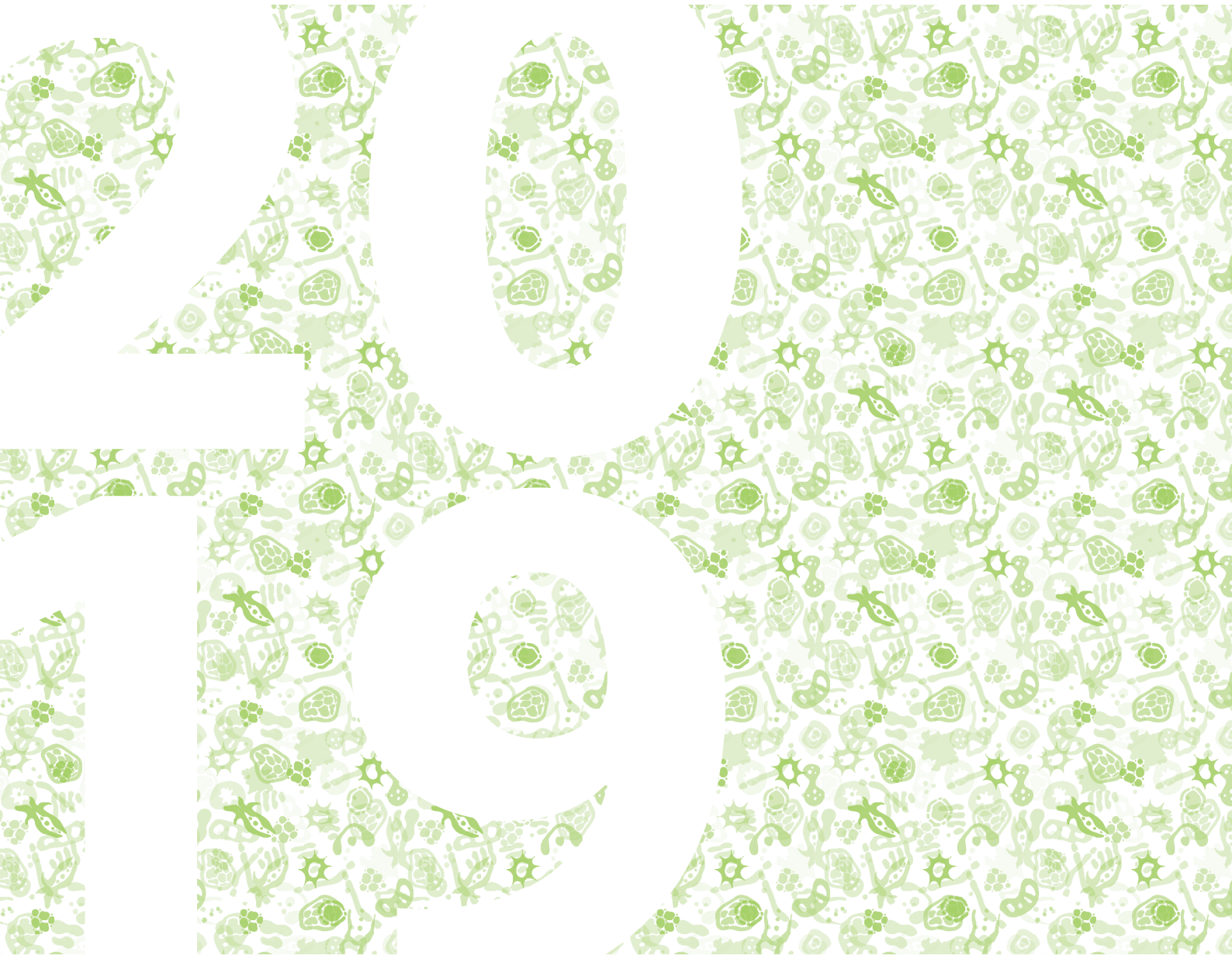
GERMS-SA: ANNUAL SURVEILLANCE REVIEW

2019

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

GERMS-SA SURVEILLANCE OFFICERS' MEETING 12-15 FEBRUARY 2019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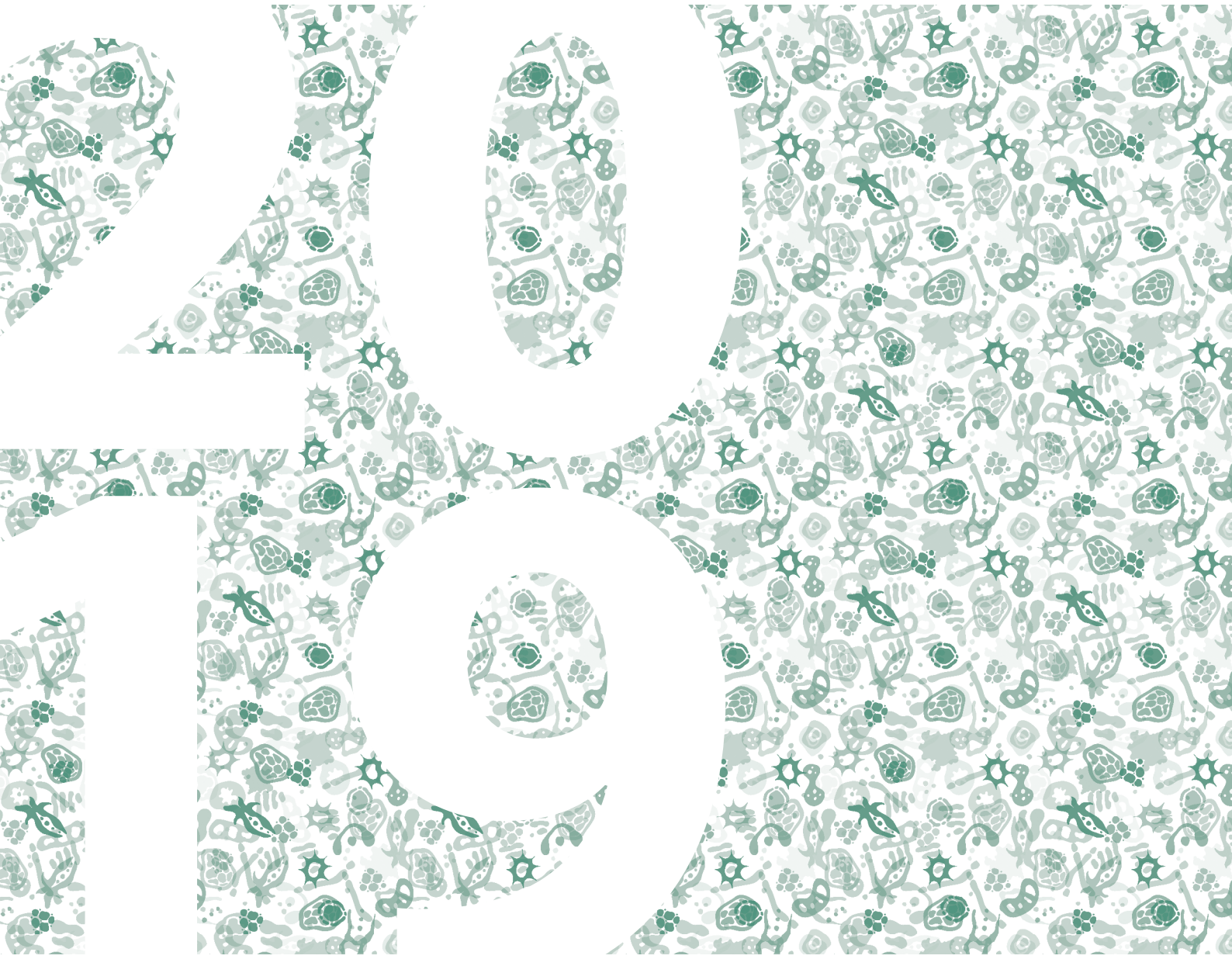

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INTRODUCTION

The National Institute for Communicable Diseases (NICD) GERMS-SA surveillance reference units report the 2019 findings which continue to be useful in reporting trends in pathogen-specific data. This year we included laboratory-based surveillance of *Streptococcus pyogenes* and *Streptococcus agalactiae*. The number of isolates received by NICD reference laboratories have increased and viability of isolates improved however audit rates are still out of target ranges. This means that we are still missing 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 2019 report also includes other NICD projects using the GERMS-SA platform; rotavirus/diarrhoeal aetio-logical surveillance. This project differs from the laboratory-based surveillance in that it is 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.

METHODS

In 2019, 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, *Salmonella enterica* serotype Paratyphi A, B and C, Nontyphoidal *Salmonella* species, *Shigella* species, *Vibrio cholerae*, Diarrhoeagenic *Escherichia coli*, *Campylobacter* species, *Listeria* species and *Streptococcus pyogenes*.
3. Vaccine-preventable diseases, e.g. *Haemophilus influenzae* type b (Hib), *Streptococcus pneumoniae* and *Streptococcus agalactiae*.
4. Healthcare-associated bloodstream infections caused by *Candida* species and ESKAPE organisms (*Enterococcus, Staphylococcus aureus, Klebsiella, Acinetobacter, Pseudomonas* and Enterobacteriaceae (*Enterobacter* and *E. coli*) and CREs.

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 2019. The population under surveillance in 2019 was estimated at 58, 8 million (Table 1). Diagnostic laboratories reported case patients to the 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 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*. Submission of *Streptococcus agalactiae* and *Streptococcus pyogenes* isolates was also introduced in 2019.

Enhanced surveillance was not conducted on any of the enteric pathogens in 2015 but restarted for *Salmonella* Typhi only in 2016 and also *Salmonella enterica* serotype Paratyphi A, B and C and Nontyphoidal *Salmonella* spp. in 2019. At ESS, surveillance officers completed clinical case report forms electronically using the Mobenzi application on mobile phones/ tablets for patients with ten laboratory-confirmed diseases: cryptococcosis, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, invasive *Salmonella* Typhi disease,

Paratyphi A,B,C, Nontyphoidal diseases, CRE, *Acinetobacter baumannii* and rifampicin-susceptible TB (7 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. 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 2018 and 2019 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2018 and 2019, 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 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, 2018 and 2019

Province	General population*		HIV-infected population**	
	2018	2019	2018	2019
Eastern Cape	6 522 734	6 712 276	796 027	804 431
Free State	2 954 348	2 887 465	371 923	374 237
Gauteng	14 717 040	15 176 116	1 885 165	1 912 525
KwaZulu-Natal	11 384 722	11 289 086	1 991 798	2 011 200
Limpopo	5 797 275	5 982 584	460 942	467 585
Mpumalanga	4 523 874	4 592 187	698 317	711 983
Northern Cape	1 225 555	1 263 875	81 739	82 622
North West	3 978 955	4 027 160	486 217	489 380
Western Cape	6 621 103	6 844 272	449 547	460 181
South Africa	**57 725 606**	**58 775 022**	**7 221 675**	**7 314 143**

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

OPERATIONAL REPORT

Site visits

In 2019, 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

GERMS-SA Laboratory and Syndromic Surveillance Officers' meeting, 12-15 February 2019 at Genesis: the aim was to discuss and integrate all surveillance projects into one under GERMS-SA and emphasize team work to different surveillance staff.

Fifteenth Surveillance Review meeting previously known as the GERMS-SA Principal Investigators' meeting), 16-17 July 2019 at PRF Centre NICD: the aim was to feedback on surveillance programme's results and reassess surveillance impact.

Surveillance audit

A total of 20 113 surveillance cases were detected by GERMS-SA in 2019. Excluding the cases of cryptococcosis (n=6 425) 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=1 198), for which no audits are performed, 4 438/12 490 (36%) 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.

Table 2. Cases detected by surveillance audit by province, 2019

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**	6425/6425 100%	1021	248	1410	1707	451	457	74	552	505	6425
	Salmonella Typhi	9/95 (9%)	0	0	4	2	0	0	0	1	2	9
	Non-typhoidal salmonellosis†	238/825 (29%)	23	8	90	56	12	10	9	9	21	238
	Shigellosis	5/33 (15%)	0	0	3	1	1	0	0	0	0	5
	Meningococcal disease	16/111 (14%)	1	0	6	3	1	0	0	1	4	16
	Haemophilus influenzae disease	105/259 (41%)	5	3	42	28	2	0	2	3	20	105
	Pneumococcal disease	627/2359 (27%)	54	30	198	139	23	27	31	38	87	627
	Streptococcus pyogenes	697/1060 (66%)	98	18	135	152	5	8	7	3	271	697
	Streptococcus agalactiae	687/1034 (66%)	45	24	308	171	22	26	6	9	76	687
	Carbapenem resistant Enterobacteriaceae (BC only)	479/1052 (46%)	N/A	10	374	63	N/A	N/A	N/A	N/A	32	479
	Acinetobacter baumannii (BC only)	659/1438 (46%)	N/A	19	465	128	N/A	N/A	N/A	N/A	47	659
Non-invasive	*Salmonella* Typhi	3/22 (14%)	0	0	1	0	0	0	0	1	1	3
	Non-typhoidal salmonellosis†	396/2437 (16%)	30	24	79	99	29	31	11	21	72	396
	Shigellosis	242/1164 (21%)	24	5	30	60	3	5	6	2	107	242
	Rifampicin-susceptible tuberculosis***	NA/1198	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1198
Total (excl crypto and RSTB)		**4438/12490 (36%)**										

Note - 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; 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.

Enhanced surveillance site performance indicators

The proportion of completed CRFs in 2019 increased compared to 2018 however still not within the target range. This was due in part to difficulties in finding TB patients (for interview and sputum collection), untimely notification of cases matching case definitions by testing laboratories and restricted access to CDW data (Table 3); 5 315/ 6 901 (77%) of cases had a case report form (CRF) completed (target=90%). The interview rate [3 832/5 315 (72%) (target=70%)] decreased from previous year as SOs continue to experience challenges in tracking patients due to late notifications and patients discharged before alert/ enrolment. 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 2019, these reports were provided quarterly.

Enhanced surveillance site quality monitoring

In 2019, 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.

SURVEILLANCE REPORTS

Enhanced surveillance site project

In 2019, 6 901 surveillance case patients were diagnosed at enhanced surveillance sites (Table 3). Of case patients with recorded HIV status, 68% (2 023/2 988) 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 (97%) were HIV-infected. HIV infection amongst patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 66%.

Table 3. Enhanced surveillance site performance indicators, 2019

Enhanced surveillance site	Case patients, n	Completed case report forms*, n (%)**		Case report forms completed by interview, n (%)***	
Addington	103	83	(81)	57	(69)
Charlotte Maxeke Johannesburg Academic [1,2]	499	438	(88)	317	(72)
Chris Hani Baragwanath/ Zola-Jabulani District [1,2,3]	1658	1038	(63)	664	(64)
Dr George Mukhari [1,2]	237	219	(92)	181	(83)
Edendale/ Greys'/ Northdale [1,2]	394	380	(96)	366	(96)
Groote Schuur/ Red Cross [1,2]	349	320	(92)	218	(68)
Helen Joseph/ Rahima Moosa Mother & Child [1,2]	403	360	(89)	253	(70)
Kimberley	144	40	(28)	0	(0)
King Edward VIII/ Inkosi Albert Luthuli Central Hospital [1,2,3]	426	338	(79)	266	(79)
Klerksdorp/ Tshepong [3]	514	278	(54)	209	(75)
Mankweng/ Polokwane/ Seshego	146	119	(82)	61	(51)
Pelonomi/ Universitas [1,2]	288	262	(91)	211	(81)
Port Elizabeth/ Dora Nginza/ Livingstone [3]	582	519	(89)	376	(72)
RK Khan [1,2,3]	259	197	(76)	169	(86)
Rob Ferreira/ Themba [3]	288	227	(79)	194	(85)
Steve Biko Pretoria Academic/ Tshwane District [1,2]	358	296	(83)	233	(79)
Tygerberg [1,2]	253	201	(79)	57	(28)
Total	**6901**	**5315**	**(77)**	**3832**	**(72)**

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 and patient interviews at certain sites are due to challenges in completing CRFs for certain pathogens and data delays from CDW. Kimberley no longer has a SO on site therefore CRFs were completed quarterly, by medical record reviews (which are a challenge to access); **Target = 90%; ***Target = 70%; [1]Sites doing CRE surveillance; [2]Sites doing *Acinetobacter baumannii* surveillance; [3]Sites doing rifampicin-susceptible TB surveillance.

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, 2019

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	1695	1530	(90)	1461	(95)	1422	(97)
Neisseria meningitidis	38	31	(82)	24	(77)	9	(38)
Streptococcus pneumoniae	893	745	(83)	616	(83)	407	(66)
Haemophilus influenzae	130	110	(85)	86	(78)	33	(38)
Salmonella Typhi	38	33	(87)	24	(73)	6	(25)
CRE	1052	798	(76)	592	(74)	157	(27)
Acinetobacter baumannii	1438	1 186	(82)	801	(68)	152	(19)
Total	**4194**	**3602**	**(86)**	**2988**	**(83)**	**2023**	**(68)**

*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.

Cryptococcus species

Results

In 2019, 6 425 patients with first episodes of laboratory-confirmed cryptococcal disease were reported. This number includes cases of meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), fungaemia (*Cryptococcus* species cultured from blood) and culture-positive disease at other sites, but excludes cases of isolated cryptococcal antigenaemia [n=352] (Table 5). A majority of patients (93%) with the first episodes were diagnosed with meningitis and 5% with fungaemia. Of the remaining patients diagnosed with cryptococcosis at other sites (n=130), most (57%) were diagnosed with a positive urine culture. Between 2018 and 2019, the incidence risk of laboratory-confirmed cryptococcosis remained stable in all provinces (overlapping 95% confidence intervals), except in North West where the incidence risk increased from 92 to 113 cases per 100 000 HIV-infected persons (Table 6). In 2019, the highest incidence risk was recorded among males aged 35-39 years; the peak incidence among females, though lower than for males, was also in the same age group (Figure 1).

Of the 6 425 case patients, age was known for 5 991 (93%) and children younger than 15 years accounted for 2% (146); 49% (72) of these were younger than 5 years. Clinical case data were collected from 1 695 case patients at ESS from January to December 2019, and completed case report forms were available for 90% (1 530) of these patients. Among patients with known HIV status (1 461), 97% (1 422) were HIV-seropositive. Of the 1 422 patients infected with HIV, 1 197 had a CD4+ T-lymphocyte (CD4) cell count test result recorded close to the time of diagnosis; the median CD4 count was 28 cells/µl (interquartile range, 10 – 62 cells/µl) and 1 105 (92%) had a CD4 cell count <200 cells/µl. Of the 807 patients with available viral load test results, 23% (186) had a viral load of <400 copies/mL, 12% (95) had viral loads of 400-10 000 copies/mL, and 65% (526) had viral loads of >10 000 copies/mL. A majority (71% [969/1 360]) of the patients with known treatment information had previously received antiretroviral treatment or were on treatment at the time of cryptococcal disease diagnosis. The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease was 34% (496/1 483).

Table 5. Number and percentage of cases of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by specimen type, South Africa, 2018-2019, n=12 835

Site of specimen	2018		2019	
	n*	%	n*	%
Cerebrospinal fluid	6103	95	5956	93
Blood	285	4	339	5
Other	22	1	130	2
Total	**6410**		**6425**	

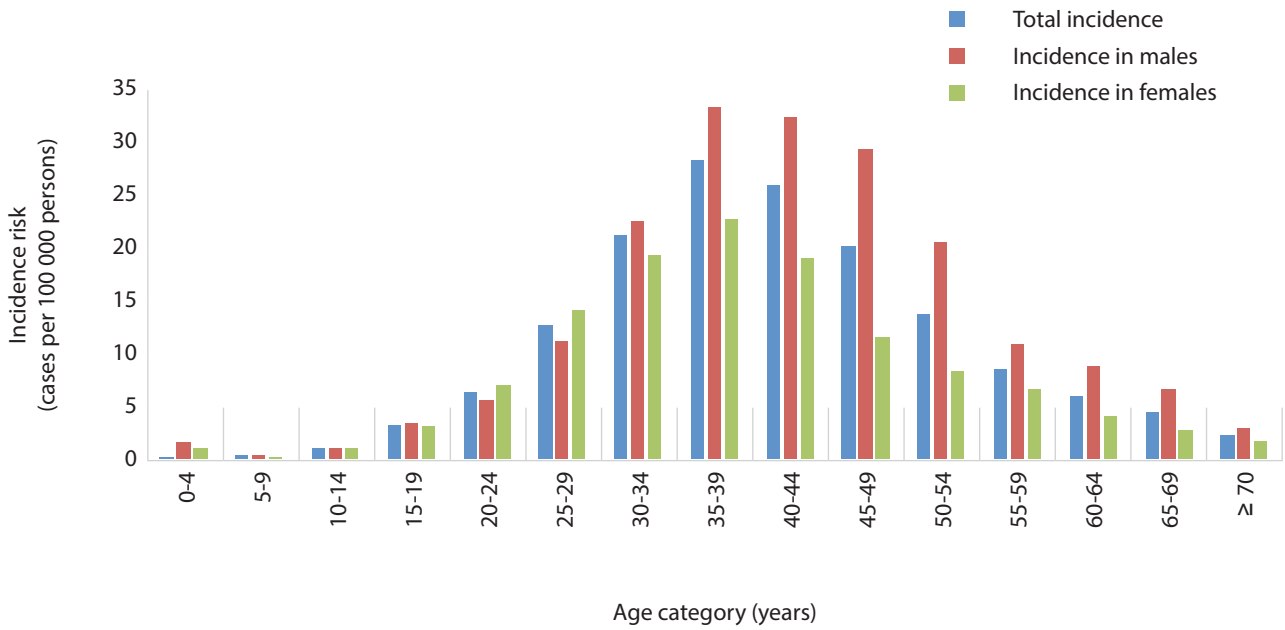
*These case numbers exclude 889 patients (537 in 2018 and 352 in 2019) who tested positive for cryptococcal antigenaemia at NHLS microbiology labs.

Table 6. Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by province, South Africa, 2018-2019, n=12 835

Province	2018		2019	
	n*	Incidence risk (95% CI)†	n*	Incidence risk (95% CI)†
Eastern Cape	920	116 (108-123)	1021	127 (119-135)
Free State	249	67 (59-75)	248	66 (58-75)
Gauteng	1520	81 (77-85)	1410	74 (70-78)
KwaZulu-Natal	1742	87 (83-92)	1707	85 (81-89)
Limpopo	505	110 (100-119)	451	96 (88-105)
Mpumalanga	503	72 (66-78)	457	64 (58-70)
Northern Cape	51	62 (45-80)	74	90 (69-110)
North West	446	92 (83-100)	552	113 (103-122)
Western Cape	474	105 (96-115)	505	110 (100-119)
South Africa	6410	89 (87-91)	6425	88 (86-90)

*These case numbers exclude patients who tested positive for cryptococcal antigenaemia. †Incidence risk 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, 2019, n=6 372



Discussion

The national incidence risk of cryptococcal meningitis or culture-confirmed cryptococcal disease remained the same between 2018 and 2019. This relatively stable incidence may be a consequence of more cases being detected through the national cryptococcal antigen screening programme. Alternatively, the underlying population of HIV-infected patients who present late and/or interrupt their treatment or those experiencing failure of ART may not be changing. The overall in-hospital case-fatality ratio associated with cryptococcosis remained high, despite some patients at GERMS-SA ESS receiving flucytosine-based induction regimens through an access programme. These results have implications for prevention and management of people living with advanced HIV disease in South Africa.

Enhanced sentinel surveillance for CRE bacteraemia in four provinces

Results

There were 2 576 cases of CRE bacteraemia (as detected by a diagnostic laboratory) reported to GERMS-SA from July 2015 through to December 2019 (Table 7). There was an increase in the number of cases from 601 in 2018 to 1 052 in 2019. In 2019, a high proportion of cases were detected from sentinel sites in Gauteng (64%; 669/1 052) followed by KwaZulu-Natal (20%; 209/1 052). In KwaZulu-Natal, there was an increase in the percentage of cases from 12% in 2018 to 20% in 2019 as well as in crease in the percentage of cases in the Western Cape from 8% in 2018 to 15% in 2019 (Table 7, Figure 2). In 2019, males accounted for 53% (556/1 052) and females 46% (481/1 052). Approximately 22% (234/1 052) of cases were aged less than one-year-old (Figure 3). Approximately 46% (479/1 052) of cases were identified by audit (Table 2). CRE isolates were available for 41% (430/1 052) of patients and submitted to NICD for antimicrobial susceptibility testing in 2019. *Klebsiella pneumoniae* was the predominant organism (80%, n=346) followed by *Serratia marcescens* (5%; n=24), *Enterobacter cloacae* (5%; n=22), and *Escherichia coli* (5%; n=9) (Figure 4).

Among isolates in 2019, 90% (n=386) were non-susceptible to ertapenem, 63% (n=272) were non-susceptible to imipenem, and 65% (n=278) were non-susceptible to meropenem and doripenem (Figure 5). Of the 430 isolates, 26 (6%) were resistant to colistin using the Sensititre reference susceptibility method (Figure 6). We confirmed carbapenemase genes in 92% (398/430) of isolates including NDM (29%; 127/430) and OXA-48 or variants (61%; 264/430) as the highest amongst all genes in 2019 (Figure 7). Five percent (21/430) 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). Susceptibility to tigecycline showed that 76% (326/429) of isolates were susceptible. HIV status was known for 74% (592/798) of cases that had a completed case report form. Of cases with known HIV status, 27% (157/592) were HIV-positive in 2019 (Table 4). Patient outcome was known for 96% (765/798) of cases, of which 38% (288/765) died in hospital.

Table 7: Number of cases of carbapenem-resistant Enterobacteriaceae (CRE) bacteraemia reported to GERMS-SA by province, July 2015 to December 2019, n=2 576 (including audit cases)

Province	2015		2016		2017		2018		2019		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Free State	1	1	3	1	11	2	11	2	17	2	43	2
Gauteng	80	68	218	67	375	78	471	78	669	64	1813	70
KwaZulu-Natal	32	27	73	23	76	16	74	12	209	20	464	18
Western Cape	4	4	29	9	21	4	45	8	157	15	256	10
Total	**117**	**100**	**323**	**100**	**483**	**100**	**601**	**100**	**1052**	**100**	**2576**	**100**

Figure 2. Distribution of CRE bacteremia cases by province, 2017-2019, n= 2 136

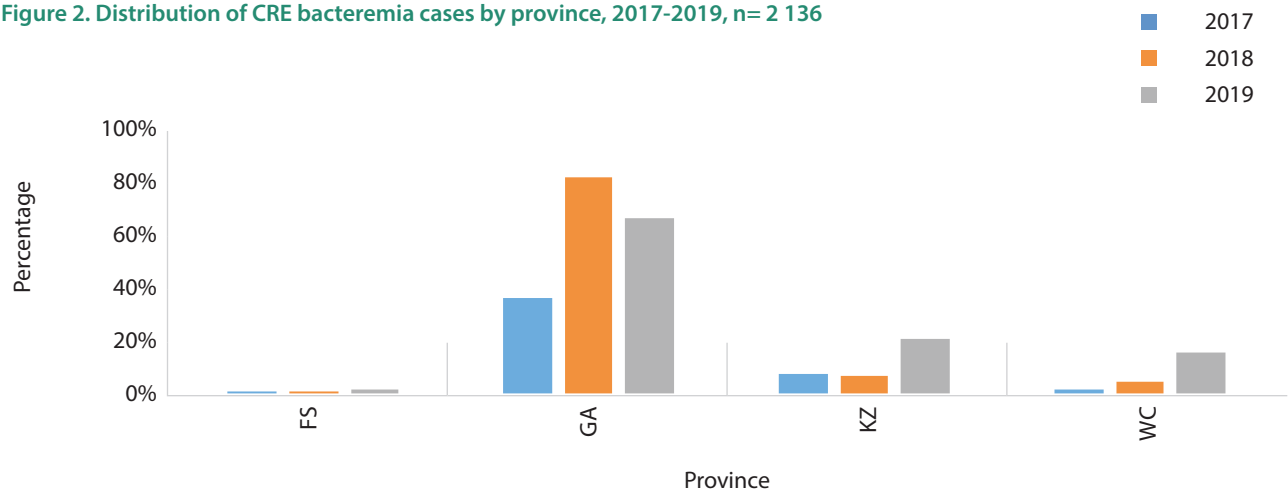


Figure 3. Distribution of CRE bacteremia by age category, 2017-2019, n= 2 136

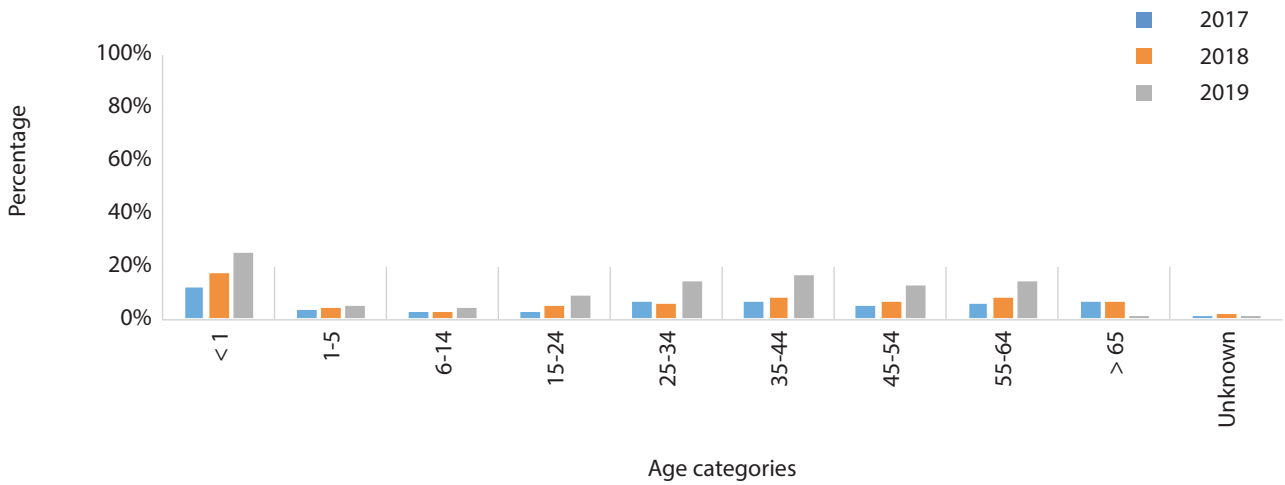


Figure 4. Enterobacteriaceae distribution by species for CRE bacteraemia surveillance, 2017-2019, n=1 031

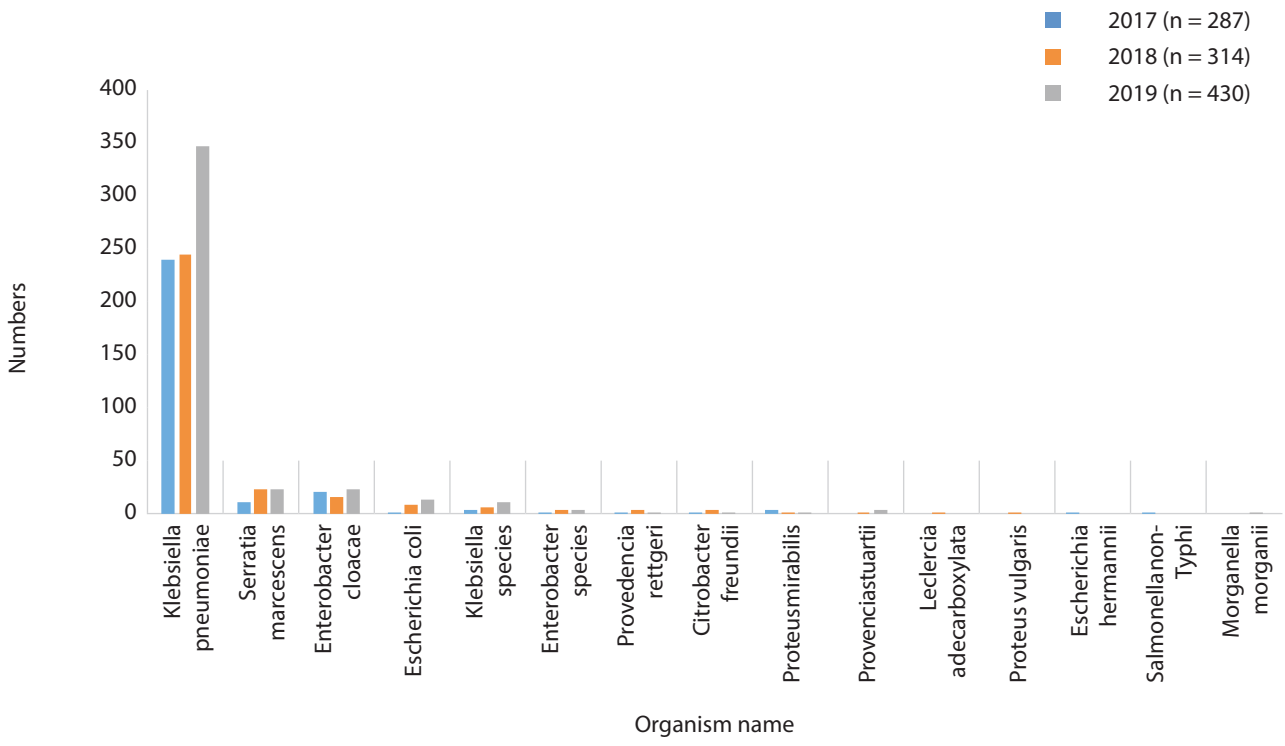


Figure 5. MIC breakpoints for carbapenem results in 2019, n=430

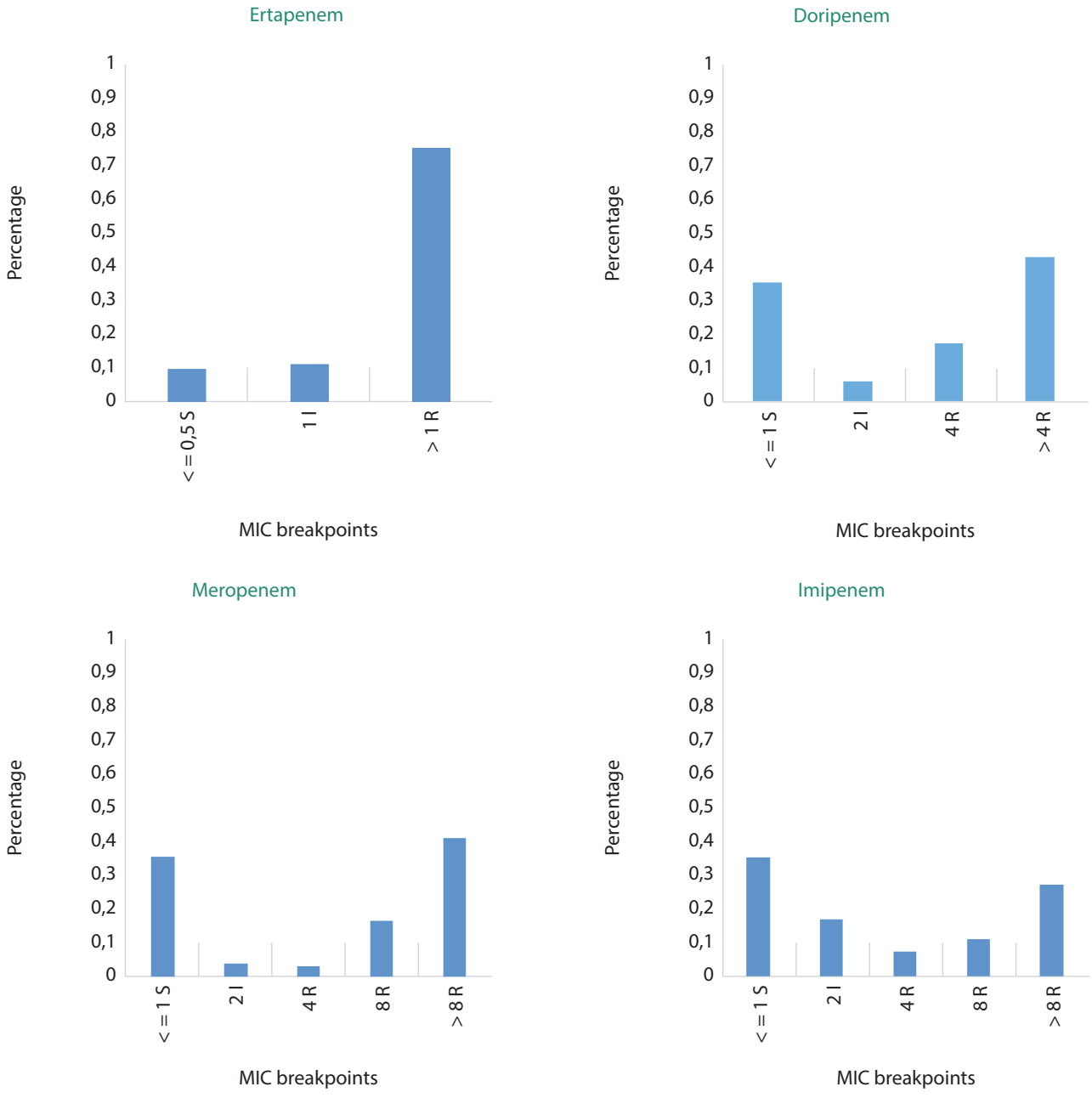


Figure 6. Confirmed colistin resistance by Sensititre, 2019, n=26

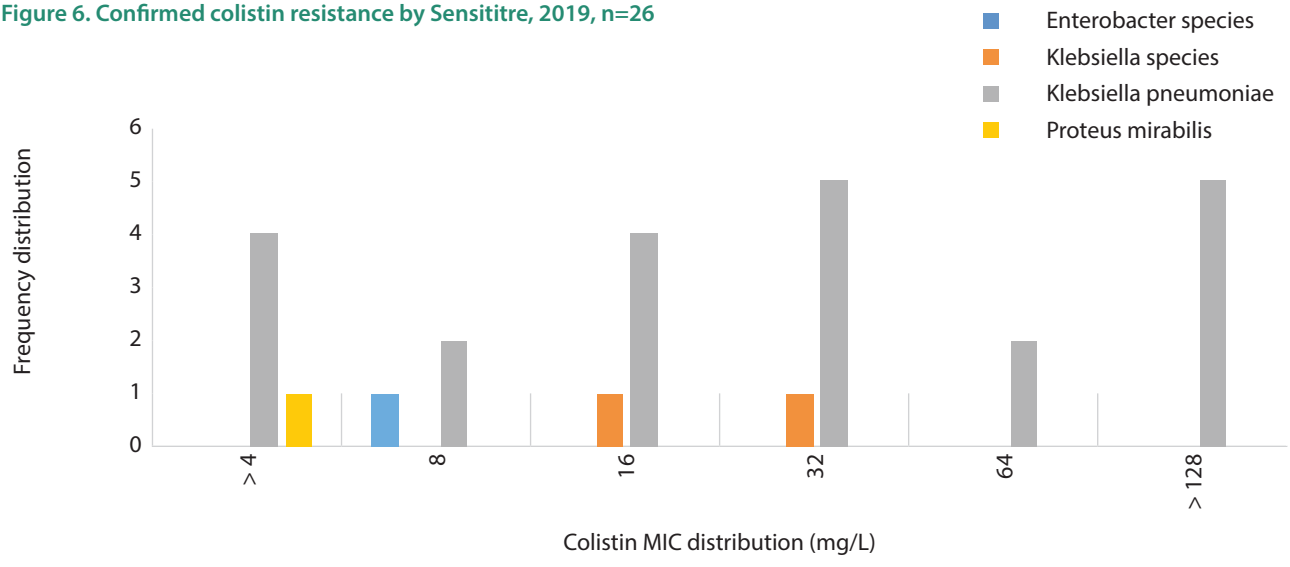


Figure 7. Distribution of carbapenemase genes in Enterobacteriaceae, 2017-2019, n=1 031

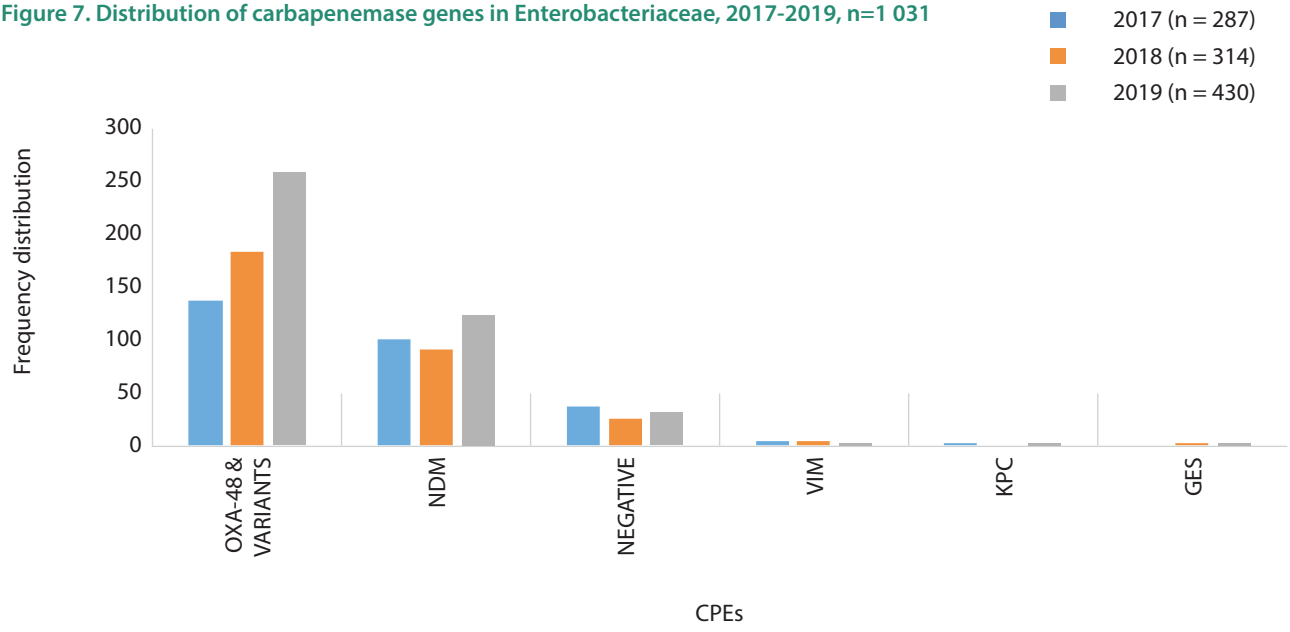
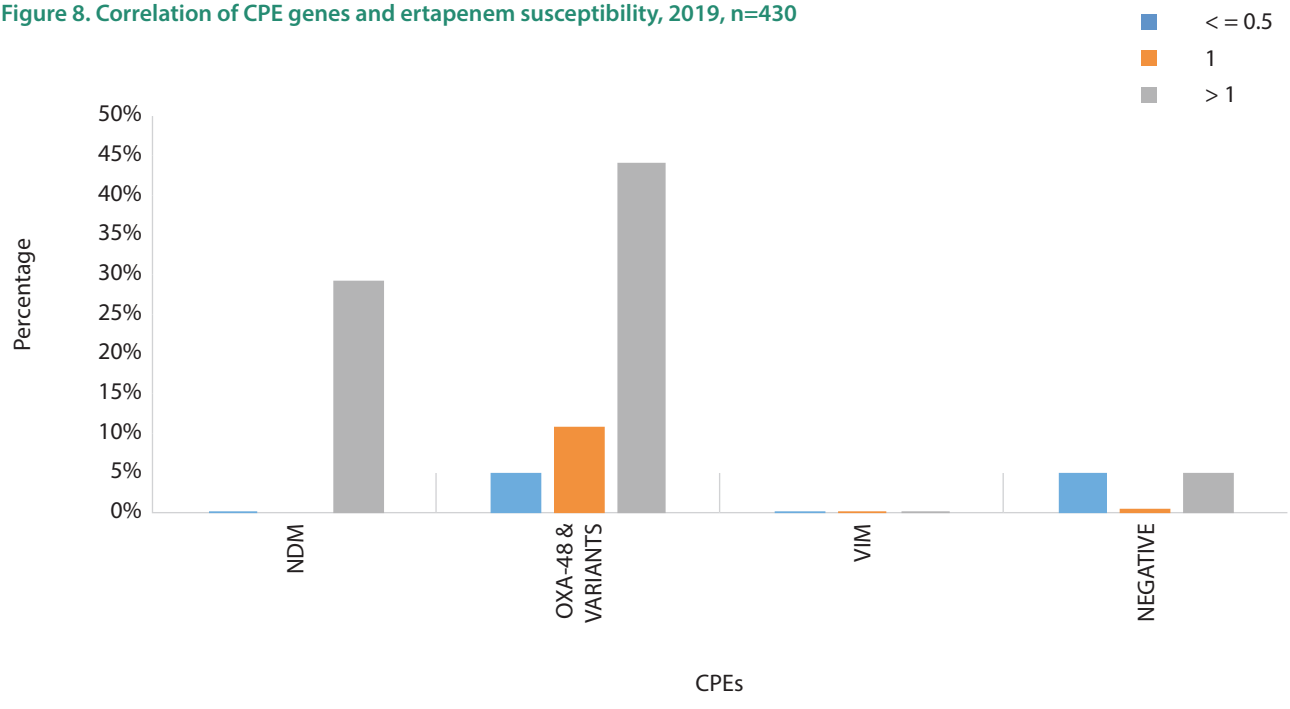


Figure 8. Correlation of CPE genes and ertapenem susceptibility, 2019, n=430



Discussion

The number of CRE bacteraemia cases detected over the surveillance period is relatively small. However, there has been an increase in 2019 compared to 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.

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

Results

In 2019, 1 438 cases of AB bacteraemia were detected in four provinces, (Table 8), of which 46% (659/1 438) were identified by audit (Table 2). Where sex was known, males accounted for 55% (n=797). The largest proportion of cases were patients aged less than one year of age (44%, n=627) (Figure 9). Clinical case data collected from enhanced surveillance sites (ESS) were available for 82% (n=1 186) of cases (Table 4). The majority of the cases were reported from ESS sites in Johannesburg and Pretoria. The susceptibility results to the most important antimicrobial agents, including colistin, is shown in Figure 10. Colistin susceptibility testing by Sensititre panels on total 1 423 isolates demonstrated that 4% (n=55) are recording breakpoint of ≥ 4 mg/L, on these isolates no plasmid mediated mcr1-5 genes were detected (Figure 11). Patient outcome was known for 55% (652/1 186) of cases, of which 60% (n=391) died in hospital. HIV status was known for 68% (801/1 186) of cases, of which 19% (n=152) were HIV-positive in 2019 (Table 4).

Table 8: Number and percentages of cases of *Acinetobacter baumannii* bacteraemia reported to GERMS-SA sentinel sites by province, South Africa, 2017 to 2019 (n=4 602) (including audit cases)

Province	2017		2018		2019		Total	
	n	%	n	%	n	%	n	%
Gauteng	918	67	1065	60	792	55	2775	60
Western Cape	139	10	197	11	153	11	489	11
KwaZulu-Natal	166	12	321	18	309	21	796	17
Free State	154	11	204	11	184	13	542	12
Total	**1377**	**100**	**1787**	**100**	**1438**	**100**	**4602**	**100**

Figure 9. Distribution of *A. baumannii* bacteraemia cases by age category, 2018-2019, n=3 225

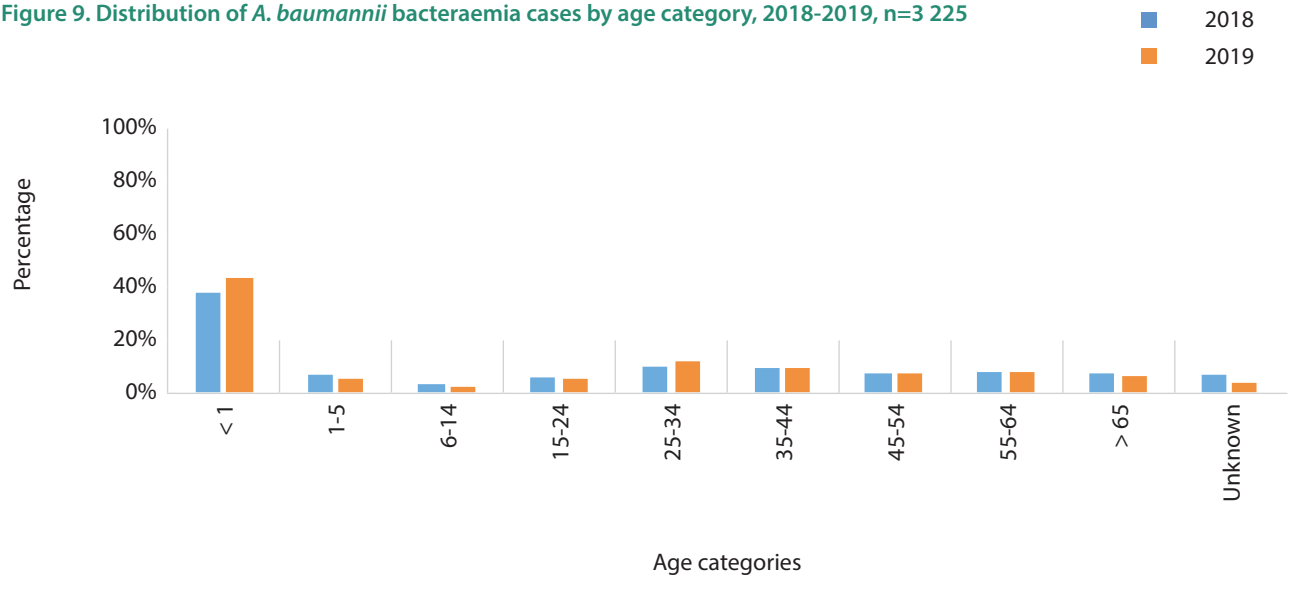


Figure 10. Proportion of viable *A. baumannii* isolates susceptible to various antimicrobial agents, 2018-2019, n= 1 447

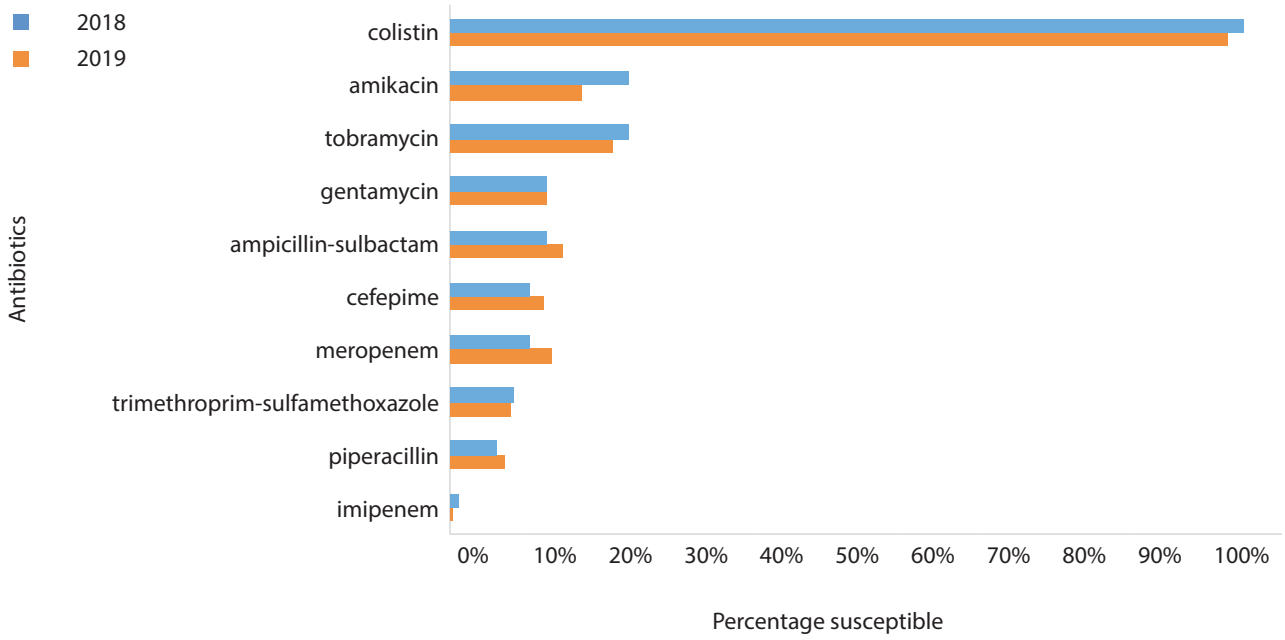
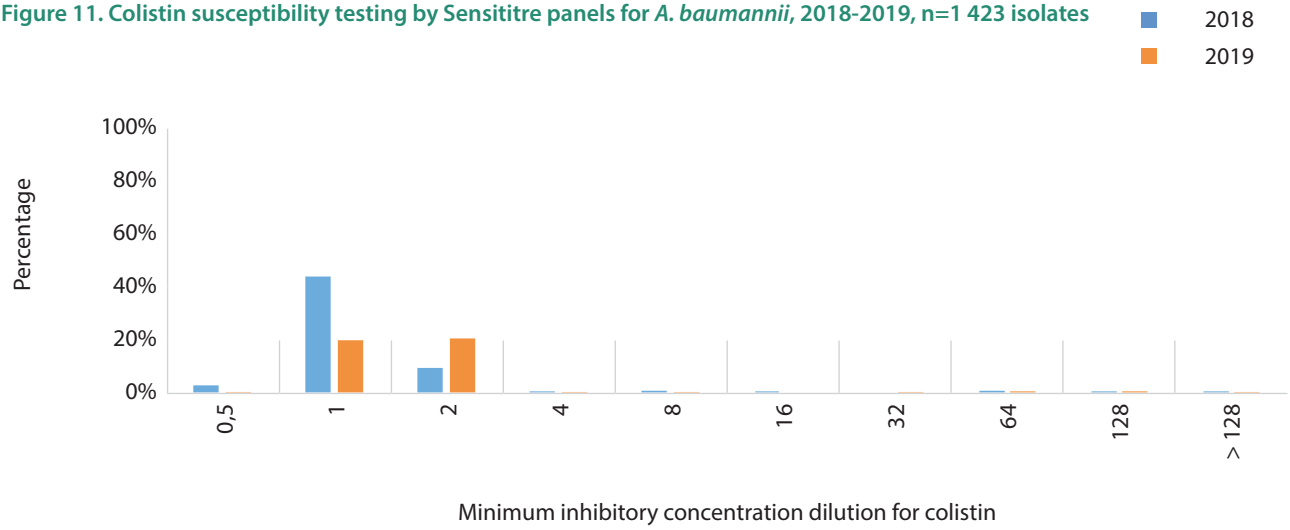


Figure 11. Colistin susceptibility testing by Sensititre panels for *A. baumannii*, 2018-2019, n=1 423 isolates



Discussion

AB bacteraemia has increased in the last year, particularly in the KwaZulu-Natal province. AB is highly prevalent in infants less than one year of age. 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.

Neisseria meningitidis

Results

In 2019, 111 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 43 (39%) viable isolates were received and 16 (14%) cases were detected on audit (Table 2). The overall disease incidence remained low at 0.19 cases per 100 000 population, similar to that in 2018 (0.22/100 000). Incidence was highest in the Western Cape Province (0.56/100 000) followed by Gauteng (0.24/100 000) and Eastern Cape Provinces (0.18/100 000) (Table 9). Most cases were sporadic, and disease peaked from winter through spring (May to October), with a further upsurge in December (Figure 12). Cerebro-spinal fluid was the most common specimen from which meningococci were identified (70/111, 63%) (Table 10). Ninety-five percent (89/94) of IMD was caused by 3 serogroups - B (36/94, 38%), Y (27/94, 29%) and W (25/94, 27%) (Table 11). Incidence of IMD was highest in children <1 year (1.14/100 000) (Figure 13). Although the different serogroups occurred across most age-categories, serogroup B was most predominant in children aged <5 years, serogroup Y in person aged 5-24 years and serogroup W in persons aged >25 years (Figure 13). Of those with known sex, IMD occurred more frequently in males (59/109, 54%). Of the viable isolates tested for antimicrobial susceptibility, 26% (11/43) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) between 0.094µg/ml and 0.25µg/ml, and all were susceptible to 3rd generation cephalosporin and ciprofloxacin.

Thirty-eight (34%) IMD patients presented to our enhanced surveillance sites and 31/38 (82%) had additional clinical information available (Table 4). The median time for each admission was 10 days (interquartile range 7-13 days). Case-fatality ratio was 19% (6/31); three patients died on the day of admission. Thirty-eight percent of patients with HIV status available were HIV-infected (9/24) (Table 4). For those who survived to discharge from hospital, 5/25 (20%) suffered sequelae following IMD. Two patients developed ongoing seizures, and one each had hearing loss, necrotic skin lesions and hydrocephalus.

Table 9: Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=236 (including audit cases)

Province	2018		2019	
	n	Incidence rate*	N	Incidence rate*
Eastern Cape	26	0,4	12	0,18
Free State	2	0,07	3	0,1
Gauteng	37	0,25	37	0,24
KwaZulu-Natal	8	0,07	13	0,12
Limpopo	4	0,07	2	0,03
Mpumalanga	2	0,04	1	0,02
Northern Cape	1	0,08	1	0,08
North West	6	0,15	4	0,1
Western Cape	39	0,59	38	0,56
South Africa	125	0,22	111	0,19

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

Figure 12. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2018-2019, n=236

Table 10. Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=236

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

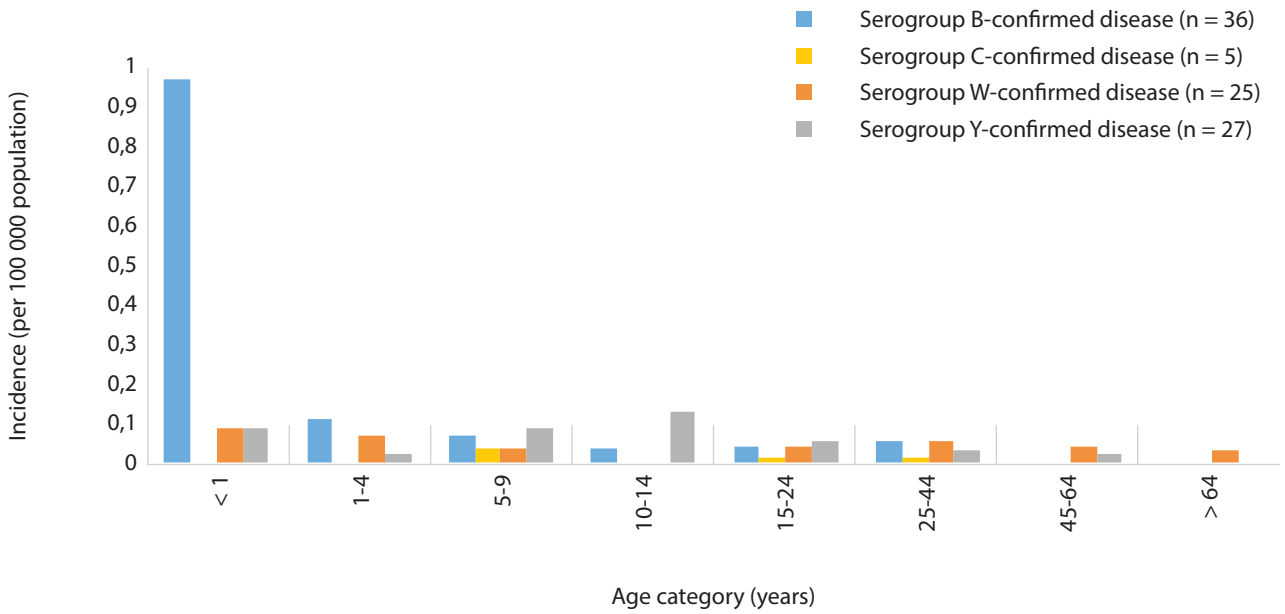
Table 11. Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2019, n=111*

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

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

Figure 13. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2019, n=111 (**specimens or viable isolates unavailable for serogrouping n=17; one isolate serogroup E).**

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



Discussion

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

Haemophilus influenzae

Results

There were 259 cases of invasive *Haemophilus influenzae* (HI) disease identified through the surveillance pro-gramme in 2019, 41% (105) were detected on audit; and 58% (149) had either viable isolates (109) or speci-mens (40) available for serotyping (Table 12). Eight cases were co-infected with invasive Streptococcus pneu-moniae. Incidence of invasive HI disease was 0.44 per 100 000 population. Gauteng Province (88/259, 34%) had the highest number of cases reported, followed by Western Cape Province (78/259, 30%) (Table 12). Twenty-eight percent of cases (41/149) were serotype b (Hib) and non-typeable (HNT) disease was found in 55% (82/149) (Table 12). Most HI cases were isolated from blood (160/259, 62%), however Hib isolates were more likely than HNT isolates to be found in CSF (17/41, 41% versus 6/82, 7%, p<0.001) (Table 13). Although HI oc-curs in all ages, invasive disease is highest in infants followed by adults aged 25-44 years (Figure 14). Hib inci-dence is still highest in infants even though significant declines have been noted since 2010 (5.2 cases per 100 000 in 2010 to 1.2 cases per 100 000 in 2019 (p<0.001)) (Figure 15 and 16). Hib incidence has remained below 0.2 per 100 000 in 1-4 year olds, since 2013 (Figure 16). HNT incidence is highest in infants (1.2 per 100 000) dropping substantially throughout the rest of childhood before increasing again in adulthood with a moderate peak from ages 25 years and older (Figure 15). Forty-one percent (12/29) of Hib isolates and 8% (5/60) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Twenty-five cases of Hib disease occurred in children <15 years of age and vaccine history was available for 32% (8/25). Three infants were <6 weeks and thus too young to receive Hib vaccine. Four children had received at least 3 doses of vaccine and were possible vaccine failures. One 3-month old child had only received one dose of Hib vaccine.

Clinical information was available for 85% (110/130) of cases presenting to the enhanced surveillance sites (ESS) (Table 4). Patients were admitted for a median of 7 days (interquartile range (IQR) 3-16). Case fatality was 27% (36/110) and median time to death was within one day of admission (IQR 0-4). There was no statistically significant difference between case fatalities of those with Hib or HNT disease (25% (5/20) vs. 23% (11/47),

p=0.5). Amongst those with known HIV status, 38% (33/86) were HIV-infected. Conditions, other than HIV, pre-disposing to HI disease were reported in 53/98 (54%) patients – the most common conditions included chronic lung disease (10), history of smoking (7), malignancy (7) and prematurity (6). Of the 19 patients at ESS with HI on CSF: eight patients died during their hospitalization, and 27% (3/11) of those who survived to discharge suffered sequelae – one developed ongoing seizures and two developed hydrocephalus.

Table 12. Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2019, n=259*

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

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

Table 13. Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2019, n=259

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

Figure 14. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2019, n=259 (age unknown for n=4; specimens or viable isolates unavailable for serotyping for n=110).

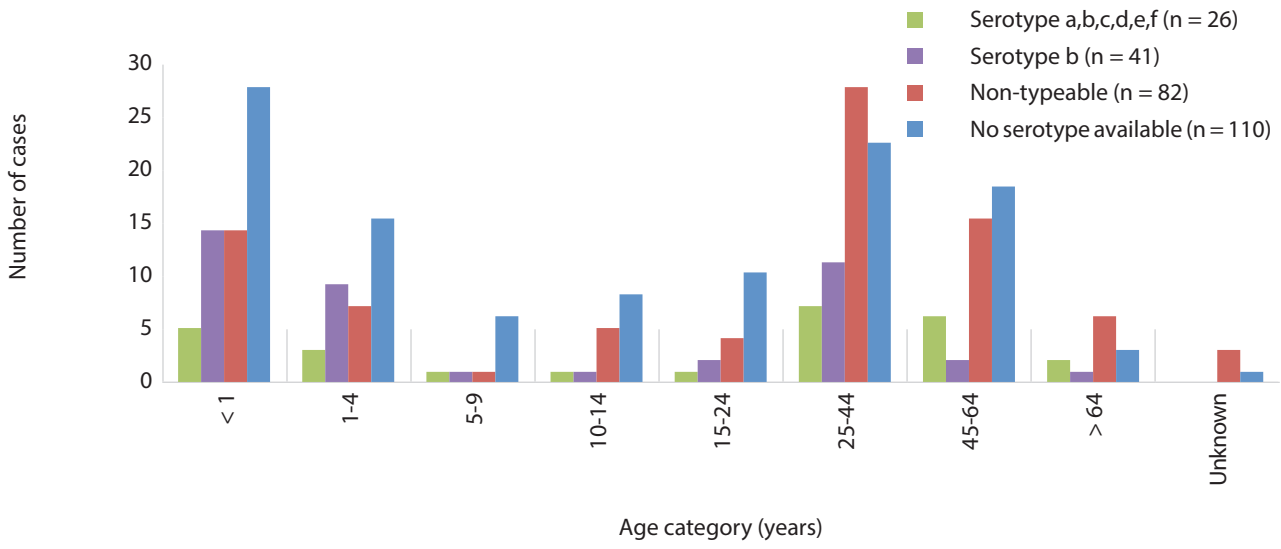


Figure 15. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2019, n=259 (age unknown, n=4; isolates unavailable for serotyping, n=110; other serotypes from cases with known age, n=26).

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

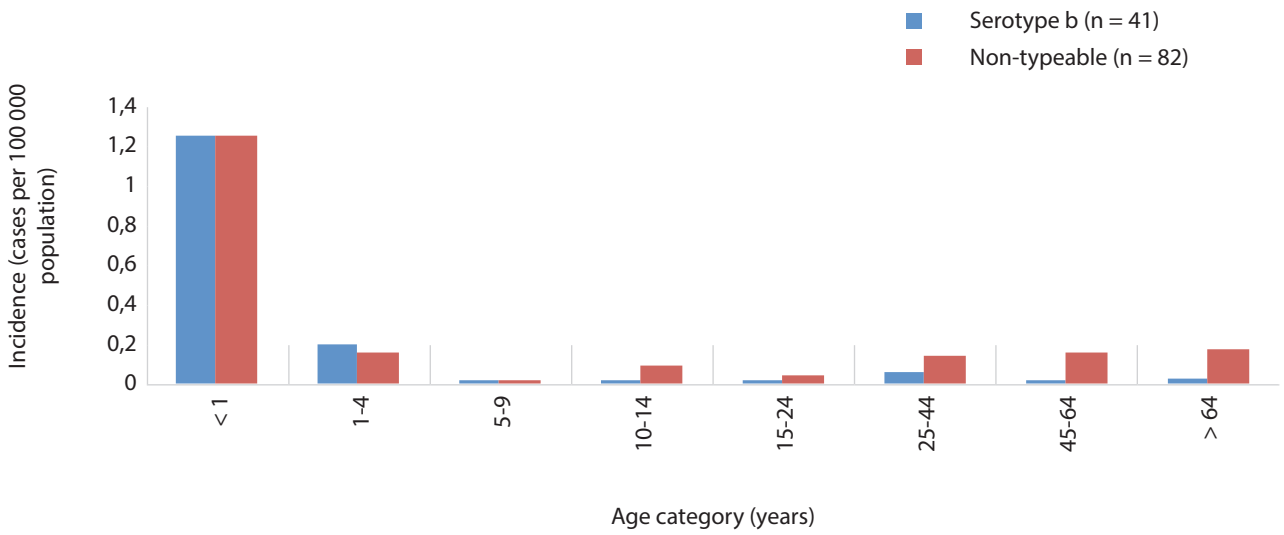
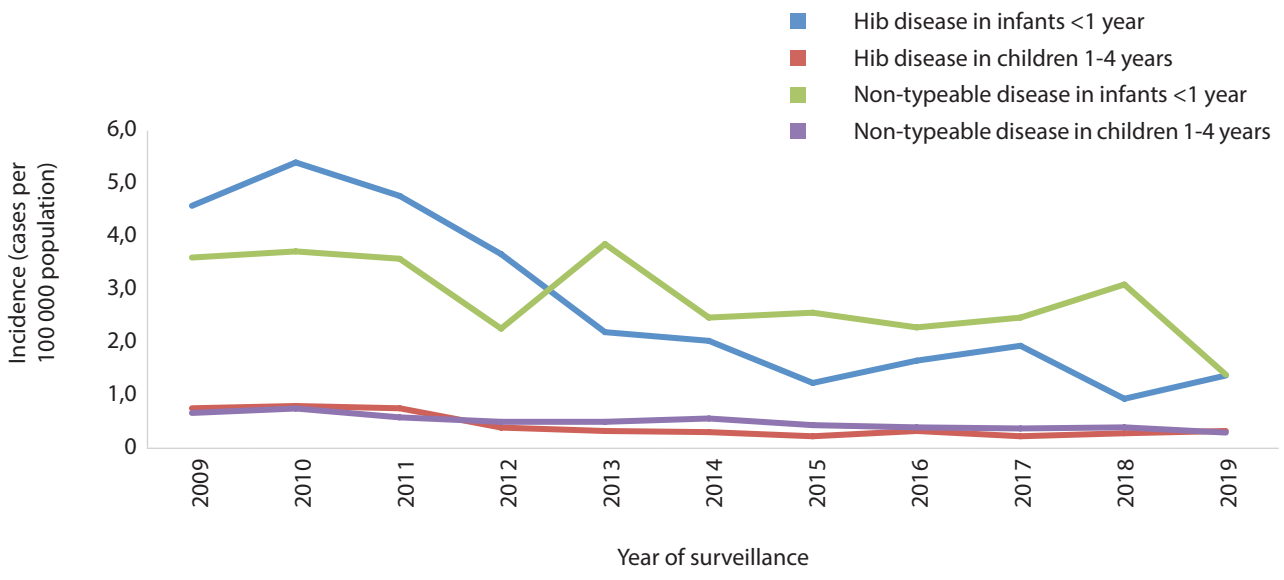


Figure 16. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2019.

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



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

Streptococcus pneumoniae

Results

Invasive pneumococcal disease (IPD) incidence for 2019 has remained the same as 2018 at 4 per 100 000 population (Table 14). The highest incidence was seen in the Western Cape (9.3 per 100 000 population) followed by Northern Cape (7.1 per 100 000) and Gauteng Provinces (5.1 per 100 000 population) (Table 14). Pneumococcal conjugate vaccine (PCV7) was introduced into the Expanded Programme on Immunisation (EPI) in 2009, and subsequently replaced by PCV13 in 2011. In 2019, peak IPD incidence occurred in infants (20 per 100 000 population), followed by adults (5-6 per 100 000 population in the 25 years and older age categories) (Figure 17). Eight patients with IPD were co-infected with invasive *Haemophilus influenzae* and one with *Neisseria meningitidis*. The majority of IPD cases were isolated from blood culture specimens (63%, 1 490/2 359) (Table 15). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 29% (413/1 386) of IPD isolates, the highest proportion was in children 1-4 years of age (51%, 40/79) (Table 16 and Figure 18). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 8% (110/1 386) of isolates from all specimens, including 8% (29/347) of IPD isolated from CSF. In 2019, serogroups 8, 12F, 19F, 7 and 14 were the most predominant serogroups causing 44% (80/180) of IPD in children <5 years-of-age, whilst serogroups 8, 12F, 3, 19A and 9N caused 43% (511/1 194) of disease in persons >5 years (Figure 19A and 19B). Only 59% (1 386/2 359) of IPD isolates were sent to NICD, of which 1 374 were serotyped (Figure 20). Of those serotyped, 22% (39/180) of isolates from children <5 years, and 30% (357/1 194) of IPD isolates from person 5 years and older were PCV13-vaccine serotypes (Table 17 and 18).

Eighty-three percent (745/893) 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) 3-13) and most deaths occurred within 2 days of admission (IQR 1-6). Overall case fatality was 33% (246/744). HIV-infection was present in 66% (407/616) of IPD patients; and 47% (27/58) of infants with maternal HIV-status available were HIV-exposed (10 HIV-infected, 14 HIV-uninfected and 3 HIV-status unknown). Forty-three percent (327/744) of patients had a condition/risk factor (excluding HIV-infection) predisposing them to IPD. The top three factors included: history of smoking (102 patients), diabetes (41 patients) and chronic lung disease (38 patients).

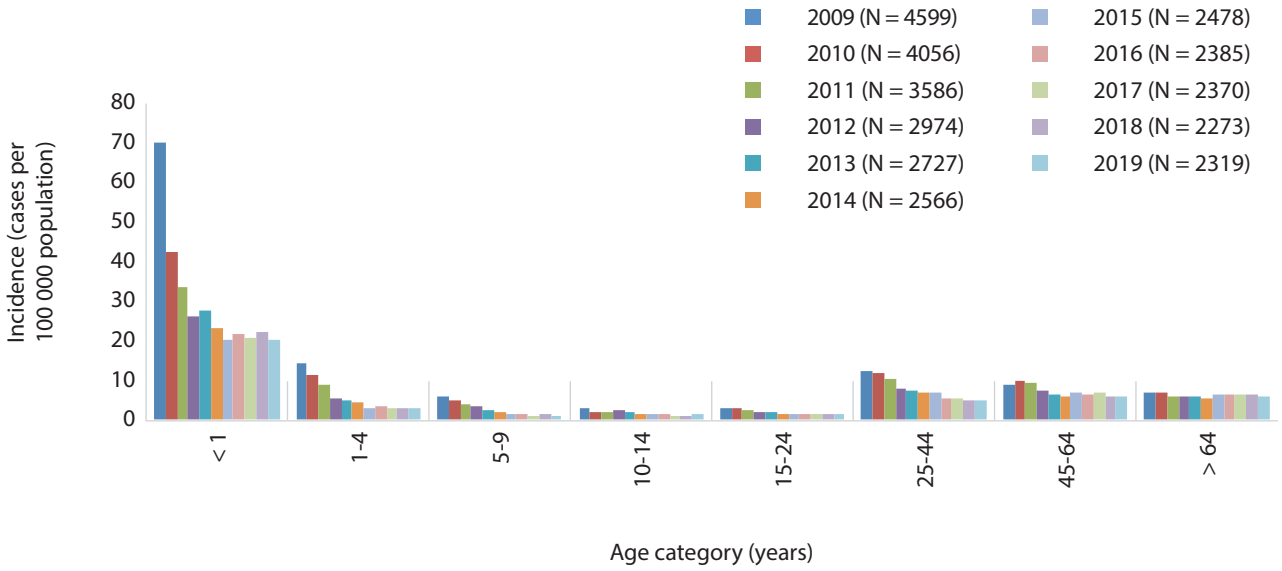
Of 180 patients at ESS with pneumococcus on CSF: 41% (73/180) died during their hospitalization, and 30% (32/107) who survived to discharge suffered at least one sequelae – these included new onset seizures (11), limb weakness/paralysis (9), hydrocephalus (4), hearing loss (4), visual loss (3) and necrotic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

Table 14. Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2018 and 2019, n=4 674 (including audit cases)

Province	2018		2019	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	259	3,96	274	4,08
Free State	106	3,59	84	2,91
Gauteng	757	5,14	776	5,11
KwaZulu-Natal	242	2,13	237	2,1
Limpopo	84	1,45	97	1,62
Mpumalanga	116	2,56	102	2,22
Northern Cape	52	4,24	90	7,12
North West	71	1,78	66	1,64
Western Cape	628	9,48	633	9,25
South Africa	2315	4,01	2359	4,01

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

Figure 17. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2019, n=33 761.



2009: N=4 760 age unknown for n=161; 2010: N=4 197, age unknown for n=141; 2011: N=3 804, age unknown for n=218; 2012: N=3 222, age unknown for n=248; 2013: N=2 865, age unknown for n=138; 2014: N=2 731, age unknown for n=165; 2015: N=2 635, age unknown for n=157; 2016: N=2 433, age unknown for n=48; 2017: N=2 440, age unknown for n=70; 2018: N=2 315, age unknown for n=42; 2019: N=2 359, age unknown for n=40

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

Table 15. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2018 and 2019, n=4 674

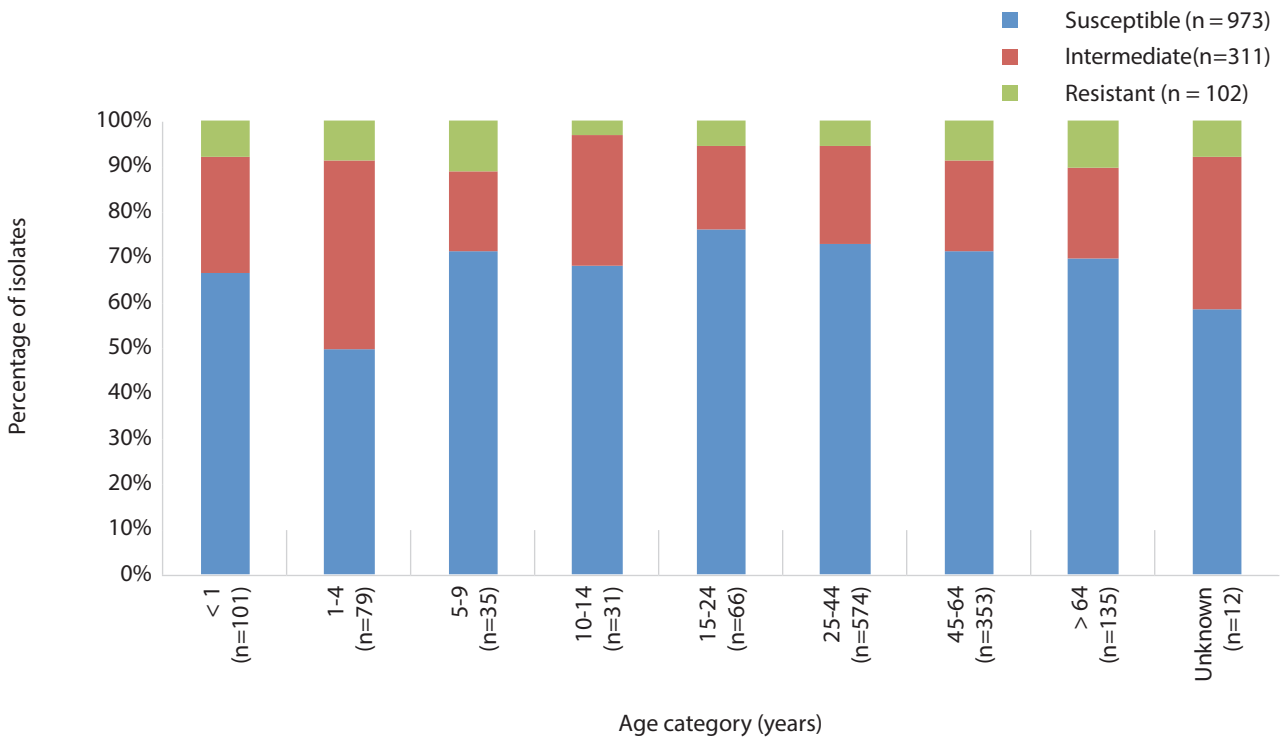
Site of specimen	2018		2019	
	n	%	n	%
Cerebrospinal fluid	795	34	700	30
Blood	1362	59	1490	63
Other	158	7	169	7
Total	**2315**		**2359**	

Table 16. Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2019, n=2 359

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

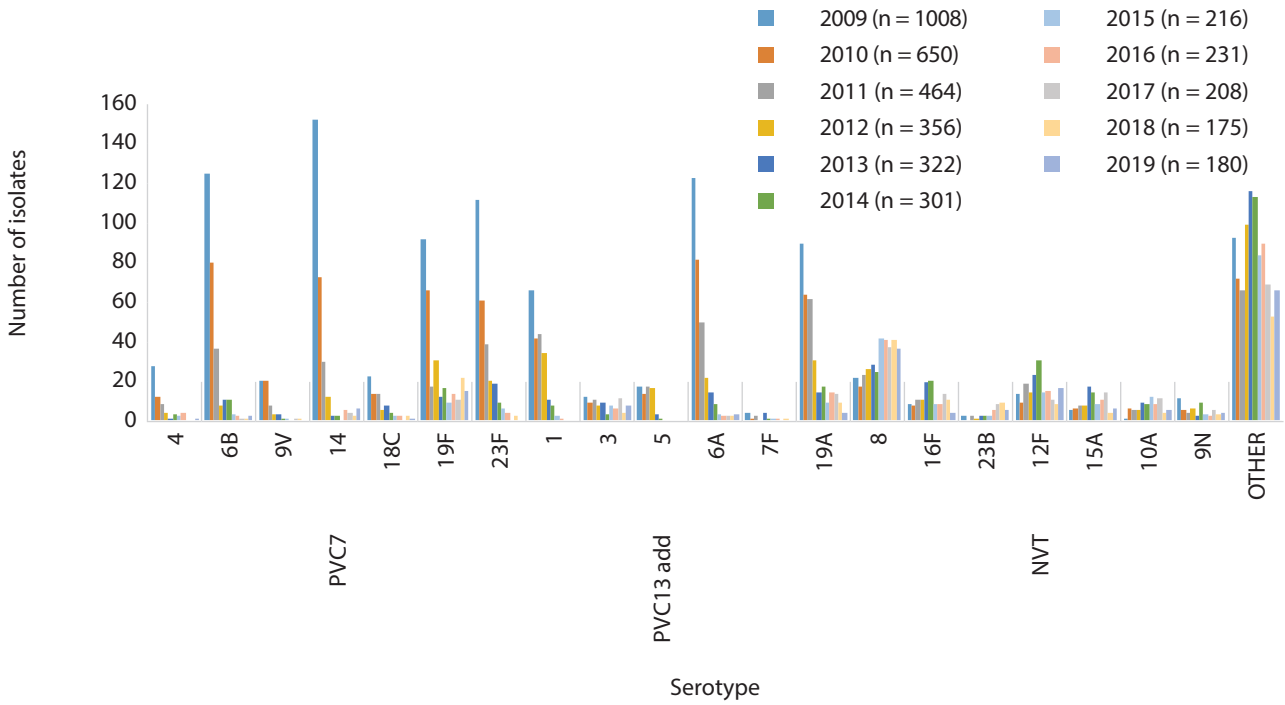
*2016 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Figure 18. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2019, n=2 359 (n=1 386 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.

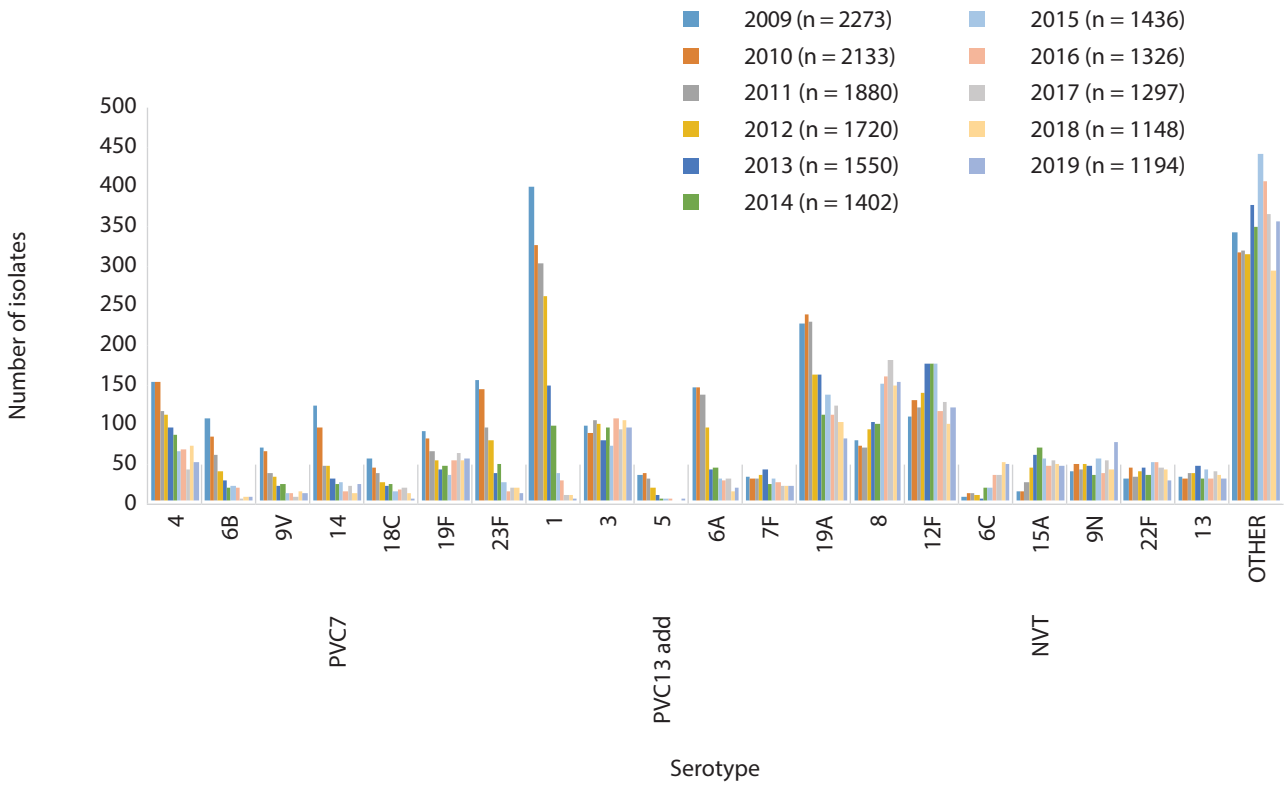
Figure 19A. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2019.



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; 2018: N=386, n=211 without viable isolates; 2019: N=361, n=181 without viable isolates

Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

Figure 19B. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children >5 years, South Africa, 2009-2019.



2009: N=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=723 without viable isolates; 2019: N=1 998, n=804 without viable isolates.

Foot note: PCV7: seven-valent pneumococcal conjugate vaccine; PCV13add: additional serotypes in the thirteen-valent pneumococcal conjugate vaccine; NVT: non-vaccine serotypes

Figure 20. Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, South Africa, 2009-2019.

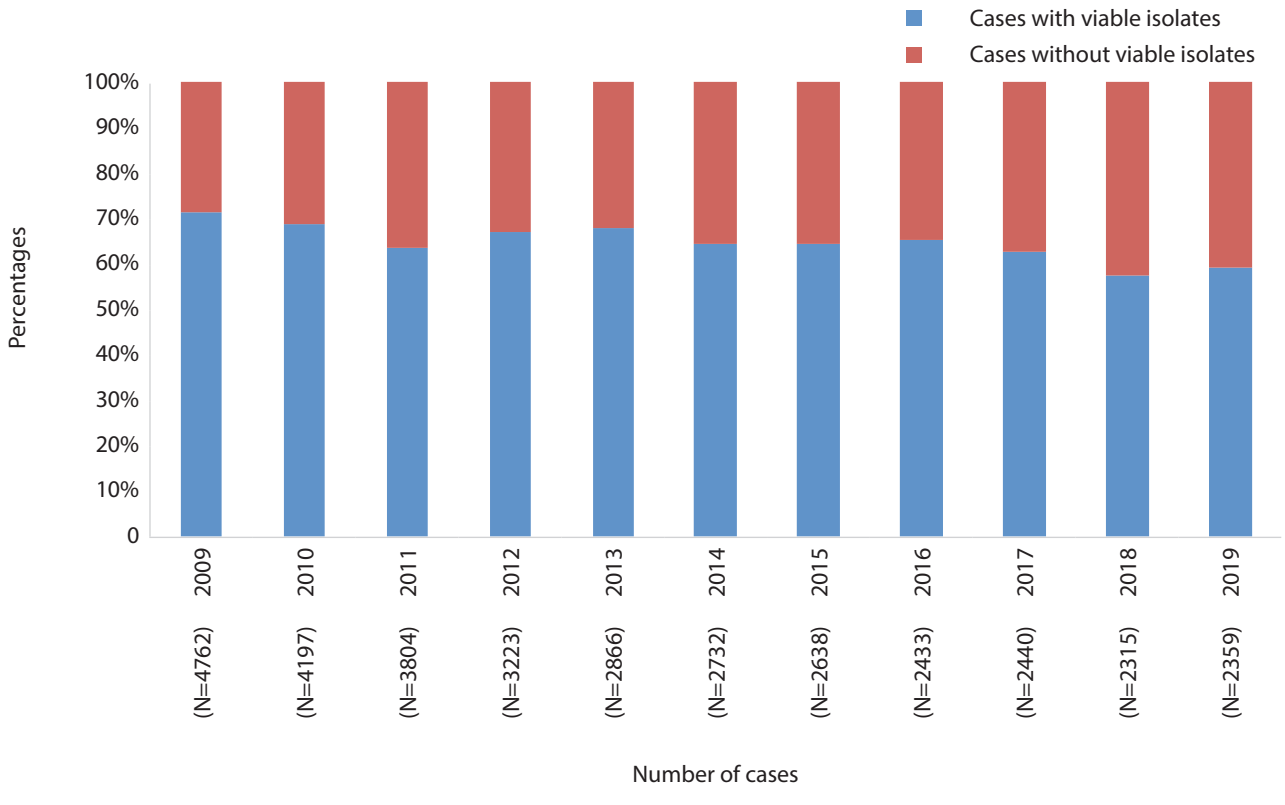


Table 17. Number and percentage of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2019, n=361 (n=180 with viable isolates)

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes**		13-valent serotypes***	
		n	%	n	%	n	%	n	%
Eastern Cape	17	2	12	0	0	2	12	3	18
Free State	7	1	14	0	0	1	14	1	14
Gauteng	68	8	12	1	1	8	12	12	18
KwaZulu-Natal	23	5	22	0	0	5	22	6	26
Limpopo	10	3	30	1	10	3	30	6	60
Mpumalanga	10	2	20	0	0	2	20	3	30
Northern Cape	1	1	100	0	0	1	100	1	100
North West	6	0	0	1	17	0	0	1	17
Western Cape	38	3	8	0	0	3	8	6	16
South Africa	180	25	14	2	1	25	14	39	22

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

Table 18. Number and percentage of invasive pneumococcal cases reported amongst adults and children >5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2019, n=1998 (n=1194 with viable isolates)

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes**		13-valent serotypes***	
		n	%	n	%	n	%	n	%
Eastern Cape	158	20	13	1	1	26	16	45	28
Free State	39	7	18	0	0	7	18	12	31
Gauteng	335	45	13	8	2	50	15	94	28
KwaZulu-Natal	62	9	15	1	2	10	16	17	27
Limpopo	36	1	3	0	0	1	3	8	22
Mpumalanga	52	7	13	3	6	7	13	19	37
Northern Cape	53	8	15	0	0	10	19	22	42
North West	17	2	12	1	6	2	12	6	35
Western Cape	442	48	11	3	1	57	13	134	30
South Africa	1194	147	12	17	1	170	14	357	30

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

Discussion

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

Group A Streptococcus (*Streptococcus pyogenes*)

Results

Thirty-four percent (363/1 060) of isolates meeting the GERMS-SA case definition for laboratory confirmed invasive Group A Streptococcus (GAS) were sent to the reference laboratory for further characterisation – these cases include isolates from skin and soft tissue infections thought to be causing systemic illness (audit Table 2). Incidence of invasive GAS was highest in infants (6.4 per 100 000) with a second peak in those aged >64 years (3 per 100 000) (Figure 21). Most cases were reported from the Western Cape Province (n=466, 44%), followed by Gauteng (208, 20%), KwaZulu-Natal (173, 16%) and Eastern Cape (159, 15%) provinces. More invasive GAS disease occurred in males (551/1 041, 52%) than females. Forty-six percent (478/1 045) of cases were identified on blood culture, followed by 41% (426/1 045) from skin and soft tissue specimens (Table 19). Of those isolates available for antimicrobial susceptibility testing, 97% (338/348) were susceptible to penicillin (MIC<0.06µg/ml) and 95% (331/348) were susceptible to erythromycin (MIC<0.25µg/ml) (Table 20).

Figure 21. Age-specific incidence rates* for laboratory-confirmed, invasive Group A Streptococcal disease, reported to GERMS-SA, South Africa, 2019, n=1 060

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

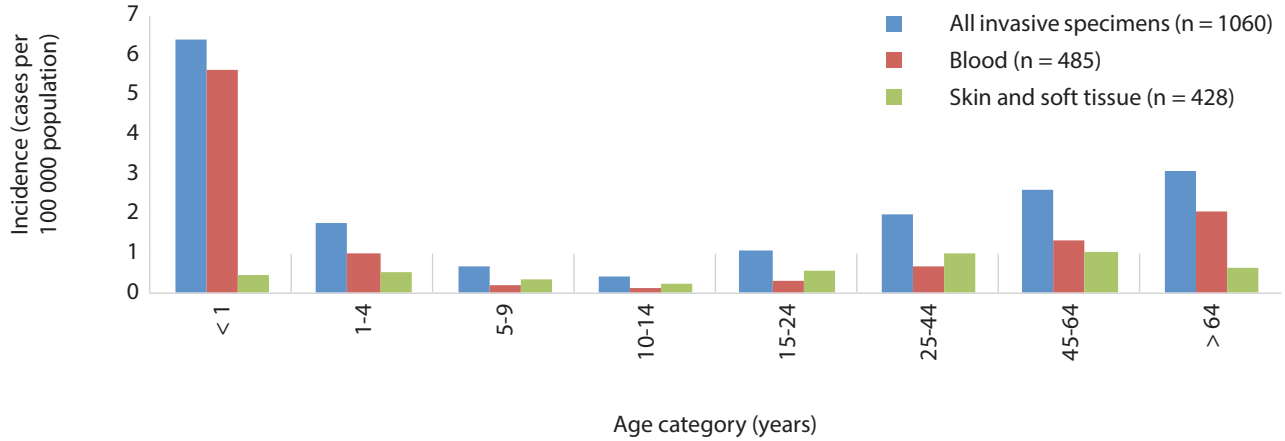


Table 19. Number and percentage of cases of invasive Group A Streptococcal disease reported to GERMS-SA by specimen type and age category, South Africa, 2019, n=1060 (age unknown for n=15)

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

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

Table 20. Number and percentage of penicillin and erythromycin susceptible and non-susceptible isolates from invasive Group A Streptococcal disease case reported to GERMS-SA, South Africa, 2019, n=1 060

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

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

Discussion

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

Group B Streptococcus (*Streptococcus agalactiae*)

Results

One thousand and thirty-four cases of invasive Group B streptococcal infections (GBS) were reported through the GERMS-SA surveillance network, of which 347 (34%) isolates were received for further characterisation. Incidence for early onset GBS (<7days) was 0.34 per 1 000 live births and 0.24 per 1 000 live births for late on-set (7-90 days) invasive disease (Table 21). Gauteng reported the highest incidence of early and late onset GBS (0.65 and 0.47 per 1 000 live births), followed by the Western Cape Province (0.46 and 0.36 per 1 000 live births) (Table 21). In infants, invasive GBS incidence was 60 per 100 000 population and decreased rapidly by month of age (Figure 22a). Whilst in persons >1 year of age, overall incidence of invasive GBS was 0.74 per 100 000, peaking in those >64 years of age (Figure 22b). In infants, most cases were isolated from blood (472/574, 82%) or cerebrospinal fluid (91/574, 16%) (Table 22). However, in persons >1 year of age blood (168/426, 39%) and soft tissue (162/426, 38%) specimens were most frequent (Table 22). Disease occurred more frequently in females (569/995, 56%) than males. Of the specimens available for serotyping, serotype III was the most predominant (166/321, 52%), followed by serotype Ia (78, 24%) (Table 23). Serotypes III and Ia were the most predominant serotypes causing invasive disease in early and late onset GBS (Figure 23). In per-sons >90 days of age, invasive GBS was caused by serotypes III, Ia, II and V (Figure 23). Ninety percent (283/316) of invasive GBS isolates were susceptible to penicillin (MIC<0.12mg/l) and 95% (296/313) were susceptible to gentamycin.

Table 21. Number of cases and incidence rates of invasive Group B Streptococcal disease reported to GERMS-SA by province and age category*, South Africa, 2019, n=1 034**

Province	Early onset (<7 days)		Late onset (7-90 days)		Age category ≥1 year	
	n	Incidence (per 1000 live births)	n	Incidence (per 1000 live births)	n	Incidence (per 100 000 population)
Eastern Cape	17	0,15	13	0,12	31	0,47
Free State	11	0,23	6	0,13	9	0,32
Gauteng	137	0,65	99	0,47	186	1,24
KwaZulu-Natal	74	0,37	43	0,21	78	0,7
Limpopo	12	0,09	11	0,09	12	0,2
Mpumalanga	17	0,21	12	0,15	8	0,18
Northern Cape	1	0,04	2	0,08	4	0,32
North West	5	0,09	5	0,09	2	0,05
Western Cape	46	0,46	36	0,36	96	1,42
South Africa	320	0,34	227	0,24	426	0,74

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

Figure 22A. Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in children <1 year of age, reported to GERMS-SA, South Africa, 2019, n=1 034 (n=574 in children <1 year, age unknown for n=34)

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

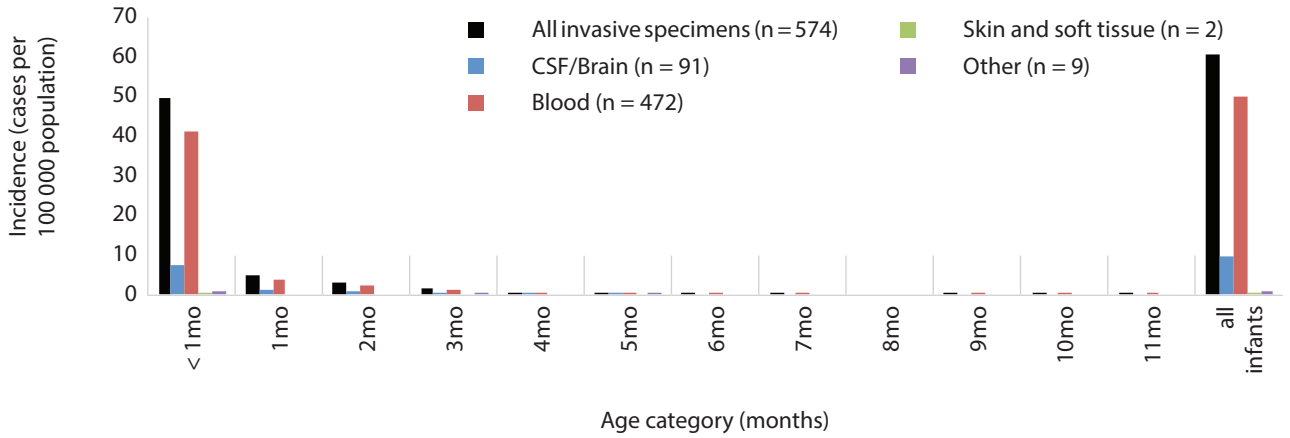


Figure 22b: Age-specific incidence rates* for laboratory-confirmed, invasive Group B Streptococcal disease in persons >1 year of age, reported to GERMS-SA, South Africa, 2019, n=1 034 (n=426 in persons >1 year, age unknown for n=34)

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

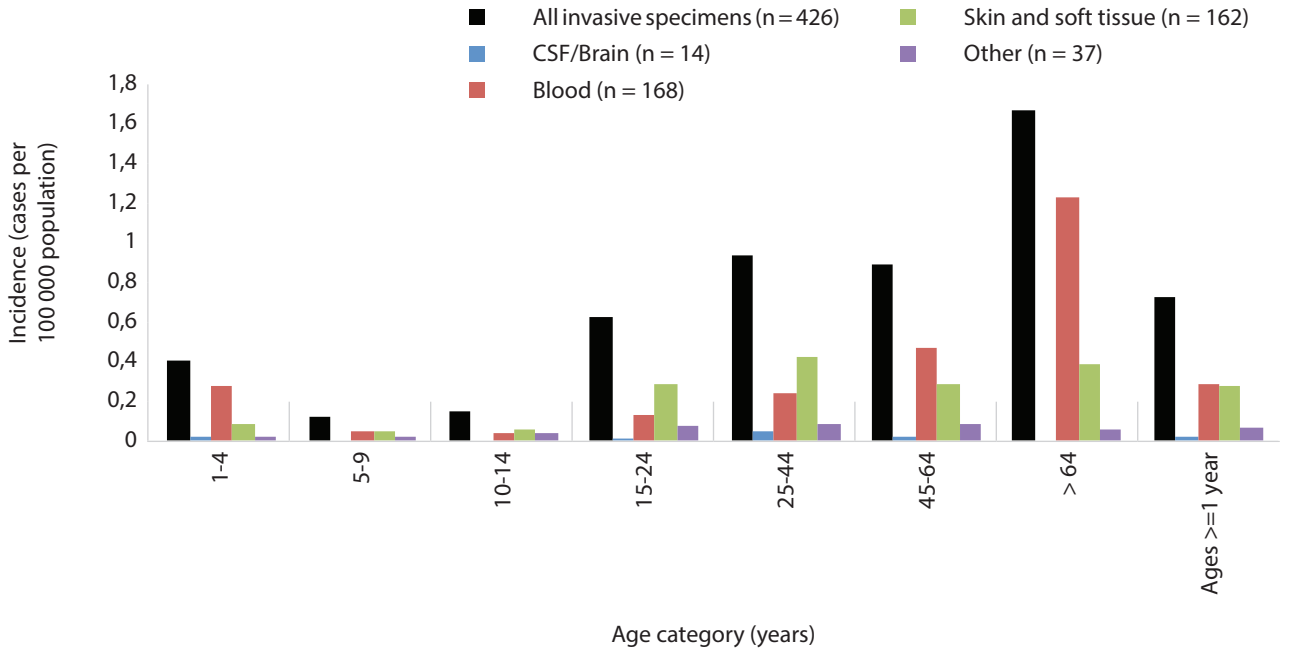


Table 22. Number and percentage of cases of invasive Group B Streptococcal disease reported to GERMS-SA by specimen type and age category*, South Africa, 2019, n=1 034

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

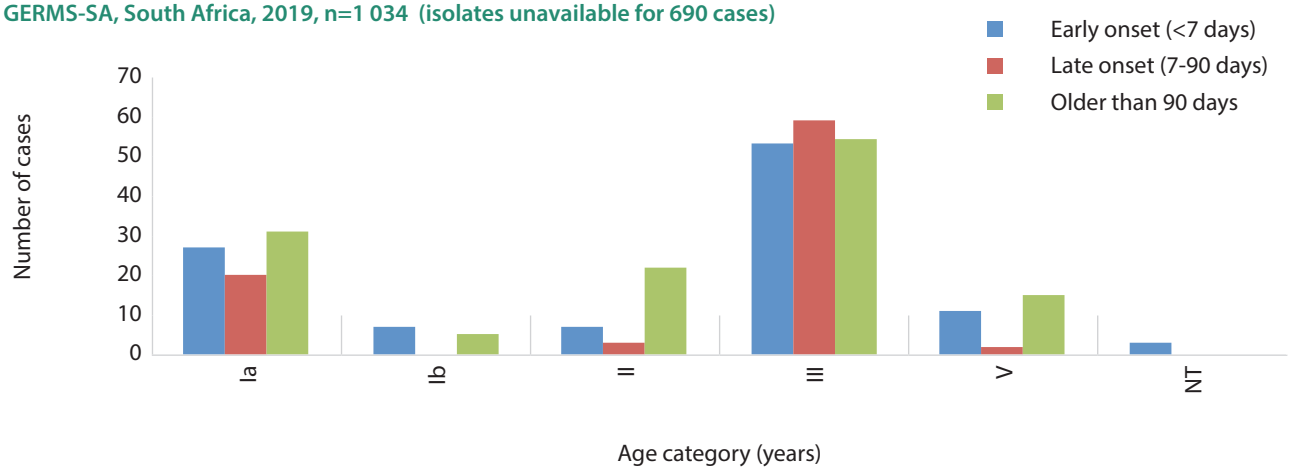
*Age unknown for n=34. **Other includes invasive specimens from bone, respiratory and gastrointestinal tracts.

Table 23. Serotype distribution of invasive Group B Streptococcal disease reported to GERMS-SA by province, South Africa, 2019, n=1 034 (all ages)

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

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

Figure 23. Numbers of cases of laboratory-confirmed, invasive Group B Streptococcal disease by serotype, reported to GERMS-SA, South Africa, 2019, n=1 034 (isolates unavailable for 690 cases)



Discussion

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

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 24. 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 24). Sixty-seven percent of cases were reported from two provinces: Gauteng (47/117, 40%) and Western Cape (32/117, 27%). The number of isolates within each age group is reported in Table 25, indicating that most isolates are from patients in the 5 to 14 year age group (36/117, 31%), followed by the 25 to 34 year age group (22/117, 19%) and the 0 to 4 year age group (21/117, 18%). Twenty percent of isolates tested were resistant to ciprofloxacin, but all isolates tested were susceptible to azithromycin (Table 26), following CLSI guidelines. Two isolates of *Salmonella* Paratyphi A and four 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 or Paratyphi B isolates.

Table 24. Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2019, n=117 (including audit reports, missing isolates, mixed and contaminated cultures).*

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	2	2
Free State	1	1
Gauteng	8	39
KwaZulu-Natal	3	14
Limpopo	2	3
Mpumalanga	1	7
Northern Cape	0	1
North West	1	1
Western Cape	5	27
Total	22	95

*Excluding *Salmonella* Paratyphi

Figure 24. Number of non-invasive and invasive cases of *Salmonella* Typhi (n=117) and Paratyphi (n=6) reported to GERMS-SA, by month of specimen collection, South Africa, 2019 (including audit reports

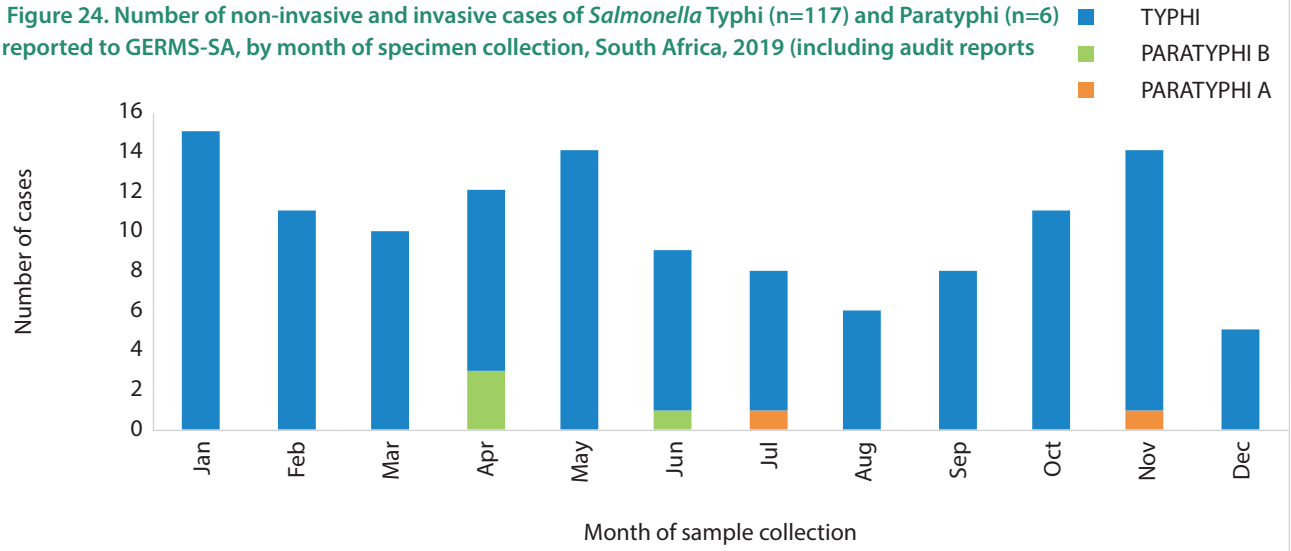


Table 25. Number of *Salmonella* Typhi cases reported to GERMS-SA by age category, South Africa, 2019, n=117 (including audit reports, missing isolates, mixed and contaminated cultures).*

Age category (years)	*Salmonella* Typhi cases
0 - 4	21
5 - 14	36
15 - 24	15
25 - 34	22
35 - 44	10
45 - 54	7
55 - 64	4
≥ 65	2
Total	117

*Excluding *Salmonella* Paratyphi

Table 26. Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2019, ciprofloxacin, n=95 and azithromycin, n=104 (excluding audit reports, missing isolates, mixed and contaminated cultures).*

Antimicrobial agent	Susceptible (%)	Resistant (%)
Ciprofloxacin (n=95)	76 (80%)	19 (20%)
Azithromycin (n=104)	104 (100%)	0

*Excluding *Salmonella* Paratyphi

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 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. The age distribution of cases is also consistent with that reported in previous years.

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. Although the proportion of isolates showing resistance to ciprofloxacin (20%) is similar to the previous year, this is of major concern. *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 5% (6/117) of total enteric fever cases.

Non-typhoidal *Salmonella* enterica (NTS)

Results

Invasive disease does not appear to have a seasonal prevalence. However, for non-invasive disease, increased numbers in the earlier months of the year and a lower incidence in the winter months reflects seasonality (Figure 25). This pattern is similar to that of previous years. The number of cases of invasive and non-invasive disease by province is shown in Table 27. Three provinces reported the highest numbers of cases of invasive disease: Gauteng (313/825, 38%), Western Cape (129/825, 16%) and KwaZulu-Natal (127/825, 15%). The same three provinces also reported the highest numbers of cases of non-invasive disease: Gauteng (968/2 437, 40%), KwaZulu-Natal (446/2 437, 18%), and Western Cape (374/2437, 15%).The number of cases of invasive and non-invasive disease, by age group, is shown in Table 28. Non-invasive disease was highest in children under five years of age (710/2 437, 29%); invasive disease was likewise most common in children under five years of age (209/825, 25%). Most invasive isolates were identified from blood cultures (92%, 763/825), although isolates were frequently identified from both blood culture and another site, including stool and other normally-sterile sites (Table 29). All isolates referred to the Centre for Enteric disease were serotyped; this included isolates submitted as part of routine laboratory-based surveillance as well as isolates submitted for outbreak investigation purposes. Although over 100 serotypes were identified, two serotypes accounted for 66% of the cases: *S. Enteritidis* (938/2 062, 45%) and *S. Typhimurium* (431/2 062, 21%). The next most common serotypes were *S. Isangi, S. Infantis, S. Heidelberg*, and *S. Newport* (Table 30). Proportions of the serotypes differed among provinces (Figure 26). *S. Enteritidis* was the most common serotype in all provinces except for Eastern Cape Province, where *S. Typhimurium* was predominant. Antimicrobial susceptibility testing was not routinely performed, but offered on request.

Figure 25. Number of non-invasive (n=2 437) and invasive (n= 825) cases of non-typhoidal *Salmonella* reported to GERMS-SA, by month of specimen collection, South Africa, 2019 (including audit reports).

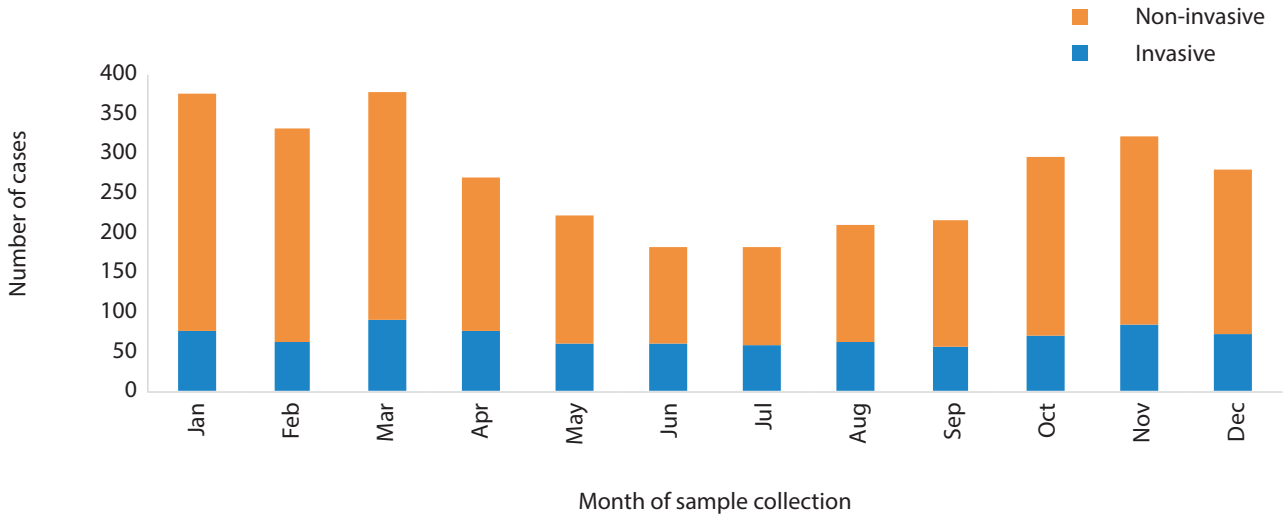


Table 27. Number of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2019, n= 3 262 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive, non-typhoidal *Salmonella* cases	Invasive non-typhoidal *Salmonella* cases
Eastern Cape	196	91
Free State	134	33
Gauteng	968	313
KwaZulu-Natal	446	127
Limpopo	67	31
Mpumalanga	112	25
Northern Cape	29	32
North West	111	44
Western Cape	374	129
Total	**2437**	**825**

Table 28. Number of cases of invasive and non-invasive non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2019, n=3 262 (including audit reports, missing isolates, mixed and contaminated cultures).

Age category (years)	Non-typhoidal *Salmonella* cases	
	Non-Invasive	Invasive
0 - 4	710	209
5 - 14	269	30
15 - 24	164	38
25 - 34	264	136
35 - 44	323	165
45 - 54	229	106
55 - 64	204	72
≥ 65	274	69
Total	**2437**	**825**

Table 29. Number of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2019, n=3 262 (including audit reports, missing, mixed and contaminated cultures).

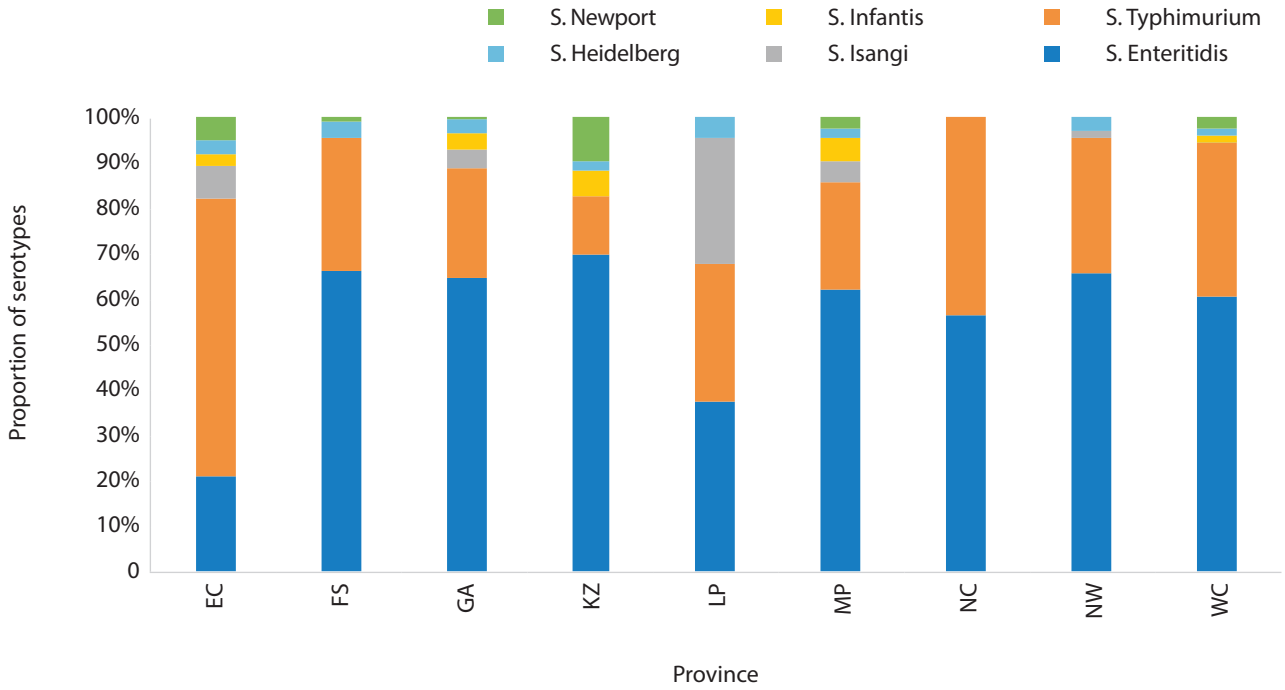
Specimen	n	%
CSF	15	1
Blood culture	763	23
Stool	2087	64
Other	397	12
Total	**3262**	**100**

*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.

Table 30. Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes by province, South Africa, 2019, n= 2062 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. Enteritidis*	*S. Typhimurium*	*S. Isangi*	*S. Infantis*	*S. Heidelberg*	*S. Newport*
Eastern Cape	25	74	9	3	4	6
Free State	56	25	0	0	3	1
Gauteng	418	158	24	24	22	2
KwaZulu-Natal	185	35	0	14	6	26
Limpopo	16	13	12	0	2	0
Mpumalanga	26	10	2	2	1	1
Northern Cape	13	10	0	0	0	0
North West	42	19	1	0	2	0
Western Cape	157	87	1	4	3	7
Total	**938**	**431**	**49**	**47**	**43**	**43**

Figure 26. Proportions of the most common non-typhoidal *Salmonella* serotypes by province, South Africa, 2019.



Discussion

Non-typhoidal salmonellosis is usually foodborne, in which case patients typically present with gastroenteritis. Invasive disease is usually associated with HIV-infection or the presence of other risk factors. As in previous years, seasonal prevalence was noted for non-invasive disease but not for invasive disease. Greater numbers reported from Gauteng and Western Cape provinces may reflect healthcare seeking behaviour and prevailing clinician testing behaviour. Children under 5 years of age bear the highest burdens of both non-invasive and invasive salmonellosis. *S. Enteritidis* was the predominant serotype, followed by *S. Typhimurium*, a pattern observed since 2012. Provincial differences in serotype proportions might reflect local transmission dynamics or undetected outbreaks, and require further investigation.

Shigella species

Results

The highest number of shigellosis cases for 2019 occurred in January through March (Figure 27). This is in keeping with the seasonal pattern noted in previous years. The primary manifestation of disease due to *Shigella* is non-invasive dysentery or diarrhoea, although invasive disease cases continue to occur (Table 31). Sixty-five percent of cases were reported from two provinces: Gauteng (438/1 197, 37%) and Western Cape (334/1 197, 28%). The predominant burden of non-invasive disease is in the under-five-years age group (447/1 164, 38%) followed by the 5 to 14 years age group (214/1 164, 18%) – Table 32. The proportion of invasive shigellosis cases was slightly lower than previous years (n=33), and the number of cases was highest among three age groups: under five years (7/33, 21%), 25 to 34 years (7/33, 21%) and 35 to 44 years (8/33, 24%). All isolates referred to the Centre for Enteric disease were serotyped; this included isolates submitted as part of routine laboratory-based surveillance as well as isolates submitted for outbreak investigation purposes. Two serotypes accounted for 61% of the cases: *S. sonnei* (269/866, 31%) and *S. flexneri* type 2a (258/866, 30%). The next most common serotypes were S. flexneri type 1b, *S. flexneri* type 3a and S. flexneri type 6 (Table 33). Proportions of the serotypes differed among provinces (Figure 28). The predominant serotype differed among provinces; *S. sonnei* and *S. flexneri* type 2a predominated in four provinces each, and *S. flexneri* type 1b predominated in one province. Antimicrobial susceptibility testing was not routinely performed, but offered on request.

Figure 27. Number of non-invasive and invasive *Shigella* cases reported to GERMS-SA, by month of specimen collection, South Africa, 2019, n = 1 197 (including audit reports).

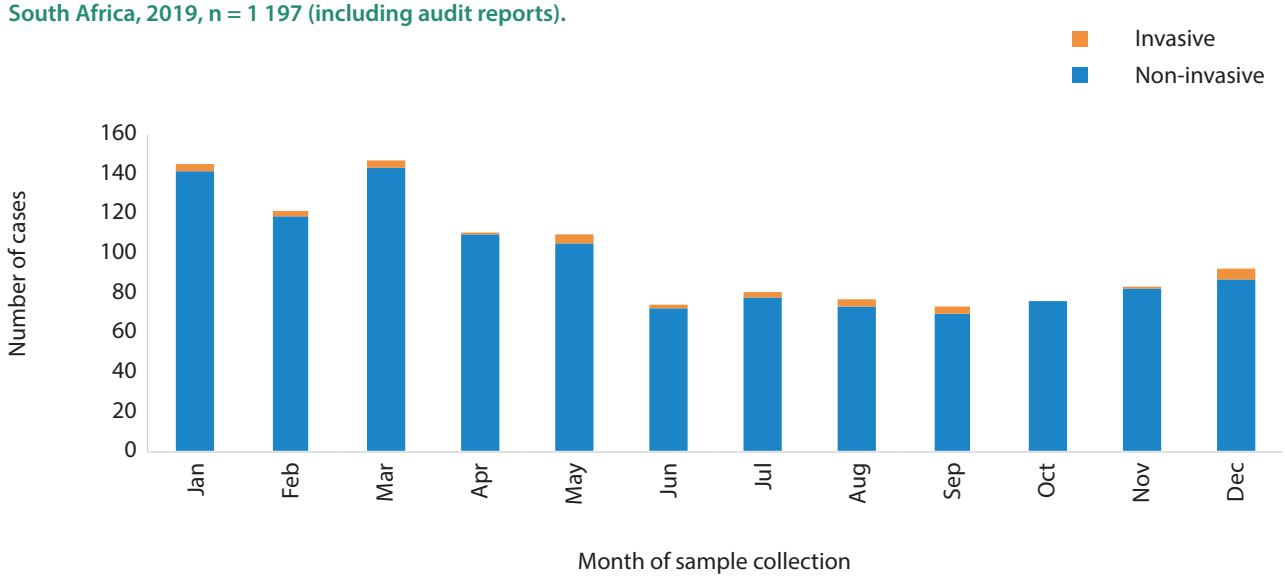


Table 31. Number of invasive and non-invasive *Shigella* cases reported to GERMS-SA by province, South Africa, 2019, n=1 197 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	159	1
Free State	51	2
Gauteng	427	11
KwaZulu-Natal	103	3
Limpopo	26	2
Mpumalanga	33	2
Northern Cape	12	0
North West	30	1
Western Cape	323	11
Total	**1164**	**33**

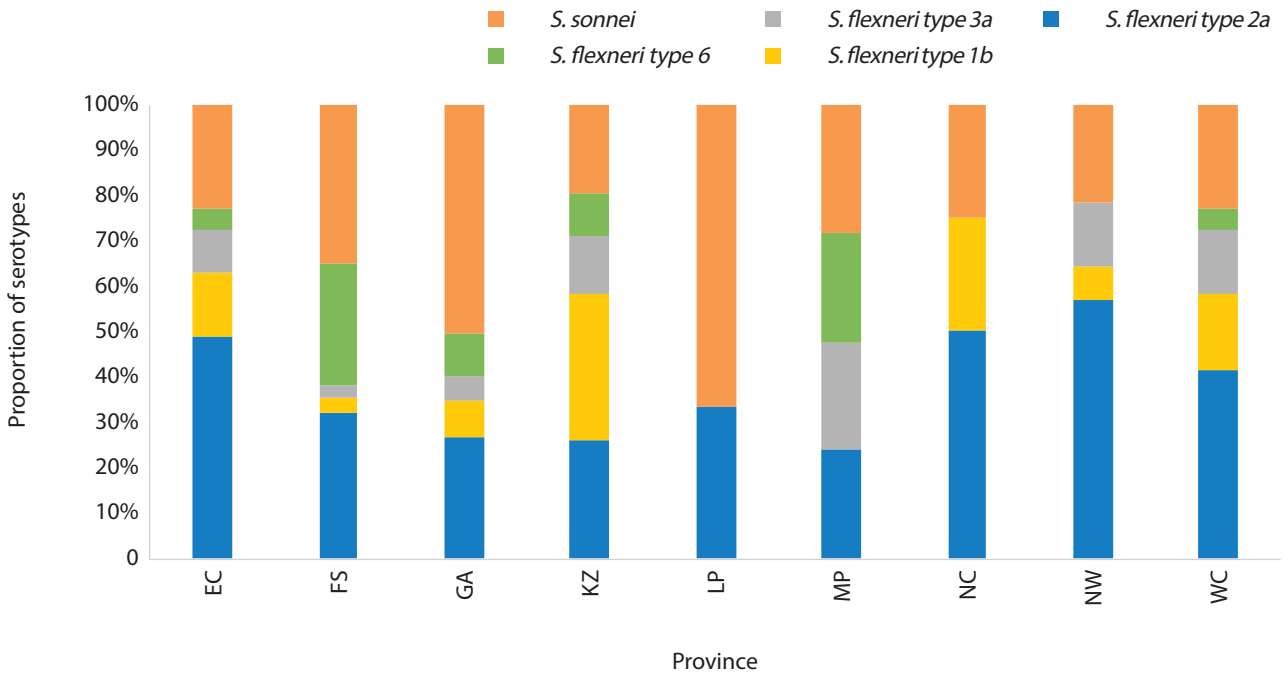
Table 32. Number of invasive and non-invasive *Shigella* cases reported to GERMS-SA by age category, South Africa, 2019, n=1 197 (including audit reports, missing isolates, mixed and contaminated cultures).

Age Category (years)	Shigellosis Cases	
	Non-invasive	Invasive
0 - 4	447	7
5 - 14	214	1
15 - 24	70	1
25 - 34	105	7
35 - 44	95	8
45 - 54	73	4
55 - 64	66	2
≥ 65	94	3
Total	**1164**	**33**

Table 33. Commonest invasive and non-invasive *Shigella* serotypes by province, South Africa, 2019, n=866 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. flexneri*	*S. flexneri*	*S. flexneri*	*S. flexneri*	*S. sonnei*
	type 2a	type 1b	type 3a	type 6	
Eastern Cape	55	16	11	5	26
Free State	11	1	1	9	12
Gauteng	91	26	20	31	171
KwaZulu-Natal	8	10	4	3	6
Limpopo	1	0	0	0	2
Mpumalanga	5	0	5	5	6
Northern Cape	2	1	0	0	1
North West	8	1	2	0	3
Western Cape	77	31	27	9	42
Total	**258**	**86**	**70**	**62**	**269**

Figure 28. Proportions of the most common *Shigella* serotypes by province, South Africa, 2019.



Discussion

Although *Shigella* infection has been associated with waterborne outbreaks in South Africa, person-to-person transmission also plays an important role. Children under five years of age bear the highest burden of shigellosis. Invasive disease appears to be decreasing. *S. sonnei* and *S. flexneri* type 2a were the predominant serotypes, in keeping with previous years. Provincial differences in serotype proportions might reflect local transmission dynamics or undetected outbreaks, and require further investigation.

Rifampicin-susceptible Tuberculosis

Results

In 2019, 507 participants were recruited and had sputum samples submitted. Valid drug susceptibility results for INH were available for 341 isolates, for which 335 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 (54%). Sixty eight percent of the patients were HIV positive. Sixty-five percent were already on ART. Twenty percent reported to have at least one episode of previous TB infection, and five per-cent reported having two or more episodes of previous TB. Sixteen percent reported to have lived with a per-son diagnosed with TB in the last 12 months. Majority of the contacts (83%) were screened for TB, of which 60% tested positive for TB. Less than half (46%) completed treatment. Table 34 shows the comparison of risk factors by INH resistance. Forty sputum samples were rejected either due to having leaked at the time of receiving at the lab or due to insufficient volume. Cultures were negative in 20% (103/507) and 4% (23/507) were contaminated, precluding further analysis. Majority of samples received were from Gauteng (38%), followed by North West (21%), Eastern Cape (20%), Kwa-Zulu Natal (14%) and Mpumalanga (7%). Thirty-two of these were isoniazid mono resistant (IMR), 81% were smear positive. North West had the highest prevalence (14.1%), fol-lowed by Eastern Cape (10.7%), Kwa-Zulu Natal (8.9 %), Mpumalanga (8.3%) and Gauteng (7.0%). The overall IMR prevalence was 9.4% [95% CI: 6.1 - 13.0%]. Only five participants reported to taking TB preventative therapy, none of these participants had INH Resistance.

Table 34. Comparison of risk factors by INH resistance

	INH Sensitive	INH mono R	Full Cohort (n)	p Value*
All lab results	309 (91)	32(9)	341	
Patients with CRFs	303 (90)	32 (10)	335	
Gender				
Male	168 (54)	14 (44)	182 (53)	0,505
Female	137 (44)	18 (56)	155 (45)	
Unknown	4 (1)	0 (0)	4 (2)	
Age Category (n=338)				
<20 years	6 (2)	3 (10)	9 (3)	0,03
20-34 years	124 (40)	7 (23)	131 (39)	
35-49 years	111 (36)	15 (48)	126 (37)	
50+ years	66 (22)	6 (19)	72 (21)	
Province (n=333)				
Eastern Cape	58 (19)	7 (22)	65 (20)	0,589
Gauteng	119 (40)	9 (28)	128 (38)	
KwaZulu-Natal	41 (14)	4 (13)	45 (14)	
Mpumalanga	22 (7)	2 (6)	24 (7)	
North West	61 (20)	10 (31)	71 (21)	
Education (completed) (n=337)				0,785
None	22 (7)	1 (3)	23 (7)	
Primary	140 (46)	16 (50)	156 (46)	
Secondary	130 (43)	13 (41)	143 (42)	
Tertiary	13 (4)	2 (6)	15 (5)	
Employment (n=337)				0,206
Full-time	41 (13)	3 (9)	44 (13)	
Part-time	23 (8)	1 (3)	23 (7)	
Self-employed	4 (1)	2 (6)	6 (2)	
Unemployed	237 (78)	26 (81)	263 (78)	

	INH Sensitive	INH mono R	Full Cohort (n)	p Value*
Healthcare worker (n=337)				0,171
No	299 (98)	30 (94)	329 (98)	
Yes	6 (2)	2 (6)	8 (2)	
Miner (ever) (n=336)				0,236
No	285 (94)	32 (100)	317 (94)	
Yes	19 (6)	0 (0)	19 (6)	
Prisoner (ever) (n=337)				0,544
No	269 (88)	28 (87)	297 (88)	
Yes	36 (12)	4 (13)	40 (12)	
Alcohol frequency (n=337)				
Never/<1 month	49 (16)	3 (9)	52 (15)	0,643
1-4 times per month	24 (8)	3 (9)	27 (8)	
>1 per week	232 (76)	23 (82)	258 (77)	
Smoking (n=337)				
Former smoker	51 (17)	8 (25)	59 (18)	0,109
Never	153 (50)	19 (59)	172 (51)	
Smoker	101 (33)	5 (16)	106 (31)	
Recreational Drug Use (n=336)				0,098
No	267 (89)	31 (97)	298 (89)	
Yes	37 (12)	1 (3)	38 (11)	
HIV status (n=337)				0,678
Negative	83(27)	10 (31)	93 (28)	
Positive	210 (69)	22 (67)	232 (68)	
Unknown	12 (4)	0 (0)	12 (4)	
Previous TB episodes				0,768
None	233 (75)	24 (75)	257 (75)	
1	63 (21)	6 (19)	63 (20)	
>=2	13 (4)	2 (6)	15 (5)	
Previous IPT (n=231)				0,603
No	204 (98)	22 (100)	226 (98)	
Yes	5 (2)	0	5 (2)	
Lived with someone with TB (n=337)				0,101
No	251 (82)	29 (91)	280 (83)	
Yes	52 (17)	2 (6)	54 (16)	
Unknown	2 (1)	1 (3)	3 (1)	

Discussion

The majority of participants with TB were co-infected with HIV highlighting its continued importance in controlling the TB epidemic. Anti-retroviral treatment has been previously shown to reduce TB incidence, and it encouraging seeing that most patients were already part of the ARV program. Number of participants on TB preventative therapy (TPT) was extremely low, only five of the 232 HIV positive participants reported being on TPT. Age and gender distribution of the participants was in keeping with the National reports, showing male dominance. The overall prevalence of IMR (9.4%) is higher than what was found in the National TB drug resistant survey 2012-2014 (5-8%), and higher than that observed last year (5%). The North West province continues to be the province with the highest IMR rate and continuous monitoring is important. 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. No significant risk factor for INH resistance was detected. A large proportion of patients exposed to TB were screened, however, completion of those testing positive for TB is poor. This indicates a gap in care cascade that 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 (78%), 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.

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Syndromic surveillance

Diarrhoeal surveillance

Introduction

In South Africa, the <5 year mortality per 1 000 live births has decreased from 79 in 2004 to 40 in 2012; a remarkable achievement. In children <5 years, diarrhoea and pneumonia are usually the major drivers of mortality in this age group although the diarrhoeal mortality rate has decreased since 2008. However, diarrhoea was still responsible for an estimated 10.2 – 5.9% of deaths in children <5 years in 2015 and regional pockets of mortality exist; the proportion of deaths attributed to diarrhoea in Mpumalanga was 24% in 2012 (1).

Large scale diarrhoeal disease studies showed that rotavirus was the most important cause of diarrhoea in children <2 years (2, 3, 4). In order to combat rotavirus disease in South Africa, a vaccine was introduced into the immunization program in August 2009. Impact studies have shown a decrease in both rotavirus-specific (54-58% reduction in children < 5 years (5) and all-cause diarrhoea (45-65% reduction in children <12 months and 40-50% reduction in children 13-24 months (6) in South Africa. The rotavirus vaccine is estimated to have contributed to a 30% decline in overall diarrhoeal mortality (7).

Despite successful introduction of the 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 (8). 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 (8). In addition, diarrhoeal mortality decreased from 3.5% to 2.9% during the same periods at this site (8).

As diarrhoeal diseases still contribute to <5 mortality and there are gaps in our knowledge around the burden in individuals >5 years and vulnerable groups including children with severe acute malnutrition, men who have sex with men, the elderly and immunocompromised people, research on diarrhoeal diseases needs to continue. Furthermore, continuous monitoring of rotavirus in children <5 years is required to ensure that the vaccine formulation and the immunisation program are functioning optimally and to identify any rotavirus strains that may escape vaccine protection.

Methods

In 2019, diarrhoeal disease surveillance was conducted at three sentinel sites, including: Chris Hani Baragwanath Academic Hospital (CHBAH, Gauteng Province), Dr George Mukhari Hospital (DGM, Gauteng/North West Province border) and Pelonomi Hospital (PNH, Free State 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 and PNH 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.

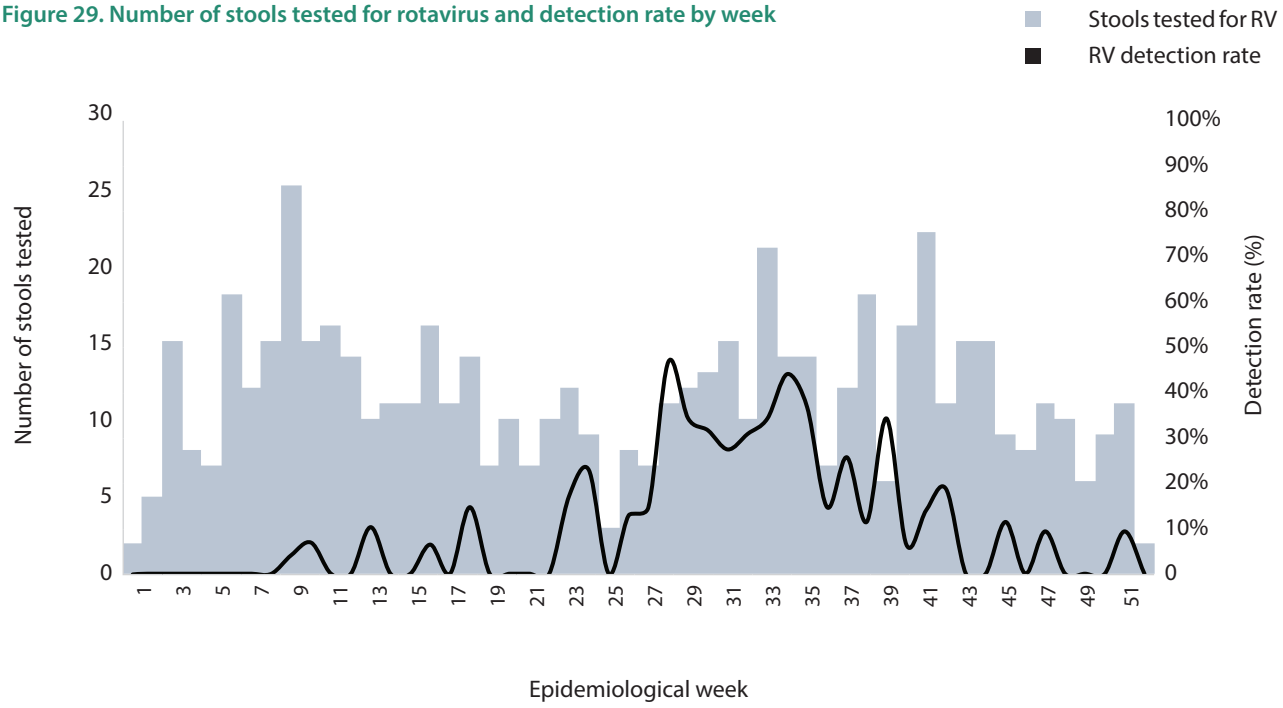
Data from a companion surveillance program (African Network for improved Diagnostics, Epidemiology and Management of Common Infectious Agents (ANDEMIA); investigating diarrhoeal diseases in all ages) was included in the analysis due to the limited cases enrolled at GERMS-SA sites.

Results

A total of 153 stool specimens were screened in 2019 with 11% (17/153) positive for rotavirus. An additional 417 specimens from ANDEMIA sites were screened in 2019 with a similar rotavirus prevalence of 12% (49/417). Rotavirus detection peaked in July with a maximum detection rate of 45% (5/11; Figure 29). A total of 60 rotavirus-positive strains were genotyped, with G3P[8] (65%; 39/60) predominant and other strains (G1P[8], G12P[6],

G2P[4], G8P[4], G8P[8], G8P[6]) detected at lower levels.
A total of 577 specimens were also screened for other enteric viruses and the following were detected: norovirus genogroup I and II in 13% (76/577); adenovirus in 22% (125/577); sapovirus in 3% (19/577) and astrovirus in 7% (38/577).

Figure 29. Number of stools tested for rotavirus and detection rate by week



Discussion

The rotavirus detection rate for 2019 (12%) was similar to 2018 (11%) and lower than the 19% noted in 2017. The G3P[8] strains that were frequently detected in 2019 have been circulating in South Africa since 2015 and were also the predominant strains in 2018 and 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 in certain sites makes it problematic to draw any conclusions regarding the prevalence of the other enteric viruses detected. However, norovirus GII detection declined in 2019 to 11% from 19% in 2018. The detection of sapovirus also decreased compared to the previous year (3% in 2019 compared to 6% in 2018) and was similar to the detection levels observed in 2017 (3%). The prevalence of adenovirus (22%) was higher than 2018 (12%) levels. Different diagnostic assays were used for detection of adenovirus which may have had an impact on the prevalence figures and require further investigation. Astrovirus prevalence was also higher in 2019 (7% in 2019 compared to 3% in 2018).

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SUMMARY

Discussion

GERMS-SA; a valuable laboratory-based surveillance programme, continues to report pathogen-specific trends. For enhanced sentinel surveillance, our surveillance officers completed 72% of case report forms by interview, reaching the target of 70%. Training and auditing of our surveillance officers data quality is continually done to improve that aspect. Even though the isolate submission and viability have increased, we still urge the labora-tories to continue sending isolates.

Opportunistic infections: Between 2018 and 2019, the laboratory-confirmed cryptococcosis incidence risk re-mained stable in all provinces. The peak incidence for men and women was in the age group of 35-39 years; however men recorded the highest incidence risk. Where we had HIV information, (n=1 461), 97% were HIV sero-positive. Of 1 422 patient infected with HIV, 969/1 360 (71%) had previously received antiretroviral treatment or 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 (34%). Rifampicin-susceptible TB surveillance looks at risk factors for TB as well as INH mono-resistance. From 5 provinces (n=507) data showed majority of participants were male (54%), almost 70% of the patients were HIV positive, 65% already on ART and only five of the 232 HIV positive participants on TB preventative therapy (TPT). Completion of those testing positive for TB was poor. Smoking continues to be a high risk factor for TB. INH mono-resistance is <10%.

Vaccine-preventable diseases: The 2019 data continue to monitor trends in IPD, Hib post-EPI vaccine introduction of PCV13 and Hib booster (2009). 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 infants. Hib-disease in children may be vaccine failures. For those that had clinical information from ESS, 27% (36/110) died in hospital and the median time to death was within one day of admission. Fifty four percent (53/98) of patients had some predisposing condition other than HIV. ***Please remember that Hib is a notifiable medical condition.*** IPD incidence remains stable across all age categories, peaks in infants and again after age 25 years. HIV-infection, infant HIV-exposure and history of smoking remain important risk factors for IPD and the overall case-fatality was 33%. Penicillin and ceftriaxone non-susceptibility remains unchanged. Clinicians should remember to check the vaccine status of children and remember to give catch-up doses.

In 2019, active surveillance for invasive GBS was introduced and no clinical data collected. Incidence of early and late onset invasive GBS disease appears low with Gauteng reporting highest incidence (0.65 and 0.47 per 1 000 live births) followed by Western Cape (0.46 and 0.36 per 1 000 live births). Disease occurred more frequently in females and most isolates in infants were from blood (472/574, 82%) or cerebrospinal fluid (91/574, 16%) with serotypes III and Ia being most predominant. Ninety percent of invasive GBS isolates were susceptible to penicillin and 95% susceptible to gentamycin.

Epidemic-prone diseases: (Notifiable medical conditions): The incidence of meningococcal disease in 2019 remained low with no outbreaks detected; WC having the highest rate and serogroup B being the predominant serogroup (36/94; 38%). High-dose penicillin is still being recommended as the drug of choice for therapy for confirmed meningococcal disease, although penicillin non-susceptibility was 26%; all were susceptible to 3rd generation cephalosporin and ciprofloxacin. Of 38 patients from our ESS, 31 had outcome information. The case fatality rate was 19% (6/31).

We received 34% (363/1 060) of isolates from the active invasive GAS surveillance since initiation in 2019. Incidence was highest in infants followed by those aged >64 years occurring mostly in males. Forty-six percent of cases were identified on blood culture, followed by 41% from skin and soft tissue specimens with the majority being highly susceptible to first line antimicrobial agents, penicillin and erythromycin.

The diagnosis of typhoid fever remains challenging and although the data may not reflect actual burden of dis-ease, numbers were comparable with 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 accounting for 5% of total enteric fever cases. Non-typhoidal salmonellosis may be foodborne or may be associ-ated with HIV-infections and seasonal prevalence was not noted for invasive disease. The proportion of invasive shigellosis cases was slightly lower than previous years; even though *Shigella* infections are associated with water-borne outbreaks in South Africa, person-to-person transmission also plays an important role.

Healthcare-associated infections: CRE numbers increased in 2018 and 2019 with the proportion of male cases greater than females. Highest proportion of sentinel site cases were from Gauteng Province (64%) followed by KwaZulu-Natal (20%). A shift to CPE mediated by OXA-48 & variants was noted. *Acinetobacter baumannii* num-bers show an increase in 2019, particularly in KwaZulu-Natal province. Highest AB bacteraemia was noticed in infants less than one year of age. The susceptibility to different antibiotics classes is extremely low.

Diarrhoeal surveillance: In 2019, rotavirus detection rate was 12% similar to 2018 and still much lower than pre-vaccine era; peaked in July with maximum rate of 45%. The G3P[8] strains which have been circulating in South Africa since 2015 and predominant in 2018 and 2016,were frequently detected in 2019. 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 decline in norovirus GII detection was noted in 2019 compared to 2018 (from 19% in 2018 to 11% in 2019). Sapovirus detection also decreased compared to 2018 (3% in 2019 compared to 6% in 2018). The prevalence of adenovirus (22%) was higher than 2018 and astrovirus prevalence also increased (3% in 2018 compared to 7% in 2019).

PUBLICATIONS

Peer-reviewed GERMS-SA and GERMS-SA-related publications 2019

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