GERMS-SA ANNUAL SURVEILLANCE REPORT FOR LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL, *HAEMOPHILUS INFLUENZAE* AND PNEUMOCOCCAL DISEASE, SOUTH AFRICA, 2017

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Executive summary

The NICD and GERMS-SA conducts national laboratory-based surveillance for *Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*, describing the epidemiology of these diseases and monitoring the impact of the pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. Participating laboratories reported case patients to the NICD using laboratory case report forms. Isolates from case patients, if available, were submitted to the NICD for phenotypic and genotypic characterisation. A surveillance audit was additionally performed for NHLS laboratories in all provinces using the NHLS Central Data Warehouse. The audit was designed to obtain basic demographic and laboratory data from additional case patients with laboratory-confirmed disease not already reported to GERMS-SA by participating laboratories. *Neisseria meningitidis* invasive disease incidence remained low for 2017, with Serogroup B predominating. Penicillin non-susceptibility was below 10%. The overall incidence of *H. influenzae* also remained low in 2017, and non-typeable disease accounted for the majority of cases. The majority of children <15 years of age with *H. influenzae* serotype b (Hib) had not been fully vaccinated, highlighting the importance of Hib vaccinations in children under 2 years. The incidence of invasive pneumococcal disease (IPD) in 2017 was similar to that in 2016, remaining low with marked reductions seen amongst all age categories post introduction of pneumococcal conjugate vaccine (PCV) into the expanded programme on immunization (EPI). Penicillin and ceftriaxone susceptibility of IPD isolates remained unchanged in 2017. HIV infection and infant HIV exposure are continued risk factors for disease. Residual disease in children <5 years was largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurred in children who have not received adequate doses of PCV-13.

Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) in collaboration with GERMS-SA (a nationwide network of clinical microbiology laboratories that participate in an active surveillance programme for pathogens of public health importance) conducts national laboratory-based surveillance for *Neisseria meningitidis, Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*. The surveillance aims to describe the epidemiology of these diseases and monitor the impact of the pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. This report summarises the findings for 2017.

Methods

Approximately 181 South African clinical microbiology laboratories participated in the GERMS-SA surveillance programme in 2017, including 26 enhanced surveillance sites (ESS).[1] The population under surveillance in 2017 was estimated at 56.5 million.[2] Diagnostic laboratories reported case patients to the NICD using laboratory case report forms according to a standard case definition: the isolation of the organism under surveillance from any normally sterile site. If available, isolates from case patients were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. Culture negative cases with a positive supplementary test e.g. Gram stain and/or antigen detection, were also reported and their samples were submitted for molecular detection of the 3 pathogens. At ESS, surveillance officers completed clinical case report forms electronically using the Mobenzi application on mobile phones for patients with laboratory-confirmed invasive meningococcal disease, invasive *H. influenzae* disease and invasive pneumococcal disease, by case patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status, and patient outcome. Case patients were followed up for the duration of their hospital admission. Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on a Microsoft Access database. A surveillance audit was performed for NHLS laboratories in all provinces using the NHLS Central Data Warehouse (CDW). The audit was designed to obtain basic demographic and laboratory data from additional case patients with laboratory-confirmed disease not already reported to GERMS-SA by participating laboratories; these cases are included in this report. Incidence was calculated using mid-year population estimates for 2016 and 2017 from Statistics South Africa.[2] Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/ NHLS.

Results and Discussion

Neisseria meningitidis

In 2017, 136 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 70 (51%) were viable isolates received and 9 (7%) were detected on audit. The overall disease incidence was 0.24 cases per 100 000 population, similar to that in 2016 (0.23/100 000). Incidence was highest in the Western Cape Province (0.75/100 000) followed by Gauteng (0.29/100 000), Eastern Cape (0.29/100 000) and Free State provinces (0.21/100 000) (Table 1). Disease peaked in the winter and spring months (June to October) with a further peak in December (Figure 1). No outbreaks of meningococcal disease were detected in 2017. Cerebrospinal fluid was the most common specimen from which meningococci were identified (94/136, 69%) (Table 2). Serogroup B (45/108, 42%) was the most common serogroup causing disease, followed by W (27/108, 25%) and Y (21/108, 19%) (Table 3; Figure 2). IMD occurred more frequently in males (73/133, 55%) than females. Incidence was highest in children <5 years with a small increase in the 15-24 year age category. Infants had the highest incidence of IMD for all serogroups (Figure 10). Of the viable isolates tested for antimicrobial susceptibility, 6% (4/70) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) >0.06µg/ml, all were susceptible to 3rd generation cephalosporin and ciprofloxacin.

Thirty-nine (29%) IMD patients presented to the enhanced surveillance sites and 35/39 (90%) had additional clinical information available. The median time for each admission was 7 days (interquartile range 5-10 days). The case-fatality ratio was 17% (6/35); 3 of these patients died on the day of admission, 2 died after 6 days and 1 after 8 days. Twenty-eight percent of patients with HIV status available were HIV-coinfected (8/29). For those who survived to discharge from hospital, 6/29 (21%) suffered sequelae following IMD. These included 1 patient requiring amputation of the toes, 1 with skin scarring following necrotic lesions, 1 developed hydrocephalus, 2 experienced new onset of seizures, and 1 with loss of vision and new onset of seizures.

Invasive meningococcal disease incidence remained low for 2017. Serogroup B predominated once again, particularly in the Western Cape Province, driving up the incidence in that province. Penicillin non-susceptibility was below 10%, justifying the continued recommendation of high-dose penicillin as the first-line therapy for confirmed IMD. Although uncommon, meningococcal disease in South Africa is a devastating illness largely affecting young children and has an in-hospital case fatality of 17%, with 21% of patients suffering sequelae post-discharge from hospital.

Table 1. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2016 and 2017, n=267 (including audit cases).

Province	2016		2017	
	n	Incidence rate*	N	Incidence rate*
Eastern Cape	15	0.21	19	0.29
Free State	2	0.07	6	0.21
Gauteng	36	0.27	41	0.29
KwaZulu-Natal	11	0.10	8	0.07
Limpopo	1	0.02	3	0.05
Mpumalanga	5	0.12	4	0.09
Northern Cape	2	0.17	1	0.08
North West	5	0.13	5	0.13
Western Cape	54	0.86	49	0.75
South Africa	**131**	**0.23**	**136**	0.24

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

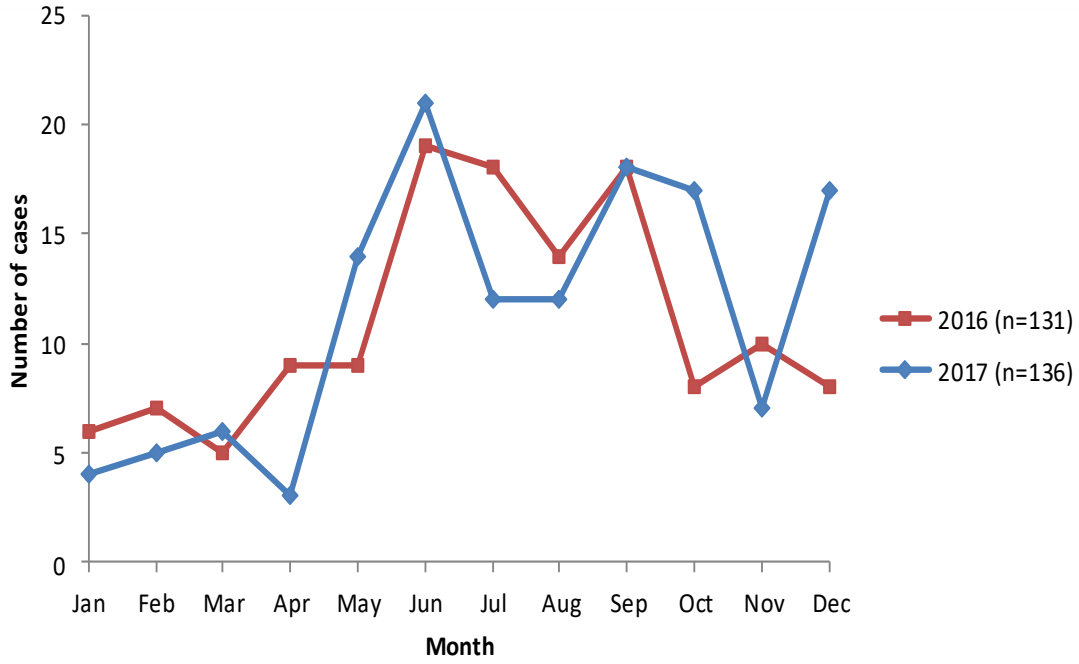

Figure 1. Numbers of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2016-2017, n=267.

Table 2. Number and percentages of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2016 and 2017, n=267.

Site of specimen	2016		2017	
	n	%	n	%
Cerebrospinal fluid	92	70	94	69
Blood	38	29	42	31
Other	1	1	0	0
Total	**131**		**136**	

Table 3. Numbers of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2017, n=136*.

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	NG**	Total
Eastern Cape	2	0	6	5	3	3	0	0	19
Free State	0	0	3		2	1	0	0	6
Gauteng	7	0	11	6	8	9	0	0	41
KwaZulu-Natal	3	0	3	0	0	2	0	0	8
Limpopo	3	0	0	0	0	0	0	0	3
Mpumalanga	3	0	0	1	0	0	0	0	4
Northern Cape	1	0	0	0	0	0	0	0	1
North West	4	0	0	0	1	0	0	0	5
Western Cape	5	0	22	2	13	6	0	1	49
South Africa	**28**	**0**	**45**	**14**	**27**	**21**	**0**	**1**	**136**

*108 (79%) with viable isolates or specimens available for serogrouping/genogrouping; ** NG: Non-groupable (including 1 that was negative for genogroups A, B, C, W, Y, X by polymerase chain reaction)

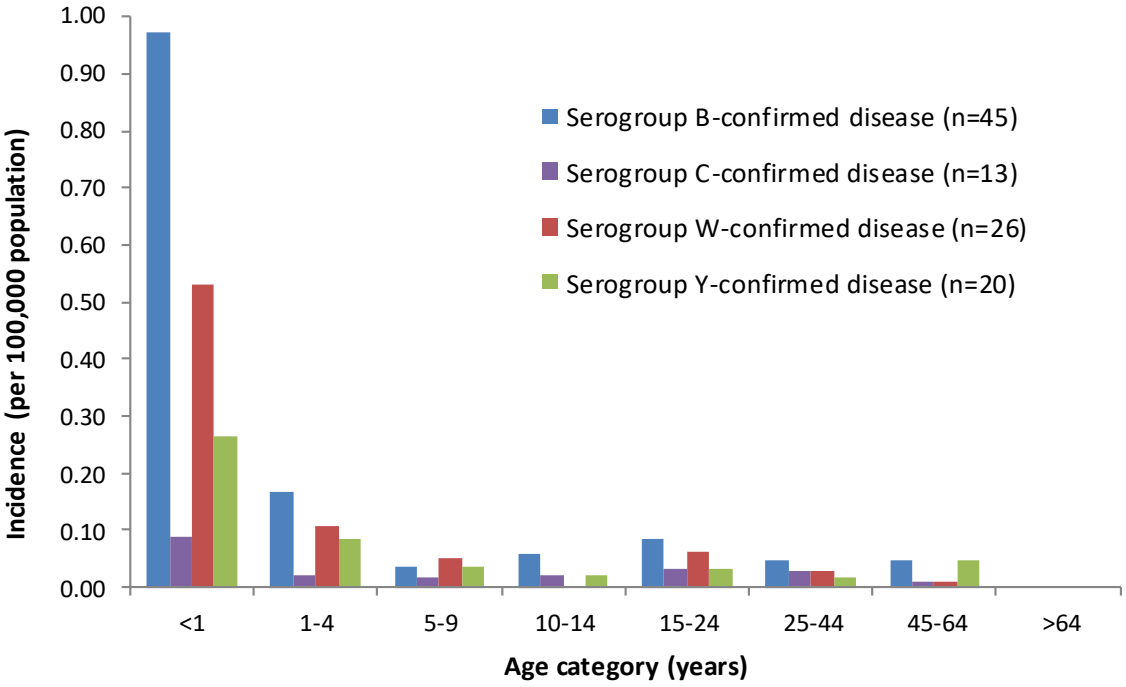

Figure 2. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2017, n=136** (**age unknown for n=3; specimens or viable isolates unavailable for serogrouping n=28; one Non-groupable specimen).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Haemophilus influenzae

There were 313 cases of invasive *H. influenzae* (HI) disease identified through the surveillance programme in 2017, of which 33% (103) were detected on audit and 59% (184) had either viable isolates (118) or specimens (66) available for serotyping (Table 4). Ten cases were co-infected with invasive *S. pneumoniae.* Western Cape Province (112/313, 36%) reported the highest number of cases, followed by Gauteng Province (84/313, 27%) (Table 4). Twenty-two percent of cases (41/184) were serotype b (Hib) and non-typeable (HNT) disease was found in 64% (118/184) (Table 4). Most cases were isolated from blood, however Hib isolates were more likely than HNT isolates to be found in CSF (19/41, 46% versus 11/118, 9%, p<0.001) (Table 5). Children <5 years had the highest burden of all types of invasive HI, followed by a second peak in the 25-44 year age group (Figure 3). Incidence of Hib in infants was 1.6 per 100 000, decreasing to 0.08 per 100 000 in 1-4 year olds, similar to that of 2016 (Figure 4 and 5). HNT incidence was also highest in infants (2.3 per 100 000) and peaked again in 45-64 year age group (0.3 per 100 000). Since 2010, Hib incidence in children <1 year has decreased significantly from 5.2 to 1.6 cases per 100 000 (p<0.001); and remained below 0.3 per 100 000 in 1-4 year olds, since 2012 (Figure 5). Seventeen percent (4/23) of Hib isolates and 7% (5/76) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Twenty-four cases of Hib disease occurred in children <15 years of age and vaccine history was available for 54% (13/24). Thirty-eight percent (5/13) of these children with invasive Hib had received appropriate doses of Hib vaccine for their age, and were possible vaccine failures, whilst 54% (7/13) had not received appropriate Hib vaccine doses for their age. The remaining child only had a verbal history of having received childhood vaccinations.

Clinical information was available for 87% (129/149) of cases presenting to the enhanced surveillance sites (ESS). Patients were admitted for a median of 9 days (interquartile range (IQR) 2-21). Case fatality was 29% (36/126) and median time to death was within one day of admission (IQR 0-9). Case fatality appeared to be lower amongst those with Hib than with HNT disease, but this did not reach statistical significance (13% (2/15) vs. 29% (14/49), p=0.3). Amongst those with known HIV status, 33% (30/92) were HIV infected. Conditions other than HIV predisposing to HI disease were reported in 71/129 (55%) patients – the most common conditions included chronic lung disease, underlying cardiac disease, malignancy, prematurity and history of smoking. Of 20 patients at ESS with HI on CSF: 25% (4/20) died during their hospitalization, and 25% (4/16) who survived to discharge suffered sequelae – these included 2 with new onset seizures, 1 with hydrocephalus and 1 with weakness of the limbs.

Overall incidence of HI remained low and HNT accounted for the majority of cases. The highest rates of disease were seen in infants for both Hib and HNT, with HNT incidence increasing with age. Case-fatality ratios were high (29%) and long-term sequelae following meningitis occurred in 25% of cases. The majority of children <15 years of age with Hib had not been fully vaccinated, highlighting the importance of Hib vaccinations in children under 2 years.

Table 4. Numbers of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2017, n=313*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	20	1	2	0	0	0	2	8	33
Free State	3	1	0	0	0	0	0	9	13
Gauteng	45	1	15	0	0	1	2	20	84
KwaZulu-Natal	22	1	3	1	1	0	2	11	41
Limpopo	3	0	5	0	0	0	0	1	9
Mpumalanga	6	0	0	1	0	0	0	1	8
Northern Cape	2	0	0	0	0	0	0	3	5
North West	4	0	2	0	0	0	1	1	8
Western Cape	24	5	14	2	0	0	3	64	112
South Africa	**129**	**9**	**41**	**4**	**1**	**1**	**10**	**118**	**313**

*184 (59%) with specimens or viable isolates available for serotyping.

Table 5. Numbers and percentages of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2017, n=313.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	28	22	19	46	9	36	11	9
Blood	62	48	21	51	15	60	72	61
Other	39	30	1	2	1	4	35	30
Total	**129**		**41**		**25**		**118**	

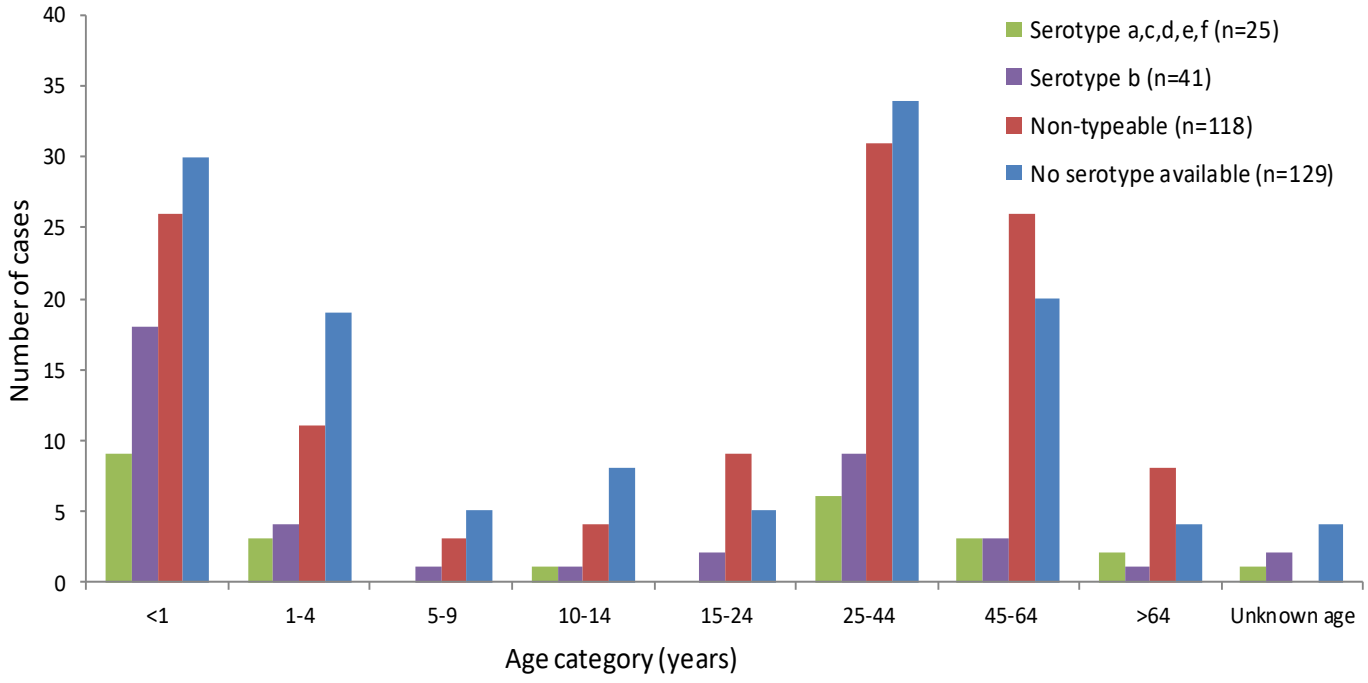

Figure 3. Numbers of laboratory-confirmed, invasive, *Haemophilus influenzae* cases reported to GERMS-SA by serotype and age group, South Africa, 2017, n=313 (age unknown for n=7; specimens or viable isolates unavailable for serotyping for n=129).

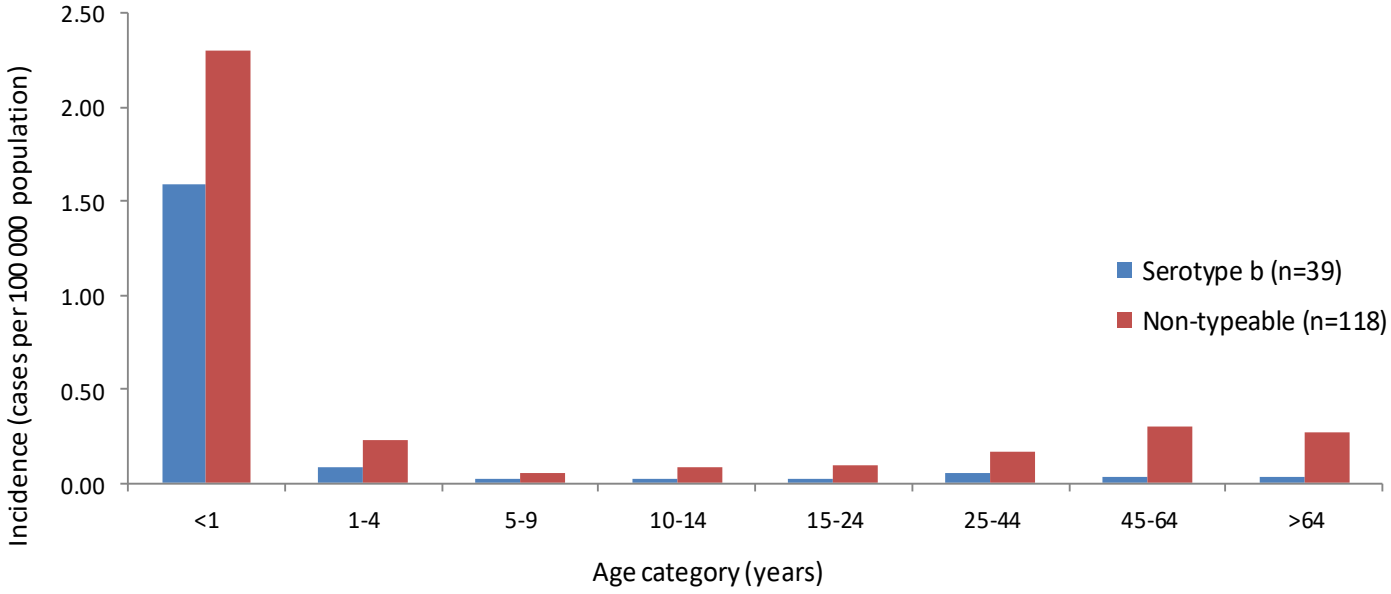

Figure 4. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype b and non-typeable, South Africa, 2017, n=313 (age unknown, n=3; viable isolates unavailable for serotyping, n=129; other serotypes from cases with known age, n=24).

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

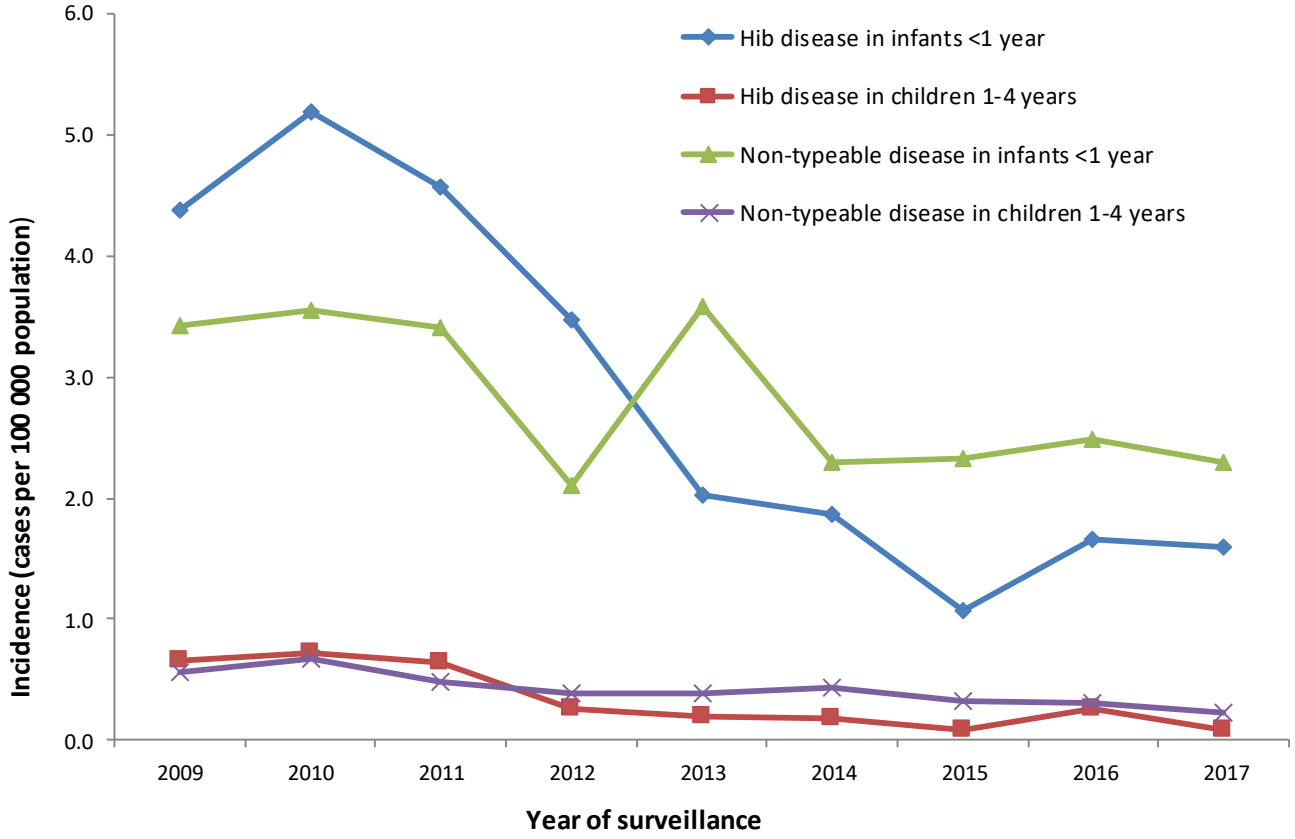

Figure 5. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b disease reported to GERMS-SA in children <5 years old, South Africa, 2009-2017.

**Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.*

Streptococcus pneumoniae

The incidence of invasive pneumococcal disease (IPD) in 2017 was similar to that in 2016 (4.3 vs 4.4 per 100 000 population, p=0.9) (Table 6). IPD incidence varied by province with the highest incidence seen in the Western Cape (10.4 per 100 000 population) followed by Gauteng Province (6.1 per 100 000 population) (Table 6).

Since the introduction of the pneumococcal conjugate vaccine (PCV-7) into the Expanded Programme on Immunisation (EPI) in 2009, and the replacement of PCV-7 with PCV-13 in 2011, there was a 79% reduction in IPD in children <5 years (from 30 per 100 000 population in 2005 to 6 per 100 000 population in 2017, p<0.001). There was also a 46% reduction in IPD in those aged five years and older (from 7 per 100 000 population in 2005 to 4 per 100 000 population in 2017). In 2017, the highest burden of IPD was still in infants (20 per 100 000 population), followed by the 45-64 year age group (7 per 100 000 population) (Figure 6). Ten patients with IPD were co-infected with invasive *H. influenzae*. The majority of cases were isolated from blood culture specimens (61%, 1480/2441) (Table 7). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 29% (439/1531) of IPD isolates, the highest proportion being in children 1-4 years of age (44%) (Table 8, Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 7% (114/1531) of isolates from all specimens, and amongst 5% (19/388) of IPD isolated from CSF. Serogroups 8, 12F, 19A, 3 and 19F were the most predominant serogroups causing IPD in 2017. Amongst children <5 years, serogroup 8 (35/201) caused the bulk of disease followed by serogroups 15A (14/201) and 19A (13/201) (Figure 8).

Unfortunately, only 55% (207/374) of IPD isolates from children <5 years-of-age were sent to the NICD for serotyping (Figure 9). Of these, 20% (41/207) were serotypes containing PCV-13 (Table 9).

Thirty-nine percent (952/2441) of IPD patients presented to the enhanced surveillance sites (ESS), and 871/952 (91%) had additional clinical information available. Patients were admitted for a median hospital stay of 8 days (interquartile range (IQR) 2-15) and most deaths occurred within 2 days of admission (IQR 1-7). Overall case fatality was 32% (274/846). HIV-coinfection was present in 64% (437/681) of IPD patients, and 37% (29/78) of infants, with maternal HIV-status available, were HIV exposed (6 HIV-infected and 23 HIV-uninfected infants). Forty-nine percent (406/825) of patients had an underlying medical condition (excluding HIV infection) predisposing them to IPD.

Of 236 patients at ESS with pneumococcus on CSF, 40% (94/236) died during their hospitalization, and 33% (47/142) who survived to discharge suffered at least one sequelae – these included new onset seizures (15), limb weakness/ paralysis (12), hearing loss (10), hydrocephalus (5), and loss of vision (4). Twenty-four episodes of IPD caused by serotypes present in the PCV-13 vaccine occurred in children <10 years-of-age at ESS. Vaccine history was available for 67% (16/24). Eighty-one percent (13/16) of these children had not received adequate PCV-13 doses for their age and 2 neonates were too young to receive vaccine. Only one child who received 3 PCV-13 doses could possibly be considered a vaccine failure.

IPD incidence remained low in 2017, with marked reductions seen amongst all age categories post introduction of PCV into the expanded programme on immunization. Children <1 year-of-age had the highest incidence of disease followed by a peak in the 45-64 year age category (a shift from the 25-44 year age category peak seen in previous years). Penicillin and ceftriaxone susceptibility of IPD isolates remain unchanged. HIV infection and infant HIV exposure remain risk factors for disease. Pneumococcal meningitis has high mortality and morbidity. Residual disease in children <5 years was largely due to non-vaccine serotypes, and the majority of vaccine-type disease occured in children who have not received adequate doses of PCV-13. Clinicians should ensure that all children (and adults with risk factors for IPD) receive adequate vaccine doses to protect them from this serious illness. The number of viable isolates submitted to the NICD for serotyping is still low, and participating laboratories are urged to remember to forward pneumococci from normally sterile sites to the NICD.

Table 6. Numbers of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2016 and 2017, n=4873 (including audit cases).

Province	2016		2017	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	208	2.95	208	3.20
Free State	147	5.14	117	4.08
Gauteng	854	6.33	868	6.08
KwaZulu-Natal	320	2.89	269	2.43
Limpopo	84	1.45	74	1.28
Mpumalanga	102	2.36	105	2.36
Northern Cape	42	3.52	53	4.37
North West	73	1.93	72	1.87
Western Cape	602	9.57	675	10.37
South Africa	2432	4.35	2441	4.32

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

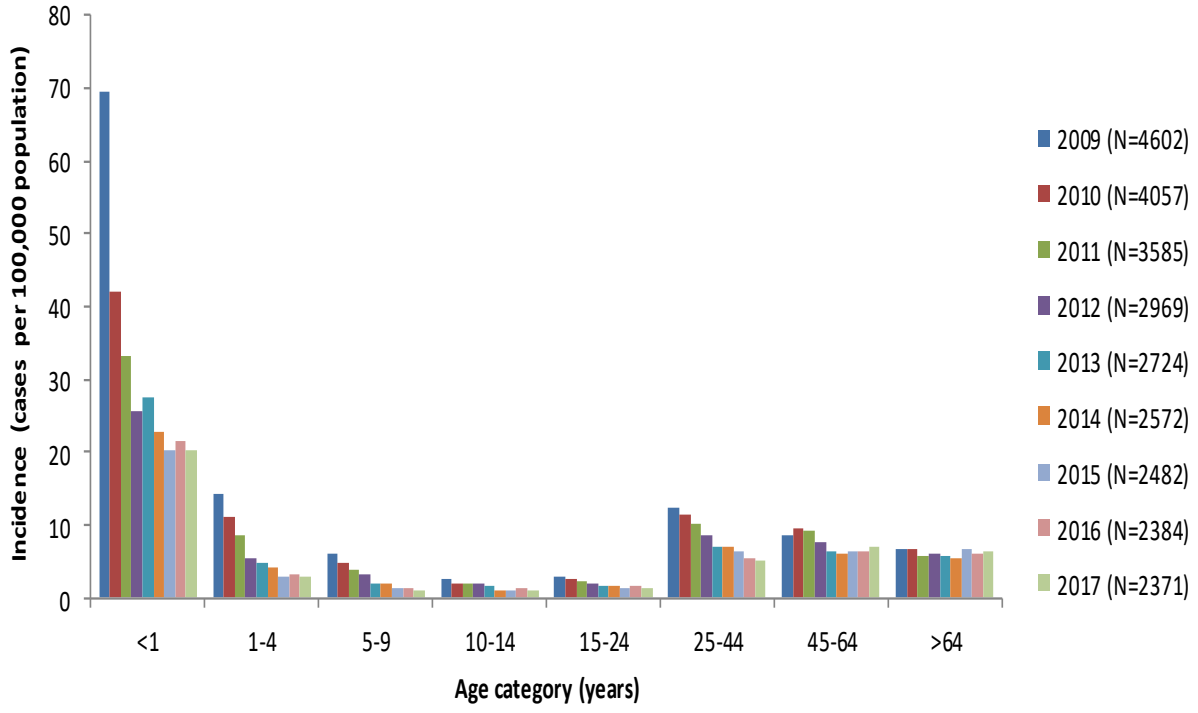

Figure 6. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease reported to GERMS-SA South Africa, 2009 through 2017.

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Table 7. Numbers and percentages of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2016 and 2017, n=4873.

Site of specimen	2016		2017	
	n	%	n	%
Cerebrospinal fluid	859	35	792	32
Blood	1379	57	1480	61
Other	194	8	169	7
Total	**2432**		**2441**	

Table 8. Numbers and percentages of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2017, n=2441.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	115	70	75	17	18	6	6
Free State	45	52	72	18	25	2	3
Gauteng	363	358	71	107	21	40	8
KwaZulu-Natal	152	70	60	38	32	9	8
Limpopo	32	31	74	10	24	1	2
Mpumalanga	40	39	60	20	31	6	9
Northern Cape	12	31	76	7	17	3	7
North West	37	28	80	5	14	2	6
Western Cape	114	413	74	109	19	39	7
South Africa	**910**	**1092**	71	**331**	22	**108**	7

*2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

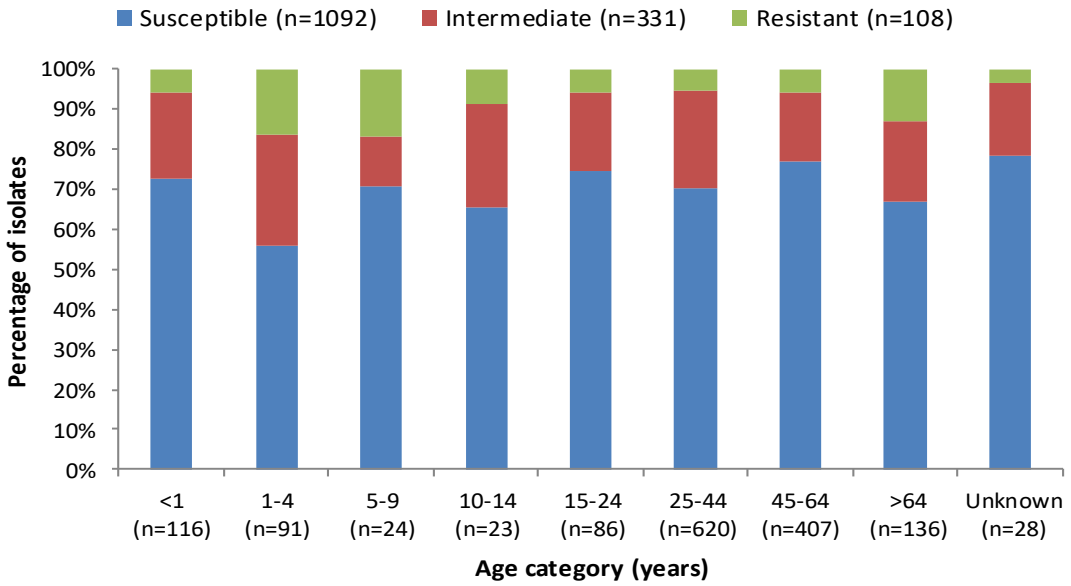

Figure 7. Numbers of laboratory-confirmed, invasive pneumococcal disease cases reported to GERMS-SA by age group and penicillin susceptibility, South Africa, 2017, n=2441 (n=1531 with viable isolates).

2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

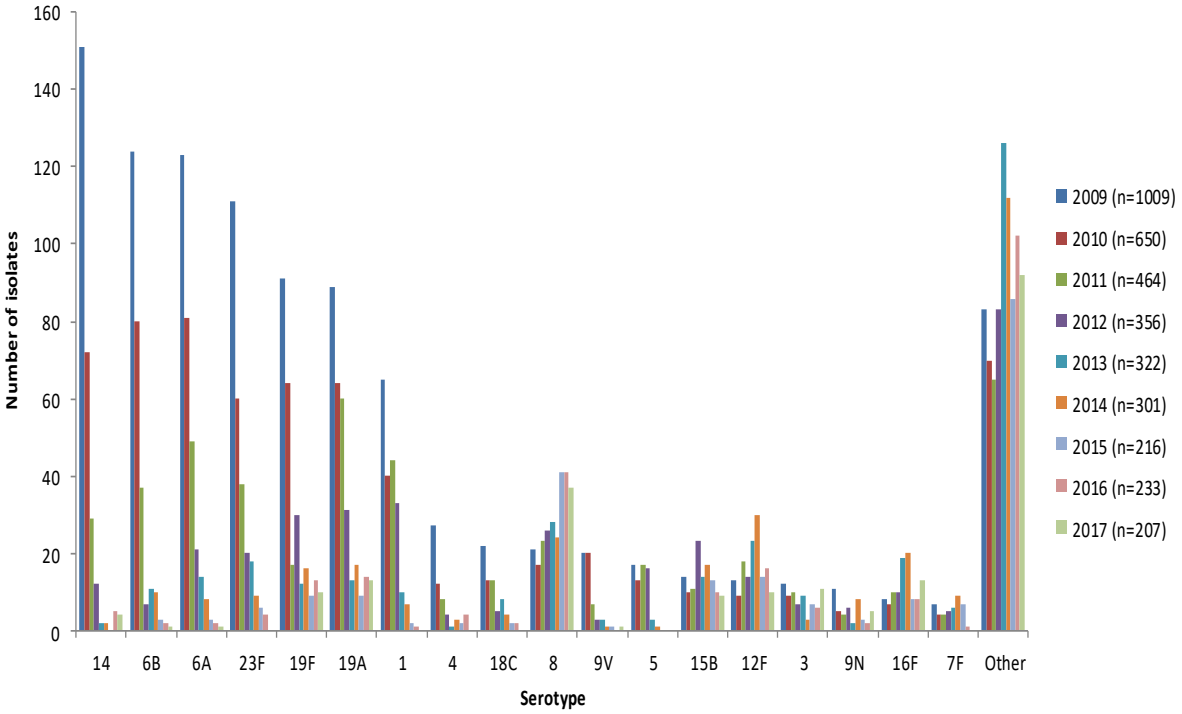

Figure 8. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA in children <5 years, South Africa, 2009-2017.

2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates; 2017: N=374, n=167 without viable isolates.

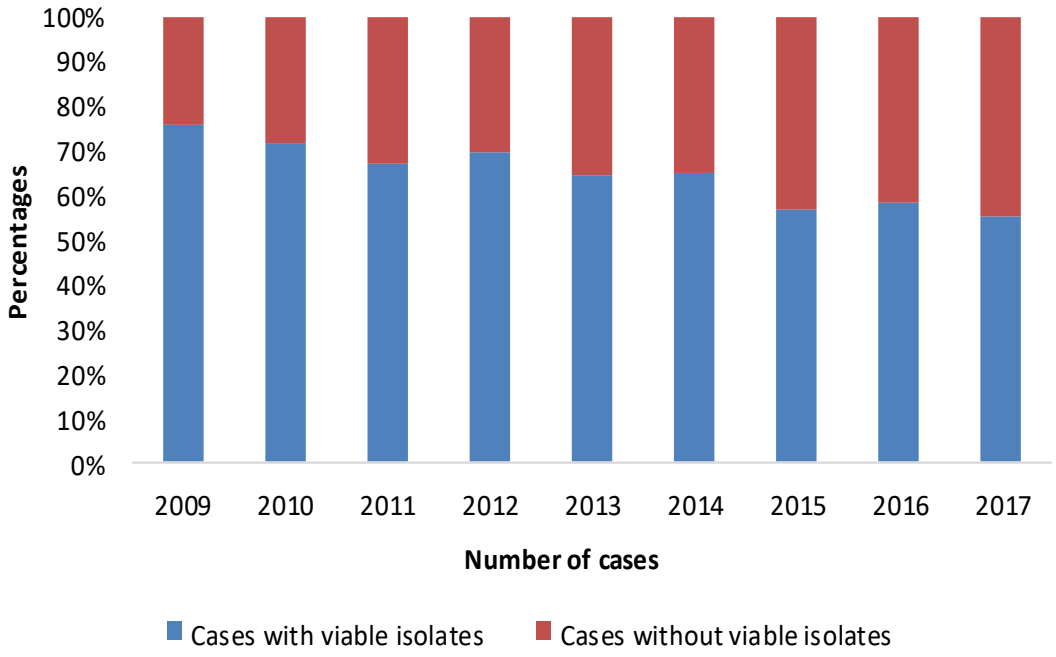

Figure 9. Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA in children <5 years, South Africa, 2009-2017.

2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates; 2017: N=374, n=167 without viable isolates.

Table 9. Numbers and percentages of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2017, n=374 (n=207 with viable isolates).

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes**		13-valent serotypes***	
		n	%	n	%	n	%	n	%
Eastern Cape	7	2	29	0	0	2	29	2	29
Free State	7	1	14	0	0	1	14	5	71
Gauteng	91	6	7	0	0	6	7	15	16
KwaZulu-Natal	15	2	13	1	7	2	13	5	33
Limpopo	11	0	0	0	0	0	0		0
Mpumalanga	7	0	0	0	0	0	0	3	43
Northern Cape	1	0	0	0	0	0	0		0
North West	5	1	20	0	0	1	20	2	40
Western Cape	63	4	6	0	0	4	6	9	14
South Africa	**207**	**16**	**8**	**1**	**0.5**	**16**	**8**	**41**	**20**

All serotypes included in each of the categories: 7-valent serotypes*: 4, 6B, 9V, 14, 18C, 19F, 23F
10-valent serotypes**: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
13-valent serotypes***: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A

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