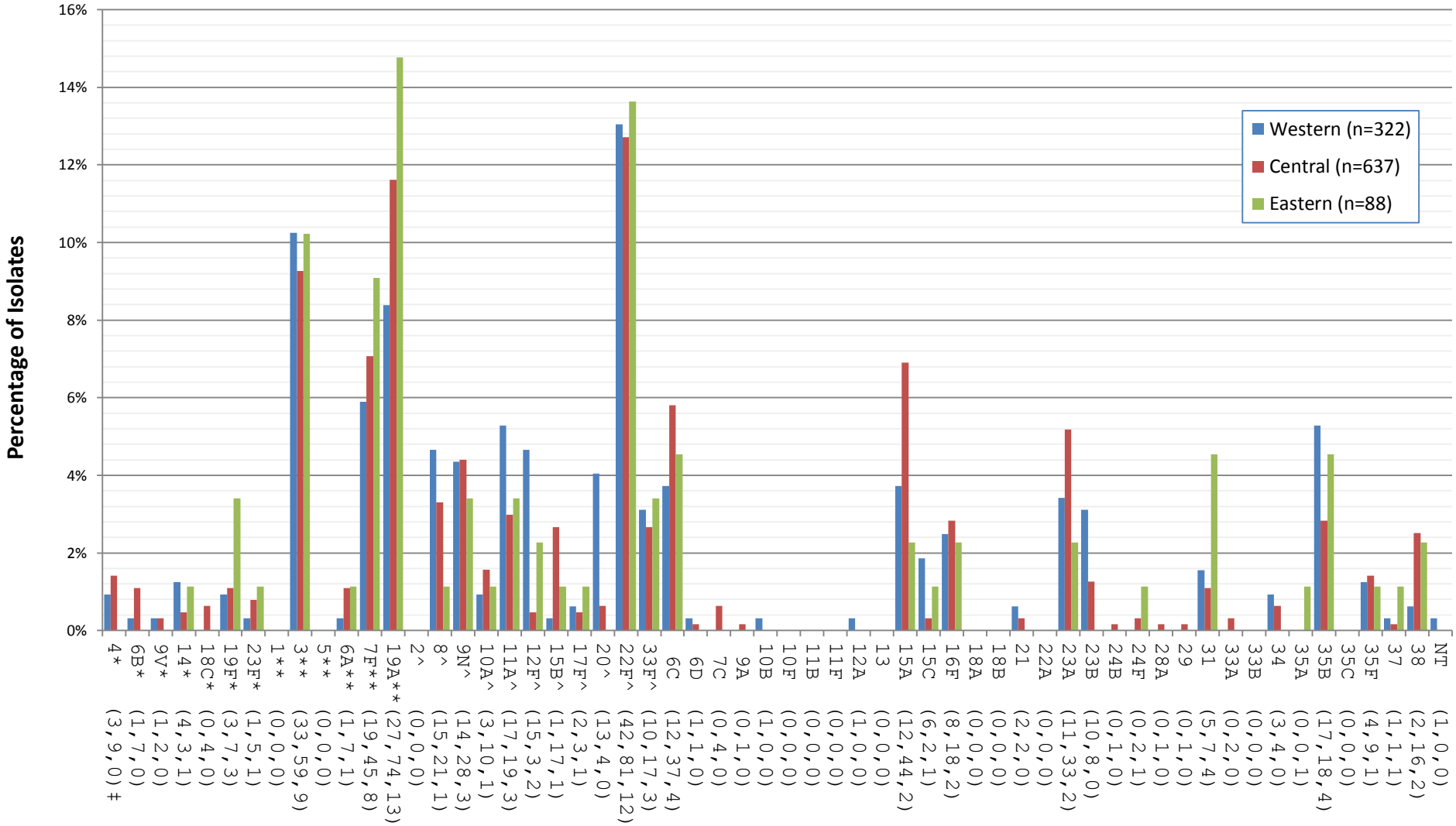
*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 24. Regional distribution of invasive *S. pneumoniae* serotypes in 50 – 64 year olds, 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 25. Regional distribution of invasive *S. pneumoniae* serotypes in ≥65 year olds, 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for Western, Central and Eastern regions, respectively.

Figure 26. Serotype 19A by region

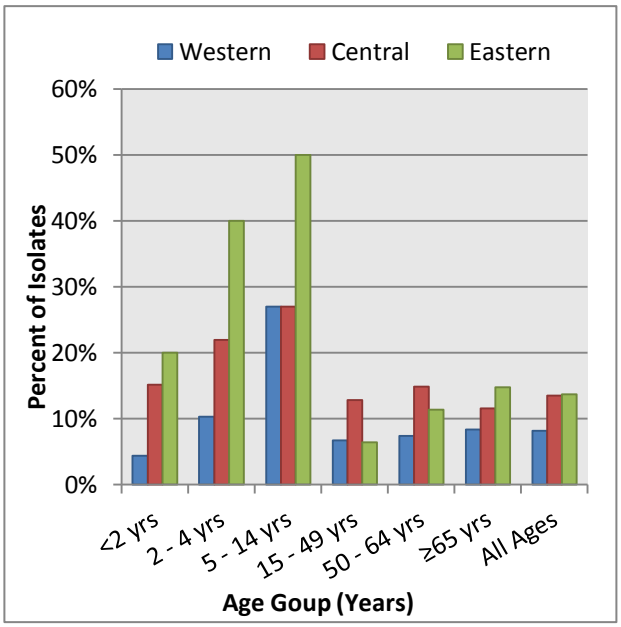


Figure 27. Serotype 7F by region

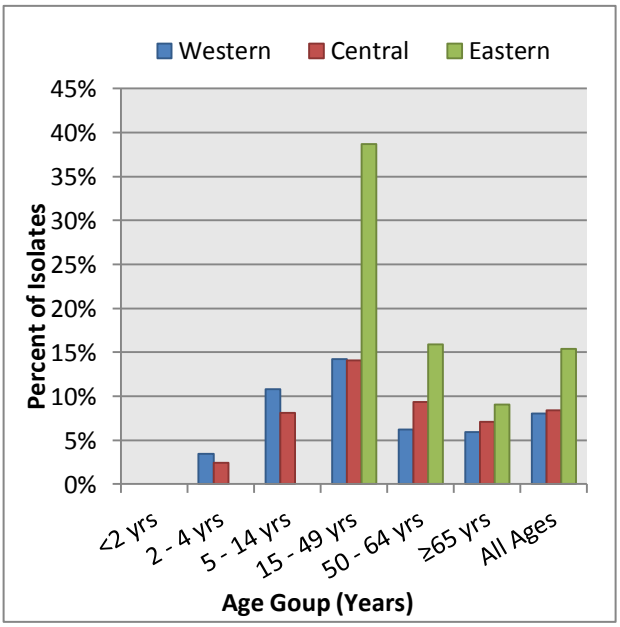


Figure 28. Serotype 3 by region

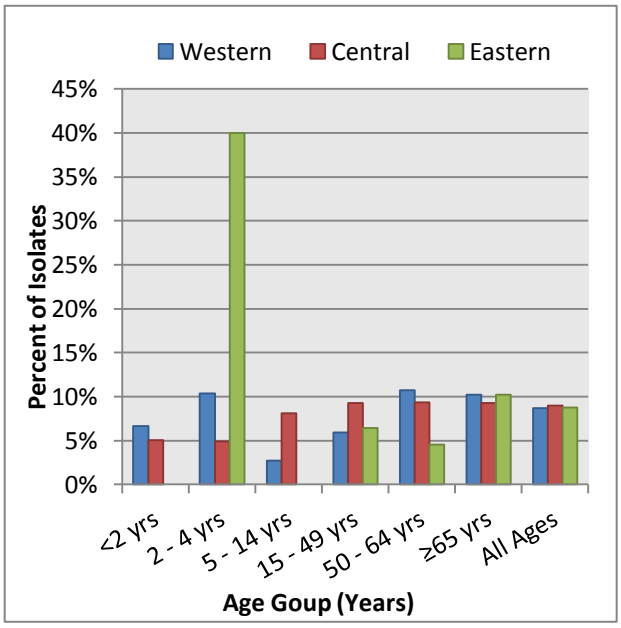
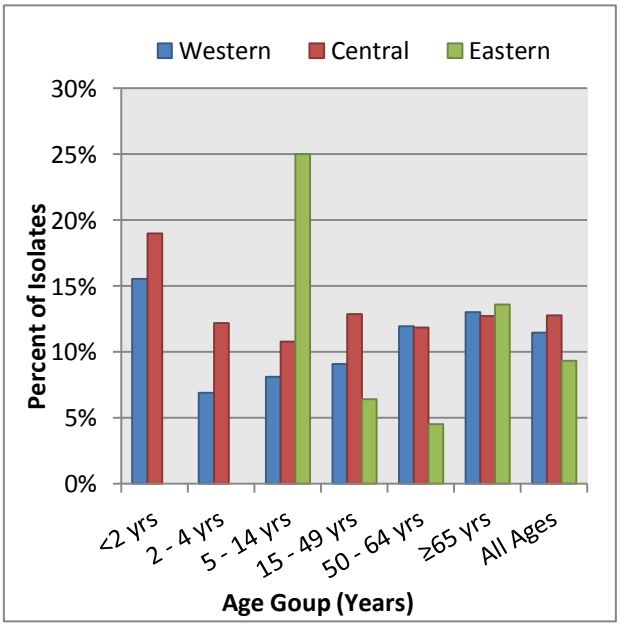


Figure 29. Serotype 22F by region



Vaccine Serotypes

Total numbers of PCV7 serotypes (4, 6B, 9V 14, 18C 19F, 23F) are very small in the <15 year old age groups, however the proportions have continued to decline in most age groups in 2013 except in children 2 - 4 years of age where proportions have increased from 1.6% (n=2) to 2.7% (n=2) from 2012 to 2013, and in the 5 – 14 year old age group with an increase from 4.8% (n=5) to 6.4% (n=5) (Figure 32).

The proportion of PCV13 serotypes (1, 3, 5, 6A, 7F and 19A) in Canada has continued to decrease in all combined age groups from 36.3% (n=952) in 2012 to 30.4% (n=783) in 2013 (Figure 31). The Eastern regions had the highest proportion of PCV13 serotypes in 2013 with 39.6% (n=72), a small decrease from 42.1% (n=75) in 2012 (Figure 30). Decreases of the PCV13 serotypes have been seen in all age groups between 2012 and 2013, which is generally due to the reduction in proportions of serotypes 7F and 19A. PCV13 serotypes represented 17.1% (n=22) of isolates in <2 year olds, 33.3% (n=27) in 2 – 4 year olds, 43.6% (n=34) of 5 – 14 year olds, 34.2% (n=182) of 15 – 49 year olds, 31.5% (n=215) of 50 – 64 year olds, and 28.3% (n=296) in those ≥65 years of age in 2013 (Figure 33).

The overall PCV7+PCV13 serotypes declined from 42.5% (n=1114) in 2012 to 35.4% (n=911) in 2013 (Figure 31). In 2013, total overall PCV7+PCV13 serotypes represented for 42.9% (n=78) of Eastern, 36.9% (n=536) of Central and 31.6% (n=297) of Western isolates. The PCV7+PCV13 serotypes in the Central and Western regions declined from 40.5% (n=586) to 32.1% (n=466); and from 29.3% (n=291) to 26.0% (n=245), respectively (Figure 30).

The proportion of isolates representing PPV23 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F) have increased in all combined age group isolates from 24.7% (n=670) in 2010 to 37.6% (n=970) in 2013 (Figure 31). The largest increase in 2013 has been observed in the <2 year old age group which increased from 26.7% (n=31) in 2012 to 47.3% (n=61) in 2013. From 2012 to 2013, the, PPV23 serotypes 2 – 4 year old age group increased from 26.8% (n=33) to 37.3% (n=28); in the 5 – 14 year old age group decreased from 2.9% (n=24) to 2.1% (n=24)in the 15 - 49 year old age group from 35.6% (n=218) to 39.8% (n=212); in the 50 – 64 year old age group from 34.0% (n=237) to 40.0% (n=273); and in the ≥65 year old age group from 30.4% (n=286) to 36.6% (n=362), respectively (Figure 34).

Table 3. Vaccine serotypes 2013

	Age Group (N)						
Vaccine*	**<2**	**2-4**	**5-14**	**15-19**	**50-64**	**≥65**	**All Ages****
PCV7	3.9% (5)	2.7% (2)	6.4% (5)	6.2% (33)	4% (27)	5.3% (55)	**5% (128)**
PCV13	17.1% (22)	33.3% (25)	43.6% (34)	34.2% (182)	31.5% (215)	28.3% (296)	**30.4% (783)**
PCV13 All	20.9% (27)	36% (27)	50% (39)	40.4% (215)	35.5% (242)	33.5% (351)	**35.4% (911)**
PPV23	47.3% (61)	37.3% (28)	25.6% (20)	39.8% (212)	40% (273)	34.6% (362)	**37.6% (970)**
PPV23 All	68.2% (88)	73.3% (55)	75.6% (59)	79.7% (424)	75.1% (512)	67.2% (704)	**70.6% (24)**
NVT Total	31.8% (41)	26.7% (20)	24.4% (19)	19.7% (105)	24.5% (167)	31.9% (334)	**27% (696)**
All	**(129)**	**(75)**	**(78)**	**(532)**	**(682)**	**(1047)**	**(2577)**

*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. *** Percentage of isolates (number of isolates).

Figure 30. Vaccine serotypes by region, 2013

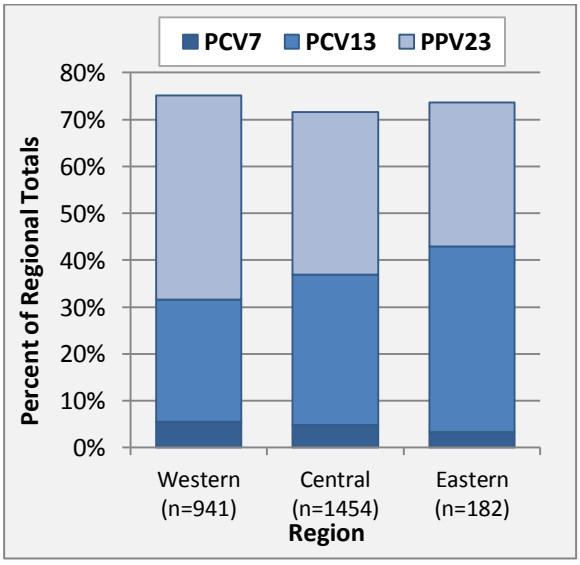


Figure 31. Vaccine serotypes 2010 - 2013

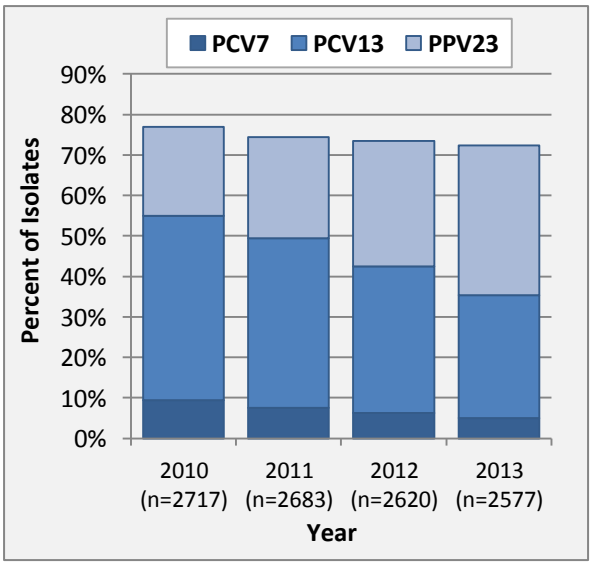


Figure 32. PCV7 serotypes (4, 6B, 9V, 14, 18C, 19F, 23F) by age group, 2010 – 2013

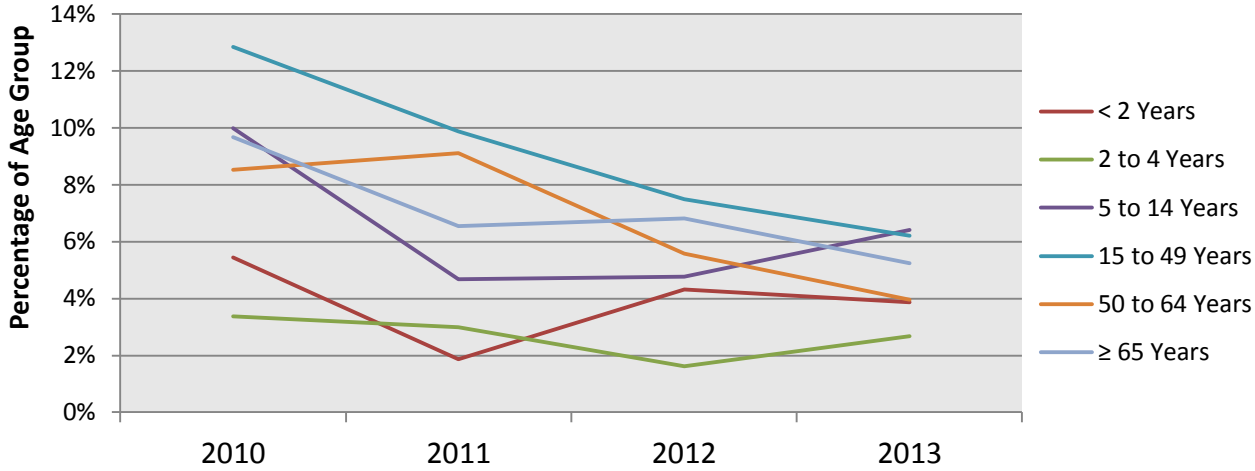


Table 4. Number of PCV7 serotype isolates

Age Group (Years)	Year			
	2010	2011	2012	2013
<2	10	3	5	5
2 - 4	5	4	2	2
5 - 14	11	6	5	5
15 - 49	75	62	46	33
50 - 64	59	63	39	27
≥65	94	60	64	55

Figure 33. PCV13 serotypes (1, 5, 7F, 3, 6A, 19A) by age group, 2010 – 2013

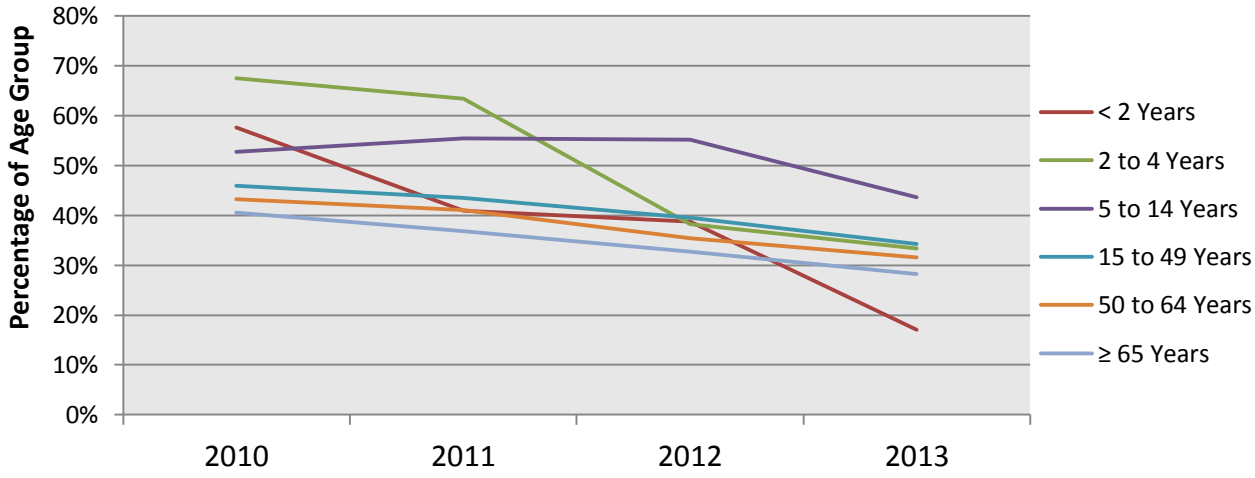


Table 5. Number of PCV13 isolates

Age Group (Years)	Year			
	2010	2011	2012	2013
<2	106	66	45	22
2 - 4	100	85	47	25
5 - 14	58	71	58	34
15 - 49	268	273	242	182
50 - 64	299	284	247	215
≥65	394	337	308	296

Figure 34. PPV23 serotypes (2, 8, 9N, 10A, 11A, 12F, 15B, 17F, 20, 22F, 33F) by age group, 2010 – 2013

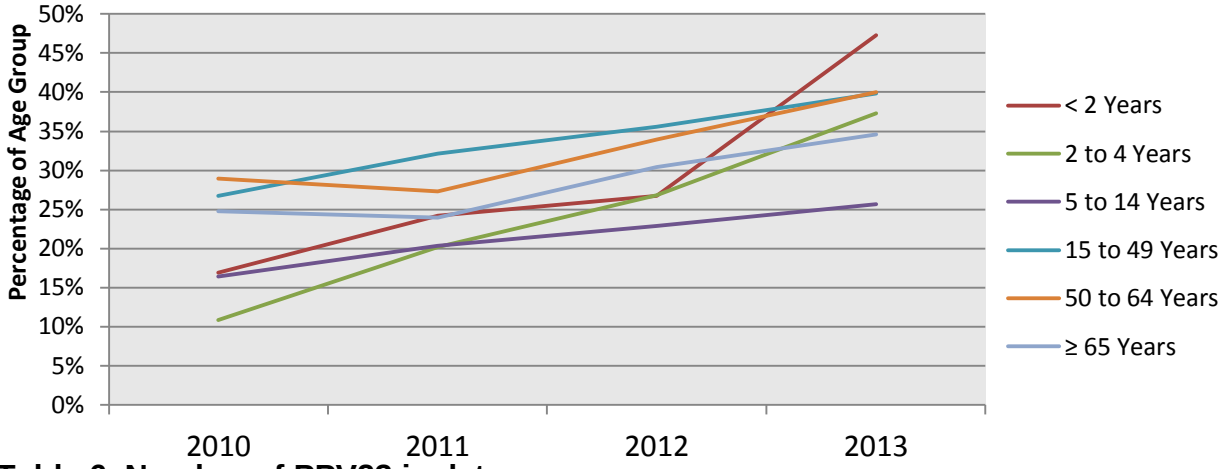


Table 6. Number of PPV23 isolates

Age Group (Years)	Year			
	2010	2011	2012	2013
<2	31	39	31	61
2 - 4	16	27	33	28
5 - 14	18	26	24	20
15 - 49	156	202	218	212
50 - 64	200	189	237	273
≥65	240	219	286	362

Figure 35. Non-vaccine serotypes by age group, 2010 – 2013

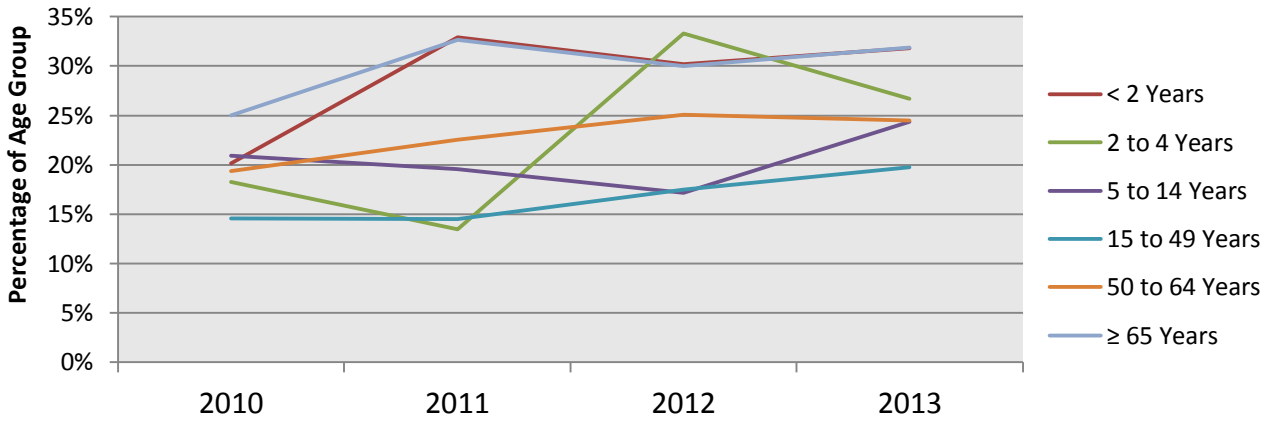


Table 7. Number of NVT isolates

Age Group (Years)	Year			
	2010	2011	2012	2013
<2	37	53	35	41
2 - 4	27	18	41	20
5 - 14	23	25	18	19
15 - 49	85	91	107	105
50 - 64	134	156	175	167
≥65	243	299	282	334

Antimicrobial Resistance of *S. pneumoniae*

As part of a joint NML/CARA program called SAVE, antimicrobial susceptibility testing was performed on 1061 *S. pneumoniae* isolates from 2013 from any age group causing IPD submitted from 8 participating jurisdictions (Saskatchewan, Manitoba, Ontario, Quebec, Nova Scotia, Prince Edward Island, New Brunswick, Newfoundland and Labrador).

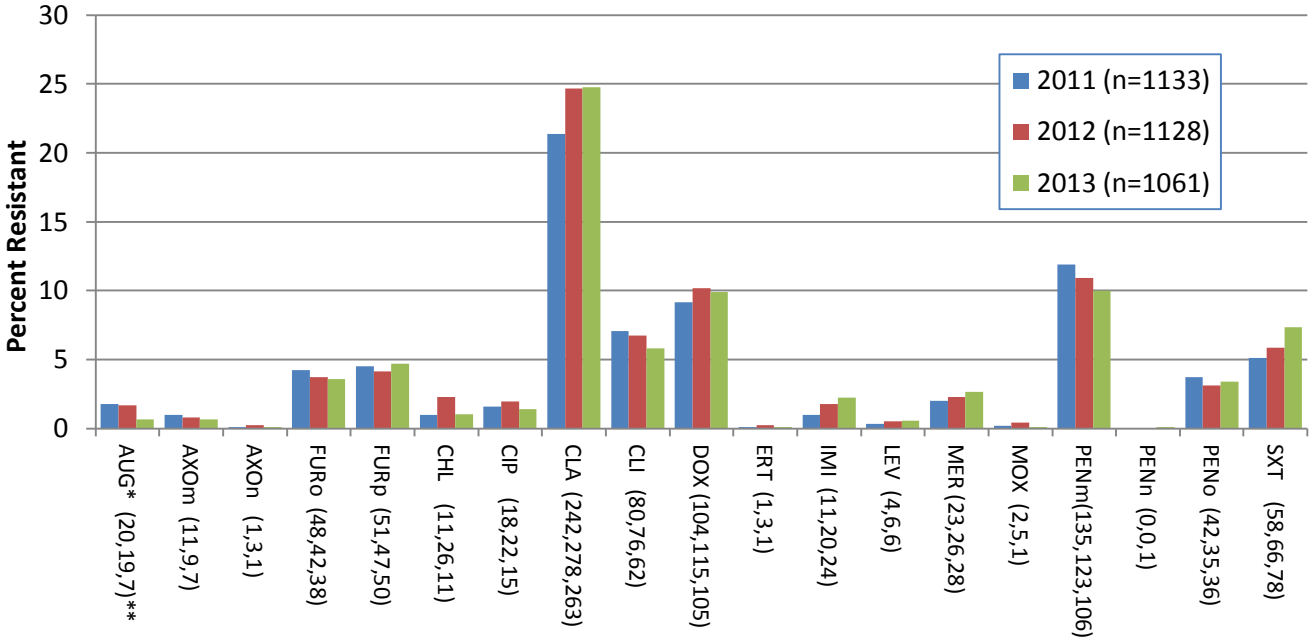
High rates of resistance were observed to clarithromycin in 2013 (24.8%, n=263), increasing slightly from 2011 levels (21.4%, n=242). Lower resistance rates were seen with penicillin using meningitis breakpoints declining from 11.9% (n=135) in 2011 to 10.0% (n=106) in 2013. Resistance to clindamycin has also declined since 2011 from 7.1% (n=80) to 5.9% (n=62) in 2013. Resistance to doxycycline has remained relatively stable since 2010, at 9.9% (n=105) in 2013, whereas trimethoprim/sulfamethoxazole resistant *S. pneumoniae* has increased from 5.1% (n=58) to 7.4% (n=78) over the same time period. There were also small increases observed in imipenem and meropenem resistance between 2011 and 2013 from 1.0% (n=11) to 2.3% (n=24); and from 2.0% (n=23) to 2.6% (n=28); respectively. No non-susceptibility to linezolid, tigecycline, or vancomycin was found (Figure 36). Regional comparison of the rates of *S. pneumoniae* antimicrobial resistance during 2013 indicate marginally higher rates of resistance in Western Canada to clarithromycin (29.8%, n=73), penicillin with meningitis breakpoints (11.0%, n=27) and trimethoprim/sulfamethoxazole (9.4%, n=23); whereas resistance to clindamycin and doxycycline was more prevalent in Central regions (6.5%, n=44; 11.5%, n=78; respectively) (Figure 37).

Serotype 15A isolates generally had the highest rates of resistance during 2013 with 40.9% (n=9) resistant to penicillin using meningitis breakpoints, 77.3% (n=17) resistant to clarithromycin, 31.8% (n=7) resistant to clindamycin, and 72.7% (n=16) resistant to doxycycline (Table 8).

In 2013, clarithromycin resistance was associated with serotypes 19A (59.6%, n=68); 10A (22.6%, n=7); 12F (81.1%, n=43); 15A (77.3%, n=17); 22F (28.0%, n=33), and 33F (81.6%, n=40) (Figure 40). Cefuroxime parenteral resistant serotypes of *S. pneumoniae* were predominately 19A (26.3%, n=30) and 35B (21.4%, n=6); and higher levels of clindamycin resistance were seen in serotypes 19A (26.3%, n=30), 33F (16.3%, n=8) and 15A (31.8%, n=7). Doxycycline resistance serotypes included 19A (33.3%, n=38) and 15A (72.7%, n=16). Imipenem and meropenem resistance was mainly associated with serotype 19A isolates (20.2%, n=23; 21.1%, n=24; respectively). Relatively high rates of resistance to penicillin (meningitis) were evident in serotypes 6A (60.0%, n=3), 6C (33.3%, n=11), 15A (40.9%, n=9), 19A (28.9%, n=33), 23A (30.0%, n=9) and 23B (38.1%, n=8), and 35B (25.0%, n=7). Trimethoprim/sulfamethoxazole resistance was associated with serotypes 19A (27.2%, n=31) and 6C (21.2%, n=7) (Figure 47).

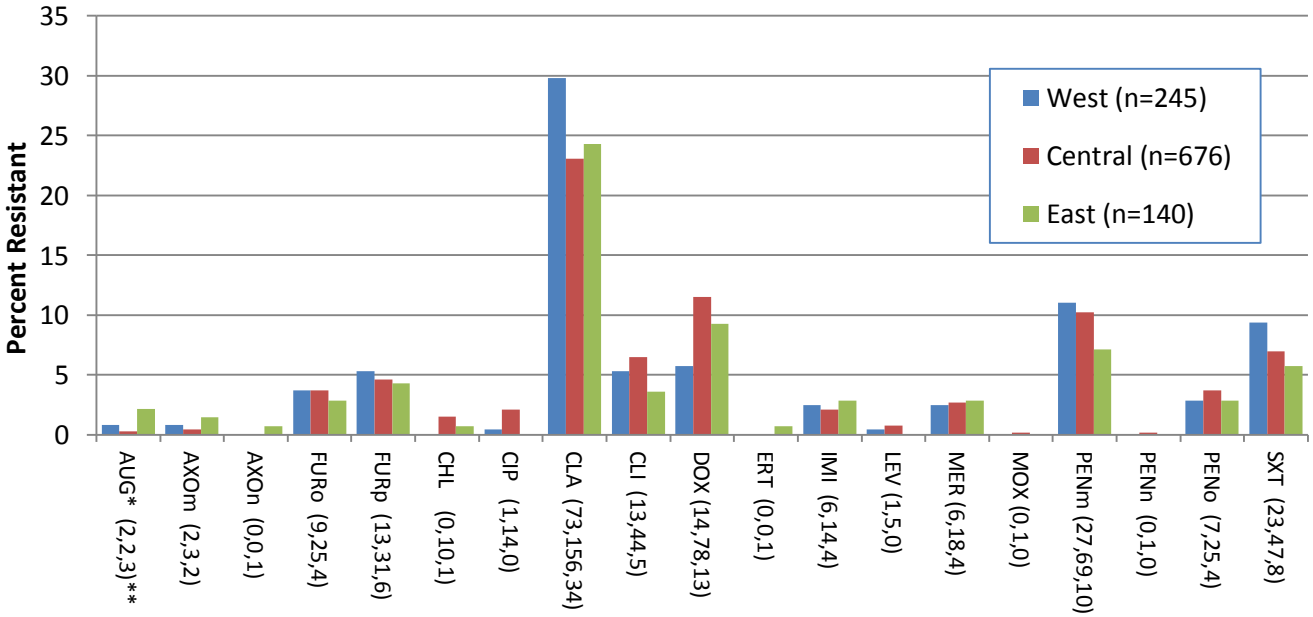
Multidrug resistance (MDR) to 3 or more classes of antimicrobials, was observed in 7.5% (n=80) of the *S. pneumoniae* tested in 2013, a slight decrease from 8.0% (n=91) observed in 2011 (Figure 38). Serotypes with the highest rates of MDR during 2013 were 15A (n=11) with 50.0% isolates resistant to 3 or more classes of antimicrobials (Figure 39) which is a decrease from 74.1% (n=20) in 2011; 19A with 28.9% (n=33), similar to 2011 levels at 29.1% (n=43); 6C with 24.2% (n=8), increasing from 8.7% (n=4) in 2011; and 19F with 23.1% (n=3), unchanged from 2011. The major MDR pattern among serotype 15A isolates was β-lactam-macrolide-clindamycin-tetracycline; for 19A and 19F β-lactam-macrolide-clindamycin-tetracycline-trimethoprim/ sulfamethoxazole; and for 6C β-lactam-macrolide- trimethoprim/sulfamethoxazole. Resistance to all 6 classes of antimicrobials was seen in 1 isolate of serotype 23F.

Figure 36. Antimicrobial resistance of *S. pneumoniae* isolates, 2011 - 2013



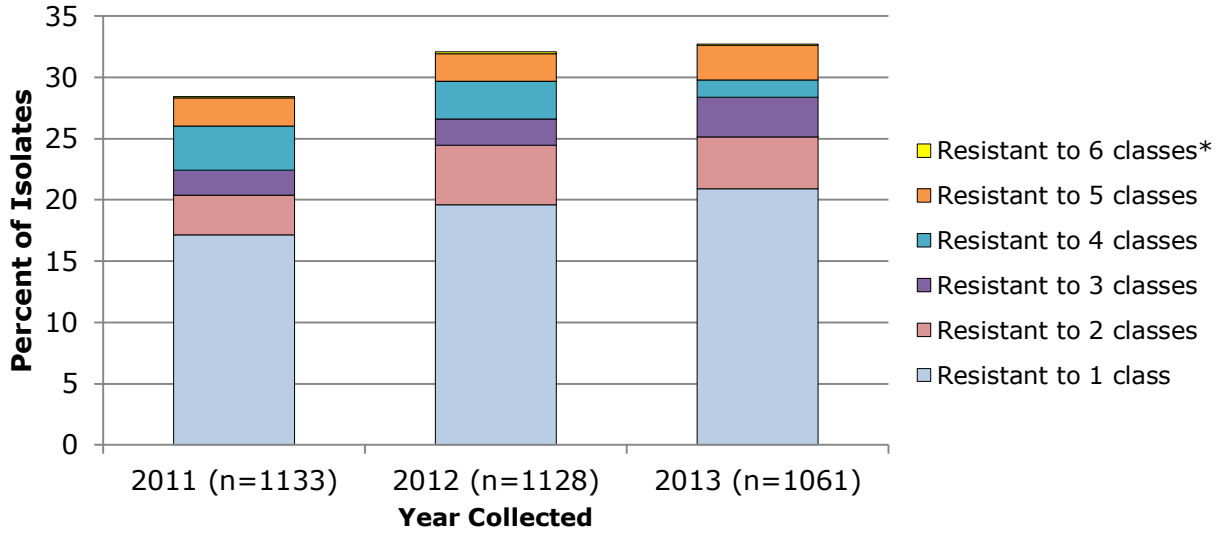
*AUG = amoxicillin/clavulanic acid; PENm = penicillin using the parenteral meningitis CLSI interpretive standard; ; PENn = penicillin using the parenteral non-meningitis interpretive standard; PENo = penicillin using the oral penicillin V interpretive standard; LEV = levofloxacin; MOX = moxifloxacin; AXOm = ceftriaxone using the parenteral meningitis interpretive standard; AXOn = ceftriaxone using the parenteral non-meningitis interpretative standard; FURo = cefuroxime using the oral interpretative standard; FURp = cefuroxime using the parenteral interpretative standard; ETP = ertapenem; IMI = imipenem; MER = meropenem; 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, 2012] interpretative breakpoints were used for DOX, all other according to CLSI[CLSI, 2011]. ** Number of isolates in 2011, 2012 and 2013, respectively.

Figure 37. Regional antimicrobial resistance of *S. pneumoniae,* 2013



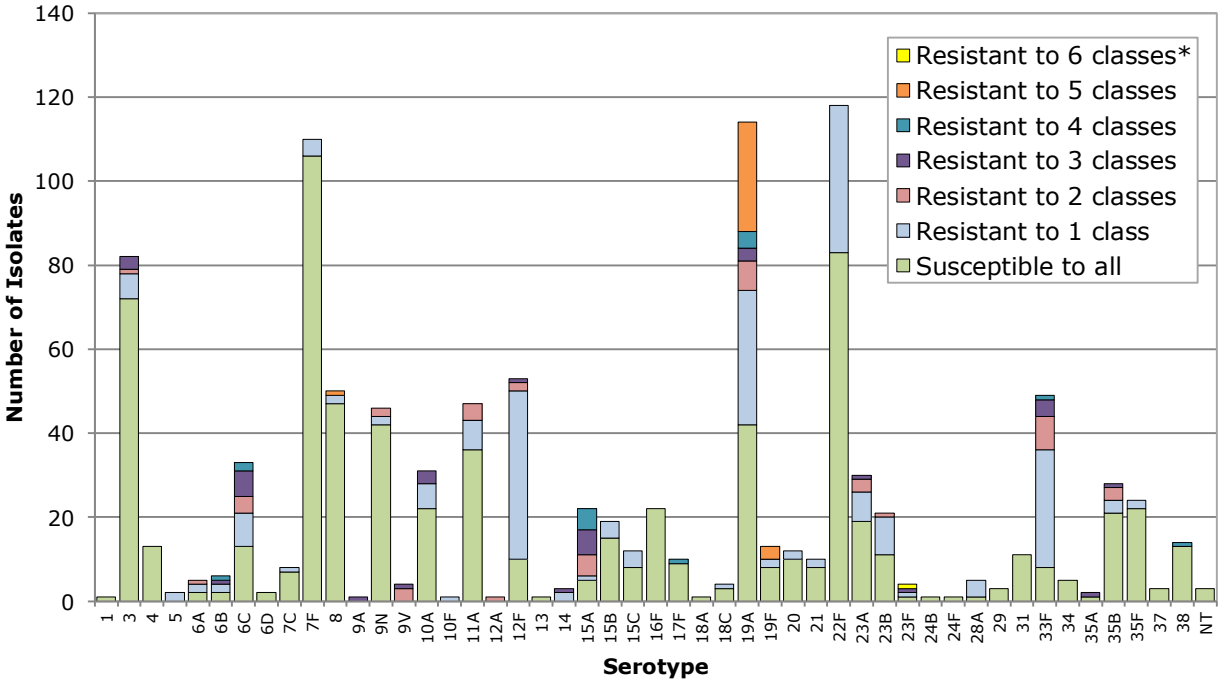
*AUG = amoxicillin/clavulanic acid; PENm = penicillin using the parenteral meningitis CLSI interpretive standard; ; PENn = penicillin using the parenteral non-meningitis interpretive standard; PENo = penicillin using the oral penicillin V interpretive standard; LEV = levofloxacin; MOX = moxifloxacin; AXOm = ceftriaxone using the parenteral meningitis interpretive standard; AXOn = ceftriaxone using the parenteral non-meningitis interpretative standard; FURo = cefuroxime using the oral interpretative standard; FURp = cefuroxime using the parenteral interpretative standard; ETP = ertapenem; IMI = imipenem; MER = meropenem; 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, 2012] interpretative breakpoints were used for DOX, all other according to CLSI[CLSI, 2011]. ** Number of isolates in Western, Central and Eastern regions, respectively.

Figure 38. Multi-drug resistance of *S. pneumoniae*, 2011 - 2013



*Antimicrobial classes include: β-lactams (amoxicillin/clavulanic acid, penicillin using meninigitis 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-sulflamethoxazole); phenicols (chloramphenicol); lincosamides (clindamycin); oxazolidinones (linezolid).

Figure 39. Multi-drug resistance of *S. pneumoniae* serotypes, 2013



*Antimicrobial classes include: β-lactams (amoxicillin/clavulanic acid, penicillin using meninigitis 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-sulflamethoxazole); phenicols (chloramphenicol); lincosamides (clindamycin); oxazolidinones (linezolid).

Table 8. Antimicrobial resistance of *S. pneumoniae* serotypes, 2013

Class	Penicllins				Cephems				Carbapenems			Fluoroquinolones		Other				
Serotype	AUG[a]	PENm	PENn	PENo	AXOm	AXOn	FURo	FURp	ERT	IMI	MER	LEV	MOX	CLA	CLI	CHL	DOX	SXT
1 (n=1)	-[b]	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3 (n=82)	-	1.2[c]	-	-	-	-	-	-	-	-	-	-	-	3.7	2.4	7.3	11.0	1.2
4 (n=13)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
5 (n=2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100
6A (n=5)	-	60.0	-	-	-	-	-	-	-	-	-	20.0	-	-	-	-	-	-
6B (n=6)	-	16.7	-	-	-	-	-	-	-	-	-	-	-	33.3	16.7	-	33.3	50.0
6C (n=33)	-	33.3	-	3.0	-	-	-	6.1	-	-	-	-	-	45.5	12.1	-	12.1	21.2
6D (n=2)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
7C (n=8)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	12.5
7F (n=110)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3.6	-
8 (n=50)	-	2.0	-	2.0	-	-	2.0	2.0	-	-	-	-	-	2.0	2.0	-	6.0	2.0
9A (n=1)	-	100	-	-	-	-	-	-	-	-	-	-	-	100	-	-	-	100
9N (n=46)	-	2.2	-	-	-	-	-	-	-	-	-	-	-	4.3	-	-	4.3	-
9V (n=4)	-	100	-	25.0	-	-	50.0	75.0	-	-	-	-	-	25.0	-	-	-	100
10A (n=31)	-	6.5	-	-	-	-	-	-	-	-	-	-	-	22.6	6.5	-	3.2	9.7
10F (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	100
11A (n=47)	-	2.1	-	-	-	-	-	-	-	-	-	2.1	-	12.8	-	-	-	10.6
12A (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	100	-	-	100	-
12F (n=53)	-	-	-	-	-	-	-	-	-	-	-	-	-	81.1	1.9	-	5.7	-
13 (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
14 (n=3)	-	33.3	-	33.3	-	-	33.3	33.3	-	-	33.3	33.3	33.3	66.7	-	-	33.3	-
15A (n=22)	-	40.9	-	-	-	-	-	9.1	-	-	-	-	-	77.3	31.8	-	72.7	-
15B (n=19)	-	-	-	-	-	-	-	-	-	-	-	-	-	10.5	-	-	5.3	5.3
15C (n=12)	-	16.7	-	-	-	-	-	-	-	-	-	-	-	16.7	-	-	-	-
16F (n=22)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
17F (n=10)	-	10.0	-	-	-	-	-	-	-	-	-	-	-	10.0	10.0	-	10.0	-
18A (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
18C (n=4)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	25.0
19A(n=114)	6.1	28.9	-	22.8	4.4	0.9	24.6	26.3	0.9	20.2	21.1	-	-	59.6	26.3	-	33.3	27.2
19F (n=13)	-	38.5	-	23.1	7.7	-	15.4	23.1	-	7.7	15.4	-	-	23.1	23.1	-	23.1	23.1
20 (n=12)	-	-	-	-	-	-	-	-	-	-	-	-	-	8.3	-	-	-	-
21 (n=10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	20.0
22F(n=118)	-	0.8	0.8	0.8	0.8	-	0.8	0.8	-	-	-	-	-	28.0	-	0.8	-	-
23A (n=30)	-	30.0	-	-	-	-	-	-	-	-	-	-	-	3.3	-	3.3	16.7	3.3
23B (n=21)	-	38.1	-	-	-	-	-	-	-	-	-	-	-	4.8	-	-	4.8	4.8
23F (n=4)	-	50.0	-	25.0	-	-	25.0	25.0	-	-	-	75.0	-	50.0	25.0	25.0	25.0	25.0
24B (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
24F (n=1)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
28A (n=5)	-	-	-	-	-	-	-	-	-	-	-	-	-	20.0	-	40.0	40.0	20.0
29 (n=3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
31 (n=11)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
33F (n=49)	-	2.0	-	-	-	-	-	-	-	-	-	-	-	81.6	16.3	-	10.2	10.2
34 (n=5)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
35A (n=2)	-	-	-	-	-	-	-	-	-	-	-	-	-	50.0	-	-	50.0	50.0
35B (n=28)	-	25.0	-	3.6	-	-	7.1	21.4	-	-	3.6	-	-	14.3	-	-	-	3.6
35F (n=24)	-	-	-	-	-	-	-	-	-	-	-	-	-	4.2	-	-	-	-
37 (n=3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
38 (n=14)	-	7.1	-	-	-	-	-	-	-	-	-	-	-	6.7	6.7	-	6.7	-
NT (n=3)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
All (n=1061)	0.7	10.0	0.1	3.4	0.7	0.1	3.6	4.7	0.1	2.3	2.6	0.6	0.1	24.8	5.8	1.0	9.9	7.4

[a]AUG = amoxicillin/clavulanic acid; PENm = penicillin using the parenteral meningitis CLSI interpretive standard; ; PENn = penicillin using the parenteral non-meningitis interpretive standard; PENo = penicillin using the oral penicillin V interpretive standard; LEV = levofloxacin; MOX = moxifloxacin; AXOm = ceftriaxone using the parenteral meningitis interpretive standard; AXOn = ceftriaxone using the parenteral non-meningitis interpretative standard; FURo = cefuroxime using the oral interpretative standard; FURp = cefuroxime using the parenteral interpretative standard; ETP = ertapenem; IMI = imipenem; MER = meropenem; 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, 2012] interpretative breakpoints were used for DOX, all other according to CLSI[CLSI, 2012].

[b] "-" denotes no resistance (0%) to the antimicrobial.

[c] Percentage of serotype total interpreted as resistant to the antimicrobial agent.

Figure 40. Clarithromycin resistance of *S. pneumoniae* serotypes collected 2011 - 2013

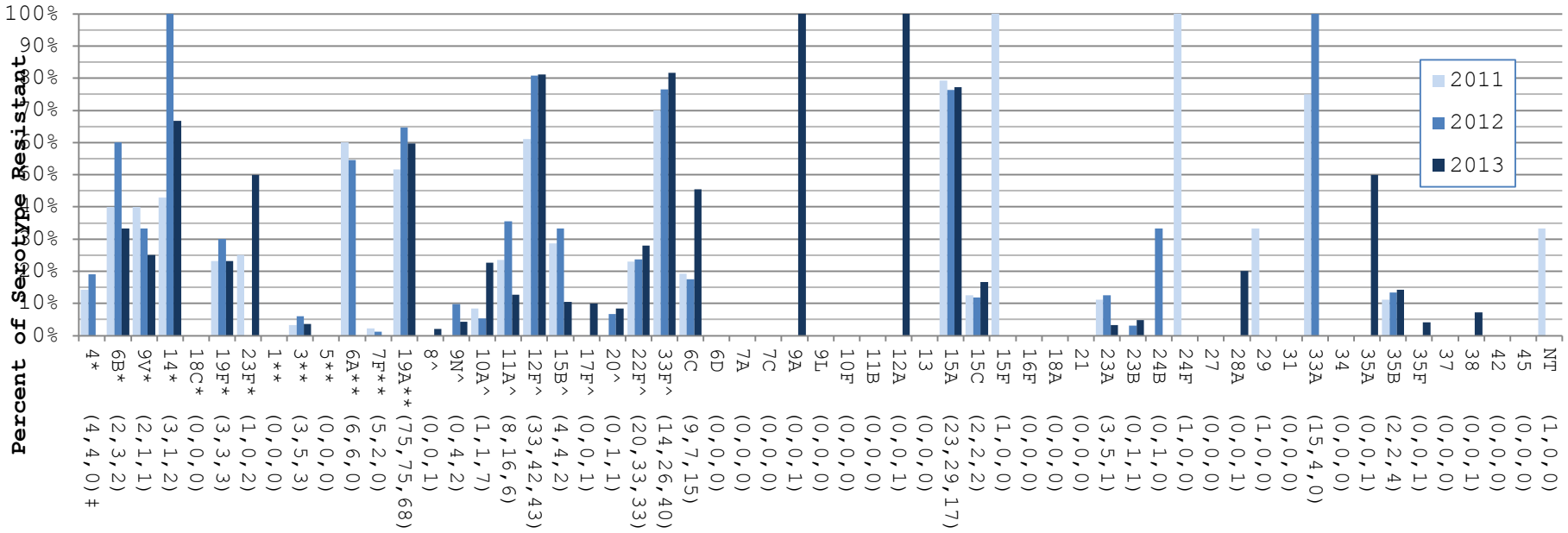
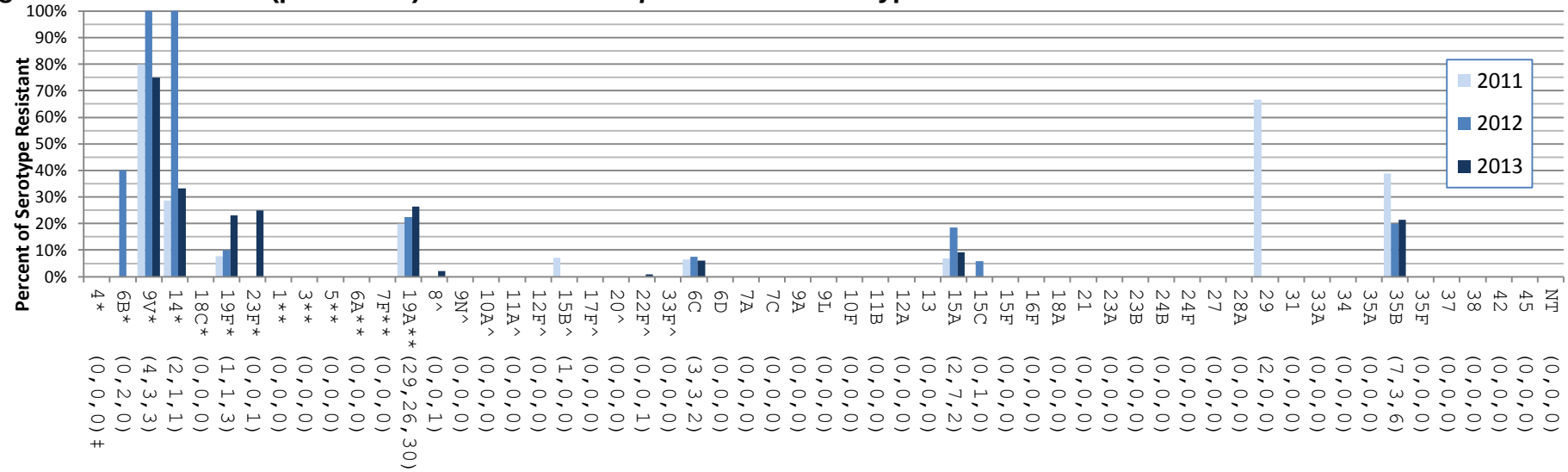


Figure 41. Cefuroxime (parenteral) resistance of *S. pneumoniae* serotypes collected 2011 – 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 42. Clindamycin resistance of *S. pneumoniae* serotypes collected 2011 – 2013

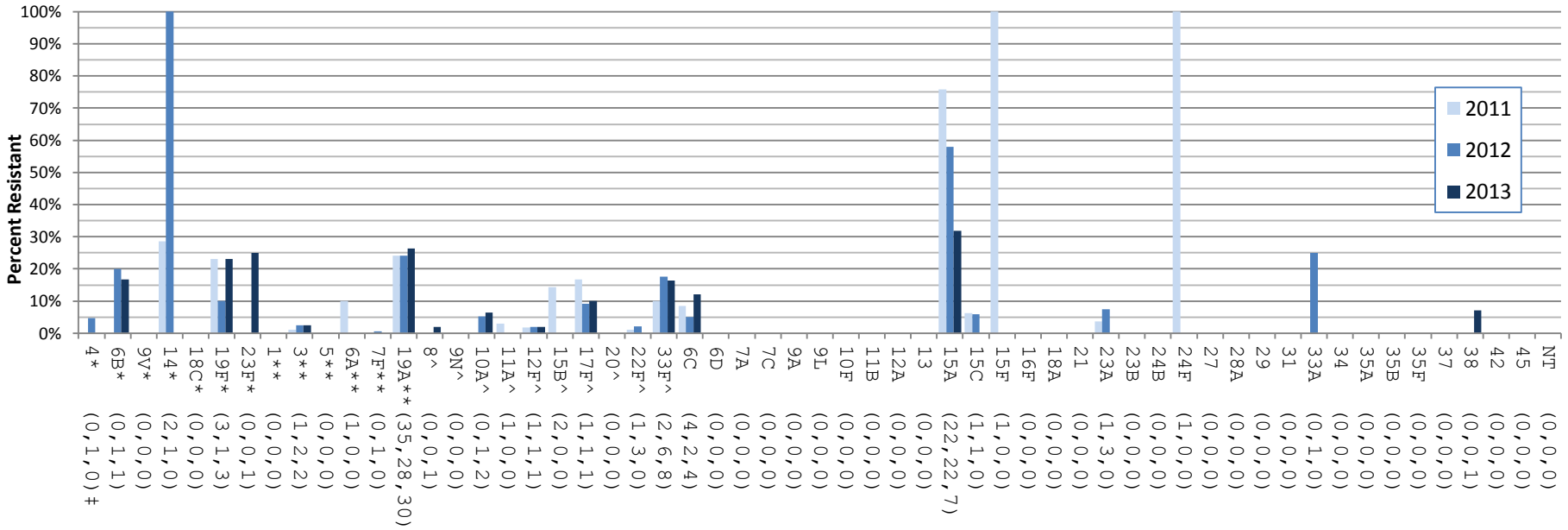
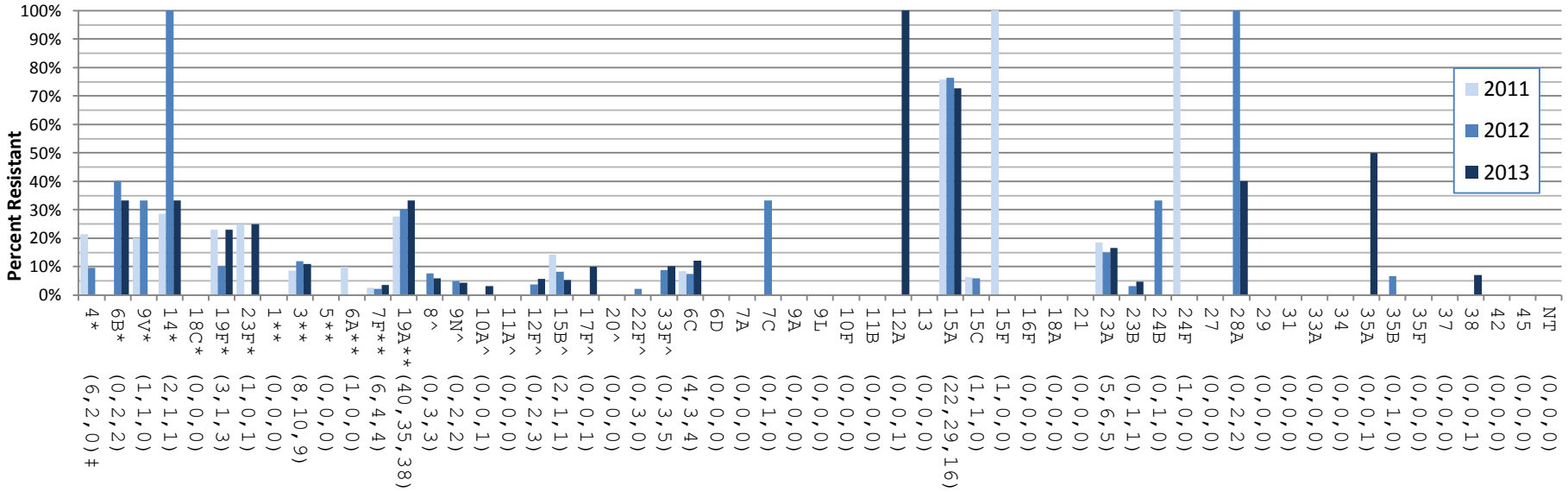


Figure 43. Doxycycline resistance of *S. pneumoniae* serotypes collected 2011 – 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 44. Imipenem resistance of *S. pneumoniae* serotypes collected 2011 – 2013

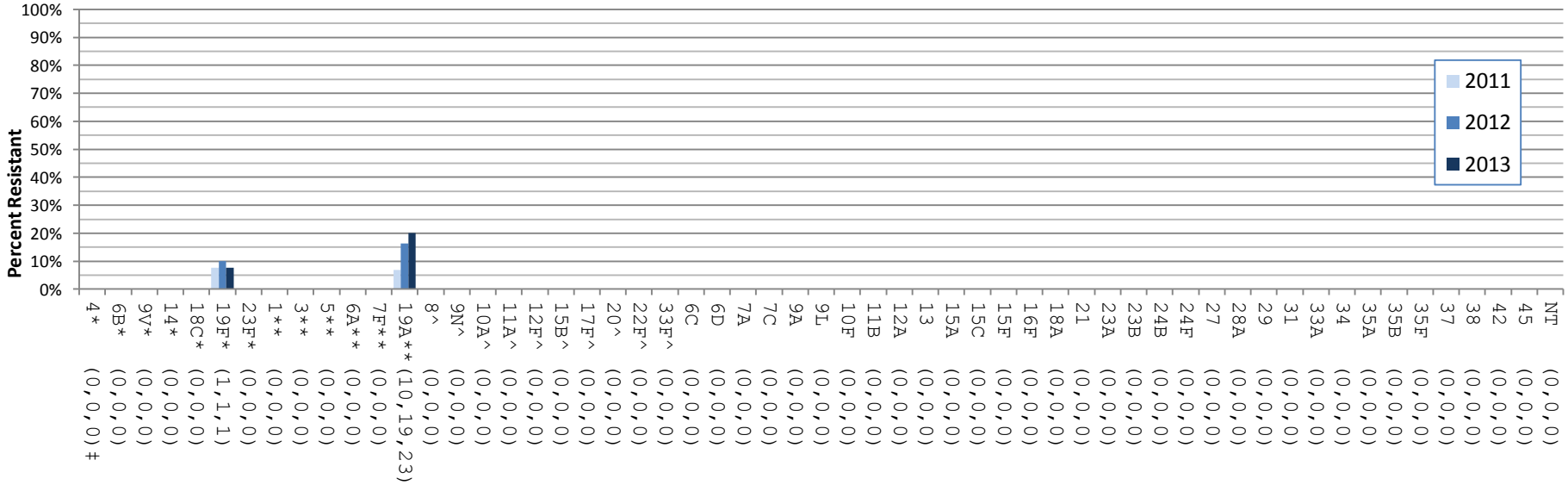
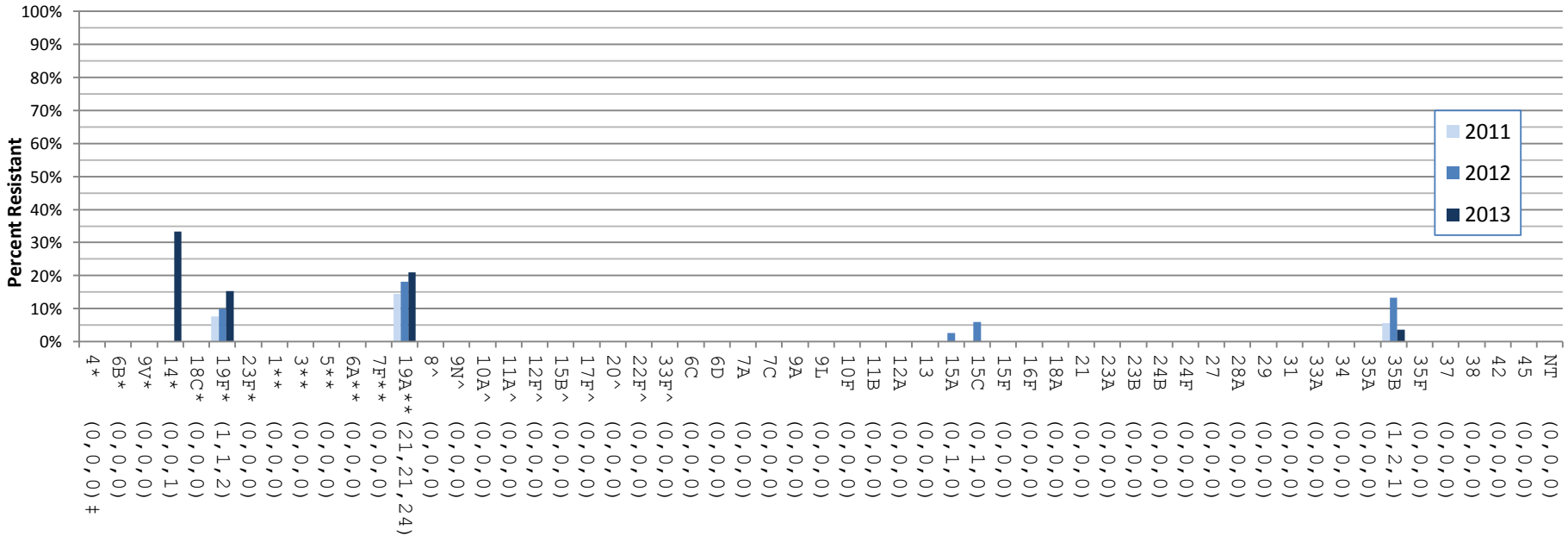


Figure 45. Meropenem resistance of *S. pneumoniae* serotypes collected 2011 – 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Figure 46. Penicillin resistance (meningitis breakpoints) of *S. pneumoniae* serotypes collected 2011 – 2013

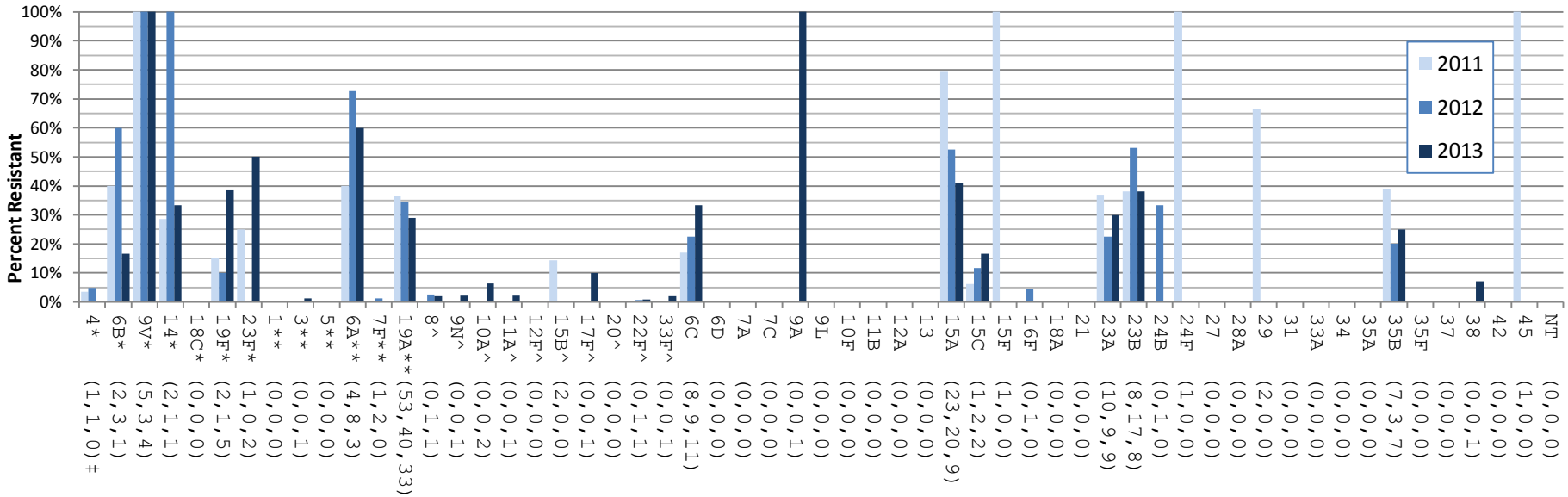
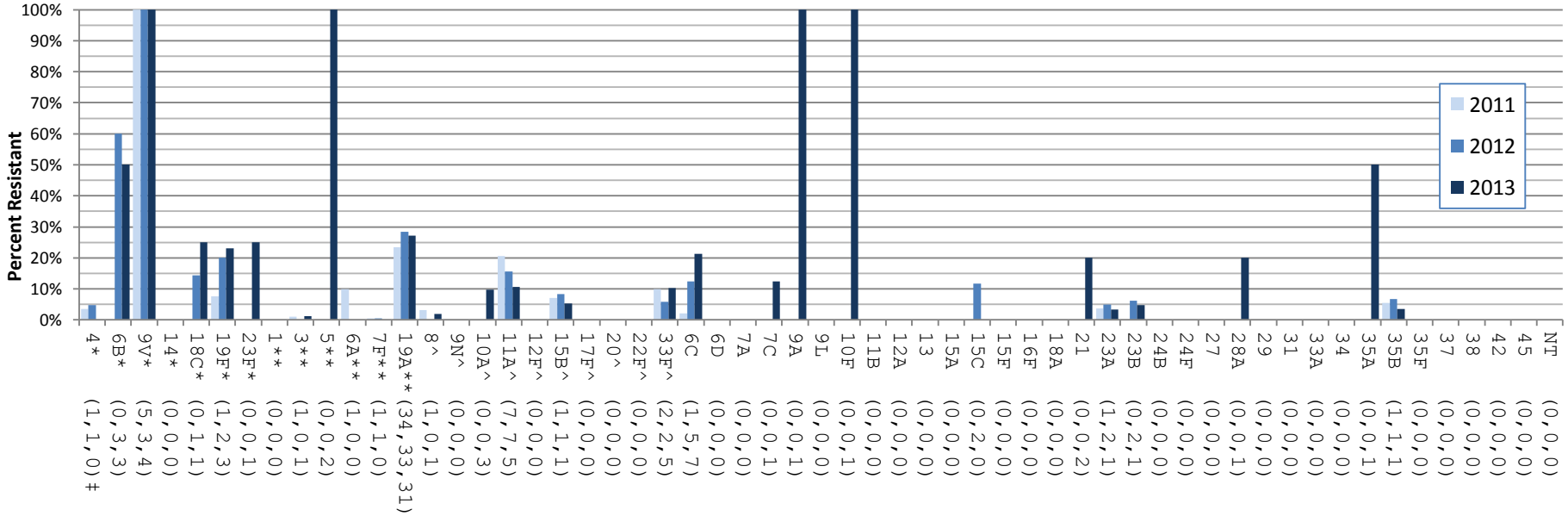


Figure 47. Trimethoprim/Sulfamethoxazole resistance of *S. pneumoniae* serotypes collected 2011 – 2013



*Component of PCV7; ** Component of PCV13; ^ Component of PPV23; ‡ Number of isolates for 2010, 2011, 2012 and 2013, respectively.

Streptococcus pyogenes (Group A *Streptococcus*)

Of the 1,294 *Streptococcus pyogenes* isolates tested at the NML by *emm* typing, 155 (12.0%) were isolated from children <15 years of age; 1096 (84.7%) from adults ≥15 years of age; and no age was available for 43 isolates. Gender information was available for 1269 isolates, of which 54.2% (n=688) were from male patients.

No major differences were observed in the relative proportions of clinical isolation sites between adults and children other than slightly more CSF and pleural fluid isolations sites observed among child isolates (2.6%, n=4 and 6.5%, n=10; respectively) than in the adults (0.2%, n=2 and 1.5%, n=16; respectively) (Figures 48, 49).

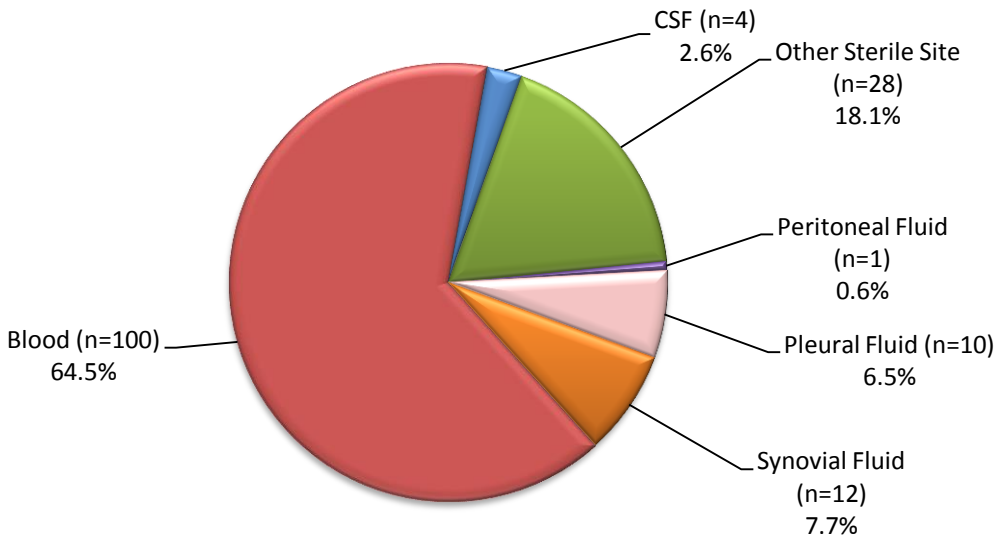
The most prevalent *emm* type in Canada during 2013 continues to be *emm*1 accounting for 28.4% (n=44) of isolates collected from children <15 years of age and 23.7% (n=260) of isolates from those ≥ 15 years of age (Figure 50, 51). *emm*89 is next most prevalent accounting for 7.1% (n=11) of child isolates and 9.9% (n=108) of adult isolates. The majority of *emm*68 (n=46), *emm*53 (n=32), *emm*80 (n=28), *emm*77 (n=14), *emm*22 (n=12) and *emm*41 (n=6) isolates were from Western Canada, whereas the majority of *emm*89 (n=90), *emm*4 (n=54), *emm*28 (n=54), *emm*12 (n=49), *emm*59 (n=33) and *emm*2 (n=277) isolates were from Central regions (Figure 52).

Among isolates from children, adults and unknown ages (n=887), *emm*1 and *emm*89 represented comparatively greater proportions of blood (26.6%, n=236 and 9.1%, n=81; respectively) than of synovial fluid isolates (10.2%, n=10 and 6.1%, n=6; respectively). Conversely, proportions of *emm*68 and *emm*82 were greater in synovial fluid (7.1%, n=7 and 8.2%, n=8; respectively) than in blood isolates (3.0%, n=27 and 1.2%, n=11, respectively) (Figure 53).

Table 9. Number of invasive *S. pyogenes* isolates from each province, 2013

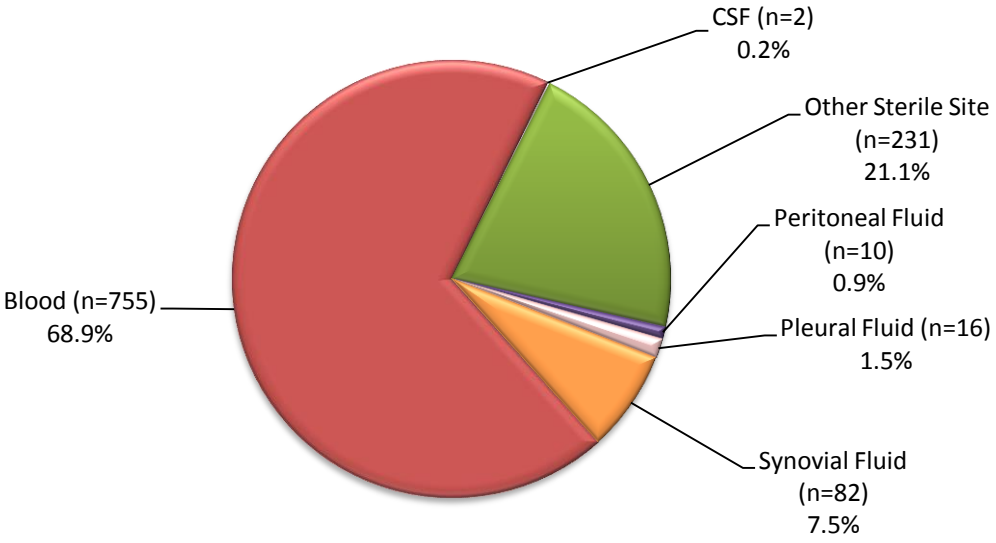
Province	< 2	2 – 4	5 – 14	15 – 49	50 – 64	≥ 65	Not Given	Total
British Columbia	3	2	9	61	23	43	1	**142**
Alberta	-	-	-	-	-	1	-	**1**
Saskatchewan	5	1	5	43	22	17	2	**95**
Manitoba	11	2	7	75	47	16	12	**170**
Ontario	27	6	26	167	115	158	19	**518**
Québec	10	8	30	121	51	91	8	**319**
New Brunswick	-	-	1	7	1	8	-	**17**
Nova Scotia	-	-	-	5	3	4	-	**12**
Prince Edward Island	-	-	-	-	1	-	1	**2**
Newfoundland and Labrador	-	-	2	3	6	1	-	**12**
Yukon Territories	-	-	-	1	1	-	-	**2**
Northwest Territories	-	-	-	2	1	1	-	**4**
Canada	**56**	**19**	**80**	**485**	**271**	**340**	**43**	**1294**

Figure 48. Clinical isolation sites of *S. pyogenes* from children <15 years of age (N=155)



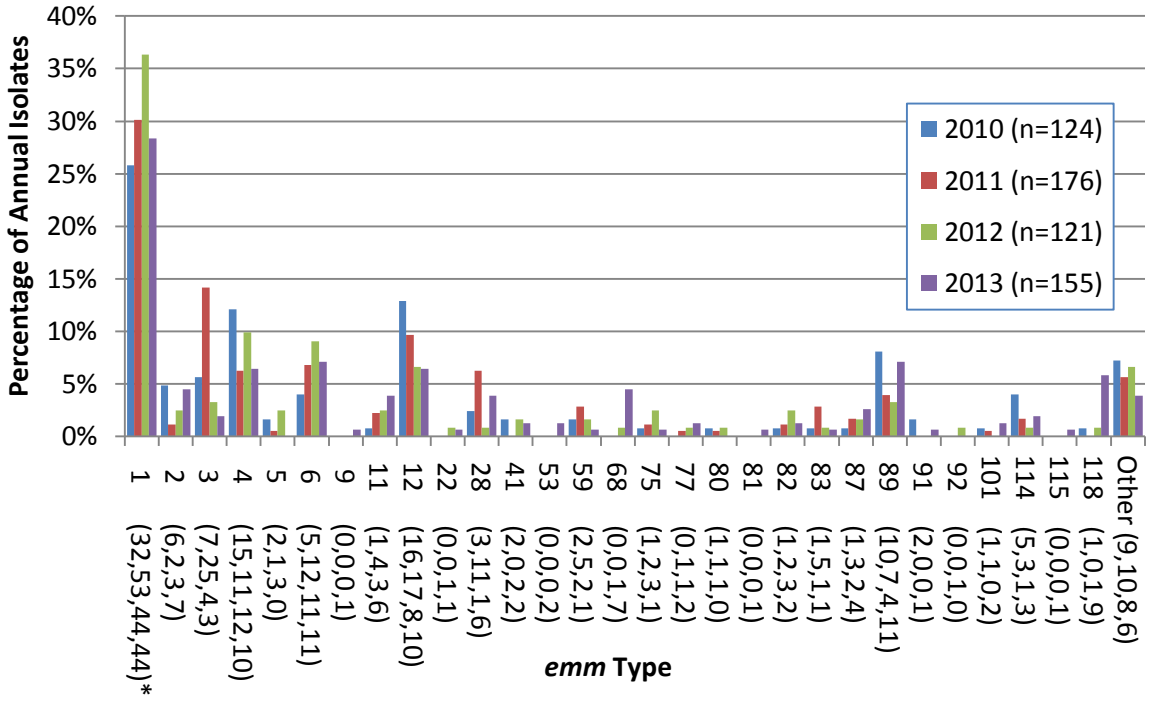
Other sterile sites include: deep tissue, biopsy and surgical samples, bone, mastoid and any clinical sources associated with necrotizing fasciitis. Patient age was not available for 43 isolates.

Figure 49. Clinical isolation sites of *S. pyogenes* from adults ≥ 15 years of age (N=1096)



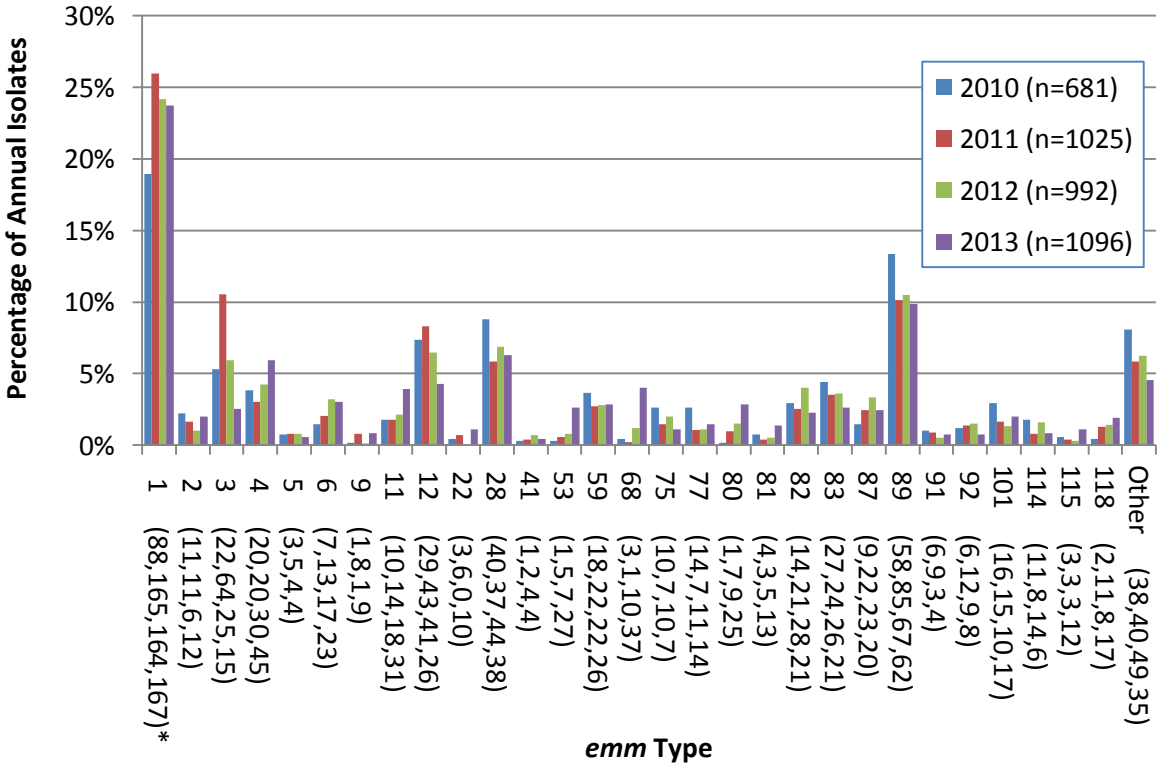
Other sterile sites include: deep tissue, biopsy and surgical samples, bone, mastoid and any clinical sources associated with necrotizing fasciitis. Patient age was not available for 43 isolates.

Figure 50. Invasive *S. pyogenes emm* types in children <15 years of age, 2010 – 2013



*Number of isolates in 2010, 2011, 2012, and 2013, respectively.

Figure 51. Invasive *S. pyogenes emm* types in adults ≥ 15 years of age, 2010 – 2013



*Number of isolates in 2010, 2011, 2012, and 2013, respectively.

Figure 52. Regional distribution of *S. pyogenes emm* types

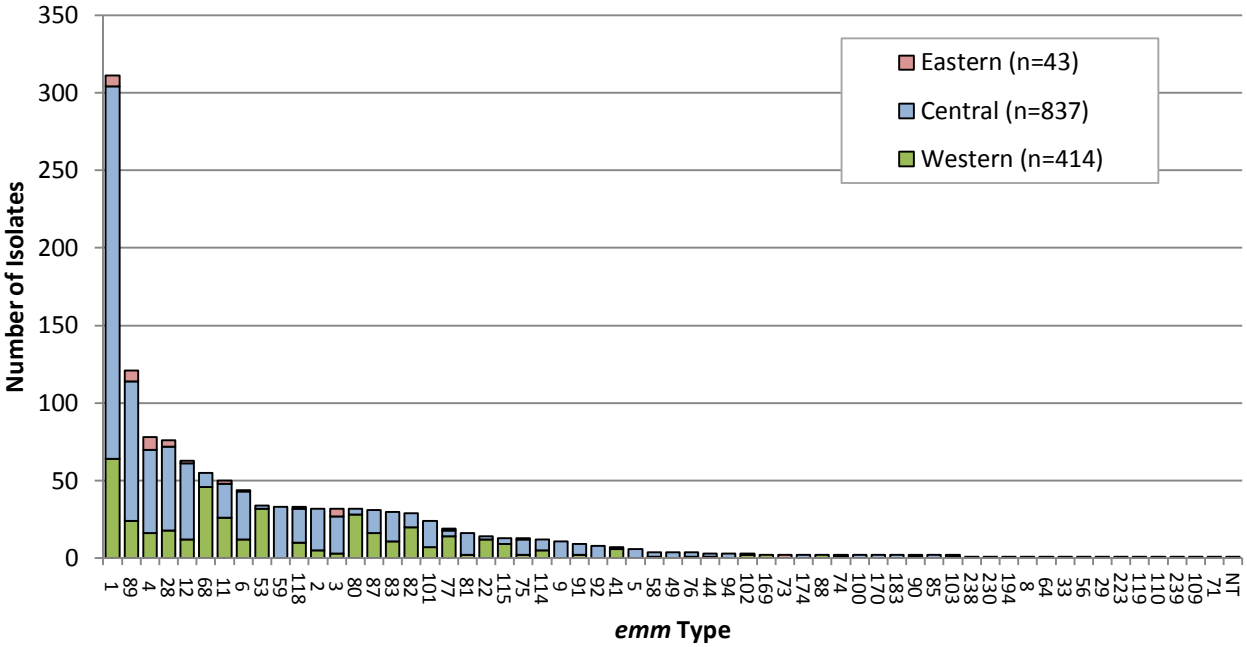


Figure 53a.Distribution of invasive *S. pyogenes emm* types from blood*, 2013

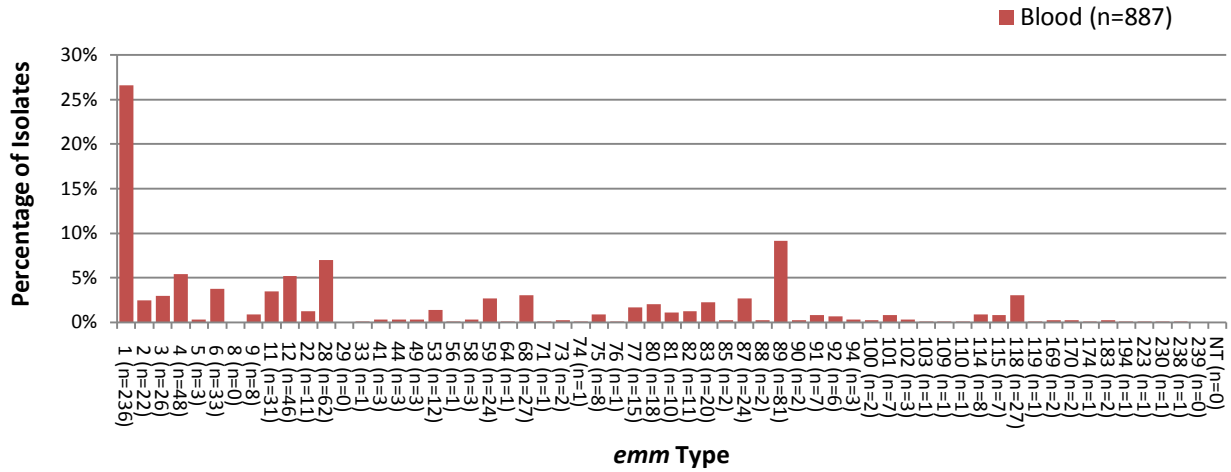


Figure 53b. Distribution of invasive *S. pyogenes emm* types from synovial fluid*, 2013

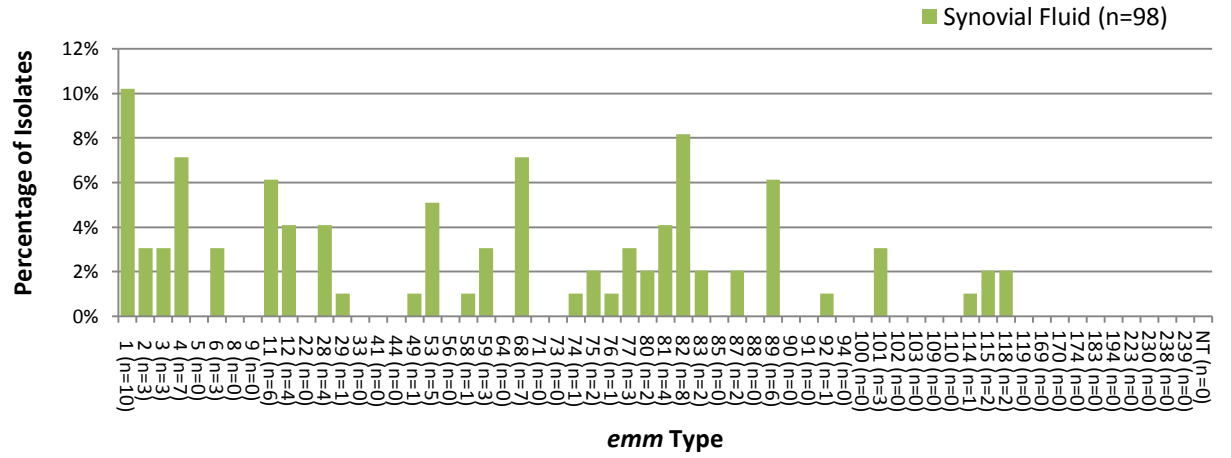
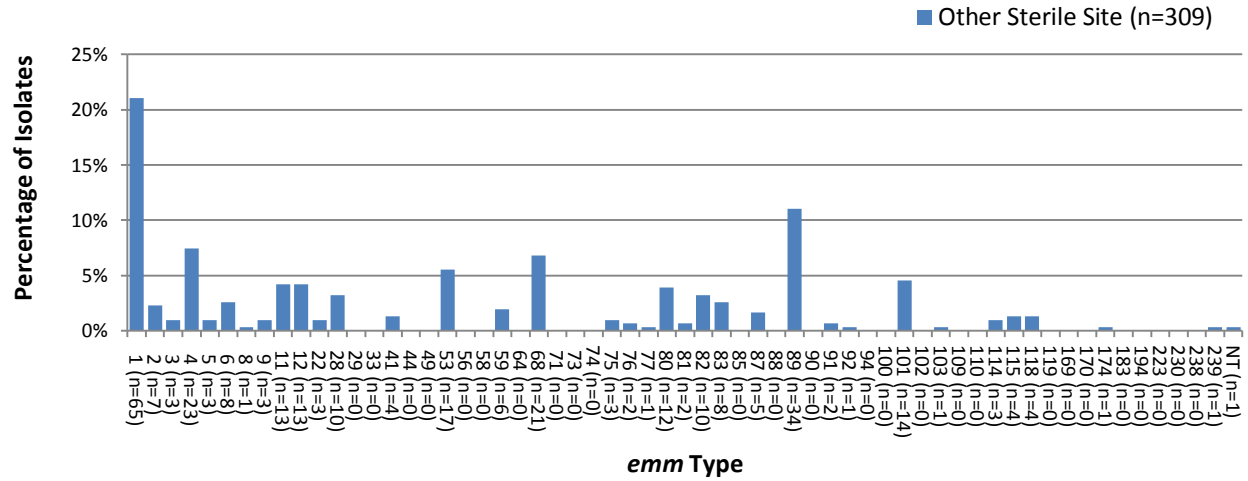


Figure 53c. Distribution of invasive *S. pyogenes emm* types from other clinical isolation sources*, 2013



* Includes isolates from child, adult and unknown age groups.

Antimicrobial Resistance of *Streptococcus pyogenes*

Of the 1,290 invasive *S. pyogenes* isolates tested by disc diffusion in 2013, 0.6% (n=8) were non-susceptible to chloramphenicol (4 resistant and 4 intermediate isolates), down from 9.4% (n=36) in 2010. Erythromycin resistance has also decreased from 14.4% (n=55) to 8.5% (n=110) from 2010 to 2013; whereas resistance to clindamycin has remained relatively unchanged at 2.2% (n=29) (Figure 54). Induced resistance to clindamycin was observed in a further 6.9% (n=89) of the isolates. No resistance was observed to penicillin or vancomycin.

Chloramphenicol non-susceptibility was observed in very few isolates including *emm*11 (n=1), *emm*89 (n=2), *emm*92 (n=1), *emm*110 (n=1), *emm*115 (n=1) and *emm*180 (n=2) (Table 11). Relatively high erythromycin (macrolide) resistance was observed among *emm*9 (72.7%, n=11), *emm*11 (61.7%, n=47), *emm*92 (87.5%, n=8), and *emm*114 (75.1%, n=12) isolates (Figure 55).

Figure 54. Antimicrobial resistance of invasive *S. pyogenes*, 2010 - 2013

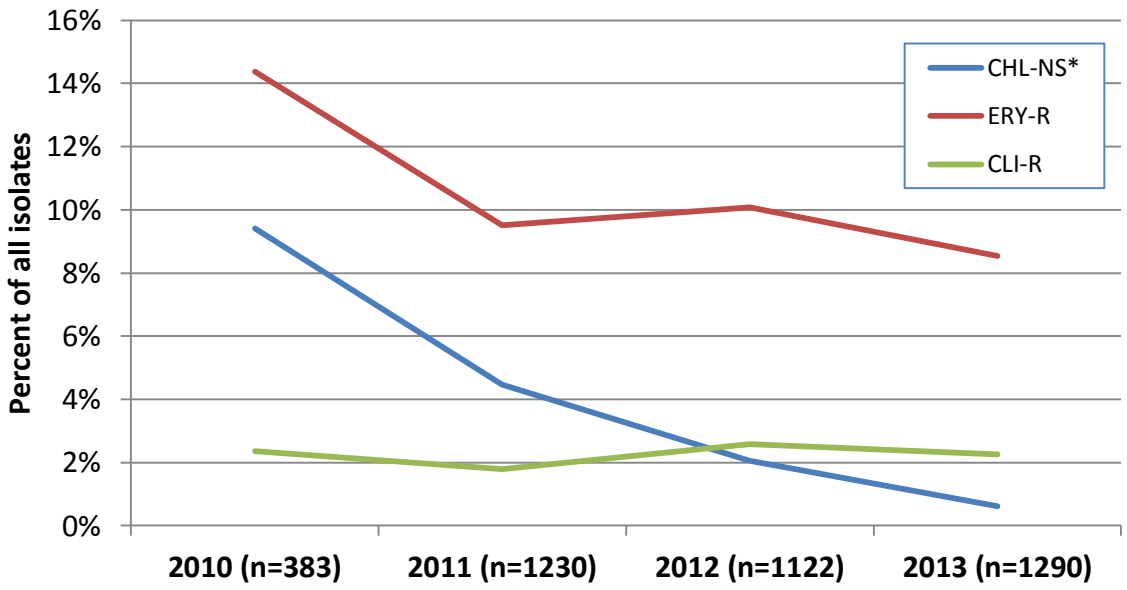


Table 10. Number of resistant *S. pyogenes* isolates

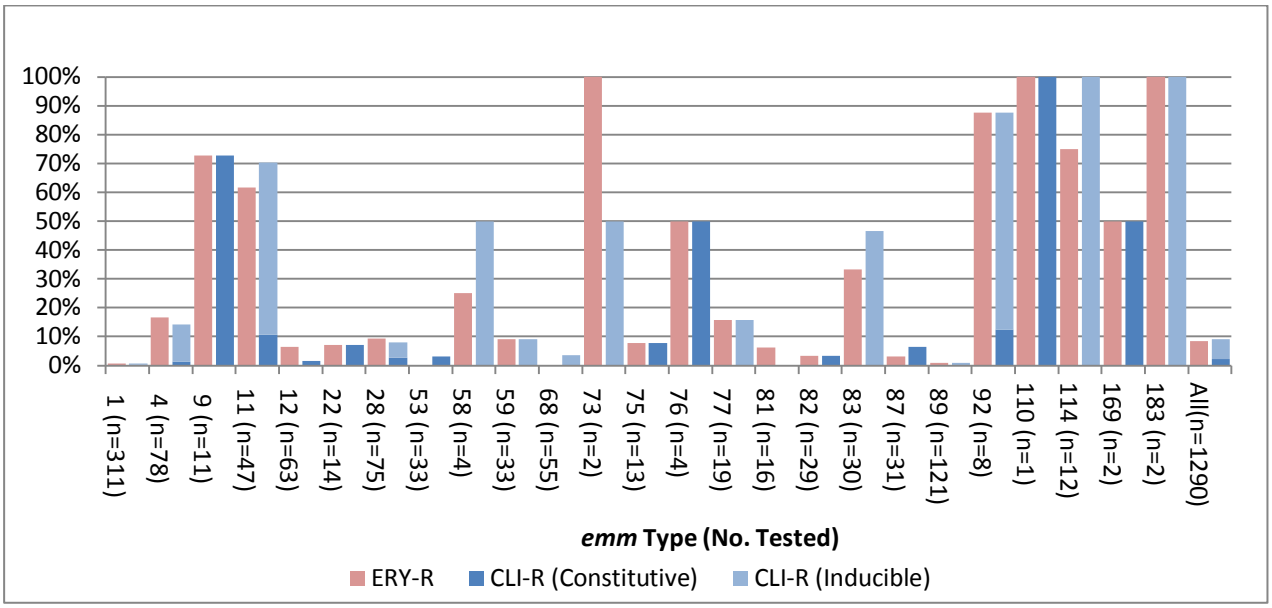
Antimicrobial	Year			
	2010	2011	2012	2013
CHL-NS*	36	55	23	8
ERY-R	55	117	113	110
CLI-R	9	22	29	29

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

Table 11. Chloramphenicol non-susceptibility of *S. pyogenes emm* types, 2010 to 2013

Emm Type	Year Collected (No. Tested)			
	2010 (n=383)	2011 (n=1230)	2012 (n=1122)	2013 (n=1290)
1	8.8% (n=7)	4.8% (n=16)	1.7% (n=5)	-
2	22.2% (n=2)	10.5% (n=2)	-	-
3	9.1% (n=1)	1.4% (n=2)	-	-
4	-	-	1.8% (n=1)	-
6	-	-	2.3% (n=1)	-
9	-	12.5% (n=1)	-	-
11	14.3% (n=1)	-	-	2.1% (n=1)
12	4.9% (n=2)	4.9% (n=5)	-	-
22	-	14.3% (n=1)	-	-
28	5.6% (n=2)	1.4% (n=1)	2.8% (n=2)	-
29	-	-	7.1% (n=1)	-
41	50% (n=1)	-	11.1% (n=1)	-
48	-	25% (n=1)	-	-
58	-	42.9% (n=3)	-	-
59	13.3% (n=2)	-	-	-
63	-	50% (n=1)	-	-
68	100% (n=1)	-	15.4% (n=2)	-
73	-	-	11.1% (n=1)	-
75	-	5.9% (n=1)	-	-
80	-	9.1% (n=1)	-	-
82	-	6.9% (n=2)	-	-
83	20% (n=3)	-	2.6% (n=1)	-
87	-	-	2.9% (n=1)	-
89	17.4% (n=8)	12.3% (n=14)	4.5% (n=5)	1.7% (n=2)
90	-	100% (n=1)	-	-
91	33.3% (n=1)	-	-	-
92	-	-	6.3% (n=1)	12.5% (n=1)
101	28.6% (n=2)	11.1% (n=2)	-	-
110	-	-	-	100% (n=1)
114	37.5% (n=3)	7.7% (n=1)	5.9% (n=1)	-
115	-	-	-	7.7% (n=1)
183	-	-	-	100% (n=2)
All	**9.4% (n=36)**	**4.5% (n=55)**	**2% (n=23)**	**0.6% (n=8)**

Figure 55. Macrolide resistance of *S. pyogenes emm* types, 2013



Invasive *Streptococcus agalactiae* (Group B *Streptococcus*)

Of the 416 *Streptococcus agalactiae* isolates tested at the NML, 16 cultures (3.8%) were early onset isolates from infants <8 days old; 7 cultures (1.7%) were late onset from infants 8 – 31 days old; 4 cultures (1.0%) were from children 1 month to 14 years old, 177 (42.5%) were from adults 15 – 64 years old, and 165 (39.7%) were from seniors ≥65 years of age, and no age was available for 47 isolates (Table 12). Isolates from male patients accounted for 52.8% (n=84) of the 159 isolates for which gender information was available.

Serotype III was most prevalent overall representing 23.8% (n=99) of all isolates tested in 2013, and 62.5% (n=10) of early onset, 57.1% (n=4) of late onset, and 50.0% (n=2) of child isolates. Serotype V was most predominant in adults and seniors with 24.3% (n=43) and 20.6% (n=34) of the isolates in these age groups, respectively (Table 12).

The majority of GBS were isolated from blood, representing 75.7% (n=315) of all isolates, followed by synovial fluids with 4.8% (n=20) of the isolates (Figure 56). Serotype III accounted for 25.7% (n=81) of blood, and 60.0% (n=6) of the CSF isolates, whereas serotype II accounted for 30.0% (n=3) of peritoneal isolates, and serotype V represented 50.0% (n=10) of synovial fluid and 25% (n=14) of other sterile site isolates (Figure 57).

Table 12. Invasive *S. agalactiae* serotypes from each age group[a], 2013

Serotype	Infant Early Onset	Infant Late Onset	Child	Adult	Senior	Not Given	Total
Ia	-	28.6%(2)	50.0%(2)	15.3%(27)	18.8%(31)	25.5%(12)	**17.8%(74)**
Ib	-	14.3%(1)	-	15.3%(27)	17.6%(29)	10.6%(5)	**14.9%(62)**
II	6.3%(1)[b]	-	-	15.3%(27)	9.7%(16)	8.5%(4)	**11.5%(48)**
III	62.5%(10)	57.1%(4)	50.0%(2)	19.2%(34)	18.2%(30)	40.4%(19)	**23.8%(99)**
IV	25.0%(4)	-	-	7.9%(14)	9.7%(16)	6.4%(3)	**8.9%(37)**
V	6.3%(1)	-	-	24.3%(43)	20.6%(34)	8.5%(4)	**19.7%(82)**
VI	-	-	-	-	2.4%(4)	-	**1.0%(4)**
VII	-	-	-	0.6%(1)	0.6%(1)	-	**0.5%(2)**
VIII	-	-	-	0.6%(1)	1.2%(2)	-	**0.7%(3)**
IX	-	-	-	0.6%(1)	0.6%(1)	-	**0.5%(2)**
NT	-	-	-	1.1%(2)	0.6%(1)	-	**0.7%(3)**
Total	**(16)**	**(7)**	**(4)**	**(177)**	**(165)**	**(47)**	**(416)**

[a] Infant Early Onset ≤ 7days, Infant Late Onset 8 – 31 days, Child = 1 month – 14 years, Adult = 15 – 64 years, Senior ≥ 65 years, NT = Non-typeable.
[b] Percentage of age group isolates (number of isolates).

Figure 56. Clinical isolation sites of *S. agalactiae*

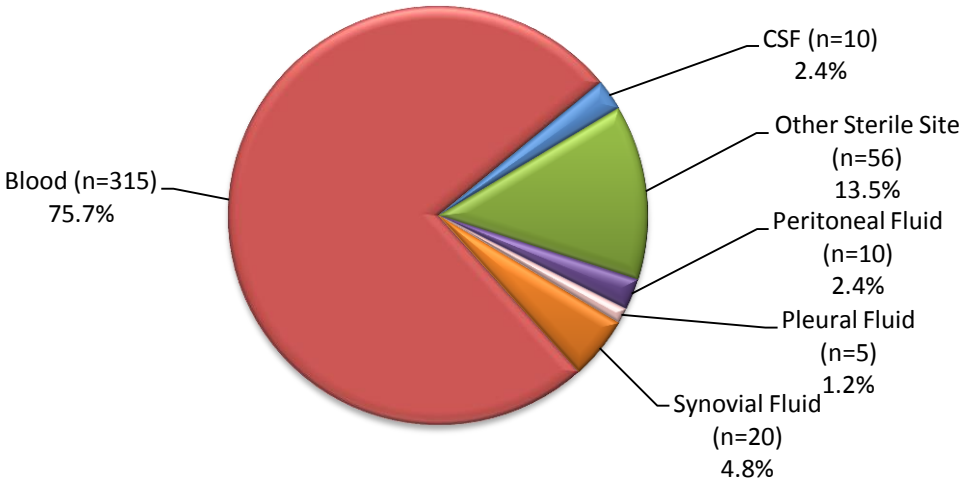


Figure 57. Invasive *S. agalactiae* serotypes by clinical isolation site

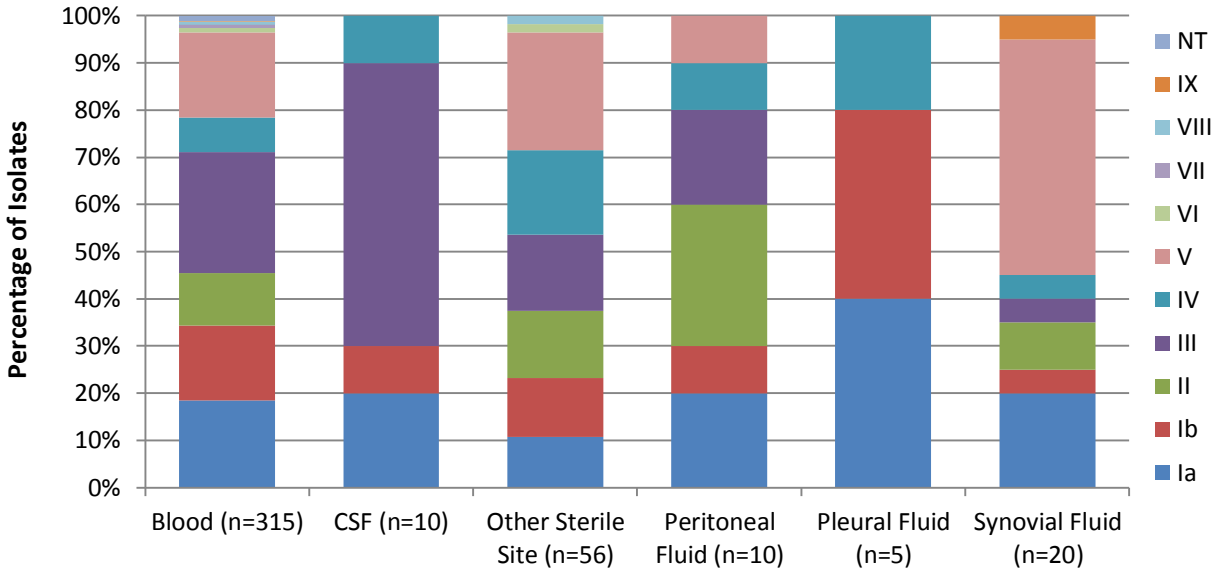
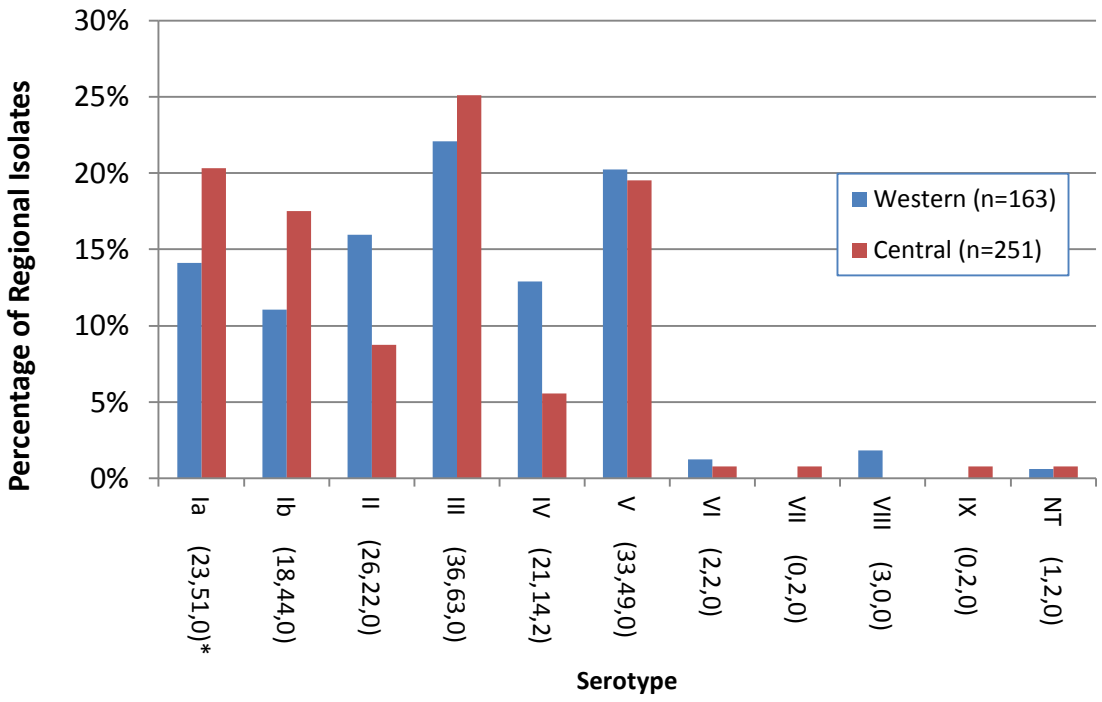


Table 13. Number of *S. agalactiae* isolates from clinical isolation sites

Serotype	Blood	CSF	Other Sterile Site	Peritoneal Fluid	Pleural Fluid	Synovial Fluid
NT	3					
IX	1					1
VIII	2		1			
VII	2					
VI	3		1			
V	57		14	1		10
IV	23	1	10	1	1	1
III	81	6	9	2		1
II	35		8	3		2
Ib	50	1	7	1	2	1
Ia	58	2	6	2	2	4

Figure 58. Regional distribution of invasive *S. agalactiae* serotypes in 2013



* Number of isolates from Western, Central and Eastern regions, respectively. To improve scale 2 serotype IV isolates representing 100% of the Eastern regional isolates were omitted from the figure.

Antimicrobial Resistance of *Streptococcus agalactiae*

Of the 420 invasive *S. agalactiae* isolates tested by disc diffusion in 2013, 1.9% (n=8) were non-susceptible (2 intermediate and 6 resistant) to chloramphenicol, remaining relatively constant since 2010 with 2.1% (n=5). Macrolide resistance has increased with clindamycin resistance increasing from 25.5% (n=84) of the isolates to 28.8% (n=121), and erythromycin resistance increasing from 40.7% (n=134) to 48.8% (n=205) between 2012 and 2013 (Figure 59).

Similarly as with the other beta hemolytic Group A *Streptococcus*, chloramphenicol non-susceptibility in Group B *Streptococci* was observed in very few isolates including serotypes Ia (n=1), III (n=2), IV (n=1) and V (n=4) (Table 15). Relatively high erythromycin (macrolide) resistance was observed among serotype II (59.6%, n=28), IV (60.5%, n=23), and V (61.2%, n=52) (Figure 60).

Figure 59. Antimicrobial resistance of invasive *S. agalactiae* (iGBS) isolated collected 2010 to 2013

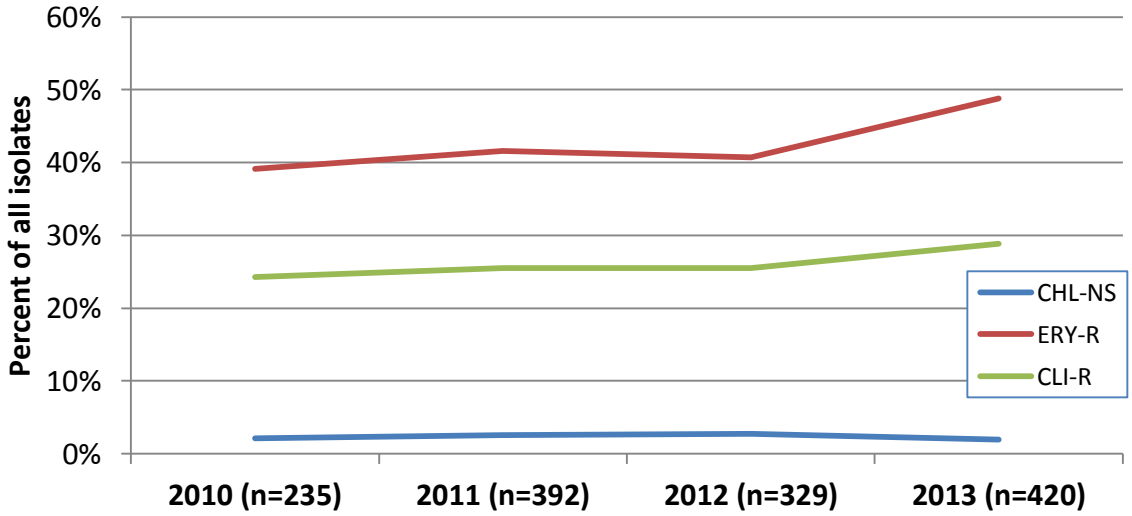


Table 14. Number of resistant *S. agalactiae* isolates

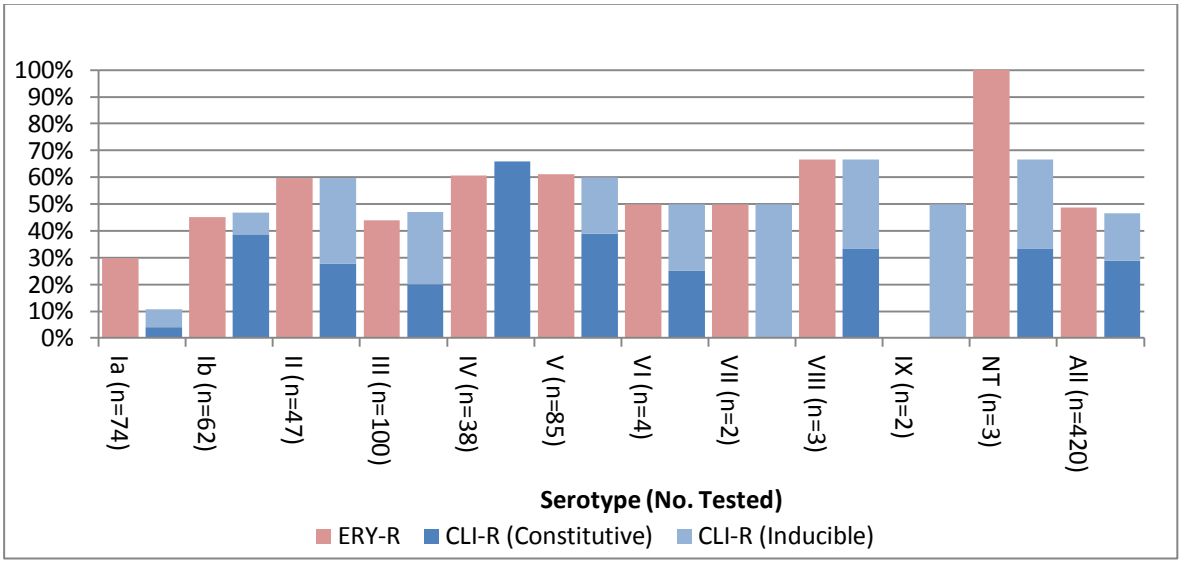
Antimicrobial	Year			
	2010	2011	2012	2013
CHL-NS	5	10	9	8
ERY-R	92	163	134	205
CLI-R	57	100	84	121

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

Table 15. Chloramphenicol non-susceptibility of *S. agalactiae* serotypes, 2010 to 2013

Serotype	Year Collected (No. Tested)			
	2010 (n=235)	2011 (n=392)	2012 (n=329)	2013 (n=420)
Ia	4.8% (n=2)	-	1.8% (n=1)	1.4% (n=1)
Ib	-	-	-	-
II	-	-	3.4% (n=1)	-
III	1.7% (n=1)	2.1% (n=2)	3.5% (n=3)	2% (n=2)
IV	5.3% (n=1)	9.8% (n=4)	11.8% (n=4)	2.6% (n=1)
V	1.8% (n=1)	3.8% (n=3)	-	4.7% (n=4)
VI	-	-	-	-
VII	-	-	-	
VIII	-	16.7% (n=1)	-	
IX	-	-	-	-
NT	-	-	-	-
All	**2.1% (n=5)**	**2.6% (n=10)**	**2.7% (n=9)**	**1.9% (n=8)**

Figure 60. Macrolide resistance of *S. agalactiae* serotypes, 2013



CONCLUSION

In *S. pneumoniae* the proportion of PCV7 serotypes remains low and continuing decreases in the predominant PCV13 serotypes 7F and 19A have been observed. The decrease of PCV13 serotypes, in addition to continuing decreases in incidence of disease in children, provides evidence of the impact of the PCV13 vaccination programs in Canada. Continued vigilance however, is required to recognize possible increases in other non-PCV13 serotypes circulating in Canada, such as serotype 22F, 23A and 23B. Although a component of the PCV13 vaccine, serotype 3 has not decreased at the rate of other constituent serotypes, raising concerns of the virulence, the immunogenicity of this serotype and the efficacy of this component of the vaccine. The continued monitoring of the relative frequency of serotypes circulating in Canada will help inform and guide the development and composition of new vaccines which will lower the total burden of disease.

Antimicrobial resistance among isolates of *S. pneumoniae* is generally declining, mainly due to the decline of highly resistant serotype 19A, but resistance to penicillins, macrolides, tetracyclines, sulfonamides and fluoroquinolones and multi-drug resistance is still common. Current antimicrobial resistance levels in Canada are relatively low, however monitoring the antimicrobial susceptibility patterns of the common *S. pneumoniae* serotypes is essential to guide empiric and directed treatments.

*S. pyogenes emm*1 and *emm*89 continue to be the dominate strains in Canada, whereas annual variability of the other *emm* types continue. Antimicrobial resistance in Group A *Streptococcus* has declined since 2010, however, due to the severity, high risk of infection and heightened public awareness of Group A *Streptococci*, the continued monitoring and surveillance of circulating serotypes and antimicrobial resistance levels are important to help identify outbreaks of disease and to inform and guide public health interventions.

S. agalactiae serotypes III and V are the predominate strains in Canada, and antimicrobial resistance is increasing, especially to macrolides. GBS causes severe outcomes in neonatal groups; however 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 *Streptococcus pneumoniae* cases serotyped in Canada, 2013

Age group	Total number of isolates serotyped	Total number of illnesses reported to CNDSS**	Percent serotyped
<1 years	51	68	75.0%
1 - 4 years	153	172	89.0%
5 – 39 years	345	444	77.7%
40 – 59 years	678	851	79.7%
≥60 years	1316	1627	80.9%
All Ages	**2577***	**3162**	**81.5%**

*Includes 34 isolates with no patient age. ** Canadian Notifiable Diseases Surveillance System, PHAC.

Table B. Proportion of invasive *Streptococcus pyogenes* cases in Canada, 2013

Age group	Total number of isolates tested	Total number of illnesses reported to CNDSS**	Percent serotyped
<1 years	43	37	116.2%
1 - 4 years	34	71	47.9%
5 – 39 years	366	497	73.6%
40 – 59 years	389	517	75.2%
≥60 years	421	536	78.5%
All Ages	**1294***	**1658**	**78.0%**

*Includes 41 isolates with no patient age. ** Canadian Notifiable Diseases Surveillance System, PHAC.

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