NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

2021

GERMS-SA: ANNUAL SURVEILLANCE REVIEW


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2021

GERMS-SA: ANNUAL SURVEILLANCE REVIEW

THE GERMS-SA ANNUAL REVIEW 2021 WAS COMPILED BY THE **NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES**, A DIVISION OF THE NATIONAL HEALTH LABORATORY SERVICE, JOHANNESBURG, SOUTH AFRICA.

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Cover photograph: Klerksdorp/ Tshepong, North West Province Surveillance team.

The National Institute for Communicable Diseases (NICD) reference units report the GERMS-SA surveillance 2021 findings which continue to be valuable in reporting trends in pathogen specific data. The far-reaching impact of COVID - 19 continued to put extraordinary pressure on both healthcare systems and our routine GERMS-SA surveillance. Having experienced four waves by 2021 resources had to be shifted towards COVID-19-related activities. With easing of lockdown regulations, introduction of COVID-19 vaccination program and decline in COVID-19 cases, diagnosis rates of other infectious diseases increased, also the number of isolates received by NICD reference laboratories showed an increase as well as better quality isolate viability. Pressure in many clinical laboratories remained and impacted the rates of audit cases which are still out of target range. Therefore, we were unable to do antimicrobial susceptibility testing and serotyping/serogrouping on these missing isolates. The fire at CMJAH, deferment of patients to other hospitals and the NHLS laboratory being closed for a few months also impacted our statistics.

We urge all microbiology laboratories, in their challenged capacities, to continue to participate in laboratory surveillance so monitoring can continue and relevant, evidence-based policies can be made. The 2021 review also includes other NICD projects using the GERMS-SA platform; rotavirus/diarrhoeal aetiological surveillance. This project differs from the laboratory-based surveillance in that it is syndromic surveillance and specimens are taken from patients with diarrhoea.

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 2021, 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 Carbapenem resistant Enterobacteriaceae and *Enterococcus* species.

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

In brief, approximately 222 South African clinical microbiology laboratories participated in the surveillance programme in 2021. The estimated population under surveillance in 2021 was at 60,1 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) (26 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 to 31 July 2022, 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 Surveillance Data Warehouse (SDW), which stores information from Disa*Lab and TrakCare laboratory information systems. Cryptococcal isolates, obtained from patients at enhanced surveillance sites, continued to be characterised by phenotypic and genotypic tests through 2013. The Antimicrobial resistance (AMR) surveillance program used the GERMS-SA platform since 2011 to 31 December 2021 as Laboratory-based Antimicrobial Resistance Surveillance (LARS) for nosocomial bacteria 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*. Enterococci surveillance was initiated only for 2021, together with CRE there was no ESS but phenotypic and genotypic testing on obtained isolates.

Enhanced surveillance was not conducted on any of the enteric pathogens in 2015 but restarted for *Salmonella* Typhi only in 2016 as well as *Salmonella enterica* serotype Paratyphi A,

B and C and Nontyphoidal *Salmonella* spp. in 2019. At ESS, for 2021, surveillance officers completed clinical case report forms electronically using the REDCap database on tablets, for patients with any of eight laboratory-confirmed diseases: cryptococcosis, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, *Streptococcus agalactiae* and *Streptococcus pyogenes*, Nontyphoidal diseases (country-wide) and rifampicin-susceptible TB (in five provinces). Surveillance officers collect data 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 2020 and 2021 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2020 and 2021, 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 ongoing 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, 2020 and 2021

Province	General population*		HIV-infected population**	
	2020	2021	2020	2021
Eastern Cape	6 734 001	6 676 590	812 694	821 514
Free State	2 928 903	2 932 441	3 76 154	377 899
Gauteng	15 488 137	15 810 388	1 939 019	1 966 032
KwaZulu-Natal	11 531 628	11 513 575	2 027 027	2 040 577
Limpopo	5 852 553	5 926 724	473 701	479 493
Mpumalanga	4 679 786	4 743 584	724 469	736 414
Northern Cape	1 292 786	1 303 047	83 448	84 248
North West	4 108 816	4 122 854	493 037	497 375
Western Cape	7 005 741	7 113 776	469 776	478 860
South Africa	**59 622 350**	**60 142 978**	**7 399 323**	**7 482 413**

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

OPERATIONAL REPORT

Site visits

In 2021, NICD staff members continued with surveillance training at enhanced surveillance sites and laboratories. Other site visits were reduced due to COVID-19 travel restrictions.

Coordination of meetings

GERMS-SA Surveillance Officers'/ Research Assistants' online (Zoom) training 12, 19 and 26 July 2021: The aim was to refresh, update and train on current GERMS-SA surveillance projects, including sentinel diarrhoeal disease surveillance and sentinel syndromic respiratory surveillance projects. New projects were introduced and challenges with electronic data collection were addressed.

Online Surveillance Review meeting previously known as the GERMS-SA Principal Investigators' meeting, 23-24 June 2021: the aim was to feedback on surveillance programme's results and reassess surveillance impact.

Surveillance audit

A total of 11 633 surveillance cases were detected by GERMS-SA in 2021 (about two-thirds of the previous year's total). Excluding the cases of cryptococcosis (n=5 004) which are all detected by audit, 1 649/6 629 (25%) of cases were detected by audit of the NHLS Corporate Data Warehouse (Table 2) and isolates not sent to the NICD by the clinical microbiology laboratories. 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, 2021

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**	5 004/5 004 (100)	830	175	1056	1279	440	335	48	295	546	5 004
	Non-typhoidal salmonellosis†	146/ 1 010 (14)	15	6	64	23	4	9	0	11	14	146
	Shigellosis	16/60 (27)	2	4	1	6	0	1	1	1	0	16
	Meningococcal *disease*	1/32 (3)	0	0	0	0	0	0	0	0	1	1
	Haemophilus influenzae disease	108/279 (39)	9	6	41	20	5	4	2	4	17	108
	Pneumococcal disease	328/1 560 (21)	39	22	100	75	5	19	18	23	27	328
	Streptococcus pyogenes	292/658 (44)	46	16	80	58	4	3	2	9	74	292
	Streptococcus agalactiae	669/1 141 (59)	46	25	345	146	14	32	3	11	47	669
Non-invasive	Non-typhoidal salmonellosis†	46/1 435 (3)	7	2	5	7	3	1	1	4	16	46
	Shigellosis	43/454 (9)	7	5	1	18	1	0	0	0	11	43
Total (excl crypto and RSTB)		**1 649/6 629 (25%)**										

*Percentage of cases detected by audit = number of cases detected on audit (n_1)/total number of cases detected by GERMS-SA (n_2) 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; †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 remained the same as in 2020. As adherence to non-pharmaceutical interventions decreased and lockdown lowered, surveillance officers resumed face-to-face interviews with patients. A challenge of poor record systems in many hospitals was still an issue 2 417/ 3 386 (71%) of cases had a case report form (CRF) completed (target=90%) (Table 3). 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. The challenges in providing these reports continued in 2021, due to delays in processing samples and results not readily available. Our roving technologist, employed for the Gauteng enhanced surveillance sites, did help to improve sending of isolates.

Enhanced surveillance site quality monitoring

In 2021, as per annual performance management and improving quality of data collection, 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 CRFs for each organism could be audited 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.

Table 3. Enhanced surveillance site performance indicators, 2021

Enhanced surveillance site	Case patients, n	Completed case report forms*, n (%)**		Case report forms completed by interview, n (%)***	
Addington	44	26	59	15	58
Charlotte Maxeke Johannesburg Academic	113	96	85	40	42
Chris Hani Baragwanath/ Zola-Jabulani District	573	392	68	189	48
Dr George Mukhari	131	109	83	47	43
Edendale/ Greys'/ Northdale	203	175	86	144	82
Groote Schuur/ Red Cross	253	184	73	46	25
Helen Joseph/ Rahima Moosa Mother & Child	426	340	80	142	42
Kimberley	47	5	11	0	0
King Edward VIII/ Inkosi Albert Luthuli Central Hospital	138	64	46	43	67
Klerksdorp/ Tshepong	156	86	55	35	41
Mankweng/ Polokwane/ Seshego	157	108	69	29	27
Pelonomi/ Universitas	108	75	69	40	53
Port Elizabeth/ Dora Nginza/ Livingstone	453	359	79	97	27
RK Khan	125	78	62	41	53
Rob Ferreira/ Themba	125	97	78	38	39
Steve Biko Pretoria Academic/ Tshwane District	128	95	74	40	42
Tygerberg	206	128	62	0	0
Total	**3 386**	**2 417**	**71**	**986**	**41**

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 due to poor record systems in many hospitals and some patients refusing to participate in surveillance during the COVID-19 pandemic. Kimberley and Tygerberg 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%.

SURVEILLANCE REPORTS

Enhanced surveillance site project

In 2021, 3 386 surveillance case patients were diagnosed at enhanced surveillance sites (Table 3). Of case patients with recorded HIV status, 72% (2 100/2 906) 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 (98%) were HIV-infected. HIV infection amongst patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 58%.

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, 2021

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	1 146	879	77	790	90	775	98
Neisseria meningitidis	15	10	67	9	90	0	0
Streptococcus pneumoniae ^	598	495	83	431	87	251	58
Haemophilus influenzae ^	132	88	67	75	85	26	35
Streptococcus pyogenes	415	242	58	168	69	57	34
Streptococcus agalactiae	600	386	64	308	80	34	11
Total	**2 906**	**2 100**	**72**	**1 781**	**85**	**1 143**	**64**

*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.

^4 mixed *Streptococcus pneumoniae* and *Haemophilus influenzae* infections, these are counted separately for each organism

Cryptococcus species

Results

During 2021, 5 004 patients with a first episode of laboratory-confirmed cryptococcal disease were reported, excluding 1 295 with isolated cryptococcal antigenaemia (i.e. without meningitis or fungaemia or culture-positive disease elsewhere) (Table 5). A majority (n=4 822, 96%) of these cases were diagnosed with cryptococcal meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), 3% (n=166) with fungaemia (*Cryptococcus* species cultured from blood) and 1% (n=16) with culture-positive disease at other sites. Only nine cases were reported from the private sector; however, audits have not been completed. Between 2020 and 2021, the national incidence risk of laboratory-confirmed cryptococcosis decreased from 76 to 67 cases per 100 000 HIV-infected persons. Although the absolute provincial incidence risks remained similar in the Eastern Cape Province over the 2 years, a decrease in the absolute incidence risk with overlapping 95% confidence intervals was noted in the Free State, Mpumalanga, Northern Cape and Western Cape provinces; and a decrease in the absolute incidence risk with no overlapping 95% confidence intervals was noted in Gauteng, KwaZulu-Natal and North West provinces. In addition, an increase in the absolute incidence risk with overlapping 95% confidence intervals was noted in the Limpopo Province (Table 6). The highest incidence risk was recorded among males aged 40-44 years and the peak incidence among females, though lower than for males, was among those aged 35-39 years (Figure 1). Age was known for 4 626 (92%) case patients; the median age was 37 years (interquartile range [IQR], 31 – 44 years) and children younger than 15 years accounted for only 2% of cases (n=86). There were 1 146 case patients reported at ESS during 2021 and case report forms were completed for 77% (n=879). Among 790 patients with known HIV status, 98% (n=775) were confirmed to be HIV-seropositive. About 61% (448/732) of case patients had previously received antiretroviral therapy (ART) or were on ART at the time of cryptococcal disease diagnosis. Of the HIV-seropositive patients, 90% (701/775) had a CD4+ T-lymphocyte (CD4) cell count test result recorded close to the time of diagnosis; the median CD4 cell count was 31 cells/µl (IQR, 13 – 68 cells/µl) and 93% (651/701) had a CD4 cell count <200 cells/µl. Viral load test results were available for 539 patients; 19% (n=104) had a viral load of <400 copies/mL, 13% (n=69) had viral loads of 400-10 000 copies/mL, and 68% (n=366) had viral loads of >10 000 copies/mL. A majority of the case patients received antifungal therapy in hospital (88%, 739/843); 62% (461/739) received a flucytosine-containing induction regimen. The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease was 40% (344/850).

Table 5. Number and percentage of cases of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by specimen type, South Africa, 2020-2021, n=10 604

Site of specimen	2020		2021	
	n*	%	n*	%
Cerebrospinal fluid	5 295	94	4 822	96
Blood	288	5	166	3
Other	17	1	16	1
Total	**5 600**		**5 004**	

*These case numbers exclude 2 076 patients (871 in 2020 and 1 295 in 2021) who only tested positive for cryptococcal antigenaemia (without meningitis or fungaemia or culture-positive disease elsewhere) 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, 2020-2021 n=10 604

Province	2020		2021	
	n*	Incidence risk (95% CI)†	n*	Incidence risk (95% CI)†
Eastern Cape	827	102 (95-109)	830	101 (97-108)
Free State	225	60 (52-68)	175	46 (39-53)
Gauteng	1 233	64 (60-67)	1 056	54 (50-57)
KwaZulu-Natal	1 479	73 (69-77)	1 279	63 (59-66)
Limpopo	423	89 (81-98)	440	92 (83-100)
Mpumalanga	397	55 (49-60)	335	45 (41-50)
Northern Cape	65	78 (59-97)	48	57 (41-73)
North West	381	77 (70-85)	295	59 (53-66)
Western Cape	570	121 (111-131)	546	114 (104-124)
South Africa	**5 600**	**76 (74-78)**	**5 004**	**67 (65-69)**

*These case numbers exclude patients who only tested positive for cryptococcal antigenaemia (without meningitis or fungaemia or culture-positive disease elsewhere).
†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).

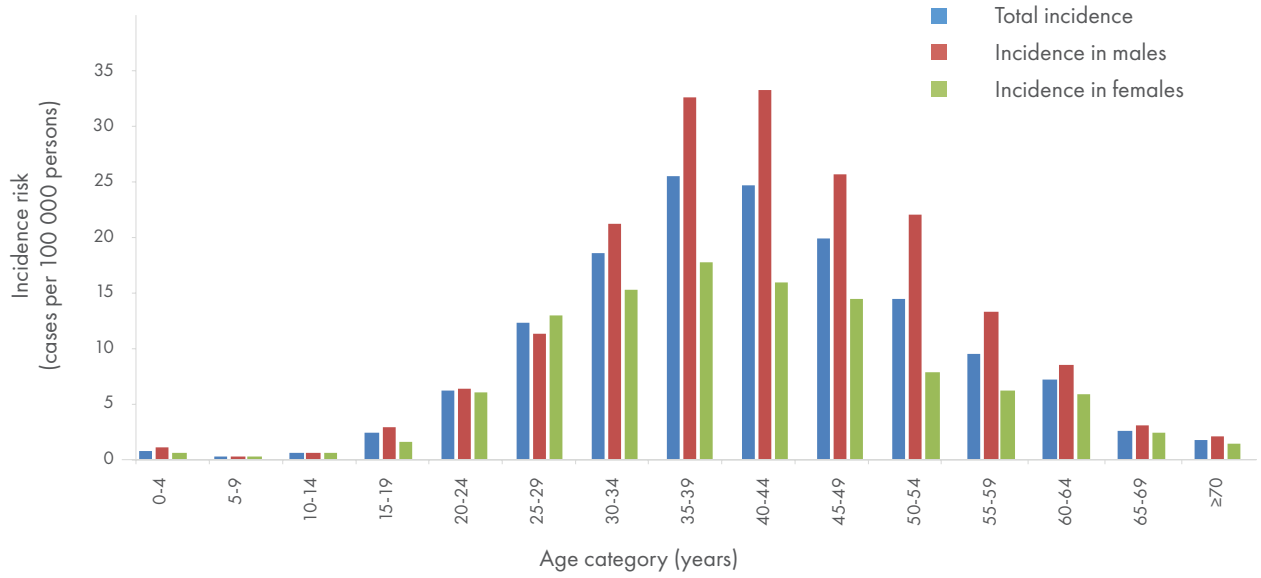


Figure 1. Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA, by sex and age group, South Africa, 2021, n= 5 360

Discussion

The national incidence risk of cryptococcal meningitis or culture-confirmed cryptococcal disease decreased overall in 2021 compared to 2020. This decrease may be related to more HIV-seropositive people initiating ART before they are at risk for opportunistic infections. However, an alternative explanation is that this decline is related to barriers to accessing the healthcare system with more COVID-19-related restriction days in 2021 compared to 2020 (https://www.gov.za/covid-19/about/about-alert-system#:~:text=Adjusted%20alert%20level%201%20is,June%20to%2025%20July%202021). An interrupted time-series analysis is being conducted by the NICD to explore this in more depth. The World Health Organization recommends cryptococcal antigen (CrAg) screening and pre-emptive fluconazole treatment for all patients with a CD4 cell count of <200 cells/µl. We only reported a small proportion of patients who were diagnosed with cryptococcal antigenaemia, mainly through provider-initiated screening, in this report. A majority of such cases are detected through the large national reflex CrAg programme [data not shown]. Timely pre-emptive fluconazole treatment given to those with antigenaemia with prevention of meningitis may be another reason for a decline in the absolute incidence risk of meningitis and culture-confirmed disease. The overall in-hospital case-fatality ratio was very high in 2021, despite >50% of the patients at GERMS-SA ESS receiving flucytosine-based induction regimens through an access programme. This may be related to a continued delayed presentation to hospital among people with symptomatic cryptococcal disease during the COVID-19 pandemic. These data indicate the need to generally strengthen the HIV programme in the country to reduce cryptococcal disease and mortality.

Neisseria meningitidis

Results

In 2021, 32 cases of laboratory-confirmed invasive *Neisseria meningitidis* were reported through the GERMS-SA surveillance programme (less that those reported in 2020 (n=50) and 2019 (n=111)) (Table 7). Only one case was detected on audit of the NHLS laboratory information system, 18 cases were detected through PCR of relevant specimens and 13 were culture positive. Cases occurred sporadically throughout the year, peaking in May and December (Figure 2). The incidence of invasive meningococcal disease (IMD) in South Africa for 2021 was 0.05 cases per 100 000 population, with the highest incidence reported from the Western Cape Province (0.2 cases per 100 000 population) followed by the Eastern Cape Province (0.07 cases per 100 000 population) (Table 7). Most organisms were identified from cerebrospinal fluid (59%, 19/32), followed by blood (41%, 13/32) (Table 8). Of 22 isolates/specimens sero/genogrouped, serogroup B (n=14) was dominant, followed by serogroups Y (n=4) and W (n=3) (Table 9). Half the IMD episodes occurred in children <5 years of age, with infants being disproportionately affected, particularly with serogroup B (incidence of serogroup B in infants 0.43 per 100 000 population) (Figure 3). There were more males (66%, 21/32) with IMD than females. Of the 13 viable isolates, 77% (10/13) were susceptible to penicillin, the other 3 had intermediate susceptibilities (penicillin minimum inhibitory concentrations between 0.19 and 0.25 µg/ml). All viable isolates were susceptible to third-generation cephalosporins, ciprofloxacin and rifampicin.

Sixty-seven percent (10/15) of cases of IMD admitted at GERMS-SA enhanced surveillance hospital sites had clinical data available (Table 4). Two cases were in adults 24-44 years and the rest were in persons less than 10 years of age (5 were infants). All patients survived their hospital stay with a median length of stay of 6 days (interquartile range 3-10 days). All nine patients with HIV results available were HIV-uninfected (Table 4). The majority of patients presented with symptoms of meningitis (8/10), one with bacteraemia and one with pneumonia. The pneumonia episode was in an adult and due to a serogroup B isolate. Of 8 cases with data available on sequelae, one infant with meningococcal meningitis was discharged with complications including hydrocephalus, new-onset seizures and neurological fallout.

Table 7. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2019-2021, n=193 (including audit cases)

Province	2019		2020		2021	
	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*
Eastern Cape	12	0.18	6	0.09	5	0.07
Free State	3	0.1	0	0	0	0
Gauteng	37	0.24	10	0.06	8	0.05
KwaZulu-Natal	13	0.12	4	0.03	3	0.03
Limpopo	2	0.03	1	0.02	0	0
Mpumalanga	1	0.02	1	0.02	1	0.02
Northern Cape	1	0.08	0	0	0	0
North West	4	0.1	1	0.02	1	0.02
Western Cape	38	0.56	27	0.39	14	0.20
South Africa	**111**	**0.19**	**50**	**0.08**	**32**	**0.05**

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

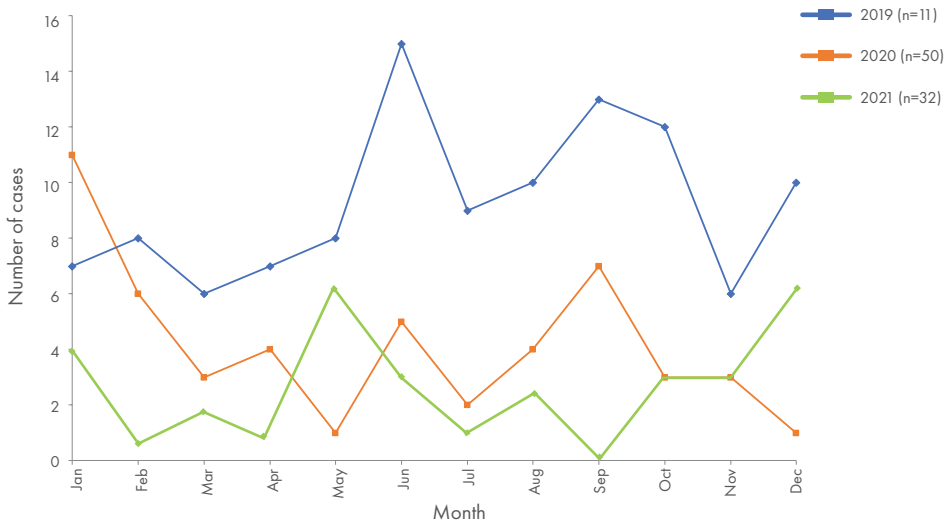


Figure 2: Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2019-2021, n=193

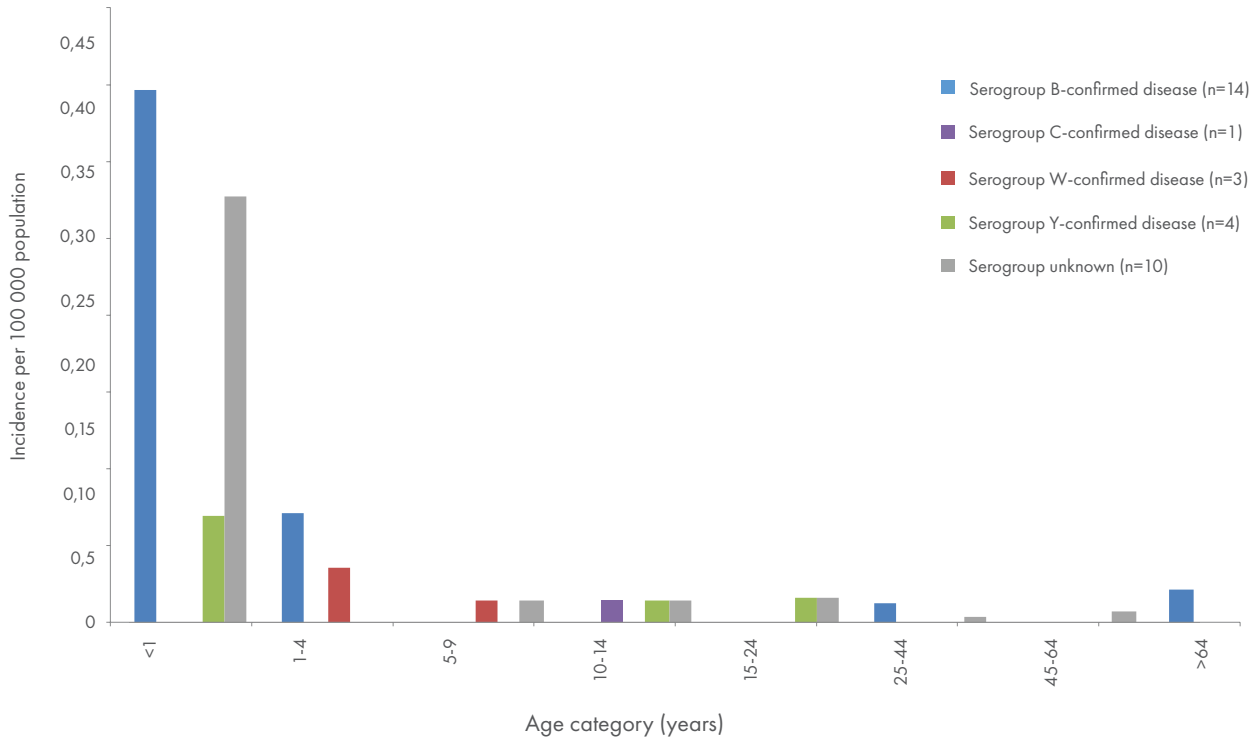
Table 8: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2019-2021, n=193

Site of specimen	2019		2020		2021	
	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*
Cerebrospinal fluid	70	63	24	48	19	59
Blood	41	37	26	52	13	41
Other	0	0	0	0	0	0
Total	**111**		**50**		**32**	

Table 9. Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2021, n=32*

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	E**	Total
Eastern Cape	3	0	1	0	1	0	0	0	5
Free State	0	0	0	0	0	0	0	0	0
Gauteng	2	0	6	0	0	0	0	0	8
KwaZulu-Natal	1	0	1	0	0	1	0	0	3
Limpopo	0	0	0	0	0	0	0	0	0
Mpumalanga	0	0	1	0	0	0	0	0	1
Northern Cape	0	0	0	0	0	0	0	0	0
North West	1	0	0	0	0	0	0	0	1
Western Cape	3	0	5	1	2	3	0	0	14
South Africa	**10**	**0**	**14**	**1**	**3**	**4**	**0**	**0**	**32**

*22 (69%) with viable isolates or specimens available for serogrouping/genogrouping; There were no non-groupable meningococcal isolates causing invasive disease in 2021.



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

Figure 3: Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2021, n=32 (specimens or viable isolates unavailable for serogrouping n=12)****

Discussion

The low incidence of IMD is believed to be a true reflection of laboratory-diagnosed meningococcal disease in South Africa in 2021, and still reflects reductions seen during the pandemic. Infants are at highest risk of IMD and although a variety of serogroups were circulating, serogroup B was dominant in most provinces and all age groups. As social activities resume to pre-COVID-19 pandemic levels, there is more opportunity for asymptomatic carriers of meningococcal bacteria to transmit meningococci to others through close contact, thus putting them at risk of developing IMD. Meningococcal disease causes severe infections and has outbreak potential, therefore clinicians are urged to consider the diagnosis in any persons presenting with fever and/or headache with rapid clinical deterioration. Third-generation cephalosporin or high dose intravenous penicillin is still recommended for treatment and should be started without delay should meningococcal disease be suspected.

Haemophilus influenzae

Results

In 2021, 279 cases of invasive *Haemophilus influenzae* (HI) disease were identified through the GERMS-SA surveillance programme. Thirty-nine percent (108/279) were audit cases, 46 (16%) were detected through PCR and 125 (45%) were available for further characterisation at the NICD (Table 2). Five cases were co-infected with *Streptococcus pneumoniae*. Invasive HI disease incidence was 0.46 cases per 100 000 population, similar to that of 2019 (0.44 per 100 000 population) (Table 10). Incidence was highest in the Western Cape Province (1.21 per 100 000 population), followed by Gauteng and Eastern Cape provinces (Table 10). Of cases available for serotyping, non-typeable HI (HNT) (n=60) was most prevalent, followed by type b (Hib) (n=48). Among all HI serotypes, most were detected from blood specimens (62%, 173/279), although significantly more cases from CSF were Hib (19/48, 40%) than HNT (7/60, 12%) and other HI serotypes (9/37, 24%) (p<0.001) (Table 11). Children <1 years had a higher incidence of Hib (1.37 cases per 100 000), HNT (0.69 per 100 000) and other serotypes (1.11 per 100 000) than other age categories (Figure 4). Hib disease in infants was similar to 2020, but higher than that of 2018 and 2019, whereas HNT disease has declined markedly in the last two years (Figure 5). Ten percent (13/126) of HI cases were non-susceptible to ampicillin, this included 4/39 Hib and 6/53 HNT episodes with ampicillin MICs >1mg/L.

Clinical information was available for 67% (88/132) of HI cases presenting at enhanced surveillance sites (ESS) (Table 4). Patients were hospitalised for a median of 8 days (IQR 1-15 days). Twenty-five percent (22/88) of patients did not survive their hospital stay, with a median time to death of one day (IQR 1-2 days) from date of specimen collection. Deaths occurred in all age categories, however more deaths occurred amongst those with HNT versus Hib (12/25 (48%) HNT died versus 1/17 (6%) Hib died, p<0.017). Of all HI cases at ESS with known HIV status, 35% (26/75) were HIV-infected (Table 4). Conditions, other than HIV, predisposing to HI disease were reported in 36/88 (41%) patients – the most common conditions included history of smoking (9), prematurity (4), chronic lung disease (4), malignancy (4) and alcoholism (3). Of the 20 surviving HI meningitis patients at ESS, 35% (7/20) suffered sequelae upon discharge – five developed ongoing seizures, three had hydrocephalus, two neurological fallout and one each suffered hearing- and vision-loss.

Hib vaccine history was available for 6/10 Hib cases in children <15 years at ESS. All the children were HIV-uninfected, one (3-months old) had not received any vaccine, one (6-months old) had received only one Hib vaccine dose, and 4 had received at least 3 doses each.

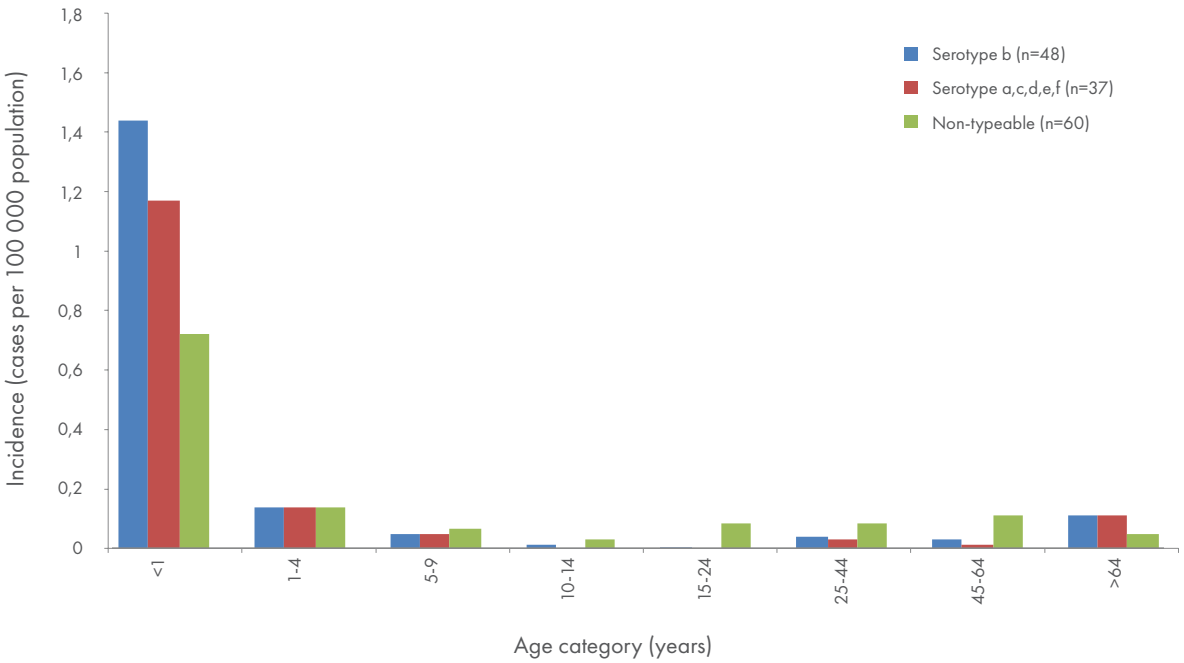
Table 10: Number of cases and incidence of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2021, n=279*

Province	Serotype									Incidence per 100 000 population**
	Serotype not available	A	B	C	D	E	F	Non-typeable	Total	
Eastern Cape	12	2	4	1	0	0	0	9	28	0.42
Free State	6	0	2	0	0	0	0	2	10	0.34
Gauteng	46	8	14	2	0	1	3	13	87	0.55
KwaZulu-Natal	24	3	7	0	0	0	1	6	41	0.36
Limpopo	7	0	1	0	0	0	0	1	9	0.15
Mpumalanga	6	0	4	0	0	0	0	0	10	0.21
Northern Cape	2	0	0	0	0	0	0	0	2	0.15
North West	5	0	1	0	0	0	0	0	6	0.15
Western Cape	26	8	15	0	2	1	5	29	86	1.21
South Africa	**134**	**21**	**48**	**3**	**2**	**2**	**9**	**60**	**279**	**0.46**

*145 (52%) with specimens or viable isolates available for serotyping.
**Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

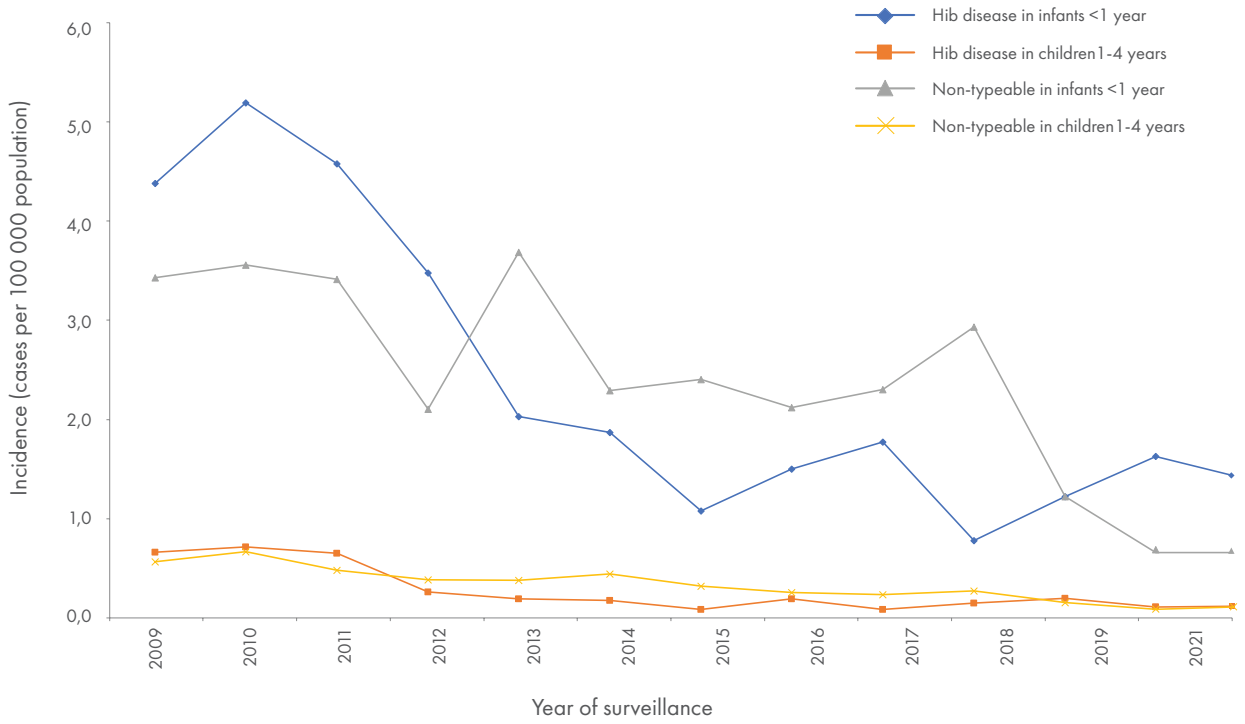
Table 11. Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2021, n=279

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	33	25	19	40	9	24	7	12
Blood	71	53	29	60	28	76	45	75
Other	30	22	0	0	0	0	8	13
Total	**134**		**48**		**37**		**60**	



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

Figure 4: Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype, South Africa, 2021, n=279 (age unknown, n=21; isolates unavailable for serotyping, n=134)



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

Figure 5: Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2021

Discussion

In 2021, invasive *Haemophilus influenzae* disease occurred at similar frequency to the pre-COVID-19 pandemic years, although a slightly higher incidence of Hib was reported in infants, while a lower incidence of HNT was documented. Primary Hib vaccination and booster doses are important in preventing invasive Hib in the community. Infants have the highest incidence of HI disease from all serotypes, however all age categories from young children to the elderly are at risk. Many persons with invasive HI had an underlying condition predisposing them to infection and over a third of those surviving an episode of meningitis were discharged from hospital with sequelae.

Streptococcus pneumoniae

Results

Of 1 560 cases of invasive pneumococcal disease (IPD) reported in 2021, 21% (328/1 560) were detected through audit of the NHLS laboratory information system, 246 (16%) through PCR of invasive body specimens and 986 (63%) were identified through culture (of which 958 were available for further characterisation) (Table 2). Incidence of IPD in South Africa was 2.59 cases per 100 000 persons, slightly higher than 2020 (2.12 per 100 000) (Table 12). The Western Cape Province had the highest incidence of IPD (7.66 per 100 000 population), followed by the Eastern Cape (3.01 per 100 000), Gauteng (2.96 per 100 000) and Free State (2.39 per 100 000) provinces (Table 12). Most cases were detected from blood specimens (69%, 1 070/1 560), followed by cerebrospinal fluid (25%, 397/1 560) (Table 13). Overall, slightly more males than females were affected (52%, 804/1 560 vs 47%, 726/1 560, sex not specified n=30). Infants had the highest IPD incidence (14.23 per 100 000), followed by adults >25 years (3.18 per 100 000) (Figure 6). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 39% (371/953) of IPD isolates, the highest proportion of penicillin non-susceptible IPD was in children 1-4 years of age (71%, 34/48) and in KwaZulu-Natal Province (24/37, 65%) (Table 14 and Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 10% (97/953) of isolates from all specimen types, including 8% (15/182) of IPD isolated from CSF. The five predominant serotypes in children <5 years included serotypes 19F, 8, 10A, 3 and 23B (Figure 8A). Whilst in persons >5 years, serotypes 8, 19A, 19F, 3 and 4 were most common (Figure 8B). Overall 34% (325/953) of serotypes causing IPD in South Africa were included in the pneumococcal 13-valent conjugate vaccine (PCV13), this varied by age-category ranging from 9% (1/11) in 10-14 year olds to 38% (95/247) of 45-64 year olds (Table 15 and Figure 9). The newly formulated PCV20 vaccine has potential coverage of 57% (543/953) of serotypes causing IPD in South Africa.

Eighty-three percent (495/598) 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 (IQR 2-14 days) and most deaths occurred within 2 days of admission (IQR 0-7 days). Overall case-fatality was 36% (177/495). HIV-infection was present in 58% (251/431) of IPD patients; and 58% (22/38) of infants with maternal HIV-status available were HIV-exposed (8 babies were HIV-infected and 14 were HIV-uninfected). Fifty-three percent (263/495) of patients had a condition/risk factor (excluding HIV-infection) predisposing them to IPD. The top five factors included: history of smoking (91 patients), chronic lung disease (29 patients), chronic cardiac or renal disease (19 patients each) and malignancy (16 patients). Of 98 patients at ESS with pneumococcus detected in CSF: 43% (42/98) died during their hospitalisation, and 25% (14/56) who survived to discharge suffered at least one sequelae upon discharge – these included new-onset seizures (8), limb weakness/paralysis (5), vision loss (5) and hydrocephalus (2).

Vaccination history was available for 9 of 12 children <10 years-of-age at ESS with IPD caused by serotypes present in the PCV13 vaccine. Two (2/9, 22%) were too young to receive vaccine; two children between 9 and 12 months-of-age had received only 2 doses and five children (56%,5/9; and 4 of whom were over 16 months-of-age) had received all 3 doses of PCV13. The serotypes responsible for disease in those who had received any PCV13 included serotypes 19F (four episodes), 19A (two episodes) and 3 (one episode).

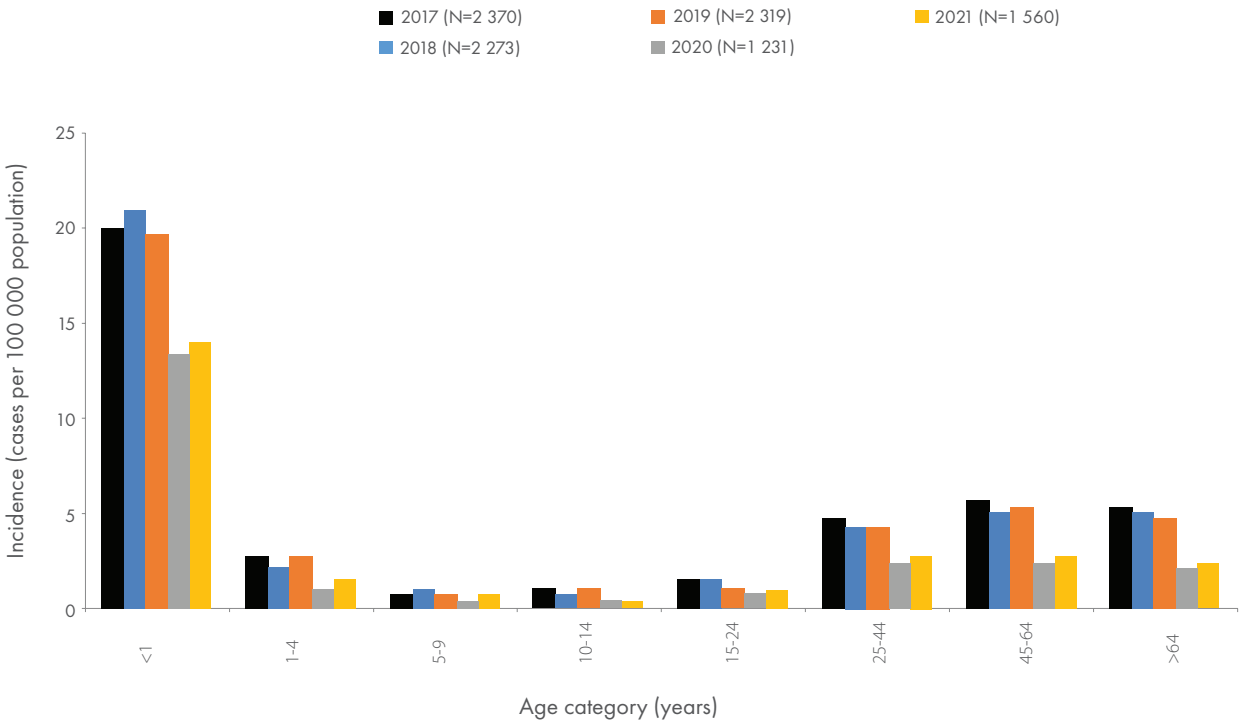
Table 12. Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2019-2021, n=5 174 (including audit cases)

Province	2019		2020		2021	
	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*
Eastern Cape	274	4.08	138	2.05	201	3.01
Free State	83	2.91	62	2.12	70	2.39
Gauteng	774	5.11	379	2.45	468	2.96
KwaZulu-Natal	237	2.10	101	0.88	118	1.02
Limpopo	96	1.62	53	0.91	44	0.74
Mpumalanga	102	2.22	42	0.90	57	1.20
Northern Cape	89	7.12	26	2.01	25	1.92
North West	66	1.64	37	0.90	32	0.78
Western Cape	631	9.25	424	6.05	545	7.66
South Africa	**2 352**	**4.01**	**1 262**	**2.12**	**1 560**	**2.59**

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

Table 13. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2019-2021, n=5 174

Site of specimen	2019		2020		2021	
	n	%	n	%	n	%
Cerebrospinal fluid	699	30	341	27	387	25
Blood	1 485	63	818	65	1 070	69
Other	168	7	103	8	103	7
Total	**2 352**		**1 262**		**1 560**	



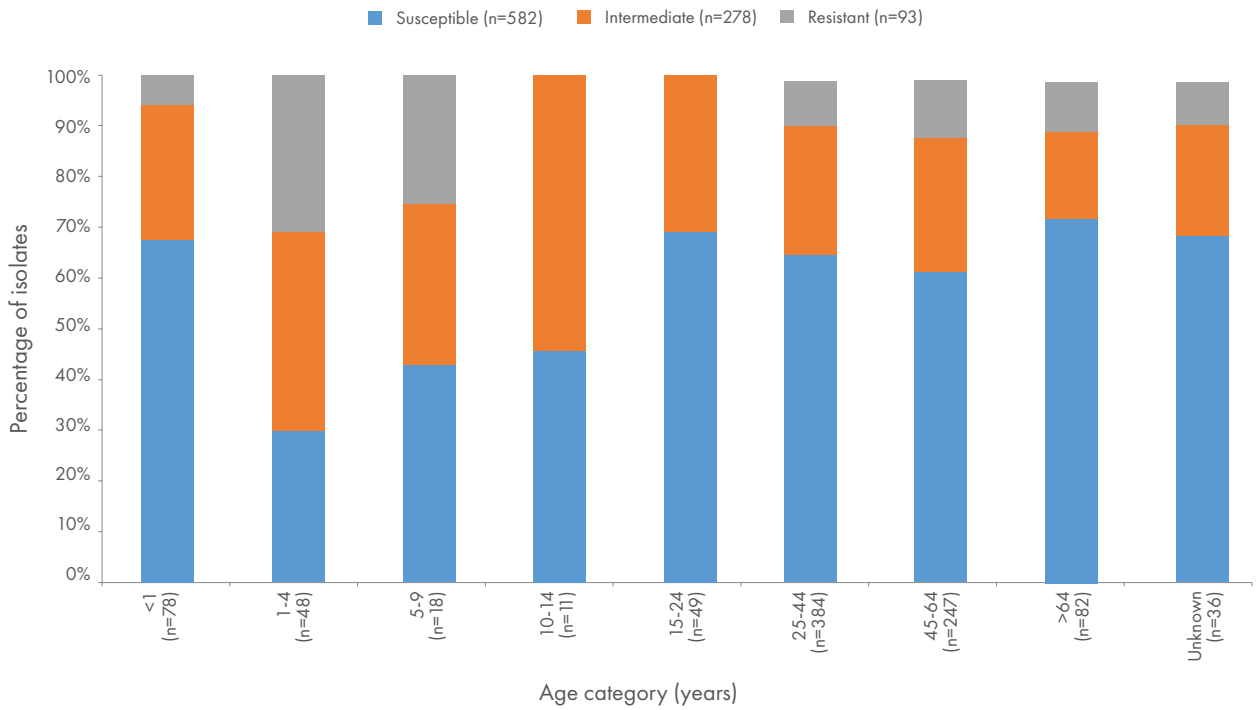
2017: N=2 440, age unknown for n=70; 2018: N=2 315, age unknown for n=42; 2019: N=2 359, age unknown for n=40; 2020: N=1 262, age unknown for n=31; 2021: N=1 560, age unknown for n=97.

Figure 6. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2017 through 2021, n=9 936

Table 14. Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2021, n=1 560

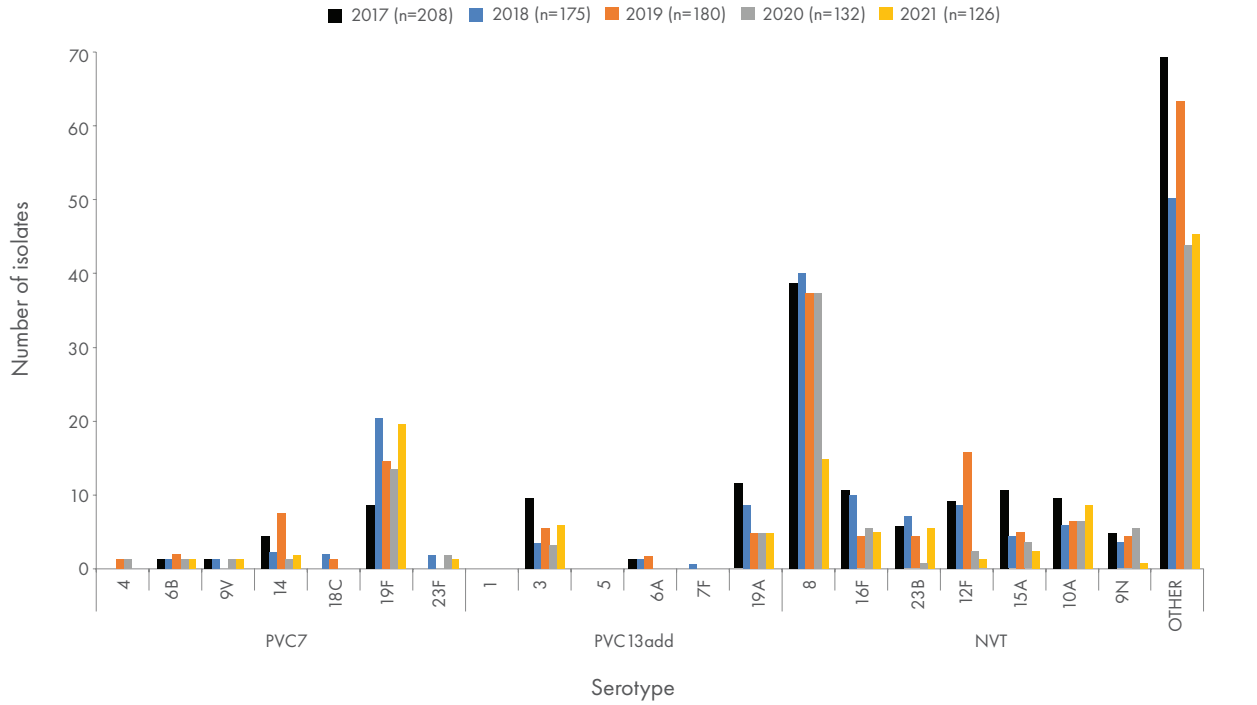
Antimicrobial agent	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	76	81	65	40	32	4	3
Free State	34	19	53	8	22	9	25
Gauteng	244	120	54	72	32	32	14
KwaZulu-Natal	81	13	35	16	43	8	22
Limpopo	17	20	74	5	19	2	7
Mpumalanga	28	18	62	8	28	3	10
Northern Cape	22	3	100	0	0	0	0
North West	24	6	75	2	25	0	0
Western Cape	81	302	65	127	27	35	8
South Africa	**607**	**582**	61	**278**	29	**93**	10

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



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

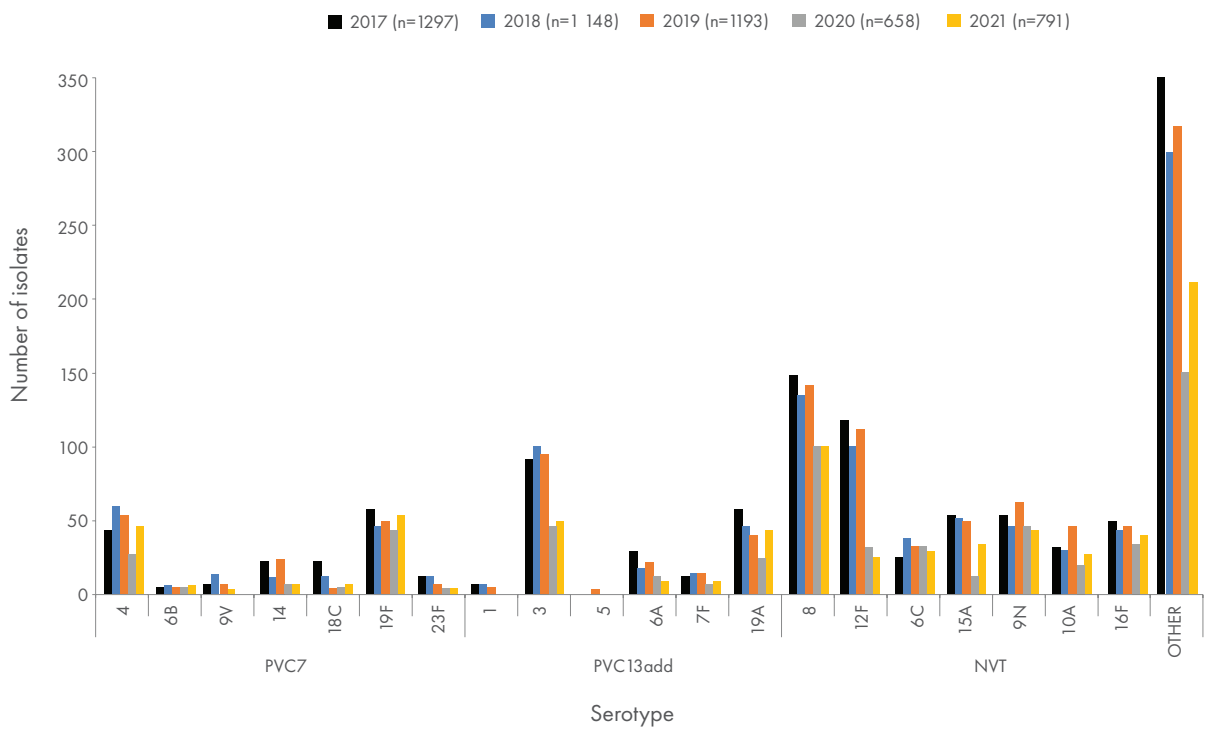
Figure 7. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age category and penicillin susceptibility, South Africa, 2021, n=1 560 (n=953 with viable isolates)



2017: N=374, n=167 without viable isolates; 2018: N=386, n=211 without viable isolates; 2019: N=361, n=181 without viable isolates; 2020: N=224, n=92 without viable isolates; 2021: N=253, n=127 without viable isolates.

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

Figure 8A: Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2017-2021



2017: N=1 996, n=699 without viable isolates; 2018: N=1 871, n=723 without viable isolates; 2019: N=1 952, n=759 without viable isolates; 2020: N=1 007, n=349 without viable isolates; 2021: N=1 210, n=419 without viable isolates.

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

Figure 8B: Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children >5 years, South Africa, 2017-2021

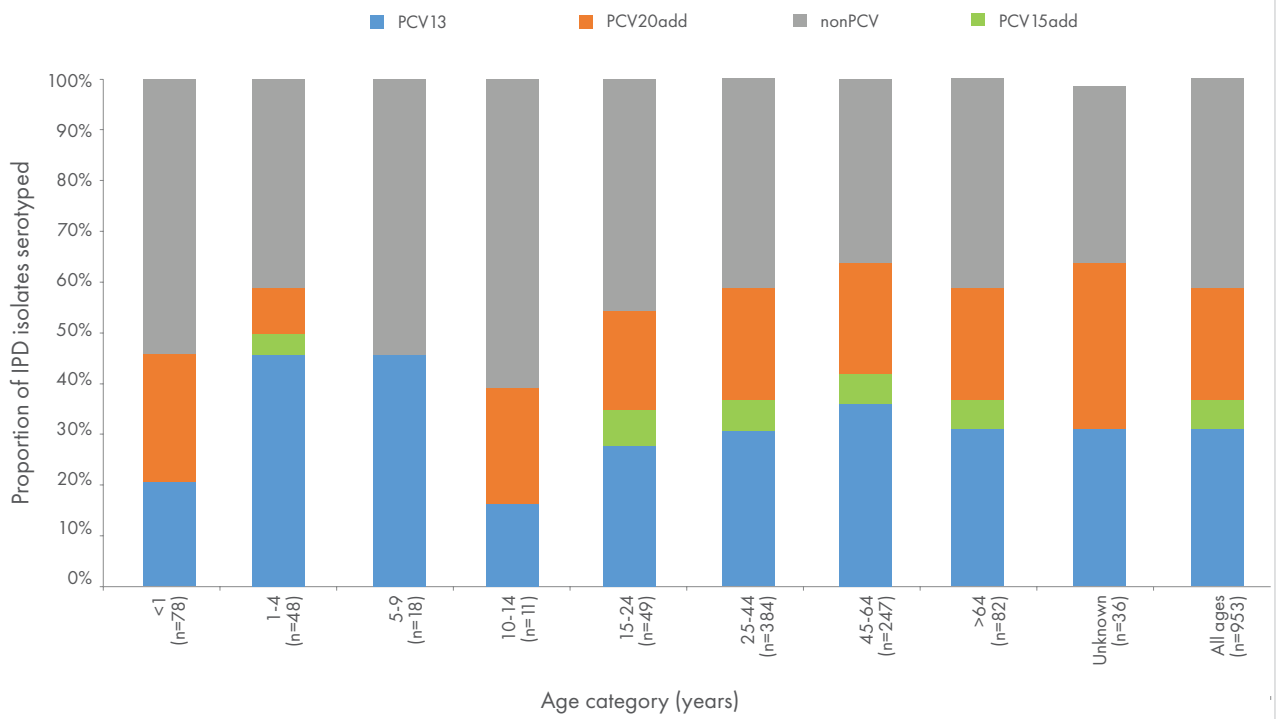
Table 15. Number and percentage of invasive pneumococcal cases reported by the serotypes contained in the 10-, 13- 15- and 20-valent pneumococcal conjugate vaccine candidates by age category, South Africa, 2021, n=1 560 (n=953 with viable isolates)

Age category	Total isolates available for serotyping	SII 10-valent serotypes		GSK 10-valent serotypes		Pfizer 13-valent serotypes		Merck 15-valent serotypes		Pfizer 20-valent serotypes	
		n	%	n	%	n	%	n	%	n	%
<1 year	78	10	13	8	10	15	19	15	19	37	47
1-4 years	48	18	38	16	33	21	44	22	46	28	58
5-9 years	18	7	39	7	39	8	44	8	44	8	44
10-14 years	11	1	9	1	9	1	9	1	9	4	36
15-24 years	49	8	16	5	10	15	31	17	35	26	53
25-44 years	384	82	21	64	17	130	34	142	37	217	57
45-64 years	247	60	24	41	17	95	38	100	40	153	62
>64 years	82	14	17	10	12	28	34	31	38	48	58
Age unknown	36	9	25	6	17	12	33	12	33	22	61
Total	**953**	**209**	22	**158**	17	**325**	34	**348**	37	**543**	57

Serotypes included in each of the pneumococcal conjugate vaccine categories:

Serum Institute India 10-valent serotypes:	1, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F
GlaxoSmithKline 10-valent serotypes:	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F
Pfizer 13-valent serotypes:	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F, 3, 6A, 19A
*Merck 15-valent serotypes:	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F, 3, 6A, 19A, 22F, 33F
*Pfizer 20-valent serotypes:	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F, 3, 6A, 19A, 22F,33F, 8, 10A, 11A, 12F,15B

* Merck PCV15 and Pfizer PCV20 are not yet licenced for use in South Africa



PCV13: 13-valent pneumococcal conjugate vaccine contains serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F; PCV15add: 15-valent vaccine contains PCV13 serotypes plus 22F and 33F; PCV20add: 20-valent vaccine contains PCV15 serotypes plus 8, 10A, 11A, 12F and 15B.

Figure 9: Potential pneumococcal serotype coverage of laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, by various pneumococcal conjugate vaccines and age categories, South Africa, 2021 (n=953 viable isolates available for serotyping)

Discussion

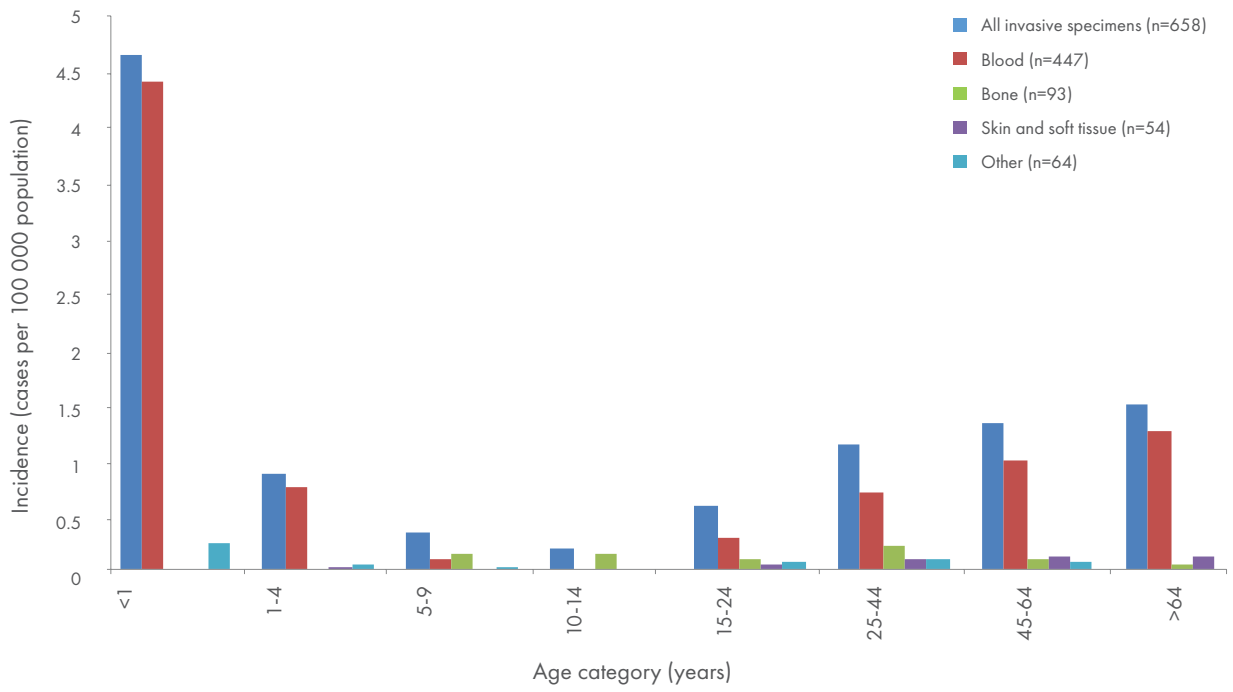
In 2021, IPD incidence remained lower than pre-COVID-19 years. Infants have the highest incidence followed by adults 25 years-and-older. Penicillin susceptibility remained high, particularly in infants. HIV-infection and HIV-exposure in infants was a dominant underlying condition amongst those with IPD. In addition, other underlying conditions (excluding HIV) predisposing to IPD were present in over half of the patients. IPD resulted in poor outcomes, with an in-hospital case-fatality ratio of 36%. In-hospital deaths were highest amongst those with pneumococcal meningitis and a quarter of meningitis survivors are discharged from hospital with sequelae. Serotype distribution varies by age-category, with serotypes 8, 19A and 19F predominating. One fifth of IPD amongst infants are still due to serotypes in PCV13, increasing to two-fifths in the 1-4 years age-category, with an overall proportion of 34%. Newer conjugate vaccines such as PCV15 and PCV20 would potentially cover 37% and 57% of current IPD in South Africa, respectively. Healthcare workers and parents need to ensure that all children are up to date with their vaccination schedule.

Group A Streptococcus *(Streptococcus pyogenes)*

Results

In 2021, of 658 episodes of invasive group A *Streptococcus* (group A strep), 44% (292/658) of isolates were not sent to the reference laboratory for further characterisation (Table 2). The invasive group A strep case definition includes individuals with group A strep isolated from sterile site specimens, as well as isolates from non-sterile site specimens with a diagnosis of septic shock or necrotising fasciitis. Incidence of invasive group A strep was highest in infants (4.72 per 100 000) with a second peak in those aged >64 years (1.52 per 100 000) (Figure 10). Incidence was highest in the Western Cape Province (3.16 per 100 000), followed by Eastern Cape (1.60 per 100 000) and Gauteng provinces (1.02 per 100 000) (Table 16A). Where sex was known, more disease occurred in males (389/642, 61%) than females. In children <5 years-of-age, 91% (87/96) of cases were diagnosed from blood culture, and amongst those >5 years of age 64% (329/517) were on blood culture, 17% (90/517) from bone specimens and 10% (50/517) from skin and soft tissue (Table 16B). Of those isolates available for antimicrobial susceptibility testing, 99% (339/342) were susceptible to penicillin (MIC<0.06µg/ml) and 95% (326/342) were susceptible to erythromycin (MIC<0.25µg/ml) (Table 17).

At enhanced surveillance sites, 58% (242/415) of invasive group A strep cases had clinical data available (Table 4). Most patients were admitted from home with a median time from admission to specimen collection of 0 days (IQR 0-4 days). Patients were admitted for a median of 7 days (IQR 2-15 days). Overall 31% (65/211) died in hospital, with most deaths occurring in persons >5 years (58/173, 34% vs 5/35, 14% in children <5 years, 3 with unknown age). Most patients with invasive group A strep had wound infections (89/203, 44%), followed by cellulitis (21%, 42/203) and necrotising fasciitis (16%, 33/203). Thirty-four percent (57/168) of patients with HIV test results available were HIV-infected (Table 4). Common risk factors for invasive group A strep included concurrent skin infections (31/203, 15%), blunt trauma or surgery in the past two weeks (16/203, 8% each).



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

Figure 10. Age-specific incidence rates* for laboratory-confirmed, invasive group A streptococcal disease, reported to GERMS-SA, South Africa, 2021, n=658

Table 16A. Number of cases and incidence rates of invasive group A streptococcal disease reported to GERMS-SA by province, South Africa, 2020-2021, n=1 104 (including audit cases)

Province	2020		2021	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	59	0.88	120	1.80
Free State	9	0.31	21	0.72
Gauteng	91	0.59	162	1.02
KwaZulu-Natal	48	0.42	86	0.75
Limpopo	5	0.09	11	0.19
Mpumalanga	10	0.21	22	0.46
Northern Cape	7	0.54	2	0.15
North West	2	0.05	9	0.22
Western Cape	215	3.07	225	3.16
South Africa	**446**	**0.75**	**658**	**1.09**

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

Table 16B. Number and percentage of cases of invasive group A streptococcal disease reported to GERMS-SA by specimen type and age category, South Africa, 2021, n=658 (age unknown for n=45)

Site of specimen	Age <5 years		Age >5 years	
	n	%	n	%
Cerebrospinal fluid/brain	5	5	12	2
Blood	87	91	329	64
Skin and soft tissue*	2	2	50	10
Bone	1	1	90	17
Other**	1	1	36	7
Total	**96**		**517**	

*Skin and soft tissue includes superficial skin swabs with an accompanying diagnosis of tissue necrosis, necrotising fasciitis or toxic shock syndrome. **Other includes invasive specimens from respiratory and gastrointestinal tracts.

Table 17. Number and percentage of penicillin and erythromycin susceptible and non-susceptible isolates from invasive group A streptococcal disease cases reported to GERMS-SA, South Africa, 2021, n=658

Antimicrobial agent	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Penicillin	316	339	99	1	0	2	1
Erythromycin	316	326	95	5	1	11	3

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

Discussion

Invasive group A strep mostly affected infants and the elderly, with infections originating potentially from disruptions to the skin. Group A strep was isolated most frequently from blood specimens for all diagnoses. Most cases were admitted from the community. In-hospital case-fatality was high, particularly amongst the elderly. Isolates were highly susceptible to first line antimicrobial agents, penicillin and erythromycin.

Group B Streptococcus *(Streptococcus agalactiae)*

Results

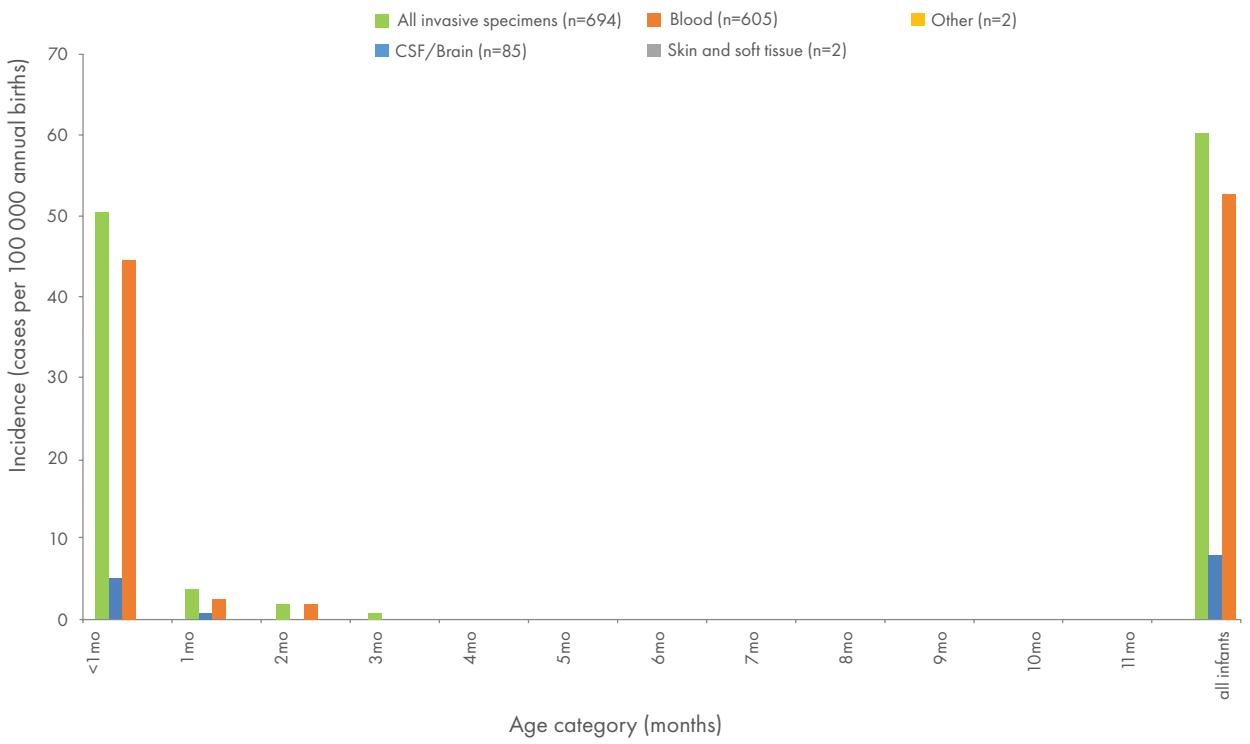
In 2021, 1 141 invasive group B streptococcal infections (group B strep) were reported through the GERMS-SA surveillance network, of which 669 (59%) episodes were detected through the NHLS laboratory information system (Table 2). Incidence for early-onset group B strep (<7 days) was 0.36 per 1 000 live births and 0.21 per 1 000 live births for late-onset (7-90 days) invasive disease (Table 18). Gauteng Province reported the highest incidence of early-onset group B strep (0.66 per 1 000 live births), while Western Cape Province reported the highest incidence of late-onset group B strep (0.35 per 1 000 live births) (Table 18). Nationally, in 2021 incidence of invasive group B strep in infants was 60 per 100 000 population, starting at 51 per 100 000 amongst neonates and decreased rapidly by advancing month of age (Figure 11A). In persons >1 year of age, overall incidence of invasive group B strep was 0.6 per 100 000, peaking at 1 per 100 000 in those >64 years of age (Figure 11B). In infants, most cases were isolated from blood (605/694, 87%) or cerebrospinal fluid (85/694, 12%) (Table 19). However, in persons >1 year of age, blood (193/333, 58%) and genitourinary tract specimens (96/333, 29%) were most frequent (Table 19). Where sex was known, in infants 52% (349/670) of disease occurred in males, however in persons >1 year most disease occurred in females (63%, 208/328). Of the specimens available for serotyping, serotype III was dominant (183/433, 40%), followed by serotype Ia (119, 26%) (Table 20). Serotypes III, Ia and V were the most dominant serotypes causing invasive disease in both early-onset group B strep and in those >90 days-of-age (Figure 12). Whereas serotypes III and Ia were the predominant serotypes amongst late-onset disease (7-90 days-of-age). Ninety-seven percent (430/442) of invasive group B strep isolates were susceptible to penicillin (MIC<0.12mg/l).

Sixty-four percent (386/600) of invasive group B strep cases at enhanced surveillance sites had clinical data available (Table 4). Median days for admission were 7 (IQR 2-16 days). Nineteen percent (71/367) of persons with invasive group B strep died, including 18% (38/206) of neonates. Underlying maternal risk factors for neonates developing invasive group B strep included: 34% (67/200) with premature rupture of membranes prior to birth, 9% (15/168) with prolonged rupture of membranes (>18 hours prior to delivery), and 3% (6/200) with pre-eclampsia. Neonatal risk factors for developing invasive group B strep included 46% (77/168) with prematurity (<37 weeks gestation), 23% (46/200) with very low birth weight (<1 500g), and 14% (28/200) who required intubation.

Table 18. Number of cases and incidence rates of invasive group B streptococcal disease reported to GERMS-SA by province and age category*, South Africa, 2021, n=1 141

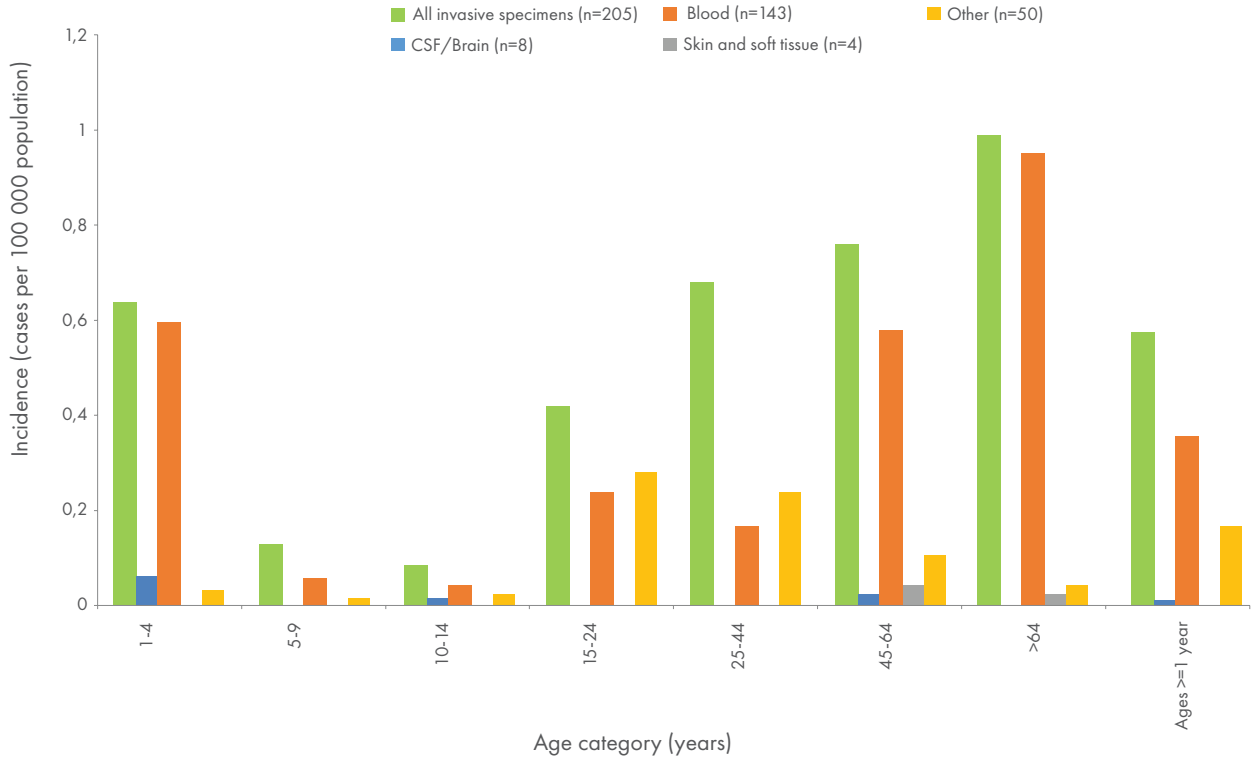
Province	Early onset (<7 days)		Late onset (7-90 days)		Age category ≥1 year	
	n	Incidence (per 1 000 live births*)	n	Incidence (per 1 000 live births*)	n	Incidence (per 100 000 population)
Eastern Cape	22	0.17	9	0.07	28	0.43
Free State	15	0.26	12	0.21	10	0.35
Gauteng	202	0.66	101	0.33	156	1.01
KwaZulu-Natal	98	0.44	39	0.18	52	0.46
Limpopo	22	0.19	18	0.16	5	0.09
Mpumalanga	28	0.30	10	0.11	14	0.30
Northern Cape	1	0.04	1	0.04	1	0.08
North West	8	0.10	2	0.02	4	0.10
Western Cape	30	0.22	48	0.35	63	0.90
South Africa	**426**	**0.36**	**240**	**0.21**	**333**	**0.56**

*N=28 cases in infants >90 days and less than one year excluded from above. **Age unknown for n=114. *Mid-year population denominators for <1 year olds were used, as live birth denominators for 2021 were unavailable at time of print.



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

Figure 11A: Age-specific incidence rates* for laboratory-confirmed, invasive group B streptococcal disease in children <1 year of age, reported to GERMS-SA, South Africa, 2021, n=694



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

Figure 11B: Age-specific incidence rates* for laboratory-confirmed, invasive group B streptococcal disease in persons ≥1 year of age, reported to GERMS-SA, South Africa, 2021, n=333

Table 19. Number and percentage of cases of invasive group B streptococcal disease reported to GERMS-SA by specimen type and age category*, South Africa, 2021, n=1 141

Site of specimen	Age <1 year		Age ≥1 years	
	n	%	n	%
Cerebrospinal fluid/brain	85	12	11	3
Blood	605	87	193	58
Skin and soft tissue	2	0	4	1
Genitourinary	1	0	96	29
Other**	1	0	29	9
Total	**694**		**333**	

*Age unknown for n=114. **Other includes invasive specimens from bone, respiratory and gastrointestinal tracts.

Table 20. Serotype distribution of invasive group B streptococcal disease reported to GERMS-SA by province, South Africa, 2021, n=1 141 (all ages)

Province	Total	Total isolates available for serotyping	Ia		Ib		II		III		IV		V		VIII	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Eastern Cape	65	17	4	22	0	0	1	6	9	50	0	0	3	17	0	0
Free State	39	9	4	36	2	18	0	0	2	18	0	0	1	9	0	0
Gauteng	556	187	50	25	11	5	11	5	74	37	7	3	34	17	0	0
KwaZulu-Natal	208	58	14	23	2	3	5	8	22	36	2	3	12	20	1	2
Limpopo	51	35	8	22	2	5	0	0	18	49	0	0	6	16	0	0
Mpumalanga	55	22	2	9	1	5	3	14	12	55	0	0	4	18	0	0
Northern Cape	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
North West	14	3	0	0	0	0	0	0	3	100	0	0	0	0	0	0
Western Cape	150	102	37	36	7	7	4	4	43	42	1	1	7	7	1	1
South Africa	**1 141**	**433**	**119**	26	**25**	5	**24**	5	**183**	40	**10**	2	**67**	15	**2**	0

There were three non-typeable (two from Limpopo and one from Western Cape) not shown in the table. Of 1 141 episodes, 433 were serotyped, 23 had insufficient specimen for serotyping, 685 did not have isolates/specimens available for serotyping at the NICD (including 669 audit cases and 16 reported cases but isolates not sent).

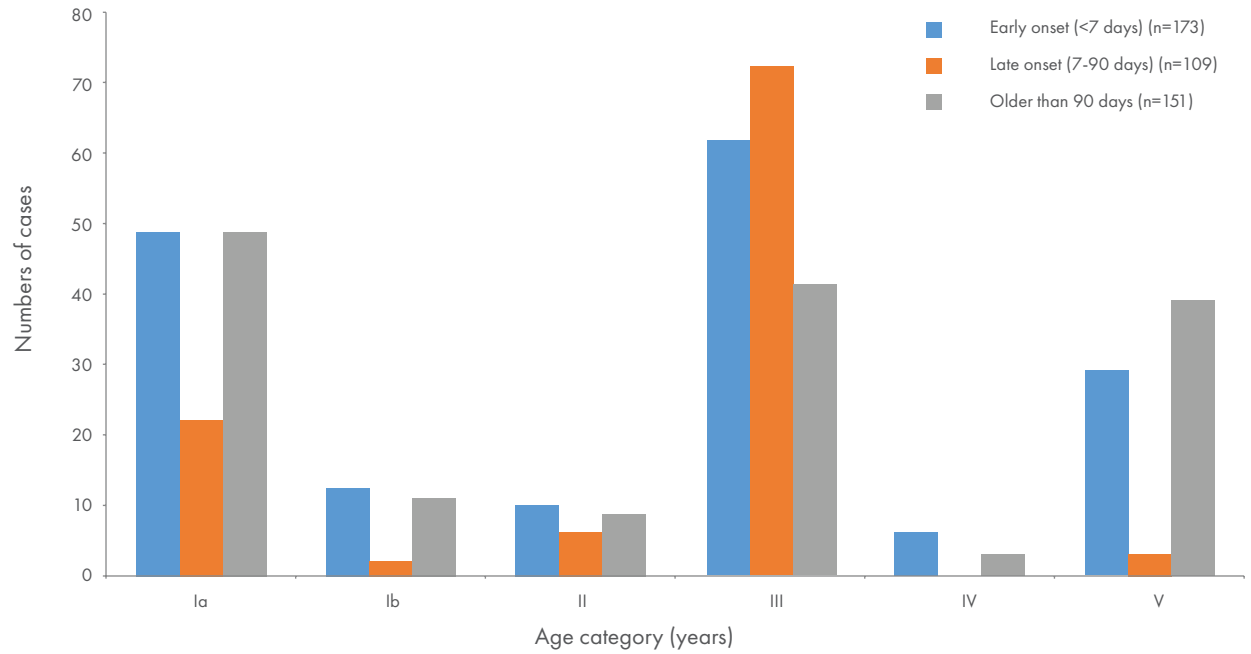


Figure 12. Numbers of cases of laboratory-confirmed, invasive group B streptococcal disease by serotype, reported to GERMS-SA, South Africa, 2021, n=1 141 (typing done for n=433)

Discussion

In South Africa, incidence of early- and late-onset group B strep varied greatly by province, possibly due to under-ascertainment of cases through poor blood culturing practices for neonates in many hospitals. Serotype III and Ia dominated across all age-categories. Majority of isolates were susceptible to penicillin, which remains the first-line antimicrobial agent for targeting neonatal sepsis. Mortality was high across all age bands. Among neonates with invasive group B strep, preterm birth was an important predisposing factor.

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

Results

A total of 131 cases of laboratory-confirmed enteric fever were identified through the active enteric fever surveillance programme of the Centre for Enteric Diseases in 2021.

The cases include *Salmonella* Typhi isolated from all sample sites, of which 80% (105/131) were blood cultures. There were no cases of enteric fever caused by *Salmonella enterica* serovars Paratyphi A, Paratyphi B or Para-typhi C. Enteric fever cases were reported from all provinces except Northern Cape and Limpopo (Table 21), but the majority (67%, 88/131) were reported from two provinces: Western Cape (51/131, 39%) and Gauteng (37/131, 28%). Most cases (89%, 117/131) were identified in the public health sector. By age group, the number of cases was highest in children aged 5 to 14 years (40/131, 31%), followed by adults aged 25 to 34 years (24/131, 18%) and adolescents and young adults aged 15 to 24 years (18/131, 14%), as shown in Table 22. An increase in the number of cases from October through December was observed (Figure 13). Of the isolates received and tested at the centre, 88% (108/123) were susceptible to ciprofloxacin and 99% (122/123) were susceptible to azithromycin (Table 23), following CLSI breakpoints.

Table 21. Number of cases of *Salmonella* Typhi by health sector and province, South Africa, 2021, n=131 (including audit reports, missing isolates, mixed and contaminated cultures)

Province	Private sector	Public sector	Total
Eastern Cape	2	4	6
Free State	0	3	3
Gauteng	6	31	37
KwaZulu-Natal	2	6	8
Limpopo	0	0	0
Mpumalanga	1	9	10
Northern Cape	0	0	0
North West	1	15	16
Western Cape	2	49	51
South Africa	**14**	**117**	**131**

Table 22. Number of cases of *Salmonella* Typhi by age category, South Africa, 2021, n=131 (including audit reports)

Age category (years)	n	%
0 - 4	17	13
5 - 14	40	31
15 - 24	18	14
25 - 34	24	18
35 - 44	13	10
45 - 54	11	8
55 - 64	1	1
≥ 65	5	2
Unknown	5	4
Total	**131**	100

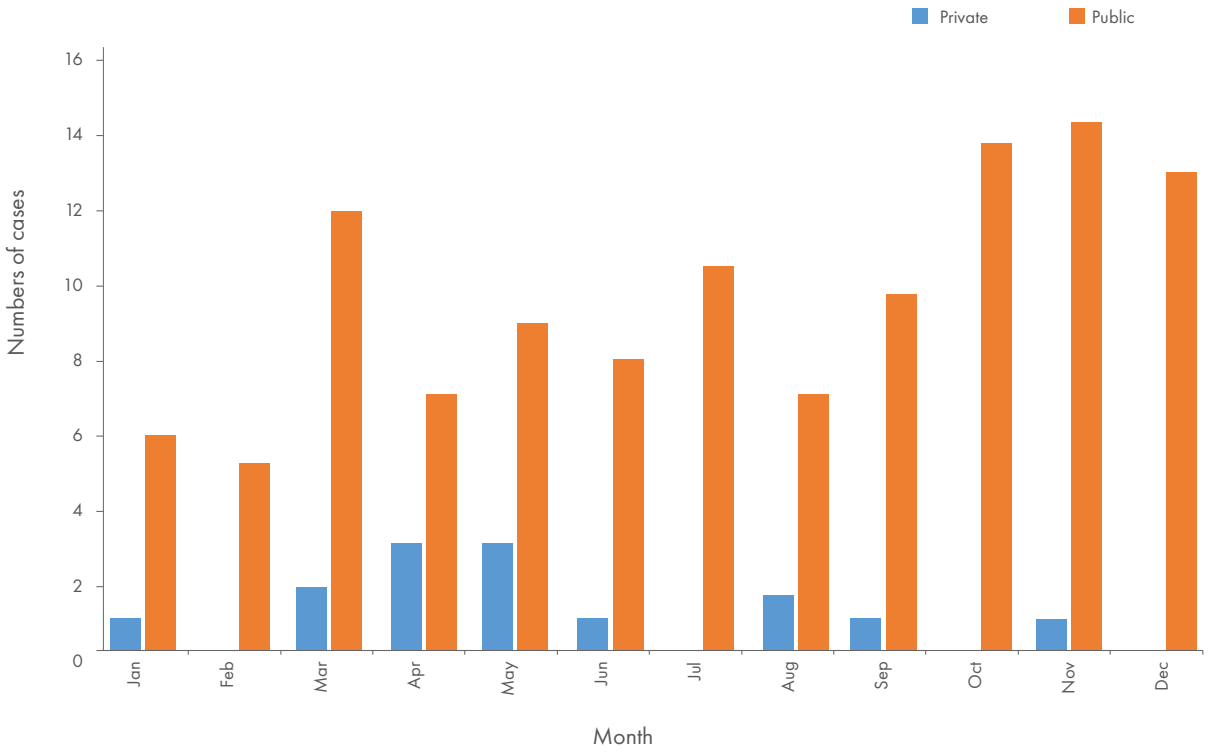


Figure 13. Number of cases of *Salmonella* Typhi by month of sample collection and health sector, South Africa, 2021, n=131

Table 23. Ciprofloxacin and azithromycin susceptibility* of viable *Salmonella* Typhi isolates received and tested at the Centre for Enteric Diseases, South Africa, 2021, n=123

Antimicrobial agent	Susceptible (%)	Resistant (%)
Ciprofloxacin	108 (88%)	15 (12%)
Azithromycin	122 (99%)	1 (1%)

*According to CLSI breakpoints

Discussion

Enteric fever caused by *Salmonella* Typhi remains endemic in South Africa. Following the outbreaks in 2005-2006, the number of culture-confirmed cases annually has remained stable at <150 cases per year. However, the number of cases in 2021 (n=131) was the highest annual total since the enteric fever outbreaks of 2005-2006. A comparison of cases by month shows a similar pattern of higher case numbers in October through January for the last three years, which could suggest seasonality (Figure 14). The age distribution of cases is similar to that reported in previous years, with children aged 5 to 14 years being most affected.

Although small, localised outbreaks of typhoid fever were identified in 2021, most cases were sporadic. The majority of cases acquired *Salmonella* Typhi infection in South Africa; few cases were imported (travel-related), mostly from neighbouring countries.

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 represent a public health risk. The diagnosis of enteric fever remains challenging; heightened clinical awareness and appropriate laboratory tests are critical in identifying cases. Culture remains the gold standard for confirming enteric fever, so prevailing clinician testing behaviour heavily influences the likelihood of detecting cases.

Greater numbers of cases reported from Gauteng and Western Cape provinces could reflect healthcare-seeking behaviour and prevailing clinician testing practices, but small localised outbreaks were also confirmed in these provinces.

Although the proportion of isolates showing resistance to ciprofloxacin (12%) is lower than recent years, this remains a major concern. *Salmonella* Typhi isolates should routinely be tested against azithromycin, which is an alternative oral antibiotic option for treating disease caused by ciprofloxacin resistant strains. Ceftriaxone may also be used as an alternative therapy, but needs to be administered parenterally. Cases of enteric fever caused by *Salmonella enterica* serovars Paratyphi A, Paratyphi B or Paratyphi C remain uncommon in South Africa, with no cases reported in 2021.

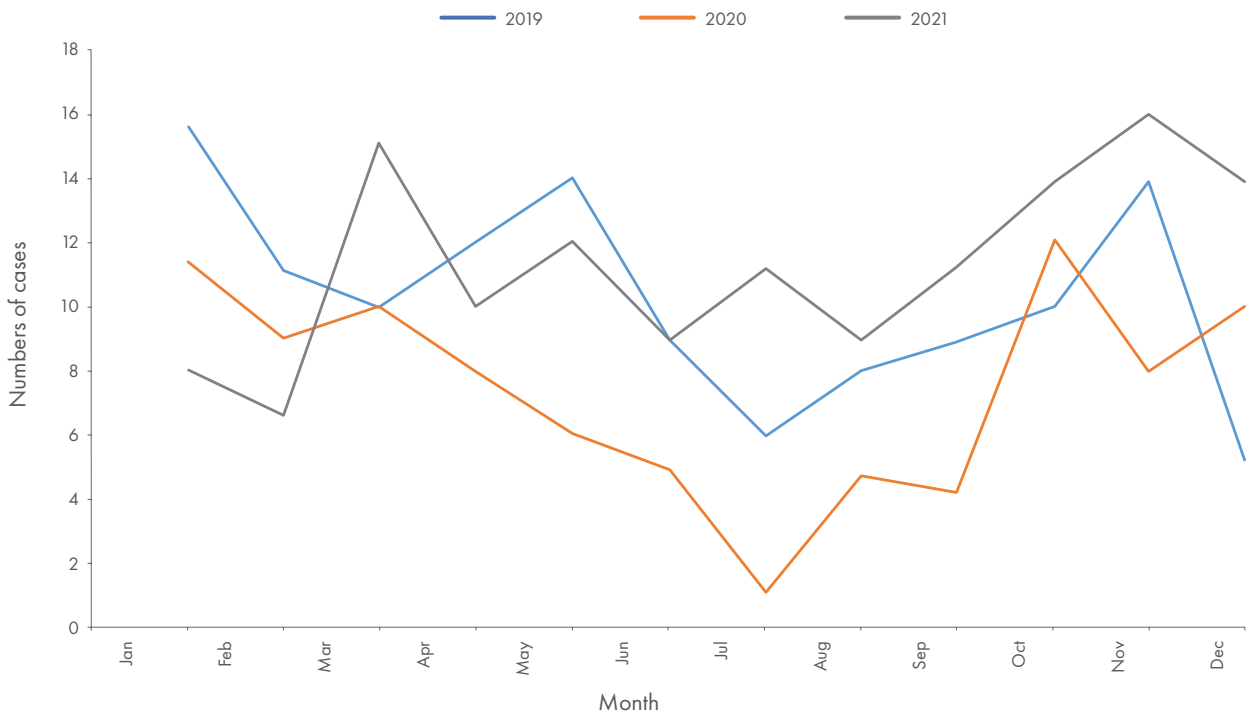


Figure 14. Number of cases of *Salmonella* Typhi reported by month and year of sample collection, South Africa, 2019 – 2021

Non-typhoidal *Salmonella* (NTS)

Results

A total of 2 445 cases of nontyphoidal salmonellosis were reported through the surveillance programme in 2021. This includes nontyphoidal *Salmonella* isolated from all sample sites, of which 41% (1 010/2 445) were indicative of invasive disease. Fifty-four percent of the total cases (1 323/2 445) were identified in the public health sector. There was a striking difference in the proportion of cases which were invasive in the public health sector (68%, 906/1 323) versus those in the private health sector (9%, 104/1 122). This could be due in part to differences in health-seeking behaviour and diagnostic practices among clinicians in the respective health sectors.

The highest numbers of cases of invasive disease were reported from Gauteng (380/1 010, 38%), followed by Western Cape (235/1 010, 23%) and Eastern Cape (121/1 010, 12%) provinces (Table 24). Gauteng also reported the highest number of cases of non-invasive disease (44%, 638/1 435), followed by Western Cape (24%, 339/1 435) and KwaZulu-Natal (8%, 123/1 435) provinces. As in previous years, although seasonal prevalence was noted for non-invasive disease (lower numbers of cases identified in the winter months); no overt seasonal pattern was noted with invasive disease (Figure 15).

Non-invasive disease was highest in children younger than five years (452/1 435, 31%) followed by persons aged 35 to 44 years (171/1 435, 12%) and 45 to 54 years (161/1 435, 11%), as shown in Table 25. Invasive disease was most common in persons aged 35 to 44 years (226/1 010, 22%) followed by children younger than five years (165/1 010, 16%) and persons aged 45 to 54 years (149/1 010, 15%). Most invasive cases were identified from blood cultures (74%, 749/1 010) – Table 26.

A total of 2 185 viable isolates were received and serotyped; this included isolates submitted as part of routine laboratory-based surveillance as well as isolates submitted for outbreak investigation purposes. A total of 71 serovars were identified, but two serovars accounted for 79% of the cases: *Salmonella* Enteritidis (1 314/2 185, 60%) and *Salmonella* Typhimurium (421/2 185, 19%). The next most common serotypes were *Salmonella enterica* subspecies *salamae, Salmonella* Hadar, *Salmonella* Muenster and *Salmonella* Isangi (Table 27). Proportions of common serovars differed among provinces, but *Salmonella* Enteritidis was the most common serotype in all provinces (Figure 16). Antimicrobial susceptibility testing was not routinely performed, but offered on request.

Table 24. Number of cases of invasive and non-invasive nontyphoidal salmonellosis by province, South Africa, 2021, n=2 445 (including audit reports)

Province	Non-invasive nontyphoidal salmonellosis	Invasive nontyphoidal salmonellosis	Total
Eastern Cape	141	121	262
Free State	108	44	152
Gauteng	638	380	1 018
KwaZulu-Natal	123	90	213
Limpopo	15	43	58
Mpumalanga	19	41	60
Northern Cape	8	7	15
North West	44	49	93
Western Cape	339	235	574
South Africa	**1 435**	**1 010**	**2 445**

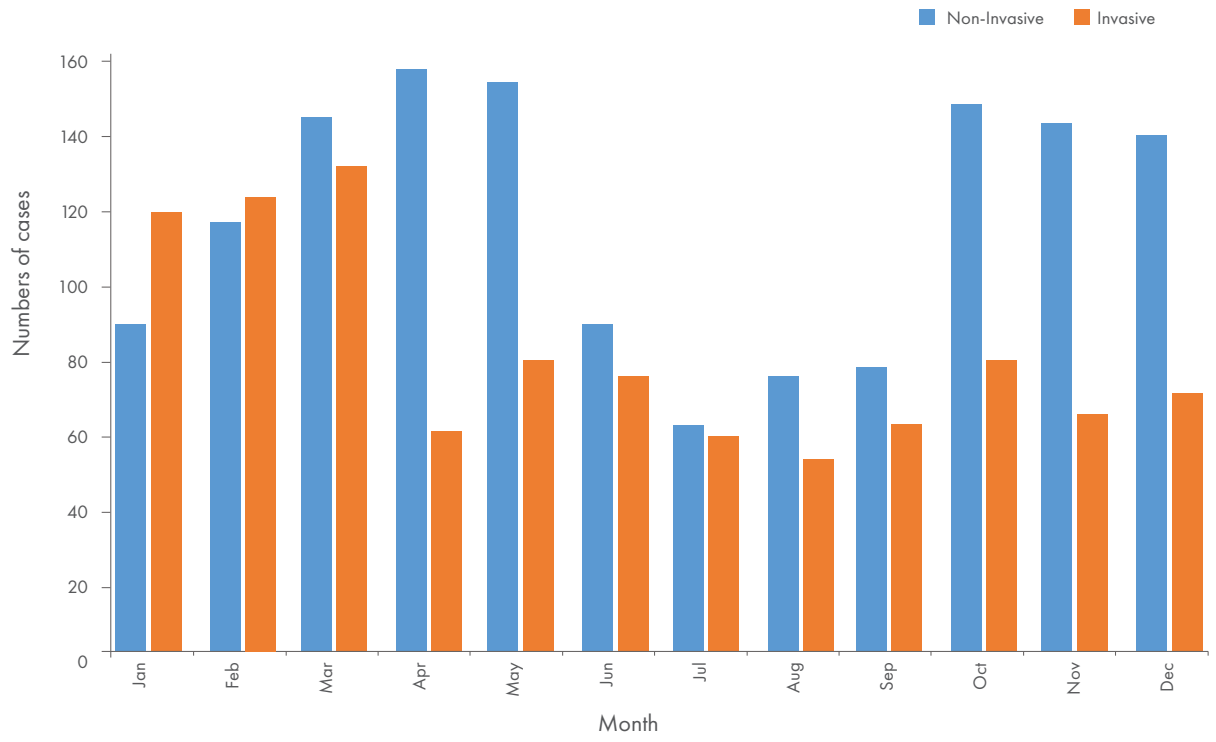


Figure 15. Number of cases of non-invasive (n = 1 435) and invasive (n = 1 010) nontyphoidal salmonellosis by month, South Africa, 2021

Table 25. Number of cases of invasive and non-invasive nontyphoidal salmonellosis by age category, South Africa, 2021, n=2 445 (including audit reports)

Age category (years)	Non-Invasive	Invasive	Total
0 - 4	452	165	617
5 - 14	141	40	181
15 - 24	72	47	119
25 - 34	148	145	293
35 - 44	171	226	397
45 - 54	161	149	310
55 - 64	120	122	242
≥ 65	157	107	264
Unknown age	13	9	22
Total	**1 435**	**1 010**	**2 445**

Table 26. Number of cases of nontyphoidal salmonellosis reported by primary anatomical site of isolation, South Africa, 2021, n=2 445 (including audit reports)

Specimen	n	%
Stool	1 435	58.7
Blood culture	749	30.6
Urine	131	5.4
CSF	6	0.2
Other	124	5.1
Total	**2 445**	**100**

Table 27. Six most common *Salmonella enterica* serovars by province, South Africa, 2021, n=2 185*

Province	*Salmonella* Enteritidis	*Salmonella* Typhimurium	*Salmonella enterica* subspecies *salamae*	*Salmonella* Hadar	*Salmonella* Muenster	*Salmonella* Isangi
Eastern Cape	137	59	8	2	0	2
Free State	74	37	10	0	0	1
Gauteng	600	127	42	13	10	11
KwaZulu-Natal	113	27	4	5	2	1
Limpopo	36	6	4	0	0	3
Mpumalanga	27	4	6	0	0	5
Northern Cape	6	4	1	0	0	0
North West	46	16	2	0	0	0
Western Cape	275	141	6	12	12	0
South Africa	**1 314**	**421**	**83**	**32**	**24**	**23**

*Includes nontyphoidal *Salmonella* isolates from invasive and non-invasive cases

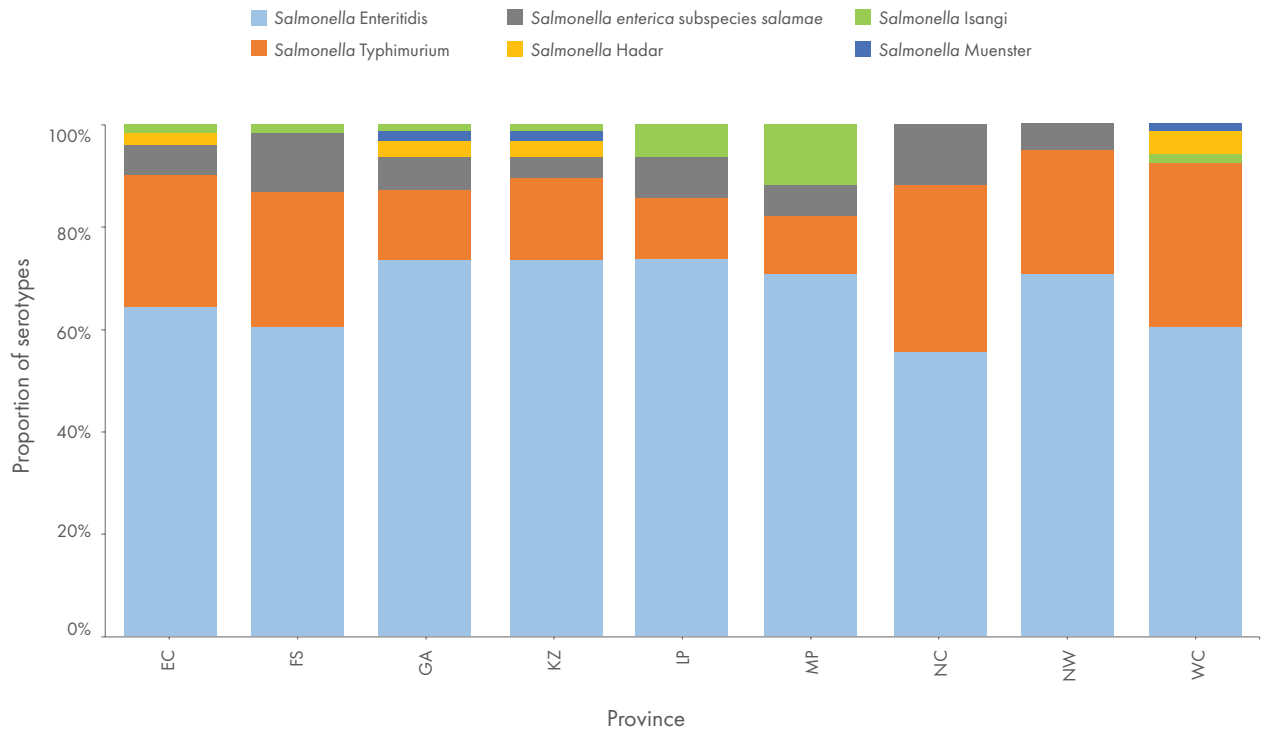


Figure 16. Proportions of the six most common *Salmonella enterica* serovars causing nontyphoidal salmonellosis by province, South Africa, 2021

Discussion

Nontyphoidal salmonellosis is usually foodborne and typically manifests as acute gastroenteritis. Invasive disease is usually associated with HIV infection or the presence of other risk factors.

More cases were reported in 2021 (n=2 445) than in 2020 (n=2 306), but the pattern suggestive of seasonality was largely preserved (Figure 17). As in previous years, although seasonal prevalence was noted for non-invasive disease (increased numbers in the earlier months of the year and low numbers in the winter months), invasive disease showed no seasonality.

Greater numbers of invasive disease reported from Gauteng and Western Cape provinces may reflect healthcare seeking behaviour and clinician testing practices. Children younger than 5 years bear the highest burden of non-invasive disease, but invasive disease was reported more commonly in adults aged 35-44 years; as in previous years, this is likely the effect of a high proportion of HIV-infected cases in this age group.

Salmonella Enteritidis was the predominant serovar, followed by *Salmonella* Typhimurium, a pattern observed since 2012. Provincial differences in serovar proportions might reflect local transmission dynamics or undetected outbreaks, and require further investigation. The noticeable increase in infections with *Salmonella enterica* sub-species *salamae* is unusual and requires monitoring and investigation.

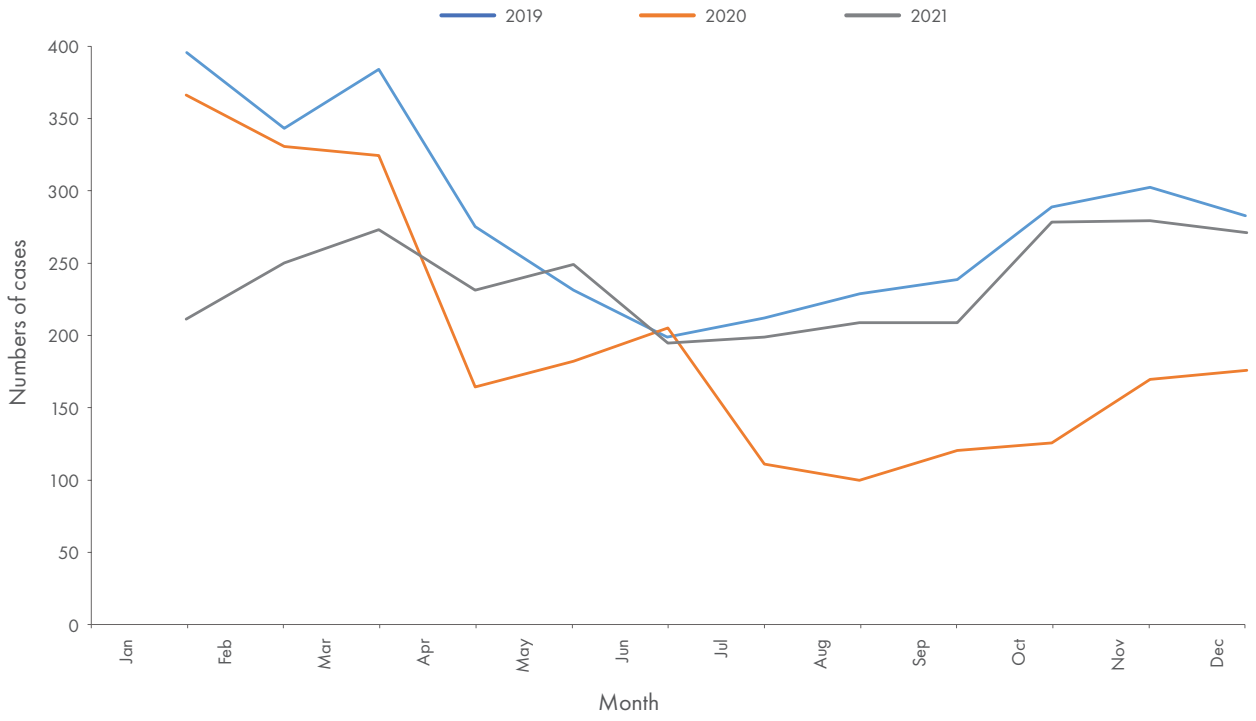


Figure 17. Number of cases of nontyphoidal *Salmonella* by month and year, South Africa, 2019 - 2021

Shigella species

Results

A total of 514 culture-confirmed cases of shigellosis was reported through the surveillance programme in 2021. Most cases (82%, 420/514) were identified in the public health sector (Table 28). The total includes *Shigella* spp. isolated from all sample sites, but in 88% (454/514) of the cases the isolate was recovered from stool or rectal swab samples reflecting non-invasive dysentery or diarrhoea (Table 29); in the remaining 12% of cases, the isolate was recovered from blood or CSF culture (32/514, 7%) or other extra-intestinal sample sites (28/514, 5%).

The highest number of shigellosis cases occurred in January through March (Figure 18). Fifty-five percent of cases were reported from Western Cape Province alone (285/514); Gauteng and KwaZulu-Natal provinces contributed 18% (92/514) and 11% (59/514) of the total cases respectively (Table 29).

Cases of shigellosis were highest in children younger than five years (207/514, 40%) followed by children 5 to 14 years of age (72/514, 14%) – Table 30. The proportion of invasive shigellosis cases remains low (7%), and as in previous years invasive disease was highest in children younger than five years (13/32, 40%).

A total of 392 viable isolates were received and serotyped; this included isolates submitted as part of routine laboratory based surveillance as well as isolates submitted for outbreak investigation purposes. The most common serotype was *S. flexneri* type 2a (140/392, 36%) followed by *S. flexneri* type 1b (64/392, 16%) and *S. sonnei* (62/392, 16%). The next most common serotypes were *S. flexneri* type 4, *S. flexneri* type 3a and *S. flexneri* type 4c (Table 31). Proportions of the serotypes differed among provinces (Figure 19). The predominant serotype differed among provinces; *S. flexneri* type 2a predominated in six provinces. Antimicrobial susceptibility testing was not routinely performed, but offered on request.

Table 28. Number of cases of shigellosis by health sector and province, South Africa, 2021, n=514 (including audit reports)

Province	Private sector	Public sector	Total
Eastern Cape	2	34	36
Free State	18	10	28
Gauteng	56	36	92
KwaZulu-Natal	9	50	59
Limpopo	0	3	3
Mpumalanga	1	2	3
Northern Cape	1	3	4
North West	1	3	4
Western Cape	6	279	285
South Africa	**94**	**420**	**514**

Table 29. Number of non-invasive and invasive or extraintestinal cases of shigellosis by province, South Africa, 2021, n=514 (including audit reports)

Province	Non-invasive	Invasive or extraintestinal	Total
Eastern Cape	31	5	36
Free State	23	5	28
Gauteng	84	8	92
KwaZulu-Natal	48	11	59
Limpopo	2	1	3
Mpumalanga	1	2	3
Northern Cape	2	2	4
North West	2	2	4
Western Cape	261	24	285
South Africa	**454**	**60**	**514**

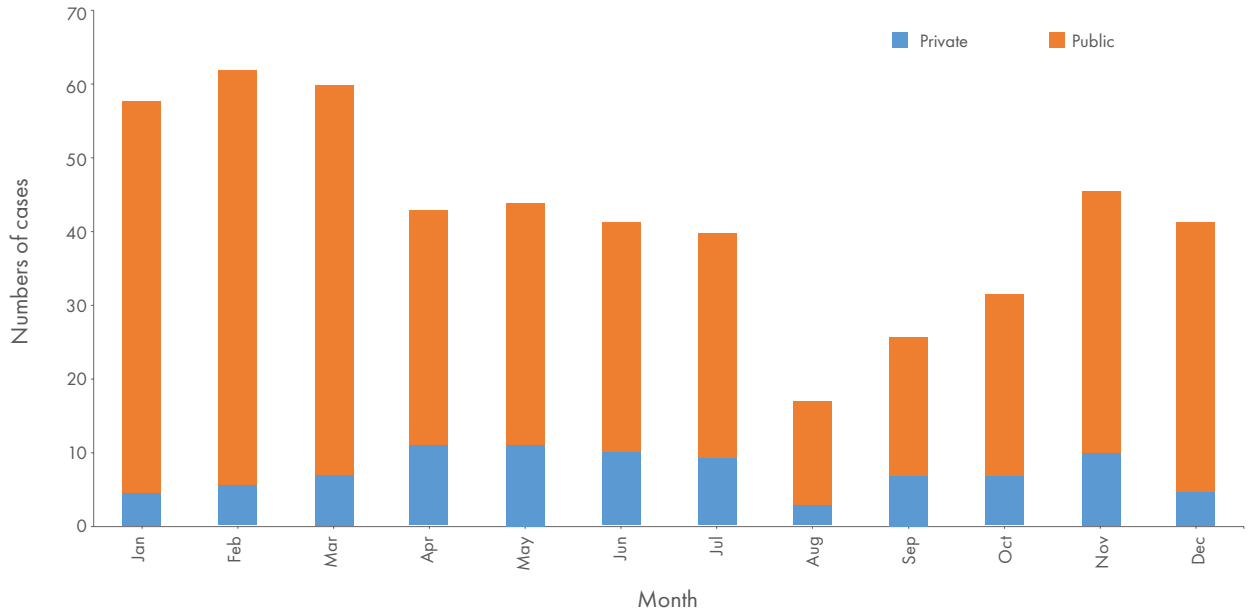


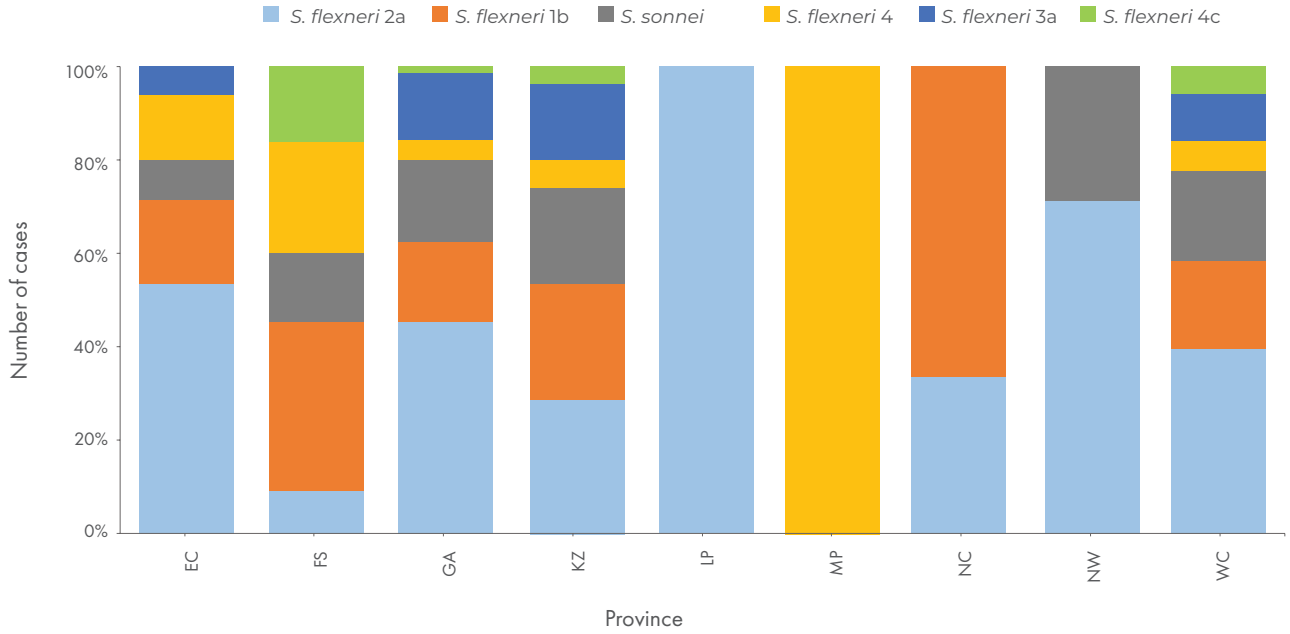
Figure 18. Number of cases of shigellosis by month and health sector, South Africa, 2021, n=514 (including audit reports)

Table 30. Number of non-invasive and invasive or extraintestinal cases of shigellosis reported by age category, South Africa, 2021, n=514 (including audit reports)

Age category (years)	Non-invasive	Invasive or extraintestinal	Total
0 - 4	183	24	207
5 - 14	68	4	72
15 - 24	19	3	22
25 - 34	47	10	57
35 - 44	45	7	52
45 - 54	38	4	42
55 - 64	16	4	20
≥ 65	34	4	38
Unknown age	4	0	4
Total	**454**	**60**	**514**

Table 31. Six most common *Shigella* species (and serotype where applicable) by province, South Africa, 2021, n=392*

Province	*S. flexneri* 2a	*S. flexneri* 1b	*S. sonnei*	*S. flexneri* 4	*S. flexneri* 3a	*S. flexneri* 4c
Eastern Cape	11	4	2	3	1	0
Free State	1	4	1	3	0	1
Gauteng	30	10	16	2	6	1
KwaZulu-Natal	7	5	5	2	4	1
Limpopo	2	0	0	0	0	0
Mpumalanga	0	0	0	1	0	0
Northern Cape	1	2	0	0	0	0
North West	2	0	1	0	0	0
Western Cape	86	39	37	22	18	12
South Africa	**140**	**64**	**62**	**33**	**29**	**15**



*Includes *Shigella* isolates from invasive, extraintestinal and non-invasive cases

Figure 19. Proportions of the most common *Shigella* species and serotypes by province, South Africa, 2021

Discussion

Although *Shigella* infection has been associated with waterborne outbreaks in South Africa, person-to-person transmission plays an important role. Children younger than five-years continue to bear the highest burden of shigellosis. The primary manifestation of disease due to *Shigella* is non-invasive dysentery or diarrhoea, and invasive disease is uncommon.

Fewer cases were reported in 2021 (n=514) than in 2020 (n=698). In contrast to previous years, there was not a typical pattern suggestive of seasonality; usually, increased numbers of cases are identified in the earlier months of the year and lower numbers in the winter months (Figure 20).

S. flexneri type 2a, *S. sonnei* and *S. flexneri* type 1b were the predominant serotypes, in keeping with previous years. Provincial differences in serotype proportions might reflect local transmission dynamics or undetected out-breaks.

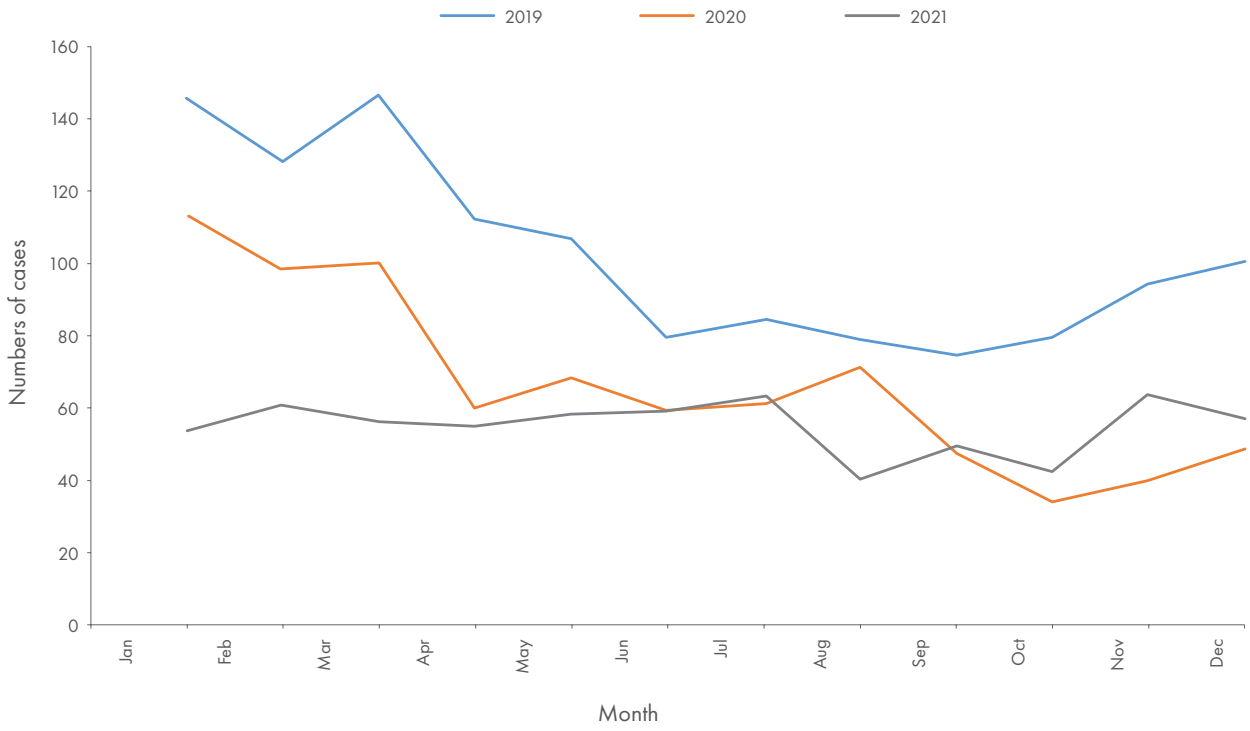


Figure 20. Number of cases of shigellosis by month and year, South Africa, 2019 - 2021 (including audit reports)

Campylobacter species

Results

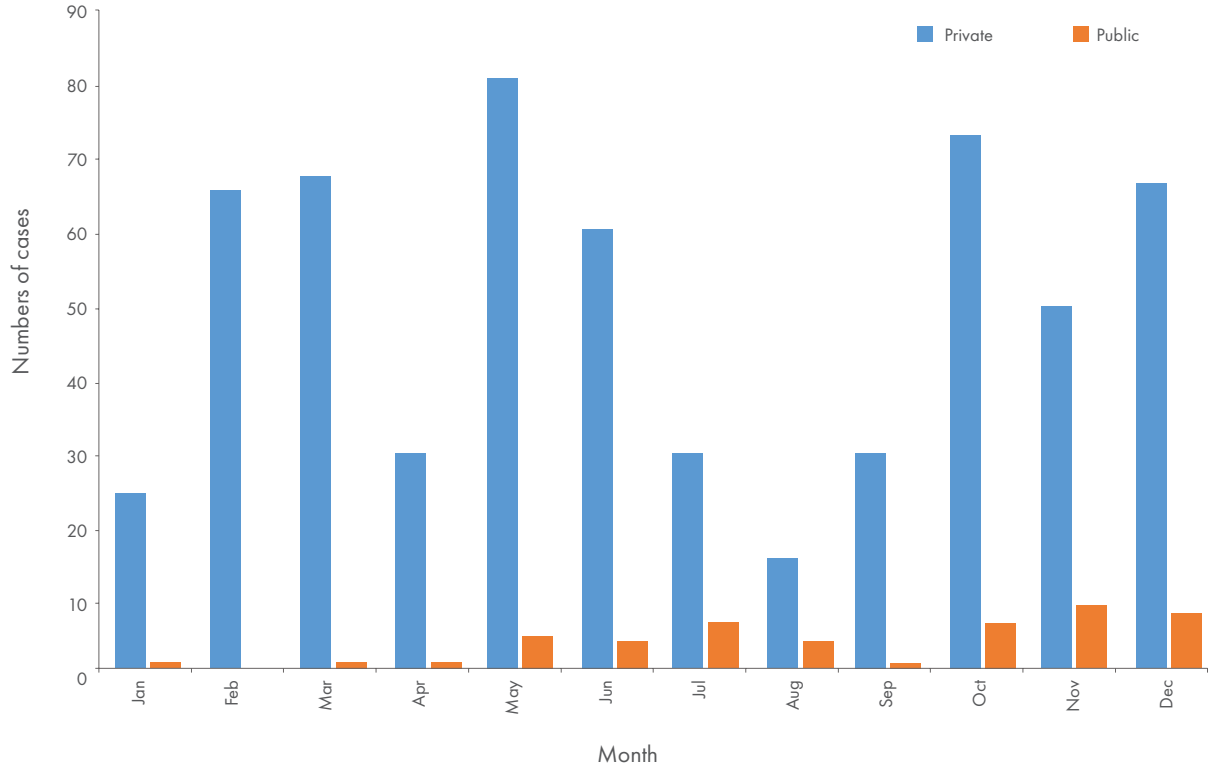
Only cases of campylobacteriosis for which isolates were received from diagnostic laboratories are reported here. Audits were not performed, so cases for which isolates were not submitted are not included in the report.

Of the 655 isolates of *Campylobacter* spp. submitted through the surveillance programme in 2021, 92% (601) were submitted by diagnostic laboratories in the private sector. This includes *Campylobacter* spp. isolated from all sample sites, but in 99% (649/655) of the cases the isolate was recovered from stool or rectal swab samples reflecting non-invasive diarrhoeal disease.

There was no apparent seasonal pattern (Figure 21). Western Cape Province reported the highest number of cases (48%) followed by Gauteng Province (41%); these two provinces alone accounted for 90% of the total cases (Table 32).

Case numbers were highest in children younger than five years (206/631, 31%) - Table 33.

Confirmatory speciation and antimicrobial susceptibility testing have not been completed.



*Only cases of campylobacteriosis for which isolates were received from diagnostic laboratories are reported. Audits were not performed.

Figure 21. Number of cases of campylobacteriosis by month and health sector, South Africa, 2021*

Table 32. Number of cases of campylobacteriosis by health sector and province, South Africa, 2021, n=655*

Province	Private sector	Public sector	Total
Eastern Cape	11	4	15
Free State	38	1	39
Gauteng	266	6	272
KwaZulu-Natal	1	1	2
Limpopo	0	0	0
Mpumalanga	1	0	1
Northern Cape	0	0	0
North West	9	0	9
Western Cape	275	42	317
South Africa	**601**	**54**	**655**

* Only cases of campylobacteriosis for which isolates were received from diagnostic laboratories are reported

Table 33. Number of *Campylobacter* spp. isolates by health sector and age category, South Africa, 2021, n=655

Age category (years)	Private sector	Public sector	n
0 - 4	189	17	206
5 - 14	60	3	63
15 - 24	70	5	75
25 - 34	57	7	64
35 - 44	58	7	65
45 - 54	44	9	53
55 - 64	35	2	37
≥ 65	81	4	85
Unknown age	7	0	7
Total	**601**	**54**	**655**

Discussion

The number of *Campylobacter* spp. isolates submitted by public sector laboratories (54/655, 8%) is very low, and strikingly disproportionate to the size of the population served in comparison to the number of isolates submitted from the private sector. However, audits of NHLS CDW data were not performed and cases in the public sector are therefore underreported. Differences in health-seeking behaviour and diagnostic practices among clinicians in the respective health sectors, as well as differences in laboratory methods utilised for culture of *Campylobacter* spp. from stool samples are also likely contributing factors.

Listeriosis

Listeriosis is classified as a category 1 notifiable medical condition. Reporting of all cases through the notifiable medical conditions (NMC) platform by healthcare workers and laboratorians is mandatory. The Centre for Enteric Diseases runs the active listeriosis surveillance programme, and every notification is followed up by the centre team. For each case, this includes contacting the diagnostic laboratory to facilitate referral of isolate(s), and contacting relevant healthcare professionals or Department of Health officials to facilitate completion of specific listeriosis case investigation forms. GERMS-SA surveillance officers at enhanced surveillance sites assist with completing the case investigation forms for cases identified at their sites.

Results

A total of 76 cases of listeriosis was notified through the NMC surveillance system in 2021. Three provinces reported 84% of the cases: Gauteng (28/76, 37%), Western Cape (26/76, 34%) and KwaZulu-Natal (10/76, 13%) – Table 34. Cases were most common among neonates ≤28 days (34%, 26/76) and adults aged 15 -49 years (34%, 26/76) - Table 35.

Twenty-two of the 76 cases (29%) were detected at ESS, but listeriosis case investigation forms were only completed for 8 cases (36%) at these sites.

Discussion

The number of listeriosis cases for 2021 (76) is below the expected range of annual cases (119-298) based on the estimated incidence of sporadic cases (2-5 cases per million population per year). The distribution of cases by province and age group is similar to that reported in 2019 and 2020.

Table 34. Number and percentage of cases of listeriosis reported from ESS by province, South Africa, 2021, n=22

Province	Total cases	Cases reported from ESS		Completed case reports	
		n	%	n	%
Eastern Cape	3	2	67	1	50
Free State	4	1	25	0	0
Gauteng	28	10	36	3	30
KwaZulu-Natal	10	1	10	0	0
Limpopo	2	2	100	2	100
Mpumalanga	1	0	0	0	0
Northern Cape	1	0	0	0	0
North West	1	0	0	0	0
Western Cape	26	6	23	2	33
South Africa	**76**	**22**	29	**8**	36

Table 35. Number and percentage of cases of listeriosis reported from ESS by age group, South Africa, 2021, n=22

Province	Total number of cases	Cases reported from ES sites	
		n	%
Neonate (≤28 days)	26	4	15
Children (1month-14 years)	0	0	0
Adults (15-49 years)	26	13	50
Adults (50-64 years)	10	3	30
Elderly (≥65 years)	14	2	14
Total	**76**	**22**	29

Vibrio cholerae

Cholera is classified as a category 1 notifiable medical condition. Reporting of all cholera cases (laboratory-confirmed and clinically suspected) through the notifiable medical conditions (NMC) platform by all healthcare workers and laboratorians is mandatory, and every notification is followed up by the Centre for Enteric Diseases team. For each case, this includes contacting the diagnostic laboratory to facilitate referral of isolate/s, and contacting relevant healthcare professionals or Department of Health officials to facilitate completion of a specific cholera case investigation form.

Results

Three cases of *Vibrio cholerae* infection were notified through the NMC surveillance system in 2020. Isolates were received for all cases, and all were confirmed to be nontoxigenic non-O1, non-O139 *V. cholerae*.

Discussion

Cases of nontoxigenic non-O1 non-O139 *V. cholerae* were identified, but these are not considered to be cholera and do not warrant a public health response. The last case of toxigenic *V. cholerae* O1 was identified in 2020.

Rifampicin-susceptible Tuberculosis

Results

COVID-19 still predominated in 2021, hampering our surveillance activities. A total of 249 sputum samples were collected from enrolled participants. Majority of samples received were from KwaZulu-Natal (25%), followed by Gauteng (24%), North West (21%), Eastern Cape (17%), and Mpumalanga (13%) provinces. Cultures were negative in 27% (68/249) of samples processed, and 2% (5/249) were contaminated, precluding further analysis. Valid drug susceptibility results for INH were available for 176 isolates, for which 163 completed CRFs were available for analysis. Eighty percent (141/176) were smear positive. Majority of participants were male (60%) while 61% were HIV positive, of which 63% (62/99) were already on ART. Fifteen percent reported to have at least one episode of previous TB infection, and six percent reported having two or more episodes of previous TB. Twenty-four percent (39/160) reported to have lived with a person diagnosed with TB in the last 12 months. Table 36 shows the comparison of risk factors by INH resistance. Isoniazid resistance was detected in 13 samples; four were from North West and Eastern Cape, two from KZN and Gauteng, and one from Mpumalanga provinces. The overall IMR prevalence was 7.4% [(95% CI: 3.5% - 11.2%)]. Only six participants reported taking TB preventative therapy, none of these participants had INH Resistance.

Table 36. Comparison of risk factors by INH resistance

	INH Sensitive	INH mono R	Full Cohort (n)	p-Value
All lab results	163 (93)	13 (7)	176	
Patients with CRFs	150 (92)	13 (8)	163	
Gender (n=175)				0.29
Male	63 (39)	7 (54)	70 (40)	0.29
Female	99 (61)	6 (46)	105 (60)	
Age Category (n=171)				0.72
<20 years	5 (3)	0 (0)	5 (3)	
20-34 years	56 (35)	6 (50)	62 (36)	
35-49 years	61 (38)	4 (33)	65 (38)	
50+ years	37 (23)	2 (16)	39 (23)	
Province (n=176)				0.526
Eastern Cape	26 (116)	4 (31)	30 (17)	
Gauteng	41 (25)	2 (15)	43 (24)	
KwaZulu-Natal	42 (26)	2 (15)	44 (25)	
Mpumalanga	21(13)	1 (8)	22 (13)	

	INH Sensitive	INH mono R	Full Cohort (n)	p-Value
North West	33 (20)	4 (31)	37 (21)	
Education (completed) (n=81)				0.056
None	2 (3)	1 (6)	3 (4)	
Primary	28 (43)	11 (69)	39 (48)	
Secondary	33 (51)	3 (19)	36 (44)	
Tertiary	2 (93)	1 (6)	3 (4)	
Education (completed) (n=163)				0.179
None	5 (3)	1(8)	6 (4)	
Primary	72 (48)	3 (23)	75 (46)	
Secondary	64 (43)	9 (69)	73 (45)	
Tertiary	9 (6)	0	9 (6)	
Employment (n=163)				0.721
Full-time	26 (17)	2 (15)	28 (17)	
Part-time	6 (4)	0 (0)	6 (4)	
Self-employed	7 (5)	0 (0)	7 (4)	
Unemployed	111 (74)	11(85)	122 (75)	
Healthcare worker (n=163)				0.675
No	148 (99)	13 (100)	161 (99)	
Yes	2 (1)	0 (0)	2 (1)	
Miner (ever) (n=161)				0.329
No	138 (93)	12 (100)	150 (93)	
Yes	11 (7)	0 (0)	11 (7)	
Prisoner (ever) (n=162)				0.111
No	128 (86)	9 (69)	137 (85)	
Yes	21 (14)	4 (31)	25 (15)	
Alcohol frequency (n=163)				0.687
Never/<1 month	118 (79)	11 (85)	129 (79)	
1-4 times per month	24 (16)	2 (15)	26 (16)	
>1 per week	8 (5)	0 (0)	8 (5)	
Smoking (n=163)				0.178
Never	76 (50)	6 (46)	82 (50)	
Former smoker	19 (13)	4 (31)	23 (14)	
Smoker	55 (37)	3 (23)	58 (36)	
Recreational Drug Use (n=163)				0.292
No	122 (81)	9 (69)	131 (80)	
Yes	28 (19)	4 (31)	32 (20)	
HIV status (n=163)				0.957
Negative	58 (39)	5 (38)	63 (39)	
Positive	91 (61)	8 (62)	99 (61)	
Unknown	1 (0.6)	0 (0)	1 (0.6)	
Previous TB episodes (n=176)				0.238
None	129 (79)	10 (77)	139 (79)	
1	26 (16)	1(8)	27 (15)	
>=2	8 (5)	2 (16)	10 (6)	
Previous IPT (n=95)				0.443
No	81 (93)	8 (100)	89 (94)	
Yes	6 (7)	0 (0)	6 (6)	
Lived with someone with TB (n=160)				0.056
No	114 (78)	7 (54)	121 (76)	
Yes	33 (22)	6 (46)	39 (24)	

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, almost two-thirds of the participants were already part of the ARV program. Number of participants reporting TB preventative therapy (TPT) exposure was extremely low, only six of the 99 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 (7.4%) is in keeping with what was found in the National TB drug resistant survey 2012-2014 (5-8%). Unfortunately, the low number of samples received during this surveillance year does not allow for any robust analysis of resistance rates and accurate comparison to previous years. The high smear-positivity is indicative of transmission, particularly in the North West Province. No significant risk factor for INH resistance was detected, however, there is weak evidence of association with previous household contact which needs to be explored. Only four of the 39 participants reported to have a close TB contact were screened, which reveals a gap in the care-cascade that requires strengthening. However, the lack of screening in 2020 and 2021 could also be due to the pressures (staff shortages etc.) of the COVID-19 pandemic. A large proportion of participants were unemployed (75%), an underappreciated factor that has an impact 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.

References

1. Govender N, Quan V, Prentice E, von Gottberg A, Keddy K, McCarthy KM, et al. GERMS-SA: A national South African surveillance network for bacterial and fungal diseases. Johannesburg, South Africa. National Institute for Communicable Diseases; 2006. National Institute for Communicable Diseases. Communicable Disease Surveillance Bulletin, 2015, 13(2). Available from: https://www.nicd.ac.za/assets/files/CommDisBull%2013(2)-June%202015.pdf
2. Statistics South Africa. Mid-year population estimates, South Africa, 2015. P0302. 3 May 2016. Available from: http://www.statssa.gov.za/publications/P0302/P03022019.pdf.
3. Thembisa Model v3.2. Johnson LF, Dorrington RE, Moolla H. Progress towards the 2020 targets for HIV diagnosis and antiretroviral treatment in South Africa. Southern African Journal of HIV Medicine 2017; 18(1): a694.
4. Clinical and Laboratory Standards Institute (CLSI) (2016): Performance standards for antimicrobial susceptibility testing; Twenty-sixth informational supplement. CLSI document M100-S26. Wayne, PA: Clinical and Laboratory Standards Institute.

Syndromic surveillance

Diarrhoeal surveillance

Large scale epidemiological studies evaluating diarrhoeal disease burden showed that rotavirus was the most important cause of disease in children <2 years (1-3). To try to reduce the burden of rotavirus disease in South Africa, the rotavirus vaccine was introduced into the immunization program in August 2009. Subsequent surveillance studies after vaccine introduction have shown a decrease in both rotavirus-specific (54-58% reduction in children <5 years; (4) and all-cause diarrhoea (45-65% reduction in children <12 months and 40-50% reduction in children 13-24 months) (5).

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 (6). 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) (6). In addition, diarrhoeal mortality decreased from 3.5% to 2.9% during the same periods at this site (6). In a Malawian study, the rotavirus vaccine was estimated to reduce overall diarrhoeal mortality by 30% (7).

As diarrhoeal diseases still contribute to morbidity and mortality in children <5 years, research needs to continue. In addition, 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. 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 2021, diarrhoeal disease surveillance was conducted at sentinel sites in three provinces as part of the GERMS-SA surveillance, including: Red Cross Children's Hospital (RCCH), Michells Plain Hospital (MPH), Eastridge Clinic (ERC, Western Cape Province), Pelonomi Hospital (PNH, Free State Province) and Klerksdorp Hospital (KDH, North West Province).

All persons 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 the patient or 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 (commercial EIA and standardised characterisation protocols) and enteric pathogens (commercial molecular detection kits and in-house real-time detection assays) screening at the Centre for Enteric Diseases, NICD.

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 in Kalafong, Mapulaneng and Matikwane hospitals) with the same enrolment criteria and testing were included in the analysis.

Results

A total of 298 stool specimens were screened in 2021 with 20% (59/298) positive for rotavirus. An additional 309 specimens from ANDEMIA sites were screened in 2021 with a rotavirus prevalence of 17% (51/309). Most of the rotavirus cases were detected between April and July (Figure 22) with G2P[4] strains predominant (69% of rotavirus cases) and G3P[8] also circulating (19% of rotavirus cases).

A total of 607 specimens were also screened for other enteric viruses and the following were detected: adenovirus in 25% (152/607); norovirus genogroup I and II in 16% (99/607); sapovirus in 6% (37/607) and astrovirus in 3% (17/607).

Specimens (n=605) were also screened for bacteria and parasites. The prevalence of various enteric pathogens included *Shigella* spp. in 15% (91/605) of cases, *Cryptosporidium* spp. in 10% (63/605), *Campylobacter jejuni/coli* in 10% (59/605), *Clostridioides difficile* in 4% (27/605), *Giardia lamblia* in 3% (21/605) and *Salmonella* spp. in 2% (13/605) of cases. Six Shiga-toxin producing *E. coli* (<1%) cases were also detected.

The majority of the cases enrolled in the GERMS-SA diarrhoeal surveillance were children <5 years (92%; 275/298). In participants >5 years, *Shigella* spp. predominated (22%; 5/23), with adenovirus (9%; 2/23), *Salmonella* spp. (9%; 2/23), norovirus (4%; 1/23) and *Cryptosporidium* spp. (4%; 1/23) also detected.

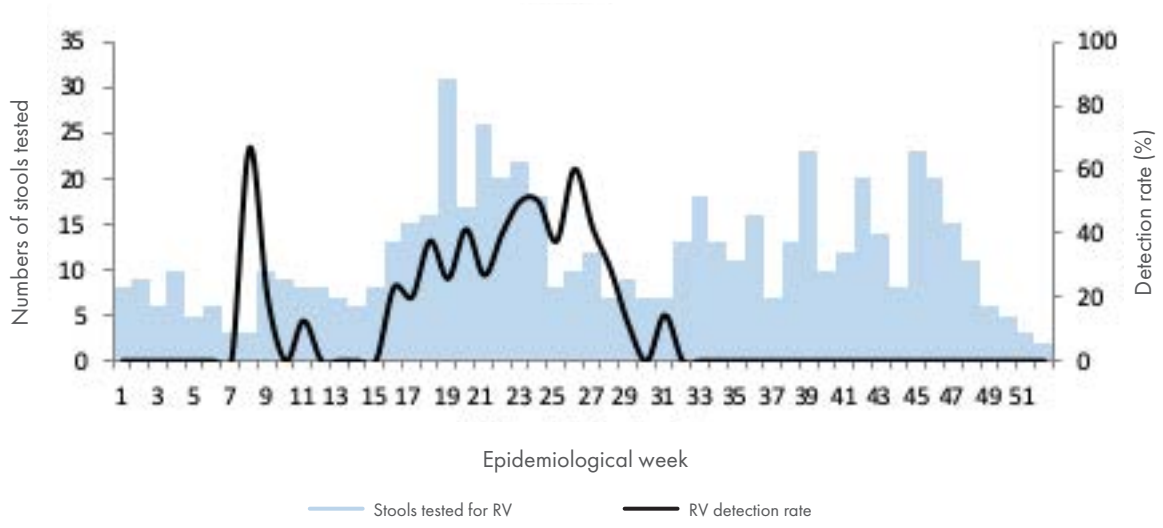


Figure 22. Number of diarrhoeal cases enrolled and the number of rotavirus positive cases per week in 2021.

Discussion

The rotavirus detection rate for 2021 (18%) was much higher than the 6% in 2020 and the 11% in 2019 and 2018 seasons. The season was also earlier in 2021 and longer than the last two years. This was probably partially due to a return to work and school as well as a reflection of sub-optimal vaccination levels during the 2020 SARS-CoV-2 pandemic.

Enteric virus prevalence trends were similar to 2020 levels for adenovirus (24% in 2020) and sapovirus (5% in 2020). However, norovirus prevalence was higher in 2021 (16%) compared to 2020 and 2019 (11%), while astrovirus prevalence was lower than 2020 and 2019 (6% in 2020 and 7% in 2019).

While the prevalence of viral pathogen increased in 2021, the prevalence of bacterial pathogens and parasites was lower than the levels seen in 2020. This may partially due to an increase in the number of cases enrolled in surveillance that could also mirror current trends in healthcare-seeking behaviour. Alternatively, it could reflect a return to pre-pandemic routines with decreased in adherence to non-pharmaceutical interventions like hand washing, social distancing and regular cleaning of frequently touched surfaces.

REFERENCES

1. Liu J, Platts-Mills JA, Juma J, Kabir F, Nkeze J, Okoi C, et al. Use of quantitative molecular diagnostic methods to identify causes of diarrhoea in children: a reanalysis of the GEMS case-control study. Lancet. 2016;388(10051):1291-301.
2. Platts-Mills JA, Babji S, Bodhidatta L, Gratz J, Haque R, Havt A, et al. Pathogen-specific burdens of community diarrhoea in developing countries: a multisite birth cohort study (MAL-ED). Lancet Glob Health. 2015;3(9):e564-75.
3. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): a prospective, case-control study. Lancet. 2013;382(9888):209-22.
4. Msimang VM, Page N, Groome MJ, Moyes J, Cortese MM, Seheri M, et al. Impact of rotavirus vaccine on childhood diarrheal hospitalization after introduction into the South African public immunization program. The Pediatric infectious disease journal. 2013;32(12):1359-64.
5. Groome MJ, Page N, Cortese MM, Moyes J, Zar HJ, Kapongo CN, et al. Effectiveness of monovalent human rotavirus vaccine against admission to hospital for acute rotavirus diarrhoea in South African children: a case-control study. Lancet Infect Dis. 2014;14(11):1096-104.
6. Makgatho E, Patel F, Solomon F, Groome MJ, Lala SG, Vallabh P, et al. The Burden of Acute Diarrheal Disease in Young Hospitalized Urban South African Children Five Years After Rotavirus Vaccine Introduction: A Retrospective Descriptive Study. The Pediatric infectious disease journal. 2019;38(7):752-6.
7. Bar-Zeev N, King C, Phiri T, Beard J, Mvula H, Crampin AC, et al. Impact of monovalent rotavirus vaccine on diarrhoea-associated post-neonatal infant mortality in rural communities in Malawi: a population-based birth cohort study. Lancet Glob Health. 2018;6(9):e1036-e44.

SUMMARY

GERMS-SA, a fundamental laboratory-based surveillance programme in the NICD continues to report pathogen-specific trends. COVID-19 continued to disrupt ongoing surveillance in 2021 in various forms. Face-to-face interaction of surveillance staff and patients was slowly introduced as further easing of restrictions came. There was sustained increase in numbers of GERMS-SA cases as hospital admissions for other diseases, not related to COVID-19, and outpatient consultations increased. The fire at CMJAH at the beginning of 2021 impacted the workload from that hospital. Training and auditing of our surveillance officers data quality is continually done to improve data quality.

Opportunistic infections: For 2021, the laboratory-confirmed **cryptococcosis** incidence risk decreased in all provinces compared to 2020. The in-hospital case-fatality rate continues to be high (40%) despite more than half of patients receiving flucytosine-based induction regimens. **Rifampicin-susceptible TB** surveillance in five provinces, over a limited surveillance time-period, showed 61% of patients being HIV-infected and 63% already on anti-retroviral treatment. Screening of TB contacts requires strengthening but this may have been a consequence of health-care access during the pandemic. A large proportion of participants were unemployed (75%), an underappreciated factor that has an impact on health delivery. For **non-typhoidal salmonellosis**, HIV infection remains to be the single most important risk factor for invasive disease and reported more commonly in adults aged 35-44 years. The noticeable increase in infections with *Salmonella enterica* subspecies *salamae* is unusual and requires monitoring and investigation.

Vaccine-preventable diseases: The 2021 data continue to monitor trends in IPD and Hib, post-EPI vaccine introduction of PCV13 and Hib booster (2009). Incidence of **invasive HI** remains low similar to that of 2019. Infants have the highest incidence of HI, with Hib predominating over HNT. Of children with Hib infection and all HIV-uninfected, vaccine failures continue to be a challenge as many were not fully vaccinated. Overall case-fatality from HI is high with a large proportion of patients with HI meningitis developing long-term sequelae. The national incidence of **invasive pneumococcal disease** remained low compared to pre-COVID-19 years across all age categories. In-hospital mortality from IPD remains high and a third of patients who survived IPD meningitis suffered sequelae. Serotype distribution of IPD is diverse with serotypes 8, 19A and 19F predominating in various age-categories. One fifth of IPD disease in infants and two-fifths in the 1-4 years age-category was caused by serotypes in PCV13. Newer conjugate vaccines such as PCV15 and PCV20 would potentially cover 37% and 57% of current IPD in South Africa, respectively. Healthcare workers and parents need to ensure that all children are up to date with their vaccination schedule. The incidence of early- and late-onset **group B strep** seems low, with large variations by province, possibly due to under-ascertainment of cases through poor blood-culturing practices particularly amongst neonates. Serotype distribution is similar to that reported by other countries, with serotype III and Ia predominating. The organism remains susceptible to first-line antimicrobial agents targeting neonatal sepsis. Mortality is high across all age bands and preterm birth remains a predisposing factor amongst a large proportion of neonates with invasive group B strep.

Epidemic-prone diseases: The incidence of **invasive meningococcal disease** in 2021 was low compared to 2020. Serogroup B was dominant in most provinces and all age groups. Penicillin non-susceptibility decreased to 23%, however all viable isolates were susceptible to third-generation cephalosporins, ciprofloxacin and rifampicin. Risk of developing IMD in creasing as social activities resume to pre-COVID-19 pandemic levels. In 2021, **enteric fever** cases were highest since 2005-2006 outbreaks. All isolates were susceptible to azithromycin and 12% were resistant to ciprofloxacin. Although ***Shigella*** infection has been associated with waterborne outbreaks in South Africa, person-to-person transmission plays an important role. Fewer cases of shigellosis were reported in 2021 than in 2020 and contrary to previous years there was no typical pattern suggestive of seasonality. The number of **listeriosis** cases for 2021 (76) is below the expected range of annual cases (119-298) based on the estimated incidence of sporadic cases (2-5 cases per million population per year). For 2021 through the NMC surveillance system, three cases of **cholera** were reported and confirmed to be nontoxigenic non-O1, non-O139 *V. cholerae*. These reported cases are not considered to be cholera and do not warrant a public health response. There was no apparent seasonal pattern for **campylobacteriosis** cases and highest case numbers were reported in children younger than five years (206/631, 31%). **Invasive group A strep** mostly affects infants and the elderly, with origin of the disease spreading mostly from the skin. In-hospital mortality is high. Isolates are highly susceptible to first line antimicrobial agents, penicillin and erythromycin.

Syndromic surveillance

Diarrhoeal surveillance: The prevalence of viral pathogens increased in 2021 while that of bacterial pathogens and parasites was lower than the levels seen in 2020 probably due to an increase in the number of cases enrolled in surveillance or return to pre-pandemic routines.

PUBLICATIONS

Peer-reviewed GERMS-SA and GERMS-SA-related publications 2021

1. 1. Meiring S, Cohen C, de Gouveia L, du Plessis M, Ganesh K, Kleynhans J, Quan V, Tempia S, von Gottberg A. Hu-man Immunodeficiency Virus Infection Is Associated with Increased Meningococcal Carriage Acquisition Among First-year Students in 2 South African Universities. Clin Infect Dis. 2021 Jul 1;73(1):e28-e38. doi: 10.1093/cid/ciaa521. PMID: 32369560; PMCID: PMC8246797.
2. Bennett JC, Hetrich MK, Quesada MG, Sinkevitch JN, Knoll MD, Feikin DR, Zeger SL, Kagucia EW, Cohen AL, Ampofo K, Brandileone MCC, Bruden D, Camilli R, Castilla J, Chan G, Cook H, Cornick JE, Dagan R, Dalby T, Danis K, de Miguel S, De Wals P, Desmet S, Georgakopoulou T, Gilkison C, Grgic-vitek M, Hammitt LL, Hilty M, Ho PL, Jayasinghe S, Kellner JD, Kleynhans J, Knol MJ, Kozakova J, Kristinsson KG, Ladhani SN, Macdonald L, Mackenzie GA, Mad'arová L, McGeer A, Mereckiene J, Morfeldt E, Mungun T, Muñoz- almagro C, Nuorti JP, Paragi M, Pilishvili T, Puentes R, Saha SK, Khan AS, Savrasova L, Scott JA, Skoczyńska A, Suga S, van der Linden M, Verani JR, von Gottberg A, Winje BA, Yildirim I, Zerouali K, Hayford K. Changes in invasive pneumococcal disease caused by streptococcus pneumoniae serotype 1 following introduction of pcv10 and pcv13: Findings from the pserenade project. Microorganisms 2021 Mar;9(4):696.
3. Knoll MD, Bennett JC, Quesada MG, Kagucia EW, Peterson ME, Feikin DR, Cohen AL, Hetrich MK, Yang Y, Sinkevitch JN, Ampofo K, Aukes L, Bacci S, Bigogo G, Brandileone MCC, Bruce MG, Camilli R, Castilla J, Chan G, Chacón GC, Ciruela P, Cook H, Corcoran M, Dagan R, Danis K, de Miguel S, De Wals P, Desmet S, Galloway Y, Georgakopoulou T, Hammitt LL, Hilty M, Ho PL, Jayasinghe S, Kellner JD, Kleynhans J, Knol MJ, Kozakova J, Kristinsson KG, Ladhani SN, Lara CS, León ME, Lepp T, Mackenzie GA, Mad'arová L, McGeer A, Mungun T, Mwenda JM, Pekka Nuorti J, Nzoyikorera N, Oishi K, De Oliveira LH, Paragi M, Pilishvili T, Puentes R, Rafai E, Saha SK, Savrasova L, Savulescu C, Anthony Scott J, Scott KJ, Serhan F, Setchanova LP, Zorko NS, Skoczyńska A, Swarthout TD, Valentiner-Branth P, van der Linden M, Vestrheim DF, von Gottberg A, Yildirim I, Hayford K, Alarcon P, Almeida SCG, Amin-Chowdhury Z, Ang M, Avdicová M, Bilima S, Born R, Bruden D, Byington CL, Chamorro G, Chow KH, Chuluunbat U, Cohen C, Colzani E, Dalby T, Deceuninck G, Dimina E, du Plessis M, Erlendsdottir H, Gierke R, Gilkison C, Givon-Lavi N, Guevara M, Hasanuzzaman M, Hossain I, Kawabata A, Klein NP, Krause V, Krizova P, Kuch A, Lefebvre B, MacDonald L, Magaziotou I, Mereckiene J, Morfeldt E, Muñoz-Almagro C, Nakamura T, Pelton SI, Pennington K, Ploy MC, Rey-Benito G, Riccardo F, Ricketson LJ, Russell F, Sánchez Eluchans NM, Sanz JC, Suga S, Sutcliffe CG, Thoon KC, Toropainen M, Tzanakaki G, Valenzuela MT, van Sorge NM, Varon E, Verani JR, Winje BA, Zerouali K. Global landscape review of serotype-specific invasive pneumococcal disease surveillance among countries using PCV10/13: The pneumococcal serotype replacement and distribution estimation (PSERENADE) project. Microorganisms. 2021 Apr 2 ;9(4):742. Available from: https://pubmed.ncbi.nlm.nih.gov/33918127/
4. Bennett JC, Hetrich MK, Quesada MG, Sinkevitch JN, Knoll MD, Feikin DR, Zeger SL, Kagucia EW, Cohen AL, Ampofo K, Brandileone MCC, Bruden D, Camilli R, Castilla J, Chan G, Cook H, Cornick JE, Dagan R, Dalby T, Danis K, de Miguel S, De Wals P, Desmet S, Georgakopoulou T, Gilkison C, Grgic-vitek M, Hammitt LL, Hilty M, Ho PL, Jayasinghe S, Kellner JD, Kleynhans J, Knol MJ, Kozakova J, Kristinsson KG, Ladhani SN, Macdonald L, Mackenzie GA, Mad'arová L, McGeer A, Mereckiene J, Morfeldt E, Mungun T, Muñoz- almagro C, Nuorti JP, Paragi M, Pilishvili T, Puentes R, Saha SK, Khan AS, Savrasova L, Scott JA, Skoczyńska A, Suga S, van der Linden M, Verani JR, von Gottberg A, Winje BA, Yildirim I, Zerouali K, Hayford K. Changes in invasive pneumococcal disease caused by streptococcus pneumoniae serotype 1 following introduction of pcv10 and pcv13: Findings from the pserenade project. Microorganisms 2021 Mar;9(4):696.
5. Skosana Z, von Gottberg A, Olorunju S, Mohale T, du Plessis M, Adams T, Mbelle N. Non-vaccine serotype pneumococcal carriage in healthy infants in South Africa following introduction of the 13-valent pneumococcal conjugate vaccine. South African Med J [Internet]. 2021 Feb 1 [cited 2021 Jul 6];111(2):143–8. Available from: https://pubmed.ncbi.nlm.nih.gov/33944725/
6. Quesada MG, Yang Y, Bennett JC, Hayford K, Zeger SL, Feikin DR, Peterson ME, Cohen AL, Almeida SCG, Ampofo K, Ang M, Bar-Zeev N, Bruce MG, Camilli R, Chacón GC, Ciruela P, Cohen C, Corcoran M, Dagan R, De Wals P, Desmet S, Diawara I, Gierke R, Guevara M, Hammitt LL, Hilty M, Ho PL, Jayasinghe S, Kleynhans J, Kristinsson KG, Ladhani SN, McGeer A, Mwenda JM, Pekka Nuorti J, Oishi K, Ricketson LJ, Sanz JC, Savrasova L, Setchanova LP, Smith A, Valentiner-Branth P, Valenzuela MT, van der Linden M, van Sorge NM, Varon E, Winje BA, Yildirim I, Zintgraff J, Knoll MD, Zahin Amin-Chowdhury, Born R, Brandileone MCC, Bruden D, Byington CL, Cameron C, Castilla J, Chan G, Chow KH, Dalby T, Danis K, de Gouveia L, de Miguel S, Deceuninck G, Del Manso M, Díaz J, Dimina E, Erlendsdottir H, Givon-Lavi

N, Kellner JD, Knol MJ, Lefebvre B, Mereckiene J, Muñoz-Almagro C, Napoli D, Nzoyikorera N, Pelton SI, Pennington K, Pilishvili T, Ploy MC, Puentes R, Suga S, Sutcliffe CG, Swarthout TD, Thoon KC, Toropainen M, Vestrheim DF, von Gottberg A. Serotype distribution of remaining pneumococcal meningitis in the mature PCV10/13 period: Findings from the PSERENADE Project. Microorganisms [Internet]. 2021 April 1 [cited 2021 Jul 7];9(4). Available from: https://pubmed.ncbi.nlm.nih.gov/33916227/

7. Nakamura T, Cohen AL, Schwartz S, Mwenda JM, Weldegebriel G, Biey JNM, Katsande R, Ghoniem A, Fahmy K, Rahman HA, Videbaek D, Daniels D, Singh S, Wasley A, Rey-Benito G, de Oliveira L, Ortiz C, Tondo E, Liyanage JBL, Sharifuzzaman M, Grabovac V, Batmunkh N, Logronio J, Heffelfinger J, Fox K, De Gouveia L, von Gottberg A, Du Plessis M, Kwambana-Adams B, Antonio M, El Gohary S, Azmy A, Gamal A, Voropaeva E, Egorova E, Urban Y, Duarte C, Veeraraghavan B, Saha S, Howden B, Sait M, Jung S, Bae S, Litt D, Seaton S, Slack M, Antoni S, Ouattara M, Van Beneden C, Serhan F. The Global Landscape of Pediatric Bacterial Meningitis Data Reported to the World Health Organization–Coordinated Invasive Bacterial Vaccine-Preventable Disease Surveillance Network, 2014–2019. J Infect Dis [Internet]. 2021 Sep 1 [cited 2021 Sep 28];224(Supplement_3):S161–73. Available from: https://pubmed.ncbi.nlm.nih.gov/34469555/
8. du Plessis M, de Gouveia L, Freitas C, Abera NA, Lula BS, Raboba JL, Nhantumbo AA, Jantjies E, Uwimana J, Phungwayo N, Maphalala G, Masona G, Muyombe J, Mugisha D, Nalumansi E, Odongkara M, Lukwesa-Musyani C, Nakazwe R, Dondo V, Macharaga J, Weldegebriel GG, Mwenda JM, Serhan F, Cohen AL, Lessa FC, von Gottberg A. The Role of Molecular Testing in Pediatric Meningitis Surveillance in Southern and East African Countries, 2008-2017. J Infect Dis. 2021 Sep 1;224(Supplement_3):S194-S203. doi: 10.1093/infdis/jiab092. PMID: 34469556;
9. Maphanga TG, Naicker SD, Kwenda S, Muñoz JF, van Schalkwyk E, Wadula J, Nana T, Ismail A, Coetzee J, Go-vind C, Mtshali PS, Mpembe RS, Govender NP; for GERMS-SA. In-vitro antifungal resistance of Candida auris isolates from bloodstream infections, South Africa. Antimicrob Agents Chemother. 2021 Jul 6:AAC0051721.
10. Naicker SD, Magobo RE, Maphanga TG, Firacative C, van Schalkwyk E, Monroy-Nieto J, Bowers J, Engelthaler DM, Shuping L, Meyer W, Govender NP. Genotype, Antifungal Susceptibility, and Virulence of Clinical South Af-rican Cryptococcus neoformans Strains from National Surveillance, 2005-2009. J Fungi (Basel). 2021 Apr 27;7(5):338.
11. Strasheim W, Perovic O, Singh-Moodley A, Kwanda S, Ismail A, Lowe M. Ward-specific clustering of methicillin-resistant Staphylococcus aureus spa-type t037 and t045 in two hospitals in South Africa: 2013 to 2017. PLoS One. 2021 Jun 29;16(6):e0253883. doi: 10.1371/journal.pone.0253883.
12. Blasich NP, Wake RM, Rukasha I, Prince Y, Govender NP. Association of semi-quantitative cryptococcal anti-gen results in plasma with subclinical cryptococcal meningitis and mortality among patients with advanced HIV disease. Med Mycol. 2021 Oct 4;59(10):1041-1047. doi: 10.1093/mmy/myab038.
13. Said H, Ratabane J, Erasmus L, Gardee Y, Omar S, Dreyer A, Ismail F, Bhyat Z, Lebaka T, van der Meulen M, Gwala T, Adelekan A, Diallo K, Ismail N. Distribution and Clonality of drug-resistant tuberculosis in South Africa. BMC Microbiol. 2021 May 28;21(1):157. doi: 10.1186/s12866-021-02232-z. PMID: 34044775; PMCID: PMC8161895.
14. Mphahlele MJ, Groome MJ, Page NA, Bhagwandin N, Mwenda JM, Steele AD. A decade of rotavirus vaccina-tion in Africa - Saving lives and changing the face of diarrhoeal diseases: Report of the 12th African Rotavirus Symposium. Vaccine. 2021 Apr 22;39(17):2319-2324. doi: 10.1016/j.vaccine.2021.03.014.

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