GERMS SOUTH AFRICA

Annual Report 2012

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

The GERMS-SA Annual Report 2012 was compiled by the National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.

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Introduction

The GERMS-SA 2012 Annual Report summarises the findings from national surveillance, including the 25 enhanced surveillance hospital sites (ESS) in all 9 provinces, for the year. Candidaemia surveillance was added to the list of surveillance pathogens in 2012; *Staphylococcus aureus* enhanced surveillance and rifampicin-resistant tuberculosis surveillance began in September 2012. For this report, *S. aureus* laboratory data are included only from January to July 2012, with ESS data included from September to December 2012, and only a narrative is included for TB surveillance. *Klebsiella pneumoniae* surveillance ended in July 2012. Laboratory information systems continued to change in 2012 (from DISA*Lab to TrakCare Lab) and audits continued to be problematic, however, for the first time, KwaZulu-Natal NHLS laboratories were included in our audits.

The Department of Health has implemented and improved on many health interventions (new vaccine introductions in the Expanded Programme on Immunisations and the Comprehensive Care, Management and Treatment Programme for HIV/AIDS) and the robust GERMS surveillance system continues to monitor the impact of these programmes on the South African population.

GERMS-SA surveillance officer meeting, Durban, August 2012.

Methods

In 2012, diseases under surveillance included:

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

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

In brief, approximately 200 South African clinical microbiology laboratories participated in the surveillance programme in 2012. The population under surveillance in 2012 was estimated at 52.3 million (Table 1). Diagnostic laboratories reported case patients to the National Institute for Communicable Diseases (NICD) using laboratory case report forms, according to standard case definitions. If available, isolates from case patients were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. From 1 July 2008, surveillance methodology for the cryptococcal project was changed, so that only enhanced surveillance sites (ESS) (25 hospitals in 9 provinces), NHLS laboratories in KZN, and laboratories in the private, mining, and military sectors were required to directly report case patients to NICD. For other cases of cryptococcosis, data were obtained directly from the NHLS Central Data Warehouse (CDW), which obtains information from Disa*Lab and TrakCare laboratory information systems. Cryptococcal isolates, obtained from patients at ESS, continued to be characterised by phenotypic and genotypic tests. From July 2010, 7 sentinel sites reported cases of *S. aureus* and *K. pneumoniae* bacteraemia and from January 2012, 9 sentinel sites reported cases of candidaemia to GERMS-SA. *K. pneumoniae* surveillance stopped in July 2012. Laboratory bacteraemic *S. aureus* surveillance continues at 3 Gauteng sites only. At ESS, surveillance officers completed clinical case report forms for patients with six laboratory-confirmed diseases (cryptococcosis, invasive salmonellosis, invasive pneumococcal disease, invasive shigellosis, invasive meningococcal disease, invasive *Haemophilus influenzae* disease and candidaemia [and from September 2012 for *S. aureus* at 3 sites and rifampicin-resistant tuberculosis at 4 sites]), by case patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status, and patient outcome. Case patients were followed up only for the duration of the hospital admission. Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on a Microsoft Access database. A surveillance audit was performed using the NHLS CDW for NHLS laboratories in all provinces. For all diseases under surveillance, except cryptococcosis, the audit was designed to obtain basic demographic and laboratory data from additional case patients with laboratory-confirmed disease not already reported to GERMS-SA by participating laboratories. For cryptococcosis, the audit was designed to obtain data from cases that were no longer reported by NHLS laboratories. Data from case patients, detected by audit, were included on the surveillance database, and have been included in this report; however, NHLS changing over from the DISA*lab to TrakCare Lab has proved difficult for our auditing purposes and all case numbers may not be reflected. Incidence was calculated using mid-year population estimates for 2011 and 2012 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2011 and 2012, using estimated population denominators from the Actuarial Society of South Africa (ASSA) 2008 model (Table 1), assuming that the HIV/AIDS prevalence amongst cases with known status was similar to those with unknown status (3). All reported incidence is expressed as cases per 100 000 population, unless otherwise stated. Reported p-

Table 1: Population denominators used to calculate incidence rates, 2011 and 2012

Province	General population*		HIV-infected population**		AIDS population**	
	2011	2012	2011	2012	2011	2012
Eastern Cape	6553889	6586307	715736	736404	60525	64849
Free State	2744120	2748506	351746	355466	35390	36010
Gauteng	12202306	12463886	1215856	1222605	126240	132375
KwaZulu-Natal	10236872	10345539	1576025	1602236	149621	158413
Limpopo	5388120	5452206	409161	423400	32285	36035
Mpumalanga	4022088	4074763	482288	492287	44827	46712
Northern Cape	1143254	1153090	76966	78711	6868	7617
North West	3496855	3546631	431576	436670	44230	45384
Western Cape	5792096	5904017	273114	278889	24533	27595
South Africa	**51 579 600**	**52 274 945**	**5 532 468**	**5 626 668**	**524 519**	**554 990**

Data sources: *Statistics South Africa; **Actuarial Society of South Africa (ASSA2008)

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values were calculated using the Mantel-Haenszel chi-squared test and p values < 0.05 were considered significant throughout. Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/NHLS, and ESS activities continued to be funded by a CDC-NICD Cooperative Agreement (U62/CCU022901).

Operational Report

Site visits

In 2012, NICD staff members undertook 38 visits to 26 surveillance sites in 8 provinces of South Africa (Table 2). This provided the opportunity to engage with staff at many laboratories and hospitals participating in the surveillance programme.

Surveillance audit

Of the 17 733 surveillance cases on the GERMS-SA database, 6663 (38%) were detected by audit of the NHLS CDW (Table 3). This percentage has been artificially inflated by the audit for cases of cryptococcosis – the number of audit cases includes 3727 of the 4897 cryptococcal cases from non-enhanced surveillance sites that, since July 2008, were not required to be reported to GERMS-SA. Only 24% (452/1920) of cases of cryptococcosis were not reported to the surveillance programme by enhanced surveillance sites that are required to report cases. Therefore, only 17% (2936/17 733) of the total GERMS-SA cases were true audit cases (not reported to the NICD by the clinical microbiology laboratories). GERMS-SA constantly strives to reduce the number of cases detected on audit by raising awareness of the surveillance programme; this is important because GERMS-SA is unable to perform additional microbiological characterisation of isolates detected only through audit.

Enhanced surveillance site performance indicators

The number of cases at enhanced surveillance sites in 2012 was similar to that in 2011. Completed CRFs were lower in 2012 compared to 2011 and this is mostly due to the addition of pathogens that cause more severe illness (candidaemia and *S. aureus*), making it more difficult to follow up patients (Table 4 and 5): 82% (3605/4384) of cases had a case report form completed (target = 90%). The interview rate continues to improve over the years [2603 (72%) of the case report forms were completed by patient interview (target = 60%)]; quality indicators also improved. Since 2007, enhanced surveillance site operational reports (ESSOR) have been provided to the site coordinators, laboratory staff and surveillance officers to enable the site team to regularly review site performance, in comparison with set targets. The main objective of these reports is to provide information regarding the overall functioning of the surveillance site, by providing indicators of laboratory participation (submission of isolates), and indicators of surveillance officer performance (completion of case report forms). By reviewing these indicators, problems with data collection can be targeted and recommendations provided to improve the site performance. In 2012, these reports were provided quarterly.

Coordination of meetings

Surveillance officer meeting, 6-7 March 2012: This meeting, convened at the NICD in Johannesburg, was attended by all surveillance officers from 9 provinces. The meeting focused on outlining the GERMS-SA surveillance programme and nested studies, improving surveillance data-capture, -entry and -reporting, and addressing occupational health and safety issues. The addition of rifampicin-resistant TB was also discussed.

Surveillance officer meeting, 22-24 August 2012: This meeting was convened in Durban, KZN, attended by 29 surveillance officers and a number of laboratory staff from the KZN sites. It included two and half days of training, and discussion of enhanced surveillance site performance indicators. The meeting focused on updates on additional projects in the GERMS-SA surveillance programme (rifampicin-resistant TB) and included training on *S. aureus* case report forms.

Principal Investigator (PI) meeting, 10-11 October 2012: Convened at the NICD, this meeting was attended by over 50 local, national and international delegates, including representatives from the Department of Health and Centers for Disease Control and Prevention. Surveillance and research activities were reviewed, and new NICD projects which could impact on the GERMS-SA network were discussed. The meeting was an opportunity to share information on all GERMS-SA pathogens and discuss the inclusion of TB on the GERMS-SA platform.

Table 2: GERMS-SA surveillance site visits between 1 January and 31 December 2012.

Date	Province	Laboratory	Hospital
16 January	WC	NHLS Groote Schuur	Groote Schuur Hospital
18 January	GA	NHLS Charlotte Maxeke Jhb Academic	Charlotte Maxeke Johannesburg Academic Hospital
24 January	WC	NHLS Tygerberg	Tygerberg Hospital
26 January	NC	NHLS Kimberly	Kimberly Hospital
01 February	GA	NHLS Leratong	Leratong Hospital
17 February	WC	Tygerberg Forensic Pathology	Tygerberg Medical School
20 February	GA	NHLS Chris Hani Baragwanath	Chris Hani Baragwanath Medical School
19 March	KZ	NHLS King Edward VIII	King Edward VIII Hospital
20 March	NW	NHLS Rustenburg & Potchefstroom	Job Tabane and Tshepong Hospitals
30 March	GA	NHLS Rahima Moosa Mother & Child	Rahima Moosa Mother & Child Hospital
13 April	GA	-	Charlotte Maxeke Jhb Academic Hospital clinicians
17 April	WC	-	Red Cross Hospital Ophthalmology & HIV Clinics
24 April	MP	NHLS Witbank Pathology	Witbank Hospital
24 & 25 April	GA	NHLS Helen Joseph	Helen Joseph Hospital
08 May	GA	-	Chris Hani Baragwanath NICU clinicians
08 May	FS	NHLS Universitas & Pelonomi	Universitas & Pelonomi Hospitals
09 May	GA	NHLS Steve Biko Pretoria Academic	Steve Biko Pretoria Academic Hospital
11 & 25 May	KZ	NHLS Greys	Greys Hospital
17 May	GA	NHLS Charlotte Maxeke Jhb Academic	Charlotte Maxeke Johannesburg Academic Hospital
29 May	GA	NHLS Steve Biko Pretoria Academic	Steve Biko Pretoria Academic Hospital
04 & 05 June	KZ	NHLS RK Khan	RK Khan Hospital
08 June	GA	NHLS Dr George Mukhari Academic	Dr George Mukhari Academic Hospital
28 June	WC	Tygerberg Forensic Pathol/ NHLS Microbiol	Tygerberg Hospital
02 August	WC	-	Groote Schuur Hospital clinicians
21 August	KZ	NHLS St Mary's	St Mary's Hospital and St Anne's Clinic
13 September	GA	NHLS Charlotte Maxeke Jhb Academic	Charlotte Maxeke Johannesburg Academic Hospital
26 September	KZ	NHLS Northdale	Northdale Hospital
16 October	WC	NHLS Tygerberg	Tygerberg Hospital
25 October	WC	NHLS Groote Schuur	Groote Schuur Hospital
25 October	LP	NHLS Polokwane & Mankweng	Polokwane and Mankweng Hospitals
08 November	GA	NHLS Chris Hani Baragwanath TB	Chris Hani Baragwanath Hospital
20 November	FS	NHLS Universitas & Pelonomi	Universitas and Pelonomi Hospitals
04 December	GA	NHLS Helen Joseph	Helen Joseph Hospital
11 December	GA	NHLS South Rand	South Rand Hospital

Table 3: Cases detected by surveillance audit by province, 2012.

	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	Typhoid**	5/47 (11%)	2	0	1	0	0	2	0	0	0	**5**
	Non-typhoidal salmonellosis†	106/647 (16%)	10	4	24	48	0	5	2	4	9	**106**
	Shigellosis	7/37 (19%)	1	0	1	3	1	0	0	0	1	**7**
	Cryptococcosis†††	4179/6817 (61%)	980	245	1057	974	132	222	8	251	310	**4179**
	Candida spp	56/532 (11%)	N/A	N/A	45	N/A	N/A	N/A	N/A	N/A	11	**56**
	Meningococcal disease	39/230 (17%)	13	3	13	4	0	1	1	2	2	**39**
	Haemophilus influenzae disease	98/327 (30%)	19	4	22	24	0	3	0	5	21	**98**
	Pneumococcal disease	717/3221 (22%)	78	61	220	231	11	32	5	54	25	**717**
	Staphylococcus aureus disease (BC only)	465/1341 (35%)	N/A	59	200	175	N/A	N/A	N/A	N/A	31	**465**
	Klebsiella pneumoniae (BC only; Jan-Jul 2012)^	527/1426 (37%)	N/A	58	239	189	N/A	N/A	N/A	N/A	41	**527**
Non-invasive	*Salmonella* Typhi**	2/16 (13%)	0	0	1	0	0	0	1	0	0	**2**
	Non-typhoidal salmonellosis†	274/1490 (18%)	34	15	67	85	5	20	3	15	30	**274**
	Shigellosis	188/1602 (12%)	18	2	48	63	3	5	6	6	37	**188**
	Cholera††	0/0 (0%)	0	0	0	0	0	0	0	0	0	**0**
	Total	**6663/ 17 733 (38%)**	**1155**	**451**	**1938**	**1796**	**152**	**290**	**26**	**337**	**518**	**6663**

*Percentage of cases detected by audit = number of cases detected on audit (n_1)/total number of cases detected by GERMS-SA (n_2) x 100; **Only *Salmonella enterica* serotype Typhi; †Including *Salmonella enterica* serotype Paratyphi; ††Only *Vibrio cholerae* O1; †††Cryptococcal cases detected by audit = number of cases not reported by enhanced surveillance sites + cases from all non-enhanced surveillance sites not required to report cases since July 2008; ^*Klebsiella* spp bacteraemia surveillance was done until end July 2012. 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.

Table 4: Enhanced surveillance site performance indicators, 2012.

Enhanced surveillance site*	Case patients, n	Completed case report forms**, n (%)***	Case report forms completed by interview, n (%)†	Completion of select data fields for interviewed patients††, (%)
Addington	145	129 (89)	70 (54)	100
Charlotte Maxeke Johannesburg Academic ^^	581	481 (83)	324 (67)	100
Chris Hani Baragwanath ^	923	724 (78)	414 (57)	100
Dr George Mukhari	208	179 (86)	149 (83)	100
Donald Gordon Medical Centre ^	1	0	0	100
Edendale/ Greys/ Northdale^^^	413	314 (76)	256 (82)	100
Groote Schuur/ Red Cross/ Victoria ^	342	320 (94)	244 (76)	100
Helen Joseph/ Rahima Moosa Mother & Child ^^	254	156 (61)	139 (89)	100
Kimberley	103	82 (80)	58(71)	100
King Edward VIII	111	81 (79)	58 (72)	100
Mankweng/Polokwane	79	74 (94)	70 (95)	100
Nelson Mandela Academic Complex	172	146 (85)	101 (69)	99
Pelonomi/ Universitas	148	126 (85)	104 (83)	100
R K Khan	196	183 (93)	159 (87)	99
Rob Ferreira/ Themba	200	179 (89)	134 (75)	99
Rustenburg	94	87 (93)	73 (84)	100
Steve Biko Pretoria Academic/ Tshwane District ^^	257	204 (79)	183 (90)	100
Tygerberg ^	157	140 (89)	67 (48)	100
TOTAL	**4384**	**3605 (82)**	**2603 (72)**	**99.8%**

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; *There were 6 surveillance officers at Chris Hani Baragwanath and 3.5 at Charlotte Maxeke Johannesburg Academic, 3 at Groote Schuur/Red Cross/Victoria, 2 at Tygerberg, 1.5 at Dr George Mukhari, Steve Biko Academic Hospital and Edendale/Greys; one surveillance officer was present at all other sites. **Low case report form completion rates at certain sites are due to challenges in completing CRFs for certain pathogens. ***Target = 90%; †Target = 60%; ††This was calculated by subtracting the proportion of "unknown" answers from a particular field on the case report form, which could easily have been answered by a patient on interview. ^Sites doing candidaemia surveillance; ^^Sites doing *S. aureus* enhanced surveillance (bacteraemia only). ^^^Northdale only started as ESS 1 September 2012.

Surveillance reports

Enhanced surveillance site project

In 2012, of 17 733 surveillance case patients detected by GERMS-SA, 4384 (25%) were diagnosed at enhanced surveillance sites. Of case patients with recorded HIV status, 76% (2420/3176) were HIV-infected (Table 5). The proportion of case patients with confirmed HIV infection varied by surveillance disease: unsurprisingly, a very high proportion of patients with AIDS-defining infections like cryptococcosis (98%) were HIV-infected; HIV infection amongst patients with invasive pneumococcal disease and non-typhoidal salmonellosis, for which HIV is a known risk factor, were 67% and 66%, respectively, and less than one third (29%) of patients with invasive meningococcal disease were HIV-infected.

Table 5: Number and percentage* of patients, diagnosed with laboratory-confirmed invasive disease at GERMS-SA enhanced surveillance sites, with confirmed HIV-1 infection, South Africa, 2012.**

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	1920	1653 (86)	1571 (95)	1532 (98)
Neisseria meningitidis	90	76 (87)	66 (87)	19 (29)
Streptococcus pneumoniae	1170	1028 (88)	892 (87)	597 (67)
Haemophilus influenzae	171	144 (87)	117 (81)	46 (39)
Salmonella species	326	277 (85)	248 (89)	164 (66)
Shigella species	16	15 (94)	12 (80)	8 (67)
Candida species	532	351 (66)	247 (70)	46 (19)
Staphylococcus aureus	159	61 (38)	23 (68)	8 (35)
Total	**4384**	**3605 (82)**	**3176 (88)**	**2420 (76)**

*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.

Salmonella enterica serotype Typhi and *S. enterica* serotypes Paratyphi A, Paratyphi B and Paratyphi C

Results

Salmonella Typhi isolates from both invasive and non-invasive sites are reported in Table 6. Cases of enteric fever were highest in October, although there was an unusual peak in July (Figure 1). The number of isolates within each age group is reported in Table 7, indicating that most isolates are from patients in the 5-34 year age group, although infection is seen in both older and younger age groups, including younger children (less than five years). Ciprofloxacin resistance remains a problem, but azithromycin resistance has not been recorded (Table 8), following EUCAST guidelines (4). One isolate of *Salmonella* Paratyphi A and of *Salmonella* Paratyphi B var Java were received from the Western Cape, from blood culture and a stool culture respectively. Both patients were adult females. Both isolates were susceptible to first and second line antimicrobials. No isolates of *Salmonella* Paratyphi C were received in 2012.

Discussion

Salmonella Typhi isolates from both invasive and non-invasive sites are included in these analyses, as both add to burden of infection in South Africa and thus represent a public health risk, although data may not reflect actual burden of disease. Strict seasonality is not observed, but case numbers are low. This is compounded by the challenges of alternative diagnostic methods for typhoid fever, including both clinical and serological. These data thus exclude those patients in whom an alternative diagnosis was made, without culture confirmation. The number of reported *Salmonella* Typhi isolates was regarded as an underestimate and thus incidence rates were not calculated. EUCAST guidelines for *Salmonella* Typhi provide break points for azithromycin, which is an alternative treatment option, as ciprofloxacin resistance emerges (4). Ceftriaxone may also be used as an alternative therapy in these cases.

Figure 1. Number of non-invasive and invasive cases of *Salmonella* Typhi (n=63) and Paratyphi (n=2) reported to GERMS-SA, by month of specimen collection, South Africa, 2012 (including audit reports).

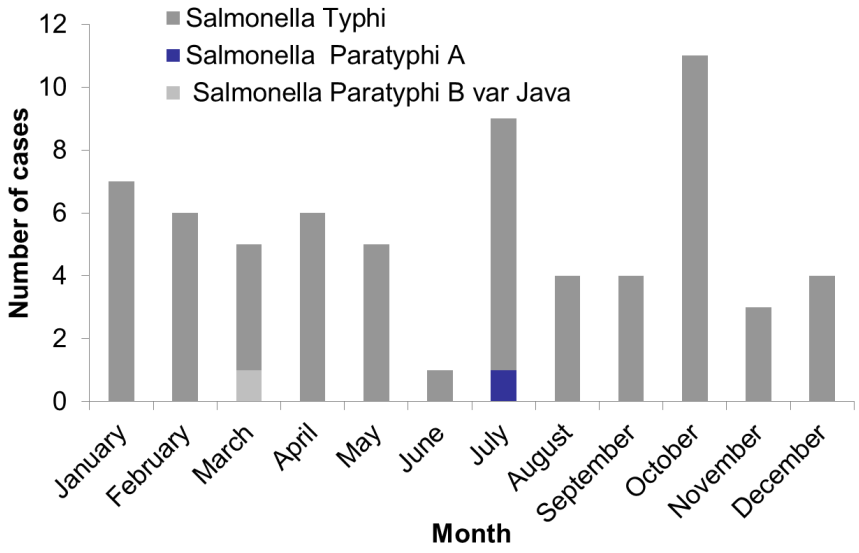


Table 6: Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2012, n=63 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	0	3
Free State	0	0
Gauteng	5	18
KwaZulu-Natal	3	9
Limpopo	0	1
Mpumalanga	3	7
Northern Cape	0	0
North West	1	0
Western Cape	4	9
South Africa	**16**	**47**

Table 7: Number of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2012, n=63 (including audit reports, missing isolates, mixed and contaminated cultures).

Age category (years)	*Salmonella* Typhi isolates
0 - 4	16
5 - 14	13
15 - 24	9
25 - 34	10
35 - 44	4
45 - 54	5
55 - 64	1
≥ 65	5
Total	**63**

Table 8: Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2012, n=56 (excluding audit reports, missing isolates, mixed and contaminated cultures). Clinically relevant antimicrobials are reported (4).

Antimicrobial agent	Susceptible (%)	Resistant (%)
Ampicillin	33 (59)	23 (41)
Chloramphenicol	36 (64)	20 (36)
Ciprofloxacin	46 (82)	10 (18)
Imipenem	56 (100)	0 (0)
Ceftriaxone	56 (100)	0 (0)
Azithromycin	56 (100)	0 (0)

Non-typhoidal *Salmonella enterica* (NTS)

Results

Invasive disease does not appear to have a seasonal prevalence; increased numbers of non-invasive disease due to NTS in the earlier months of the year and December reflect seasonality, although a lower peak occurred in the winter months (Figure 2). The number of cases of invasive and non-invasive disease, by province, reported to GERMS-SA, is stated in Table 9. The number of cases of invasive and non-invasive disease, by age group, is shown in Table 10. Most invasive isolates were identified from blood cultures, although isolates were frequently identified from both blood culture and another site, including stool and other normally-sterile sites (Table 11). Resistance to first-line antimicrobial agents and the fluoroquinolones was noted (Table 12), as well as ESBL production (119/1721 (7%) of all NTS). *Salmonella* Enteritidis was the most common NTS isolated (Table 13).

Discussion

Non-typhoidal salmonellosis may be a food-borne disease, for which data are poorly captured in South Africa, and where the patients normally present with gastroenteritis, or may be an AIDS-defining illness, in which case the organism frequently becomes invasive. Seasonal prevalence was noted in 2012 for non-invasive disease, however an unusual peak in case numbers between May and July in non-invasive isolates reflects a nosocomial outbreak of *Salmonella* gastroenteritis in the Eastern Cape, rather than seasonality (5). Incidence rates have only been calculated for invasive NTS, due to differences in stool-taking practices in adult and paediatric medical care. Antimicrobial resistance remains a cause for concern in invasive and non-invasive cases. *Salmonella* Enteritidis was the commonest serotype, as noted in 2011 (6).

Figure 2. Number of non-invasive (n=1490) and invasive (n=647), non-typhoidal *Salmonella* (NTS) cases, reported to GERMS-SA, by month of specimen collection, South Africa, 2012 (including audit reports).

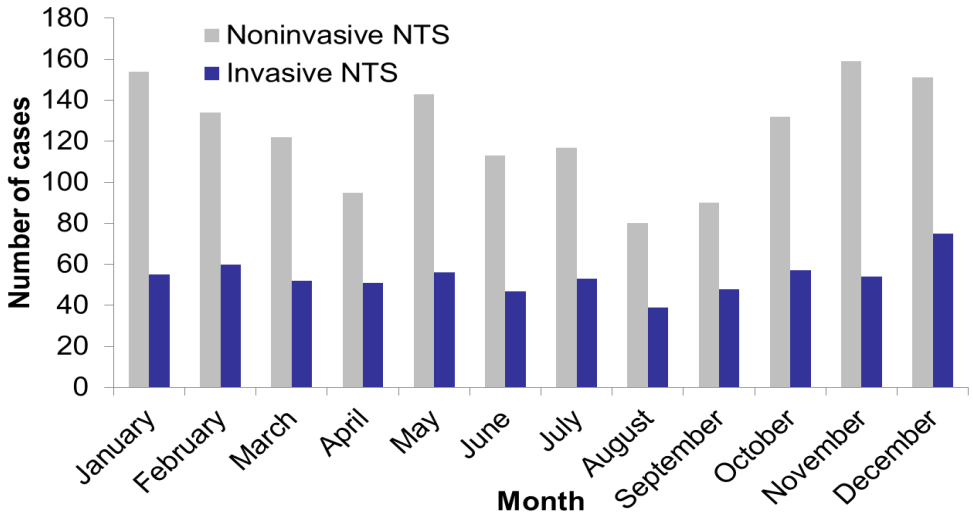


Table 9: Number* of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2012, n= 2137 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive, non-typhoidal *Salmonella* isolates	Invasive, non-typhoidal *Salmonella* isolates
Eastern Cape	183	41
Free State	36	16
Gauteng	560	313
KwaZulu-Natal	239	118
Limpopo	10	6
Mpumalanga	64	33
Northern Cape	13	11
North West	16	5
Western Cape	369	104
South Africa	**1490**	**647**

*Incidence rates were not calculated as there may have been regional differences in specimen collection practices.

Table 10: Number of cases and incidence rates for invasive* and non-invasive non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2012, n= 2137 (including audit reports, missing isolates, mixed and contaminated cultures).

Age Category (years)	Cases		
	Non-invasive	Invasive	Incidence rate for invasive disease**
0 - 4	519	171	3.23
5 - 14	147	26	0.26
15 - 24	97	37	0.37
25 - 34	176	103	1.14
35 - 44	173	126	1.79
45 - 54	131	72	1.49
55 - 64	73	41	1.30
≥ 65	92	36	1.36
Unknown	82	35	-
Total	**1490**	**647**	**1.24**

*Incidence rates for non-invasive non-typhoidal *Salmonella* were not calculated because specimens may not have been submitted for culture from all patients with gastroenteritis due to non-typhoidal *Salmonella* in clinical practice; **Incidence rates are expressed as cases per 100 000 population.

Table 11: Number of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2012, n=2137 (including audit reports, missing, mixed and contaminated cultures).

Specimen	n	%
CSF	22	1
Blood culture	535	25
Stool	1233	58
Other	347	16
Total	**2137**	**100**

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

Table 12: Antimicrobial susceptibility test results for all non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2012, n=1721 (excluding audit reports, missing isolates, mixed and contaminated cultures). Clinically relevant antimicrobials for non-invasive and invasive strains are reported (4).

Antimicrobial agent	Susceptible (%)		Resistant (%)	
Ampicillin	1503	(87)	218	(13)
Trimethoprim- Sulphamethoxazole	1532	(89)	189	(11)
Chloramphenicol	1523	(89)	198	(11)
Ciprofloxacin	1579	(92)	142	(8)
Imipenem	1721	(100)	0	(0)
Ceftriaxone	1602	(93)	119	(7)

Table 13: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2012, n=1303 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	Serotype				
	Dublin	Enteritidis	Heidelberg	Isangi	Typhimurium
Eastern Cape	4	15	3	2	112
Free State	0	10	0	1	12
Gauteng	7	382	16	13	146
KwaZulu-Natal	17	84	8	5	41
Limpopo	0	6	0	2	0
Mpumalanga	2	42	2	4	7
Northern Cape	0	8	0	0	6
North West	0	0	0	0	1
Western Cape	7	212	11	3	112
South Africa	**37**	**759**	**40**	**30**	**437**

Shigella species

Results

Slightly increased numbers from January to April in 2012 suggest seasonality (Figure 3). Although the primary burden of disease due to *Shigella* is non-invasive dysentery or diarrhoea, invasive disease remains an important cause of morbidity in South Africa (Table 14). The predominant burden of disease, including both invasive and non-invasive shigellosis, is in the under-five-year age group (Table 15). Quinolone resistance remains low, but fluoroquinolone resistance appears to be emerging (Table 16). ESBL-production is rarely documented, but remains important. Predominant serotypes confirm that *S. sonnei* remains the most common cause of shigellosis in South Africa (Table 17). *S. dysenteriae* type 1 was not isolated in 2012 (data not shown). Four (0.3%) of 1433 *Shigella* isolates were ESBL-producers. Of these, a single *S. flexneri* 6 was from a blood culture in an adult; the remainder were from non-invasive specimens from children less than five years of age.

Discussion

Shigella infection is largely due to water-borne outbreaks in South Africa, although person-to-person transmission may play a role. Resistance to fluoroquinolones remains low, but should continue to be monitored. ESBL-production is rarely documented, but must be monitored as ESBL-producing subtypes appear common to those in other nosocomial pathogens (7). Although *S. dysenteriae* type 1 isolates are not reported as there were no isolates in South Africa in 2012, the potential for future epidemics remains in the absence of safe water or sanitation and the availability of a vaccine.

Figure 3. Number of non-invasive and invasive *Shigella* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2012, n=1639 (including audit reports).

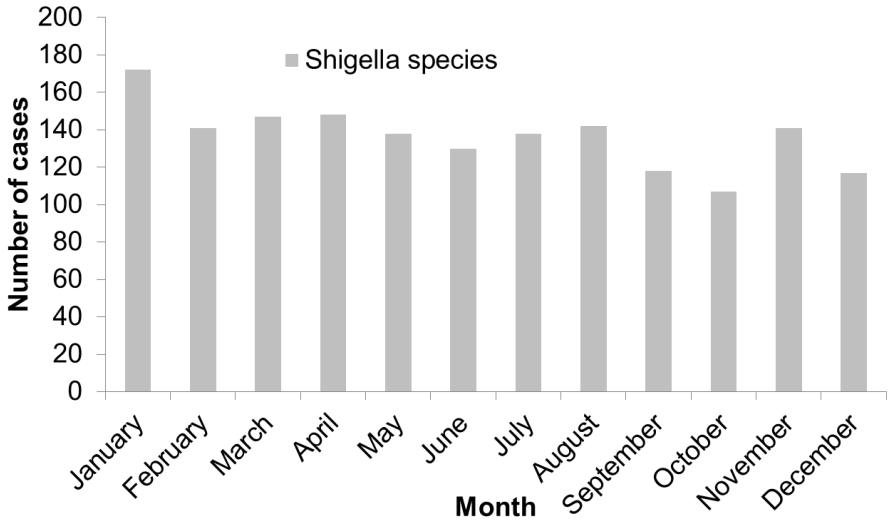


Table 14: Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2012, n=1639 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	271	6
Free State	63	2
Gauteng	581	12
KwaZulu-Natal	224	8
Limpopo	4	1
Mpumalanga	33	2
Northern Cape	31	0
North West	8	0
Western Cape	387	6
South Africa	**1602**	**37**

Table 15: Number of cases* and incidence rates for *Shigella* (invasive and non-invasive) reported to GERMS-SA by age category, South Africa, 2012, n=1639 (including audit reports, missing isolates, mixed and contaminated cultures).**

Age Category (years)	Cases		
	Non-invasive	Invasive	Incidence rate for invasive disease**
0 - 4	739	13	0.25
5 - 14	292	6	0.06
15 - 24	65	5	0.05
25 - 34	143	4	0.04
35 - 44	110	2	0.03
45 - 54	84	1	0.02
55 - 64	54	0	0.00
≥ 65	68	3	0.11
Unknown	47	3	-
Total	**1602**	**37**	**0.07**

*Cases may be under-reported due to local clinical practices: no mixed infections were identified. **Incidence rates are expressed as cases per 100 000 population.

Table 16: Antimicrobial susceptibility test results for *Shigella* isolates received by GERMS-SA, South Africa, 2012, n=1433 (excluding audit reports, missing isolates, mixed and contaminated cultures). Clinically relevant antimicrobials for non-invasive and invasive strains are reported (4).

Antimicrobial agent	Susceptible	(%)	Resistant	(%)
Ampicillin	815	(57)	618	(43)
Trimethoprim- Sulphamethoxazole	247	(17)	1186	(83)
Chloramphenicol	978	(68)	455	(32)
Nalidixic acid	1428	(99.6)	5	(0.4)
Ciprofloxacin	1432	(99.9)	1	(0.1)
Imipenem	1433	(100)	0	(0)
Ceftriaxone	1429	(99.7)	4	(0.3)

Table 17: Commonest invasive and non-invasive *Shigella* serotypes reported to GERMS-SA by province, South Africa, 2012, n=1476 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. flexneri* type 1b	*S. flexneri* type 2a	*S. flexneri* type 3a	*S. flexneri* type 6	*S. sonnei*
Eastern Cape	51	86	34	14	73
Free State	0	20	16	4	20
Gauteng	24	120	66	69	289
KwaZulu-Natal	3	49	20	20	81
Limpopo	1	0	0	0	0
Mpumalanga	1	7	3	8	16
Northern Cape	0	16	0	2	6
North West	0	1	0	0	0
Western Cape	37	157	46	34	82
South Africa	**117**	**456**	**185**	**151**	**567**

Diarrhoeagenic *Escherichia coli* (DEC)

Results

An increased number of cases were identified in October and November (Figure 4). Enteropathogenic *E. coli* (EPEC) remains the commonest cause of diarrhoea, due to this pathogen, identified in South Africa (Table 18). Most cases were identified in children less than 5 years of age (Table 19). No specific serotypes predominated. Among the EHEC/STEC isolates, two isolates of sorbitol-negative *E. coli* O157 were received (data not shown).

Discussion

Fewer isolates were received than in the previous years, possibly due to financial constraints within the health care system (6), but there is a suggestion of seasonality with increased case numbers in the last quarter of the year. The predominance of cases in younger children under five years of age may reflect, in part, specimen-taking practices, as well as the burden of diarrhoeal disease in this age group (Table 19). Incidence rates were not calculated as numbers were not viewed as being fully representative. Actual burden of disease due to diarrhoeagenic *E. coli* is probably greatly underestimated in South Africa, as management is primarily syndromic and centres on rehydration. As a result, clinicians are unlikely to prioritise stool-taking in uncomplicated cases of diarrhoea. Disease in the past appears to have been primarily associated with water-borne outbreaks, due to high levels of faecal contamination in water sources, and this trend appears to be continuing. Identification of EHEC/STEC was primarily incidental, as there are currently no useful biochemical markers in sorbitol-positive isolates (8).

Figure 4. Number of diarrhoeagenic *Escherichia coli* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2012, n=86.

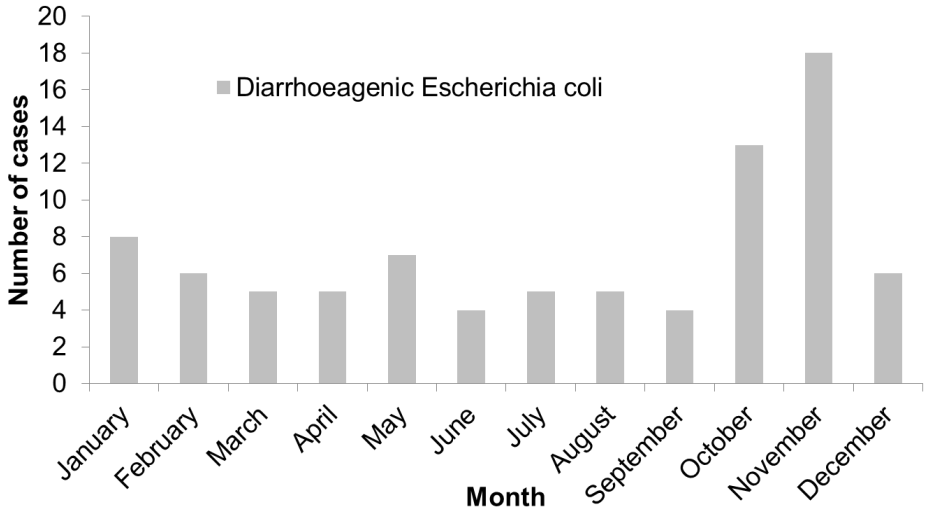


Table 18: Number of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by province, South Africa, 2012, n=86.

Province	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC	Mixed pathotype*
Eastern Cape	3	3	1	0	11	0	0
Free State	0	0	0	0	0	0	0
Gauteng	5	0	3	1	9	0	2
Kwazulu-Natal	1	2	1	0	5	0	0
Limpopo	0	0	0	0	0	0	0
Mpumalanga	9	6	0	3	8	4	0
Northern Cape	0	0	0	0	0	0	0
North West	0	0	0	0	0	0	0
Western Cape	3	2	1	1	2	0	0
South Africa	**21**	**13**	**6**	**5**	**35**	**4**	**2**

DAEC: diffusely-adherent *E. coli*; EAggEC: enteroaggregative *E. coli*; STEC/EHEC: Shiga-toxigenic *E. coli* or enterohaemorrhagic *E. coli*; EIEC: enteroinvasive *E. coli*; EPEC: enteropathogenic *E. coli*; ETEC: enterotoxigenic *E. coli.*
*Mixed pathotype: contained virulence genes from more than one pathotype.

Table 19: Number of diarrhoeagenic *E. coli* isolates reported to GERMS-SA by age category, South Africa, 2012, n=86.

Age category (years)	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC	Mixed pathotype*
0 - 4	8	10	3	0	25	2	2
5 - 14	1	2	0	2	2	0	0
15 - 24	1	0	0	1	2	0	0
25 - 34	3	1	1	0	0	0	0
35 - 44	1	0	0	0	2	0	0
45 - 54	1	0	0	0	1	1	0
55 - 64	3	0	0	0	0	0	0
≥ 65	0	0	1	1	1	1	0
Unknown	3	0	1	1	2	0	0
Total	**21**	**13**	**6**	**5**	**35**	**4**	**2**

DAEC: diffusely-adherent *E. coli*; EAggEC: enteroaggregative *E. coli*; STEC/EHEC: Shiga-toxigenic *E. coli* or enterohaemorrhagic *E. coli*; EIEC: enteroinvasive *E. coli*; EPEC: enteropathogenic *E. coli*; ETEC: enterotoxigenic *E. coli.*
*Mixed pathotype: contained virulence genes from more than one pathotype.

Vibrio cholerae O1

No cases of *Vibrio cholerae* O1 were reported in South Africa in 2012.

Cryptococcus species

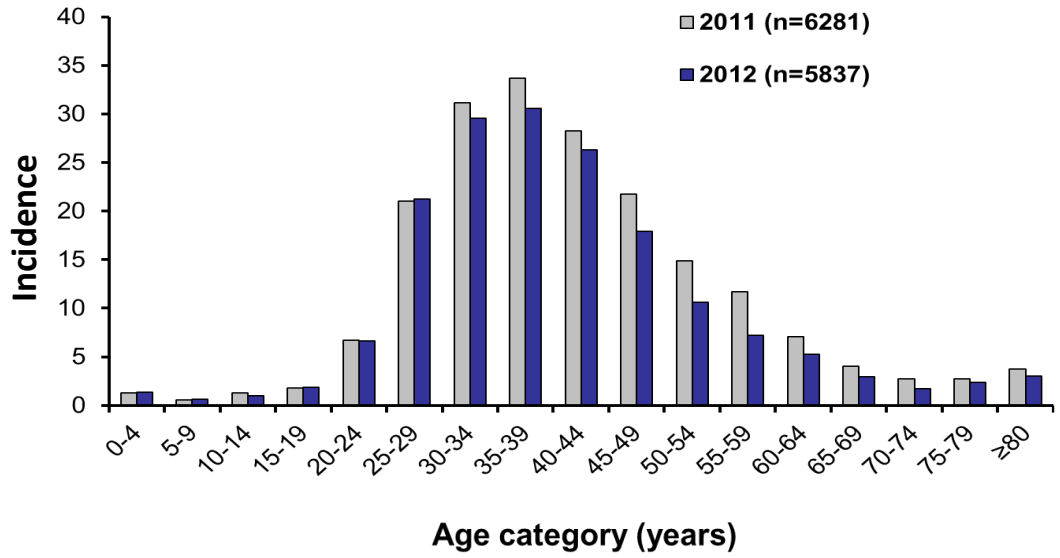
Results

During 2012, 6817 case patients, with laboratory-confirmed, incident cryptococcal episodes, were reported. The incidence of cryptococcal disease in the HIV-infected population has decreased in the Eastern Cape, Free State, Limpopo, Mpumalanga and North West provinces and has increased in Gauteng, Northern Cape and Western Cape provinces (Table 20). The highest incidence was recorded among patients aged 35-39 years: 31 cases per 100 000 persons in the general population (Figure 5). One hundred and fifty-five children younger than 15 years had laboratory-confirmed cryptococcosis; 72/155 (46%) were younger than 5 years of age. Where sex was known (6748/6817, 99%), 47% of patients were female. Most patients (89%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 9% were diagnosed with fungaemia (Table 21). Ninety-six patients were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. At enhanced surveillance sites, 1920 patients were diagnosed with cryptococcosis, with viable isolates received from 1177 (61%) patients. Isolates were speciated from all these cases; 1131 (96%) were identified as *Cryptococcus neoformans* and 46 (4%) were identified as *Cryptococcus gattii.* Cases of *C. gattii* disease were diagnosed in seven provinces: Gauteng (n=18), Mpumalanga (n=14), KwaZulu-Natal (n=5), North West (n=4), Limpopo (n=2), Free State (n=2) and Western Cape (n=1). The in-hospital case-fatality ratio for patients at enhanced surveillance sites did not change significantly between 2011 and 2012 [463/1476 (31%) vs. 529/1639 (32%); p=0.6].

Discussion

The burden of laboratory-confirmed cryptococcal disease continued to be high in 2012 with an overall incidence of 119 cases per 100 000 HIV-infected persons. Approximately 300 more incident cases were detected by GERMS-SA in 2012 compared with 2011. This increase was largely due to improved surveillance case detection in 2012; for the first time, NHLS laboratories in KwaZulu-Natal were subjected to a surveillance audit. However, the surveillance audit may still not have detected all cases in KwaZulu-Natal because some laboratories still do not use an electronic laboratory information system. Also with the changeover from DISA*Lab to TrakCare Lab, not all cases may have been picked up by the CDW; hence the decrease in cryptococcosis incidence may not be a true reflection of disease burden but rather an artefact of the laboratory information system. The GERMS-SA programme now undertakes annual national audits of all public-sector laboratories. Most patients continued to be diagnosed with meningitis. More men were diagnosed with cryptococcal disease than women. This may reflect the lower ART coverage and initiation of ART at low CD4+ T-lymphocyte counts among South African men. *C. neoformans* was the predominant pathogen causing disease and the small number of patients who were infected with *C. gattii* were diagnosed across the country. The in-hospital case-fatality ratio remained high and unchanged. Implementation of cryptococcal screening to detect disease earlier could potentially change the epidemiology of disease and reduce mortality.

Figure 5. Incidence* of laboratory-confirmed cryptococcal disease reported to GERMS-SA by age category, South Africa, 2011 and 2012, n=12 118 (age unknown for 1249 cases).



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

Table 20: Number of cases and incidence of cryptococcal disease detected by GERMS-SA by province, South Africa, 2011 and 2012, n=13 367.

Province	2011		2012	
	n	Incidence**	n	Incidence**
Eastern Cape	1226	171	1109	151
Free State	347	99	317	89
Gauteng	1899	156	1976	162
KwaZulu-Natal	1043*	66	1906*	119
Limpopo	409	100	177	42
Mpumalanga	622	129	365	74
Northern Cape	61	79	68	86
North West	453	105	307	70
Western Cape	490	179	592	212
South Africa	**6550**	**117**	**6817**	**119**

*A surveillance audit was performed for NHLS KZN laboratories for the first time in 2012 detecting additional cases that had not been reported passively; **Incidence was calculated using HIV-infected population denominators determined by the Actuarial Society of South Africa model and are expressed as cases per 100 000 population.

Table 21: Number and percentage of cases of cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012, n=13 367.

Site of specimen	2011		2012	
	n	%	n	%
Cerebrospinal fluid	5827	89	6097	89
Blood	665	10	624	9
Other	58	1	96	2
	6550		**6817**	

Candida species

Results

In 2012, 532 cases of candidaemia were detected from nine sentinel hospitals (Table 22). The vast majority of cases occurred among children aged 0-4 years and 146 (29%) of all cases occurred among neonates (≤28 days of age) (Figure 6). Where sex was known, 54% (282/519) of patients were male. Clinical data were collected for 351 (66%) patients. The overall crude case-fatality ratio was high (145/347; 42%). Although HIV infection is not an independent risk factor for candidaemia, 19% (46/247) of patients who were diagnosed with candidaemia were also HIV-infected. In total, 528 viable isolates were processed in the reference laboratory and at least one viable isolate was available for 410 (77%) cases of candidaemia. Overall, *Candida albicans* was the most common species followed by *Candida parapsilosis* and *Candida glabrata*; the species distribution differed significantly between Gauteng and Western Cape (Table 23). All *Candida* isolates had an amphotericin B minimum inhibitory concentration (MIC) ≤ 1 µg/ml (apart from two *C. krusei* isolates with an MIC of 2 µg/ml). Susceptibility results for five common *Candida* species and three antifungal drugs are summarised in Table 24. In Gauteng and the Western Cape, the percentage of *C. parapsilosis* isolates that were susceptible to fluconazole (27/130 (21%) vs. 7/11 (64%); p=0.001) and voriconazole (38/130 (30%) vs. 10/11 (91%); p<0.001) differed significantly.

Discussion

Culture-confirmed candidaemia represents the tip of the iceberg for this common hospital-associated infection because blood culture is an insensitive means of diagnosis. Despite this limitation, enhanced surveillance has provided insight into the clinical epidemiology of candidaemia diagnosed at mostly public-sector hospitals in two provinces. Overall, most cases of candidaemia were diagnosed among young children, predominantly neonates, and almost half of patients died in hospital. The epidemiology of candidaemia is clearly different between Gauteng and Western Cape. In Gauteng, *C. albicans* and *C. parapsilosis* were equally detected whereas *C. albicans* and *C. glabrata* were the two most common species in the Western Cape. Knowledge of local hospital or hospital unit epidemiology should guide empiric treatment choices. In Gauteng, amphotericin B remains the empiric drug of choice for candidaemia because of the high prevalence of azole-resistant *C. parapsilosis* isolates. Caspofungin is also a reasonable choice in settings where this drug is available. In the Western Cape, high-dose fluconazole or amphotericin B are both reasonable choices for empiric treatment of candidaemia.

Table 22: Number of cases of candidaemia detected by GERMS-SA by enhanced surveillance site, Gauteng and Western Cape, 2012, n=532.

Enhanced surveillance site	n
Charlotte Maxeke Johannesburg Academic	116
Chris Hani Baragwanath	222
Groote Schuur	40
Helen Joseph/ Rahima Moosa	27
WITS Donald Gordon Medical Centre	1
Red Cross	19
Steve Biko Pretoria Academic	64
Tygerberg	42
Victoria	1
Total	**532**

Table 23: *Candida* species distribution for cases of candidaemia with a viable bloodstream isolate, Gauteng and Western Cape, 2012, n=410.

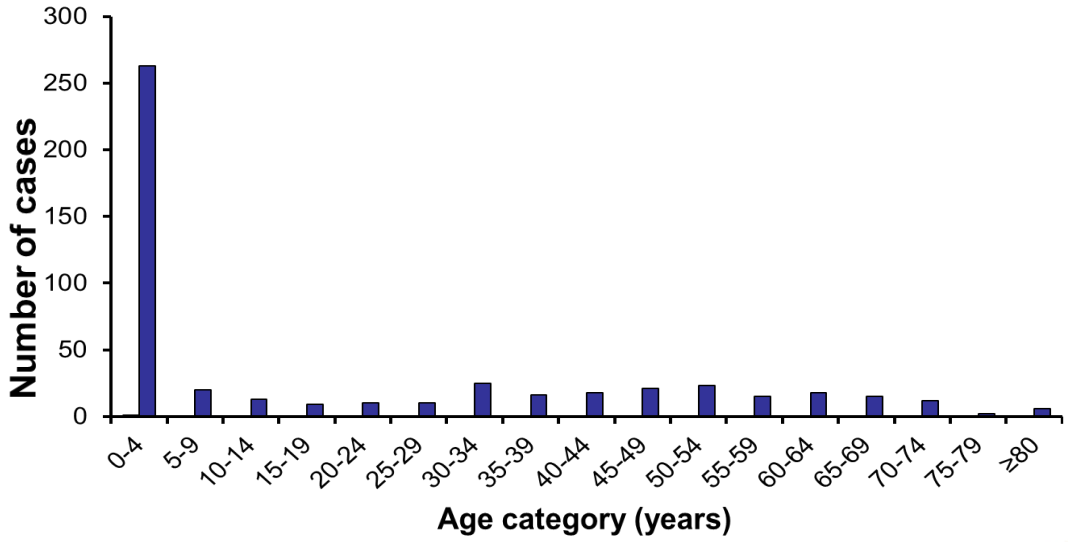
Species	Gauteng	Western Cape	Overall
	N (%)	N (%)	N (%)
Candida albicans	132 (40)	39 (49)	171 (42)
Candida parapsilosis	131 (40)	11 (14)	142 (35)
Candida glabrata	29 (9)	14 (18)	43 (10)
Candida tropicalis	18 (5)	9 (11)	27 (7)
Candida krusei	4 (1)	4 (5)	8 (2)
Other *Candida* species	16 (5)	3 (4)	19 (5)
Total	**330 (100)**	**80 (100)**	**410 (100)**

Table 24: Number and percentage of *Candida* bloodstream isolates (five commonest species only) susceptible* to fluconazole, voriconazole and caspofungin by broth microdilution testing, Gauteng and Western Cape, 2012, n=391.

Susceptible to Antifungal agent:	C. albicans (n=171)	C. parapsilosis (n=142)	C. glabrata ** (n=43)	C. tropicalis (n=27)	C. krusei (n=8)
Fluconazole	165/165 (100%)	34/141 (24%)	N/A	27/27 (100%)	N/A
Voriconazole	165/165 (100%)	48/141 (34%)	N/A	27/27 (100%)	7/8 (88%)
Caspofungin	165/167 (99%)	141/141 (100%)	35/43 (81%)	26/27 (96%)	7/8 (88%)

*Based on CLSI M27-S4 (2013) species-specific breakpoints; **Caspofungin MIC for 8 *C. glabrata* isolates was 0.25 µg/ml intermediate); denominators vary because of missing antifungal susceptibility results for some isolates

Figure 6. Number of cases of laboratory-confirmed candidaemia reported to GERMS-SA by age category, Gauteng and Western Cape, 2012, n=496 (age unknown for 36 cases).



Neisseria meningitidis

Results

In 2012, 191 cases of meningococcal disease were reported, and an additional 39 cases were identified on audit: a total of 230 cases of laboratory-confirmed meningococcal disease were identified by the surveillance system during the year (Table 25). Overall incidence decreased from 2011 (0.66 cases per 100,000 population in 2011 compared to 0.44/100,000 in 2012, p<0.001). The number of cases reported was greatest during the winter and spring months (Figure 7). Of all cases reported, cerebrospinal fluid (CSF) was the most common specimen yielding meningococci (Table 26), and the number of cases diagnosed on blood culture remained similar in 2012 compared to 2011 (p=0.3). Serogroup W was the most predominant in South Africa (72/176, 41%) (Table 27), similar to the proportion in 2011 (137/275, 50%; p=0.08). Minor year-on-year fluctuations of disease by province were noted. Rates of disease were highest in the Western and Eastern Cape (Table 25). In Gauteng, the incidence of meningococcal disease was estimated at 0.62/100 000, and most of that disease was due to serogroup W (29/56, 52%). In Western Cape, serogroup B was the most common meningococcal serogroup (21/45, 47%). Risk of disease was greatest amongst children less than five years of age. Age and serogroup-specific incidence rates show that infants were at greatest risk of disease for the three most common serogroups (Figure 8). Preliminary analysis of case-fatality ratios, as calculated at enhanced surveillance sites where in-hospital outcome is specifically looked for, was 7/76 (9%) in 2012, compared to 19/105 (18%) in 2011 (p=0.1). Of the viable isolates tested for antimicrobial resistance, 5% (6/129) of isolates had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and would be considered non-susceptible.

Discussion

Incidence of disease continues to decline in all provinces except Western and Eastern Cape. Serogroup W disease remained the predominant serogroup. Changes in meningococcal disease incidence in provinces may reflect changes in ability to confirm disease in the laboratory and changes in reporting to the surveillance network, or may reflect true changes in incidence. Case-fatality ratios have not changed significantly compared to 2011. The prevalence of non-susceptibility to penicillin remained low in 2012. The clinical relevance of increased MICs is unclear, and penicillin is, at present, still being recommended as the drug of choice for therapy for confirmed meningococcal disease.

Figure 7. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2011-2012, n=570.

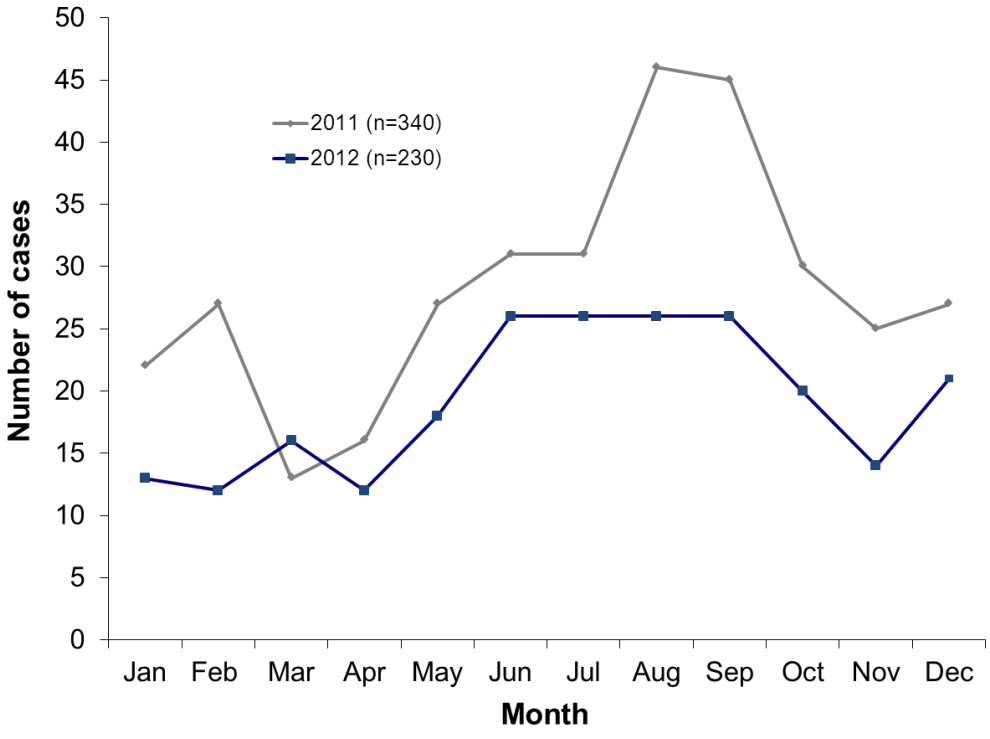
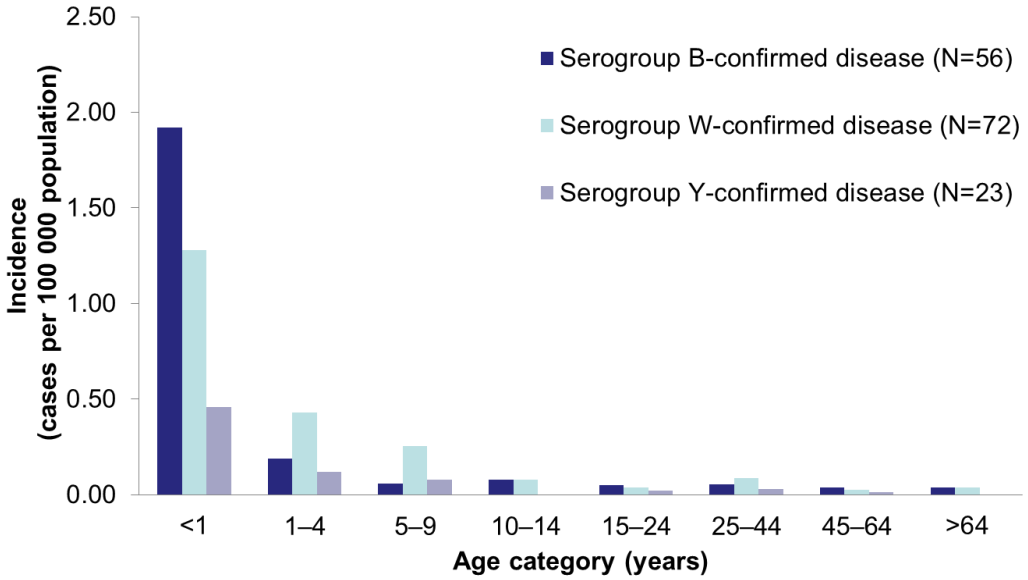


Figure 8. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, W and Y, South Africa, 2012, n=230 (age unknown for n=8; specimens or viable isolates unavailable for serogrouping n=54).**



*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.
**Other serogroups: serogroup A, n=2; serogroup C, n=21; non-groupable, n=2.

Table 25: Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2011 and 2012, n=570 (including audit cases).

Province	2011		2012	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	49	0.75	49	0.75
Free State	27	0.98	12	0.44
Gauteng	133	1.09	77	0.63
KwaZulu-Natal	40	0.39	26	0.25
Limpopo	9	0.17	3	0.06
Mpumalanga	19	0.47	6	0.15
Northern Cape	6	0.52	2	0.17
North West	5	0.14	8	0.23
Western Cape	52	0.90	47	0.81
South Africa	**340**	**0.66**	**230**	**0.44**

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

Table 26: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012, n=570.

Site of specimen	2011		2012	
	n	%	n	%
CSF	254	75	162	70
Blood	84	25	67	29
Other	2	0.6	1	0.4
Total	**340**	**≈100**	**230**	**≈100**

Table 27: Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2012, n=230*.

Province	Serogroup							
	Serogroup not available	A	B	C	W	Y	NG**	Total
Eastern Cape	16	0	11	6	10	6	0	49
Free State	3	0	4	2	2	0	1	12
Gauteng	21	1	14	5	29	7	0	77
KwaZulu-Natal	5	0	3	3	11	4	0	26
Limpopo	3	0	0	0	0	0	0	3
Mpumalanga	1	0	2	0	2	1	0	6
Northern Cape	1	0	0	0	1	0	0	2
North West	2	1	1	2	2	0	0	8
Western Cape	2	0	21	3	15	5	1	47
South Africa	**54**	**2**	**56**	**21**	**72**	**23**	**2**	**230**

*176 (77%) with viable isolates or specimens available for serogrouping; ** NG: Non-groupable

Haemophilus influenzae

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2012 was 229, while an additional 98 cases were identified during the national audit (total number of cases available for analysis was 327). Of these, 192 (59%) had isolates or specimens available for serotyping, and 69/192 (36%) were confirmed as serotype b (Table 28). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (43/69, 62% vs. 6/88, 7%, p<0.001) (Table 29). In 2012, a total of 49 cases of *H. influenzae* serotype b (Hib) were reported amongst children <5 years (Figure 9). Serotype b was the commonest serotype of *H. influenzae* causing disease amongst infants (Figure 10). Rates of Hib disease as recorded by our surveillance network amongst infants <1 year of age were similar over the last 4 years (p=0.2, chi-squared test for trend) (Figure 11). Twenty-three percent of serotype b strains were non-susceptible to ampicillin (MIC>1mg/L, all producing beta lactamase), 11 of 47 isolates tested, while 9% (7/75) of non-typeable strains were non-susceptible (p=0.06).

Discussion

Since the introduction of the Hib conjugate vaccine into the Expanded Programme on Immunisation (EPI) for South Africa in 1999, there has been a reduction in cases reported due to this serotype (9). Population-based studies in South Africa before the introduction of the conjugate Hib vaccine had demonstrated annual rates of invasive Hib disease of 170 per 100 000 infants below one year of age (10;11) and any increases noted recently were small in comparison to the substantial decline in disease subsequent to the introduction of the vaccine. Recognising that our surveillance system underestimates disease, reported cases of Hib disease amongst children <1 year are being monitored carefully. In April 2009, the updated infant vaccination programme in South Africa introduced a booster dose of conjugate Hib vaccine given at 18 months as part of a combination vaccine (Pentaxim: diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*Haemophilus influenzae* type-b conjugate). The first children benefiting from this would have received a dose in November 2010. It is hoped that this booster will improve long-term protection against disease and impact on on-going Hib transmission in the community (12). Rates of Hib in children <1 year have stabilised in the last 4 years. This could be related to interventions such as improved prevention and treatment of HIV in infants, the introduction of the booster dose of Hib vaccine, or changes in diagnosis and reporting of cases. More data are needed to evaluate the relative contribution of these factors and we urge clinical and laboratory staff to continue reporting all cases of *H. influenzae.*

Figure 9. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2012, n=327 (age unknown for n=24; specimens or viable isolates unavailable for serotyping for n=135).

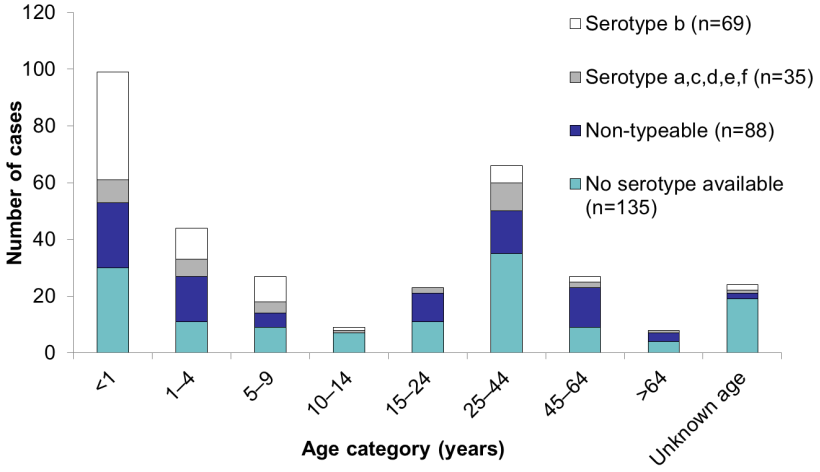
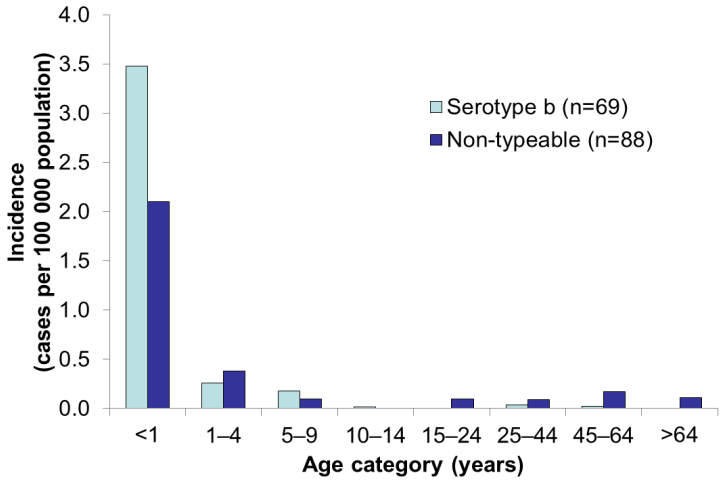
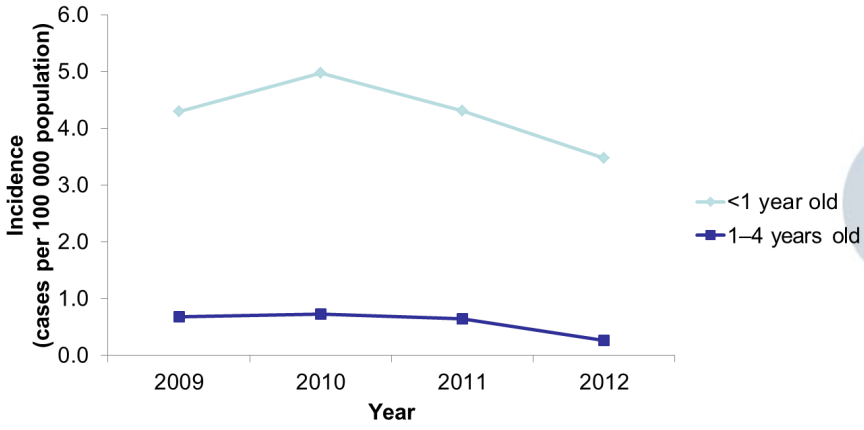


Figure 10. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2012, n=327 (age unknown, n=24; viable isolates unavailable for serotyping, n=135; other serotypes from cases with known age, n=34).



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

Figure 11. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2012.



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

Table 28: Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2012, n=327*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	25	0	5	0	2	1	1	0	34
Free State	5	0	9	0	0	1	0	2	17
Gauteng	33	8	25	0	0	2	5	33	106
KwaZulu-Natal	26	0	5	0	0	1	1	14	47
Limpopo	2	0	1	0	0	0	0	0	3
Mpumalanga	6	0	5	0	0	0	1	1	13
Northern Cape	2	1	2	0	0	0	1	2	8
North West	5	0	2	0	0	0	0	0	7
Western Cape	31	3	15	1	0	3	3	36	92
South Africa	**135**	**12**	**69**	**1**	**2**	**8**	**12**	**88**	**327**

*192 (59%) with specimens or viable isolates available for serotyping.

Table 29: Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2012, n=327.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
CSF	34	25	43	62	18	51	6	7
Blood	50	37	23	33	17	49	69	78
Other	51	38	3	4	0	0	13	15
Total	**135**		**69**		**35**		**88**	

Streptococcus pneumoniae

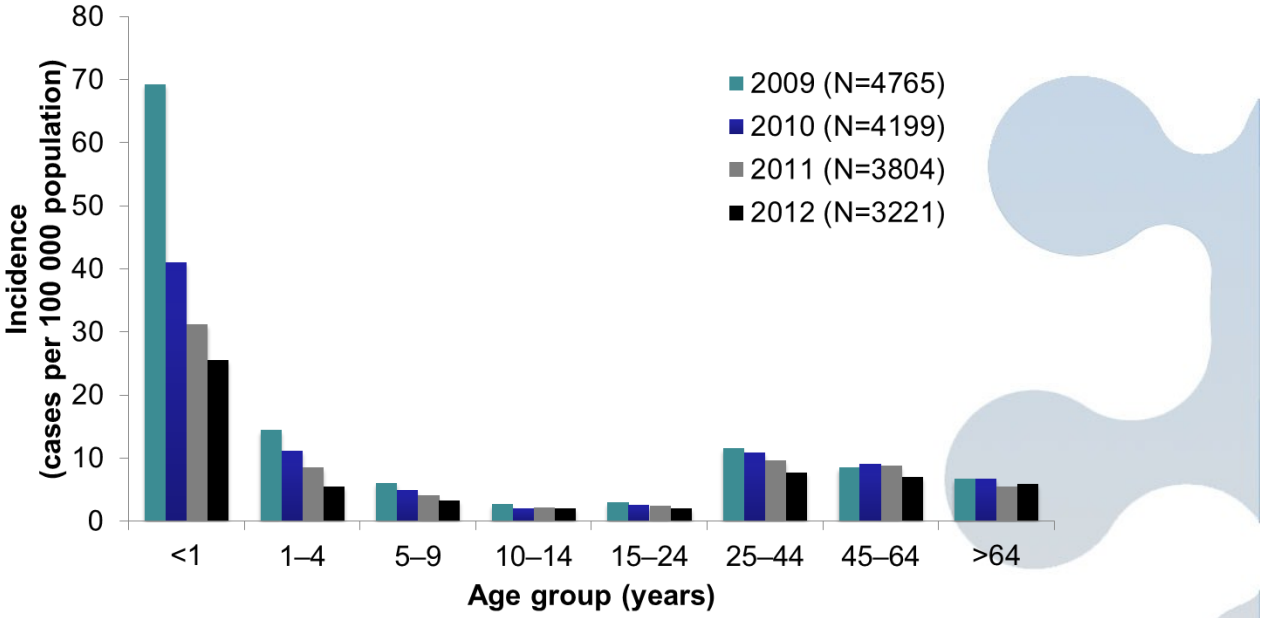
Results

The 7-valent polysaccharide-protein conjugate pneumococcal vaccine (PCV-7) was introduced into the Expanded Programme on Immunisations (EPI) in South Africa from 1 April 2009. In April 2010, this vaccine was replaced by the 13-valent formulation (PCV-13). Incidence of reported invasive pneumococcal disease (IPD) varied widely by province (Table 30). The age group at highest risk of disease in South Africa was infants <1 year of age, and there was an on-going significant reduction in disease since 2009 ($p<0.001$ chi-squared test for trend) (Figure 12). The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 31). Prevalence of non-susceptible strains ranged from 22% to 36% in different provinces (Table 32). Penicillin non-susceptible isolates were most common amongst children less than 5 years of age (Figure 13). Ceftriaxone non-susceptibility was detected amongst 5% (117/2160) of all IPD cases; and no reduction was seen from 2011 (5%, 126/2409). Amongst isolates from CSF specimens, 4% (31/834) were non-susceptible. The number of cases amongst children less than 5 years of age due to common serotypes for the period 2009-2012 are in Figure 14. The percentage of disease in 2012 amongst children less than 5 years of age due to PCV7 and newer valency vaccine formulations are shown in Table 33. The number of isolates in this age group available for serotyping has decreased in the last four years (1009/1337 [75%] in 2009, 649/909 [71%] in 2010 and 468/680 [69%] in 2011, 353/509 [69%] in 2012).

Discussion

Differences in IPD incidence by province have been documented for several years, and are partly due to differences in specimen-taking practices and laboratory reporting, however real differences in disease incidence cannot be excluded. The decreases in incidence of disease in children <1 year of age are partly due to the introduction of PCV7 in South Africa. When our data are analysed by HIV co-infection, vaccine and non-vaccine serotypes have decreased in HIV-infected infants, suggesting that HIV prevention and treatment improvements have also substantially impacted on this opportunistic disease (14). We urge clinicians to continue taking relevant specimens when pneumococcal disease is suspected and laboratorians to send all pneumococci isolated from normally sterile site specimens. On-going surveillance will assist in evaluating pneumococcal disease in our country at this time of multiple interventions.

Figure 12. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2012.



2009: N=4765; age unknown for n=163; 2010: N=4199; age unknown for n=142; 2011: N=3804; age unknown for n=219; 2012: N=3221, age unknown for n=256.

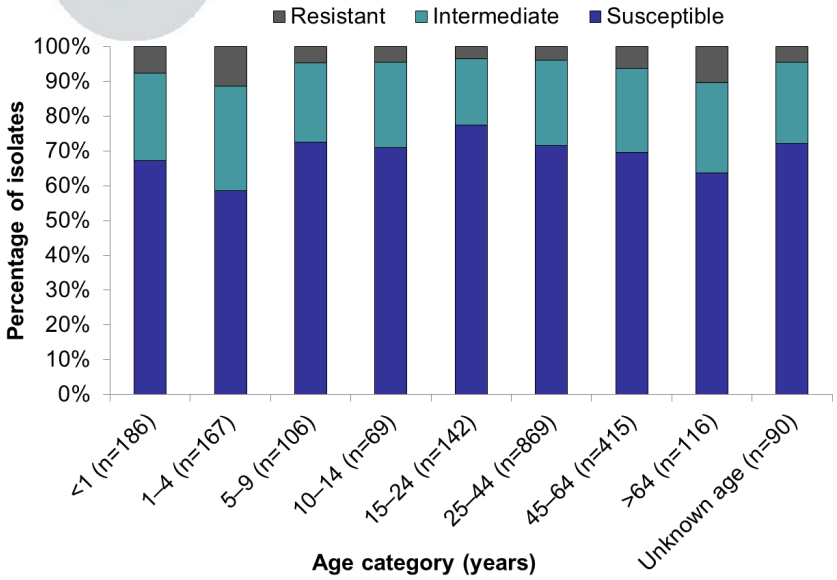
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

Table 30: Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2011 and 2012, n=7025.

Province	2011		2012	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	343	5.23	314	4.77
Free State	228	8.31	224	8.15
Gauteng	1593	13.05	1266	10.16
KwaZulu-Natal	550	5.37	576	5.57
Limpopo	61	1.13	75	1.38
Mpumalanga	206	5.12	167	4.10
Northern Cape	66	5.77	50	4.34
North West	194	5.55	132	3.72
Western Cape	563	9.72	417	7.06
South Africa	**3804**	**7.38**	**3221**	**6.16**

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

Figure 13. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2012, n=3221 (n=2160 with viable isolates).



2012 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Table 31: Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012, n=7025.

Site of specimen	2011		2012	
	n	%	n	%
CSF	1580	42	1383	43
Blood	1785	47	1501	47
Other	439	11	337	10
	3804	**100**	**3221**	**100**

Table 32: Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2012, n=3221.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	107	133	64	61	29	13	6
Free State	72	111	73	39	26	2	1
Gauteng	374	638	72	202	23	52	6
KwaZulu-Natal	287	197	68	73	25	19	7
Limpopo	32	33	77	10	23	0	0
Mpumalanga	55	75	67	31	28	6	5
Northern Cape	7	33	77	9	21	1	2
North West	77	43	78	11	20	1	2
Western Cape	50	246	67	94	26	27	7
South Africa	**1061**	**1509**	**70**	**530**	**25**	**121**	**6**

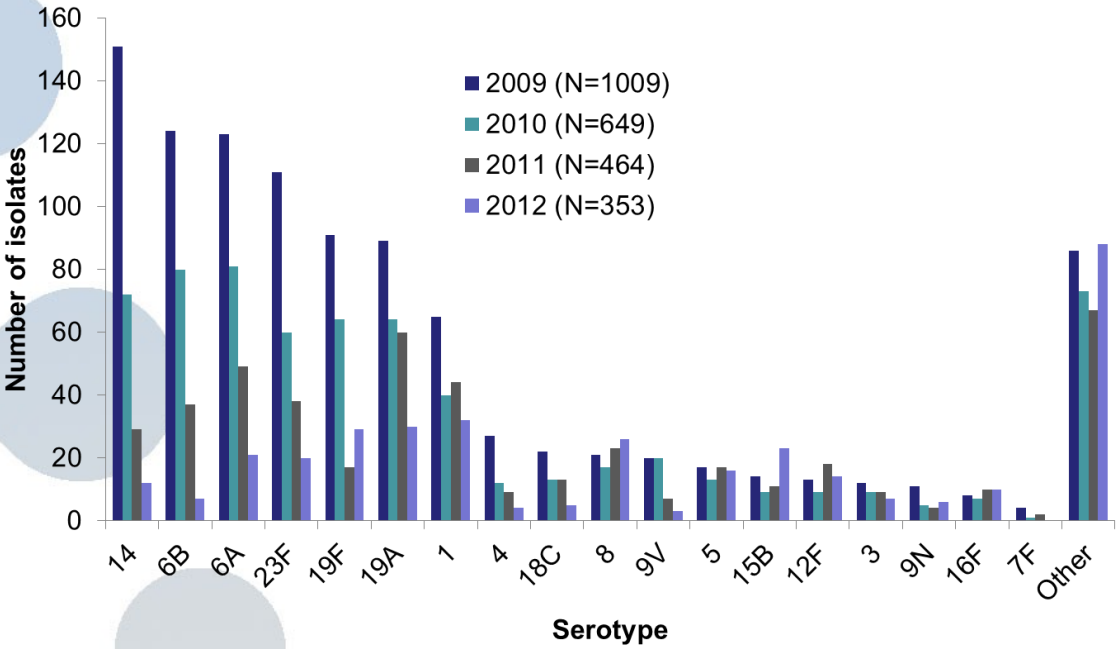
*2012 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Table 33: Number and percentage of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2012, n=508 (n=353 with viable isolates).

Province	Total isolates available for serotyping	7-valent serotypes*		Serotype 6A#		10-valent serotypes*		13-valent serotypes*	
		n	%	n	%	n	%	n	%
Eastern Cape	36	13	36	3	8	17	47	22	61
Free State	30	9	30	2	7	12	40	14	47
Gauteng	160	24	15	8	5	54	34	76	48
KwaZulu-Natal	49	12	24	2	4	18	37	24	49
Limpopo	5	1	20		0	2	40	3	60
Mpumalanga	16	5	31	2	13	5	31	10	63
Northern Cape	7	2	29	1	14	2	29	3	43
North West	6		0		0	2	33	3	50
Western Cape	44	14	32	3	7	16	36	24	55
South Africa	**353**	**80**	**23**	**21**	**6**	**128**	**36**	**179**	**51**

*7-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F; 10-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F; 13-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A.
Cross-protection with 6B has been demonstrated (13).

Figure 14. Pneumoccocal serotypes, in descending order, causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2012.



(2009: N=1337, n=1009 with viable isolates; 2010: N=909; n=649 with viable isolates; 2011: N=695, n=464 with viable isolates; 2012; N=509, n=353 with viable isolates)

Case-control study to estimate effectiveness of a pneumococcal conjugate vaccine (PCV) against invasive pneumococcal disease (IPD) in South Africa

A case-control study to assess the effectiveness of the 7-valent pneumococcal conjugate vaccine (PCV-7) against invasive pneumococcal disease (IPD) was conducted from March 2010 through November 2012. A manuscript describing the results of this study is currently being finalised. Preliminary results were described in the 2011 GERMS-SA annual report (6).

PCV-13 replaced PCV-7 in June 2011. Since this time we have been conducting a study aiming to evaluate the effectiveness of PCV-13 against laboratory confirmed vaccine-serotype IPD compared to no vaccination among HIV-infected and -uninfected children eligible to receive PCV through the routine vaccination programme in South Africa. Up to the 12th June 2013 for the PCV-13 study, we screened 178 children <5 years and all were age-eligible. Of the age-eligible cases, 117 cases have completed enrolment of cases and controls. These case-control sets consist of 98 HIV-uninfected cases with 518 controls and 19 HIV -infected cases with 82 controls. Overall, HIV-uninfected cases have a higher average number of controls per case (5.3 controls) than HIV-infected cases (4.3 controls). The numbers of HIV-infected cases enrolled into the PCV-13 component of the study are lower than projected. This decrease in HIV-infected IPD cases is possibly due to the improved Prevention-of-Mother -to-Child-Transmission (PMTCT) programme and increased access to antiretroviral treatment for children. We have added new case enrolment sites to try and address the decrease in numbers of HIV-infected cases. The enrolment of HIV-infected controls has also proved challenging for the above reasons, but has improved significantly with the inclusion of HIV clinics as a source of controls.

Klebsiella pneumoniae

Results

In 2012, higher numbers of *Klebsiella pneumoniae* (KP) than *Staphylococcus aureus* (SA) isolates were recorded through GERMS-SA surveillance, particularly in Gauteng province (Figure 15). From January through July 2012, 1426 cases of *Klebsiella pneumoniae* bloodstream infections were reported (Table 34). The highest number of cases (n=843; 59%) was detected from Gauteng province (Table 34).The lowest number of cases was detected during winter (June-July), though distribution was high throughout the year (Figure 16). Of the viable *K. pneumoniae* isolates tested for antimicrobial resistance, 239 (75%) were extended spectrum β-lactamase (ESBL) producers (Figure 17). A total number of 160 (50%) isolates were susceptible to ciprofloxacin, 292 (92%) to tigecycline, 297 (94%) to ertapenem and 202 (65%) to piperacillin/tazobactam (Table 35).

Discussion

Sentinel surveillance for *K. pneumoniae* bacteraemia was initiated in July 2010 through GERMS-SA. Incidence has not been reported. In 2012, over 70% of the isolates were submitted to the reference laboratory. Amongst the submitted isolates, two-thirds were ESBL producers. *K. pneumoniae* isolates were distributed almost equally throughout the year with a decline of the trend line during winter months in all four provinces.

Figure 15. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* (1426) and *Staphylococcus aureus* (1148) bacteraemia reported to GERMS-SA sentinel sites by provinces, January-July 2012.

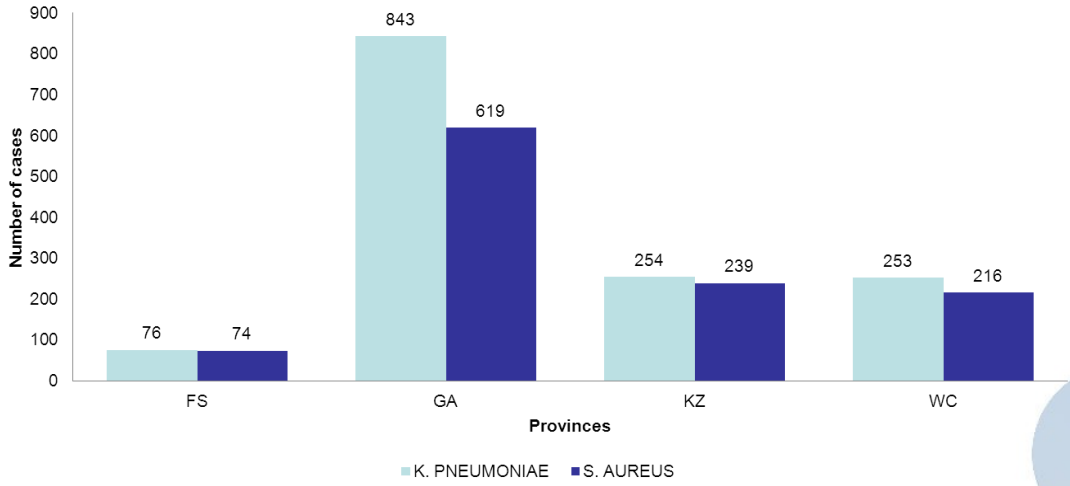


Table 34: Number of *Klebsiella pneumoniae* cases reported to GERMS-SA sentinel sites by province, South Africa, January-July 2012, n=1426 (including audit cases).

Province	n	%
Free State	76	5
Gauteng	843	59
KwaZulu-Natal	254	18
Western Cape	253	18
Total	**1426**	**100**

Figure 16. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA from sentinel sites by month, and trend line analysis January-July 2012, n=1426.

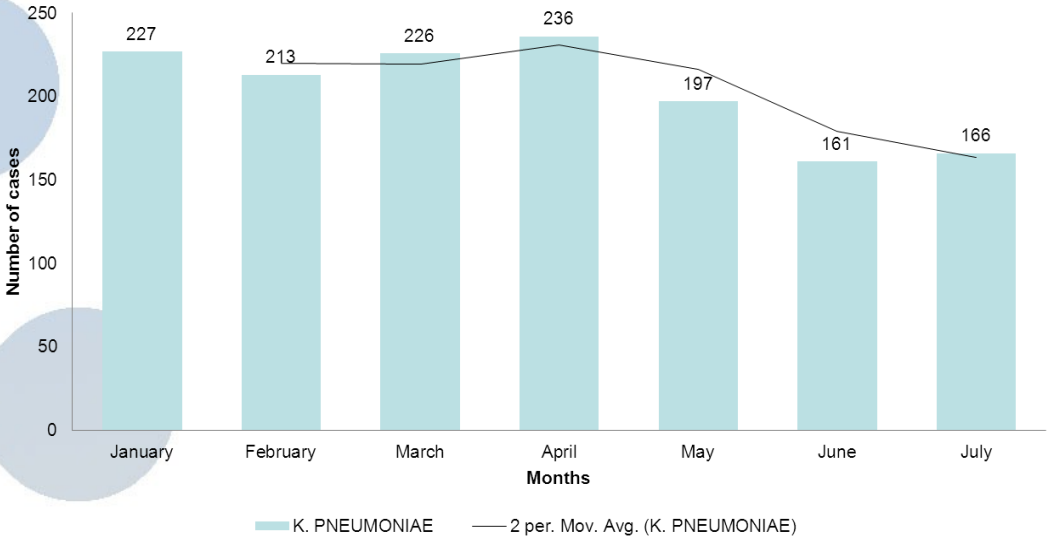


Figure 17. Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites, by ESBL production, January-July 2012, n=317.

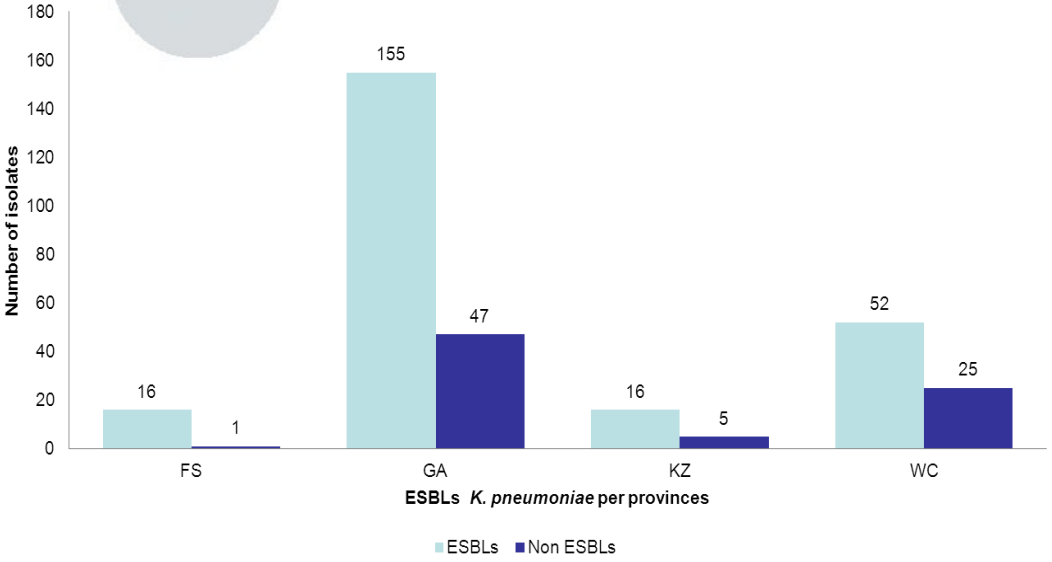


Table 35. Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites, by susceptibility to ertapenem, ciprofloxacin, tigecycline and piperacillin/tazobactam, January-July 2012, n=317.

Province	Antimicrobial agents							
	Piperacillin/tazobactam		Ertapenem		Ciprofloxacin		Tigecyline	
	S*	NS**	S	NS	S	NS	S	NS
Free State	7	10	13	4	7	10	17	0
Gauteng	121	79	190	12	103	99	183	19
KwaZulu-Natal	17	2	19	2	10	11	20	1
Western Cape	57	20	75	2	40	37	72	5
Total	**202**	**111**	**297**	**20**	**160**	**157**	**292**	**25**

*S=susceptible; **NS=non susceptible

Staphylococcus aureus

Results

The number of cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA from January through July 2012 was 1148. (Table 36). Of these, the majority of cases were detected from sentinel sites in Gauteng (54%) followed by KwaZulu-Natal (21%) and Western Cape (19%) (Table 36). The numbers of cases were equally distributed throughout the whole year, though there was a decline during the autumn season, which picked up in the winter months (Figure 18). Resistance to oxacillin (MRSA) was determined in 289 (44 %) isolates. 99.4% of *S. aureus* isolates were susceptible to vancomycin and 82% to clindamycin. Three non-susceptible vancomycin isolates were noted in 2012. Ninety-six percent of isolates were susceptible to mupirocin (Table 37).

Discussion

Incidence of *S. aureus* bacteraemia was not calculated and cases could not be separated into hospital- versus community-acquired categories because only laboratory-based data were available. The percentage of *S. aureus* isolates which were MRSA was as high as 44% of the total number submitted to the AMRRU. Clindamycin-resistant *S. aureus* isolates occurred at high rates (18%) and the three vancomycin non-susceptible isolates identified have not yet been confirmed with the reference method.

Figure 18. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by month, January-July 2012, and trend line analysis, n=1148.

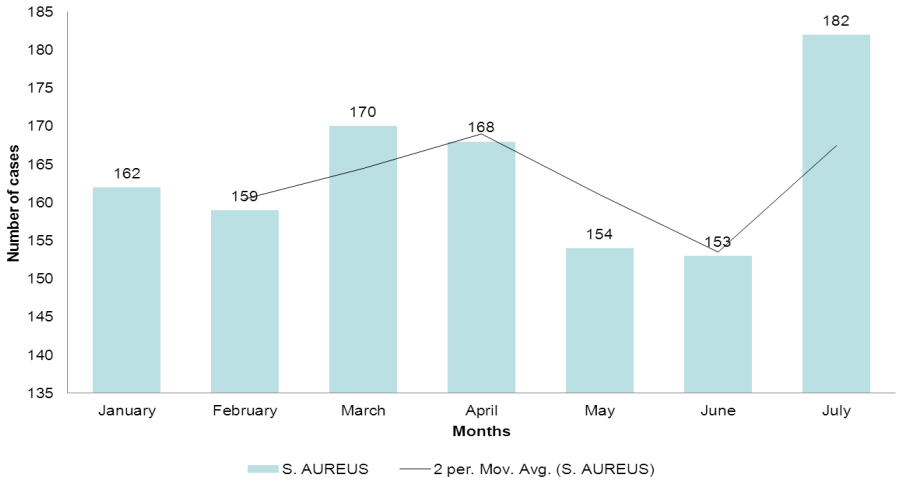


Table 36: Number of *Staphylococcus aureus* cases reported to GERMS-SA sentinel sites by province, South Africa, January-July 2012, n=1148 (including audit cases).

Province	n	%
Free State	74	6
Gauteng	619	54
KwaZulu-Natal	239	21
Western Cape	216	19
Total	**1148**	**100**

Table 37: Number of viable, laboratory-confirmed *Staphylococcus aureus* reported by GERMS-SA sentinel sites, with reported susceptibility testing to clindamycin (n=534), vancomycin (n=534), mupirocin (n=503) and oxacillin (n=661), January-July 2012.

Province	Antimicrobial agents							
	Oxacillin		Clindamycin		Vancomycin		Mupirocin	
	S*	NS**	S	NS	S	NS	S	NS
Free State	7	5	7	3	10	0	9	0
Gauteng	233	199	303	58	359	2	325	13
KwaZulu-Natal	23	7	23	12	35	0	33	2
Western Cape	109	58	109	19	127	1	117	4
Total	**372**	**289**	**442**	**92**	**531**	**3**	**484**	**19**

*S:=susceptible; **NS=non-susceptible

Rifampicin-resistant Tuberculosis

South Africa (SA) has a high incidence of tuberculosis (TB) with large absolute numbers of drug-resistant cases (15). In 2012, SA initiated a phased nationwide implementation of Xpert MTB/RIF rapid diagnostic testing for TB suspects. To date, over 1 million tests have been performed, with a national average of 14.55% MTB positivity and 7.14% rifampicin resistance. Through GERMS -SA, the Centre for Tuberculosis has initiated a sentinel surveillance system for rifampicin-resistant TB in SA to estimate the burden of resistance to other TB drugs, estimate the sensitivity and specificity of rifampicin resistance as a predictor of Multi-Drug-Resistant TB, to identify prevalent rifampicin–resistant strains and to determine the impact of implementation of the Xpert MTB/RIF rapid diagnostic testing on the epidemiology of rifampicin-resistant TB over time. Four GERMS enhanced surveillance sites have been initiated in Gauteng, Mpumalanga, Northern Cape and Eastern Cape. Surveillance activities in the pilot site in the Gauteng province are currently being evaluated to optimise the processes and outputs in order to meet the stated objectives. Ultimately, surveillance will include one enhanced site per province.

Discussion

In 2012 the GERMS-SA laboratory-based surveillance programme has continued to provide robust data for public health action, reporting on 17 733 cases of laboratory-confirmed disease. In addition to the usual opportunistic, epidemic-prone and vaccine-preventable diseases under surveillance it has added 3 new priority diseases to its enhanced surveillance repertoire, namely *Candida* spp., *Staphylococcus aureus* and rifampicin-resistant tuberculosis (TB).

Already our enhanced surveillance data on candidaemia has shown extremely high in-hospital mortality, with a large difference in antifungal susceptibility profiles between isolates from Gauteng and the Western Cape. In the last quarter of 2012, enhanced surveillance for *Staphylococcus aureus* bacteraemia and rifampicin-resistant tuberculosis was started at selected sites. The aim of the staphylococcal enhanced surveillance is to describe epidemiological differences between hospital-associated and community-associated methicillin-resistant *Staphylococcus aureus* (MRSA), whilst enhanced rifampicin-resistant tuberculosis surveillance will attempt to describe the outcomes and clinical differences between patients with rifampicin mono-resistant TB and multidrug-resistant TB.

Although three-quarters of patients presenting at enhanced surveillance sites with a GERMS-SA related infection were co-infected with HIV, there are multiple other factors that affect the epidemiology of the diseases under surveillance, namely water and sanitation, overcrowding and housing, vaccine availability and uptake, antiretroviral therapy rollout, and prevention of mother to child transmission programmes. These factors all impact on our surveillance data. This has been detected in the continued downward trend of invasive pneumococcal disease in the vaccinated and unvaccinated populations, the stabilisation of *Haemophilus influenzae* type b disease in infants, the outbreak of non-typhoidal salmonellosis in the Eastern Cape and the change in gender profile for cryptococcosis.

Antimicrobial susceptibility of pathogens to empiric therapy continues to be monitored. Concerns have been raised over the continued increase in ciprofloxacin resistance of *Salmonella* Typhi; however azithromycin and ceftriaxone remain effective alternative therapies. Penicillin remains the drug of choice for meningococcal disease, and ceftriaxone in adequate high doses is still effective for empiric treatment of pneumococcal meningitis. Vancomycin should be added if high level resistance (MIC ≥ 1 µg/ml) is confirmed or if there is a poor clinical response after 48 hours.

The continued strength of the GERMS-SA surveillance programme is the on-going participation of the public and private sector laboratories. The NICD reference laboratories require submission of isolates for serotyping/serogrouping, antimicrobial susceptibility testing and molecular work for analysis and feedback to stakeholders in order to improve the health of all South Africans. We thank you all for your participation in this national surveillance programme and encourage you to continue to partner with us in future.

Publications

1. **Crowther-Gibson P, Cohen C, Klugman K, de Gouveia L, von Gottberg A,** for the Group for Enteric, Respiratory, and Meningeal Disease Surveillance in South Africa (GERMS-SA). Risk Factors for Multidrug-Resistant Invasive Pneumococcal Disease in South Africa, a Setting with High HIV Prevalence, in the Prevaccine Era from 2003 to 2008. *Antimicrobial Agents and Chemotherapy* 2012, 56(10):5088-5095.
2. **du Plessis M, Moodley C, Mothibeli K, Fali A, Klugman K, von Gottberg A,** for the Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa (GERMS-SA). Population Snapshot of Invasive Serogroup B Meningococci in South Africa from 2005 to 2008. *Journal of Clinical Microbiology* 2012, 50(8):2577-2584.
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GERMS-Related (Cryptococcal screening work)

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