NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

GERMS-SA: ANNUAL SURVEILLANCE REVIEW

Surveillance Officers meeting, 2 – 5 August 2022, Birchwood Conference Centre

2022

GERMS-SA: ANNUAL SURVEILLANCE REVIEW

THE GERMS-SA ANNUAL REVIEW 2022 WAS COMPILED BY THE NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES (NICD), A DIVISION OF THE NATIONAL HEALTH LABORATORY SERVICE (NHLS), JOHANNESBURG, SOUTH AFRICA.

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INTRODUCTION

The National Institute for Communicable Diseases (NICD) reference units report the GERMS-SA surveillance 2022 findings that continue to be appreciated in reporting trends in pathogen-specific data. The beginning of 2022 saw the NHLS laboratories starting on their back foot, with NHLS Diagnostic Media Productions in Sandringham shutting down because of structural challenges. This impacted negatively on the number of isolates received by NICD reference laboratories in terms of numbers and isolate viability. Despite the support of the GERMS-SA rover technician in collecting isolates/samples and plates from the largest Johannesburg hospitals, along with case patient notification reports from the Surveillance Data Warehouse (SDW) and Notifiable Medical Conditions (NMC), the shortage of staff in reference laboratories persisted, affecting the proportion of submitted isolates. Consequently, we were unable to do antimicrobial susceptibility testing and serotyping/serogrouping on these missing isolates. The Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM) requested the submission of *Cryptococcus* spp. isolates to monitor 5-flucytosine from the Western Cape Province and all other laboratories for sites implementing the use of 5FC for cryptococcal meningitis.

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. We thank you for your ongoing service to the health of all South Africans.

METHODS

In 2022, 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*.

The methods applied 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 2022. The estimated population under surveillance in 2022 was at 60.6 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 KwaZulu-Natal (KZN), and laboratories in the private, mining, and military sectors were required to send cryptococcal isolates to the NICD. All other cases of cryptococcosis were detected through 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. Between 2015 and 31 July 2022, no isolates were collected, and all cryptococcal cases were detected through the NHLS SDW. On 1 September 2022, Cryptococcus surveillance for flucytosine susceptibility testing started. Cryptococcus isolates from all NHLS laboratories with flucytosine access sites and all Western Cape Province NHLS laboratories were submitted to the NICD. For this annual report, only cryptococcal data from the current and immediate previous year(s) was analysed. Thus, some fraction of cases reported as incidents in these 2 years might be misclassified because they were not cross-checked against a line list of individuals who had cryptococcal disease or antigenaemia in the years prior to the analysis period. This could lead to an overestimation of the disease incidence in these 2 years.

Enhanced surveillance (ES) was not conducted on any of the enteric pathogens in 2015; however, ES was restarted in 2016 for *Salmonella* Typhi, and in 2019 for Nontyphoidal *Salmonella* species and *Salmonella* enterica serotype Paratyphi A, B, and C. The Centre for Enteric Diseases (CED) runs the active surveillance

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

At ESS, for 2022, surveillance officers completed clinical case report forms electronically using the REDCap database on tablets for patients with eleven laboratory-confirmed diseases: cryptococcosis, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, invasive Group A Streptococcus disease, invasive Group B Streptococcus disease, invasive *Salmonella* Typhi disease, Paratyphi A,B,C, Nontyphoidal diseases (country-wide), Listeriosis (still paper-based) and rifampicin-susceptible TB (in seven provinces), 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. The influence was calculated using mid-year population estimates for 2021 and 2022 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2021 and 2022 using the Thembisa model (Table 1) (3). All reported incidence is expressed as cases per 100 000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test, and p values <0.05 were considered significant throughout. Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand, and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/NHLS. 2022 saw the resignation of two surveillance officers who were not replaced due to posts being frozen.

Table 1. Population denominators used to calculate incidence rates, South Africa, 2021 and 2022

Province	General population*		HIV-infected population**	
	2021	2022	2021	2022
Eastern Cape	6 676 590	6 676 691	821 514	830 855
Free State	2 932 441	2 921 611	377 899	379 618
Gauteng	15 810 388	16 098 571	1 966 032	1 992 630
KwaZulu-Natal	11 513 575	11 538 325	2 040 577	2 052 723
Limpopo	5 926 724	5 941 439	479 493	485 124
Mpumalanga	4 743 584	4 720 497	736 414	748 004
Northern Cape	1 303 047	1 308 734	84 248	85 046
North West	4 122 854	4 186 984	497 375	502 030
Western Cape	7 113 776	7 212 142	478 860	487 388
South Africa	**60 142 978**	**60 604 992**	**7 482 413**	**7 563 419**

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

OPERATIONAL REPORT

Site visits

In 2022, NICD staff members continued with site visits and surveillance training at enhanced surveillance sites and laboratories.

Co-ordination of meetings

GERMS-SA staff training meeting for surveillance officers and research assistants at the Birchwood Conference Centre Johannesburg, 2-5 August 2022: The aim was to give feedback on GERMS-SA surveillance output, as well as to refresh, update, and train staff on current GERMS-SA surveillance projects, including all sentinel syndromic and laboratory-based surveillance programmes. The new head of division was introduced, and challenges with electronic data collection and meeting targets were addressed.

Surveillance audit

A total of 12 995 surveillance cases were detected by GERMS-SA in 2022 (about two-thirds of the previous year's total). Excluding the cases of cryptococcosis (n=4 551), which are all detected by audit, 2 627/8 444 (31%) of cases were detected by audit of the NHLS Corporate Data Warehouse (Table 2), and isolates were not sent to the NICD by the clinical microbiology laboratories (excluding *Cryptococcus* spp.). 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, 2022

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**	4 551/4 551 (100)	728	177	1 026	1 076	373	283	52	288	548	4 551
	Nontyphoidal salmonellosis†	525/1 582 (33)	54	39	191	96	17	40	11	36	41	525
	Shigellosis	66/119 (55)	12	6	12	23	0	3	0	7	3	66
	Meningococcal disease	9/70 (13)	0	1	4	1	0	1	0	0	2	9
	Haemophilus influenzae disease	143/349 (41)	11	7	57	31	7	5	2	6	17	143
	Pneumococcal disease	441/1 859 (24)	44	22	173	94	15	22	19	21	31	441
	Streptococcus pyogenes	452/947 (48)	43	22	145	72	10	20	1	9	130	452
	Streptococcus agalactiae	629/1 086 (58)	20	19	275	176	23	55	4	16	41	629
Non-invasive	Nontyphoidal salmonellosis†	228/1 603 (14)	36	14	57	57	4	9	6	8	37	228
	Shigellosis	134/829 (16)	6	6	38	47	0	2	3	0	32	134
Total (excl crypto and RSTB)		**2 627/8 444 (31%)**										

*Percentage of cases detected by audit = number of cases detected on audit (n1)/total number of cases detected by GERMS-SA (n2) x 100;**All cases of cryptococcal disease are detected by LIS audit and no isolates are received; therefore this disease is excluded from the total; †Excludes cases of *Salmonella enterica* serovars Typhi, and serovars Paratyphi A, B and C; 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 was higher than that in 2021. Although restrictions to the records department were relaxed and surveillance officers resumed face-to-face interviews with patients, poor record systems in many hospitals are still an issue (Table 3); 3 045/ 3 598 (85%) of cases had a case report form (CRF) completed (target=90%). The interview rate remained the same as the previous year, partly due to delayed notifications resulting in patients being discharged before alert, making it difficult for surveillance officers (SOs) to make follow-ups; 1 251 (41%) of the CRFs were completed by patient interview (target=70%). The loss of surveillance staff at sites impacted heavily on consenting and interview rates. Since 2007, enhanced surveillance site operational reports (ESSOR) have been provided to the site co-ordinators, laboratory staff, and SOs 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 SO performance (completion of CRFs). By reviewing these indicators, problems with data collection can be targeted, and recommendations are provided to improve the site's performance. The challenges in providing these reports continued in 2022, 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 the sending of isolates. In addition, there was increased training at sites and strengthened monitoring and evaluation systems.

Table 3. Enhanced surveillance site performance indicators, 2022

Enhanced surveillance site	Case patients, n	Completed case report forms*, n (%)**		Case report forms completed by interview, n (%)***	
Addington	52	44	85	20	45
Charlotte Maxeke Johannesburg Academic	158	137	87	72	53
Chris Hani Baragwanath/ Zola-Jabulani District	663	548	83	267	49
Dr George Mukhari	127	114	90	56	49
Edendale/ Greys'/ Northdale	186	182	98	119	65
Groote Schuur/ Red Cross	315	267	85	101	38
Helen Joseph/ Rahima Moosa Mother & Child	356	320	90	158	49
Kimberley/ Robert Mangaliso Sobukwe	49	25	51	0	0
King Edward VIII	104	82	79	37	45
Klerksdorp/ Tshepong	196	120	61	64	53
Mankweng/ Polokwane/ Seshego	190	166	87	53	32
Pelonomi/ Universitas	112	90	80	43	48
Port Elizabeth/ Dora Nginza/ Livingstone	479	447	93	140	31
RK Khan	107	85	79	36	42
Rob Ferreira/ Themba	129	123	95	40	33
Steve Biko Pretoria Academic/ Tshwane District	172	124	72	27	22
Tygerberg	203	171	84	18	11
Total	**3 598**	**3 045**	**85**	**1 251**	**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. *Increased report form completion rates after re-training SOs and improved monitoring/ evaluating systems at sites. Patient interviews are still low at certain sites due to delayed notifations; therefore, patients were discharged/ demised before the alert. Kimberly shared a post with NMC; therefore, most CRFs were completed by medical reviews (which are a challenge to access); **Target = 90%; ***Target = 70%.

Enhanced surveillance site quality monitoring

In 2022, as per annual performance management and improving quality of data collection, SOs were audited in terms of quality of work. CRFs from a fixed time period were randomly selected for each SO 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 the entry of incorrect data. Data training was done regularly to overcome these errors.

SURVEILLANCE REPORTS

Enhanced surveillance site project

In 2022, 3 598 surveillance case patients were diagnosed at enhanced surveillance sites (Table 3). Of case patients with recorded HIV status, 59% (1 467/2 504) were HIV-infected (Table 4). The proportion of case patients with confirmed HIV infection varied by surveillance disease; unsurprisingly, a very high proportion of patients with AIDS-defining infections like cryptococcosis (97%) were HIV-infected. HIV infection among patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 58%.

Table 4. Numbers and percentages* of patients diagnosed with laboratory-confirmed invasive disease at GERMS-SA enhanced surveillance sites, with confirmed HIV-1 infection **, South Africa, 2022

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	1 076	966	90	940	97	915	97
Neisseria meningitidis	22	17	77	15	88	3	20
Streptococcus pneumoniae^	746	657	88	637	97	368	58
Haemophilus influenzae^	166	140	84	130	93	33	25
Streptococcus pyogenes	504	402	80	383	95	96	25
Streptococcus agalactiae^	525	429	82	399	93	52	13
Total	**3 039**	**2 611**	**86**	**2 504**	**96**	**1 467**	**59**

*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 co-infections counted separately under each pathogen: 2 *Streptococcus pneumoniae* and *Streptococcus agalactiae* mixed episodes, and 2 *Streptococcus pneumoniae* and *Haemophilus influenzae* mixed episodes.

Cryptococcus species

Results

During 2022, 4 821 episodes of laboratory-confirmed cryptococcal disease were reported. This included 4 551 first episodes (among 4 551 patients) and 270 recurrent episodes (among 226 patients) (Table 5). By comparison, 5 149 episodes were reported in 2021, of which 4 939 were incidental and 210 recurrent (among 184 patients). We excluded cases of isolated cryptococcal antigenaemia (i.e. positive blood cryptococcal antigen test without concurrent meningitis, fungaemia, or culture-positive disease elsewhere) from these analyses.

A majority (n=4 444, 98%) of the incident cases were diagnosed as cryptococcal meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), 2% (n=87) as fungaemia (*Cryptococcus* species cultured from blood), and 0.4% (n=20) as culture-positive disease at other sites (Table 6). Between 2021 and 2022, the national incidence risk of laboratory-confirmed cryptococcosis decreased from 66 (95% CI 64-68) to 60 (95% CI 58-62) cases per 100 000 people living with HIV (Table 7). Over these 2 years, incidence risks with overlapping 95% confidence intervals were noted in most provinces except KwaZulu-Natal, where a substantial decrease in incidence was noted. The highest incidence risk in 2022 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 and 40-44 years (Figure 1). Age was known for 3 798 (84%) case patients; the median age was 38 years (interquartile range [IQR], 31-45 years), and children younger than 15 years accounted for 2% of cases (n=83). There were 1 076 case patients with a first episode reported at ESS during 2022, and case report forms were completed by 90% (n=966). Among 940 patients with known HIV status, 97% (n=915) were HIV-seropositive (Table 4). A majority of HIV-seropositive patients (90% [820/915]) had previously received antiretroviral therapy (ART) or were on antiretroviral treatment at the time of their cryptococcal disease diagnosis. The median CD4 cell count recorded close to the time of cryptococcal disease was 36 cells/µl (IQR, 15-73 cells/µl); 93% (760/819) had a CD4 cell count <200 cells/µl. Viral load test results were available for 650 patients; 21% (n=137) had a viral load of <400 copies/mL, 13% (n=89) had viral loads of 400-10 000 copies/mL, and 66% (n=426) had viral loads of >10 000 cop-ies/mL. A majority of the case patients received antifungal therapy in-hospital (89%, 803/907); 52% (401/773) received a flucytosine-containing induction regimen. The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease was 38% (344/913). The in-hospital mortality was higher among individuals who did not receive a flucytosine-containing induction regimen (46% [214/467] compared to those who did (25% [101/398]).

Table 5. Number of incident and recurrent episodes of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA, South Africa, 2021-2022, n=9 970

Year	Cases (incident episodes)	Cases with recurrent episodes	Total recurrent episodes*	Total episodes
2021	4 939	184	210	5 149
2022	4 551	226	270	4 821
Total	**9 490**	**410**	**480**	**9 970**

*Some cases had more than one recurrent episode.

Table 6. Number and percentage of incident cases of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by specimen type, South Africa, 2021-2022, n=9 490

Site of specimen	2021		2022	
	n*	%	n*	%
Cerebrospinal fluid	4 771	97	4 444	98
Blood	154	3	87	2
Other	14	0.3	20	0.4
Total	**4 939**		**4 551**	

*These case numbers exclude 2 721 patients (1 338 in 2021 & 1 383 in 2022) who tested positive for cryptococcal antigenaemia at NHLS microbiology labs.

Table 7. Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by province, South Africa, 2021-2022, n=9 490

Province	2021		2022	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	828	101 (94-108)	728	88 (81-94)
Free State	171	45 (38-52)	177	47 (40-53)
Gauteng	1 016	52 (48-55)	1 026	51 (48-55)
KwaZulu-Natal	1 249	61 (58-65)	1 076	52 (49-56)
Limpopo	427	89 (81-97)	373	77 (69-85)
Mpumalanga	339	46 (41-51)	283	38 (33-42)
Northern Cape	47	56 (40-72)	52	61 (45-78)
North West	293	59 (52-66)	288	57 (51-64)
Western Cape	569	119 (109-129)	548	112 (103-122)
South Africa	**4 939**	**66 (64-68)**	**4 551**	**60 (58-62)**

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

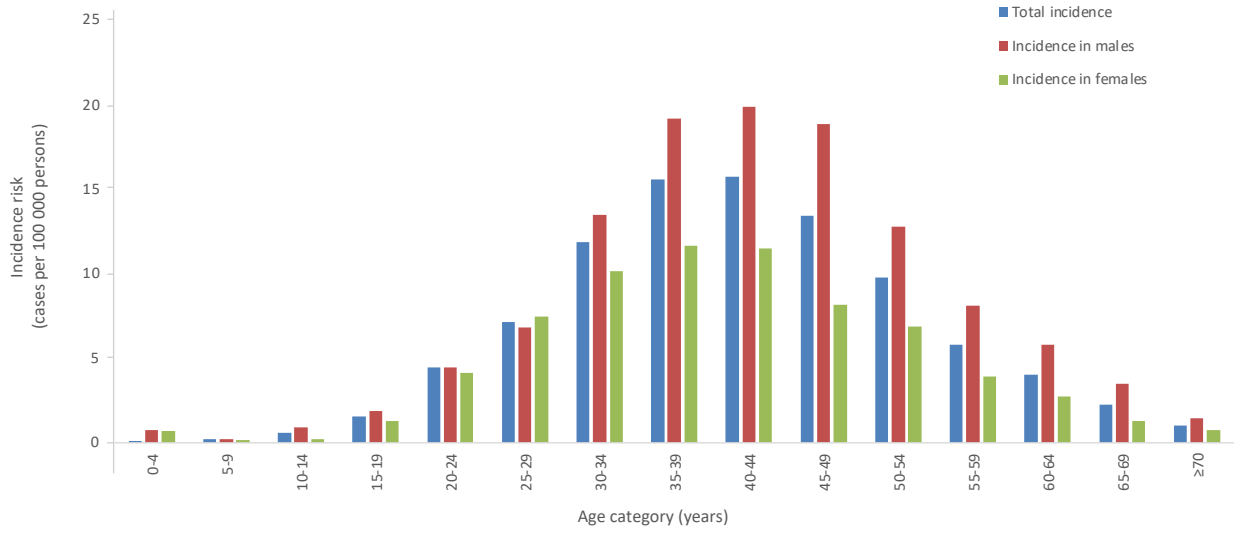

Figure 1. Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA , by sex and age group, South Africa, 2022, n= 3 798

Discussion

In 2022, the national incidence risk for cryptococcal meningitis or culture-confirmed cryptococcal disease decreased compared to the previous year. This decline was most marked in KwaZulu-Natal Province. This decrease in new cases may be explained by individuals initiating ART earlier before they are at risk for opportunistic infections or by screening and pre-emptive treatment of patients with cryptococcal antigenaemia through the reflex CrAg programme. However, the total number of episodes (including recurrent disease) did not change substantially. The burden on the healthcare system therefore persists, with many thousands of patients annually requiring hospital admission for management of cryptococcosis. The South African standard treatment guidelines were updated in mid-2022 to recommend 1 week of flucytosine and amphotericin B deoxycholate followed, by a week of high-dose fluconazole as induction for cryptococcal meningitis. The in-hospital mortality for patients at GERMS-SA ESS remained high in 2022, particularly among those who did not receive flucytosine-based induction therapy. Regimens containing flucytosine are preferred due to the survival benefits demonstrated in randomised-controlled trials and observational studies. However, there was a concerning drop in the proportion of patients at ESS receiving flucytosine-based induction through a national access programme, decreasing from 62% in 2021 (data not shown) to 52% in 2022. This decline could be attributed to clinicians' reluctance to prescribe flucytosine, a lack of awareness regarding its benefits and/or availability, or issues related to stock shortages. Urgent steps are needed to enhance access to, and promote the use of flucytosine. The former will be remedied by the inclusion of flucytosine in the national tender for Supply and Delivery of Anti-infective Medicines from October 2023.

Neisseria meningitidis

Results

In 2022, 70 laboratory-confirmed invasive meningococcal disease (IMD) episodes were reported through the GERMS-SA surveillance programme. Twenty-nine viable isolates were sent to the NICD for further characterisation, 32 episodes were diagnosed through molecular methods only, and nine cases were detected through an audit of the NHLS laboratory information system (Table 2). The incidence of IMD in South Africa for 2022 was 0.12 per 100 000 population (Figure 2), ranging between provinces from 0.35 episodes per 100 000 in the Western Cape to 0.04 in Mpumalanga (Table 8). The highest incidence was reported in infants (<1 year of age) at 1.6 episodes per 100 000, followed by children 1-4 years of age (0.31 per 100 000) - (Figure 3). No clusters were reported during 2022 and most episodes occurred in the winter through spring months (Figure 4). Most episodes were diagnosed from cerebrospinal fluid (45/70, 64%), and the rest from blood cultures (Table 9). Where sex was known, there were more males (61%, 41/67) with IMD than females. Where serogrouping could be done (45/70, 64%), serogroup B (15), Y (14) and W (11) were most common (Table 10). Among infants, serogroup B was dominant (incidence 0.60 per 100 000), whereas among persons 15-24 years old, most episodes were serogroup Y (incidence 0.07 per 100 000) - (Figure 5). Of 29 viable isolates, 45% (13/29) were susceptible to penicillin, 52% (15/29) had intermediate susceptibility (penicillin minimum inhibitory concentrations (MIC) between 0.094 and 0.25µg/ml), and one was penicillin resistant (MIC 0.38µg/ml). Two isolates were ciprofloxacin resistant (7%, 2/29, ciprofloxacin MIC >0.12µg/ml, one serogroup Y and one serogroup W, both were rifampicin sensitive, penicillin intermediate and nalidixic acid resistant). All viable isolates were susceptible to third-generation cephalosporins, and rifampicin.

In 2022, 77% (17/22) of IMD episodes reported from GERMS-SA enhanced surveillance site hospitals had clinical data collected (Table 4). Median age was 2 years (range 2 months to 64 years) and patients stayed a median of eight days in hospital (interquartile range 3-12 days). The majority of patients were admitted with meningitis (94%, 16/17). In-hospital case-fatality was 12% (2/17). One patient with bacteraemia died and one with meningi-tis. Twenty percent (3/15) of persons were HIV-coinfected (Table 4). Five patients (33%, 5/15) were discharged with sequelae, two of whom had multiple sequelae. These included five persons with neurological fallout, one with new onset seizures and one with necrotic skin lesions.

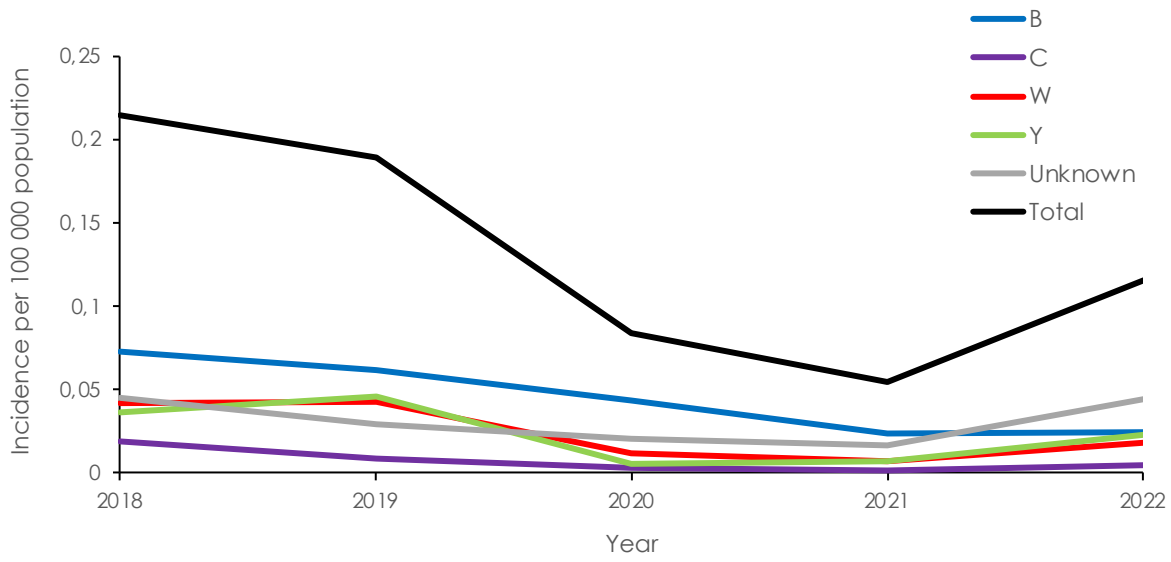

Figure 2. Incidence of invasive meningococcal disease by serogroup, South Africa, 2018-2022 (n=388)

Table 8. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2019-2022, n=264 (including audit cases)

Province	2019		2020			2021		2022
	n*	Incidence risk (95% CI)†	n*	Incidence risk (95% CI)†	n*	Incidence risk (95% CI)†	n*	Incidence risk (95% CI)†
Eastern Cape	12	0.18	6	0.09	5	0.07	5	0.07
Free State	3	0.10	0	0.00	0	0.00	3	0.10
Gauteng	37	0.24	10	0.06	8	0.05	23	0.14
KwaZulu-Natal	13	0.12	4	0.03	3	0.03	6	0.05
Limpopo	2	0.03	1	0.02	0	0.00	3	0.05
Mpumalanga	1	0.02	1	0.02	1	0.02	2	0.04
Northern Cape	1	0.08	0	0.00	0	0.00	1	0.08
North West	4	0.10	1	0.02	1	0.02	2	0.05
Western Cape	38	0.56	27	0.39	15	0.20	25	0.35
South Africa	**111**	**0.19**	**50**	**0.08**	**33**	**0.05**	**70**	**0.12**

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

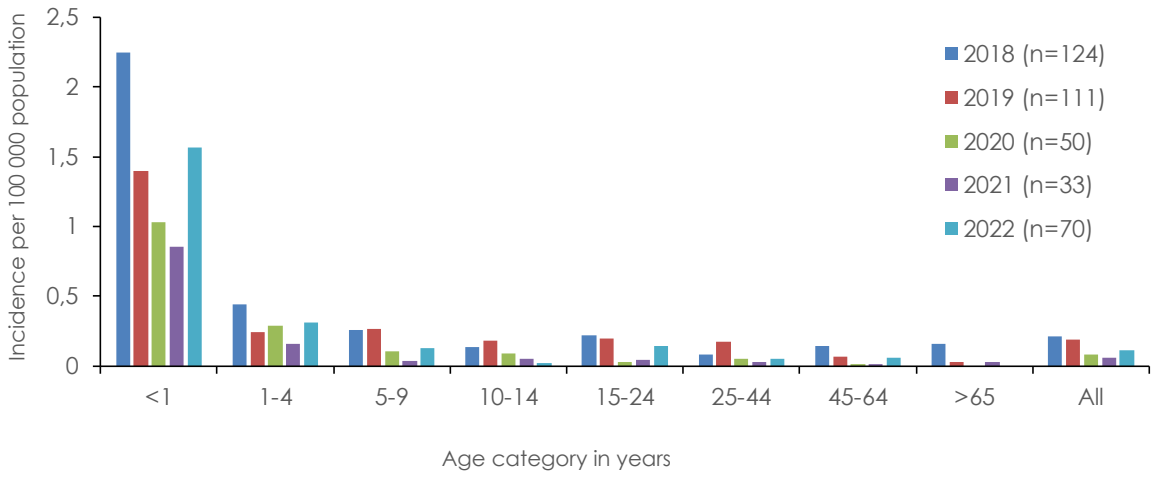

Figure 3. Incidence of invasive meningococcal disease by age-category, South Africa, 2018-2022 (n=388)

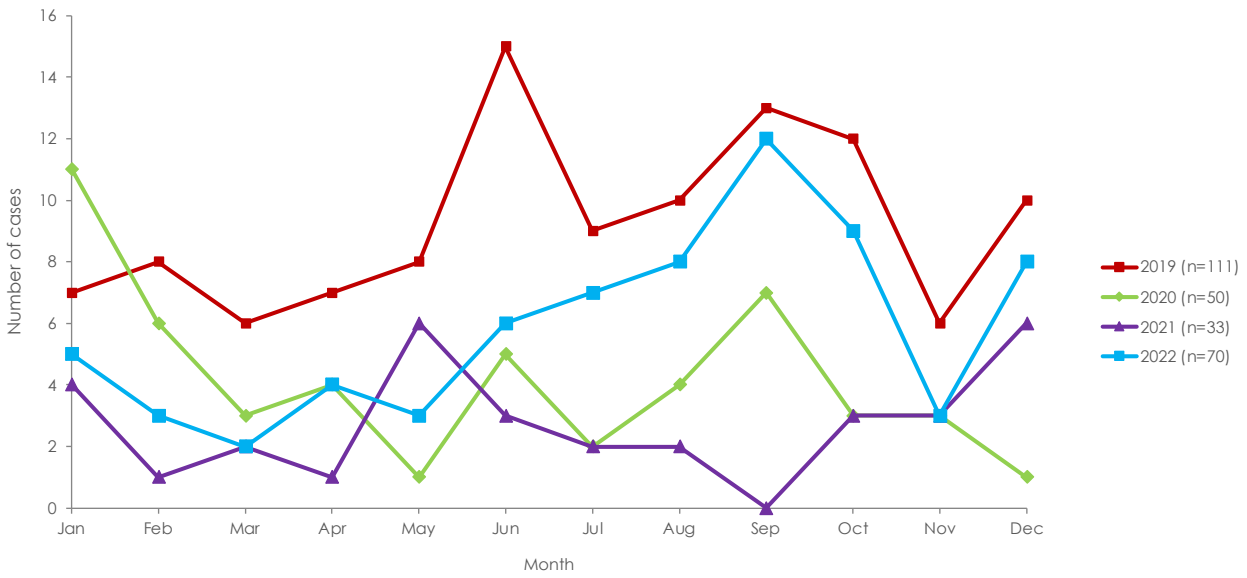

Figure 4. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2019-2022, n=264

Table 9. Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2019-2022, n=264

Site of specimen	2019		2020		2021		2022	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	70	63	24	48	20	61	45	64
Blood	41	37	26	52	13	39	25	36
Other	0	0	0	0	0	0	0	0
Total	**111**		**50**		**33**		**70**	

Table 10. Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2022, n=70*

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	E**	Total
Eastern Cape	1	0	3	0	1	0	0	0	5
Free State	1	0	1	0	1	0	0	0	3
Gauteng	16	0	0	0	3	4	0	0	23
KwaZulu-Natal	2	0	3	1	0	0	0	0	6
Limpopo	0	0	0	0	0	3	0	0	3
Mpumalanga	1	0	1	0	0	0	0	0	2
Northern Cape	0	0	1	0	0	0	0	0	1
North West	0	0	0	1	0	1	0	0	2
Western Cape	6	0	6	1	6	6	0	0	25
South Africa	**27**	**0**	**15**	**3**	**11**	**14**	0	0	**70**

*43 (61%) with viable isolates or specimens available for serogrouping/ genogrouping. There were no non-groupable meningococcal isolates causing invasive disease in 2022.

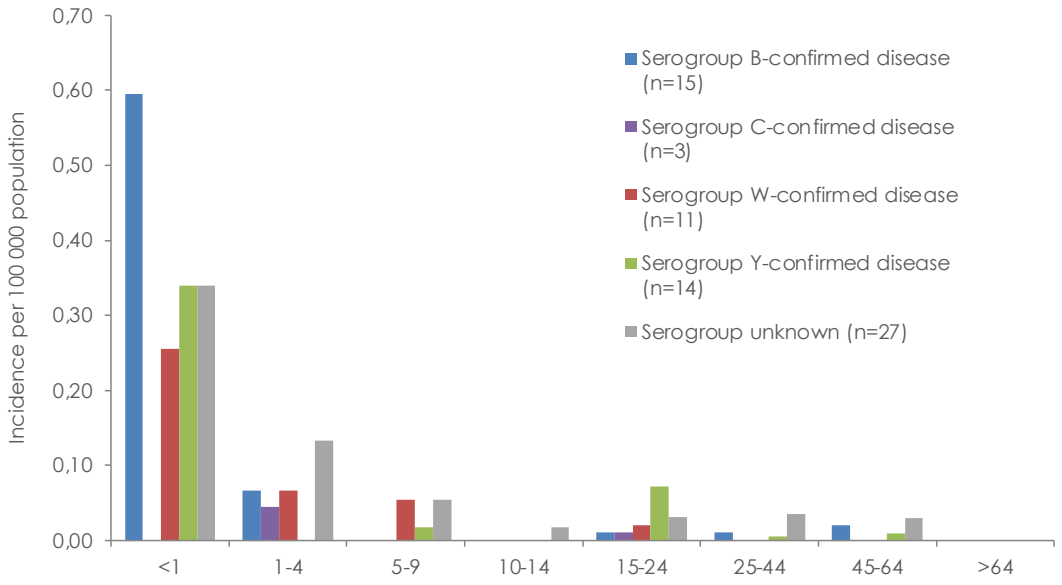

Figure 5. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2022, n=70 (**specimens or viable isolates unavailable for serogrouping n=27)**

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

Discussion

In 2022, IMD incidence was double that in 2021 but had not yet reached the 2019 incidence rate (pre-COVID-19 pandemic). Although many episodes did not have a serogroup reported, the incidence of all circulating serogroups increased from 2021 to 2022, with serogroups B, W, and Y occurring in equal numbers in the Western Cape Province (the province with the highest burden of disease). The increase in penicillin non-susceptible isolates is concerning, and these isolates (including the two ciprofloxacin-resistant isolates) will be sequenced for further analysis. However, up until 2021, penicillin non-susceptibility was due to the presence of various penA mosaics, which were present in a variety of lineages; therefore, the increase is unlikely to be due to the expansion of a single lineage/clone. IMD is a serious infection with a high case-fatality, and a third of those surviving to discharge developed long-term sequelae. Clinicians are urged to consider the diagnosis in any person presenting with fever and/or headache with rapid clinical deterioration. On suspicion of IMD, immediate initiation of third-generation cephalosporin or high dose intravenous penicillin is still recommended.

Haemophilus influenzae

Results

In 2022, 349 episodes of invasive *Haemophilus influenzae* (HI) disease were identified through the GERMS-SA surveillance programme: 156 (45%) viable isolates were received at the NICD reference laboratory, 50 (14%) were detected through molecular testing only, and 143 (41%) were detected through an audit of the NHLS laboratory information system (Table 2). Four episodes were co-infected with *Streptococcus pneumoniae*, one cultured from cerebrospinal fluid and three cultured from blood specimens. In South Africa, the incidence of invasive HI was 0.58 per 100 000 population, ranging from 1.59 per 100 000 in the Western Cape to 0.11 in Mpumalanga Province (Figure 6 and Table 11). Of the 177 episodes with a known serotype, the majority were non-typeable (HNT, 112), followed by type B (Hib, 42). Most HI occurred in infants <1 year (6.38 episodes per 100 000 population), and HNT had the highest serotype-specific incidence for all age categories, except ages 1-4 years, where Hib was more common (Figures 7 and 8). Among all HI episodes and from all serotypes, blood was the most common specimen type (229/349, 66%) - (Table 12). Eight percent (12/156) of HI cases were non-susceptible to ampicillin; this included 17% (6/36) of Hib, 4% (4/100) of HNT, and 10% (2/20) of serotype F episodes with ampicillin MICs >1mg/L.

At enhanced surveillance sites, 84% (140/166) of HI episodes had clinical information collected. The median admission time was 10 days (interquartile range (IQR) 4-19 days).

Twenty-four percent (33/140) of patients died in hospitals, with a median time to death of two days (IQR 1-12 days) from the specimen collection date. Deaths occurred in patients of all serotypes and all age categories. Case-fatality increased with increasing age (ranging from 18% (6/34) among infants <1 year to 38% (3/8) among those >64 years, p=0.982). A quarter of persons with HI infection with a known HIV status were living with HIV (33/130) - (Table 4). Conditions other than HIV predisposing to HI disease were reported in 54% of (76/140) patients; the most common conditions included ever having tuberculosis (13%, 18), prematurity (32% of infants, 11/34), malignancy (6%, eight), chronic lung disease (5%, seven), and diabetes (4%, six). Twenty (14%, 20/140) HI episodes at ESS were diagnosed as meningitis. Of these, three patients died (15%, 3/20), and 18% (3/17) of survivors suffered sequelae at discharge from the hospital. All three had hydrocephalus, including one child with new onset seizures and visual loss.

Among 10 children <15 years admitted to ESS with Hib infection, Hib conjugate vaccination history was available for seven children. All seven were HIV-uninfected and had no reported underlying risk factors for HI disease. Two (29%, 2/7) children had never received any Hib vaccine although they were eligible age-wise, and five had received at least one dose. Of the five, two children had received three doses of the Hib vaccine and were not yet eligible for the 18-month booster dose, one child had received two doses but skipped the 14-week dose, and two had only received their 6-week dose yet were old enough to have received further doses of the vaccine.

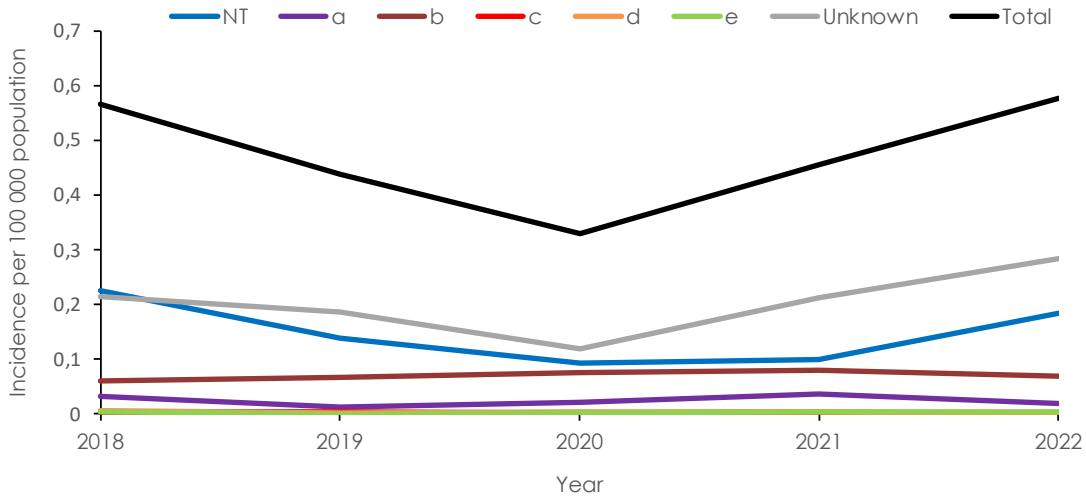

Figure 6. Incidence of invasive *Haemophilus influenzae* disease by serogroup, South Africa, 2018-2022 (n=1 404)

Table 11. Number of cases and incidence of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2022, n=349*

Province	Serotype									
	Serotype not available	A	B	C	D	E	F	Non-typeable	Total	Incidence per 100 000 population**
Eastern Cape	12	4	6	0	0	0	2	17	41	0.61
Free State	7	0	3	0	0	0	1	4	15	0.51
Gauteng	71	4	10	0	0	0	3	20	108	0.67
KwaZulu-Natal	34	0	3	0	0	0	0	6	43	0.37
Limpopo	9	0	1	0	0	0	0	0	10	0.17
Mpumalanga	5	0	0	0	0	0	0	0	5	0.11
Northern Cape	3	0	0	0	0	1	0	1	5	0.38
North West	6	0	0	0	0	0	0	1	7	0.17
Western Cape	25	4	19	0	0	1	3	63	115	1.59
South Africa	172	12	42	0	0	2	9	112	349	0.58

*177 (51%) 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.

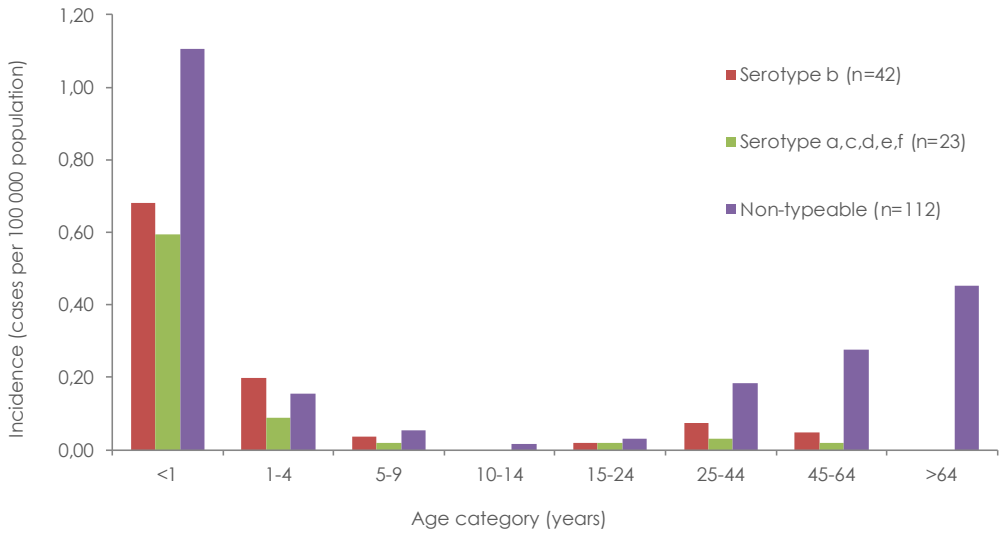

Figure 7. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype, South Africa, 2022, n=349 (age unknown, n=14; isolates unavailable for serotyping, n=172)

*177 (51%) 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.

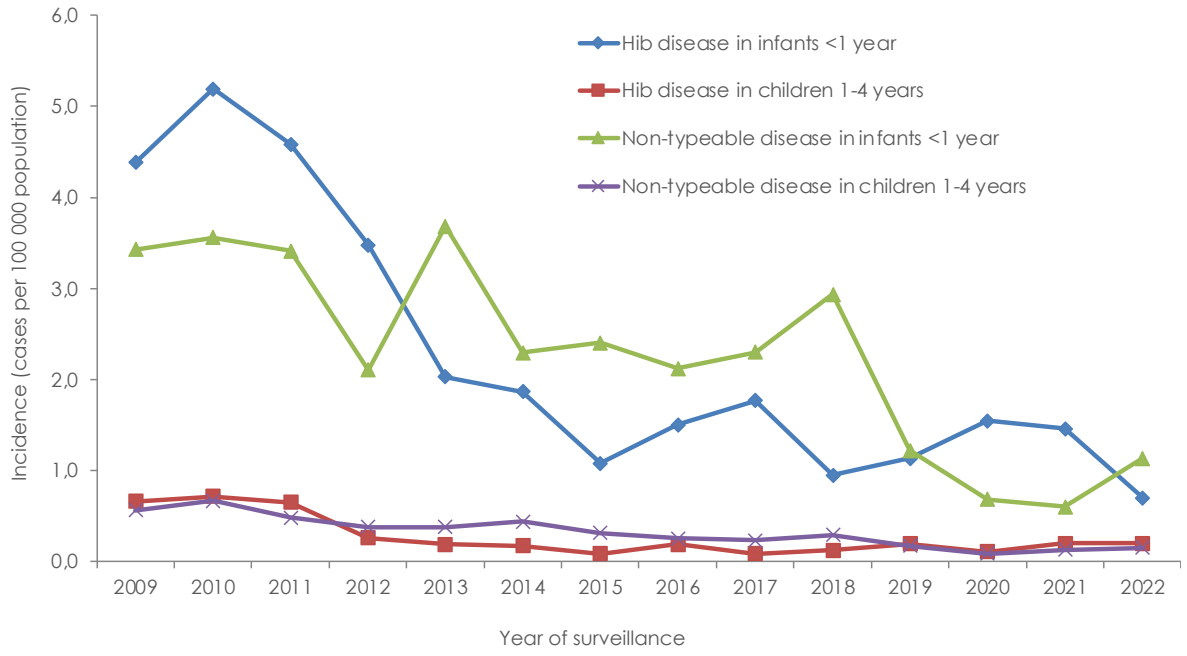

Figure 8. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b and non-typeable disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2022

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

Table 12. Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2022, n=349

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	23	13	19	45	9	39	8	7
Blood	109	63	22	52	14	61	84	75
Other	40	23	1	2	0	0	20	18
Total	**172**		**42**		**23**		**112**	

Discussion

Invasive HI disease in 2022 has returned to pre-COVID-19 pandemic levels, with non-typeable disease dominating in almost all age categories. Case-fatality was high for all episodes of HI infection, and many with meningitis suffered long-term sequelae. Over half the people with HI disease had some sort of predisposing condition. Hib disease has continued to decline in children <1 year, however, we noted that almost a third of children with Hib disease had missed all their age-eligible doses of Hib vaccine, and over 40% had skipped at least one dose. Primary Hib vaccination and booster doses are important in preventing invasive Hib in the community, particularly among premature infants.

Streptococcus pneumoniae

Results

In 2022, 1 859 episodes of invasive pneumococcal disease (IPD) were reported to the GERMS-SA surveillance programme: 1 144 (62%) viable isolates were sent to the NICD reference laboratory for further characterisation, 274 (15%) were identified at NICD through molecular testing only, and 441 (24%) were detected through the NHLS laboratory information system (Table 2). Incidence of IPD was 3.1 per 100 000 population in South Africa, lower than the pre-COVID-19 pandemic incidence in 2019 of 4.0 per 100 000 (Table 13). The incidence in the Western Cape Province (9.8 per 100 000) was three times higher than the national incidence, while in other provinces, IPD incidence ranged between 1.1-3.2 per 100 000 (Table 13). By age category, incidence peaked in infants (<1 year, 12.9 per 100 000), with a second peak in adults 45-64 years of age (4.7 per 100 000) - (Figure 9). Where sex was known, 53% (960/1 821) were male. Most episodes were diagnosed from blood specimens (71%, 1 311/1 859) and cerebrospinal fluid (23%, 425/1 859) - (Table 14). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was demonstrated in 35% (398/1 144) of all cultured isolates (Table 15). Persons from KwaZulu-Natal (46%, 23/50) and children 1-4 years of age (63%, 45/72) had the highest proportion of non-susceptible isolates (Table 15 and Figure 10). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 8% (94/1 144) of isolates from all specimen types. The top three serotypes occurring in children <5 years included serotypes 19F, 8 and 3, while in those >5 years, serotypes 8, 19A, and 3 dominated (Figures 11a and 11b). Overall, the potential coverage of serotypes in the 13-valent pneumococcal conjugate vaccine was 31% (435/1 392) and 60% (842/1 392) for the 23-valent polysaccharide vaccine (Figure 12 and Table 16). This fluctuated with the different age categories and the various vaccine formulations.

At enhanced surveillance sites (ESS), 88% (657/746) of persons with IPD had clinical data collected. Patients were hospitalised for a median of 6 days (interquartile range (IQR): 1-13 days). In-hospital case-fatality was 33% (217/655) and increased to 54% (27/50) among those >64 years. Most deaths occurred within 2 days of specimen collection (IQR 1-6 days). Of those with known status, 58% (368/637) were HIV infected. Thirty-three percent (15/45) of infants with maternal HIV-status available were HIV-exposed (four babies were HIV-infected and 11 were HIV-uninfected). Fifty-three percent (346/655) of patients had a condition/risk factor (excluding HIV infection) predisposing them to IPD. The top five factors included: history of smoking (17%, 113 persons), ever having tuberculosis (17%, 113), alcohol abuse (7%, 49), diabetes (7%, 47), and chronic lung disease (4%, 29).

Of 125 people at ESS with pneumococcus detected in CSF, 48% (60/125) died during their hospitalisation, and 26% (17/65) who survived to discharge suffered at least one sequelae upon discharge (four persons had >1 sequelae). Sequelae included new-onset seizures (eight), limb weakness/paralysis (five), necrotic skin lesions (three), hearing loss (three), amputation (two), and vision loss (one).

Eighteen children <10 years of age at ESS had IPD caused by serotypes present in PCV13; these included nine serotypes 19F, four serotypes 3, three serotypes 19A, and one each for serotypes 4 and 6A. Vaccination history was unavailable for four children: one child (13 months old) had not received any PCV13 doses, two babies were too young to have received the 6-week dose, and 11 were fully vaccinated for age (10 had received three doses of vaccine and one child had received only two doses). The serotypes responsible for disease in those who had received any PCV13 included serotypes 19F (seven episodes), 19A (two episodes), and 3 (two episodes).

Table 13. Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2019-2022, n=7 002 (including audit cases)

Site of specimen	2019		2020		2021		2022	
	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*
Eastern Cape	274	4.08	136	2.02	201	3.01	224	3.35
Free State	83	2.91	62	2.12	70	2.39	62	2.12
Gauteng	774	5.11	377	2.43	465	2.94	515	3.20
KwaZulu-Natal	237	2.10	99	0.86	116	1.01	158	1.37
Limpopo	96	1.62	52	0.89	45	0.76	69	1.16
Mpumalanga	102	2.22	41	0.88	56	1.18	53	1.12
Northern Cape	89	7.12	26	2.01	25	1.92	27	2.06
North West	66	1.64	36	0.88	32	0.78	48	1.15
Western Cape	631	9.25	413	5.90	539	7.58	703	9.75
South Africa	**2 352**	**4.01**	**1 242**	**2.08**	**1 549**	**2.58**	**1 859**	**3.07**

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

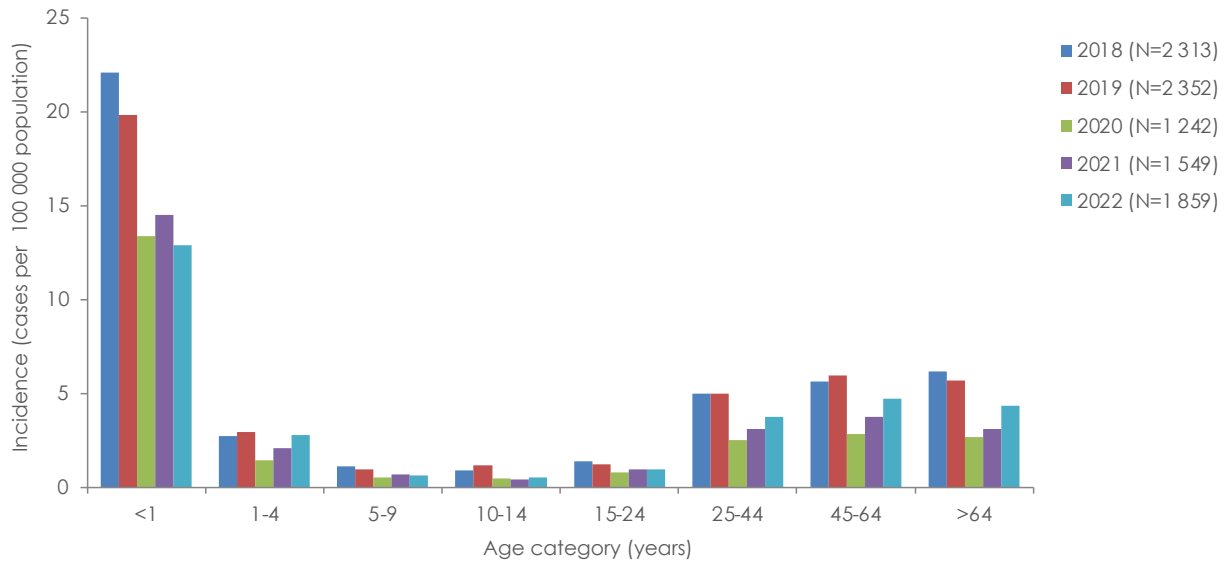

Figure 9. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2018 through 2022, n=10 546

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

Table 14. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2019-2022, n=7 002

Site of specimen	2019		2020		2021		2022	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	701	30	340	27	385	25	425	23
Blood	1 484	63	806	65	1 067	69	1 311	71
Other	167	7	96	8	97	6	123	7
Total	**2 352**		**1 242**		**1 549**		**1 859**	

Table 15. Number and percentage of penicillin-susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2022, n=1 144

Province	Isolate not available	Susceptible*		Resistant*	
	n	n	%	n	%
Eastern Cape	72	91	60	61	40
Free State	25	29	78	8	22
Gauteng	300	130	60	85	40
KwaZulu-Natal	108	27	54	23	46
Limpopo	25	31	70	13	30
Mpumalanga	30	15	65	8	35
Northern Cape	20	6	86	1	14
North West	26	14	64	8	36
Western Cape	109	403	68	191	32
South Africa	**715**	**746**	**65**	**398**	**35**

*2021 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; resistant, ≥0.12mg/L.

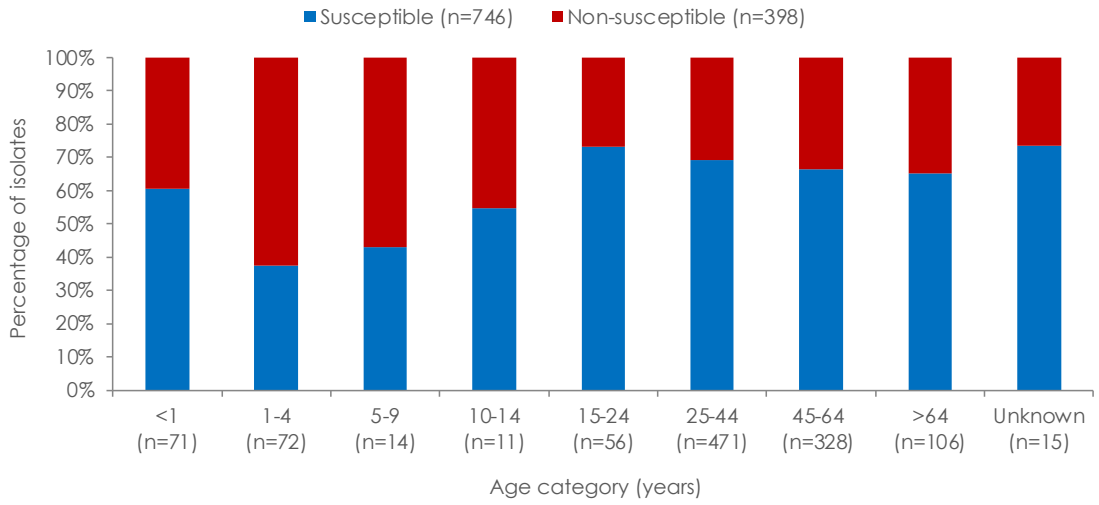

Figure 10. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2022, n=1 859 (n=1 144 with viable isolates)

2021 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible,MIC ≤0.06mg/L; non-susceptible >0.06mg/L

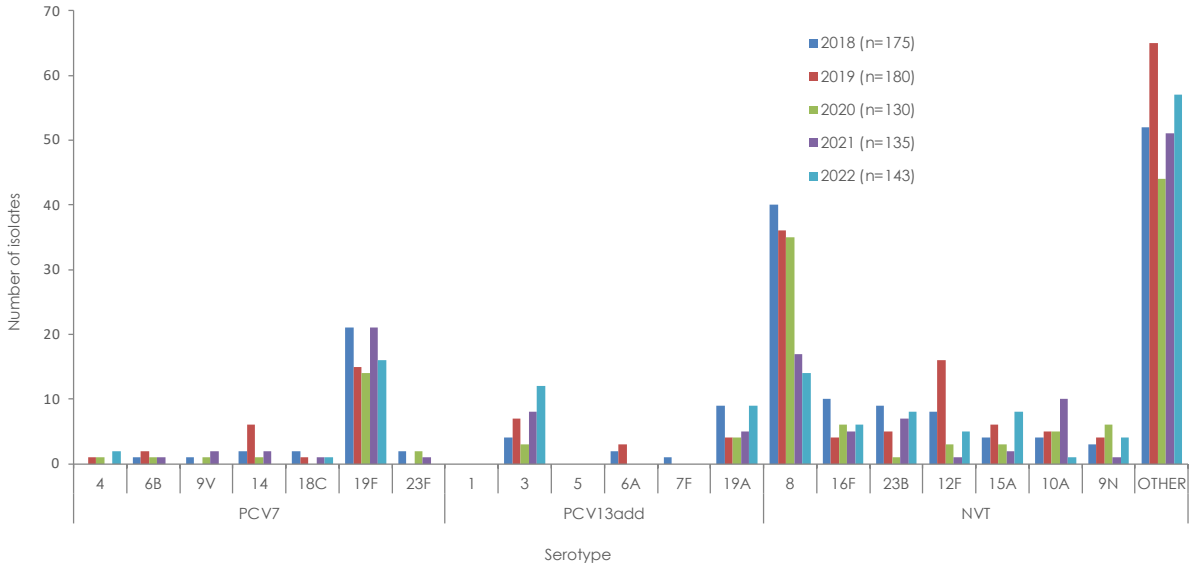

Figure 11a. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2018-2022

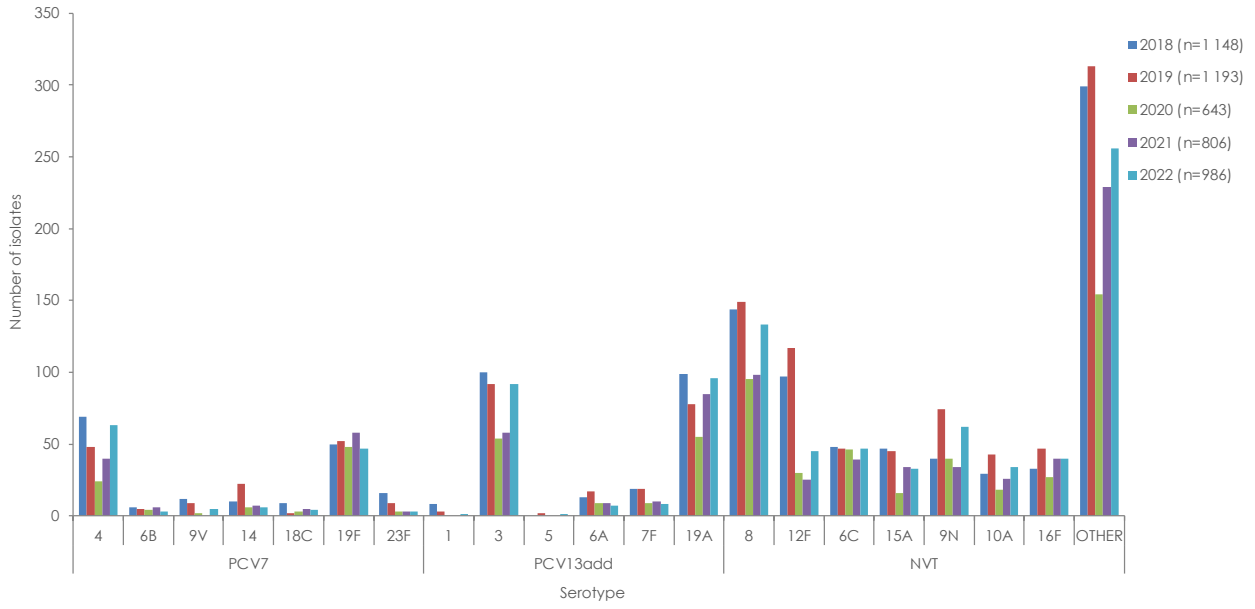

Figure 11b: Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in adults and children >5 years, South Africa, 2018-2022

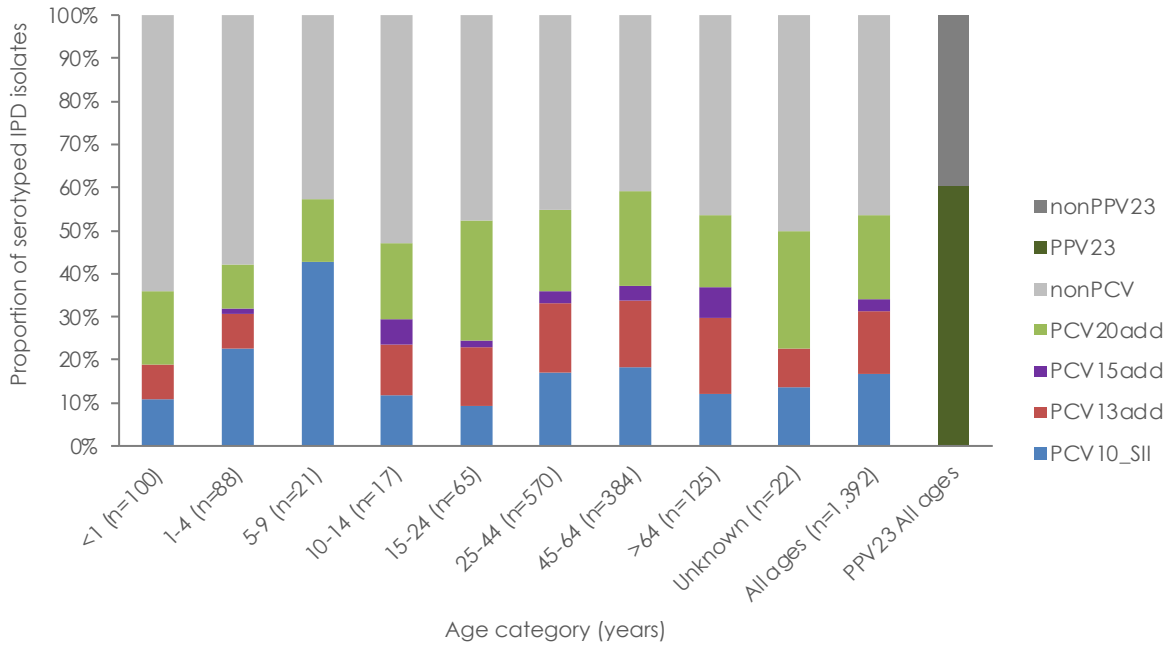

Figure 12. Potential pneumococcal serotype coverage of laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, by various pneumococcal conjugate vaccines and age categories, South Africa, 2022 (n=1 144 viable isolates and n=246 PCR-positive specimens available for serotyping)

PCV10_SII: 10-valent pneumococcal conjugate vaccine from Serum Institute India contains serotypes 1, 5, 6A, 6B, 7F, 9V, 14, 19A, 19F and 23F; PCV13add: 13-valent vaccine contains PCV10_SII serotypes plus serotypes 3, 4 and 18C; 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.PPV23: serotypes in PCV13 less 6A, plus 2,8,9N,10A,11A,12F,15B,17F,20,22F,33F.

Table 16. Number and percentage of invasive pneumococcal cases reported by the serotypes contained in the 10-, 13-,15-, and 20-valent pneumococcal conjugate vaccine candidates and the 23-valent pneumococcal polysaccharide vaccine by age category, South Africa, 2022, n=1 859 (n=1 144 with viable isolates)

Age category (years)	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		23-valent serotypes	
		n	%	n	%	n	%	n	%	n	%	n	%
<1	71	7	10	8	11	15	21	15	21	31	44	36	51
1-4	72	18	25	11	15	25	35	25	35	33	46	35	49
5-9	14	7	50	3	21	7	50	7	50	9	64	9	64
10-14	11	2	18	2	18	2	18	3	27	6	55	7	64
15-24	56	4	7	6	11	13	23	14	25	32	57	37	66
25-44	471	84	18	73	16	159	34	174	37	280	59	325	69
45-64	328	67	20	45	14	122	37	133	41	213	65	236	72
>64	106	13	12	13	12	34	32	42	40	62	58	76	72
unk	15	1	7	3	20	3	20	3	20	8	53	8	53
		203	18	**164**	14	**380**	33	**416**	36	**674**	59	**769**	67

Serotypes included in each of the pneumococcal conjugate vaccine categories:

Serum Institute India 10-valent serotypes:	1, 5, 6A, 6B, 7F, 9V, 14, 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
23-valent serotypes:	1, 4, 5, 6B, 7F, 9V, 14, 18C, 19F, 23F, 3, 19A, 22F, 33F, 8, 10A, 11A, 12F,15B, 2, 9N, 17F, 20

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

Discussion

IPD incidence has increased year-on-year since 2020 for almost all age categories but has not yet returned to pre-COVID-19 levels. Once again, the Western Cape Province had a disproportionately high burden of IPD, warranting further investigation. Overall, infants continue to have the highest incidence, followed by adults of 25 years and older, potentially driven by the high rate of comorbidities (including HIV-infection and previous tuberculosis infections) in the adult population. Case-fatality from IPD remains high, with a third of patients succumbing to the infection; this increases to just under 50% for those with meningitis and over 50% for those older than 64 years. In both children and adults, serotypes 8 and 3 dominate, with 19F and 19A also featuring in the top three places, respectively. A third of all serotyped IPD episodes in South Africa were due to serotypes in PCV13, ranging from 19% in infants to 43% in 5-9 year-olds; however, many breakthrough infections in fully vaccinated children were reported. As South Africa moves forward with changes in pneumococcal conjugate vaccine formulations in the expanded programme on immunisation, it is important that IPD surveillance in South Africa be continued.

Group A Streptococcus *(Streptococcus pyogenes)*

Results

In 2022, 947 episodes of invasive group A Streptococcus (group A strep) were reported through the GERMS-SA surveillance programme, of which 470 (52%) were sent to the reference laboratory for further characterisation (Table 2). The case definition for an invasive group A strep infection included individuals with group A strep isolated from a sterile site specimen or isolates from non-sterile site specimens with an accompanying diagnosis of septic shock, necrotising fasciitis, or necrotic tissue. Overall incidence was 1.6 episodes per 100 000 persons (similar to 2019, 1.7 per 100 000). Infants had the highest incidence (5.5 per 100 000) followed by adults >64 years (2.4 per 100 000) - (Figure 13). The incidence was highest in the Western Cape Province (5.2 per 100 000), followed by the Eastern Cape (1.8 per 100 000) and Gauteng (1.6 per 100 000) Provinces (Table 17). Where sex was known, infections occurred more often in males (59%, 531/904) than females. Most episodes were diagnosed from blood cultures; however, persons aged >5 years had a more diverse range of specimen types than children <5 years (57% (446/787) of episodes in persons >5 years were from blood culture versus 90% (115/128) in children <5 years, p<0.001) - (Figure 14, Table 18). All isolates tested (470/470) were susceptible to penicillin (MIC<0.06µg/ml), and 95% (447/470) were susceptible to erythromycin (MIC<0.25µg/ml) - (Table 19).

At enhanced surveillance sites, 80% (402/504) of persons with invasive group A strep had clinical data collected (Table 4). Most specimens were taken at admission to the hospital (median 0 days, interquartile range (IQR) 0-4 days from admission date), and people spent a median of 7 days in the hospital (IQR 2-18 days). In-hospital mortality was 26% (103/402) with most deaths occurring on day 2 of admission (IQR 1-7 days). Mortality was lower in children <5 years of age (15%, 7/47) than in persons >5 years of age (26%, 87/336). Most patients with invasive group A strep had wound infections (33%, 134/402), followed by necrotizing fasciitis (21%, 83/402) and cellulitis (19%, 77/402). Common risk factors for developing group A strep included having had previous surgery (15%, 60/402), a penetrating trauma (15%, 59/402), or a skin infection (12%, 49/402) in the previous two weeks. Twenty-five percent of persons with invasive group A strep were HIV-coinfected (96/383).

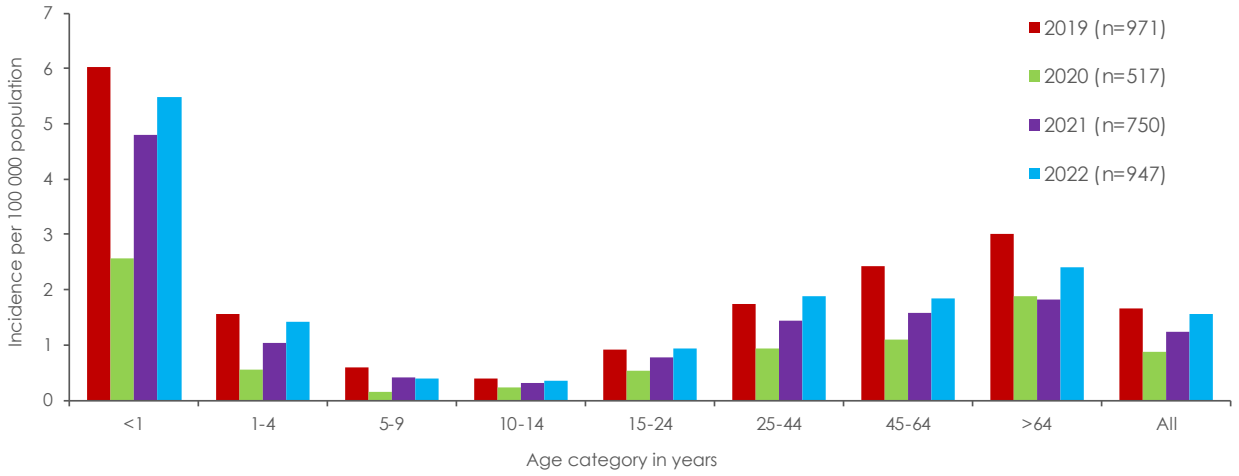

Figure 13. Incidence of invasive *Streptococcus pyogenes* by age category, South Africa, 2018-2022 (n=3 185)

Table 17. Number of cases and incidence rates of invasive group A streptococcal disease reported to GERMS-SA by province, South Africa, 2019-2022, n=3 185 (including audit cases)

Province	2019		2020		2021		2022	
	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*	n	Incidence rate*
Eastern Cape	143	2.13	71	1.05	151	2.26	122	1.83
Free State	22	0.76	11	0.38	21	0.72	35	1.20
Gauteng	199	1.31	96	0.62	176	1.11	263	1.63
KwaZulu-Natal	162	1.44	49	0.42	92	0.80	98	0.85
Limpopo	8	0.13	5	0.09	11	0.19	20	0.34
Mpumalanga	11	0.24	11	0.24	23	0.48	21	0.44
Northern Cape	7	0.55	7	0.54	3	0.23	2	0.15
North West	2	0.05	3	0.07	9	0.22	10	0.24
Western Cape	417	6.09	264	3.77	264	3.71	376	5.21
South Africa	**971**	**1.65**	**517**	**0.87**	**750**	**1.25**	**947**	**1.56**

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

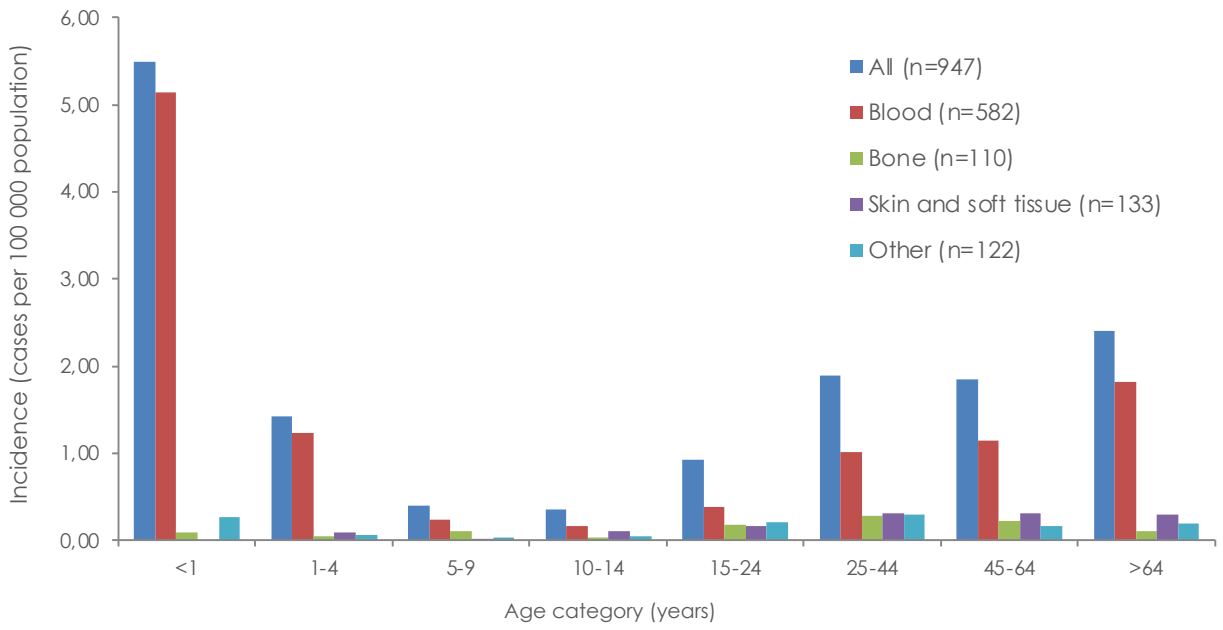

Figure 14. Age-specific incidence rates* for laboratory-confirmed, invasive group A streptococcal disease, reported to GERMS-SA, South Africa, 2022, n=947

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

Table 18. Number and percentage of cases of invasive group A streptococcal disease reported to GERMS-SA by specimen type and age category, South Africa, 2022, n=947 (age unknown for n=32)

Site of specimen	Age <5 years		Age >5 years	
	n	%	n	%
Cerebrospinal fluid/brain	3	2	8	1
Blood	115	90	446	57
Skin and soft tissue*	4	3	127	16
Bone	3	2	107	14
Other**	3	3	16	12
Total	**128**		**787**	

*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, genitourinary and gastrointestinal, tracts.

Table 19. 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, 2022, n=470

Site of specimen	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Penicillin	477	470	100	0	0	0	0
Erythromycin	477	447	95	2	0.4	20	4

*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 infections occurred mostly in infants and the elderly, with the majority of infections diagnosed through blood culture. The organism likely originated from a breech to the skin through recent surgery or trauma. Although isolates were highly susceptible to first-line antimicrobial agents, in-hospital case fatality was high, particularly for the elderly.

Group B Streptococcus *(Streptococcus agalactiae)*

Results

In 2022, 1 086 laboratory-confirmed episodes of invasive group B streptococcus (group B strep) were reported through the GERMS-SA network: 411 (38%) viable isolates were sent to the NICD reference laboratory for further characterisation; 46 (4%) were identified at NICD through molecular testing only; and 629 (58%) were detected through the NHLS laboratory information system (Table 2). Nationally, incidence for invasive group B strep fluctuated through the COVID-19 pandemic years but has stabilised at rates slightly higher than 2019 (Figures 15a and 15b). In 2022, infants had by far the highest incidence - 75 times higher than in persons >1 year of age (53.59 per 100 000 population <1 year versus 0.71 per 100 000 population >1 year, p<0.001). However, among the >1 year age category, those aged 25-44 years had the highest incidence in 2022 (0.76/100 000) - (Figure 15a). The incidence per 1 000 live births in 2022 was 0.29 for early-onset (<7 days of life) and 0.20 for late-onset (7-90 days) invasive group B strep disease (Figure 15b). Numbers of laboratory-confirmed episodes vary by Province, with Gauteng, KwaZulu-Natal, and Western Cape Provinces reporting the highest numbers (Table 20). In infants, most cases were isolated from blood (485/615, 89%) or cerebrospinal fluid (66/615, 11%) - (Table 21 and Figure 16a). However, in persons >1 year of age, blood (190/423, 45%) and genitourinary tract specimens (163/423, 39%) (particularly from younger adults of reproductive age) were most frequent (Table 21, Figure 16b). Where sex was known, among infants, 50% (287/572) of episodes occurred among females; however, among people >1 year of age, 70% (295/420) occurred among females (p<0.001). Of the isolates that were serotyped, serotypes III (38%), Ia (31%) and V (13%), were most common for all presentations (early-onset, late-onset and disease in >1 year age group) - (Table 22, Figure 17a). Serotype III dominated across all specimen types, particularly in CSF specimens (78%, 29/37), whereas blood specimens were equally likely to be serotype III (33%, 112/336) or Ia (33%, 110/336). Of the few (12%, 20/164) genitourinary specimens typed, 40% (8/20) were serotype III (Figure 17b). All (412/412) invasive group B strep isolates tested were sensitive to penicillin (MIC<0.12mg/L), 77% (318/412) to erythromycin (MIC<0.5mg/L), and 5% (19/412) to tetracycline (MIC<2mg/L).

In 2022, 82% (429/525) of group B strep episodes occurring at enhanced surveillance sites had clinical data collected (Table 4). The median length of hospital stay was 7 days (IQR 1-16 days). Overall, 18% (76/412) of patients with outcome data died, 20% (41/204) of those <1, and 16% (31/190) >1 year-of-age (p=0.226). Most deaths occured on day 2 of admission (IQR 1-10 days). Among 171 neonates, 22% (37/171) died. Underlying maternal risk factors for neonates developing invasive group B strep included: 23% (39/171) with premature rupture of membranes prior to birth and 8% (14/171) with pre-eclampsia. Neonatal risk factors for developing invasive group B strep included 43% (74/171) born prematurely (<37 weeks gestation), 18% (30/171) with very low birth weight (<1500g), and 22% (37/171) who required intubation. Of a subset of 95 episodes of invasive group B strep with a diagnosis of intrauterine sepsis, there were 2 deaths. Eighty-four percent (80/95) of women with intrauterine sepsis were pregnant or postpartum at the time of the infection. Among these pregnancies, 88% (70/80) resulted in the death of the neonate/foetus.

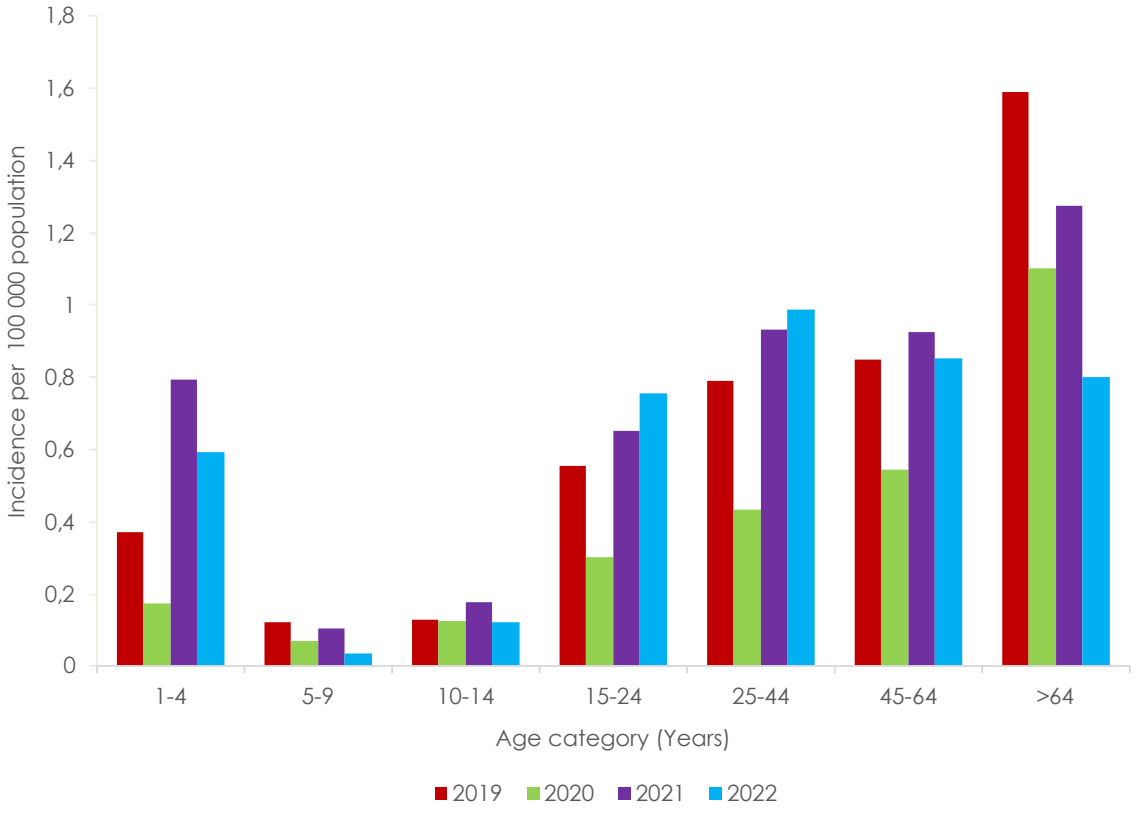

Figure 15a. Incidence of laboratory-confirmed invasive Group B Streptococcus by age category (>12 months) and year reported to GERMS-SA, South Africa, 2019-2022 (N=4 052, n=174 with unknown age

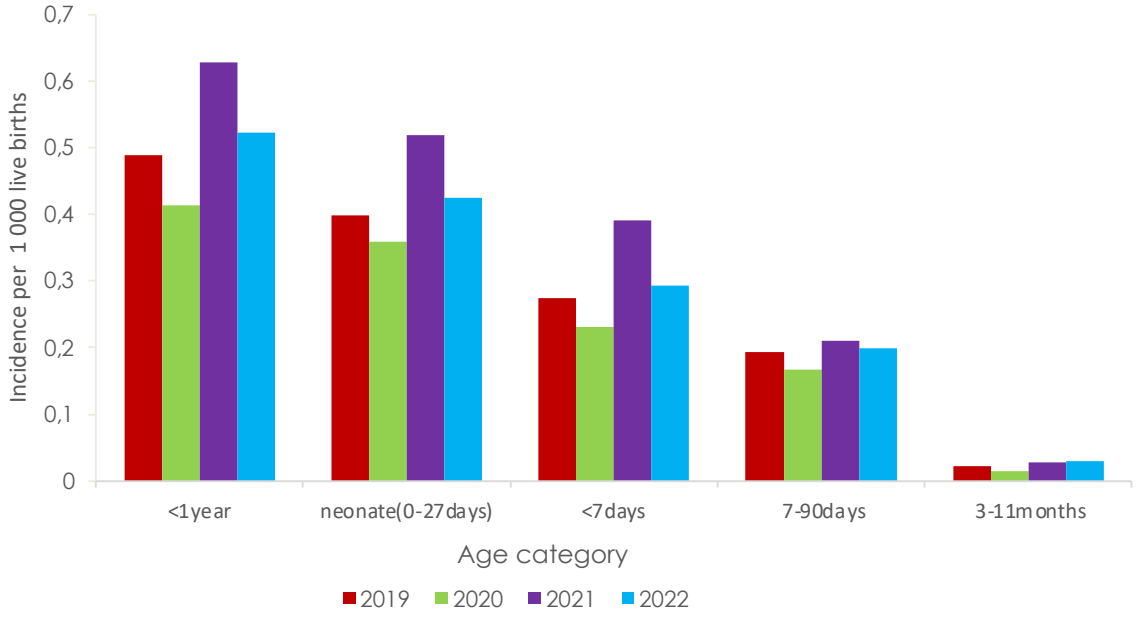

Figure 15b. Incidence of invasive Group B Streptococcus per 1 000 live births by age category (<12 months) and year reported to GERMS-SA, South Africa, 2019-2022 (n=2 417)

Table 20. Number of cases and incidence rates of invasive group B streptococcal disease reported to GERMS-SA by province and age category*, South Africa, 2022, n=1 086 (age unknown for n=48)

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	9		22		20	
Free State	9		7		23	
Gauteng	142		100		195	
KwaZulu-Natal	100		38		76	
Limpopo	11		9		13	
Mpumalanga	39		11		9	
Northern Cape	0		0		2	
North West	3		5		6	
Western Cape	32		42		79	
South Africa	**345**	**0.29**	**234**	**0.20**	**423**	**0.71**

*N=36 cases in infants >90 days and less than one year excluded from above. *Denominators included mid-year population estimates for >1 year olds and live births for early and late onset episodes*.

Table 21. Number and percentage of cases of invasive group B streptococcal disease reported to GERMS-SA by specimen type and age category*, South Africa, 2022, n=1 086

Site of specimen	Age <1 year		Age >1 years	
	n	%	n	%
Cerebrospinal fluid/brain	66	11	14	3
Blood	548	89	190	45
Skin and soft tissue	0	0	17	4
Genitourinary**	1	0	163	39
Other***	0	0	47	11
Total	**615**		**423**	

*Age unknown for n=48. **Genitourinary specimens include uterine tissue, products of conception and placental tissue ***Other includes invasive specimens from bone, respiratory and gastrointestinal tracts.

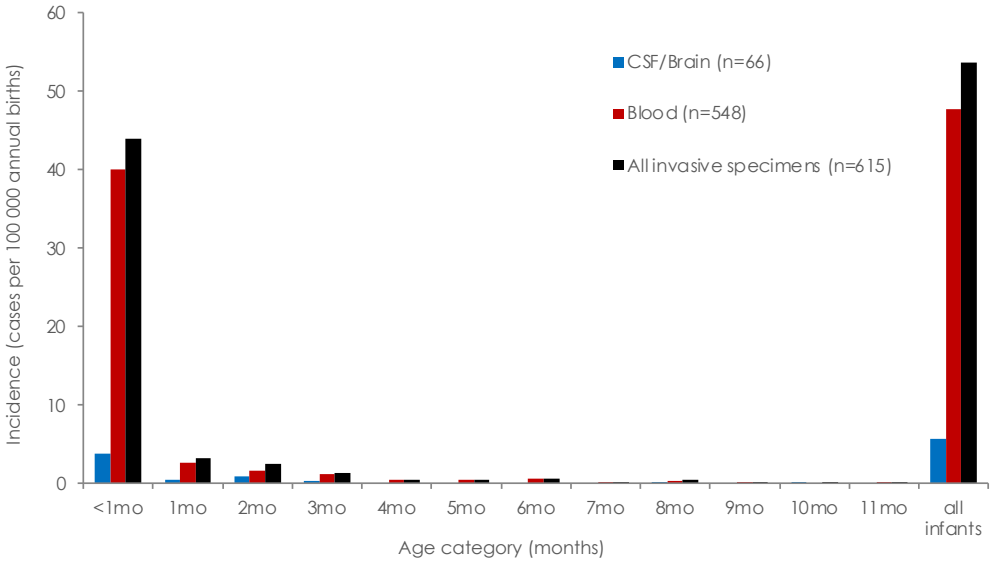

Figure 16a. Age-specific incidence rates* for laboratory-confirmed, invasive group B streptococcal disease in children <1 year of age, reported to GERMS-SA, South Africa, 2022, n=615

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

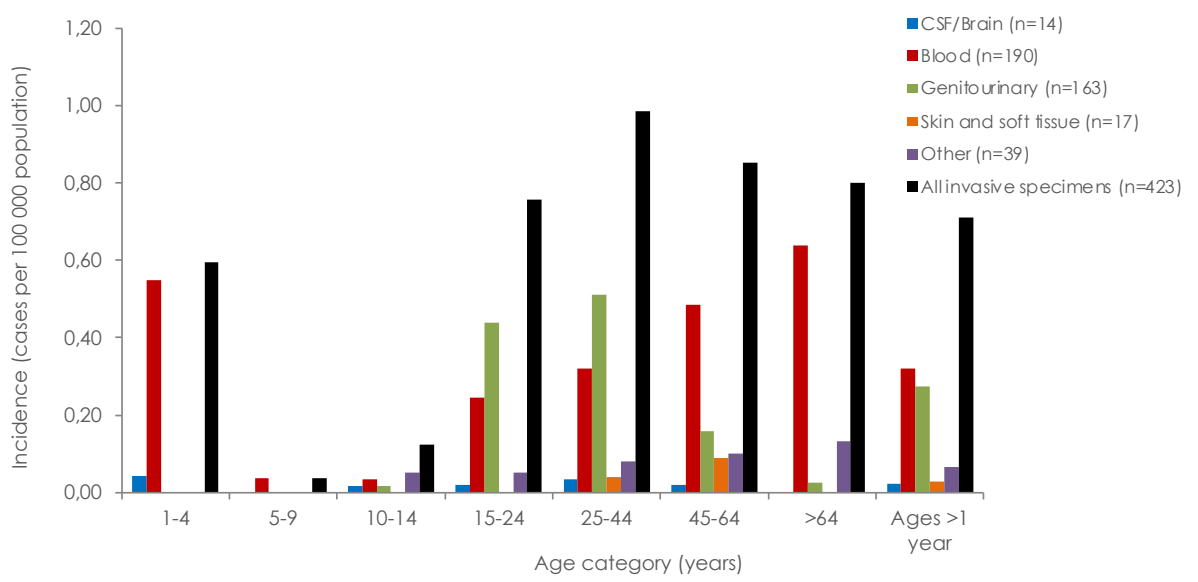

Figure 16b. Age-specific incidence rates* for laboratory-confirmed, invasive group B streptococcal disease in persons ≥1 year of age, reported to GERMS-SA, South Africa, 2022, n=423

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population. n=615 episodes in children<1 year and n=48 episodes with age unknown)

Table 22. Serotype distribution of invasive group B streptococcal disease reported to GERMS-SA by province, South Africa, 2022, n=1 086 (age unknown n=48)

Province	Total	Isolates available for sero-typing	Ia		Ib		II		III		IV		V		VIII	
			n	%	n	%	n	%	n	%	n	%	n	%	n	%
Eastern Cape	55	31	6	19	2	6	2	6	17	55	1	3	3	10	0	0
Free State	41	19	7	37	1	5	0	0	6	32	1	5	3	16	1	5
Gauteng	473	175	45	26	14	8	7	4	74	42	10	6	23	13	0	0
KwaZulu-Natal	233	49	15	31	2	4	3	6	12	24	3	6	13	27	1	2
Limpopo	38	12	2	17	1	8	1	8	5	42	1	8	1	8	0	0
Mpumalanga	63	8	3	38	1	13	1	13	1	13	0	0	2	25	0	0
Northern Cape	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
North West	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Western Cape	163	112	46	41	8	7	7	6	38	34	2	2	8	7	2	2
South Africa	**1 086**	**406**	**124**	**31**	**29**	**7**	**21**	**5**	**153**	**38**	**18**	**4**	**53**	**13**	**4**	**1**

Of 1 086 episodes, 406 were serotyped, five were non-typeable (one each from Eastern Cape, Free State, and Gauteng Provinces, and two from the Western Cape Province), 15 had insufficient specimen for serotyping, 660 did not have isolates/specimens available for serotyping at the NICD (including 629 audit cases, and 31 reported cases but isolates not sent).

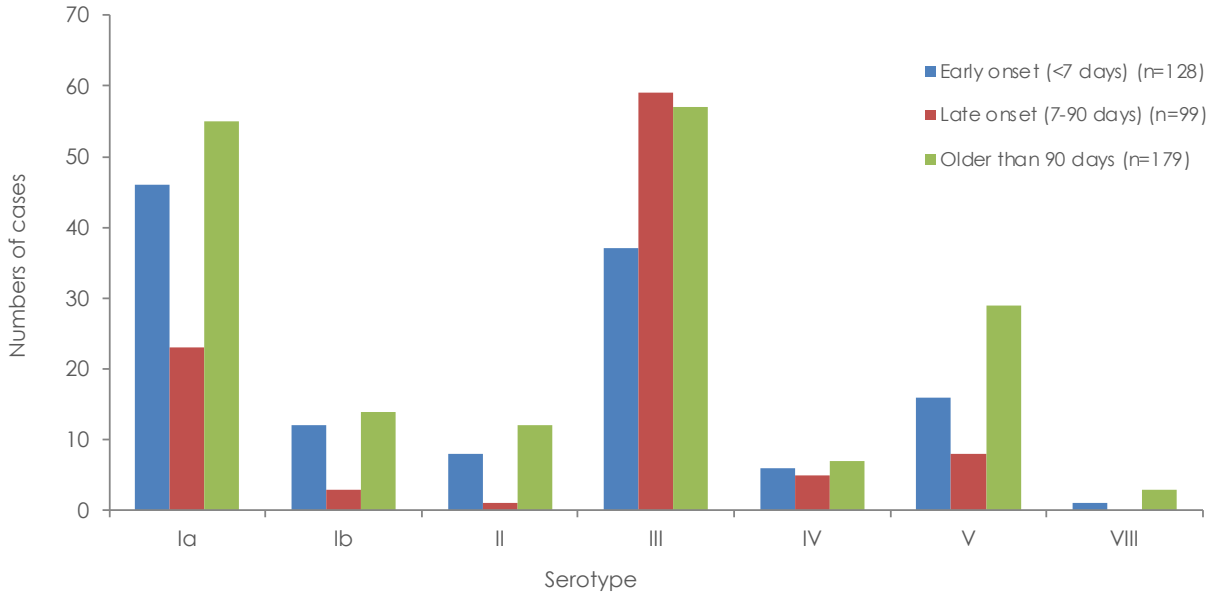

Figure 17a. Numbers of cases of laboratory-confirmed, invasive group B streptococcal disease by serotype, reported to GERMS-SA, South Africa, 2022, n=1 086 (typing done for n=406, 4 with unknown age)

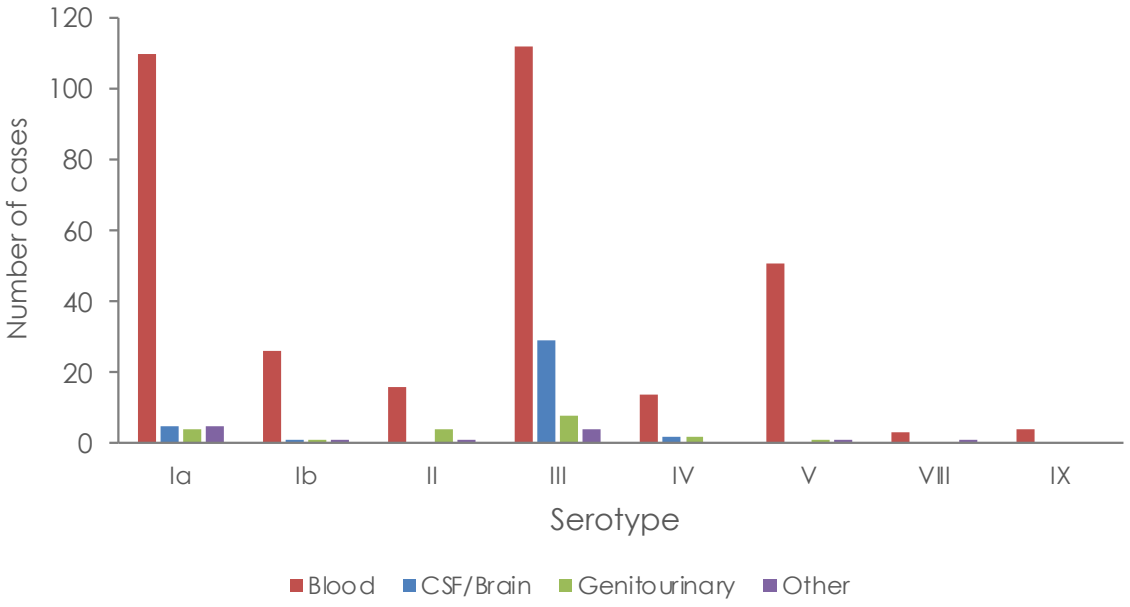

Figure 17b. Numbers of cases of laboratory-confirmed, invasive group B streptococcal disease by serotype and specimen type, reported to GERMS-SA, South Africa, 2022, n=1 086 (typing done for n=406)

Discussion

Infants, particularly neonates, carry a huge burden of invasive group B strep disease in South Africa. Smaller numbers of cases identified in less populated provinces may be a reflection of under-ascertainment of cases through lower rates of blood cultures performed, particularly amongst hospitalised neonates. The extremely poor pregnancy outcome amongst women with laboratory-confirmed intrauterine sepsis is concerning as it highlights the large role that group B strep has as a cause of stillbirth and spontaneous abortion. Serotypes III and Ia were once again dominant across all age categories and specimen types. Opportunely, the majority of isolates were susceptible to penicillin, which is still the first-line antimicrobial agent for targeting neonatal sepsis.

Enteric fever (typhoid and paratyphoid fever): *Salmonella enterica* serovar Typhi and *Salmonella enterica* serovars Paratyphi A, Paratyphi B, and Paratyphi C

Results

A total of 204 cases of laboratory-confirmed enteric fever were identified through the active enteric fever surveillance programme of the Centre for Enteric Diseases in 2022.

The cases include *Salmonella* Typhi isolated from all sample sites, of which 84% (171/204) were blood cultures. Enteric fever cases were reported from all provinces except the Northern Cape Province (Table 23); half the cases (were reported from Gauteng Province (51%, 104/204), followed by Western Cape Province (20%, 40/204) and North West Province (26%, 25/204). Most cases (90%, 183/204) were identified in the public health sector. By age group, the number of cases was highest in children aged 5 to 14 years (29%, 60/204), followed by adolescents and young adults aged 15 to 24 years (18%, 37/204), and adults aged 25 to 34 years (18%, 37/204), as shown in Table 24. An increase in the number of cases was observed from January to February, May to June and from October through December (Figure 18). Of the isolates received and tested at the centre, 90% (161/178) were susceptible to ciprofloxacin and 99% (176/178) were susceptible to azithromycin (Table 25a), following CLSI breakpoints. Three isolates of Paratyphi A were identified. No isolates of Paratyphi B or Paratyphi C were reported or identified.

Seventy-nine (79/204; 39%) cases were reported from ESS, and 43/79 (54%) had additional information on variable completeness available (Table 25b). Patients were aged between one and 52 years, with a median age of 23 years. HIV status was known for 39/43 (91%), of which 12/39 (31%) were HIV-infected. Two (2/43; 5%) deaths were reported.

Table 23. Number of cases of *Salmonella* Typhi and Paratyphi A by health sector and province, South Africa, 2022, n = 204 (including audit reports, missing isolates, mixed and contaminated cultures)

Province	Private sector	Public sector	Total
Eastern Cape	1	3	4
Free State	0	7	7
Gauteng	14	90	104
KwaZulu-Natal	2	10	12
Limpopo	0	6	6
Mpumalanga	1	4	5
Northern Cape	0	0	0
North West	1	25	26
Western Cape	2	38	40
South Africa	**21**	**183**	**204**

Table 24. Number of cases of *Salmonella* Typhi and Paratyphi A by age category, South Africa, 2022, n = 204 (including audit reports)

Age category (years)	n	%
0 - 4	18	9
5 - 14	60	29
15 - 24	37	18
25 - 34	37	18
35 - 44	24	12
45 - 54	18	9
55 - 64	3	1
≥ 65	1	0
Unknown	6	3
Total	**204**	**100**

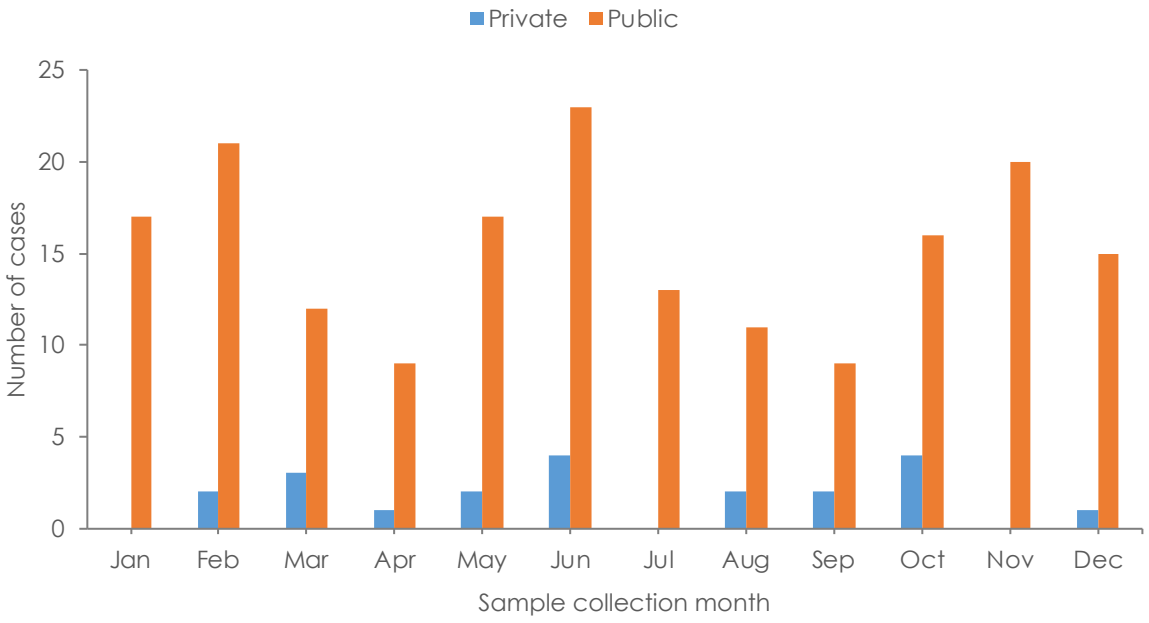

Figure 18. Number of cases of *Salmonella* Typhi and Paratyphi A by month of sample collection and health sector, South Africa, 2022

Table 25a. Ciprofloxacin and azithromycin susceptibility* of viable *Salmonella* Typhi and Paratyphi A isolates received and tested at the Centre for Enteric Diseases, South Africa, 2022 (n = 178)

Antimicrobial agent	Susceptible (%)	Non-susceptible (%)
Ciprofloxacin	161 (90%)	17 (10%)
Azithromycin	176 (99%)	2 (1%)

*According to CLSI breakpoints

Table 25b: Number and percentage of cases of *Salmonella* Typhi and Paratyphi reported from ESS by province, South Africa, 2022 (n = 79)

Province	Total cases	Cases reported from ESS		Completed case reports	
		n	%	n	%
Eastern Cape	4	1	25	0	0
Free State	7	2	29	1	50
Gauteng	104	30	29	17	57
KwaZulu-Natal	12	3	25	1	33
Limpopo	6	5	83	3	60
Mpumalanga	5	1	20	0	0
Northern Cape	0	0	0	0	0
North West	26	22	85	9	41
Western Cape	40	15	38	12	80
South Africa	**204**	**79**	**39**	**43**	**54**

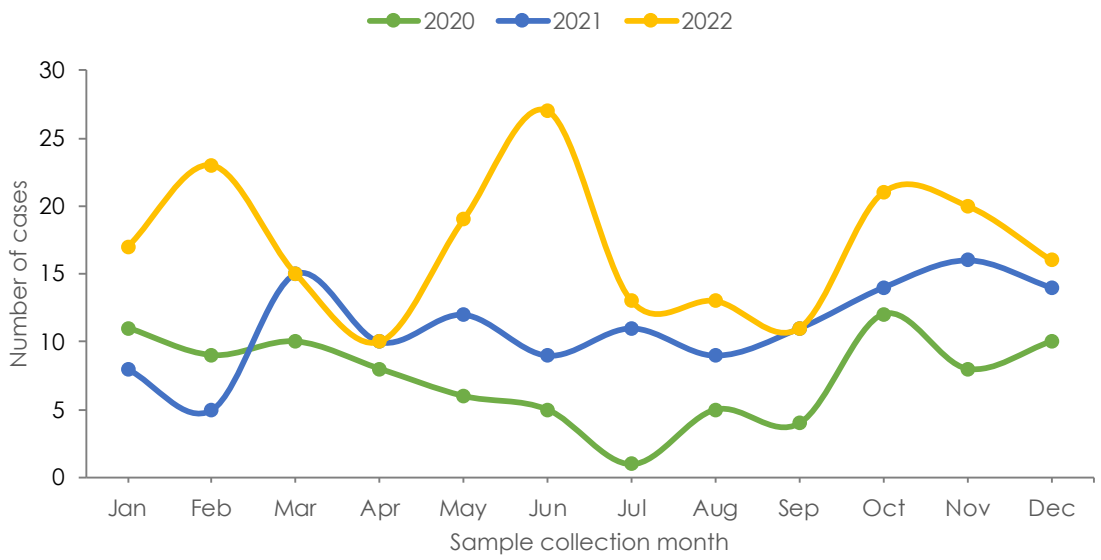

Figure 19. Number of cases of *Salmonella* Typhi and Paratyphi reported by month and year of sample collection, South Africa, 2020 – 2022

Discussion

Enteric fever caused by *Salmonella* Typhi remains endemic in South Africa. Following the outbreaks in 2005-2006 the number of culture-confirmed cases per year has remained stable at <150 cases per year from 2006 through 2021. The number of cases in 2022 (n=204) is the highest annual total reported since 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, although higher case numbers were also observed in May to June 2022 due to a localised outbreak in Gauteng (Figure 19). The age distribution of cases is similar to that reported in previous years, with children aged 5 to 14 years being most affected. More than half the cases were sporadic. However, the increase in the number of cases in Gauteng was driven by specific small localised clusters (outbreaks) as defined by the genetic relatedness of isolates on core-genome multilocus sequence typing analysis of whole genome sequencing data. Cases from an outbreak strain originating in North West Province have also been identified in other Provinces, including Gauteng. The majority of cases acquired *Salmonella* Typhi infection in South Africa.

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. Reported cases significantly underrepresent the true number of cases. Culture remains the gold standard for confirming enteric fever, so high index of suspicion and appropriate laboratory testing is critical to identifying cases. The number of cases reported from different provinces may also reflect healthcare-seeking behaviour and prevailing clinician testing practices.

Although the proportion of isolates showing resistance to ciprofloxacin (10%) is lower than in 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 it 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 only 3 cases of S. Paratyphi A reported in 2022.

Nontyphoidal *Salmonella enterica (NTS)*

Results

A total of 3 185 cases of nontyphoidal salmonellosis were reported through the surveillance programme in 2022. This includes nontyphoidal *Salmonella* isolated from all sample sites, of which 50% (1 582/3 185) were indicative of invasive disease (Table 26). Sixty-nine percent of the total cases (2 203/3 185) were identified in the public health sector. There was a striking difference in the proportion of cases that were invasive in the public health sector (1 471/1 582, 93%) versus those in the private health sector (111/1 582, 7%). This could be due in part to differences in health-seeking behaviour and diagnostic practices among clinicians in the respective health sectors. Of the 1 603 non-invasive nontyphoidal salmonellosis cases reported, 54% (871/1 603) were reported by the private sector, and 46% (732/1 603) were reported by the public sector.

The highest numbers of cases of invasive disease were reported from Gauteng Province (565/1 582, 36%), followed by Western Cape (330/1 582, 21%), KwaZulu-Natal (189/1 582, 12%), and Eastern Cape (178/1 582, 11%) provinces (Table 26). Gauteng Province also reported the highest number of cases of non-invasive disease (539/1 603, 34%), followed by Western Cape (467/1 603, 29%), KwaZulu-Natal (194/1 603, 12%), and Eastern Cape (190/1 603, 12%) 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 for invasive disease (Figure 20). Non-invasive disease was highest in children younger than five years (406/1 603, 25%), followed by people aged 35 to 44 years (203/1 603, 13%), and people aged 5 to 14 years (194/1 603, 12%), as shown in Table 27. Invasive disease was most common in people aged 35 to 44 years (369/1 582, 23%) followed by children younger than five years (237/1 582, 15%), and people aged 45 to 54 years (220/1 582, 14%). Most invasive cases were identified from blood cultures (1043/1 582, 66%) - (Table 28).

A total of 2 060 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. More than 70 serovars were identified, but two serovars accounted for 89% of the cases: *Salmonella* Enteritidis (1433/2 060, 70%) and *Salmonella* Typhimurium (393/2 060, 19%). The next most common serotypes were *Salmonella enterica* subspecies *salamae*, *Salmonella* Isangi, *Salmonella* Infantis and *Salmonella* Muenchen (Table 29). Proportions of common serovars differed among provinces, but *Salmonella* Enteritidis was the most common serotype in all Provinces (Figure 21). Antimicrobial susceptibility testing was not routinely performed, but was offered on request.

Table 26: Number of cases of invasive and non-invasive nontyphoidal salmonellosis by Province, South Africa, 2022, n = 3 185 (including audit reports)

Province	Non-invasive nontyphoidal salmonellosis	Invasive nontyphoidal salmonellosis	Total
Eastern Cape	190	178	368
Free State	116	75	191
Gauteng	539	565	1 104
KwaZulu-Natal	194	189	383
Limpopo	15	63	78
Mpumalanga	25	73	98
Northern Cape	16	16	32
North West	41	93	134
Western Cape	467	330	797
South Africa	**1 603**	**1 582**	**3 185**

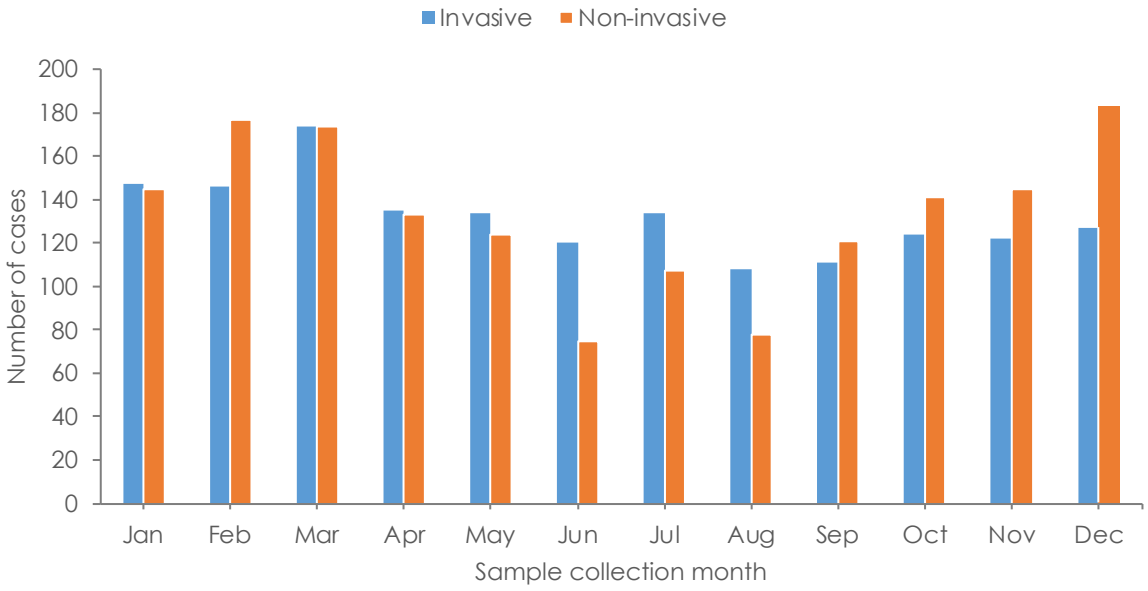

Figure 20. Number of cases of non-invasive (n = 1 603) and invasive (n = 1 582) nontyphoidal salmonellosis by month, South Africa, 2022

Table 27. Number of cases of invasive and non-invasive nontyphoidal salmonellosis by age category, South Africa, 2022, n = 3 185 (including audit reports)

Age category (years)	Non-Invasive	Invasive	Total
0 - 4	406	237	643
5 - 14	194	54	248
15 - 24	95	88	183
25 - 34	159	203	362
35 - 44	203	369	572
45 - 54	169	220	389
55 - 64	149	189	338
≥ 65	177	146	323
Unknown age	51	76	127
Total	**1 603**	**1 582**	**3 185**

Table 28. Number of cases of nontyphoidal salmonellosis reported by primary anatomical site of isolation, South Africa, 2022, n = 3 185 (including audit reports).

Age category (years)	n	%
Stool	1 603	50.3
Blood culture	1 043	32.7
Urine	237	7.4
CSF	15	0.5
Other	287	9.0
Total	**3 185**	**100**

Table 29. Six most common *Salmonella enterica* serovars by province, South Africa, 2022 (2 060/3 185) *

Province	*Salmonella* Enteritidis	*Salmonella* Typhimurium	*Salmonella enterica* subspecies *salamae*	*Salmonella* Isangi	*Salmonella* Infantis	*Salmonella* Muenchen
Eastern Cape	106	72	9	53	1	5
Free State	94	21	3	0	4	2
Gauteng	587	96	37	6	13	5
KwaZulu-Natal	143	15	9	0	11	4
Limpopo	33	6	3	4	2	1
Mpumalanga	26	5	4	2	2	1
Northern Cape	11	2	0	0	0	0
North West	62	10	2	3	2	1
Western Cape	371	166	12	3	8	22
South Africa	**1 433**	**393**	**79**	**71**	**43**	**41**

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

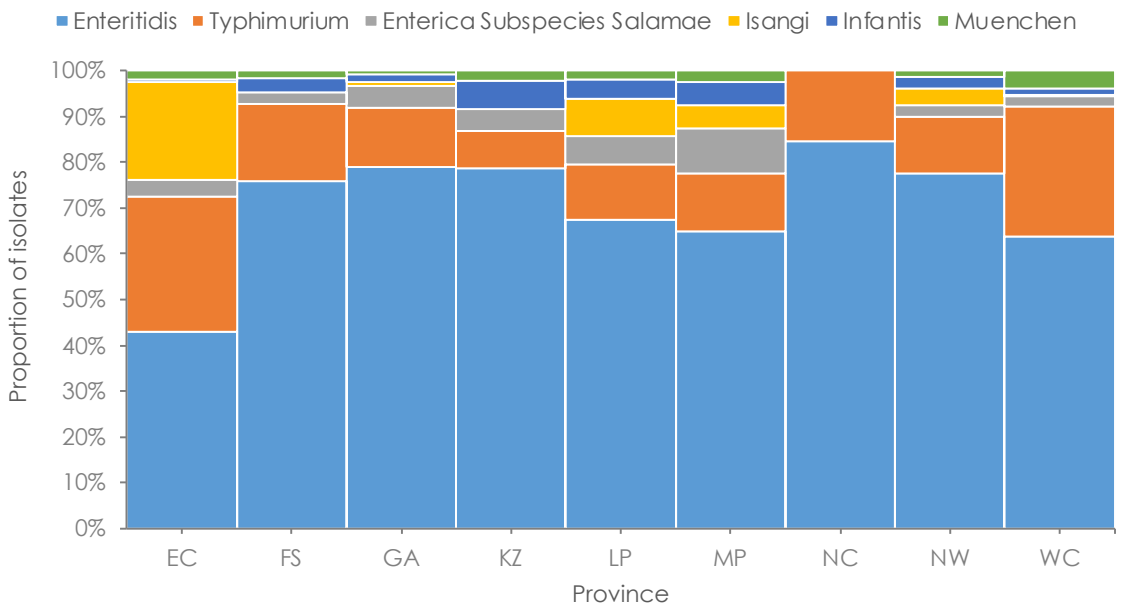

Figure 21. Proportions of the six most common *Salmonella enterica* serovars causing nontyphoidal salmonellosis by province, South Africa, 2022.

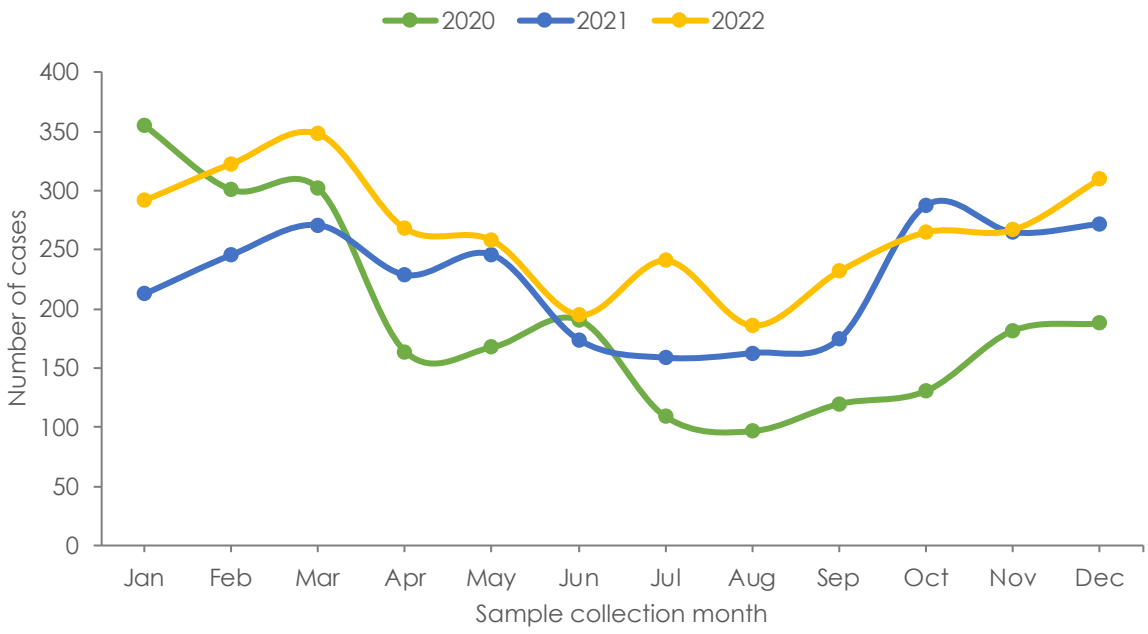

Figure 22. Number of cases of nontyphoidal *Salmonella* by month and year, South Africa, 2020 - 2022.

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 2022 (n=3 185) than in 2021 (n = 2 445) or 2020 (n = 2 306), but the pattern suggestive of seasonality was largely preserved (Figure 22). As in previous years, although seasonal prevalence was noted for non-invasive disease (increased numbers in the earlier and later months of the year and low numbers in the winter months), invasive disease showed no seasonality.

Greater numbers of invasive diseases reported from the 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.

Shigella species

Results

A total of 948 culture-confirmed cases of shigellosis were reported through the surveillance programme in 2022. The public health sector accounted for 74% (705/948) of cases (Table 30). The total includes *Shigella* spp. isolated from all sample sites, but in 87% (829/948) of the cases, the isolate was recovered from stool or rectal swab samples reflecting non-invasive dysentery or diarrhoea (Table 31); in the remaining 13% of cases, the isolate was recovered from blood or CSF culture (55/948, 6%) or other extra intestinal sample sites (64//948, 7%).

Higher numbers of shigellosis cases also occurred in January and February, with a small peak in cases in July and November (Figure 23). Thirty-nine percent of cases were reported from Western Cape province (372/948); Gauteng and KwaZulu-Natal provinces contributed 25% (238/948) and 17% (165/948) of the total cases, respectively (Table 31).

Cases of shigellosis were highest in children younger than five years (328/948, 35%), followed by children 5 to 14 years of age (140/948, 15%) (Table 32). The proportion of invasive shigellosis cases remains low (6%), and as in previous years, invasive disease was highest in children younger than five years (24/55, 44%).

A total of 725 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. sonnei* (305/725, 42%) and *S. flexneri* type 2a (242/725, 33%), followed by *S. flexneri* type 1b (80/725, 11%), and the next most common serotypes were *S. flexneri* type 4, *S. flexneri* type 3a and *S. flexneri* type 6 (Table 33). Proportions of the serotypes differed among provinces (Figure 24). The predominant serotype differed among provinces; *S. sonnei* predominated in six Provinces, while *S. flexneri* type 2a predominated in Western Cape Province. Antimicrobial susceptibility testing was not routinely performed but was offered on request.

Table 30. Number of cases of shigellosis by health sector and province, South Africa, 2022, n = 948 (including audit reports)

Province	Private sector	Public sector	Total
Eastern Cape	7	77	84
Free State	24	16	40
Gauteng	128	110	238
KwaZulu-Natal	59	106	165
Limpopo	0	10	10
Mpumalanga	6	8	14
Northern Cape	2	3	5
North West	6	14	20
Western Cape	11	361	372
South Africa	**243**	**705**	**948**

Table 31. Number of non-invasive and invasive or extra intestinal cases of shigellosis by province, South Africa, 2022, n = 948 (including audit reports)

Province	Non-invasive	Invasive or extra intestinal	Total
Eastern Cape	70	14	84
Free State	32	8	40
Gauteng	206	32	238
KwaZulu-Natal	137	28	165
Limpopo	7	3	10
Mpumalanga	10	4	14
Northern Cape	5	0	5
North West	9	11	20
Western Cape	353	19	372
South Africa	**829**	**119**	**948**

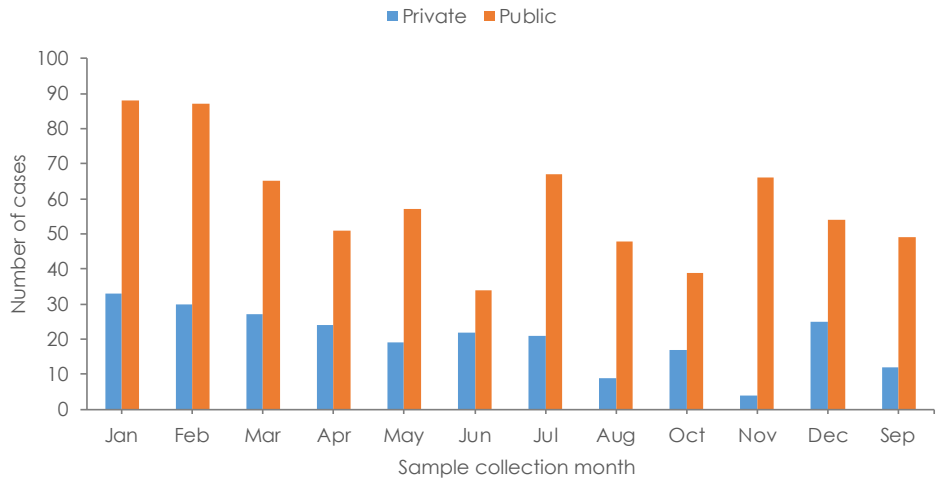

Figure 23. Number of cases of shigellosis by month and health sector, South Africa, 2022, n = 948 (including audit reports)

Table 32. Number of non-invasive and invasive or extra intestinal cases of shigellosis reported by age category, South Africa, 2022, n = 948 (including audit reports)

Province	Non-invasive	Invasive or extra intestinal	Total
0 - 4	294	34	328
5 - 14	127	13	140
15 - 24	36	11	47
25 - 34	100	22	122
35 - 44	94	9	103
45 - 54	49	9	58
55 - 64	55	8	63
≥ 65	63	9	72
Unknown age	11	4	15
Total	**829**	**119**	**948**

Table 33. Six most common *Shigella* species (and serotype where applicable) by province, South Africa, 2022 (725/948) *

Province	*S. sonnei*	*S. flexneri* type 2a	*S. flexneri* type 1b	*S. flexneri* type 4	*S. flexneri* type 3a	*S. flexneri* type 6
Eastern Cape	27	22	9	4	1	1
Free State	17	3	1	3	1	1
Gauteng	113	44	9	7	8	4
KwaZulu-Natal	59	23	17	4	4	2
Limpopo	3	3	3	0	0	0
Mpumalanga	8	2	0	0	0	1
Northern Cape	1	1	1	0	0	0
North West	10	8	0	0	0	1
Western Cape	67	136	40	25	18	13
South Africa	**305**	**242**	**80**	**43**	**32**	**23**

*Includes *Shigella* isolates from invasive, extra intestinal and non-invasive cases. Twenty-five different serovars of *Shigella* were identified with the six most common serovars listed on the table above accounting for 76% (725/948) of the total.

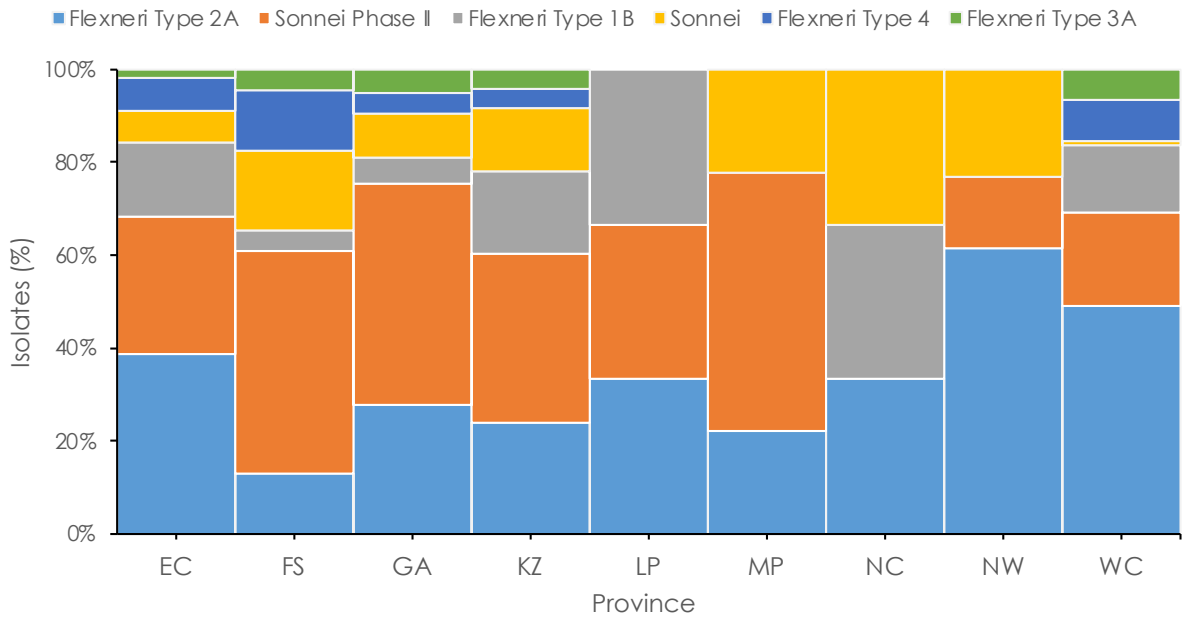

Figure 24. Proportions of the most common *Shigella* species and serotypes by province, South Africa, 2022

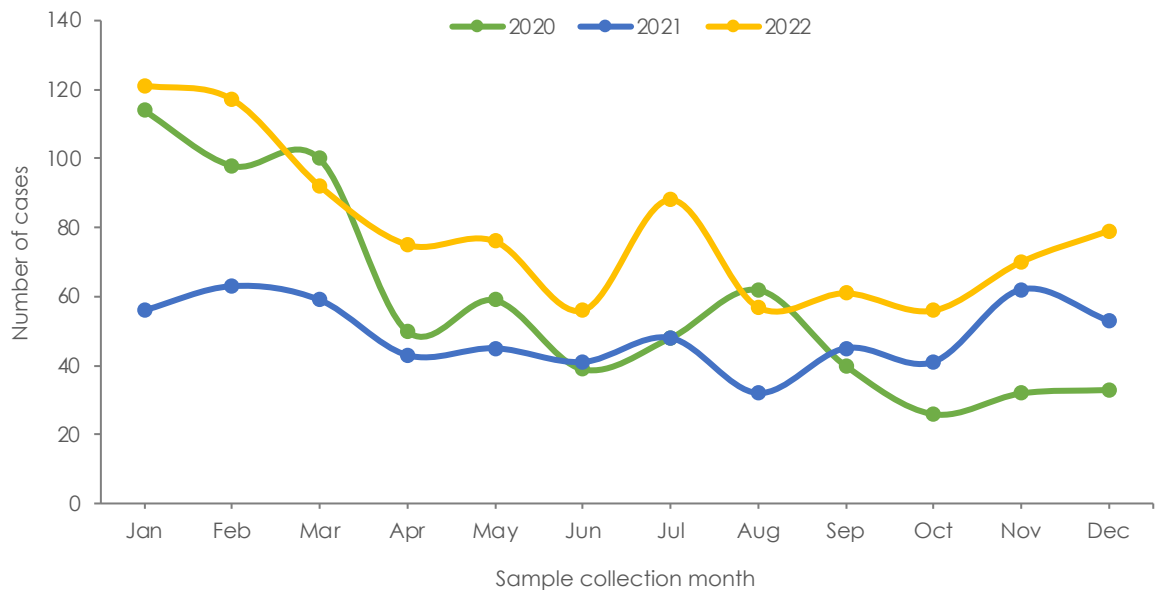

Figure 25. Number of cases of shigellosis by month and year, South Africa, 2020 - 2022 (including audit reports)

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.

Larger case numbers were reported in 2022 (n = 948) than in 2020 (n = 698) and 2021 (n = 514). Usually, increased numbers of cases are identified in the earlier months of the year and lower numbers in the winter months. No typical pattern of seasonality was noted in 2021, but in 2022, there were more cases in January and February. (Figure 25).

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 outbreaks.

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.

Seven hundred and ten (88%) of the 804 isolates of *Campylobacter* spp. submitted through the surveillance programme in 2022 were submitted by diagnostic laboratories in the private sector (Table 34). This includes *Campylobacter* spp. isolated from all sample sites, but in 98% (788/804) of the cases, the isolate was recovered from stool or rectal swab samples reflecting non-invasive diarrhoeal disease.

Case numbers appeared higher in the warmer months, January to February and November to December (Figure 26). Western Cape province reported the highest number of cases (384/804, 48%) followed by Gauteng Province (323/804, 40%); these two provinces alone accounted for 88% of the total cases (Table 34).

Case numbers were highest in children younger than five years (244/804, 30%) (Table 35).

Confirmatory speciation and antimicrobial susceptibility testing have not been completed.

Table 34. Number of cases of campylobacteriosis by health sector and province, South Africa, 2022, n = 804*

Province	Non-invasive	Invasive or extra intestinal	Total
Eastern Cape	6	22	28
Free State	46	0	46
Gauteng	313	10	323
KwaZulu-Natal	2	1	3
Limpopo	0	0	0
Mpumalanga	8	1	9
Northern Cape	1	1	2
North West	9	0	9
Western Cape	325	59	384
South Africa	**710**	**94**	**804**

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

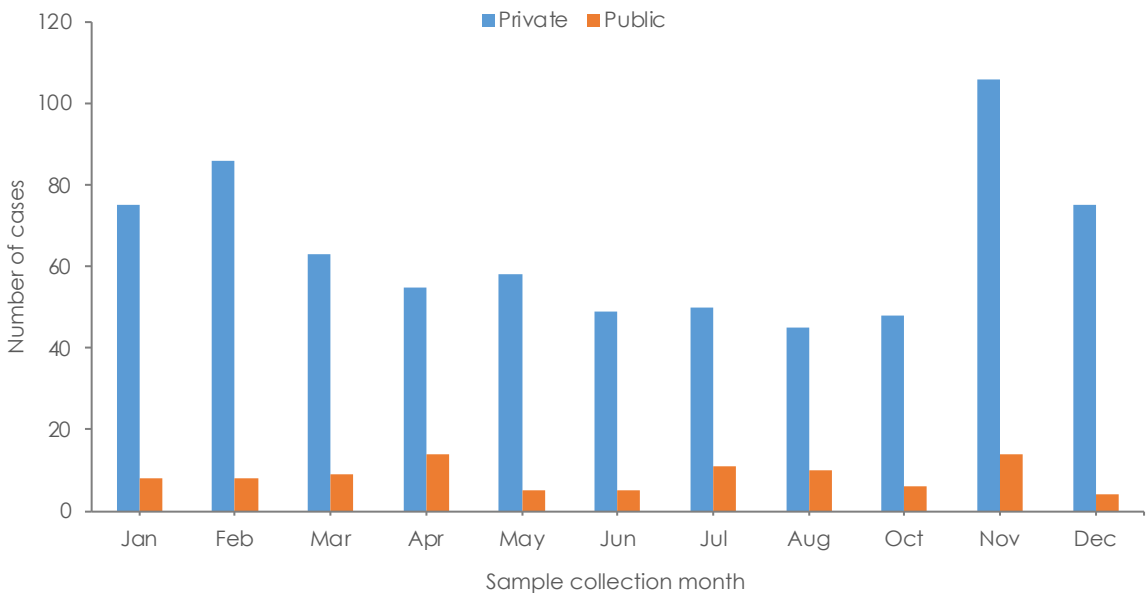

Figure 26. Number of cases of campylobacteriosis by month and health sector, South Africa, 2022.*

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

Table 35. Number of *Campylobacter* spp. isolates by health sector and age category, South Africa, 2022, n = 804*

Age category (years)	Private sector	Public sector	n
0 - 4	209	35	244
5 - 14	83	3	86
15 - 24	69	4	73
25 - 34	55	14	69
35 - 44	68	15	83
45 - 54	71	12	83
55 - 64	57	6	63
≥ 65	84	4	88
Unknown	14	1	15
Total	**710**	**94**	**804**

Discussion

As seen in 2020 and 2021, the number of *Campylobacter* spp. isolates submitted by public sector laboratories (94/804, 12%) 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 the culture of *Campylobacter* spp. from stool samples, are also likely contributing factors.

Listeriosis

Results

A total of 88 cases of listeriosis were notified through the NMC surveillance system in 2022. Three provinces reported 76% of the cases: Western Cape (33/88, 38%), Gauteng (20/88, 23%), and KwaZulu-Natal Provinces (17/88, 19%) (Table 36). Cases were most common among adults aged 15 -49 years (35/88, 40%), followed by neonates ≤28 days (24/88, 27%) (Table 37. Gender was known for (87/88; 99%) and females accounted for (50/87; 57%) of cases.

Twenty-seven of 88 cases (31%) were detected at ESS sites, and listeriosis case investigation forms were completed for 17 cases (63%) at these sites (Table 37). Patients were aged between 0 and 85 years with a median age of 41 years, with 65% (11/17) being female. HIV status was known for 88% (15/17) of the cases, of which six were HIV-infected. Five (5/17; 29%) deaths were reported and one pregnancy associated case that resulted in a still-birth was also reported.

Table 36. Number and percentage of cases of listeriosis reported from ESS by province, South Africa, 2022 (n = 27)

Province	Total cases	Cases reported from ESS		Completed case reports	
		n	%	n	%
Eastern Cape	11	4	36	3	75
Free State	4	2	50	1	50
Gauteng	20	8	40	5	63
KwaZulu-Natal	17	3	18	2	67
Limpopo	0	0	0	0	0
Mpumalanga	1	1	100	1	100
Northern Cape	1	0	0	0	0
North West	1	1	100	0	0
Western Cape	33	8	24	5	63
South Africa	**88**	**27**	**31**	**17**	**63**

Table 37. Number and percentage of cases of listeriosis reported from ESS by age group, South Africa, 2022 (n = 27)

Province	Total cases	Cases reported from ESS	
		n	%
Neonate (≤28 days)	24	4	17
Children (1month-14 years)	4	0	0
Adults (15-49 years)	35	14	40
Adults (50-64 years)	9	3	33
Elderly (≥65 years)	13	4	31
Unknown age	3	2	67
Total	**88**	**27**	**31**

Discussion

The number of listeriosis cases for 2022 (88) 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). As seen previously, most cases are reported from Western Cape, Gauteng and KwaZulu-Natal Provinces; with a lower percentage of cases reported from Gauteng in 2022 compared with 2020 and 2021. In contrast to previous years, more cases were reported in the 15 -49 year age group (35/88, 40%) than in neonates ≤28 days (24/88, 27%) in 2022.

Vibrio cholerae

Results

Four isolates were received for testing, and all were confirmed to be nontoxigenic non-O1, non-O139 *V. cholerae.*

Discussion

Four cases of nontoxigenic non-O1 non-O139 *V. cholerae* were identified in 2022, but these do not meet the case definition for a cholera case and do not warrant a public health response. Prior to this reporting period, the last case of toxigenic *V. cholerae* O1 was identified in 2020.

Rifampicin-susceptible Tuberculosis

Results

Participants with confirmed Rifampicin-susceptible TB were enrolled from the following seven provinces: Eastern Cape, Free State, Gauteng, KwaZulu-Natal (KZN), Limpopo, Mpumalanga and North West and 583 sputum samples were collected. Majority of samples received were from Gauteng (36%), followed by KwaZulu-Natal (30%), North West (23%), Eastern Cape (6%) with Free State, Limpopo and Mpumalanga Provinces contributing less than 5% each. Sixty-five percent (244/371) of sputum samples were smear positive, 154 were culture negative and 23 contaminated. Valid drug susceptibility results for INH were available for 399 isolates, for which 371 completed case report forms (CRFs) were available for analysis. Risk factor analysis was limited to participants with completed CRFs. More than half (58%) of the samples were from male participants. Sixty-seven percent (250/371) of the participants were HIV positive with 45% (113/250) already on ART. Nineteen percent reported to have at least one episode of previous episode of TB infection. Table 38 shows the comparison of risk factors by INH resistance. Isoniazid resistance was detected in 48 samples (13%); 15 each were from Gauteng, KwaZulu-Natal and North West, two from Eastern Cape, and one from Mpumalanga. The overall Isoniazid (INH) Mono Resistance (IMR) prevalence was 13% [(95% CI: 9.5% - 16.1%)]. Only ten participants reported taking TB preventative therapy, and one of these participants had INH Resistance.

Table 38. Comparison of risk factors by INH resistance.

	INH mono Sensitive n=323 (87%)	INH mono resistant n=48 (13%)	Total N=371	p Value
Gender				0,359
Female	137 (42)	17 (35)	154 (42)	
Male	186 (58)	31 (65)	217 (58)	
Age category (n=365)				0,145
<20	5 (2)	1 (2)	6 (2)	
20-34	126 (40)	12 (26)	138 (38)	
35-49	109 (34)	23 (49)	132 (36)	
50+	78 (25)	11 (23)	89 (24)	
Province				0.69*
EC	14 (4)	2 (4)	16 (4)	
FS	4 (1)	0 (0)	4 (1)	
GP	125 (39)	15 (31)	140 (38)	
KZN	91 (28)	15 (31)	106 (29)	
LP	1 (0)	0 (0)	1 (0)	
MP	7 (2)	1 (2)	8 (2)	
NW	81 (25)	15 (31)	96 (26)	
Education				0,926
No formal	23 (7)	4 (8)	27 (7)	
Primary	112 (35)	17 (35)	129 (35)	
Secondary	173 (54)	26 (54)	199 (54)	
Tertiary	15 (5)	1 (2)	16 (4)	
Employment (n=368)				0,449
Full-time employment	31 (10)	2 (4)	33 (9)	
Part-time employment	22 (7)	5 (11)	27 (7)	
Self-employed	7 (2)	0 (0)	7 (2)	
Unemployed	261 (81)	40 (85)	301 (82)	0,659
Healthcare worker				
No	320 (99)	48 (100)	368 (99)	
Yes	3 (1)	0 (0)	3 (1)	
HIV status				0,833
Negative	85 (26)	14 (29)	99 (27)	
Positive	219 (68)	31 (65)	250 (67)	
Unknown	19 (6)	3 (6)	22 (6)	
Previous TB (n=370)				0,434
No	263 (81)	37 (77)	300 (81)	
Yes	59 (18)	11 (23)	70 (19)	
Unknown	1 (0)	0 (0)	1 (0)	
IPT (n=250)				0,885
No	195 (89)	29 (94)	224 (90)	
Yes	9 (4)	1 (3)	10 (4)	
Unknown	15 (7)	1 (3)	16 (6)	

*p-value for EC, GP, KZN and NW only

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, however, less than half of those who were HIV positive were already part of the ARV program. The number of participants on TB preventative therapy (TPT) was extremely low, with less than 5% (10/250) of HIV positive participants reported being on TPT. This shows a gap in the implementation of the TPT programme which requires strengthening. Age and gender distribution of the participants was in keeping with the National reports, showing male dominance. A large proportion of participants were unemployed (82%), higher than the previous year (75%) an underappreciated factor that has an impact on health access. The overall prevalence of IMR (13%) was higher than what was re-ported in the National TB drug resistant survey 2012-2014 (5-8%), and higher than the previous year (2021: 7.4%). Unfortunately, the low number of samples received during the previous two surveillance years (within the COVID pandemic) does not allow for robust analysis of resistance rates and robust comparison to previous years. The high smear positivity is indicative of transmission of IMR, particularly in Gauteng, KwaZulu-Natal and North West provinces, which also have the highest IMR rates. No significant risk factor for INH resistance was detected. The findings of this surveillance has important public health importance, and even though the surveillance was conducted only at a few sites, the results obtained are useful and insightful to understand the epidemic and monitor trends.

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SUMMARY

In 2022, GERMS-SA continued to be a fundamental laboratory-based surveillance programme at the NICD to report pathogen specific trends. The face-to-face interaction of surveillance staff and patients improved after the COVID19 changes but loss of surveillance staff, and posts being frozen, impacted heavily on our consenting rates and interviews done although the number of completed CRFs almost reached target. Case patient alert reports were generated by SDW and NMC to promote prompt tracing of patients meeting the case definitions. Data quality constantly improved through training and auditing of our surveillance officers' data.

Opportunistic infections: In 2022, the laboratory-confirmed cryptococcosis incidence risk decreased in all provinces compared to 2021. Although more than half of patients receive flucytosine-based induction regimens, the in-hospital case-fatality rate remained high (38%). The proportion of patients at ESS receiving flucytosine-based induction through a national access program, decreased to 52% in 2022. **Rifampicin-susceptible TB** surveillance in seven provinces, over a limited surveillance time-period, showed 67% of patients being HIV-infected and 45% already on anti-retroviral treatment. TPT program requires strengthening, only ten participants reported taking TB preventative therapy. A large proportion of participants were unemployed (82%), an underappreciated factor that has an impact on health access. For **nontyphoidal salmonellosis,** HIV infection remains the single most important risk factor for invasive disease and reported more commonly in adults aged 35-44 years. Provincial differences in serovar proportions might reflect local transmission dynamics or undetected outbreaks, and require further investigation.

Vaccine-preventable diseases: The 2022 data continue to monitor trends in IPD and Hib, post-EPI vaccine introduction of PCV13 and Hib booster (2009). Incidence of **invasive HI** returned to pre-COVID-19 pandemic levels. Infants had the highest incidence of HI, with HNT predominating over Hib. 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 was 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. Western Cape Province had a disproportionately high burden of IPD. In-hospital mortality from IPD remained high and a third of patients who survived IPD meningitis suffered sequelae. Serotype distribution of IPD was diverse with serotypes 8, 3, 19F and 19A predominating in various age-categories. One fifth of IPD disease in infants and two-fifths in the 5-9 years age category was caused by serotypes in PCV13. As South Africa moves forward to changes in pneumococcal conjugate vaccine formulations in the expanded programme on immunisation, it is important that IPD surveillance in South Africa is continued. In South Africa, infants particularly neonates carry a huge burden of invasive **group B strep disease.** Fewer cases were identified in less populated provinces, possibly due to under-ascertainment of cases through poor blood-culturing practices particularly amongst neonates. Serotype distribution was 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.

Epidemic-prone diseases: (Notifiable medical conditions): The incidence of **invasive meningococcal disease** in 2022 was double that in 2021. Serogroup B, W and Y occurring in equal numbers were dominant in the Western Cape Province. The increase in penicillin non-susceptible isolates is concerning and these isolates will be sequenced for further analysis. IMD is a serious infection with a high case-fatality and a third of those surviving to discharge developed long-term sequelae. In 2022, the highest number of **enteric fever** cases were reported since 2006. Cases from an outbreak strain originating in North West province were identified in other provinces. All isolates were susceptible to azithromycin and 10% were resistant to ciprofloxacin. Although ***Shigella*** infection has been associated with waterborne outbreaks in South Africa, person-to-person transmission plays an important role. More cases of shigellosis were reported in 2022 than in 2021. Contrary to previous years, typical pattern suggestive of seasonality was noted in January and February. The number of listeriosis cases for 2022 (88) was 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 2022 through the NMC surveillance system, four cases of cholera were reported and confirmed to be nontoxigenic non-O1, non-O139 *V. cholerae*. These reported cases were not considered to be **cholera** and do not warrant a public health response. Highest case numbers of **campylobacteriosis** appeared in the warmer months, January to February and November to December and were reported in children younger than five years (244/804, 30%). **Invasive group A strep** mostly affected infants and the elderly, with origin of the disease spread-ing mostly from the skin. In-hospital mortality is high. Isolates were highly susceptible to first line antimicrobial agents, penicillin and erythromycin.

PUBLICATIONS

Peer-reviewed GERMS-SA and GERMS-SA-related publications 2022

1. Mashau RC, Meiring ST, Quan VC, Nel J, Greene GS, Garcia A, Menezes C, Reddy DL, Venter M, Stacey S, Madua M, Boretti L, Harrison TS, Meintjes G, Shroufi A, Trivino-Duran L, Black J, Govender NP; GERMS-SA. Outcomes of flucytosine-containing combination treatment for cryptococcal meningitis in a South African na-tional access programme: a cross-sectional observational study. Lancet Infect Dis. 2022 Jun 21:S1473-3099(22)00234-1. doi: 10.1016/S1473-3099(22)00234-1.
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