GERMS

SOUTH AFRICA

# Annual Surveillance Review 2018

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

**The GERMS-SA Annual Report 2018 was compiled by the National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.**


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## Introduction

NICD reference laboratories report their GERMS-SA surveillance findings for 2018.

Surveillance continues to be useful in reporting trends in pathogen-specific data however the number of isolates received by NICD reference laboratories continues to decrease with worsening viability of isolates. This means that we have fewer isolates for antimicrobial susceptibility testing and serotyping/ serogrouping. We urge all microbiology laboratories, in their challenged capacities, to continue participating in laboratory surveillance so monitoring can continue and relevant, evidence-based policies can be made. The 2018 report also includes all NICD projects using our GERMS-SA platform. These include STI, rotavirus/diarrhoeal aetiological surveillance and zoonosis surveillance. These projects differ from the laboratory-based surveillance in that some are syndromic surveillance and specimens are taken from patients.

We encourage all laboratory staff to continue participating in the NICD surveillance programmes. We thank you for your ongoing service to the health of all South Africans.

Bekiwe Ncwana, NMC trainer (centre) showing surveillance officers (L-R: Nkosinathi Mbhele, Nokuthula Nzuza, Rachel Nare and Nthabiseng Motati) the Notifiable Medical Conditions App – 18 April 2018.

## Methods

In 2018, diseases under surveillance included:

1. Opportunistic infections associated with HIV, e.g. cryptococcosis, invasive pneumococcal disease (IPD) and rifampicin-susceptible *Mycobacterium tuberculosis*
2. Epidemic-prone diseases, e.g. *Neisseria meningitidis*, *Salmonella enterica* serotype Typhi, *Shigella* species, *Vibrio cholera,* diarrhoeagenic *Escherichia coli* and listeriosis
3. Vaccine-preventable diseases, e.g. *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* and rotavirus
4. Hospital infections, e.g. *Staphylococcus aureus*, Carbapenem resistant Enterobacteriaceae and *Candida* species

The methods utilised by the GERMS-SA surveillance programme have been previously described in detail (1).

In brief, approximately 222 South African clinical microbiology laboratories participated in the surveillance programme in 2018. The population under surveillance in 2018 was estimated at 57,7 million (Table 1). Diagnostic laboratories reported case patients to the National Institute for Communicable Diseases (NICD) using laboratory case report forms, according to standard case definitions. If available, isolates from case patients were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. From 1 July 2008 to 31 December 2013, surveillance methodology for the cryptococcal project was changed, so that only enhanced surveillance sites (ESS) (29 hospitals in 9 provinces), NHLS laboratories in KZN, and laboratories in the private, mining, and military sectors were required to directly report case patients to NICD. In 2015 and 2016, no laboratories were required to directly report case patients or send isolates to NICD. For these cases of cryptococcosis, data were obtained directly from the

*Continued on page 5...*

NHLS Corporate Data Warehouse (CDW), which stores information from Disa*Lab and TrakCare laboratory information systems. Cryptococcal isolates, obtained from patients at ESS, continued to be characterised by phenotypic and genotypic tests through 2013. Carbapenam Resistant Enterobacteriaceae (CRE) surveillance started in July 2015 in four provinces and these organisms were requested to be sent: *Klebsiella* spp., *Enterobacter* spp., *Citrobacter* spp., *Serratia* spp., *E. coli*., *Providentia* spp., *Proteus* spp., *Salmonella* spp., *Morganella* spp. and *Acinetobacter baumannii.*

Enhanced surveillance was not conducted on any of the enteric pathogens in 2015 but restarted for *Salmonella* Typhi only in 2016. At ESS, surveillance officers completed clinical case report forms electronically using the Mobenzi application on mobile phones/ tablets for patients with eight laboratory-confirmed diseases: cryptococcosis, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, invasive *Salmonella* Typhi disease and rifampicin-susceptible TB [9 sites]), 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 only 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 CDW. For all diseases under surveillance, except cryptococcosis and rifampicin-susceptible TB, 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. For cryptococcosis, the audit was designed to obtain data from cases that were no longer reported by NHLS laboratories. Data from case patients, detected by audit, were included on the surveillance database, and have been included in this report; Incidence was calculated using mid-year population estimates for 2017 and 2018 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2017 and 2018, using the Thembisa model (Table 1) (3). All reported incidence is expressed as cases per 100 000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test and p values <0.05 were considered significant throughout. 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 M140159 (previously M08-11 -17) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/NHLS.

**Table 1.** Population denominators used to calculate incidence rates, South Africa, 2017 and 2018

| Province | General population* | | HIV-infected population** | |
|---|---|---|---|---|
| | 2017 | 2018 | 2017 | 2018 |
| Eastern Cape | 6 498 683 | 6 522 734 | 785 266 | 796 027 |
| Free State | 2 866 678 | 2 954 348 | 368 972 | 371 923 |
| Gauteng | 14 278 669 | 14 717 040 | 1 852 088 | 1 885 165 |
| KwaZulu-Natal | 11 074 784 | 11 384 722 | 1 967 748 | 1 991 798 |
| Limpopo | 5 778 442 | 5 797 275 | 453 531 | 460 942 |
| Mpumalanga | 4 444 212 | 4 523 874 | 682 723 | 698 317 |
| Northern Cape | 1 213 996 | 1 225 555 | 80 762 | 81 739 |
| North West | 3 856 174 | 3 978 955 | 482 017 | 486 217 |
| Western Cape | 6 510 312 | 6 621 103 | 436 771 | 449 547 |
| South Africa | 56 521 948 | 57 725 606 | 7 109 879 | 7 221 675 |

Data source: *Statistics South Africa, **Thembisa Model

## Operational Report

**Site visits**

In 2018, NICD staff members continued with site visits to feedback, train and trouble-shoot at laboratories, hospitals and clinics linked to GERMS surveillance. Feedback is important to maintain or improve surveillance participation.

**Coordination of meetings**

Notifiable Medical Conditions (NMC) meeting combined with annual Surveillance officers' meeting, April 2018: the aims of this meeting were to understand notification forms and how to complete them, NMC App, categories of NMC list and role of SOs in NMC.

GERMS-SA NICD Surveillance Review: due to financial constraints it was decided to hold this meeting every second year.

**Surveillance audit**

A total of 15 659 surveillance cases were detected by GERMS-SA in 2018. Excluding the cases of cryptococcosis (n=6 353) which are all detected by audit, as isolates are no longer required to be sent to the NICD, and cases of rifampicin-susceptible TB (n=2 064), for which no audits are performed, 3 277/7 242 (45%) of cases were not reported to the NICD by the clinical microbiology laboratories, but were detected by audit of the NHLS Corporate Data Warehouse (Table 2). GERMS-SA constantly strives to reduce the number of cases detected on audit by raising awareness of the surveillance programme; this is important because GERMS-SA is unable to perform additional microbiological characterisation of isolates detected only through audit.

**Enhanced surveillance site performance indicators**

The proportion of completed CRFs in 2018 was lower than that in 2017 . This was due in part to difficulties in finding TB patients (for interview and sputum collection) and untimely notification on cases meeting case definition by testing laboratories (Table 3): 4 397/ 6 148 (72%) of cases had a case report form (CRF) completed (target = 90%). The interview rate slightly increased from previous year however SOs continue experiencing challenges in tracking patients due to late notifications resulting in them completing CRFs through medical records: [3 348/4 397 (76%) of the CRFs were completed by patient interview (target=70%)]. Since 2007, enhanced surveillance site operational reports (ESSOR) have been provided to the site coordinators, laboratory staff and surveillance officers to enable the site team to regularly review site performance, in comparison with set targets. The main objective of these reports is to provide information regarding the overall functioning of the surveillance site, by providing indicators of laboratory participation (submission of isolates), and indicators of surveillance officer performance (completion of CRFs). By reviewing these indicators, problems with data collection can be targeted, and recommendations are provided to improve the site performance. In 2018, these reports were provided quarterly.

**Enhanced surveillance site quality monitoring**

In 2018, surveillance officers (SOs) were audited in terms of quality of work. CRFs from a fixed time period were randomly selected for each surveillance officer so that there were 7 CRFs (one for each organism) to audit per SO. The medical record files were drawn and the GERMS-coordinating staff filled in a modified clean CRF from the original source data and compared their CRF with the original SO CRF. A scoring system was set up and, although the scores varied widely amongst SOs, many of the errors were ones of omission and overlooking information rather than entry of incorrect data. Data training was done regularly to overcome these errors.


**L-R:** Martha Bodiba (data analyst) and Sunnieboy Njikho (field project coordinator) with surveillance officers Lesley Ingle and Tumelo Tlhomelang outside NHLS Rob Ferreira

Project manager Mokupi Manaka (centre) with WC field project coordinator (FPC) and surveillance officers. **L-R front** Cecilia Miller (FPC) and Nazila Shalabi. **L-R back** Priscilla Mouton, Zama Mfundisi and Cheryl Mentor.

**Table 2.** Cases detected by surveillance audit by province, 2018

| Surveillance case | | Percentage of cases detected by audit* $n_1/n_2$ (%) | Number of cases detected by audit | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | EC | FS | GA | KZ | LP | MP | NC | NW | WC | SA |
| Invasive | Cryptococcosis** | 6 353/6 353 (100%) | 907 | 245 | 1 508 | 1 739 | 505 | 501 | 51 | 446 | 451 | 6 353 |
| | *Salmonella* Typhi | 11/77 (14%) | 0 | 0 | 2 | 5 | 1 | 0 | 0 | 1 | 2 | 11 |
| | Non-typhoidal salmonellosis† | 396/648 (61%) | 25 | 19 | 113 | 61 | 20 | 26 | 3 | 6 | 123 | 396 |
| | Shigellosis | 22/36 (61%) | 0 | 1 | 9 | 3 | 0 | 0 | 0 | 2 | 7 | 22 |
| | Listeriosis | 92/348 (26%) | 5 | 1 | 45 | 17 | 5 | 7 | 1 | 1 | 10 | 92 |
| | Meningococcal disease | 23/125 (18%) | 1 | 0 | 9 | 4 | 2 | 0 | 0 | 4 | 3 | 23 |
| | *Haemophilus influenzae* disease | 116/327 (35%) | 13 | 4 | 38 | 29 | 5 | 6 | 1 | 5 | 15 | 116 |
| | Pneumococcal disease | 653/2 314 (28%) | 79 | 41 | 221 | 126 | 58 | 24 | 11 | 45 | 48 | 653 |
| | Carbapenem resistant Enterobacteriaceae (BC only) | 275/601 (46%) | N/A | 4 | 223 | 37 | N/A | N/A | N/A | N/A | 11 | 275 |
| | *Acinetobacter baumannii* (BC only) | 338/713 (47%) | N/A | 18 | 216 | 84 | N/A | N/A | N/A | N/A | 20 | 338 |
| Non-invasive | *Salmonella* Typhi | 1/14 (7%) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 1 |
| | Non-typhoidal salmonellosis† | 754/1 229 (61%) | 73 | 36 | 147 | 160 | 54 | 70 | 9 | 25 | 180 | 754 |
| | Shigellosis | 596/805 (74%) | 46 | 40 | 108 | 96 | 5 | 9 | 0 | 13 | 279 | 596 |
| | Cholera†† | 0/5 (N/A) | 0 | 0 | 2 | 1 | 2 | 0 | 0 | 0 | 0 | 5 |
| | Rifampicin-susceptible tuberculosis*** | NA/2 064 | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| Total (excl crypto and RSTB) | | 3 277/7 242 (45%) | | | | | | | | | | |

Percentage of cases detected by audit = number of cases detected on audit (n1)/total number of cases detected by GERMS-SA (n2) x 100;**All cases of cryptococcal disease are detected by LIS audit and no isolates are received; therefore this disease is excluded from the total; ***Audits are not performed on TB cases, therefore this organism is excluded from the total; †Excluding *Salmonella enterica* serotype Paratyphi; ††Only *Vibrio cholerae* O1; EC: Eastern Cape; FS: Free State; GA: Gauteng; KZ: KwaZulu-Natal; LP: Limpopo; MP: Mpumalanga; NC: Northern Cape; NW: North West; WC: Western Cape; SA: South Africa; BC: Blood culture. *Acinetobacter baumannii* cases demonstrated from 1st August until 31st December 2018.

## Surveillance reports

## Enhanced surveillance site project

In 2018, 6 148 surveillance case patients were diagnosed at enhanced surveillance sites (Table 3). Of case patients with recorded HIV status, 75% (2 584/3 431) were HIV-infected (Table 4). The proportion of case patients with confirmed HIV infection varied by surveillance disease: unsurprisingly, a very high proportion of patients with AIDS-defining infections like cryptococcosis (93%), RSTB (73%) were HIV-infected. HIV infection amongst patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 70%.

**Table 3.** Enhanced surveillance site performance indicators, 2018

| Enhanced surveillance site | Case patients, n | Completed case report forms*, | | Case report forms completed by interview, n | |
|---|---|---|---|---|---|
| Addington [2] | 89 | 80 | (90) | 65 | (81) |
| Charlotte Maxeke Johannesburg Academic [2] | 392 | 384 | (98) | 309 | (80) |
| Chris Hani Baragwanath/ Zola-Jabulani District [1,2] | 1 456 | 992 | (68) | 699 | (70) |
| Dr George Mukhari [2] | 164 | 147 | (90) | 109 | (74) |
| Edendale/ Greys'/ Northdale [2] | 301 | 285 | (95) | 266 | (93) |
| Groote Schuur/ Red Cross [2] | 202 | 180 | (89) | 120 | (67) |
| Helen Joseph/ Rahima Moosa Mother & Child [2] | 340 | 297 | (87) | 222 | (75) |
| Kimberley | 75 | 54 | (72) | 21 | (39) |
| King Edward VIII/ Inkosi Albert Luthuli Central Hospital [1,2] | 305 | 122 | (40) | 114 | (93) |
| Klerksdorp/ Tshepong [1] | 598 | 362 | (61) | 302 | (83) |
| Mankweng/ Polokwane/ Seshego | 119 | 60 | (50) | 17 | (28) |
| Pelonomi/ Universitas [2] | 144 | 129 | (90) | 94 | (73) |
| Port Elizabeth/ Dora Nginza/ Livingstone [1] | 622 | 444 | (71) | 323 | (73) |
| RK Khan [1,2] | 508 | 202 | (40) | 175 | (87) |
| Rob Ferreira/ Themba [1] | 355 | 228 | (64) | 208 | (91) |
| Steve Biko Pretoria Academic/ Tshwane District [2] | 305 | 280 | (92) | 196 | (70) |
| Tygerberg [2] | 173 | 151 | (87) | 108 | (72) |
| Total | 6 148 | 4 397 | (72) | 3 348 | (76) |

Note - The percentage (in brackets) in each cell was calculated using the numerator from that cell and the corresponding denominator from the cell to the left; *Low case report form completion rates at certain sites are due to challenges in completing CRFs for certain pathogens; **Target = 90%; ***Target = 70%; [1]Sites doing rifampicin-susceptible TB surveillance, [2]sites doing CRE and *A. baumannii* surveillance. *A. baumannii* enhanced surveillance started from 1st August and data are reflecting until 31st December 2018.

**Table 4.** Numbers and percentage* of patients diagnosed with laboratory-confirmed invasive disease at GERMS-SA enhanced surveillance sites, with confirmed HIV-1 infection **, South Africa, 2018

| Pathogen | Case patients, n | Case patients with completed case report forms, n (%)* | | Case patients with known HIV status, n (%) | | Case patients with confirmed HIV infection, n (%)** | |
|---|---|---|---|---|---|---|---|
| *Cryptococcus* species | 6 353 | 1 489 | (23) | 1 177 | (79) | 1 382 | (93)† |
| *Neisseria meningitidis* | 51 | 44 | (86) | 36 | (82) | 6 | (17) |
| *Streptococcus pneumoniae* | 875 | 758 | (87) | 567 | (75) | 397 | (70) |
| *Haemophilus influenzae* | 152 | 133 | (88) | 91 | (68) | 47 | (52) |
| *Salmonella* Typhi | 24 | 21 | (88) | 17 | (81) | 3 | (18) |
| CRE | 601 | 516 | (86) | 375 | (73) | 91 | (24) |
| *Acinetobacter baumannii* | 713 | 603 | (85) | 387 | (64) | 88 | (23) |
| Rifampicin-susceptible TB | 2 064 | 854 | (41) | 781 | (91) | 570 | (73) |
| Total | 10 833 | 4 418 | (41) | 3 431 | (78) | 2 584 | (75) |

*The percentage (in brackets) in each cell was calculated using the numerator from that cell and the corresponding denominator from the cell to the left. **HIV infection was confirmed by an age-appropriate, laboratory test and recorded by surveillance officers at enhanced surveillance sites. †The percentage (in brackets) was calculated using the numerator from that cell and the corresponding denominator from cell "case patients with completed case report forms".

## *Cryptococcus* species

**Results**

During 2018, 6 353 case patients with laboratory-confirmed incident cryptococcal disease (including meningitis, fungaemia and culture-positive disease at other sites but excluding cryptococcal antigenaemia [n=861]) were reported (Table 5). Between 2017 and 2018, the incidence increased in Limpopo province, remained stable in six provinces (overlapping 95% confidence intervals) and decreased in Gauteng and KwaZulu-Natal. In 2018, the highest incidence was recorded among males aged 40 -44 years; the peak incidence among females was in the group aged 30-34 years (Figure 1). One hundred and thirty eight children younger than 15 years had laboratory-confirmed cryptococcosis; 60 (43%) of these were younger than 5 years of age. Most patients (96%) with incident disease were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species) and 3% with fungaemia (Table 6). In 2018, 22 patients were diagnosed by culture of urine and other specimen types. Clinical case data were collected from patients at ESS from January to December 2018. For 2018, completed case report forms were available for 90% (1 489/1 661) of patients. Of these, 79% (1 177/1 489) patients knew their HIV status, and 93% (1 382/1 489) were HIV-seropositive. Of 1382 patients infected with HIV, 841 (61%) were antiretroviral treatment (ART) – experienced. Among ART-experienced patients, 618 (73%) were on ART at the time of diagnosis of cryptococcal disease. Among 1 178 HIV-infected patients who had a CD4+ T-lymphocyte (CD4) count test result recorded close to the time of diagnosis, 1 078 (92%) had a CD4 count <200 cells/µl; the median CD4 count was 33 cells/µl (interquartile range, 13 – 79). The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease was 33% (486/1 489).

**Discussion**

The incidence of cryptococcal meningitis or culture-confirmed cryptococcal disease was decreased slightly between 2017 and 2018. Despite the increased coverage of antiretroviral treatment, this relatively stable incidence may be a consequence of more cases being detected through the national cryptococcal antigen screening programme. Alternatively, more patients may be at risk for cryptococcal disease because of interruption or failure of ART. The in-hospital case-fatality ratio associated with cryptococcosis remained high.

**Table 5.** Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by province, South Africa, 2017-2018, n=12 989

| Province | 2017 | | 2018 | |
|---|---|---|---|---|
| | n* | Incidence (95% CI)† | n* | Incidence (95% CI)† |
| Eastern Cape | 789 | 100 (93-107) | 907 | 114 (107-121) |
| Free State | 239 | 65 (57-73) | 245 | 66 (58-74) |
| Gauteng | 1 859 | 100 (96-105) | 1508 | 80 (76-84) |
| KwaZulu-Natal | 1 899 | 97 (92-101) | 1739 | 87 (83-91) |
| Limpopo | 404 | 89 (80-98) | 505 | 100 (100-119) |
| Mpumalanga | 500 | 73 (67-80) | 501 | 72 (65-78) |
| Northern Cape | 46 | 57 (40-73) | 51 | 62 (45-80) |
| North West | 493 | 102 (93-111) | 446 | 92 (83-100) |
| Western Cape | 407 | 93 (84-102) | 451 | 100 (91-110) |
| South Africa | 6 636 | 93 (91-96) | 6 353 | 88 (86-90) |

*These case numbers exclude patients who tested positive for cryptococcal antigenaemia. †Incidence was calculated using mid-year population denominators determined by the Thembisa model and is expressed as cases per 100 000 HIV-infected persons (refer to Table 1).

**Figure 1.** Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA , by gender and age group, South Africa, 2018, n=5 774

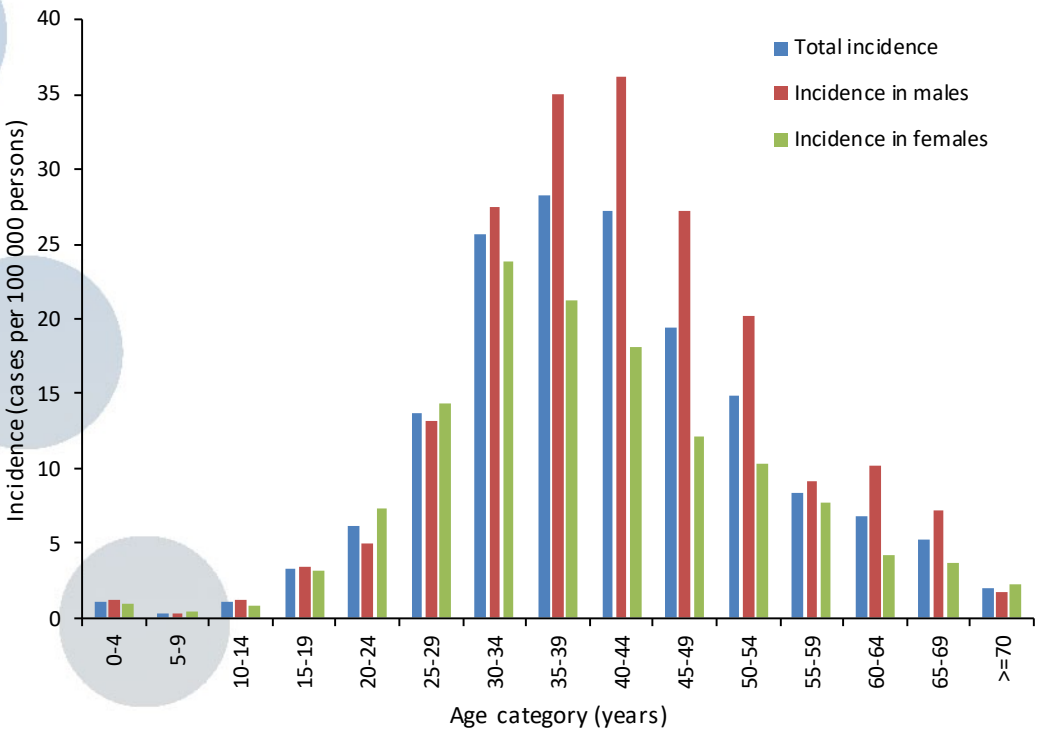



**Table 6.** Number and percentage of cases of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by specimen type, South Africa, 2017-2018, n=12 989

| Site of specimen | 2017 | | 2018 | |
|---|---|---|---|---|
| | n* | % | n* | % |
| Cerebrospinal fluid | 6 294 | 95 | 6 126 | 96 |
| Blood | 238 | 3 | 205 | 3 |
| Other | 104 | 2 | 22 | 1 |
| Total | 6 636 | | 6 353 | |

*These case numbers exclude patients who tested positive for cryptococcal antigenaemia.

## Enhanced sentinel surveillance for CRE bacteraemia in four provinces

**Results**

There were 1 524 cases of CRE bacteraemia (as detected by a diagnostic laboratory) reported to GERMS-SA from July 2015 through to December 2018 (Table 7). During the two-year period (2017-2018), the proportion of males (611/1 084, 56%) was higher compared to females (467/1 084, 44%); p=0.70. Approximately 26% (n=281/1 084) of cases were aged less than one-year-old. The median age of cases was 31 years old (IQR <1-52); p=0.29 (Figure 2). There was an increase in the number of cases from 483 in 2017 to 601 in 2018. In 2018, a high proportion of cases were detected from sentinel sites in Gauteng (471/601; 78%) followed by KwaZulu-Natal (74/601; 12%). In KwaZulu-Natal, there was a decrease in the proportion of cases from 16% in 2017 to 12% in 2018 and an increase in the proportion of cases in the Western Cape from 4% in 2017 to 7% in 2018; p=0.07 (Figure 3). Less than half of the cases in 2018 (275/601; 46%) were identified by audit (Table 2). CRE isolates were available for 52% (314/601) of patients and submitted to NICD for antimicrobial susceptibility testing in 2018. *Klebsiella pneumoniae* was the predominant organism (244; 78%) followed by *Serratia marcescens* (23; 7%) *Enterobacter cloacae* (15; 5%), and *Escherichia coli* (9; 3%) (Figure 4). Among isolates in 2018, 71% (220) were non-susceptible to ertapenem, 39% (120) non-susceptible to imipenem, and 41% (129) non-susceptible to meropenem and doripenem (Figure 5). Isolates available from 2015 to 2018 showed that 6% (63/1 021) were resistant to colistin using the Sensititre reference susceptibility method (Figure 6). None of these isolates tested positive for plasmid mediated genes, *mcr*- 1-5. We confirmed carbapenemase genes in 91% (287/314) of isolates including NDM (94/314; 30%) and OXA-48 or variants (187/314; 60%) as the highest amongst all genes in 2018 (Figure 7). Ten percent (18/185) of isolates were susceptible to ertapenem with an MIC ≤ 0.5 mg/L but were OXA-48 positive. A shift was noted among CRE mediated by OXA-48 & variants (Figure 8). Susceptible to tigecycline showed that 79% (470/592) of isolates were susceptible. Patient outcome was known for 79% (n=476) of cases, of which 35% (n=167) died in hospital. HIV status was known for 73% (375/516) of cases, of which 24% (n=91) were HIV-positive in 2018 (Table 4).

**Discussion**

The number of CRE bacteraemia cases detected over the surveillance period is relatively small. However, there has been an increase in 2017 and 2018 of these highly-resistant organisms which has an impact on the public-sector health system in terms of patient outcomes and healthcare costs. Most cases were detected in Gauteng and KwaZulu-Natal. We noted a shift to CPE mediated by OXA-48 & variants; these enzymes are not easily detected in the laboratory. In addition, the OXA genes are located on a very efficient transposon with the potential for point mutations, which would render them even more difficult to detect. Plasmid mediated colistin resistance has not been detected amongst our isolates.

**Table 7.** Number of cases of carbapenem-resistant Enterobacteriaceae (CRE) bacteraemia reported to GERMS-SA by province, July 2015 to December 2018, n=1 524 (including audit cases)

| Province | 2015 | | 2016 | | 2017 | | 2018 | | Total | |
|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | n | % |
| Free State | 1 | 1 | 3 | 1 | 11 | 2 | 11 | 2 | 26 | 2 |
| Gauteng | 80 | 68 | 218 | 67 | 375 | 78 | 471 | 78 | 1 144 | 75 |
| KwaZulu-Natal | 32 | 27 | 73 | 23 | 76 | 16 | 74 | 12 | 255 | 18 |
| Western Cape | 4 | 4 | 29 | 9 | 21 | 4 | 45 | 8 | 99 | 6 |
| Total | 117 | 100 | 323 | 100 | 483 | 100 | 601 | 100 | 1 524 | 100 |

**Figure 2.** Distribution of cases of CRE bacteraemia by age category, n=1 084

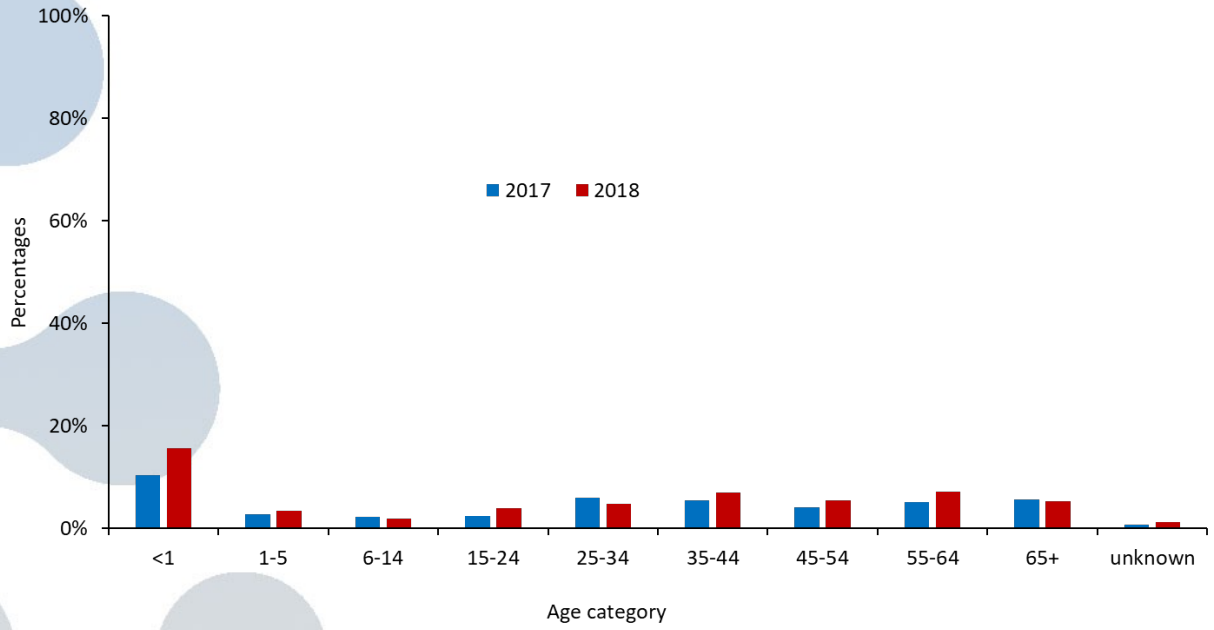



**Figure 3.** Distribution of cases of CRE bacteraemia by province, n=1 084

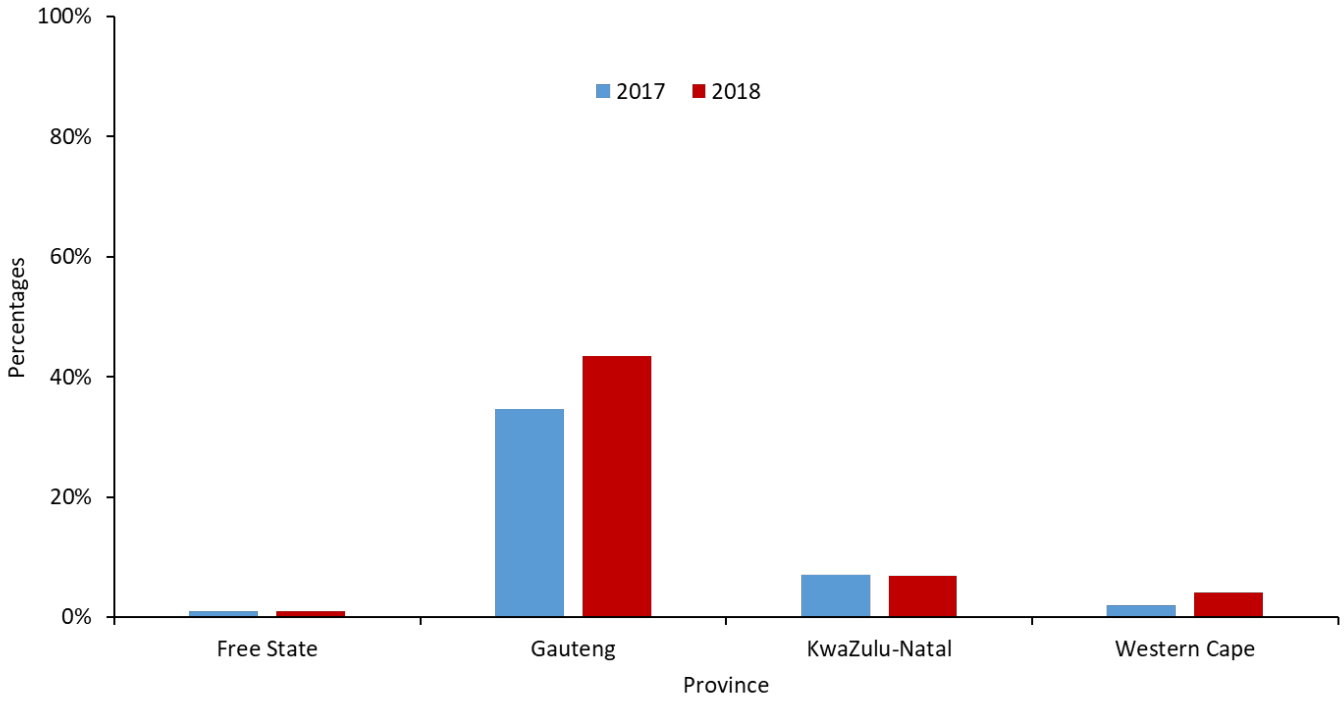


**Figure 4.** Enterobacteriaceae distribution by species for CRE bacteraemia surveillance, n=601

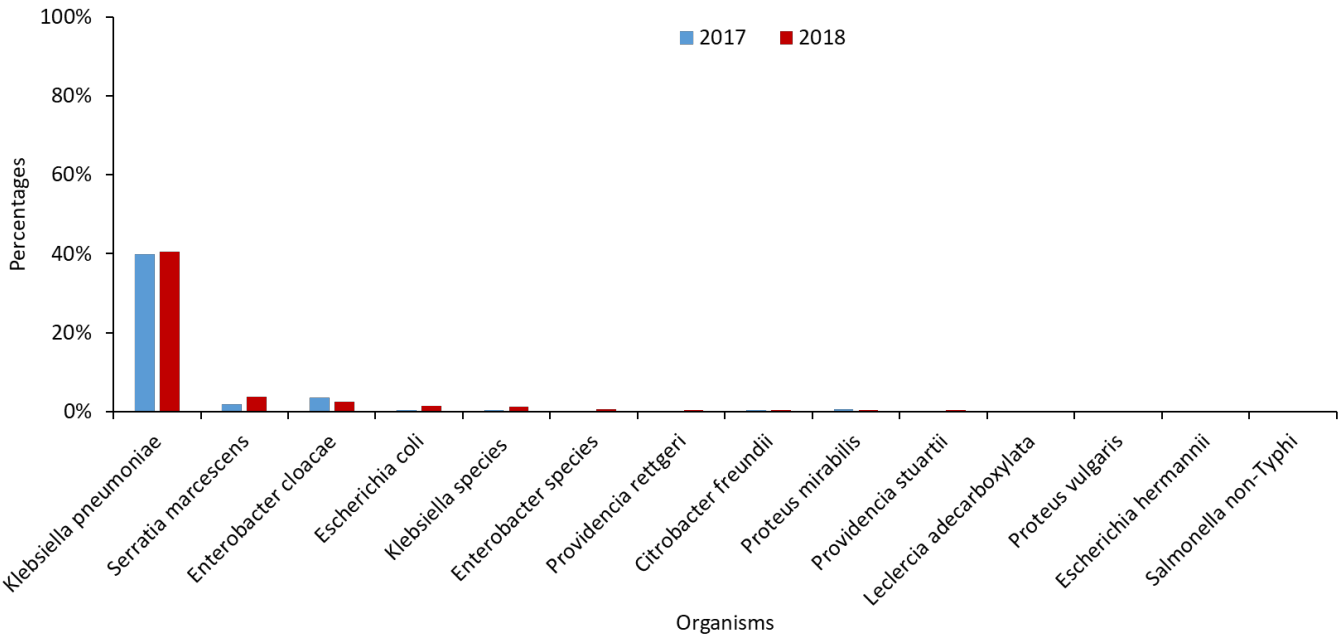



**Figure 5.** Carbapenems AST results, n=598

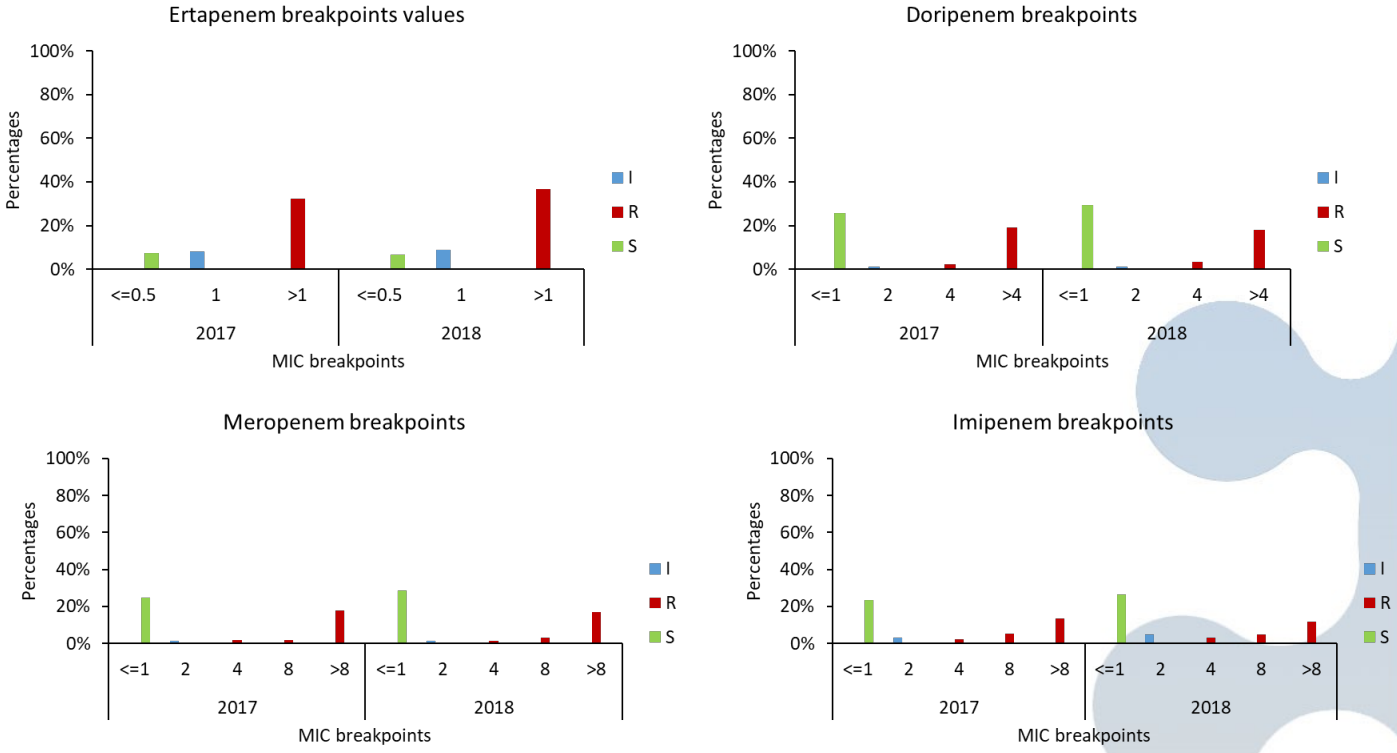


**Figure 6.** Colistin resistance by Sensititre, from total of 1 021 isolates from 2015 until December 2018, 135 (13%) resistant to colistin by MicroScan, 63 (6%) were confirmed by Sensititre

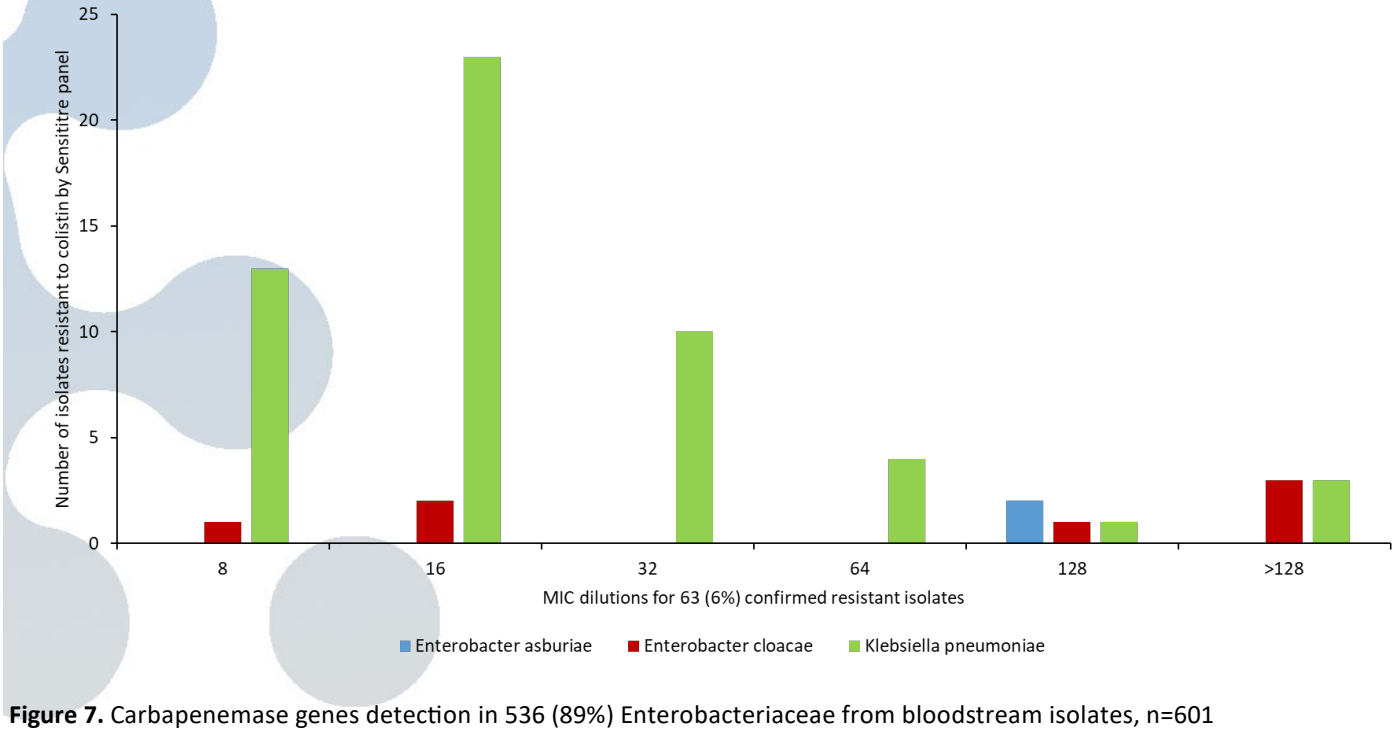



**Figure 7.** Carbapenemase genes detection in 536 (89%) Enterobacteriaceae from bloodstream isolates, n=601

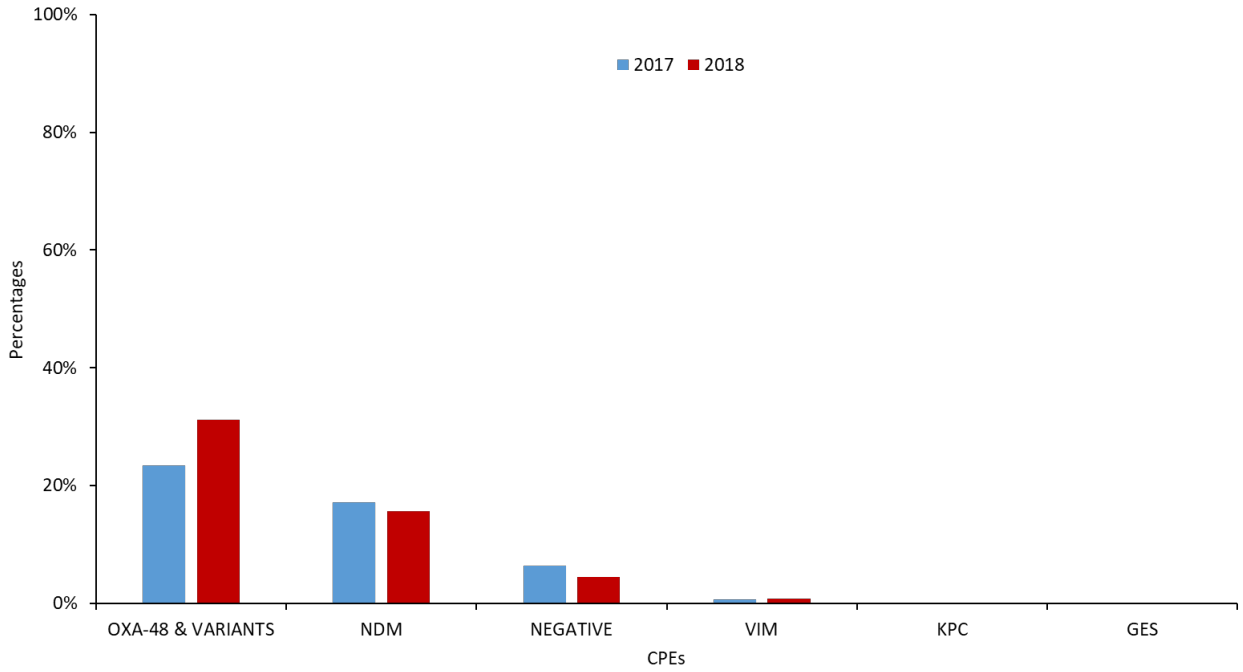
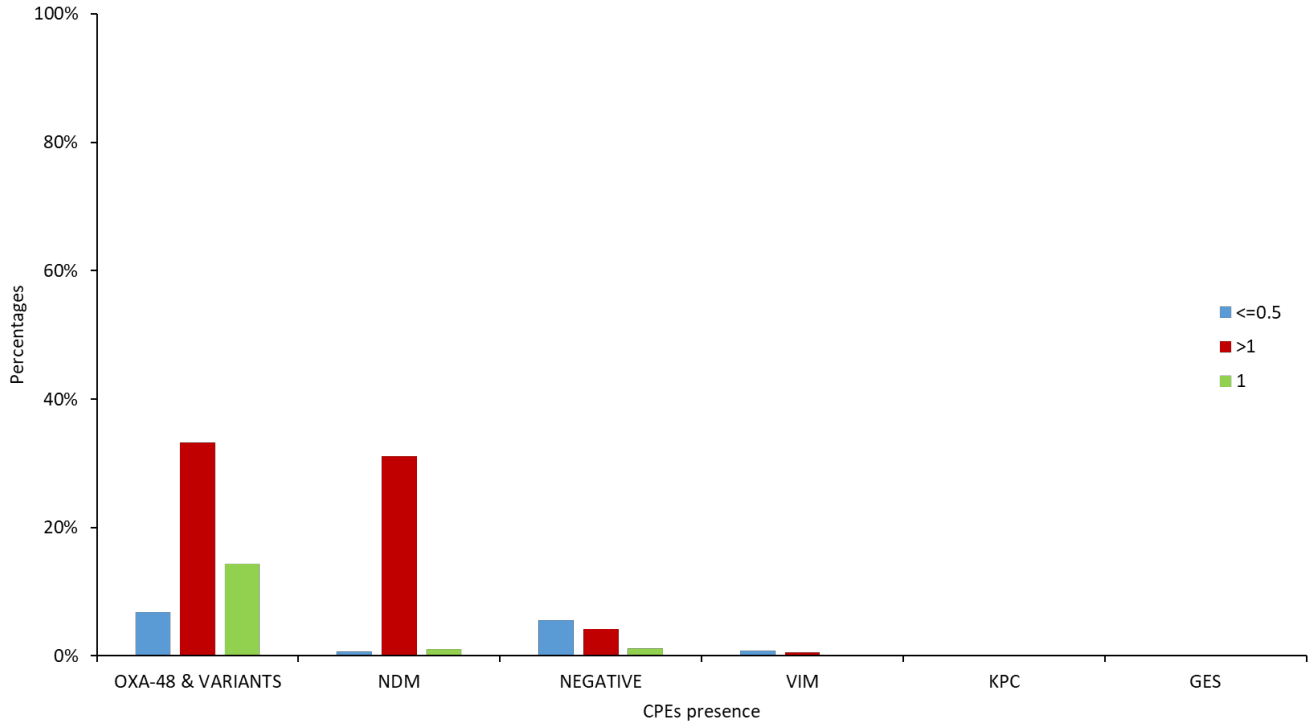


**Figure 8.** Correlation of CPEs and ertapenem susceptibility, predicting presence of enzymes is 93%




## Laboratory-based sentinel surveillance for *Acinetobacter baumannii* bacteraemia in the Gauteng, Free State, KwaZulu-Natal and Western Cape

**Results**

In 2018, 1 787 cases of AB bacteraemia were detected in four provinces, (Table 8), of which 47% (338/713) were identified by audit (enhanced surveillance began in August 2018) (Table 2). Where sex was known, males accounted for 53% (n=952). The largest proportion of patients were neonates (29%, n=516) (Figure 9). Clinical case data collected from enhanced surveillance sites (ESS) were available for 85% (n=603) of cases (Table 4). The majority of the cases were reported from ESS sites in Johannesburg and Pretoria (Table 3). Susceptibility to the most important antimicrobial agents including colistin is shown in Figure 10. Patient outcome was known for 77% (n=550) of cases, of which 37% (n=206) died in hospital. HIV status was known for 64% (387/603) of cases, of which 23% (n=88) were HIV-positive in 2018 (Table 4).

**Discussion**

AB bacteraemia has increased in the last year, particularly in the Kwa-Zulu Natal province. AB is highly prevalent in neonates and young children. The susceptibility to different classes of antibiotics is critically low; assessing clinical significance of the organism per individual case is required to be able to optimize patient management. For the optimization of antibiotic treatment and assessment of significance of the organism causing severe infection, enhanced surveillance showed that risk factors play critical roles such as duration of hospital stay, previous use of antibiotics and surgical interventions.

**Table 8.** Number and percentages of cases of *Acinetobacter baumannii* bacteraemia reported to GERMS-SA sentinel sites by province, South Africa, 2017 and 2018 (n=3 164) (including audit cases)

| Province | 2017 | | 2018 | | Total | |
|---|---|---|---|---|---|---|
| | n | % | n | % | n | % |
| Gauteng | 918 | 67 | 1 065 | 60 | 1 983 | 63 |
| Western Cape | 139 | 10 | 197 | 11 | 336 | 11 |
| KwaZulu-Natal | 166 | 12 | 321 | 18 | 487 | 15 |
| Free State | 154 | 11 | 204 | 11 | 358 | 11 |
| Total | 1 377 | 100 | 1 787 | 100 | 3 164 | 100 |

**Figure 9.** Distribution of *A. baumannii bacteraemia* cases by age category, 2018, n=1 787

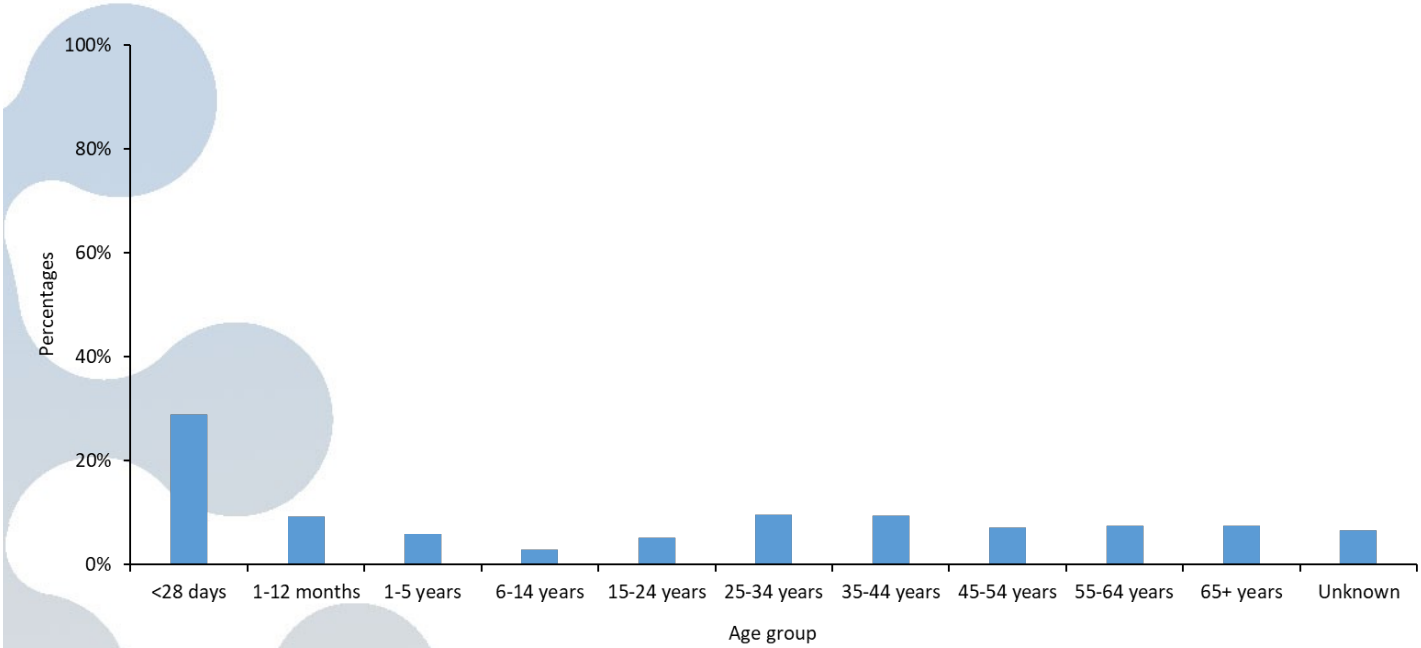
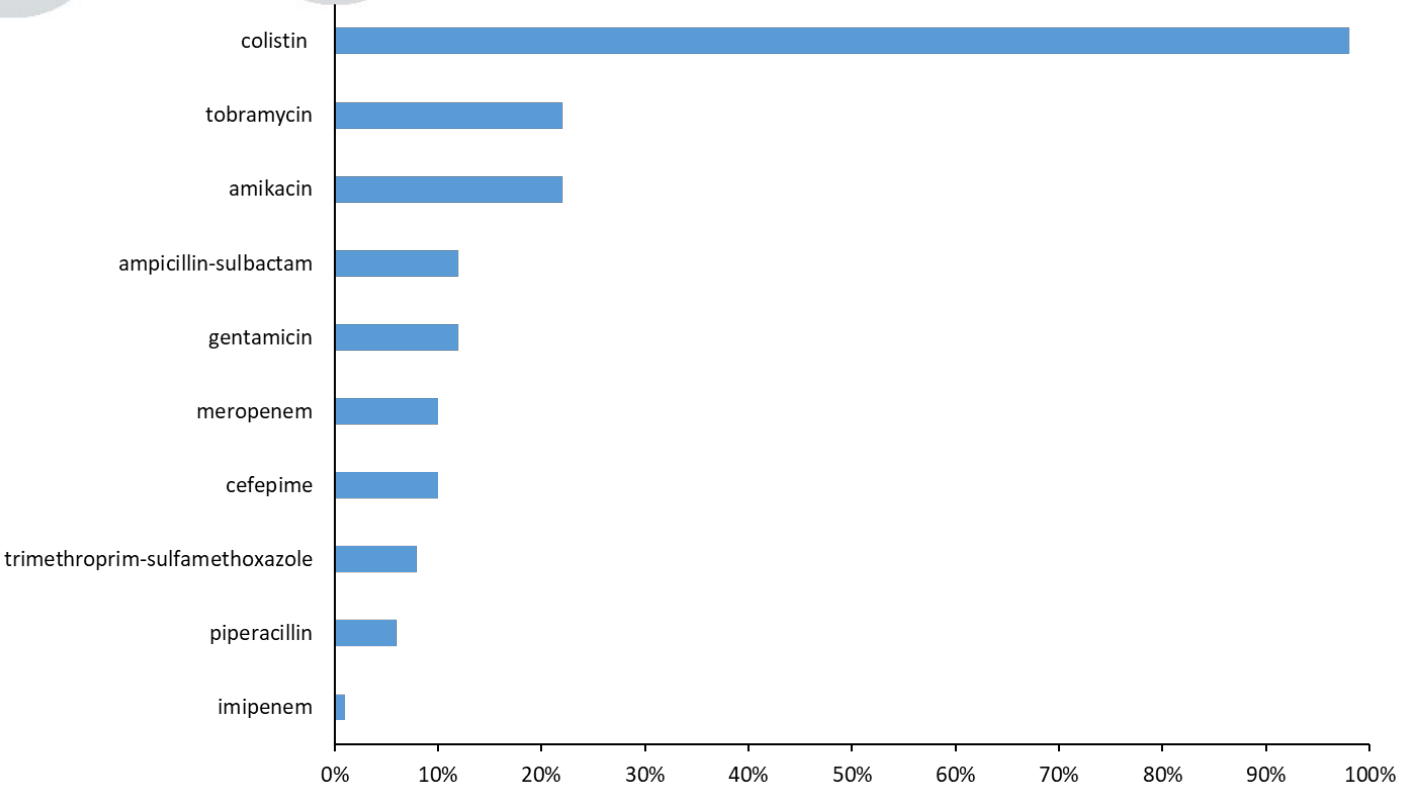



**Figure 10.** Proportion of *A. baumannii* isolates susceptible to various antimicrobial agents, 2018, n=775



## *Neisseria meningitidis*

**Results**

In 2018, 125 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 49 (39%) viable isolates were received and 23 (18%) cases were detected on audit (Table 2). The overall disease incidence was 0.22 cases per 100 000 population, similar to that in 2017 (0.24/100 000). Incidence was highest in the Western Cape Province (0.59/100 000) followed by Eastern Cape (0.40/100 000), Gauteng (0.25/100 000) and North West provinces (0.15/100 000) (Table 9). Disease peaked in winter, from May to September, with a further peak in December (Figure 11). Once again no outbreaks of meningococcal disease were detected in 2018. Cerebrospinal fluid was the most common specimen from which meningococci were identified (82/125, 66%) (Table 10). Serogroup B (42/98, 43%) was the most common serogroup causing disease, followed by W (24/98, 24%) and Y (21/98, 21%) (Table 11). IMD occurred equally in females (63/124, 51%) and males. Incidence of IMD was highest in children <1 year for all serogroups (Figure 12). Of the viable isolates tested for antimicrobial susceptibility, 12% (6/49) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) between 0.094µg/ml and 0.25µg/ml, and all were susceptible to 3$^{rd}$ generation cephalosporin and ciprofloxacin.

Fifty-one (41%) IMD patients presented to our enhanced surveillance sites and 44/51 (86%) had additional clinical information available (Table 4). The median time for each admission was 8 days (interquartile range 6-11 days). Case-fatality ratio was 12% (5/43); three patients died on the day of admission. Seventeen percent of patients with HIV status available were HIV-infected (6/36) (Table 4). For those who survived to discharge from hospital, 3/23 (13%) suffered sequelae following IMD. All three had skin scarring from necrotic lesions and two of these patients required reconstructive surgery to correct the deformity.

**Discussion**

IMD epidemiology remains largely unchanged from previous years: IMD incidence is low with serogroup B disease causing the majority of episodes. A small increase in the proportion of serogroup Y cases is noted, particularly in the Eastern Cape Province where it now predominates. High-dose penicillin is still recommended as first-line therapy for confirmed IMD, along with provision of ciprofloxacin as chemoprophylaxis to close contacts. Although uncommon, meningococcal disease in South Africa is a devastating illness affecting all age groups. In 2018, in -hospital case fatality was 12%, with 13% of survivors suffering sequelae post discharge from hospital.

**Table 9.** Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2017 and 2018, n=261 (including audit cases)

| Province | 2017 | | 2018 | |
|---|---|---|---|---|
| | n | Incidence rate* | N | Incidence rate* |
| Eastern Cape | 18 | 0.28 | 26 | 0.40 |
| Free State | 8 | 0.28 | 2 | 0.07 |
| Gauteng | 42 | 0.29 | 37 | 0.25 |
| KwaZulu-Natal | 8 | 0.07 | 8 | 0.07 |
| Limpopo | 4 | 0.07 | 4 | 0.07 |
| Mpumalanga | 4 | 0.09 | 2 | 0.04 |
| Northern Cape | 0 | 0.00 | 1 | 0.08 |
| North West | 5 | 0.13 | 6 | 0.15 |
| Western Cape | 47 | 0.72 | 39 | 0.59 |
| South Africa | 136 | 0.24 | 125 | 0.22 |

**Figure 11.** Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2017-2018, n=261

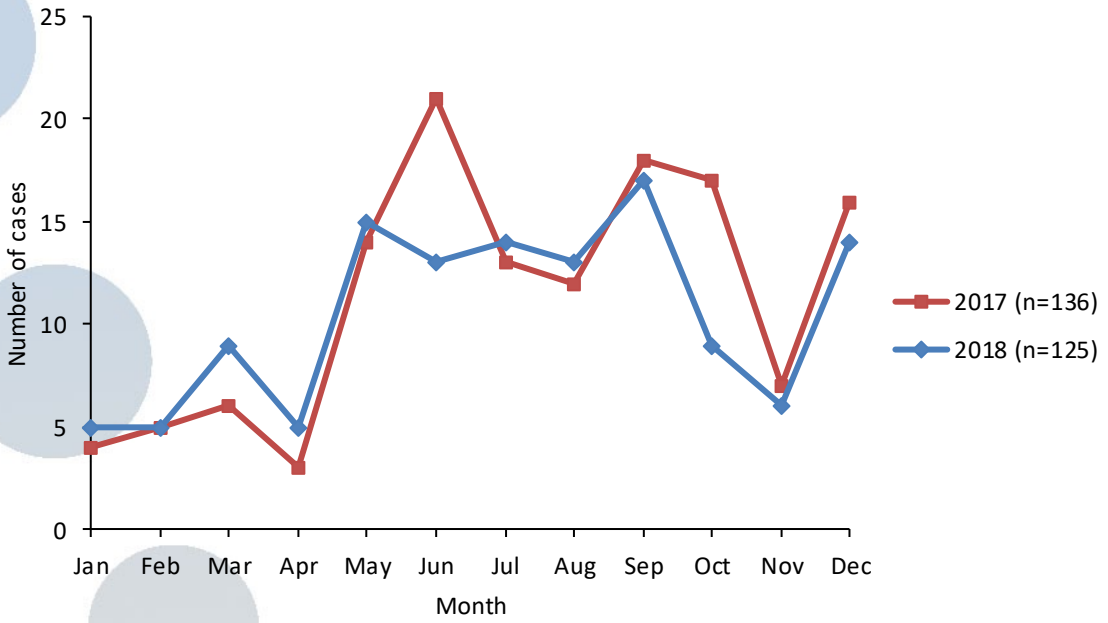



**Table 10.** Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2017 and 2018, n=261

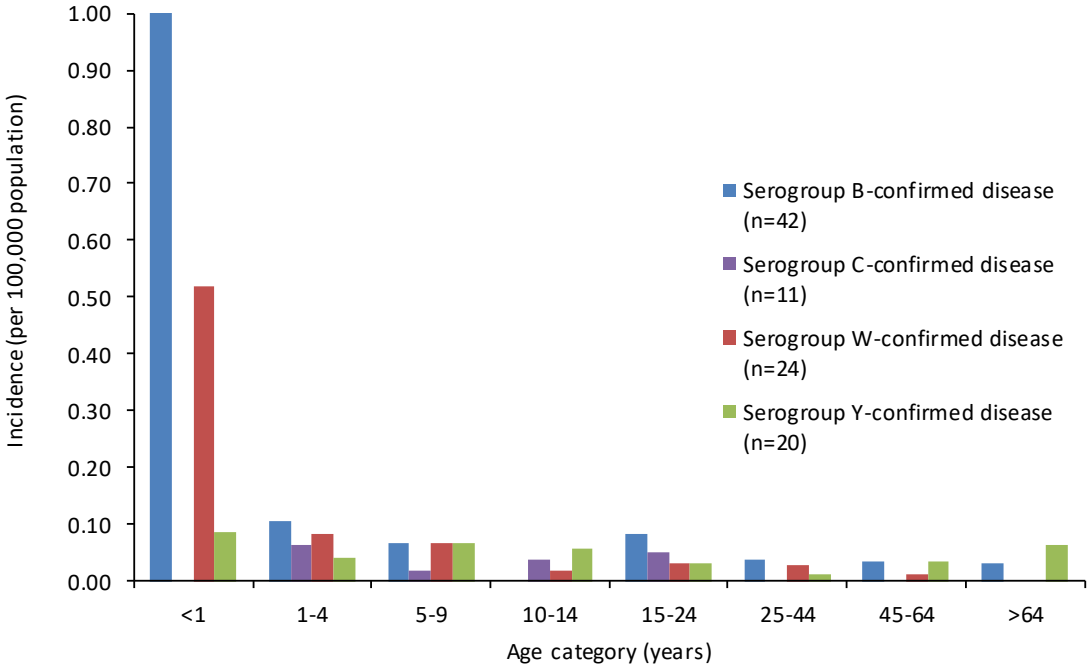
| Site of specimen | 2017 | | 2018 | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid | 93 | 68 | 82 | 66 |
| Blood | 42 | 31 | 43 | 34 |
| Other | 1 | 1 | 0 | 0 |
| Total | 136 | | 125 | |

**Table 11.** Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2018, n=125*

| Province | Serogroup | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Serogroup not available | A | B | C | W | Y | Z | NG** | Total |
| Eastern Cape | 2 | 0 | 7 | 4 | 4 | 9 | 0 | 0 | 26 |
| Free State | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 2 |
| Gauteng | 10 | 0 | 12 | 3 | 8 | 4 | 0 | 0 | 37 |
| KwaZulu-Natal | 4 | 0 | 2 | 0 | 1 | 1 | 0 | 0 | 8 |
| Limpopo | 2 | 0 | 1 | 0 | 1 | 0 | 0 | 0 | 4 |
| Mpumalanga | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 2 |
| Northern Cape | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| North West | 4 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 6 |
| Western Cape | 3 | 0 | 17 | 4 | 10 | 5 | 0 | 0 | 39 |
| South Africa | 27 | 0 | 42 | 11 | 24 | 21 | 0 | 0 | 125 |

*98 (78%) with viable isolates or specimens available for serogrouping/genogrouping; ** NG: Non-groupable

**Figure 12.** Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2018, n=125** (**age unknown for n=1; specimens or viable isolates unavailable for serogrouping n=27).




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

## *Haemophilus influenzae*

**Results**

There were 327 cases of invasive *Haemophilus influenzae* (HI) disease identified through the surveillance programme in 2018, 35% (116) were detected on audit; and 61% (201) had either viable isolates (142) or specimens (59) available for serotyping (Table 12). Four cases were co-infected with invasive *Streptococcus pneumoniae*. Western Cape Province (101/327, 31%) had the highest number of cases reported, followed by Gauteng Province (93/327, 28%) (Table 12). Seventeen percent of cases (34/201) were serotype b (Hib) and non-typeable (HNT) disease was found in 64% (129/201) (Table 12). Most HI cases were isolated from blood (200/327, 61%), however Hib isolates were more likely than HNT isolates to be found in CSF (8/34, 24% versus 15/129, 12%, p=0.01) (Table 13).

Children <1 year had the highest numbers of all types of invasive HI, followed by the 25-44 years age group (Figure 13). 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 0.8 cases per 100 000 in 2018 (p<0.001)) (Figure 14 and 15). Hib has remained below 0.2 per 100 000 in 1-4 year olds, since 2013 (Figure 15). HNT incidence is highest in infants (2.9 per 100 000) dropping substantially throughout the rest of childhood before increasing again in adulthood with a moderate peak in the >64 years age category (0.3 per 100 000) (Figure 14).

Thirty-five percent (9/26) of Hib isolates and 13% (11/86) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Seventeen cases of Hib disease occurred in children <15 years of age and vaccine history was available for 29% (5/17). Eighty percent (4/5) of these children with invasive Hib had received at least 3 doses of Hib vaccine, and were possible vaccine failures (including one fully vaccinated child who had underlying congenital cardiac disease). One 4-month old child had only received one dose of Hib vaccine.

Clinical information was available for 88% (133/152) of cases presenting to the enhanced surveillance sites (ESS) (Table 4). Patients were admitted for a median of 7 days (interquartile range (IQR) 2-13). Case fatality was 27% (36/133) 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 (13% (2/15) vs. 36% (21/59), p=0.2). Amongst those with known HIV status, 52% (47/91) were HIV-infected. Conditions other than HIV predisposing to HI disease were reported in 71/133 (53%) patients – the most common conditions included history of smoking, chronic lung disease and prematurity. Of the 19 patients at ESS with HI on CSF: one patient died during their hospitalization, and 22% (4/18) of those who survived to discharge suffered sequelae – these included three with hearing loss and one with hydrocephalus.

**Discussion**

Overall incidence of HI remains low and HNT accounts for the majority of cases. Highest rates of disease are seen in infants for both Hib and HNT, with HNT incidence increasing in the elderly. Case-fatality ratios are high (27%) and long-term sequelae following meningitis occurred in 22% of cases. Although many of the children with Hib disease had been fully vaccinated, only few vaccine histories were attainable. It is extremely important for clinicians and infection control nurses in the hospitals to make a thorough note of vaccine histories when encountering children with this devastating vaccine preventable illness and ensure appropriate use of vaccinations offered in the infant immunization programme.

**Table 12.** Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2018, n=327*

| Province | Serotype | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | Serotype not available | a | b | c | d | e | f | Non-typeable | Total |
| Eastern Cape | 14 | 1 | 4 | 0 | 0 | 0 | 2 | 24 | 45 |
| Free State | 4 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 7 |
| Gauteng | 42 | 5 | 9 | 1 | 1 | 1 | 5 | 29 | 93 |
| KwaZulu-Natal | 30 | 3 | 4 | 1 | 1 | 1 | 0 | 8 | 48 |
| Limpopo | 5 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 |
| Mpumalanga | 6 | 1 | 1 | 0 | 0 | 0 | 1 | 5 | 14 |
| Northern Cape | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 4 |
| North West | 7 | 1 | 0 | 0 | 0 | 0 | 0 | 2 | 10 |
| Western Cape | 17 | 8 | 16 | 0 | 2 | 0 | 3 | 55 | 101 |
| South Africa | 126 | 19 | 34 | 2 | 4 | 2 | 11 | 129 | 327 |

*201 (61%) with specimens or viable isolates available for serotyping.

**Table 13.** Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2018, n=327

| Site of specimen | No serotype available | | Serotype b | | Serotypes a, c, d, e, f | | Non-typeable | |
|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % |
| Cerebrospinal fluid | 26 | 21 | 8 | 24 | 12 | 32 | 15 | 12 |
| Blood | 64 | 51 | 24 | 70 | 24 | 63 | 88 | 68 |
| Other | 36 | 28 | 2 | 6 | 2 | 5 | 26 | 20 |
| Total | 126 | | 34 | | 38 | | 129 | |

**Figure 13.** Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2018, n=327 (age unknown for n=12; specimens or viable isolates unavailable for serotyping for n=126).

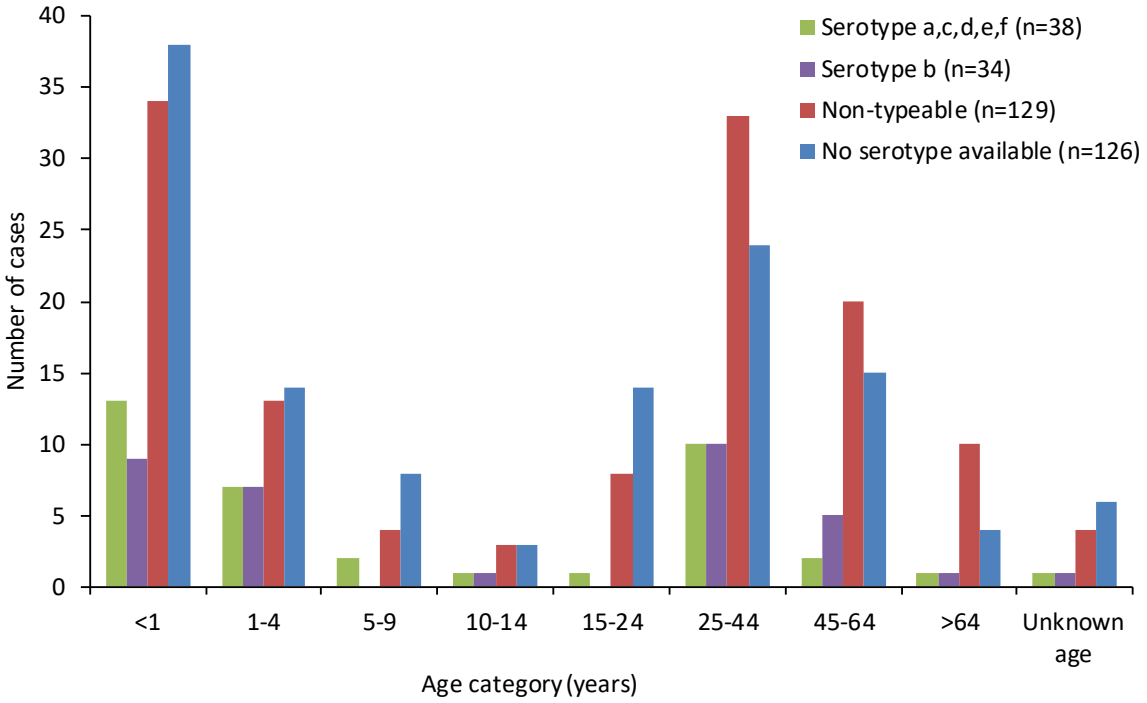
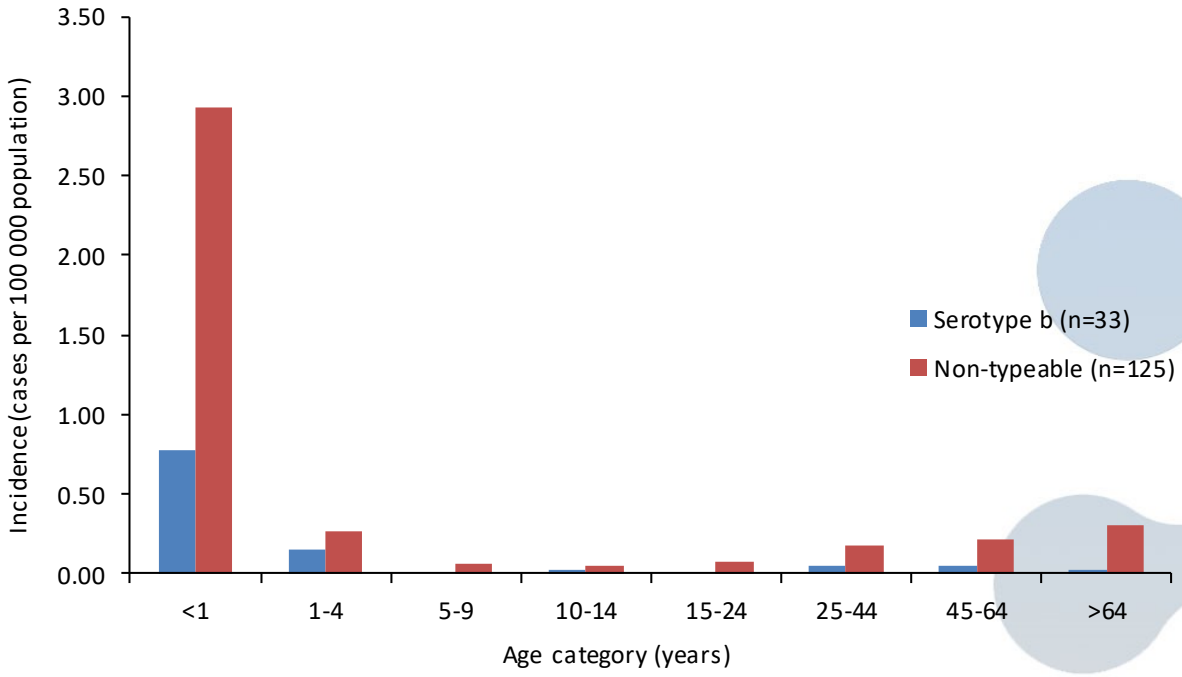
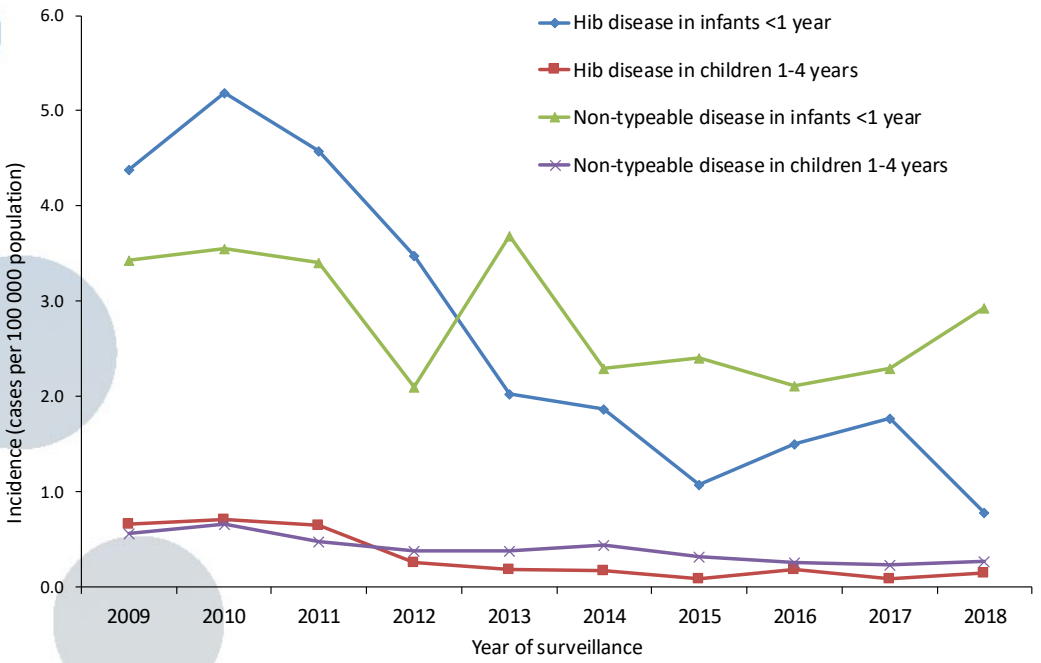



**Figure 14.** Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2018, n=327 (age unknown, n=5; viable isolates unavailable for serotyping, n=126; other serotypes from cases with known age, n=38).




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

**Figure 15.** Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2018.




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

## *Streptococcus pneumoniae*

**Results**

Incidence of invasive pneumococcal disease (IPD) in 2018 was 4 per 100 000 population, similar to that of 2017 (Table 14). IPD incidence varies greatly by province with the highest incidence seen in the Western Cape (9.5 per 100 000 population) followed by Gauteng Province (5.1 per 100 000 population) (Table 14). Pneumococcal conjugate vaccine (PCV7) was introduced into the Expanded Programme on Immunisation (EPI) in 2009, and subsequently replaced by PCV13 in 2011. Between 2009 and 2013 there were substantial reductions in IPD in all age categories and this reduction has been sustained over recent years.

In 2018, the highest incidence of IPD remains in infants (21 per 100 000 population), drops to 3 per 100 000 population in 1-4 year olds and then increases again from 25 years and above to 5 -6 per 100 000 population in the older age-categories (Figure 16). Four patients with IPD were co-infected with invasive *Haemophilus influenzae*. The majority of IPD cases were isolated from blood culture specimens (59%, 1 362/2 314) (Table 15). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 30% (402/1 335) of IPD isolates, the highest proportion was in children 1-4 years of age (56%, 36/64) (Table 16 and Figure 17). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 8% (96/1238) of isolates from all specimens, and amongst 7% (25/365) of IPD isolated from CSF. In 2018, serogroups 8, 19F, 16F, 19A and 12F were the most predominant serogroups causing IPD in children <5 years-of-age, whilst serogroups 8, 3, 19A, 12F and 4 caused the majority of disease in persons ≥5 years (Figure 18A and 18B). Only 45% (170/375) of IPD isolates from children <5 years-of-age were sent to the NICD for serotyping (Figure 19). Of these, 26% (44/170) were serotypes contained in PCV13 (Table 17).

Eighty-seven percent (758/875) of IPD patients presenting to our enhanced surveillance sites (ESS) had clinical information available. (Table 4). Patients were admitted for a median hospital stay of 7 days (interquartile range (IQR) 2-14) and most deaths occurred within 2 days of admission (IQR 0-5). Overall case fatality was 32% (244/758). HIV-infection was present in 70% (397/567) of IPD patients; and 45% (38/85) of infants with maternal HIV-status available were HIV-exposed (7 HIV-infected, 20 HIV-uninfected and 11 HIV-status unknown). Forty-five percent (341/758) of patients had a condition/risk factor (excluding HIV-infection) predisposing them to IPD. The top three factors included: history of smoking (98 patients), chronic lung disease (45 patients) and chronic renal disease (41 patients). Of 206 patients at ESS with pneumococcus on CSF: 35% (73/206) died during their hospitalization, and 23% (30/133) who survived to discharge suffered at least one sequelae – these included new onset seizures (13), limb weakness/paralysis (9), hearing loss (7), necrotic skin lesions (4) and hydrocephalus (1). Twenty-four 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 79% (19/24) of these children. Twenty-six percent (5/19) were too young to receive vaccine; 16% (3/19) of children eligible to receive vaccine had not received any PCV doses; 26% (5/19) had received all 3 doses of PCV; and 32% (6/19) had only received one dose of PCV at 6 weeks of age.

The serotypes responsible for disease in those who had received PCV13 included serotypes 19F, 19A, 23F, 6A and 14.

**Discussion**

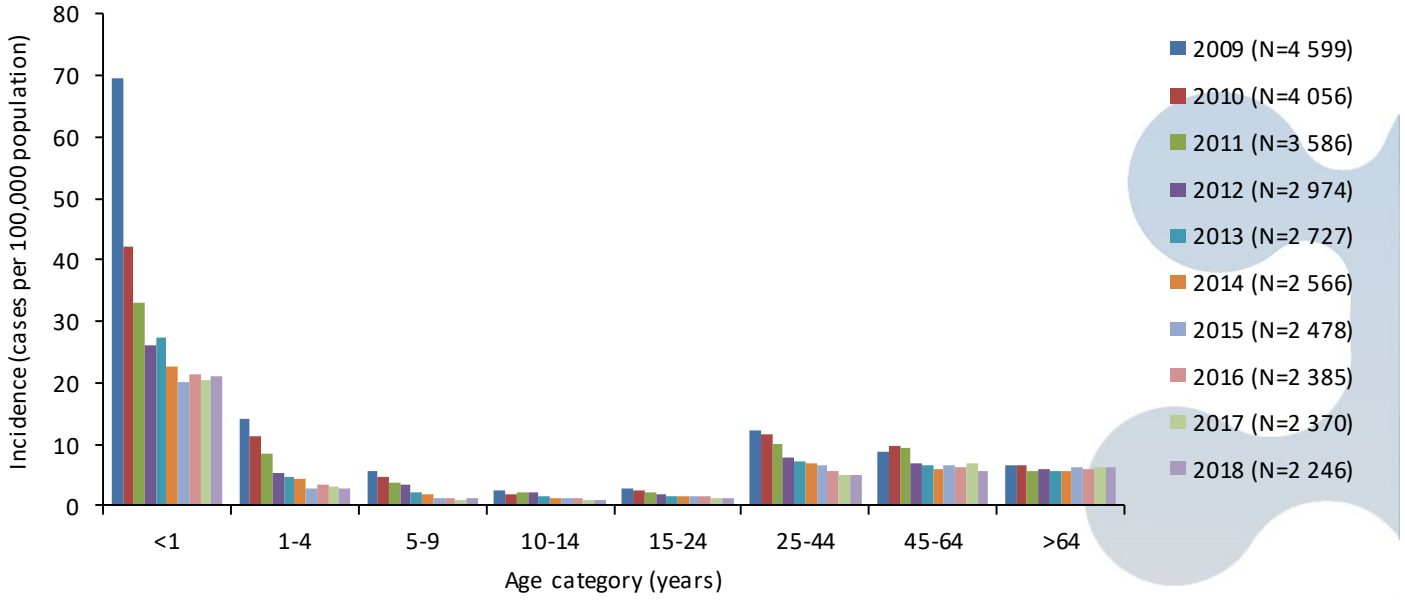
IPD incidence remains low for 2018, with sustained reductions seen amongst all age categories post PCV introduction. Infants still have the highest disease incidence, peaking again after age 25 years. Penicillin and ceftriaxone susceptibility of IPD isolates remain unchanged. HIV-infection and infant HIV-exposure remain risk factors for IPD. Pneumococcal disease has a high mortality and morbidity. Residual disease in children <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 ≥ 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. The small number of viable isolates submitted to the NICD for serotyping is concerning, and we urge laboratories to remember to forward pneumococci from normally sterile sites to the NICD to ensure ongoing reporting of IPD serotype data.

**Table 14.** Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2017 and 2018, n=4 754 (including audit cases)

| Province | 2017 | | 2018 | |
|---|---|---|---|---|
| | n | Incidence rate* | n | Incidence rate* |
| Eastern Cape | 208 | 3.20 | 258 | 3.96 |
| Free State | 109 | 3.80 | 106 | 3.59 |
| Gauteng | 891 | 6.24 | 757 | 5.14 |
| KwaZulu-Natal | 269 | 2.43 | 242 | 2.13 |
| Limpopo | 66 | 1.14 | 84 | 1.45 |
| Mpumalanga | 99 | 2.23 | 116 | 2.56 |
| Northern Cape | 53 | 4.37 | 52 | 4.24 |
| North West | 70 | 1.82 | 71 | 1.78 |
| Western Cape | 675 | 10.37 | 628 | 9.48 |
| South Africa | 2 440 | 4.32 | 2 314 | 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 16.** Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2018, n=31 401.




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=2 314, age unknown for n=68.

**Table 15.** Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2017 and 2018, n=4 754

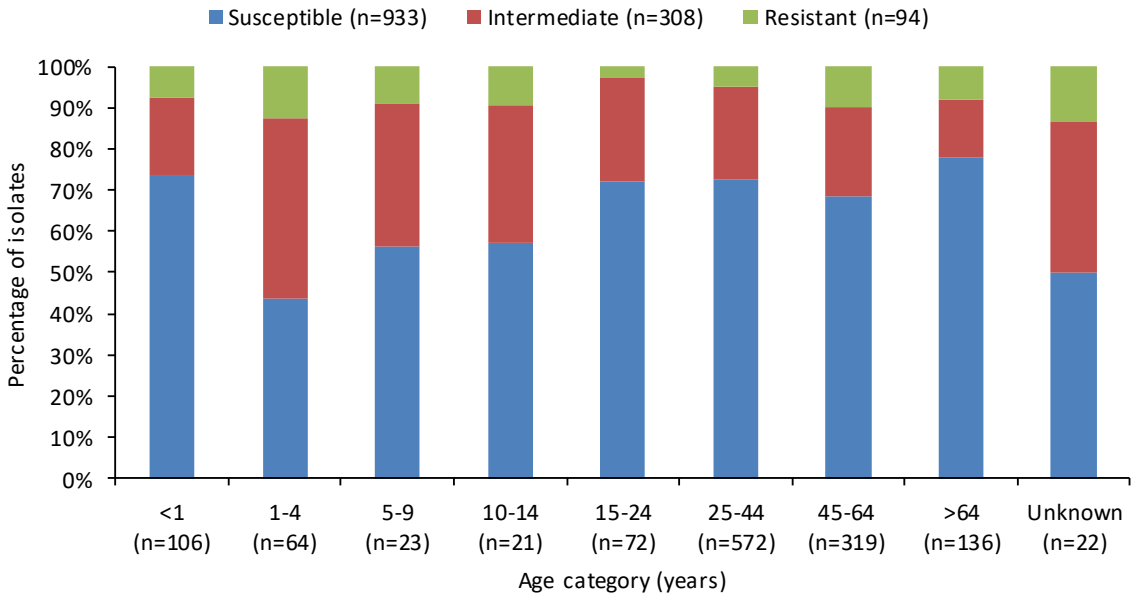
| Site of specimen | 2017 | | 2018 | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid | 792 | 32 | 794 | 34 |
| Blood | 1 480 | 61 | 1 362 | 59 |
| Other | 168 | 7 | 158 | 7 |
| Total | 2 440 | | 2 314 | |

**Table 16.** Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2018, n=2 314

| Province | Isolate not available | Susceptible* | | Intermediate* | | Resistant* | |
|---|---|---|---|---|---|---|---|
| | n | n | % | n | % | n | % |
| Eastern Cape | 122 | 101 | 74 | 30 | 22 | 5 | 4 |
| Free State | 55 | 38 | 75 | 11 | 22 | 2 | 4 |
| Gauteng | 372 | 258 | 67 | 92 | 24 | 35 | 9 |
| KwaZulu-Natal | 135 | 71 | 66 | 28 | 26 | 8 | 7 |
| Limpopo | 72 | 7 | 58 | 5 | 42 | 0 | 0 |
| Mpumalanga | 41 | 51 | 68 | 19 | 25 | 5 | 7 |
| Northern Cape | 15 | 26 | 70 | 10 | 27 | 1 | 3 |
| North West | 53 | 13 | 72 | 5 | 28 | 0 | 0 |
| Western Cape | 114 | 368 | 72 | 108 | 21 | 38 | 7 |
| South Africa | 979 | 933 | 70 | 308 | 23 | 94 | 7 |

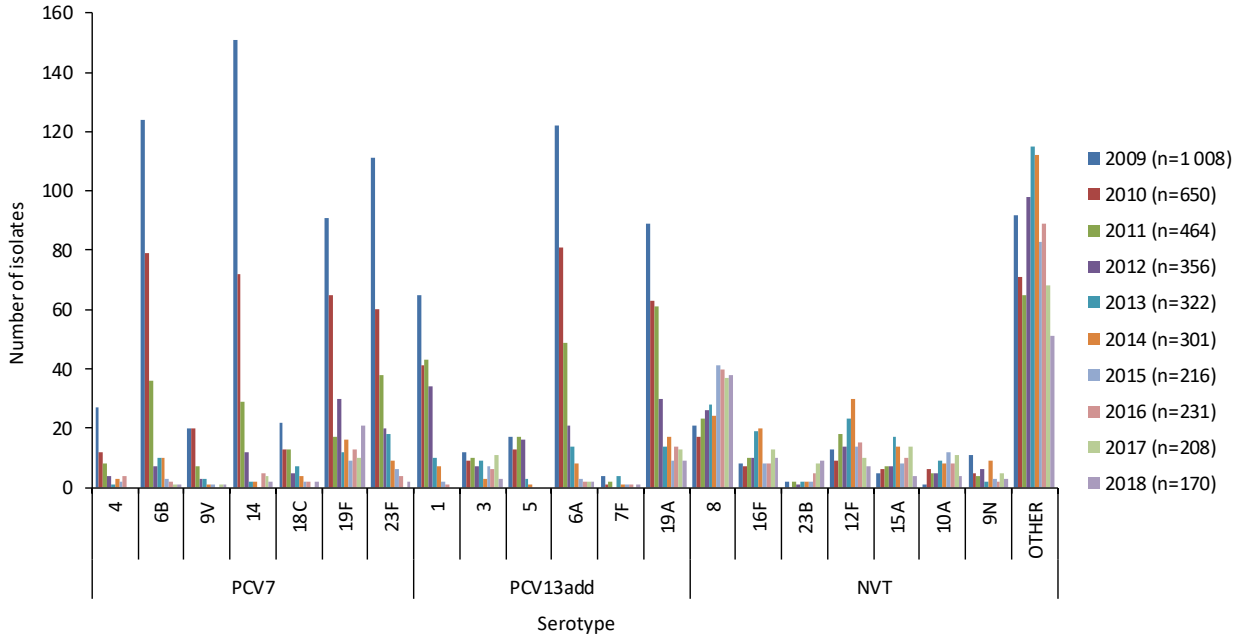
*2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

**Figure 17.** Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2018, n=2 314 (n=1 335 with viable isolates).



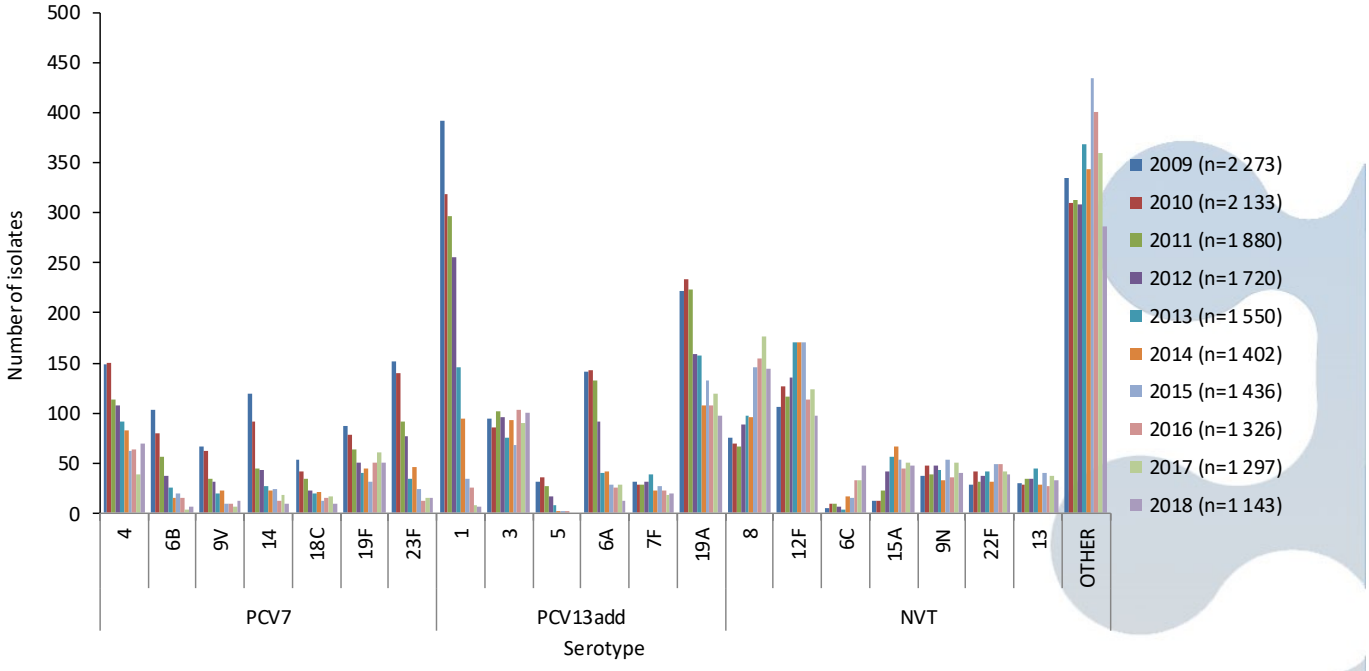

2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

**Figure 18a.** Most common pneumococcal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2017.




2009: N=1 336, 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 18b.** Most common pneumococcal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children >5 years, South Africa, 2009-2018.




2009: N=3 264, n=991 without viable isolates; 2010: N=3 146; n=1 013 without viable isolates; 2011: N=2 891, n=1 011 without viable isolates; 2012: N=2 462, n=742 without viable isolates; 2013: N=2 229, n=679 without viable isolates; 2014: N=2 101, n=699 without viable isolates; 2015: N=2 097, n=661 without viable isolates; 2016: N=1 986, n=660 without viable isolates; 2017: N=1 996, n=699 without viable isolates; 2018: N=1 871, n=728 without viable isolates.

**Figure 19.** Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, in children <5 years, South Africa, 2009-2018.

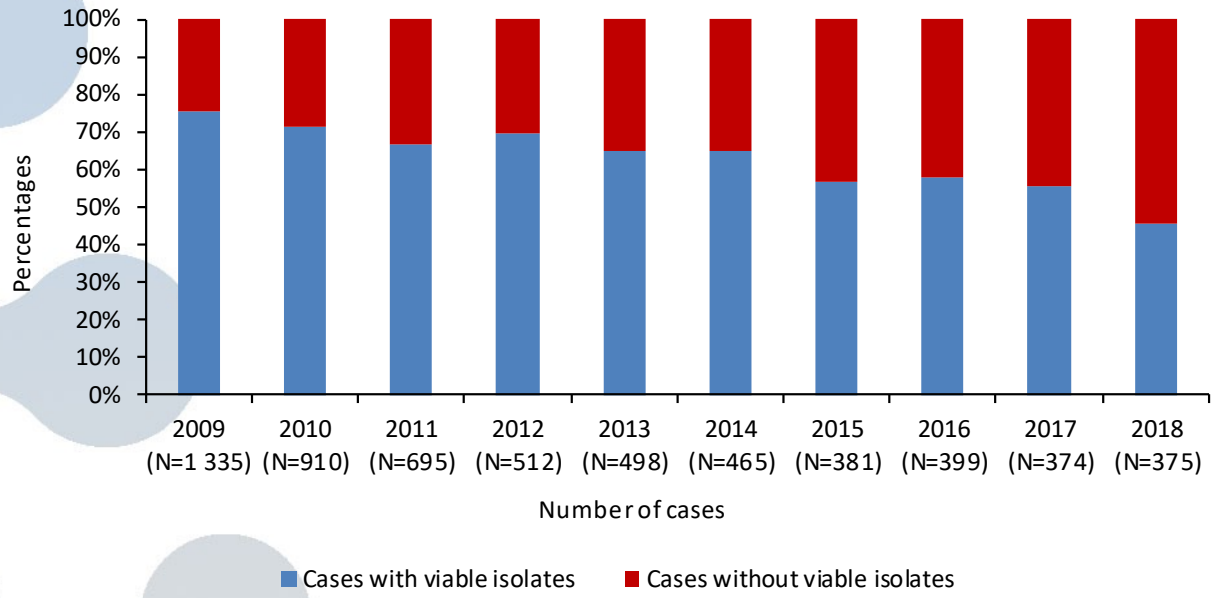



**Table 17.** Number and percentage of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2018, n=375 (n=170 with viable isolates)

| Province | Total isolates available for serotyping | 7-valent | | Serotype 6A# | | 10-valent | | 13-valent | |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | n | % |
| Eastern Cape | 11 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 18 |
| Free State | 6 | 3 | 50 | 0 | 0 | 3 | 50 | 3 | 50 |
| Gauteng | 72 | 15 | 21 | 0 | 0 | 16 | 22 | 22 | 31 |
| KwaZulu-Natal | 18 | 4 | 22 | 0 | 0 | 4 | 22 | 6 | 33 |
| Limpopo | 1 | 0 | 0 | 1 | 100 | 0 | 0 | 1 | 100 |
| Mpumalanga | 7 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 14 |
| Northern Cape | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| North West | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Western Cape | 52 | 7 | 13 | 1 | 2 | 7 | 13 | 9 | 17 |
| South Africa | 170 | 29 | 17 | 2 | 1 | 30 | 18 | 44 | 26 |

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

## Enteric fever (typhoid and paratyphoid fever): *Salmonella enterica* serotype Typhi and *S. enterica* serotypes Paratyphi A, Paratyphi B and Paratyphi C

**Results**

Typhoid fever cases with *Salmonella* Typhi isolates from all sample sites (therefore indicative of both invasive and non-invasive disease) are reported in Table 18. Cases of enteric fever (including typhoid fever (*Salmonella* Typhi) and paratyphoid fever (*S. enterica* serotypes Paratyphi A, Paratyphi B and Paratyphi C)) were highest in January, although there was no marked seasonality (Figure 20). The number of isolates within each age group is reported in Table 19, indicating that most isolates are from patients in the 5 to 14 year and 25 to 34 year age groups, although infection is seen in both older and younger age groups, including younger children (less than five years). Ciprofloxacin resistance is problematic, and a single isolate was shown to be resistant to azithromycin (Table 20), following CLSI guidelines. Five isolates of *Salmonella* Paratyphi A and seven isolates of *Salmonella* Paratyphi B were identified. No isolates of *Salmonella* Paratyphi C were reported or identified. No antimicrobial susceptibility testing was conducted on *S. enterica* serotypes Paratyphi A, Paratyphi B and Paratyphi C isolates.

**Discussion**

Typhoid fever remains endemic in South Africa. Typhoid outbreaks occurred in 2005-2006, but since then the number of culture-confirmed typhoid fever cases annually has remained stable at <150 cases per year. Most cases are typically sporadic, but small clusters have also been identified. Although imported travel-related cases are reported, the majority of cases are locally acquired reflecting ongoing, albeit it low-level, transmission.

*Salmonella* Typhi isolates from both invasive and non-invasive sites are included in these analyses, as both add to the burden of infection in South Africa and thus represent a public health risk. The diagnosis of enteric fever remains challenging; clinical index of suspicion and appropriate laboratory tests are critical in identifying cases. Given the limitations of serological testing, culture (and more recently, PCR) remains the gold standard for confirmation of disease. Therefore, the prevailing clinician testing behaviour heavily influences the likelihood of detecting enteric fever cases. Although this data may not reflect actual burden of disease, numbers were comparable with previous non-outbreak years. Although strict seasonality is not observed, as in previous years the greatest number of cases were seen during January. Greater numbers reported from Gauteng and Western Cape provinces may reflect healthcare seeking behaviour and prevailing clinician testing behaviour. The number of reported *Salmonella* Typhi isolates is regarded as an underestimate and thus incidence rates were not calculated. *Salmonella* Typhi should routinely be tested against azithromycin, which is an alternative treatment option, as ciprofloxacin resistance emerges. Continual monitoring of resistance to these two antimicrobials has become mandatory. Ceftriaxone may also be used as an alternative therapy. Paratyphoid fever remains uncommon in South Africa, accounting for 11% (12/103) of total enteric fever cases.

**Table 18.** Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2018, n=91 (including audit reports, missing isolates, mixed and contaminated cultures).

| Province | Non-invasive *Salmonella* Typhi | Invasive *Salmonella* Typhi |
|---|---|---|
| Eastern Cape | 1 | 4 |
| Free State | 0 | 1 |
| Gauteng | 8 | 30 |
| KwaZulu-Natal | 0 | 8 |
| Limpopo | 1 | 9 |
| Mpumalanga | 2 | 7 |
| Northern Cape | 0 | 0 |
| North West | 0 | 1 |
| Western Cape | 2 | 17 |
| South Africa | 14 | 77 |

**Figure 20.** Number of non-invasive and invasive cases of *Salmonella* Typhi (n=91) and Paratyphi (n=12) reported to GERMS-SA, by month of specimen collection, South Africa, 2018 (including audit reports).

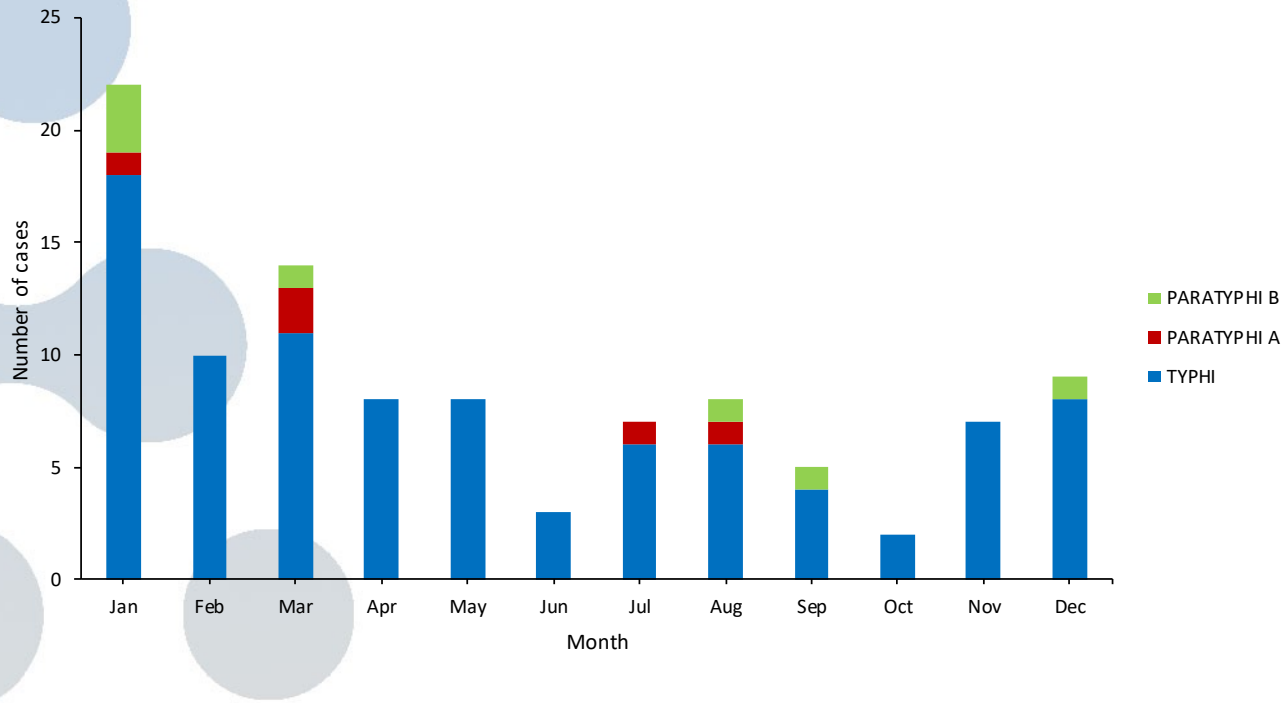



**Table 19.** Number of *Salmonella* Typhi cases reported to GERMS-SA by age category, South Africa, 2018, n=91 (including audit reports, missing isolates, mixed and contaminated cultures).

| Age category (years) | *Salmonella* Typhi cases |
|---|---|
| 0 - 4 | 5 |
| 5 - 14 | 28 |
| 15 - 24 | 13 |
| 25 - 34 | 18 |
| 35 - 44 | 11 |
| 45 - 54 | 9 |
| 55 - 64 | 4 |
| ≥ 65 | 2 |
| Unknown | 1 |
| Total | 91 |

**Table 20.** Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2018, ciprofloxacin, n=74 and azithromycin, n=71 (excluding audit reports, missing isolates, mixed and contaminated cultures).

| Antimicrobial agent | Susceptible (%) | Resistant (%) |
|---|---|---|
| Ciprofloxacin (n=74) | 57 (77%) | 17 (23%) |
| Azithromycin (n=71) | 70 (99%) | 1 (1%) |

## Non-typhoidal *Salmonella enterica* (NTS)

**Results**

Invasive disease does not appear to have a seasonal prevalence; increased numbers of non-invasive disease in the earlier months of the year and a lower incidence in the winter months reflect seasonality (Figure 21). The number of cases of invasive and non-invasive disease by province is stated in Table 21. The number of cases of invasive and non-invasive disease, by age group, is shown in Table 22; non-invasive disease was highest in children under five years of age, whilst invasive disease was most common in adults aged 35 – 44 years. Most invasive isolates were identified from blood cultures (87%, 563/648), although isolates were frequently identified from both blood culture and another site, including stool and other normally-sterile sites (Table 23). Serotyping and antimicrobial susceptibility testing of referred isolates was undertaken on request, or when associated with an outbreak.

**Discussion**

Non-typhoidal salmonellosis may be foodborne, in which case patients typically present with gastroenteritis, or may be associated with HIV-infection, in which case the organism frequently becomes invasive. As in previous years, seasonal prevalence was noted in 2018 for non-invasive disease.

**Figure 21.** Number of non-invasive (n=1 229) and invasive (n= 648) cases of non-typhoidal *Salmonella* reported to GERMS-SA, by month of specimen collection, South Africa, 2018 (including audit reports).

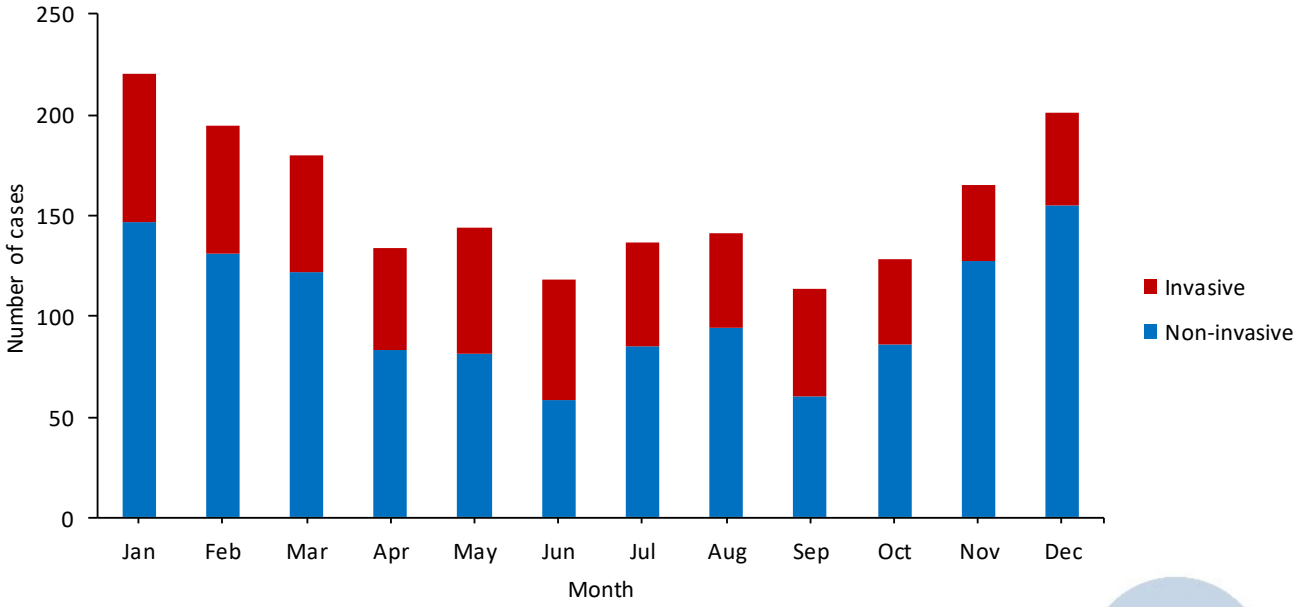



**Table 21.** Number of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2018, n= 1 877 (including audit reports, missing isolates, mixed and contaminated cultures).

| Province | Non-invasive, non-typhoidal *Salmonella* cases | Invasive non-typhoidal *Salmonella* cases |
|---|---|---|
| Eastern Cape | 204 | 53 |
| Free State | 53 | 26 |
| Gauteng | 236 | 208 |
| KwaZulu-Natal | 296 | 84 |
| Limpopo | 63 | 26 |
| Mpumalanga | 96 | 40 |
| Northern Cape | 23 | 17 |
| North West | 54 | 36 |
| Western Cape | 204 | 158 |
| Unknown | 0 | 0 |
| South Africa | 1 229 | 648 |

**Table 22.** Number of cases of invasive and non-invasive non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2018, n=1 877 (including audit reports, missing isolates, mixed and contaminated cultures).

| Age Category (years) | Cases | |
|---|---|---|
| | Non-invasive | Invasive |
| 0 - 4 | 243 | 117 |
| 5 - 14 | 125 | 25 |
| 15 - 24 | 112 | 43 |
| 25 - 34 | 184 | 120 |
| 35 - 44 | 194 | 144 |
| 45 - 54 | 122 | 83 |
| 55 - 64 | 99 | 42 |
| ≥ 65 | 103 | 38 |
| Unknown | 47 | 36 |
| Total | 1 229 | 648 |

**Table 23.** Number of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2018, n=1 877 (including audit reports, missing, mixed and contaminated cultures).

| Specimen | n | % |
|---|---|---|
| CSF | 13 | 0.7 |
| Blood culture | 563 | 30 |
| Stool | 882 | 47 |
| Other | 419 | 22.3 |
| Total | 1 877 | 100 |

*Many cases had multiple isolates of the same serotype, including those with isolates from an invasive site of origin and a second isolate from stool, or isolates from two different normally-sterile sites.

## *Shigella* species

**Results**

The highest number of shigellosis cases for 2018 occurred in January through March (Figure 22). which is in keeping with previous years (2008 – 2015, and 2017) when increased cases during summer months suggested seasonality. The primary manifestation of disease due to *Shigella* is non-invasive dysentery or diarrhoea, although invasive disease cases continue to occur (Table 24). The predominant burden of disease, including both invasive and non-invasive shigellosis, is in the under-five-year age group (Table 25). Serotyping and antimicrobial susceptibility testing of referred isolates was undertaken by request or when associated with an outbreak.

**Discussion**

Although *Shigella* infection has been associated with water-borne outbreaks in South Africa, person-to-person transmission also plays an important role. Invasive disease appears to be decreasing.

**Figure 22.** Number of non-invasive and invasive *Shigella* cases reported to GERMS-SA, by month of specimen collection, South Africa, 2018, n = 841 (including audit reports).

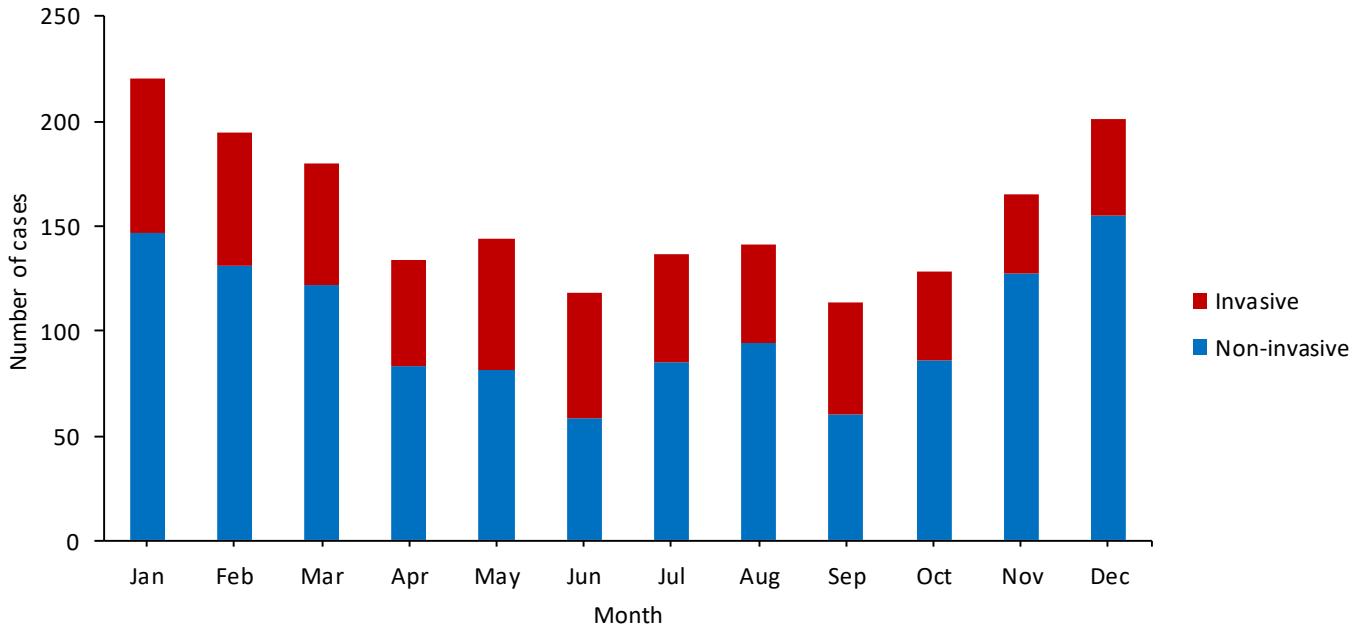



**Table 24.** Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2018, n=841 (including audit reports, missing isolates, mixed and contaminated cultures).

| Province | Non-invasive *Shigella* | Invasive *Shigella* |
|---|---|---|
| Eastern Cape | 147 | 0 |
| Free State | 50 | 1 |
| Gauteng | 136 | 19 |
| KwaZulu-Natal | 137 | 3 |
| Limpopo | 6 | 1 |
| Mpumalanga | 20 | 1 |
| Northern Cape | 5 | 0 |
| North West | 21 | 4 |
| Western Cape | 283 | 7 |
| South Africa | 805 | 36 |

**Table 25.** Number of invasive and non-invasive *Shigella* cases reported to GERMS-SA by age category, South Africa, 2018, n=841 (including audit reports, missing isolates, mixed and contaminated cultures).

| Age Category (years) | Cases | |
|---|---|---|
| | Non-invasive | Invasive |
| 0 - 4 | 323 | 13 |
| 5 - 14 | 119 | 3 |
| 15 - 24 | 41 | 2 |
| 25 - 34 | 87 | 4 |
| 35 - 44 | 64 | 5 |
| 45 - 54 | 52 | 0 |
| 55 - 64 | 54 | 2 |
| ≥ 65 | 49 | 5 |
| Unknown | 16 | 2 |
| Total | 805 | 36 |

## *Vibrio cholerae* O1

**Results**

Five cases of *Vibrio cholerae* O1 were identified in 2018 (Table 26). Two epidemiologically linked cases were confirmed to be imported from Zimbabwe during the Zimbabwean cholera outbreak, and two sporadic case-patients each reported close contact with traveller/s recently returned from Zimbabwe prior to the onset of their respective illnesses. The fifth case was an isolated sporadic case, and the source of infection could not be established.

**Discussion**

Cholera is not endemic in South Africa. Infrequent, sporadic cholera cases are reported and are typically imported (travel-related). The notable exception is the 2008-2009 cholera outbreak which began as a spill-over from neighbouring Zimbabwe.

During 2018, imported and sporadic cases were identified. However, prompt and effective public health response in all cases ensured that local transmission did not occur.

**Table 26**. Number of cholera cases reported to GERMS-SA by province and month of diagnosis, South Africa, 2018, n = 5*

| Province | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| GA | | | | | | | | | | | 2 | | 2 |
| KZ | | | 1 | | | | | | | | | | 1 |
| LP | | | | | | | | | | | | 2 | 2 |
| Total | | | 1 | | | | | | | | 2 | 2 | 5 |

*Four cases (those diagnosed during October and November) had either travelled to Zimbabwe or reported close contact with a person recently returned from travel to Zimbabwe, prior to illness onset.

## *Listeria monocytogenes*

**Results**

The highest case numbers occurred in January through March 2018, prior to the identification of the source of the outbreak. Following the announcement on 4 March 2018 that the source of the outbreak was identified and the implicated food products recalled, the number of cases sharply declined. The outbreak was officially declared over on 3 September, by which time the number of new cases had decreased to ≤5 cases per week. Table 27 shows the provincial distribution of cases. Although cases occurred in all provinces, 78% were reported from three provinces: Gauteng (209/386, 54%), Western Cape (60/386, 16%) and KwaZulu-Natal (34/386, 9%). Where age is available, neonates ≤28 days accounted for 43% (162/377) of the cases, and 33% (124/377) of the cases were adults aged 15-49 years (Figure 23). All laboratory-confirmed cases were classified as listeriosis, regardless of primary anatomical site of isolation (Table 28). *L. monocytogenes* was most commonly isolated from blood culture (70%) followed by CSF (12%).

**Discussion**

GERMS-SA played a vital role in supporting the listeriosis outbreak investigation during 2017 and 2018. Now that listeriosis is a notifiable medical condition, routine surveillance will assist in detecting unusual trends in case numbers which may indicate outbreaks, to allow for rapid investigation and response.

**Table 27.** Number of listeriosis cases reported to GERMS-SA, by province, South Africa, 2018, n=386 (including audit reports, missing isolates, mixed and contaminated cultures).

| Province | Number of cases |
|---|---|
| Eastern Cape | 23 |
| Free State | 11 |
| Gauteng | 209 |
| KwaZulu-Natal | 34 |
| Limpopo | 18 |
| Mpumalanga | 19 |
| Northern Cape | 1 |
| North West | 11 |
| Western Cape | 60 |
| Unknown | 0 |
| South Africa | 386 |

**Figure 23.** Number of listeriosis cases reported to the Centre for Enteric Diseases, by age group and gender, South Africa, 2018, n = 386 (including audit reports).

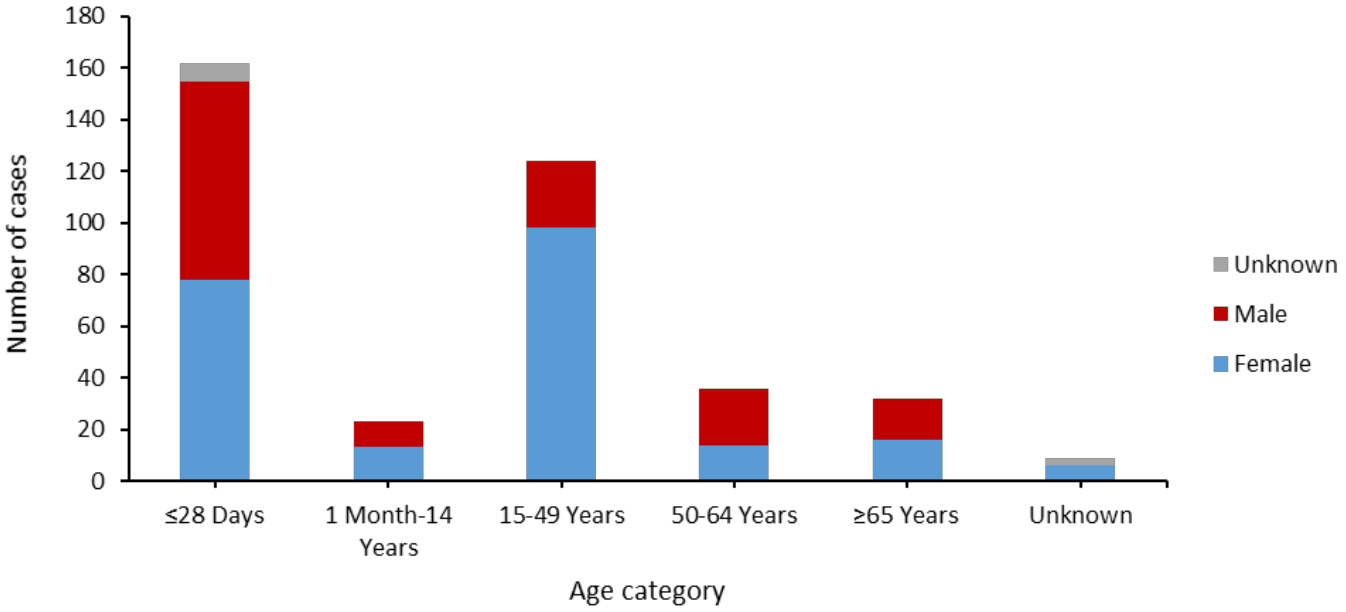



**Table 28.** Number of listeriosis cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2018, n=386 (including audit reports, missing, mixed and contaminated cultures).

| Specimen | n | % |
|---|---|---|
| CSF | 47 | 12.2 |
| Blood culture | 272 | 70.5 |
| Stool | 5 | 1.3 |
| Other | 62 | 16 |
| Total | 386 | 100 |

*Many cases had multiple isolates from different body sites

## Rifampicin-susceptible Tuberculosis

**Results**

In 2018, 854 participants were recruited and had sputum samples submitted. Valid drug susceptibility results for INH were available for 664 isolates, for which 603 completed CRFs were available for analysis. Participants enrolled, were from five provinces (Eastern Cape, Gauteng, KZN, Mpumalanga and North West). Majority of participants were male (56%). Almost 70% of the patients were HIV positive. Sixty-five percent were already on ART and 24% were due to initiate therapy. Twenty-four percent reported to have at least one episode of previous TB infection. Forty percent reported to have lived with a person diagnosed with TB in the last 12 months. Only 43% of these contacts were screened for TB, of which 80% tested positive for TB. Treatment was completed in only 38% of patients. Table 29 shows the comparison of risk factors by INH resistance. Cultures were negative in 18% (143/791) and 7% (52/791) were contaminated, precluding further analysis. Majority of samples received were from Gauteng (38%), followed by North West (20%), Kwa-Zulu Natal (19%), Mpumalanga and Eastern Cape both at 11%. Thirty-three of these were isoniazid mono resistant (IMR), 90% were smear positive. North West had the highest prevalence (8.4%), followed by Kwa-Zulu Natal (6.0%), Eastern Cape (5.7%), Gauteng (4.3%), and Mpumalanga (3%). The overall IMR prevalence was 5%. Only 12 participants reported taking INH prophylactic therapy, three of these participants had INH Resistance.

**Discussion**

The majority of TB cases were co-infected with HIV highlighting its continued importance in controlling the TB epidemic. Antiretroviral treatment has been previously shown to reduce TB incidence, and it is encouraging seeing that almost 90% were part of the ARV program. Age and gender distribution of the participants was in keeping with the National reports and, with what is observed on the TB dashboard. The overall prevalence of IMR (5%) is in keeping with what was found in the National TB drug resistant survey (5-8%). It is also interesting to note the high smear positivity rate of IMR cases, which is indicative of transmission, particularly in the North West province. The only significant risk factor for IMR was IPT (although numbers were very small). A low proportion of patients exposed to TB were screened, indicating that contact tracing of index cases is not as optimal as it should be, and requires strengthening. The high prevalence of smoking, which is a known risk factor for TB, is an important health issue that is often overlooked leading to poor lung health and increased long-term susceptibility to TB and other infections. A large proportion of participants were unemployed (69%), an underappreciated factor that impacts on health delivery. The findings of this surveillance has important public health importance, and even though the surveillance was conducted only at a few sites, the results obtained are useful and insightful to understand the epidemic and monitor trends.

**Table 29.** INH Mono Resistance Risk Factor Table

| | | INH Sensitive | INH mono R | Full Cohort (n) |
|---|---|---|---|---|
| **All lab results** | | 624 (94) | 40 (6) | 664 |
| **Patients with CRFs** | | 570 (95) | 33 (5) | 603 |
| **Gender** | | | | |
| | Male | 318 (56) | 18 (55) | 336 (56) |
| | Female | 252 (44) | 15 (45) | 267 (44) |
| **Age Category** | | | | |
| | <20 years | 16 (3) | 0 (0) | 16 (3) |
| | 20-34 years | 217 (38) | 14 (42) | 231 (38) |
| | 35-49 years | 222 (39) | 15 (45) | 237 (39) |
| | 50+ years | 113 (20) | 4 (12) | 117 (19) |
| | unknown | 2 (0) | 0 (0) | 2 (0) |
| **Province** | | | | |
| | Eastern Cape | 66 (12) | 4 (12) | 70 (11) |
| | Gauteng | 222 (39) | 10 (30) | 232 (38) |
| | KwaZulu-Natal | 109 (19) | 7 (21) | 116 (19) |
| | Mpumalanga | 64 (11) | 2 (6) | 66 (11) |
| | North West | 109 (19) | 10 (30) | 119 (20) |
| **Education (completed)** | | | | |
| | None | 28 (5) | 2 (6) | 30 (5) |
| | Primary | 151 (26) | 8 (24) | 159 (26) |
| | Secondary | 358 (63) | 22 (67) | 380 (63) |
| | Tertiary | 32 (6) | 1 (3) | 33 (5) |

| | | INH Sensitive | INH mono R | Full Cohort (n) |
|---|---|---|---|---|
| **All lab results** | | 624 (94) | 40 (6) | 664 |
| **Patients with CRFs** | | 570 (95) | 33 (5) | 603 |
| **Employment** | | | | |
| | Full-time | 101 (18) | 7 (21) | 108 (18) |
| | Part-time | 54 (9) | 2 (6) | 56 (9) |
| | Self-employed | 18 (3) | 2 (6) | 20 (3) |
| | Unemployed | 397 (70) | 22 (67) | 419 (69) |
| **Healthcare worker** | | | | |
| | No | 554 (97) | 31 (94) | 585 (97) |
| | Yes | 15 (3) | 2 (6) | 17 (3) |
| **Miner (ever)** | | | | |
| | No | 552 (97) | 32 (97) | 584 (97) |
| | Yes | 16 (3) | 1 (3) | 17 (3) |
| **Prisoner (ever)** | | | | |
| | No | 501 (88) | 28 (85) | 529 (88) |
| | Yes | 67 (12) | 5 (15) | 72 (12) |
| **Alcohol frequency** | | | | |
| | Never/<1 month | 451 (79) | 29 (88) | 480 (80) |
| | 1-4 times per month | 72 (13) | 2 (6) | 74 (12) |
| | >1 per week | 45 (8) | 2 (6) | 47 (8) |
| **Smoking** | | | | |
| | Never | 329 (58) | 21 (64) | 350 (58) |
| | Former smoker | 107 (19) | 5 (15) | 112 (19) |
| | Smoker | 133 (23) | 7 (21) | 140 (23) |
| **Recreational Drug Use** | | | | |
| | No | 515 (90) | 32 (97) | 547 (91) |
| | Yes | 53 (9) | 1 (3) | 54 (9) |
| **HIV status** | | | | |
| | Negative | 159 (28) | 8 (24) | 167 (28) |
| | Positive | 394 (69) | 24 (73) | 418 (69) |
| | Unknown | 17 (30 | 1 (3) | 18 (3) |
| **Previous IPT** | | | | |
| | No | 378 (98) | 21 (88) | 399 (97) |
| | Yes | 9 (2.3) | 3 (13) | 12 (3) |
| **Previous TB episodes** | | | | |
| | None | 437 (77) | 23 (70) | 460 (77) |
| | 1 | 112 (20) | 7 (21) | 119 (20) |
| | >=2 | 19 (3) | 3 (9) | 22 (4) |
| **Lived with someone with TB** | | | | |
| | No | 453 (81) | 25 (76) | 478 (80) |
| | Yes | 108 (19) | 8 (24) | 116 (20) |

* Fisher's exact

## References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**Hats off to our great staff!!!**

**Together, everyone achieves more!!!**

## Syndromic surveillance

## Diarrhoeal surveillance

**Introduction**

The mortality rate of children less than five years of age in South Africa has decreased from 78.1 per 1000 live births in 2003 to 37-40 deaths per 1000 live births in 2015 (1). However, these rates still exceed the World Health Organization sustainable development goal (SDG) 3 target of ≤25 deaths per 1000 live births. Diarrhoea, pneumonia and HIV infection have been identified as important causes of death in children <5 years outside the neonatal period. Mortality data from Statistics South Africa revealed a reduction in the annual number of diarrhoea-associated deaths in children <5 years from 9310 in 2009 to 2031 in 2016, equating to an enormous decrease of 78%. The dramatic decline is attributed to multiple interventions, including the introduction of the blue drop status for water quality management within municipalities, the HIV prevention of mother to child transmission (PMTCT) program, improved antiretroviral therapy (ART) roll-out, and the impact of rotavirus vaccine. Rotavirus is the most important cause of severe diarrhoea and death in children <5 years. The rotavirus vaccine is an oral monovalent vaccine administered to children at 6 and 14 weeks of age, and was introduced into the national immunization program in August 2009.

Rotavirus vaccine is estimated to have contributed at least 30% to the decline in diarrhoeal mortality (2). Impact studies have shown a decrease in both rotavirus-specific (54-58% reduction in children < 5 years (3) and all-cause diarrhoea (45-65% reduction in children <12 months and 40-50% reduction in children 13 -24 months (4) in South Africa. A recently published study showed that despite successful introduction of rotavirus vaccine and improvements in access to safe water and sanitation, acute diarrhoeal diseases were still responsible for 15% of hospital admissions in children < 5 years at a tertiary hospital in South Africa (5). The incidence of diarrhoeal diseases for 2016 (612 per 100,000) was 58% lower than the 2006–2008 (pre-vaccine introduction) rates (1 470 per 100 000) (5). In addition, diarrhoeal mortality decreased from 3.5% to 2.9% during the same periods (5). Continuous monitoring of diarrhoeal disease and rotavirus in children <5 years is required to ensure that both the vaccine formulation and the immunisation program are functioning optimally and to identify any rotavirus strains that may escape vaccine protection.

**Methods**

In 2018, diarrhoeal disease surveillance was conducted at four sentinel sites, including: Chris Hani Baragwanath Academic Hospital (CHBAH, Gauteng Province), Dr George Mukhari Hospital (DGM, Gauteng/North West Province border), Pelonomi Hospital (PNH, Free State Province) and Dora Nginza Hospital (DNH, Eastern Cape Province). All children <5 years admitted to a sentinel hospital for the treatment of acute diarrhoea (as defined by the World Health Organization, and of ≤7 days duration) were approached for enrolment. Enrolment was conducted systematically from Monday to Friday (08:00 – 17:00), after informed consent was obtained from a parent or guardian. Demographic, clinical and outcome data were collected in a structured questionnaire by dedicated surveillance officers. Stool specimens were collected for rotavirus and enteric virus screening. Specimens from CHBAH, PNH and DNH were screened at the Centre for Enteric Diseases, NICD for rotavirus (commercial EIA and standardised characterisation protocols) and other enteric viruses. Specimens from DGM were screened at the MRC-Diarrhoeal Pathogens Research Unit laboratory at Sefako Makgatho Health Sciences University for rotavirus using the same standardised protocols.

**Results**

A total of 280 stool specimens were screened in 2018 with 11% (30/280) positive for rotavirus (Figure 24). Rotavirus detection peaked in July with a maximum detection rate of 42% (15/36). A total of 19 rotavirus-positive strains were genotyped, with G3P [8] (73%; 14/19) being predominant and other strains (G1P[8], G9P[6], G8P[4]) detected at lower levels. A total of 199 specimens were also screened for other enteric viruses and the following were detected: norovirus genogroup I and II in 21% (41/199); adenovirus in 12% (24/199); sapovirus in 6% (11/199) and astrovirus in 3% (6/199) (Figure 25).

**Discussion**

The rotavirus detection rate for 2018 (11%) was lower than the 19% noted in 2017 and much lower than rates reported in the pre-vaccine era. The G3P[8] strains that were frequently detected in 2018 have been circulating in South Africa since 2015 and were also the predominant strains in 2016. The frequency of rotavirus genotype distribution simply reflects the changing and unpredictable nature of rotavirus genotype circulation, with no rotavirus genotype/s independently associated with increased severity having been identified as yet. The limited number of specimens screened for enteric viruses as well as the limited sites surveyed makes it problematic to draw any conclusions regarding the prevalence of the other enteric viruses detected. However, a substantial increase in norovirus GII detection was noted in 2018 compared to 2017 (19% in 2018 compared to 8% in 2017). Additional typing of these strains will be performed to establish if new strains or variants of norovirus were circulating in 2018. The detection of sapovirus also increased compared to the previous year (6% in 2018 compared to 3% in 2017) and was similar to the detection levels observed in 2016 (7%). The prevalence of adenovirus (12%) remained constant and astrovirus prevalence was similar (3% in 2018 compared to 4% in 2017) in the last two years of surveillance.

**Figure 24.** Number of diarrhoeal cases enrolled at sentinel hospital sites and the number of rotavirus detections per month, South Africa, 2018.

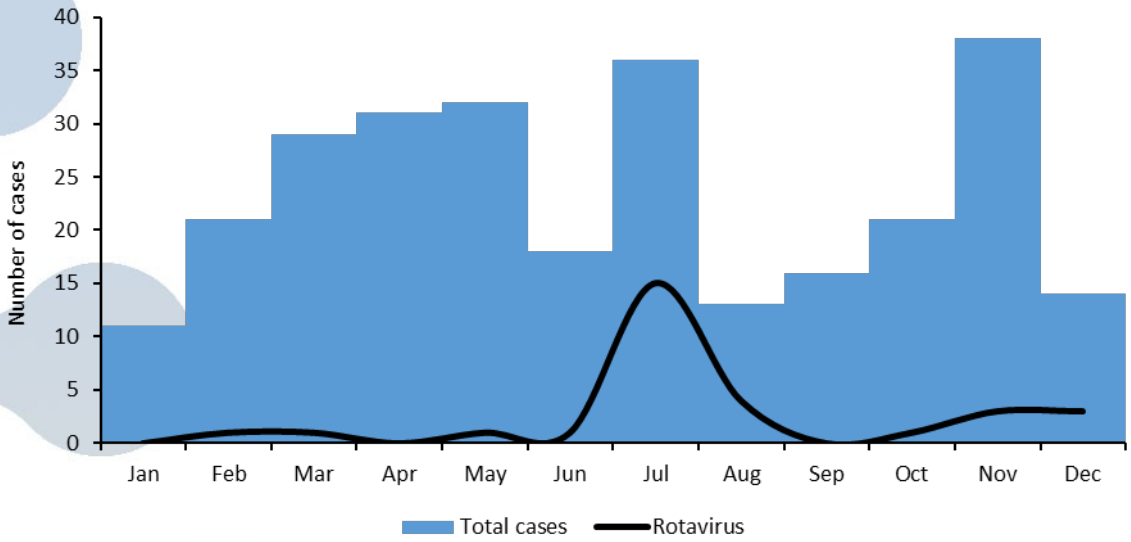
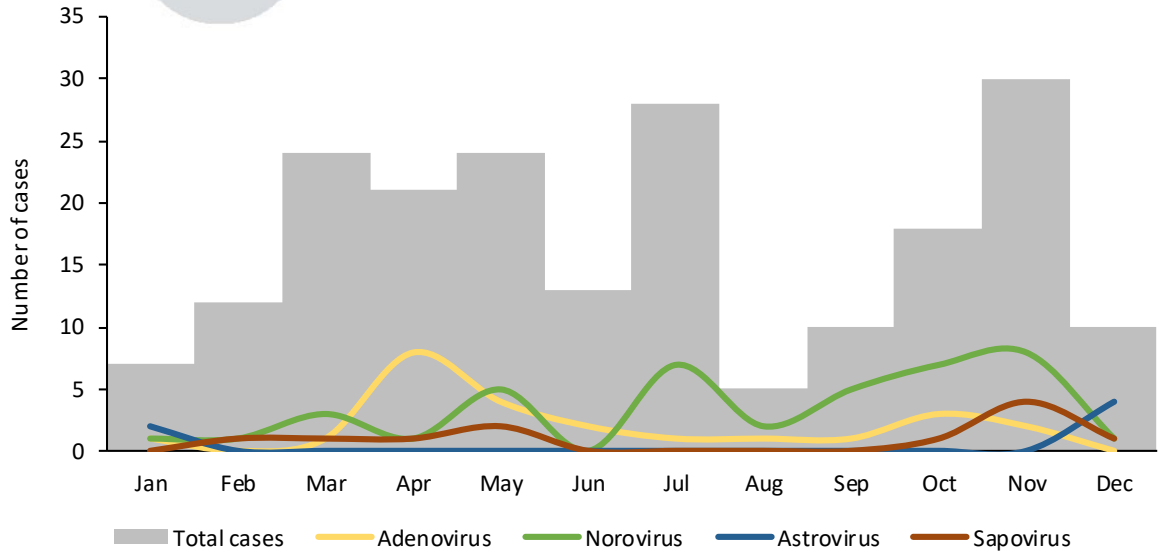



**Figure 25.** Number of diarrhoeal cases enrolled at sentinel hospital sites and the number of enteric viruses detected per month, South Africa, 2018.

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# Aetiological surveillance of Sexually Transmitted Infection Syndromes at sentinel sites: GERMS SA 2018


**Executive Summary**

Sentinel aetiological surveillance of STI syndromes was conducted at primary healthcare facilities in four South African provinces in the year 2018. *Neisseria gonorrhoeae* was the predominant cause of MUS; and syndromic management with dual antimicrobial therapy, which also covers *Chlamydia trachomatis*, the second most common pathogen, is rational. Extensively-drug resistant (XDR) *Neisseria gonorrhoeae* was not detected – all isolates were susceptible to extended-spectrum cephalosporins. Herpes simplex virus was the commonest detectable cause of genital ulceration, supporting the continued use of acyclovir in syndromic management. The syndromic management of VDS remains complex: the commonest causes, bacterial vaginosis and candidiasis, are not considered as STIs; however, a significant proportion of patients with either condition were co-infected with STI pathogens. The VDS treatment algorithms in the latest 2018 STI syndromic management guidelines have been amended to include treatment for STI pathogens based on sexual risk behaviour. The HIV seroprevalence among STI patients was high, underlining the importance of linkage to universal HIV counselling and testing in primary healthcare settings.


**Background**

In South Africa, STIs are managed principally at primary healthcare facilities (PHCs) using standard syndromic management guidelines (1). Periodic aetiological surveillance of the three main STI syndromes i.e. Male Urethritis Syndrome (MUS), Vaginal Discharge Syndrome (VDS) and Genital Ulcer Syndrome (GUS), is critical in validating the existing treatment algorithms. The monitoring of *Neisseria gonorrhoeae* antimicrobial susceptibility profiles is essential for identifying the emergence of extensively-drug resistant (XDR) gonorrhoea that is now a category 3 Notifiable Medical Condition (2). The PHC STI syndromic management guidelines were recently updated (in 2018) based on the demographic and aetiological data obtained from national and sentinel surveillance studies conducted by the NICD Centre for HIV & STI and GERMS-SA.

Major changes included the removal of the age cut-off of 35 years in the VDS algorithm that stratified symptomatic females into STI and non-STI groups for treatment. Instead, treatment for sexually transmitted causes of VDS is now based on an assessment of sexual risk behaviour. Additionally, owing to the periodic stock-outs of benzathine penicillin, alternative treatment recommendations for syphilis were included in the GUS treatment algorithm for adult males and non-pregnant females, and even for pregnant women in the event that benzathine penicillin reserves are not available for this patient category. In 2018 STI aetiological surveillance was conducted in the following provinces: Gauteng (Alexandra Healthcare Centre); Northern Cape (Kimberley City Clinic) and Limpopo (Rethabile Healthcare Centre).

**Objectives**

The primary objectives of surveillance were to determine the aetiologies of the three major STI syndromes (MUS, GUS, VDS) and the susceptibility profiles of *Neisseria gonorrhoeae* isolates. Secondary objectives were to determine co-infections (e.g. HIV) among patients presenting with STI Syndromes.

**Methods:**

Consecutive consenting patients presenting with MUS, VDS or GUS at the selected PHCs between January and December 2018 (and up to 31 January 2019 for Kimberley City Clinic) were included in the surveillance. Inclusion criteria were STI patients aged 18 years and above with a new episode of clinically confirmed MUS, VDS and/ or GUS. The target sample size per site was as follows: 100 cases each of MUS and GUS and approximately 150-200 cases of MUS (in order to obtain at least 100 viable gonococcal isolates from each site). Following eligibility and informed consent procedures, a nurse-administered questionnaire was used to document demographic and clinical information. Swabs were used for the sampling of genital discharge (vaginal, endocervical, urethral) and genital ulcers. Additionally, a 10ml specimen of venous blood was collected from each participant.

**Result**

**Patient demographic and clinical characteristics**

Of 680 participants, 328 (48%) were male (Table 30). Median age of participants was 27 years (IQR 24 - 33) and the majority were of black African ethnicity (96%) and of self-reported heterosexual orientation (99.3%). With respect to high risk sexual behaviours: median age at sexual debut was 18 years (IQR 16-19), and less than 20% self-reported condom use at last sexual encounter. Condom use was significantly lower at the Limpopo Province site (9.7%). Approximately one-quarter of participants had been diagnosed with an STI syndrome within the preceding 12-month period; and this proportion was significantly higher for the Northern Cape at 43% ($p = 0.001$).

Overall, over 25% of all patients reported having multiple sexual partners in the past 3 months, and that their most recent sexual encounter was with a non-regular partner (this proportion was significantly lower for Limpopo compared to the other two provinces). A significantly greater proportion of patients in Gauteng reported having sex with a partner in another province (32%) or country (24%) in the preceding 3-month period. Approximately 76% of patients reported knowledge of their HIV status. Overall 28% of males had been medically circumcised; this was lowest for Gauteng Province (22%). The majority of patients (656/680; 96.5%) presented with one STI syndrome; multiple (two or more) STI syndromes were present in 24 patients (3.5%; 95% CI 2.4 – 5.2).

**Table 30.** Demographic and behavioural characteristics of participants with STI syndromes (N=680)

| Variable | All N=680 | AHC (GP) N=344 | KCC (NC) N=200 | RHC (LP) N=136 | p-value |
|---|---|---|---|---|---|
| Males | 328 (48.2) | 205 (59.6) | 90 (45.0) | 33 (24.3) | <0.001 |
| Current age, Median(IQR) | 27 (24- 33) | 28 (25- 33) | 26 (23- 33) | 27 (23- 34) | 0.164 |
| Black Africans | 651 (95.7) | 341 (99.1) | 174 (87.0) | 136 (100) | <0.001 |
| Age at first sex, Median(IQR) | 18 (16- 19) | 17 (16- 19) | 18 (16- 20) | 18 (16- 19) | 0.236 |
| Heterosexual orientation (self-reported) | 675(99.3) | 342 (99.4) | 198 (99.0) | 135 (99.3) | 0.875 |
| Condom use at most recent sexual encounter | 128 (18.2) | 77 (22.4) | 38 (19.0) | 13 (9.7) | 0.004 |
| Sex with someone living outside province in the past 3 months | 169 (24.9) | 111 (32.3) | 39 (19.5) | 19 (14.0) | <0.001 |
| Sex with someone living outside the country in the past 3 months | 96 (14.1) | 83 (24.1) | 3 (1.5) | 10 (7.4) | <0.001 |
| Most recent sexual encounter with a non-regular sexual partner | 192 (28.2) | 110 (32.0) | 57 (28.5) | 25 (18.4) | 0.01 |
| Reported two or more sexual partners in the past 3 months | 188 (27.7) | 111 (32.3) | 60 (30.0) | 17 (12.5) | <0.001 |
| STI syndrome diagnosed in the past 12 months | 163 (24.0) | 39 (11.3) | 86 (43.0) | 38 (27.9) | 0.001 |
| Main syndrome diagnosed | | | | | |
| MUS only | 258 (37.9) | 161 (46.8) | 70 (35.0) | 27 (19.9) | |
| VDS only | 291 (42.8) | 94 (27.30 | 97 (48.5) | 100 (73.5) | <0.001 |
| GUS only | 107 (25.7) | 77 (22.4) | 24 (12.0) | 6 (4.4) | |
| >=2 syndromes | 24 (3.5) | 12 (3.5) | 9 (4.5) | 3 (2.2) | |
| Know their HIV status | 516 (75.9) | 246 (71.5) | 170 (85.0) | 100 (73.5) | 0.001 |
| Males medically circumcised* | 92 (28.1) | 46 (22.4) | 38(42.2) | 8 (24.2) | 0.002 |

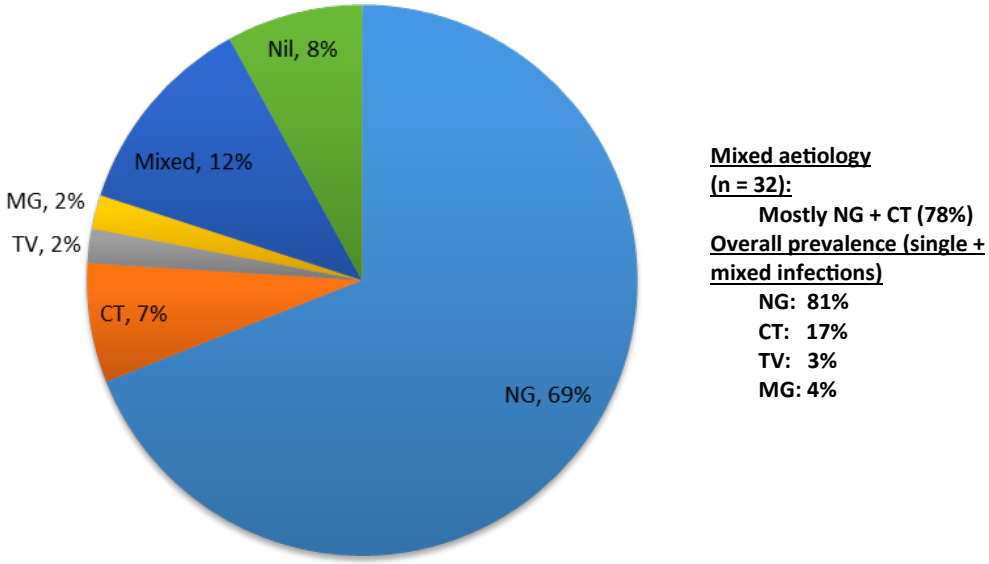
*among 328 males

Key: Alexandra Healthcare Centre (AHC); Gauteng Province (GP); Kimberley City Clinic (KCC); Northern Cape (NC); Rethabile Healthcare Centre (RHC); Limpopo Province (LP)

**Laboratory results**
**STI Syndrome aetiologies**
**MUS**

Among 261 patients presenting with MUS, *Neisseria gonorrhoeae* was the commonest cause (211, 80.8%; 95% CI 75.6 – 85.2), followed by *Chlamydia trachomatis* (45, 17.2%; 95% CI 13.1 – 22.4) (Figure 26). The majority of patients (209, 70.8%; 95% CI 65.4 – 75.8) had infections caused by single agents. *Trichomonas vaginalis* and *Mycoplasma genitalium* accounted for less than 5% of MUS. Multiple pathogens were detected in approximately 12.3% (32; 95% CI 8.8 – 16.9): the majority of these mixed infections (30; 93.8%) were caused by *Neisseria gonorrhoeae* together with one or more STI pathogens, mostly *Chlamydia trachomatis* (25; 78.1%). An STI pathogen was detected in approximately 92% of specimens (241; 95%CI 88.4 – 95.0); approximately 8% of specimens (20; 95% CI 5.0 – 11.6) had no identifiable STI aetiology. There were no significant differences in MUS aetiology by site. All gonococcal culture isolates (n = 172) were exquisitely sensitive to extended-spectrum cephalosporins on minimum inhibitory concentration (MIC) testing (cefixime $MIC_{50}$ <0.016 µg/ml, $MIC_{90}$ <0.016 µg/ml; ceftriaxone $MIC_{50}$ 0.002 µg/ml, $MIC_{90}$ 0.004 µg/ml).

**Figure 26.** Relative prevalence of STI pathogens in MUS (N = 261)




Key: *Neisseria gonorrhoeae* (NG); *Chlamydia trachomatis* (CT); *Trichomonas vaginalis* (TV); *Mycoplasma genitalium* (MG)

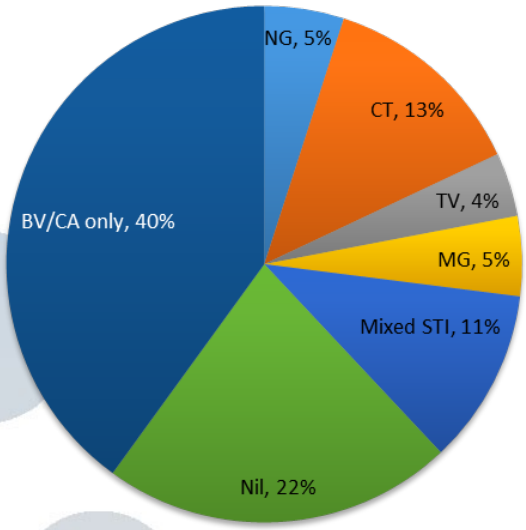
**VDS**

Among 312 women with VDS (Figure 27), less than 50% had a detectable STI pathogen in single or mixed infections (120; 95% CI 33.2 – 44.0). The commonest STI aetiology was *Chlamydia trachomatis* (67, 21.5%; 95% CI 17.2 – 26.4), followed by *Neisseria gonorrhoeae* (36, 11.6%; 95% CI 8.4 – 15.6). *Trichomonas vaginalis* accounted for approximately 10% (30, 9.6%; 95% CI 6.8 – 13.4) of infections, and *Mycoplasma genitalium* for 8% (26, 8.3%; 95% CI 5.7 – 12.0). Overall, single STI pathogens were detected in 145 VDS cases (27.6%; 95% CI 22.9 – 32.8); and mixed infections with multiple (two or more) STI pathogens in 34 (10.9%; 95% CI 7.9 – 14.9). Most VDS cases were attributed to conditions that are not traditionally considered to be STIs: bacterial vaginosis (BV) was identified in 145/312 (46.5%; 95% CI 41.0 – 52.1). Vulvovaginal candidiasis (CA) accounted for 85 (27.2%; 95% CI 22.6 – 32.4). An identifiable pathogen or cause was not found for 68 (21.8%; 95% CI 17.5 – 26.7) of VDS cases.

A significant proportion of VDS patients had co-infection with STI and non-STI aetiologies. Only 11.5% (36/312; 95% CI 8.4 – 15.6) of VDS cases tested for all causes had a sole STI aetiology; whereas 26.9% (84/312; 95% CI 22.3 – 32.1%) had an STI plus BV and/or CA.

Overall 73 VDS cases (23.4%) had BV-STI co-infections, and 14 VDS cases (4.5%) had CA-STI co-infections. Therefore 73/145 patients with BV (50.3%; 95% CI 42.2 – 58.5) and 14/85 patients with CA (16.5%; 95% CI 9.9 – 26.1) had STI co-infections. There were no significant differences in VDS aetiology by site.

**Figure 27.** Relative prevalence of VDS aetiologies (N = 312)




**Any STI pathogen (single/ mixed infections): 38.5% (120/312)**
**Overall prevalence**
**NG : 12%**
**CT : 22%**
**TV : 10%**
**MG : 8%**

**STI only: 11.5% (36/312)**

**BV: 46.5% (145/312)**
**Overall BV with STI: 23.4% (73/312)**
**Of those with BV: 50% had STI (73/145)**

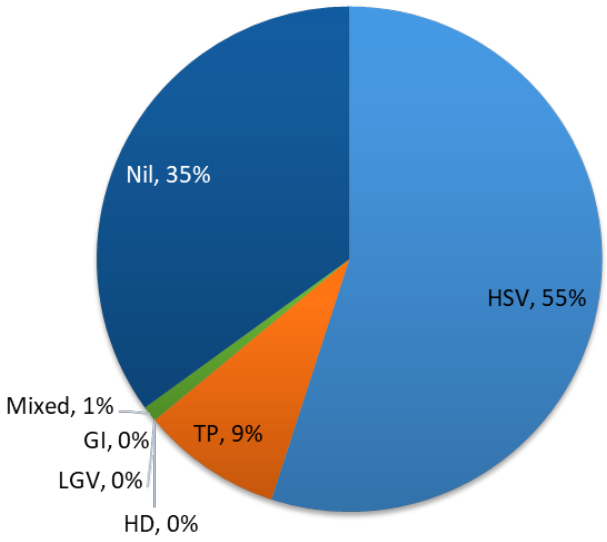
**CA: 20% (87/431)**
**Overall CA with STI: 4.5% (14/312)**
**Of those with CA: 16.5% had STI (14/85)**

Key: *Neisseria gonorrhoeae* (NG); *Chlamydia trachomatis* (CT); *Trichomonas vaginalis* (TV); *Mycoplasma genitalium* (MG); bacterial vaginosis (BV); vulvovaginal candidiasis (CA)

**GUS**

Among 131 GUS cases (Figure 28), the major cause was herpes simplex virus (HSV) in 55.0% (72; 95% CI 46.3 – 63.4); followed by *Treponema pallidum* (TP) in 9.2% (12/131; 95% CI 5.2 – 15.5). Type-specific PCR revealed that all HSV-associated ulceration was caused by HSV-2. Most cases of genital herpes were HSV-2 serology positive and represented reactivation disease (56/72, 77.8%; 95% CI 66.5 – 86.0), as opposed to first-episode HSV-2 ulceration. Most pathogen-detectable cases had a single aetiology (82/131, 63%). Only 1 patient had mixed aetiology with HSV and TP co-infection. An ulcer-derived pathogen was not identified in approximately 35% GUS cases (48; 95% CI 28.7 – 45.3). Statistical analysis to reliably detect significant aetiological differences by site was limited by small sample sizes for GUS.

**Figure 28.** Relative prevalence of STI pathogens in GUS (N = 131)




**Mixed aetiology ≈ 1% (1/131)**
**HSV + TP (1)**

Key: herpes simplex virus (HSV); *Treponema pallidum* (TP); lymphogranuloma venereum (LGV); granuloma inguinale (GI)

**Serological results**

HIV co-infection rates were as follows: 40.5% (61/143; 95% CI 32.3 – 49.2) in GUS; 22.4% (128/428; 95% CI 18.1 – 27.4) in VDS and 18.4% (103/482; 95% CI 14.1 – 23.6) in MUS. The relative prevalence of HIV co-infection in VDS was significantly lower for the Northern Cape site (11%) than for sites in other provinces (p = 0.001).

**Discussion and Conclusions**

This surveillance study provides a snapshot of STI Syndrome aetiologies across several South African provinces in 2018. Overall the study found that the majority of participants enrolled with STI syndromes were young and reported high risk sexual behaviour, such as young age at sexual debut and unprotected sex at last sexual encounter. STI/HIV control interventions, such as knowledge of HIV status, condom use and voluntary male medical circumcision need to be strengthened across all provinces. *Neisseria gonorrhoeae* was the predominant cause of male urethritis syndrome. Based on our data, syndromic management for MUS in the South African public health sector should include cover for the two leading causes, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. XDR gonorrhoea was not detected through surveillance, suggesting that the current first-line dual regimen of ceftriaxone-azithromycin is appropriate for the treatment of gonorrhoea.

Bacterial vaginosis was the leading cause of VDS, and prevalent in almost 50% of females. A significant proportion of women with BV were co-infected with one or more STI pathogens. These findings suggest that BV is associated with risk factors for traditional STI infections, and support reconfiguration of the management algorithm for VDS to increase the predictive value of the algorithm for STI pathogens by assessing behavioural risk.

Herpes simplex virus-2 remains the leading cause of pathogen-detectable GUD in Gauteng, and this supports the use of anti-viral therapy in the syndromic management guidelines

The HIV prevalence among patients presenting with STI syndromes such as VDS and GUS is significantly higher than the STATS-SA 2018 estimated prevalence of 19% for adults aged 15-49 years in the general South African population. This underscores the importance of linkage to universal HIV testing and treatment for STI patients; and support the recently adopted national policy of universal testing and treatment (early ARV initiation) in those who are HIV-infected.

Treatment guidelines are available at:
http://www.nicd.ac.za/wp-content/uploads/2019/03/2018-STI-syndromic-management-guidelines.pdf

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**Data management and statistical analysis**: Tendesayi Kufa-Chakezha, Gloria de Gita, Thabitha Mathega

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## Zoonotic aetiologies in febrile adults in the Mnisi Community, Mpumalanga Province, South Africa, 2018

**Introduction**

The Mnisi area is a malaria endemic area in rural Mpumalanga and shares 75% of its boundaries with wildlife reserves. Contact between wildlife, livestock and humans is frequent. Zoonoses cause infectious diseases in humans who interact with livestock, domestic animals and vectors. A high prevalence of zoonotic infections was observed in a previous study at 3 public health clinics in Mnisi (1). A single sentinel site was established at the community health clinic in Hluvukani for the NICD surveillance programme in 2014. The aim of the study was to investigate selected zoonotic diseases in an agropastoral rural community in South Africa.

**Methods**

The methodology has remained the same. Consenting adult (≥18 years) volunteers presenting to the clinic with fever (>37.5 °C) or a history of fever, and on whom a malaria rapid test was done, were enrolled and a questionnaire administered. Acute and convalescent blood samples were collected and for 2018 laboratory tests for arboviruses (West Nile, Chikungunya, Sindbis and Rift Valley fever virus), leptospirosis, Q fever and brucellosis were done (Table 31). In addition, malaria PCR was done on all samples.

**Table 31.** Panel of tests performed

| Test | Test particulars | Samples tested | Interpretation of results |
|---|---|---|---|
| Arbovirus Haemagglutination Inhibition test | Arbovirus Haemagglutination Inhibition test (In-house) | Convalescent serum samples, or acute samples where convalescent samples not available | As described in Swanepoel *et al.,* 1986 (2) |
| West Nile IgM ELISA | Anti-West Nile Virus (IgM) ELISA (Euroimmun Medizinische Labordiagnostika AG, Germany) | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |
| Chikungunya IgM ELISA | Anti-Chikungunya Virus (IgM) ELISA (Euroimmun Medizinische Labordiagnostika AG, Germany) | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |
| Sindbis IgM ELISA | Arbovirus In-house IgM Capture ELISA (In-house) | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |
| Rift Valley fever Inhibition ELISA (IgG and IgM) | Rift Valley fever Inhibition ELISA (IgG and IgM) (In-house) | Convalescent serum samples, or acute samples where convalescent samples not available | As described in *Paweska et al.,* 2005 (3) |
| Q fever IgG ELISA* | Panbio® *Coxiella burnetii (Q fever) IgG ELISA (Standard Diagnostics Inc., Republic of Korea)* | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |
| *Leptospira IgM ELISA* | Panbio® *Leptospira IgM ELISA (Standard Diagnostics Inc., Republic of Korea).* | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |
| *Brucella IgM and IgG ELISA* | Vircell® Brucella IgM and IgG ELISA (Vircell S.L., Spain) | Convalescent serum samples, or acute samples where convalescent samples not available | Index values calculated using run-based cut-off values. As per manufacturer's recommendations |

**Results**

In 2018 we enrolled more adults with acute febrile illness than in 2017 (n=62). Thirty-seven percent (23/62) did not return for follow up blood samples. Of those who did, the median time to return was 21 days (10-31 days). The median age was 39 years (IQR 28-49 years) and 62% were female.

Sixty of sixty-two patients (97%) had contact with animals, 95% with chickens, 89% with dogs, 69% with cattle and goats, 63% with rodents. Half of the patients had been previously bitten by ticks or fleas. Thirteen percent (13%) had attended a dip tank and this ranged from 3 years to 40 plus years. All patients had eaten meat. Seventy-one percent had slaughtered animals (chickens). Only three patients had consumed raw cow's milk (two of them heated it), none consumed goat's milk. Only one patient (2%) knew of abortions in her/ her neighbour's animals. Illness duration ranged from 2-3 days (mean of 2 days). Twenty-seven percent (17/62) of patients had no systemic symptoms, majority presented with muscle pain (48%) followed by gastro-intestinal symptoms (30%) and respiratory symptoms (21%). Eighty-two percent (51/62) received an antibiotic at the clinic and 5% (3/62) were referred to the hospital.

Only 30 samples were tested for the full spectrum of laboratory tests and 43% (13/30) of patients showed evidence of a recent or past infection/exposure for at least one of the zoonotic diseases tested (Table 32). Malaria PCR was positive for the one patient in whom the rapid test was positive.

**Table 32.** Laboratory results

| Laboratory test positive | Number of patients positive/ samples tested | % positive |
|---|---|---|
| Q fever IgG | 7/30 | 23.3% |
| *Leptospira IgM* | 3/62 | 4.8% |
| *Brucella IgG* | 3/60 | 5% |
| Malaria PCR | 1/41 | 2% |
| West Nile IgM ELISA | 1/40 | 2.5% |
| Chikungunya IgM ELISA | 1/40 | 2.5% |
| Sindbis IgM ELISA | 1/40 | 2.5% |
| Rift Valley fever Inhibition ELISA (IgG and IgM) | 1/40 | 2.5% |

**Conclusions**

The numbers were higher for 2018. Animal contacts are common, majority of patients seek health care early and antibiotic use is high. Bacterial zoonoses were more prevalent than viral pathogens. Q fever was more prevalent this year than the previous two years, Leptospirosis prevalence was similar over the last 3 years.

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## Summary

The GERMS-SA laboratory-based surveillance a valuable surveillance programme in reporting pathogen-specific trends. For enhanced sentinel surveillance, the percentage of case report forms done on interview was 76% (still reaching the target of 70%) and ongoing training and auditing of our surveillance officer data quality is done to continually improve that aspect. Sadly the isolate submission and viability have declined and we urge the laboratories to continue sending isolates.

**Opportunistic infections:** The epidemiology of cryptococcal meningitis or culture-confirmed cryptococcal disease was slightly decreased between 2017 and 2018. *Cryptococcus* spp, incidence remained stable across provinces for 2017 and 2018. The peak incidence in men was in the 40-44 year old age group; in women it was in the 30-34 year old age group. Where we had HIV information, (n=1 489), 93% were HIV sero-positive. Of 1 382 patient infected with HIV, 841 (61%) were on ART-experienced and 618/841 (73%) were on ART at the time of diagnosis of cryptococcal disease. Patients still come into hospital with a low CD4 count and the in-hospital case fatality rate continues to be high (33%).
Rifampicin-susceptible TB surveillance looks at risk factors for TB as well as INH mono-resistance. From 5 provinces (n=603) data showed majority of participants were male (56%), almost 70% of the patients were HIV positive and 65% already on ART with 24% about to initiate treatment. There was poor contact tracing and poor completion of treatment. Smoking continues to be a high risk factor for TB. INH mono-resistance is <10%.

**Vaccine-preventable diseases:** The 2018 data continues to monitor the trends in IPD and Hib post-EPI vaccine introduction of PCV13 and the Hib booster. Hib disease remains low, infants being the most affected with Hib and non-typeable disease (HNT). Hib isolates were more likely than HNT isolates to be found in CSF than blood. Non-typeable disease is highest in all age groups. Hib-disease in children may be vaccine failures. For those that had clinical information from ESS, 27% (36/133) died in hospital and the median time to death was within one day of admission. Fifty three percent (71/133) of patients had some predisposing condition other than HIV. ***Please remember that Hib is a notifiable medical condition.*** There is a continued decrease in IPD , incidence peaks in infants and again after age 25 years. HIV-infection and infant HIV-exposure remain risk factors for IPD and overall case fatality was 32% . Penicillin and ceftriaxone non-susceptibility remains unchanged. Clinicians should remember to check the vaccine status of children and remember to give catch-up doses.

**Epidemic-prone diseases:** The incidence of meningococcal disease remained similar to that in 2017 with no outbreaks detected; WC having the highest rate and serogroup B being the predominant serogroup (42/98; 43%). High-dose penicillin is still being recommended as the drug of choice for therapy for confirmed meningococcal disease, although penicillin non-susceptibility was 12%; all were susceptible to 3rd generation cephalosporin and ciprofloxacin. Of 51 patients from our ESS, 43 had outcome information. The case fatality rate was 12% (5/43).
The diagnosis of typhoid fever remains challenging and although the data may not reflect actual burden of disease, numbers were comparable to previous non-outbreak years. For *Salmonella* Typhi, azithromycin is an alternative treatment option since the emergence of ciprofloxacin resistance; continual monitoring of resistance to these two antibiotics has become mandatory.

Paratyphoid fever remains rare in South Africa. Non-typhoidal salmonellosis may be foodborne or may be associated with HIV-infection. Although *Shigella* infection has been associated with water-borne outbreaks in South Africa, person-to-person transmission also plays and important role. Cholera in South Africa is not endemic, only travel-related sporadic cases are infrequently reported.

**Listeriosis** was declared a Notifiable Medical Condition following the listeriosis outbreak of 2017-2018. Seventy right percent of cases were reported from three provinces: Gauteng (54%), WC (16%) and KZN (9%). Neonates accounted for 43% of cases, 33% of cases in adults 15-49 years. The situations reports are available on the NICD webpage.

**Healthcare associated infections:** CRE numbers increased in 2017 and 2018 with the proportion of male cases greater than females. Highest proportion of sentinel site cases were from Gauteng Province (78%) followed by KwaZulu-Natal (12%). A shift to CPE mediated by OXA-48 & variants was noted. *Acinetobacter baumannii* numbers show an increase in 2018, particularly in KwaZulu-Natal province. Highest AB bacteraemia was noticed in neonates and young children. The susceptibility to different antibiotics classes is extremely low.

**Diarrhoeal surveillance:** In 2018, rotavirus detection rate deceased to 11% much lower than pre-vaccine era; peaked in July with maximum rate of 42%. The G3P[8] strains which have been circulating in South Africa since 2015 and predominant in 2016 were frequently detected in 2018. However, no rotavirus genotype has been associated with increased severity and genotype frequency distribution simply reflects the changing and unpredictable nature of rotavirus genotype circulation globally. The limited number of specimens screened for enteric viruses as well as the limited sites surveyed makes it difficult to draw any conclusions regarding the prevalence of the other enteric viruses detected. However, a substantial increase in norovirus GII detection was noted in 2018 compared to 2017 (19% in 2018 compared to 8% in 2017). Sapovirus detection also increased compared to 2017 (6% in 2018 compared to 3% in 2017). The prevalence of adenovirus (12%) remained constant and astrovirus prevalence was similar (3% in 2018 compared to 4% in 2017) in the last two years of surveillance.

**STI aetiological surveillance:** Overall the study found that the majority of participants enrolled with STI syndromes were young and reported high risk sexual behaviour, such as young age at sexual debut and unprotected sex at last sexual encounter. *Neisseria gonorrhoeae* was the predominant cause of male urethritis syndrome. Based on our data, syndromic management for MUS in the South African public health sector should include cover for the two leading causes, *Neisseria gonorrhoeae* and *Chlamydia trachomatis.* Bacterial vaginosis was the leading cause of VDS, and prevalent in almost 50% of females. A significant proportion of women with BV were co-infected with one or more STI pathogens. These findings suggest that BV is associated with risk factors for traditional STI infections, and that the management algorithm for VDS should be reconfigured to increase the predictive value of the algorithm for STI pathogens. Herpes simplex virus-2 remains the leading cause of pathogen-detectable GUD in Gauteng, and this supports the use of antiviral therapy in the syndromic management guidelines. HIV co-infection rates were as follows: 40.5% (61/143; 95% CI 32.3 – 49.2) in GUS; 22.4% (128/428; 95% CI 18.1 – 27.4) in VDS and 18.4% (103/482; 95% CI 14.1 – 23.6) in MUS, significantly higher than the STATS-SA 2018 estimated prevalence of 19% for adults aged 15-49 years in the general South African population. This underscores the importance of linkage to universal HIV testing and treatment for STI patients; and support the recently adopted national policy of early ARV initiation for those who are HIV-infected.

**Zoonotic diseases in acutely febrile patients**: This study is in acute febrile adults attending one rural Mpumalanga clinic bordered by the Kruger National Park and where the populations of human, livestock, domestic animals and wildlife are in frequent contact. Only 30 samples were tested for the full spectrum of laboratory tests: leptospirosis, Q fever and brucellosis and 43% of patients showed evidence of a recent or past infection/ exposure for at least one of the zoonotic diseases tested. One rapid malaria test was positive and it was confirmed on PCR The numbers were higher for 2018, animal contacts were common, majority of patients sought health care early and antibiotic use was high.

***The GERMS-SA publications and effects on policy are as a result of the isolates that your participating laboratories submit and the work that you at your clinics and hospitals permit. We encourage all laboratory and clinical staff to continue participating in the NICD surveillance programmes. We thank you for your continued support of GERMS-SA .***

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