# GERMS-SA ANNUAL SURVEILLANCE REPORT FOR LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL, *HAEMOPHILUS INFLUENZAE*, PNEUMOCOCCAL, GROUP A STREPTOCOCCAL AND GROUP B STREPTOCOCCAL INFECTIONS, SOUTH AFRICA, 2019

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**Summary**

The Centre for Respiratory Diseases and Meningitis (CRDM), of the National Institute for Communicable Diseases (NICD), through the GERMS-SA platform, performs national laboratory-based surveillance on five invasive bacterial diseases including: *Neisseria meningitidis, Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Streptococcus agalactiae.* The surveillance programme aims to describe the epidemiology of these invasive infections and monitor the impact of preventive measures, such as routine vaccination, over time. Diagnostic microbiology laboratories in South Africa are requested to submit isolates meeting the GERMS-SA surveillance case definition to the CRDM reference laboratory for further phenotypic and genotypic characterisation. Basic demographic data are collected from the patients' laboratory reports for all isolates detected. At selected enhanced surveillance hospital sites, trained surveillance officers interview the patients and review the medical records for all *Neisseria meningitidis, Haemophilus influenzae* and pneumococcal disease episodes. Invasive meningococcal disease incidence remained low in 2019 with serogroup B causing most disease in young infants, serogroup Y responsible for a peak in adolescents and serogroup W predominating through adulthood. In-hospital case fatality for IMD was 19%, with 20% of survivors suffering sequelae post-hospital discharge. Incidence of invasive *Haeomophilus influenzae* remained low with non-typeable *Haemophilus influenzae* causing most disease. Infants had the highest rates of *H. influenzae* type b and non-typeable (HNT) disease, with HNT incidence increasing into adulthood. In-hospital case fatality was 27% and long-term sequelae following meningitis occurred in 27% of survivors. Invasive pneumococcal disease (IPD) incidence has remained stable over the past 5 years across all age categories. Infants still have the highest disease incidence, with disease peaking again after age 25 years. Residual IPD in children aged <5 years is largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurs in children who have not received adequate doses of pneumococcal conjugate vaccine (PCV13). Serotypes causing IPD in those aged ≥5 years remain diverse including both vaccine and non-vaccine serotypes. Infants and the elderly experience the highest incidence of invasive Group A Streptococcal (GAS) infections in South Africa with the

majority of isolates being susceptible to first-line antibiotics. In 2020, clinical data will be collected from persons with invasive GAS infections admitted to our enhanced surveillance sites and molecular typing of all the 2019 and 2020 isolates will commence. Incidence of early and late onset invasive Group B Streptococcus (GBS) appears low, however this may be due to low specimen taking practices in many areas of South Africa. Most invasive GBS in infants was caused by serotypes III and Ia, although a range of serotypes was found to be causing invasive GBS in other age groups. This was the first year of active surveillance for invasive GBS and no clinical data were collected. Clinical laboratories are encouraged to send all isolates meeting the GERMS-SA case definition to the NICD so that further characterisation and serotyping can be done. In 2020, enhanced clinical surveillance will begin for both GAS and GBS at selected sites in order to report on risk factors predisposing to invasive infections and outcome following infection.

**Introduction**

The Centre for Respiratory Diseases and Meningitis (CRDM), of the National Institute for Communicable Diseases (NICD), through the GERMS-SA platform, performs national laboratory-based surveillance on invasive bacterial diseases such as: *Neisseria meningitidis, Haemophilus influenzae*, *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Streptococcus agalactiae.* The surveillance aims to describe the epidemiology of these diseases and monitor the impact of routine pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. Surveillance has been ongoing since 2003, however this is the first year of *Streptococcus pyogenes* (Group A Streptococcus) and *Streptococcus agalactaie* (Group B Streptococcus) surveillance. This report summarises the findings for all pathogens in 2019.

**Methods**

Approximately 220 South African clinical microbiology laboratories participated in the GERMS-SA surveillance programme in 2019, including 31 enhanced surveillance hospital sites (ESS).[1]

The South African population under surveillance in 2019 was estimated at 58.8 million, with 954 532 births.[2,3] HIV-prevalence in South Africa is 13.5%, with 7.94 million persons living with HIV.[2]

The standard case definition for all five pathogens included the detection of the organism under surveillance from any normally sterile site. In addition, non-invasive isolates of *Streptococcus pyogenes* from skin or soft tissue were accepted if the accompanying diagnosis was necrotising fasciitis or septic shock syndrome. Diagnostic microbiology laboratories reported case patients to the NICD using laboratory case report forms and submitted available isolates from case patients on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. Only antimicrobial susceptibility testing was performed on *Streptococcus pyogenes* isolates in 2019. Genotypic characterisation of these isolates will be conducted at a later stage. Culture-negative cases with a positive supplementary test e.g. Gram stain and/or antigen detection were also reported, and samples were submitted for molecular detection of *Streptococcus pneumoniae, Haemophilus influenzae* or *Neisseria meningitidis*. Repeat isolates from the same patient were counted as a single case if they occurred within 21 days of the first culture.

At ESS surveillance officers completed clinical case report forms using the Mobenzi application on electronic tablets for patients with laboratory-confirmed invasive meningococcal, invasive *H. influenzae* 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 the 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 2018 and 2019 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.

***Neisseria meningitidis***

**Results**

In 2019, 111 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 43 (39%) viable isolates were received and 16 (14%) cases were detected on audit. The overall disease incidence remained low at 0.19 cases per 100 000 population, similar to that in 2018 (0.22/100 000). Incidence was highest in the Western Cape Province (0.56/100 000) followed by Gauteng (0.24/100 000) and Eastern Cape provinces (0.18/100 000) (Table 1). Most cases were sporadic, and disease peaked from winter through spring (May to October), with a further upsurge in December (Figure 1). Cerebrospinal fluid was the most common specimen from which meningococci were identified (70/111, 63%) (Table 2). Ninety-five percent (89/94) of IMD was caused by 3 serogroups - B (36/94, 38%), Y (27/94, 29%) and W (25/94, 27%) (Table 3). Incidence of IMD was highest in children <1 year (1.14/100 000) (Figure 2). Although the different serogroups occurred across most age-categories, serogroup B was most predominant in children aged <5 years, serogroup Y in persons aged 5-24 years and serogroup W in persons aged ≥25 years. (Figure 2) Of those with known sex, IMD occurred more frequently in males (59/109, 54%). Of the viable isolates tested for antimicrobial susceptibility, 26% (11/43) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) between 0.094µg/ml and 0.25µg/ml, and all were susceptible to 3rd generation cephalosporin and ciprofloxacin.

**Table 1.** Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=236 (including audit cases).

| Province | 2018 | | 2019 | |
|---|---|---|---|---|
| | n | Incidence rate* | N | Incidence rate* |
| Eastern Cape | 26 | 0.40 | 12 | 0.18 |
| Free State | 2 | 0.07 | 3 | 0.10 |
| Gauteng | 37 | 0.25 | 37 | 0.24 |
| KwaZulu-Natal | 8 | 0.07 | 13 | 0.12 |
| Limpopo | 4 | 0.07 | 2 | 0.03 |
| Mpumalanga | 2 | 0.04 | 1 | 0.02 |
| Northern Cape | 1 | 0.08 | 1 | 0.08 |
| North West | 6 | 0.15 | 4 | 0.10 |
| Western Cape | 39 | 0.59 | 38 | 0.56 |
| **South Africa** | **125** | **0.22** | **111** | 0.19 |

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

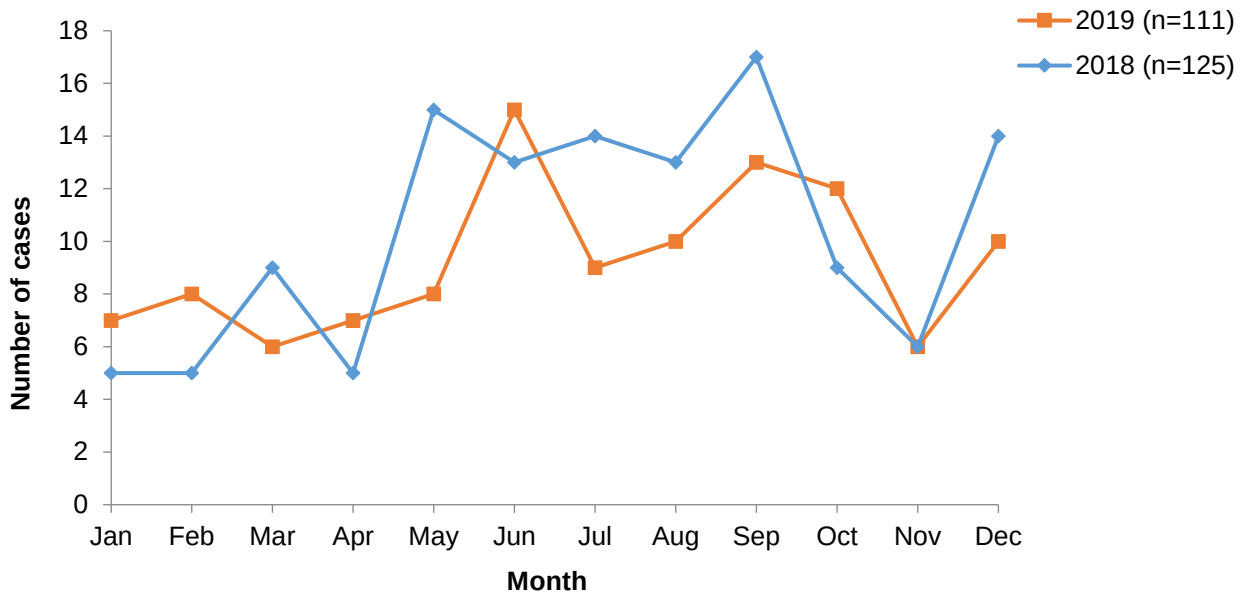


**Figure 1.** Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2018-2019, n=236.

**Table 2.** Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=236**.**

| Site of specimen | 2018 | | 2019 | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid | 82 | 66 | 70 | 63 |
| Blood | 43 | 34 | 41 | 37 |
| Other | 0 | 0 | 0 | 0 |
| **Total** | **125** | | **111** | |

**Table 3.** Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2019, n=111*.

| Province | Serogroup | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Serogroup not available | A | B | C | W | Y | Z | E** | Total |
| Eastern Cape | 1 | 0 | 2 | 0 | 1 | 8 | 0 | 0 | 12 |
| Free State | 0 | 0 | 0 | 0 | 2 | 1 | 0 | 0 | 3 |
| Gauteng | 7 | 0 | 10 | 2 | 12 | 6 | 0 | 0 | 37 |
| KwaZulu-Natal | 3 | 0 | 6 | 0 | 3 | 1 | 0 | 0 | 13 |
| Limpopo | 1 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 2 |
| Mpumalanga | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| Northern Cape | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 |
| North West | 1 | 0 | 2 | 0 | 0 | 1 | 0 | 0 | 4 |
| Western Cape | 4 | 0 | 14 | 3 | 7 | 9 | 0 | 1 | 38 |
| **South Africa** | **17** | **0** | **36** | **5** | **25** | **27** | **0** | **1** | **111** |

*94 (85%) with viable isolates or specimens available for serogrouping/genogrouping; There were no Non-groupable meningococcal isolates causing invasive disease in 2019.

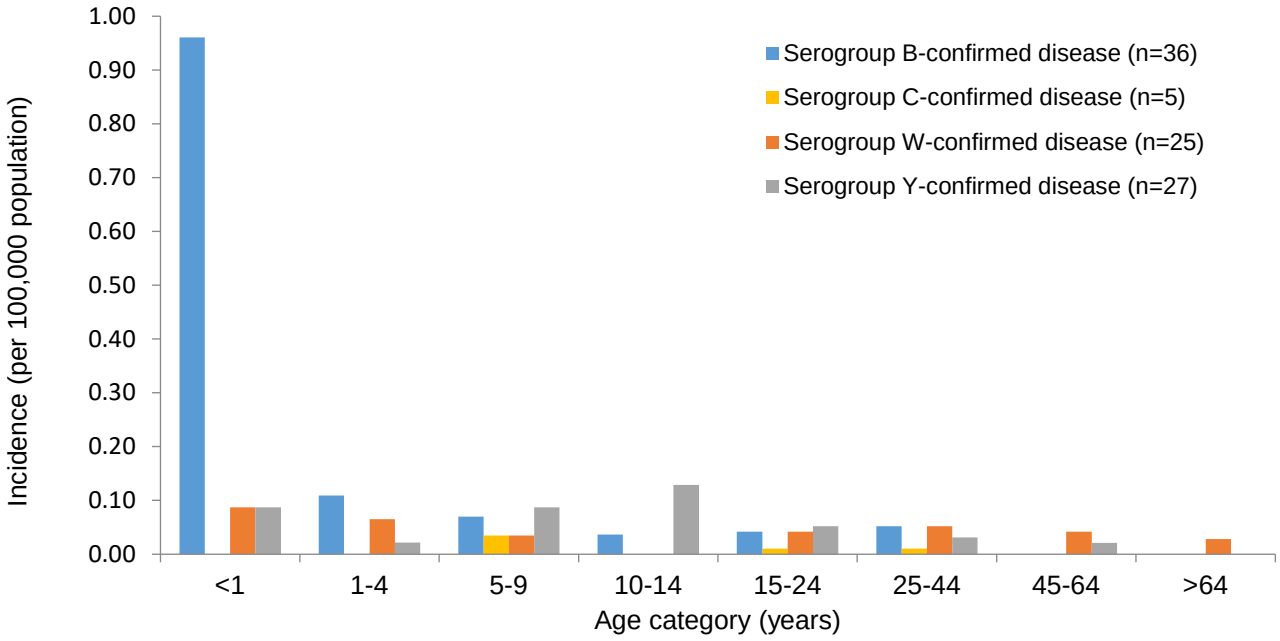


**Figure 2.** Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2019, n=111** (**specimens or viable isolates unavailable for serogrouping n=17; one isolate serogroup E).

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

Thirty-eight (34%) IMD patients presented to the enhanced surveillance sites and 31/38 (82%) had additional clinical information available. The median time for admissions was 10 days (interquartile range 7-13 days). The case-fatality ratio was 19% (6/31); three patients died on the day of admission. Thirty-eight percent of patients with HIV status available were HIV-infected (9/24). For those who survived to discharge from hospital, 5/25 (20%) suffered sequelae following IMD. Two patients developed ongoing seizures, and one each had hearing loss, necrotic skin lesions and hydrocephalus.

**Discussion**

Incidence of IMD in South Africa remains low with a variety of serogroups (B, Y and W) causing disease in the different age-categories. Burden is highest in infants, particularly serogroup B disease, whilst serogroup Y disease has been responsible for a peak in 10-14 year olds. All IMD isolates were susceptible to third generation cephalosporins and an increase in penicillin non-susceptibility of the meningococci was noted. Third generation cephalosporins are frequently used as empiric therapy in patients presenting with meningitis/bacteraemias. Before switching over to high-dose penicillin once IMD is confirmed, clinicians should establish susceptibility of meningococcal isolates to penicillin. Provision of ciprofloxacin as chemoprophylaxis is recommended to all close contacts. Although uncommon, meningococcal disease in South Africa is a devastating illness affecting all age groups. In 2019, in-hospital case fatality was 19%, with 20% of survivors suffering sequelae post discharge from hospital.

***Haemophilus influenzae***

**Results**

There were 259 cases of invasive *Haemophilus influenzae* (HI) disease identified through the surveillance programme in 2019 - 41% (105) were detected on audit and 58% (149) had either viable isolates (109) or specimens (40) available for serotyping (Table 4). Eight cases were co-infected with invasive *Streptococcus pneumoniae*. Incidence of invasive HI disease was 0.44 per 100 000 population. Gauteng Province (88/259, 34%) had the highest number of cases reported, followed by Western Cape Province (78/259, 30%) (Table 4). Twenty-eight percent of cases (41/149) were serotype b (Hib) and non-typeable (HNT) disease was found in 55% (82/149) (Table 4). Most HI cases were isolated from blood (160/259, 62%), however Hib isolates were more likely than HNT isolates to be found in cerebrospinal fluid (CSF) (17/41, 41% versus 6/82, 7%, $p<0.001$) (Table 5). Although HI occurs in all ages, invasive disease is highest in infants followed by adults aged 25-44 years (Figure 3). Hib incidence is still highest in infants even though significant declines have been noted since 2010 (5.2 cases per 100 000 in 2010 to 1.2 cases per 100 000 in 2019 ($p<0.001$)) (Figure 4 and 5). Hib incidence has remained below 0.2 per 100 000 in 1-4 year olds since 2013 (Figure 5). HNT incidence is highest in infants (1.2 per 100 000) dropping substantially throughout the rest of childhood before increasing again in adulthood with a moderate peak from ages 25 years and older (Figure 4). Forty-one percent (12/29) of Hib isolates and 8% (5/60) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Twenty-five cases of Hib disease occurred in children <15 years of age and vaccine history was available for 32% (8/25). Three infants were <6 weeks and thus too young to receive Hib vaccine. Four children had received at least 3 doses of vaccine and were possible vaccine failures. One 3-month old child had only received one dose of Hib vaccine.

**Table 4.** Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2019, n=259*.

| Province | Serotype | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Serotype not available | a | b | c | d | e | f | Non-typeable | Total |
| Eastern Cape | 6 | 2 | 7 | 0 | 1 | 0 | 2 | 7 | 25 |
| Free State | 3 | 0 | 1 | 0 | 0 | 0 | 1 | 3 | 8 |
| Gauteng | 44 | 3 | 10 | 0 | 0 | 0 | 4 | 27 | 88 |
| KwaZulu-Natal | 28 | 0 | 5 | 0 | 0 | 0 | 1 | 8 | 42 |
| Limpopo | 2 | 0 | 1 | 0 | 0 | 0 | 0 | 2 | 5 |
| Mpumalanga | 0 | 0 | 4 | 0 | 0 | 0 | 2 | 0 | 6 |
| Northern Cape | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 |
| North West | 3 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 5 |
| Western Cape | 22 | 3 | 12 | 1 | 0 | 0 | 5 | 35 | 78 |
| **South Africa** | **110** | **8** | **41** | **2** | **1** | **0** | **15** | **82** | **259** |

*149 (58%) with specimens or viable isolates available for serotyping.

**Table 5.** Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2019, n=259.

| Site of specimen | No serotype available | | Serotype b | | Serotypes a, c, d, e, f | | Non-typeable | |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % |
| Cerebrospinal fluid | 19 | 17 | 17 | 41 | 9 | 35 | 6 | 7 |
| Blood | 60 | 55 | 21 | 51 | 17 | 65 | 62 | 76 |
| Other | 31 | 28 | 3 | 7 | 0 | 0 | 14 | 17 |
| **Total** | **110** | | **41** | | **26** | | **82** | |

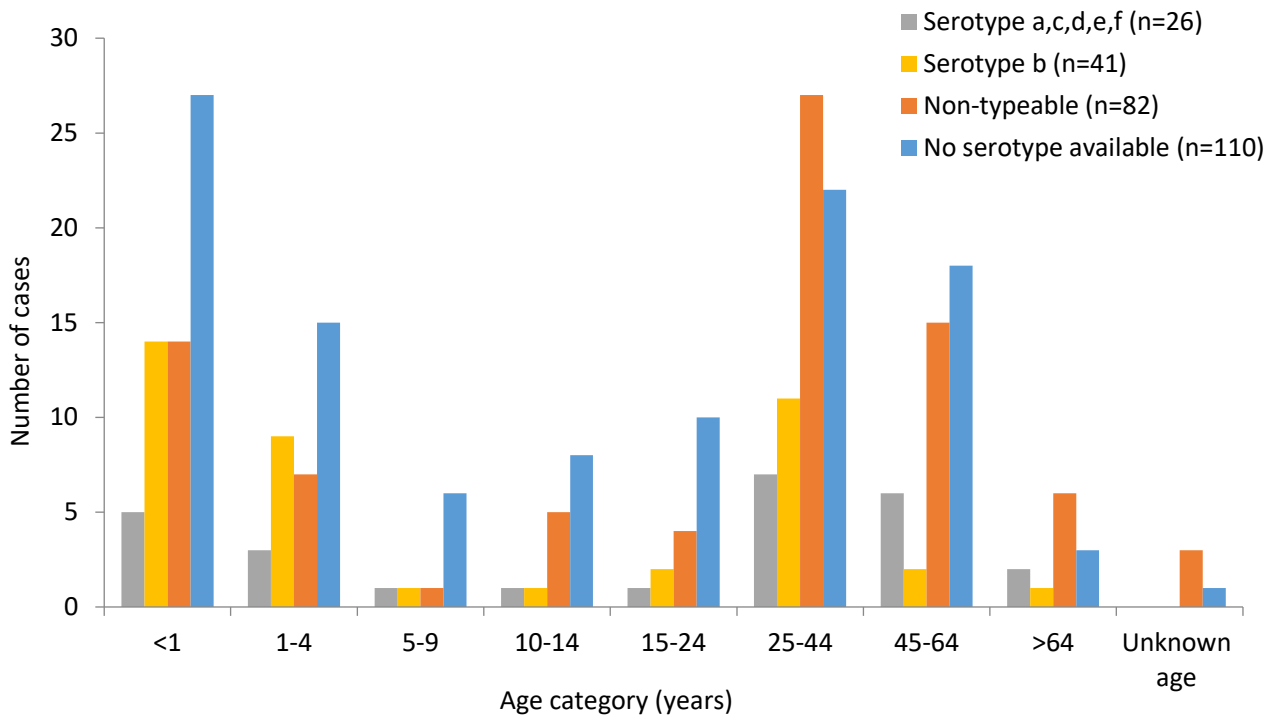


**Figure 3.** Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2019, n=259 (age unknown for n=4; specimens or viable isolates unavailable for serotyping for n=110).

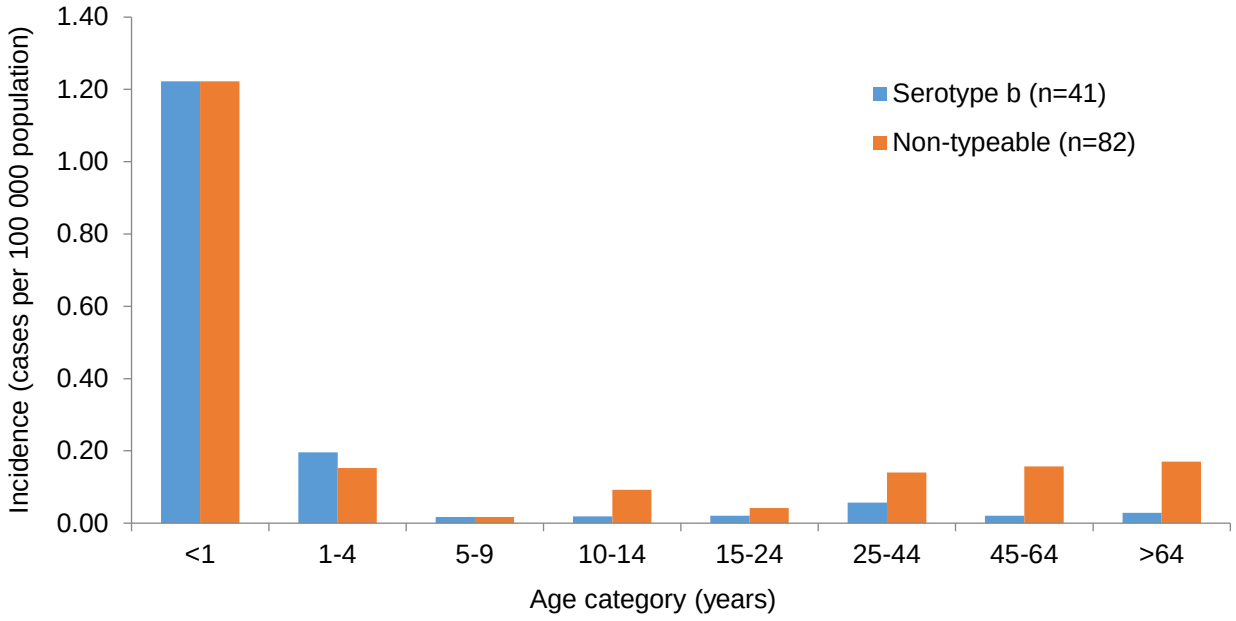


**Figure 4.** Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2019, n=259 (age unknown, n=4; isolates unavailable for serotyping, n=110; other serotypes from cases with known age, n=26).

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

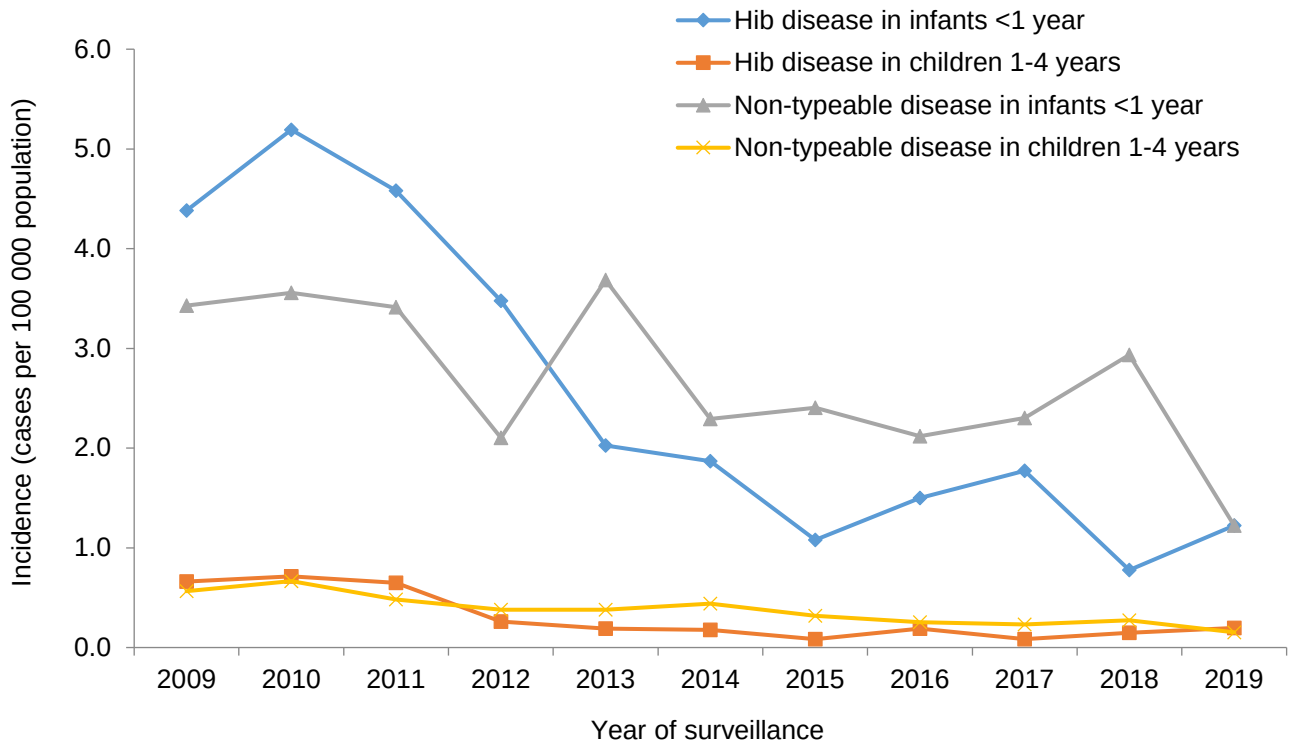


**Figure 5.** Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2019.
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Clinical information was available for 85% (110/130) of cases presenting to the ESS. Patients were admitted for a median of 7 days (interquartile range (IQR) 3-16). Case fatality was 27% (36/110) and median time to death was within one day of admission (IQR 0-4). There was no statistically significant difference between case fatalities of those with Hib or HNT disease (25% (5/20) vs. 23% (11/47), p=0.5). Amongst those with known HIV status, 38% (33/86) were HIV-infected. Conditions other than HIV predisposing to HI disease were reported in 53/98 (54%) patients – the most common conditions included chronic lung disease (10), history of smoking (7), malignancy (7) and prematurity (6). Of the 19 patients at ESS with HI on CSF: eight patients died during their hospitalization, and 27% (3/11) of those who survived to discharge suffered sequelae – one developed ongoing seizures and two developed hydrocephalus.

**Discussion**

Overall incidence of HI remained low in 2019 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 in adults. Many adults with invasive HI infection had an underlying chronic condition, such as chronic lung disease or malignancy. Case-fatality rates are high (27%) and long-term sequelae following meningitis occurred in 27% of survivors. Although many of the children with Hib disease had been fully vaccinated, only a few vaccine histories were obtainable.

***Streptococcus pneumoniae***

**Results**

Invasive pneumococcal disease (IPD) incidence for 2019 remained the same as 2018 at 4 per 100 000 population (Table 6). The highest incidence was seen in the Western Cape (9.3 per 100 000 population) followed by Northern Cape (7.1 per 100 000) and Gauteng provinces (5.1 per 100 000 population) (Table 6). Pneumococcal conjugate vaccine (PCV7) was introduced into the Expanded Programme on Immunisation (EPI) in 2009, and subsequently replaced by PCV13 in 2011. In 2019, peak IPD incidence occurred in infants (20 per 100 000 population), followed by adults (5-6 per 100 000 population in the 25 years and older age categories) (Figure 6). Eight patients with IPD were co-infected with invasive *Haemophilus influenzae* and one with *Neisseria meningitidis*. The majority of IPD cases were isolated from blood specimens (63%, 1490/2359) (Table 7). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 29% (413/1386) of IPD isolates and the highest proportion was in children 1-4 years of age (51%, 40/79) (Table 8 and Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 8% (110/1386) of isolates from all specimens including 8% (29/347) of IPD isolated from CSF. In 2019, serogroups 8, 12F, 19F, 7 and 14 were the most predominant serogroups causing 44% (80/180) of IPD in children <5 years-of-age, whilst serogroups 8, 12F, 3, 19A and 9N caused 43% (511/1194) of disease in persons >5 years (Figure 8A and 8B). Only 59% (1386/2359) of IPD isolates were sent to NICD, of which 1374 were serotyped (Figure 9). Of those serotyped, 22% (39/180) of isolates from children <5 years, and 30% (357/1194) of IPD isolates from person 5 years and older were PCV13-vaccine serotypes (Table 9 and 10).

**Table 6.** Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=4674 (including audit cases).

| Province | 2018 | | 2019 | |
|---|---|---|---|---|
| | n | Incidence rate* | n | Incidence rate* |
| Eastern Cape | 259 | 3.96 | 274 | 4.08 |
| Free State | 106 | 3.59 | 84 | 2.91 |
| Gauteng | 757 | 5.14 | 776 | 5.11 |
| KwaZulu-Natal | 242 | 2.13 | 237 | 2.10 |
| Limpopo | 84 | 1.45 | 97 | 1.62 |
| Mpumalanga | 116 | 2.56 | 102 | 2.22 |
| Northern Cape | 52 | 4.24 | 90 | 7.12 |
| North West | 71 | 1.78 | 66 | 1.64 |
| Western Cape | 628 | 9.48 | 633 | 9.25 |
| **South Africa** | **2315** | **4.01** | **2359** | **4.01** |

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

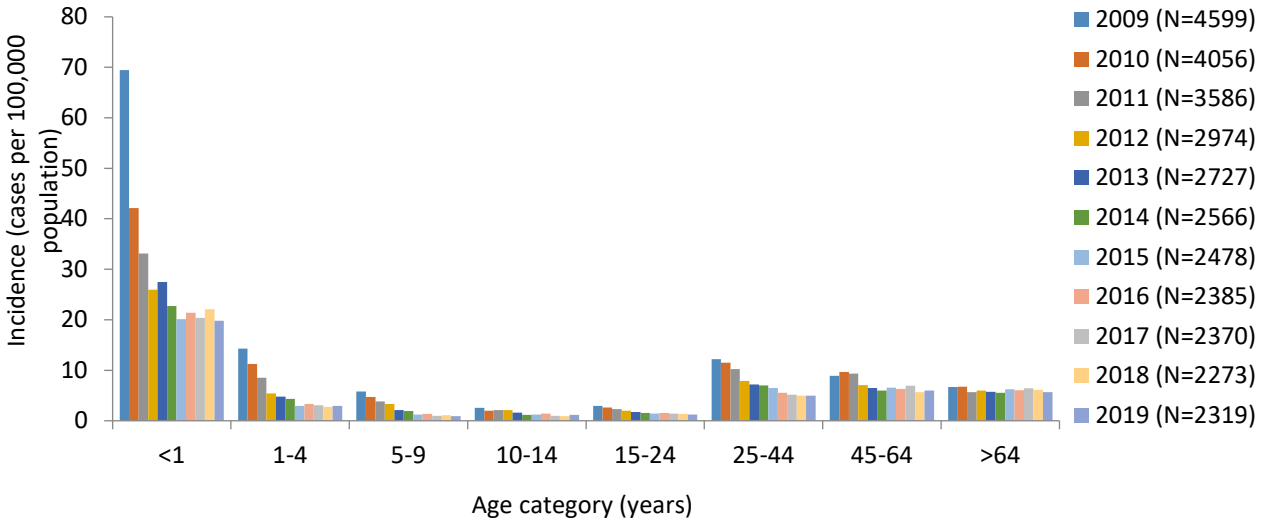


**Figure 6.** Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2019, n=33,761.
2009: N=4,760 age unknown for n=161; 2010: N=4,197, age unknown for n=141; 2011: N=3,804, age unknown for n=218; 2012: N=3,222, age unknown for n=248; 2013: N=2,865, age unknown for n=138; 2014: N=2,731, age unknown for n=165; 2015: N=2,635, age unknown for n=157; 2016: N=2,433, age unknown for n=48; 2017: N=2,440, age unknown for n=70; 2018: N=2,315, age unknown for n=42; 2019: N=2359, age unknown for n=40
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

**Table 7.** Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=4674.

| Site of specimen | 2018 | | 2019 | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid | 795 | 34 | 700 | 30 |
| Blood | 1362 | 59 | 1490 | 63 |
| Other | 158 | 7 | 169 | 7 |
| **Total** | **2315** | | **2359** | |

**Table 8.** Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2019, n=2359.

| Province | Isolate not available | Susceptible* | | Intermediate* | | Resistant* | |
|---|---|---|---|---|---|---|---|
| | n | n | % | n | % | n | % |
| Eastern Cape | 99 | 119 | 68 | 44 | 25 | 12 | 7 |
| Free State | 38 | 34 | 74 | 7 | 15 | 5 | 11 |
| Gauteng | 364 | 297 | 72 | 78 | 19 | 37 | 9 |
| KwaZulu-Natal | 152 | 50 | 59 | 26 | 31 | 9 | 11 |
| Limpopo | 51 | 37 | 80 | 7 | 15 | 2 | 4 |
| Mpumalanga | 39 | 43 | 68 | 16 | 25 | 4 | 6 |
| Northern Cape | 36 | 38 | 70 | 11 | 20 | 5 | 9 |
| North West | 43 | 17 | 74 | 4 | 17 | 2 | 9 |
| Western Cape | 151 | 338 | 70 | 118 | 24 | 26 | 5 |
| **South Africa** | **973** | **973** | **70** | **311** | **22** | **102** | **7** |

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

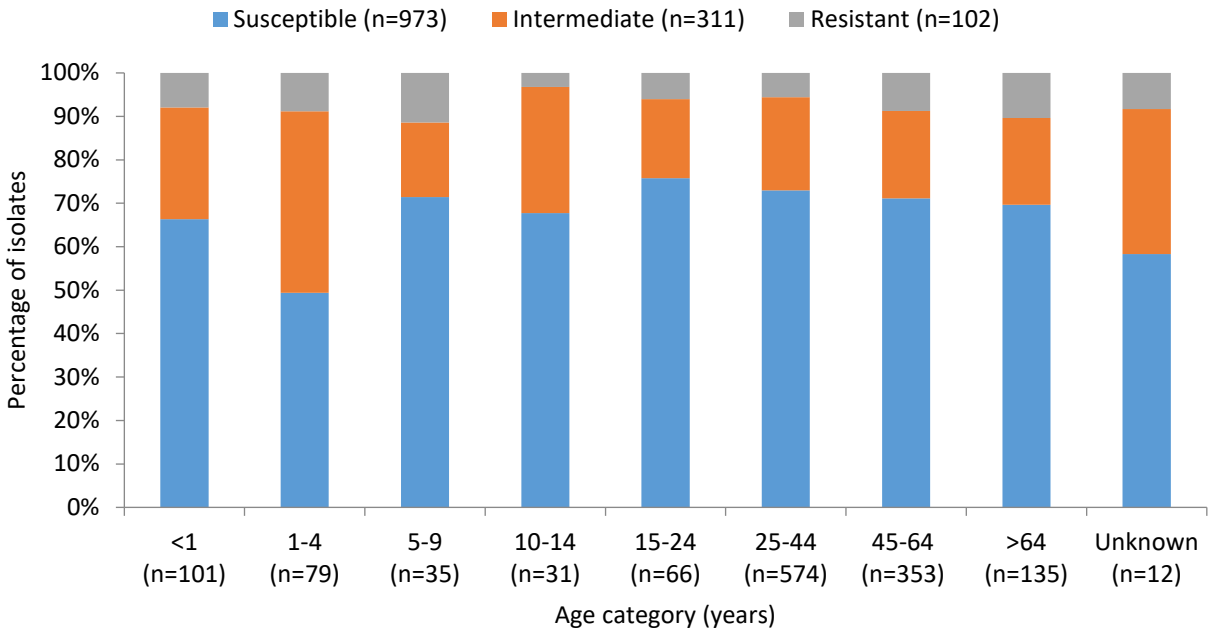


**Figure 7.** Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2019, n=2359 (n=1386 with viable isolates).
2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

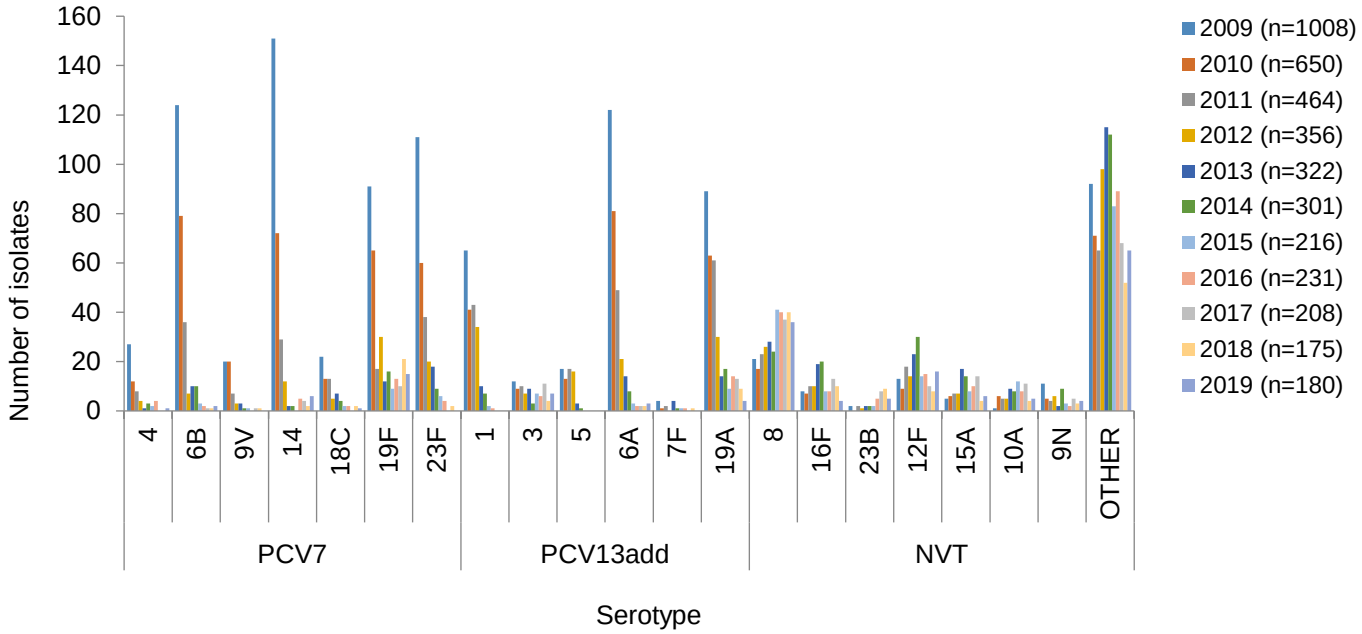


**Figure 8a.** Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2019.
2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable 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; 2018: N=386, n=211 without viable isolates; 2019: N=361, n=181 without viable isolates
Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

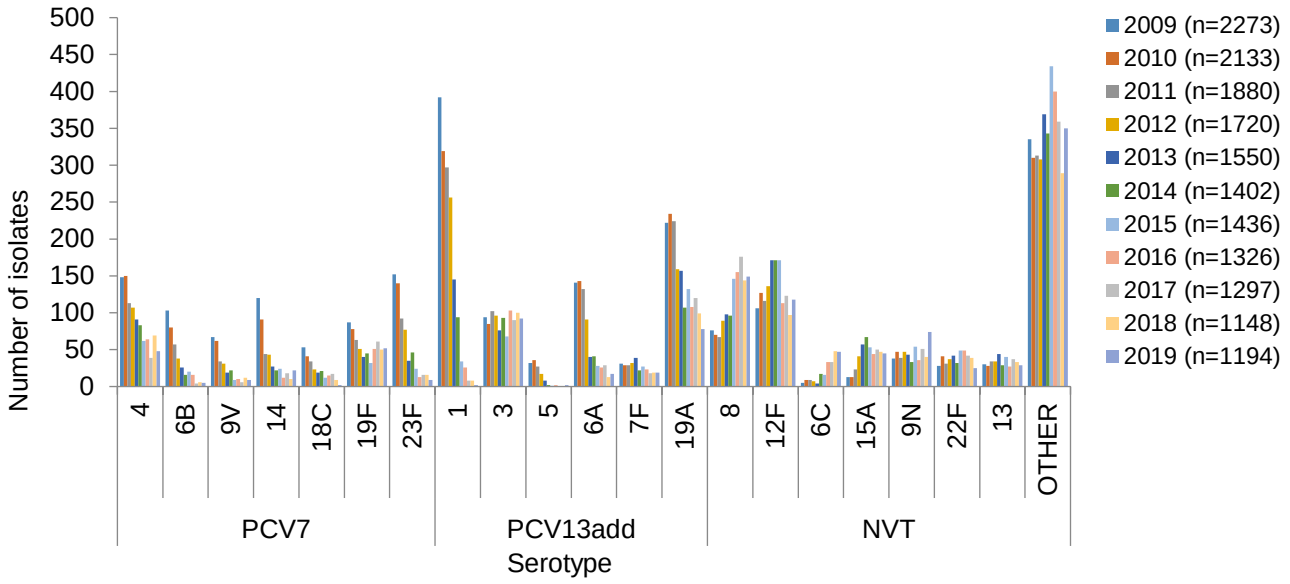


**Figure 8b.** Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children ≥5 years, South Africa, 2009-2019.
2009: N=3264, n=991 without viable isolates; 2010: N=3146; n=1013 without viable isolates; 2011: N=2891, n=1011 without viable isolates; 2012: N=2462, n=742 without viable isolates; 2013: N=2229, n=679 without viable isolates; 2014: N=2101, n=699 without viable isolates; 2015: N=2097, n=661 without viable isolates; 2016: N=1986, n=660 without viable isolates; 2017: N=1996, n=699 without viable isolates; 2018: N=1871, n=723 without viable isolates; 2019: N=1998, n=804 without viable isolates.
Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

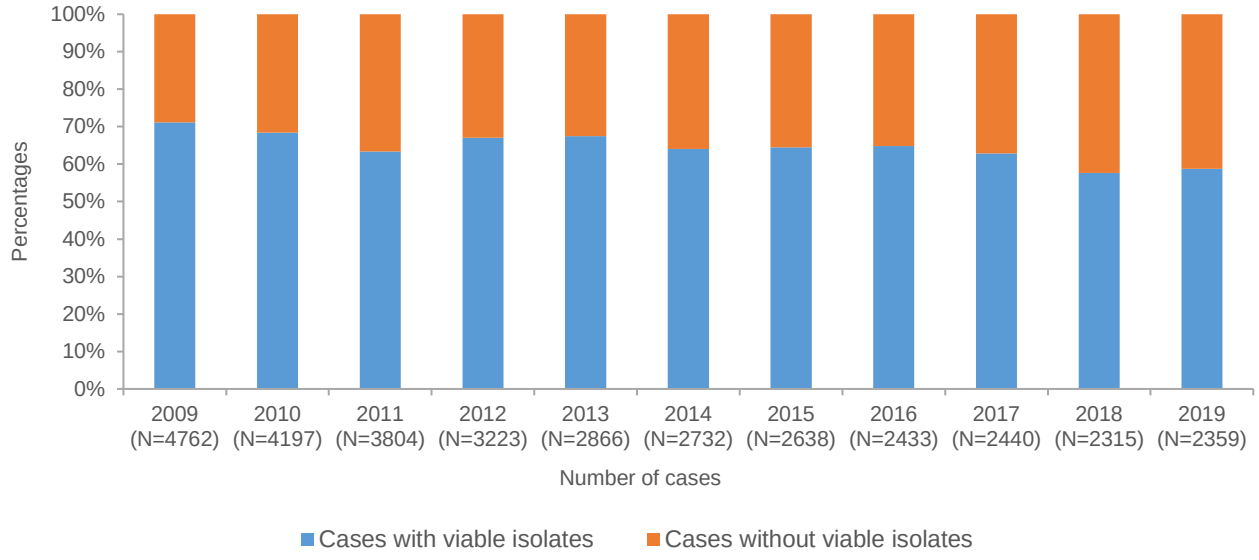


**Figure 9.** Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, South Africa, 2009-2019.

**Table 9.** Number and percentage 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, 2019, n=361 (n=180 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 | 17 | 2 | 12 | 0 | 0 | 2 | 12 | 3 | 18 |
| Free State | 7 | 1 | 14 | 0 | 0 | 1 | 14 | 1 | 14 |
| Gauteng | 68 | 8 | 12 | 1 | 1 | 8 | 12 | 12 | 18 |
| KwaZulu-Natal | 23 | 5 | 22 | 0 | 0 | 5 | 22 | 6 | 26 |
| Limpopo | 10 | 3 | 30 | 1 | 10 | 3 | 30 | 6 | 60 |
| Mpumalanga | 10 | 2 | 20 | 0 | 0 | 2 | 20 | 3 | 30 |
| Northern Cape | 1 | 1 | 100 | 0 | 0 | 1 | 100 | 1 | 100 |
| North West | 6 | 0 | 0 | 1 | 17 | 0 | 0 | 1 | 17 |
| Western Cape | 38 | 3 | 8 | 0 | 0 | 3 | 8 | 6 | 16 |
| **South Africa** | **180** | **25** | **14** | **2** | **1** | **25** | **14** | **39** | **22** |

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
# Cross-protection with 6B has been demonstrated

**Table 10.** Number and percentage of invasive pneumococcal cases reported amongst adults and children >5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2019, n=1998 (n=1194 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 | 158 | 20 | 13 | 1 | 1 | 26 | 16 | 45 | 28 |
| Free State | 39 | 7 | 18 | 0 | 0 | 7 | 18 | 12 | 31 |
| Gauteng | 335 | 45 | 13 | 8 | 2 | 50 | 15 | 94 | 28 |
| KwaZulu-Natal | 62 | 9 | 15 | 1 | 2 | 10 | 16 | 17 | 27 |
| Limpopo | 36 | 1 | 3 | 0 | 0 | 1 | 3 | 8 | 22 |
| Mpumalanga | 52 | 7 | 13 | 3 | 6 | 7 | 13 | 19 | 37 |
| Northern Cape | 53 | 8 | 15 | 0 | 0 | 10 | 19 | 22 | 42 |
| North West | 17 | 2 | 12 | 1 | 6 | 2 | 12 | 6 | 35 |
| Western Cape | 442 | 48 | 11 | 3 | 1 | 57 | 13 | 134 | 30 |
| **South Africa** | **1194** | **147** | **12** | **17** | **1** | **170** | **14** | **357** | **30** |

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
# Cross-protection with 6B has been demonstrated

Eighty-three percent (745/893) of IPD patients presenting to ESS had clinical information available. Patients were admitted for a median hospital stay of 7 days (interquartile range (IQR) 3-13) and most deaths occurred within 2 days of admission (IQR 1-6). Overall case fatality was 33% (246/744). HIV-infection was present in 66% (407/616) of IPD patients; and 47% (27/58) of infants with maternal HIV-status available were HIV-exposed

(10 HIV-infected, 14 HIV-uninfected and 3 HIV-status unknown). Forty-three percent (327/744) of patients had a condition/risk factor (excluding HIV-infection) predisposing them to IPD. The top three factors included: history of smoking (102 patients), diabetes (41 patients) and chronic lung disease (38 patients).

Of 180 patients at ESS with pneumococcus on CSF, 41% (73/180) died during their hospitalization, and 30% (32/107) who survived to discharge suffered at least one sequelae – these included new onset seizures (11), limb weakness/paralysis (9), hydrocephalus (4), hearing loss (4), visual loss (3) and necrotic skin lesions (1). Eighteen episodes of IPD caused by serotypes present in the PCV13 vaccine occurred in children <10 years-of-age at ESS. Vaccine history was available for 67% (12/18) of these children. Seventeen percent (2/12) were too young to receive vaccine; 25% (3/12) of children eligible to receive vaccine had not received any PCV doses; 25% (3/12) had received all 3 doses of PCV; one child had received two doses; and 25% (3/12) had only received one dose of PCV at 6 weeks of age. The serotypes responsible for disease in those who had received any PCV13 included serotypes 19F (3 episodes), 6A (2 episodes), 14 and 6B (one each).

**Discussion**

IPD incidence has remained stable over the past 5 years across all age categories. Infants still have the highest disease incidence, with disease peaking again after age 25 years. Penicillin and ceftriaxone susceptibility of IPD isolates remained unchanged from 2018. HIV-infection, infant HIV-exposure and history of smoking remained important risk factors for IPD. Pneumococcal disease has a high mortality and high rate of sequelae following infection. Residual disease in children aged <5 years is largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurs in children who have not received adequate doses of PCV13. Serotypes causing IPD in those aged >5 years remain diverse including both vaccine and non-vaccine serotypes. Clinicians should ensure that all children (and adults with risk factors for IPD) receive adequate PCV doses to protect them from this serious illness.

**Group A *Streptococcus* (*Streptococcus pyogenes*)**

**Results**

Thirty-four percent (363/1060) of isolates meeting the GERMS-SA case definition for laboratory confirmed invasive Group A Streptococcus (GAS) were sent to the reference laboratory for further characterisation – these cases included isolates from skin and soft tissue infections thought to be causing systemic illness. Incidence of invasive GAS was highest in infants (6.4 per 100 000) with a second peak in those aged >64 years (3 per 100 000) (Figure 10). Most cases were reported from the Western Cape Province (n=466, 44%), followed by Gauteng (208, 20%), KwaZulu Natal (173, 16%) and Eastern Cape (159, 15%) provinces. More invasive GAS disease occurred in males (551/1041, 52%) than females. Forty-six percent (478/1045) of cases were identified on blood culture, followed by 41% (426/1045) from skin and soft tissue specimens (Table 11). Of those isolates available for antimicrobial susceptibility testing, 97% (338/348) were susceptible to penicillin (MIC<0.06µg/ml) and 95% (331/348) were susceptible to erythromycin (MIC<0.25µg/ml) (Table 12).

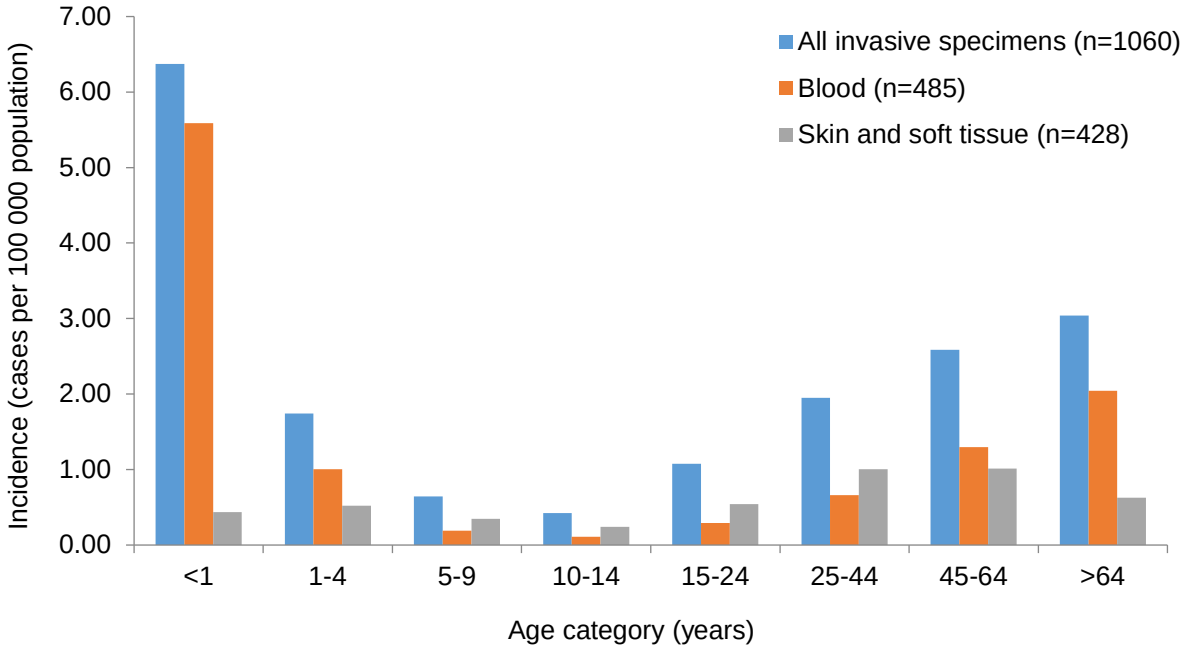


**Figure 10.** Age-specific incidence rates* for laboratory-confirmed, invasive Group A Streptococcal disease, reported to GERMS-SA, South Africa, 2019, n=1060.
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

**Table 11.** Number and percentage of cases of invasive Group A Streptococcal disease reported to GERMS-SA by specimen type and age category, South Africa, 2019, n=1060 (age unknown for n=15).

| Site of specimen | Age <5 years | | Age ≥5 years | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid/brain | 7 | 5 | 8 | 1 |
| Blood | 110 | 72 | 368 | 41 |
| Skin and soft tissue | 29 | 19 | 397 | 45 |
| Bone | 4 | 3 | 72 | 8 |
| Other* | 3 | 2 | 47 | 5 |
| **Total** | **153** | | **892** | |

*Other includes invasive specimens from respiratory, genitourinary and gastrointestinal tracts

**Table 12.** Number and percentage of penicillin and erythromycin susceptible and non-susceptible isolates from invasive Group A Streptococcal disease case reported to GERMS-SA, South Africa, 2019, n=1060.

| Antimicrobial agent | Isolate not available | Susceptible* | | Intermediate* | | Resistant* | |
|---|---|---|---|---|---|---|---|
| | n | n | % | n | % | n | % |
| Penicillin | 712 | 338 | 97 | 8 | 2 | 2 | 1 |
| Erythromycin | 712 | 331 | 95 | 1 | 0 | 16 | 5 |

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

**Discussion**

Infants and the elderly experience the highest incidence of invasive GAS infections in South Africa. Of the isolates characterized, the majority were highly susceptible to the first line antimicrobial agents, penicillin and erythromycin. This was the first year of active surveillance for invasive GAS and clinical laboratories are encouraged to send all invasive GAS isolates meeting the case definition to the NICD so that further phenotypic and genotypic characterisation can be performed. In 2020, clinical data will be collected from persons with invasive GAS infections admitted to our enhanced surveillance sites and molecular typing of all the 2019 and 2020 isolates will commence.

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

**Results**

One thousand and thirty-four cases of invasive Group B streptococcal infections (GBS) were reported through the GERMS-SA surveillance network, of which 347 (34%) isolates were received for further characterisation. Incidence for early onset GBS (<7days) was 0.34 per 1000 live births and 0.24 per 1000 live births for late onset (7-90 days) invasive disease (Table 13). Gauteng Province reported the highest incidence of early and late onset GBS (0.65 and 0.47 per 1000 live births), followed by the Western Cape Province (0.46 and 0.36 per 1000 live births) (Table 13). In infants, invasive GBS incidence was 60 per 100 000 population and decreased rapidly by month of age (Figure 11a). Whilst in persons >1 year of age, overall incidence of invasive GBS was 0.74 per 100 000, peaking in those >64 years of age (Figure 11b). In infants, most cases were isolated from blood (472/574, 82%) or cerebrospinal fluid (91/574, 16%) (Table 14). However, in persons >1 year of age blood (168/426, 39%) and soft tissue (162/426, 38%) specimens were most frequent (Table 14). Disease occurred more frequently in females (569/995, 56%) than males. Of the specimens available for serotyping, serotype III was the most predominant (166/321, 52%), followed by serotype Ia (78, 24%) (Table 15). Serotypes III and Ia were the most predominant serotypes causing invasive disease in early and late onset GBS (Figure 12). In persons >90 days of age, invasive GBS was caused by serotypes III, Ia, II and V (Figure 12). Ninety percent (283/316) of invasive GBS isolates were susceptible to penicillin (MIC<0.12mg/l) and 95% (296/313) were susceptible to gentamycin.

**Table 13.** Number of cases and incidence rates of invasive Group B Streptococcal disease reported to GERMS-SA by province and age category*, South Africa, 2019, n=1034**.

| Province | Early onset (<7 days) | | Late onset (7-90 days) | | Age category ≥1 year | |
|---|---|---|---|---|---|---|
| | n | Incidence (per 1000 live births) | n | Incidence (per 1000 live births) | n | Incidence (per 100 000 population) |
| Eastern Cape | 17 | 0.15 | 13 | 0.12 | 31 | 0.47 |
| Free State | 11 | 0.23 | 6 | 0.13 | 9 | 0.32 |
| Gauteng | 137 | 0.65 | 99 | 0.47 | 186 | 1.24 |
| KwaZulu-Natal | 74 | 0.37 | 43 | 0.21 | 78 | 0.70 |
| Limpopo | 12 | 0.09 | 11 | 0.09 | 12 | 0.20 |
| Mpumalanga | 17 | 0.21 | 12 | 0.15 | 8 | 0.18 |
| Northern Cape | 1 | 0.04 | 2 | 0.08 | 4 | 0.32 |
| North West | 5 | 0.09 | 5 | 0.09 | 2 | 0.05 |
| Western Cape | 46 | 0.46 | 36 | 0.36 | 96 | 1.42 |
| **South Africa** | **320** | **0.34** | **227** | **0.24** | **426** | **0.74** |

*N=27 cases in infants >90 days and less than one year excluded from above. **Age unknown for n=34.

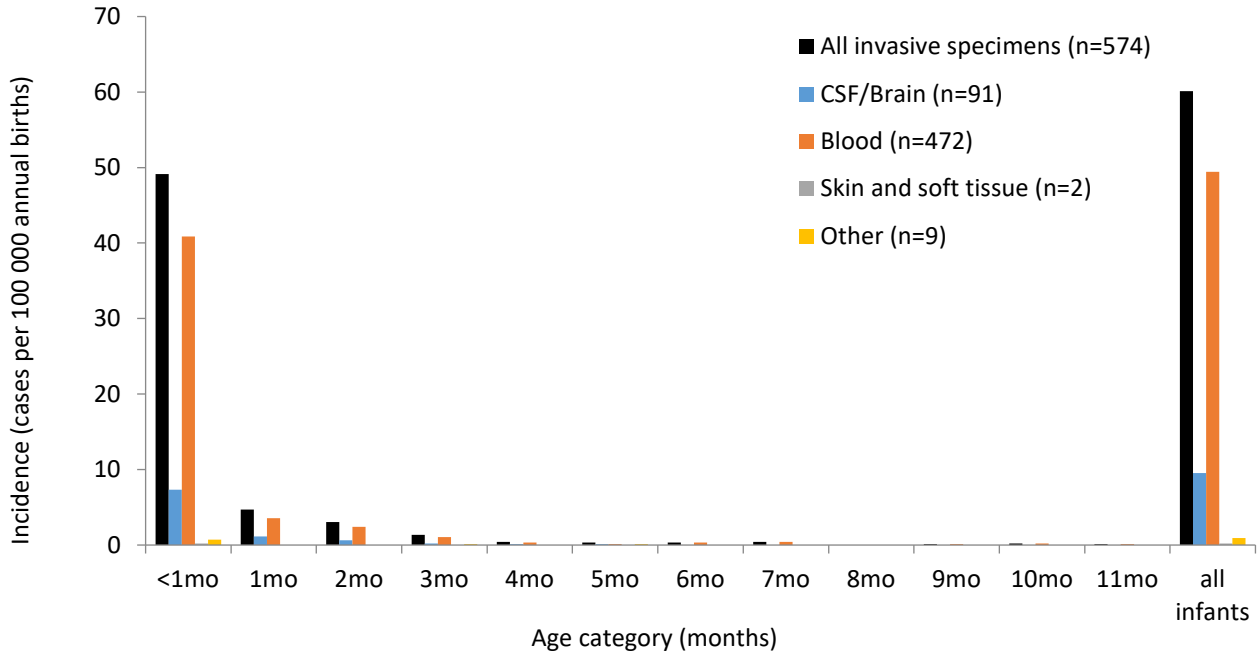


**Figure 11a.** Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in children <1 year of age, reported to GERMS-SA, South Africa, 2019, n=1034 (n=574 in children <1 year, age unknown for n=34).

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

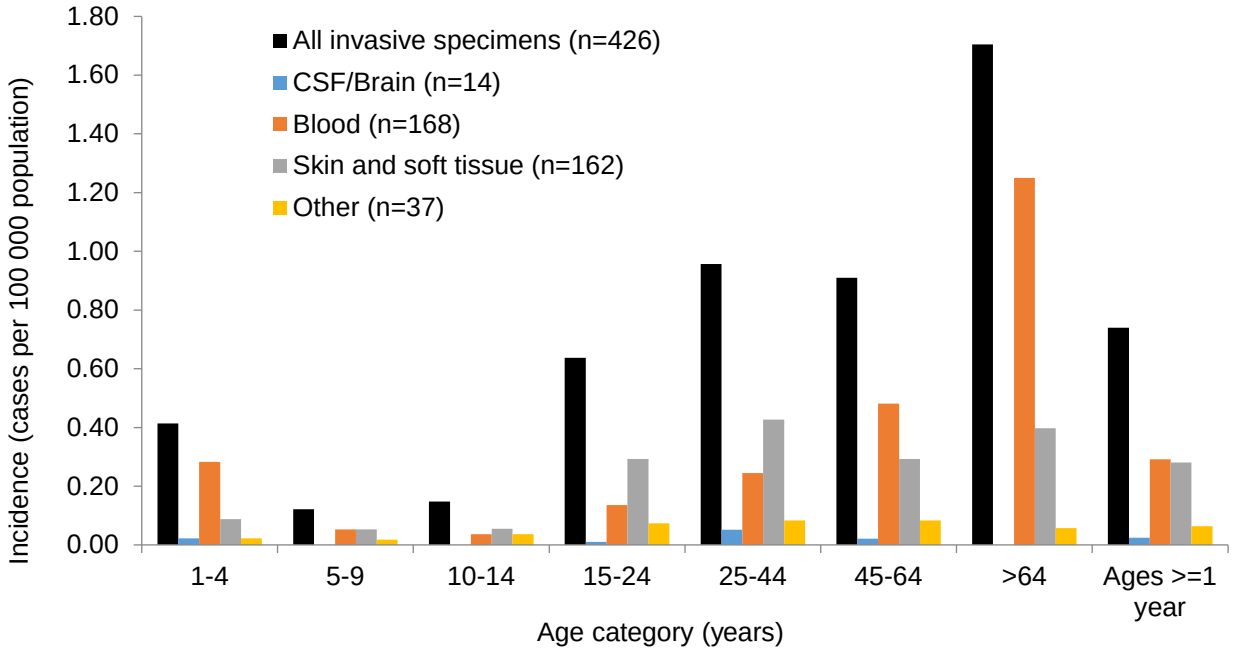


**Figure 11b.** Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in persons ≥1 year of age, reported to GERMS-SA, South Africa, 2019, n=1034 (n=426 in persons ≥1 year, age unknown for n=34).

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

**Table 14.** Number and percentage of cases of invasive Group B Streptococcal disease reported to GERMS-SA by specimen type and age category*, South Africa, 2019, n=1034.

| Site of specimen | Age <1 year | | Age ≥1 years | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid/brain | 91 | 16 | 14 | 3 |
| Blood | 472 | 82 | 168 | 39 |
| Skin and soft tissue | 9 | 2 | 162 | 38 |
| Genitourinary | 0 | 0 | 45 | 11 |
| Other** | 2 | 0 | 37 | 9 |
| **Total** | **574** | | **426** | |

*Age unknown for n=34. **Other includes invasive specimens from bone, respiratory and gastrointestinal tracts.

**Table 15.** Serotype distribution of invasive Group B Streptococcal disease reported to GERMS-SA by province, South Africa, 2019, n=1034 (all ages).

| Province | Total isolates available for serotyping | Ia | | Ib | | II | | III | | V | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | n | % | n | % |
| Eastern Cape | 21 | 3 | 14 | 0 | 0 | 3 | 14 | 9 | 43 | 4 | 19 |
| Free State | 7 | 0 | 0 | 0 | 0 | 1 | 14 | 4 | 57 | 0 | 0 |
| Gauteng | 140 | 31 | 22 | 3 | 2 | 13 | 9 | 68 | 49 | 11 | 8 |
| KwaZulu-Natal | 34 | 12 | 35 | 1 | 3 | 1 | 3 | 16 | 47 | 2 | 6 |
| Limpopo | 16 | 0 | 0 | 1 | 6 | 2 | 13 | 11 | 69 | 0 | 0 |
| Mpumalanga | 12 | 2 | 17 | 0 | 0 | 2 | 17 | 7 | 58 | 1 | 8 |
| Northern Cape | 1 | 0 | 0 | 0 | 0 | 1 | 100 | 0 | 0 | 0 | 0 |
| North West | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 50 |
| Western Cape | 111 | 30 | 27 | 7 | 6 | 9 | 8 | 51 | 46 | 9 | 8 |
| **South Africa** | **321** | **78** | **24** | **12** | **4** | **32** | **10** | **166** | **52** | **28** | **9** |

In addition, there was one mixed III/Ia isolate from Free State, one mixed III/V from Western Cape, and three non-typeable (one from Gauteng and two from KwaZulu Natal).

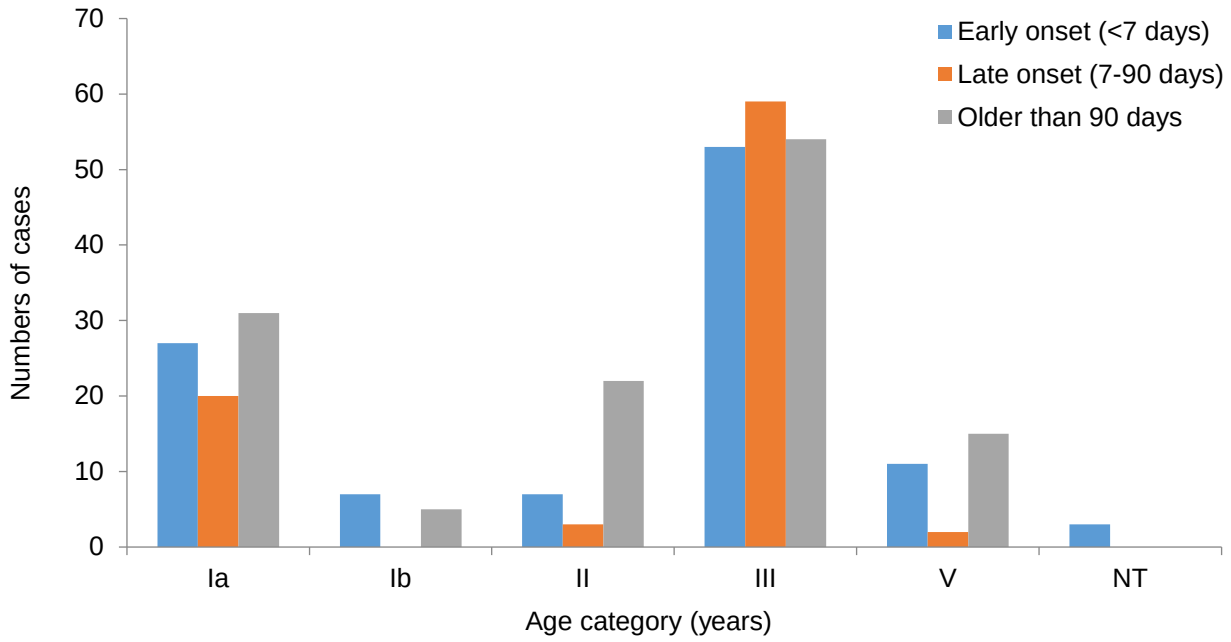


**Figure 12.** Numbers of cases of laboratory-confirmed, invasive Group B Streptococcal disease by serotype, reported to GERMS-SA, South Africa, 2019, n=1034 (isolates unavailable for 690 cases).

**Discussion**

Incidence of early and late onset invasive GBS appears low, however this may be due to decreased case ascertainment in many areas of South Africa. Most invasive GBS in infants was caused by serotypes III and Ia, although a range of serotypes was found to be causing invasive GBS in other age groups. This was the first year of active surveillance for invasive GBS and no clinical data was collected. Clinical laboratories are encouraged to send all GBS isolates meeting the GERMS case definition to the NICD so that further characterisation and serotyping can be done. In 2020, enhanced clinical surveillance will begin at selected sites in order to report on risk factors predisposing to invasive GBS and outcome following infection.

**Conclusions**

Incidence of invasive meningococcal and *Haemophilus influenzae* disease remained low for 2019, with rates of invasive pneumococcal disease being stable over the past 5 years. Infants have the highest rates of invasive meningococcal, *Haemophilus influenzae*, pneumococcal, GAS and GBS infections, despite routine vaccination programmes targeting pneumococcal and *Haemophilus influenzae* type b disease prevention in young children. There was a wide diversity of serogroups/serotypes of the different organisms circulating in South Africa, making targeting of residual disease difficult to achieve through limited vaccination options. Despite the low incidence of disease, in-hospital case-fatality remains high for invasive meningococcal, *Haemophilus influenzae* and pneumococcal disease, with high rates of sequelae amongst survivors. This highlights the importance of continued active surveillance of these infections and others such as Group A and B streptococcus in order to understand the disease burden and monitor serotype/serogroup diversity for future vaccine targets.

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