GERMS SOUTH AFRICA

Annual Report 2011

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

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Cover photograph: GERMS-SA Principal Investigator's meeting, 26-27 September 2011, NICD

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Introduction

The 2011 Annual Report summarises the findings from national surveillance, including the enhanced surveillance sites (ESS) at 25 hospitals in all 9 provinces, for the year. In 2011, a reduction in numbers of organisms reported has been noted across all pathogens under surveillance. The following factors may have influenced this to varying degrees: difficulties in conducting audits, the financial situation of the NHLS in 2011, and the improvement and introduction of multiple health interventions.

As in previous years audits were done through the Central Data Warehouse (CDW), however because of the roll out of TrakCare Lab to replace Disa*Lab throughout the country, there have been challenges with the auditing processes; KwaZulu-Natal has still not been audited fully. The financial situation that the National Health Laboratory Services (NHLS) faced at the end of 2011 may also have impacted on specimen-taking practises which further impacts laboratory-based surveillance. The
department of Health has implemented and improved on multiple health interventions and GERMS-SA, as a mature surveillance system, is well positioned to monitor the impact of national interventions such as new vaccine introductions and addition of booster vaccines; the Comprehensive Care, Management and Treatment Programme for HIV/AIDS; and the Prevention of Mother To Child Transmission of HIV (PMTCT).

The National Microbiology Surveillance Unit Team, 2012

Methods

In 2011, 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,* and diarrhoeagenic *Escherichia coli*
3. Vaccine-preventable diseases, e.g. *Haemophilus influenzae* type b (Hib), and *Streptococcus pneumoniae*
4. Nosocomial infections, e.g. *Staphylococcus aureus* and *Klebsiella* 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 2011. The population under surveillance in 2011 was estimated at 50.5 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 to GERMS-SA.

At ESS, surveillance officers completed clinical case report forms for patients with 6 laboratory-confirmed diseases (cryptococcosis, invasive salmonellosis, invasive pneumococcal disease, invasive shigellosis, invasive meningococcal disease, invasive *Haemophilus influenzae* disease), 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 8 provinces (excluding KZN) between 1 January and 31 December 2011, and for KZN between 1 October and 31 December 2011. 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

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Table 1: Population denominators used to calculate incidence rates, 2010 and 2011

Province	General population*		HIV-infected population**		AIDS population**	
	2010	2011	2010	2011	2010	2011
Eastern Cape	6 743 823	6 829 959	695 707	715 736	57 821	60 525
Free State	2 824 570	2 759 644	348 832	351 746	36 085	35 390
Gauteng	11 192 029	11 328 203	1 207 378	1 215 856	122 551	126 240
KwaZulu-Natal	10 645 508	10 819 128	1 550 955	1 576 025	143 549	149 621
Limpopo	5 439 552	5 554 657	394 221	409 161	28 508	32 285
Mpumalanga	3 617 513	3 657 181	472 882	482 288	44 720	44 827
Northern Cape	1 103 918	1 096 731	74 963	76 966	6 044	6 868
North West	3 200 649	3 253 390	427 023	431 576	44 222	44 230
Western Cape	5 223 908	5 287 863	266 180	273 114	21 119	24 533
South Africa	**49 991 470**	**50 586 756**	**5 438 141**	**5 532 468**	**504 619**	**524 519**

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

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cryptococcosis, the audit was designed to obtain data from case patients, which were no longer reported by NHLS laboratories in 8 provinces. 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 rates were calculated using mid-year population estimates for 2010 and 2011 from Statistics South Africa (Table 1) (2). Incidence rates in the HIV-infected and AIDS populations were calculated for 2010 and 2011, 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 rates are expressed as cases per 100 000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test and p-values < 0.05 were considered significant throughout.

Ethics approval for the ongoing activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and from relevant University and Provincial Ethics Committees for the various enhanced surveillance sites. Surveillance activities were funded by the NICD/NHLS, and ESS activities continued to be mostly funded by a CDC-NICD Cooperative Agreement (U62/CCU022901).

Operational report

Site visits

In 2011, NICD staff members undertook 34 visits to 25 surveillance sites in all 9 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 17 981 surveillance cases on the GERMS-SA database, 7012 (39%) 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 include 4684 cryptococcal cases from non-enhanced surveillance sites that, since July 2008, were not required to report these cases to GERMS-SA. Only 13% (243/1915) of cases of cryptococcosis were not reported to the surveillance programme by enhanced surveillance sites which are required to report cases. Therefore, the corrected percentage of non-reported cases detected by audit would be 19% (2571/13 540). Overall, 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 performance of enhanced surveillance sites improved with respect to meeting performance targets in 2011 (Table 4): 88% (3590/4074) of cases had a case report form completed (target = 90%) and 2434 (68%) of the case report forms were completed by patient interview (target = 60%); quality indicators also improved in 2011. 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 are provided to improve the site performance. In 2011, these reports were provided quarterly.

Coordination meetings

Surveillance officer meeting, 21-22 February 2011: This meeting, convened at the NICD in Johannesburg, was attended by 29 surveillance officers from 9 provinces. The meeting focused on outlining the GERMS surveillance programme and nested studies, improving surveillance data-capture, -entry and -reporting, and addressing occupational health and safety issues.

Surveillance officer meeting, 21-22 July 2011: This meeting was convened at the NICD, attended by all surveillance officers, and included two 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, and on IPD study update, training, and discussion of the introduction of PCV13 into the EPI and its effect on the IPD study.

Principal Investigator (PI) meeting, 26-27 September 2011: Convened at the NICD, this meeting was attended by over 50 local, national and international delegates, including representatives from the Department of Health and CDC. 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 the early operations of the IPD case-control study, and to raise proposals for new studies such as Group B *Streptococcus* surveillance, the PCV13 case-control study, TRAC phase 2, and enhancing *Klebsiella* and *Staphylococcus* surveillance.

Steering Committee meeting, 27 September 2011: Convened

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at the NICD after the PI meeting, this was attended by 11 committee members and 9 invited observers. The meeting covered how new pathogens will be selected with regards to NDoH priorities. In future the Steering committee will be replaced by a broader external advisory committee for the entire NICD.

Table 2: GERMS-SA surveillance site visits between 1 January and 31 December 2011

Date	Province	Laboratory	Hospital
23 May 2011	Eastern Cape	NHLS Nelson Mandela Academic Complex	Nelson Mandela Academic Complex, Mthatha
24 May 2011	Eastern Cape	NHLS East London	Frere Hospital, East London
		Ampath	East London
		Pathcare	Beacon Bay Life Hospital, East London
5 April 2011	Free State	NHLS Pelonomi	Pelonomi Hospital
		NHLS Universitas	Universitas Hospital
26 January 2011	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
17 March 2011	Gauteng	NHLS CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
		NHLS CHBH	Chris Hani Baragwanath Hospital
15 April 2011	Gauteng	NHLS Steve Biko Academic	Steve Biko Academic Hospital
22 June 2011	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
25 July 2011	Gauteng	NHLS CHBH	Chris Hani Baragwanath Hospital
5 August 2011	Gauteng	NHLS Helen Joseph	Helen Joseph Hospital and Rahima Moosa Mother and Child Hospital
15 August 2011	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
20 September 2011	Gauteng	Lancet Pretoria	
8 July 2011	KwaZulu Natal	NHLS Addington	Addington Hospital
		NHLS King Edward VIII	King Edward VIII Hospital
3 November 2011	Limpopo	NHLS Mankweng	Mankweng Hospital
		NHLS Polokwane	Polokwane Hospital
23-24 March 2011	Mpumalanga	NHLS Rob Ferreira	Rob Ferreira Hospital
		NHLS Themba	Themba Hospital
6 April 2011	Northern Cape	NHLS Kimberley	Kimberley Hospital
27 January 2011	North West	NHLS Tshepong	Tshepong Hospital
15 March 2011	North West	NHLS Job Shimankana Tabane	Job Shimankana Tabane Hospital
14 June 2011	North West	NHLS Job Shimankana Tabane	Job Shimankana Tabane Hospital
23-24 February 2011	Western Cape	NHLS Greenpoint	
		NHLS Groote Schuur	Groote Schuur Hospital
		NHLS Tygerberg	
		NHLS Worcester	
		NHLS East London	
		NHLS Mthatha	
10 March 2011	Western Cape	NHLS Tygerberg	Khayelitsha District Hospital
30 March 2011	Western Cape	NHLS Groote Schuur	Red Cross Children's Hospital/ Groote Schuur Hospital/ Victoria Hospital
4 May 2011	Western Cape	NHLS Tygerberg	Tygerberg Hospital

Table 3: Cases detected by surveillance audit by province, 2011

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**	5/63 (8)	2	0	3	0	0	0	0	0	0	**5**
	Non-typhoidal salmonellosis†	111/608 (18)	10	3	42	42	2	7	0	4	1	**111**
	Shigellosis	18/67 (27)	0	0	13	3	0	1	0	0	1	**18**
	Cryptococcosis††	4684/6599 (71)	1123	320	1291	276	359	475	32	390	418	**4684**
	Meningococcal disease	36/325 (11)	13	4	11	1	3	3	0	1	0	**36**
	Haemophilus influenzae disease	83/391 (21)	13	9	32	0	3	10	1	3	12	**83**
	Pneumococcal disease	744/3608 (21)	132	67	292	0	33	69	10	80	61	**744**
	Klebsiella disease	462/1601 (29)	-	53	370	-	-	-	-	-	39	**462**
	Staphylococcus aureus disease	409/1649 (25)	-	55	288	-	-	-	-	-	66	**409**
Non-invasive	Salmonella Typhi**	3/9 (33)	1	0	0	2	0	0	0	0	0	**3**
	Non-typhoidal salmonellosis†	276/1441 (19)	29	5	81	85	10	17	8	29	12	**276**
	Shigellosis	181/1618 (11)	26	5	59	43	8	7	8	9	16	**181**
	Cholera	0/2 (0)	0	0	0	0	0	0	0	0	0	**0**
	Total	**7012/17 981 (39)**	**1349**	**521**	**2482**	**452**	**418**	**589**	**59**	**516**	**626**	**7012**

*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; ††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; 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, 2011

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	164	158 (96)	109 (69)	98
Charlotte Maxeke Johannesburg Academic	476	461 (97)	286 (62)	100
Chris Hani Baragwanath	866	773 (89)	479 (62)	100
Dr George Mukhari	278	210 (76)	167 (80)	100
Edendale/ Greys	299	296 (99)	202 (68)	100
Groote Schuur/ Red Cross/ Victoria	326	310 (95)	190 (61)	100
Kimberley	114	88 (77)	57 (65)	98
King Edward VIII	153	124 (81)	84 (68)	100
Mankweng/Polokwane	92	79 (86)	60 (76)	100
Nelson Mandela Academic Complex	175	145 (83)	116 (80)	100
Pelonomi/ Universitas	142	114 (80)	85 (75)	100
R K Khan	213	204 (96)	179 (88)	100
Rob Ferreira/ Themba	237	218 (92)	159 (73)	100
Rustenburg	133	121 (91)	89 (74)	100
Steve Biko Pretoria Academic/ Tshwane District	220	144 (65)	103 (72)	100
Tygerberg	186	145 (78)	69 (48)	100
TOTAL	**4074**	**3590 (88)**	**2434 (68)**	**99**

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, 3 at Charlotte Maxeke Johannesburg Academic and 3 at Groote Schuur/Red Cross/ Victoria in 2011; one surveillance officer was present at all other sites; **Low case report form completion rates at certain sites are due to the turnover of surveillance staff – if other reasons for low completion of case report forms were detected, these were addressed at those sites. ***Target = 90%; †Target = 60%; ††This was calculated by subtracting the number of "unknown" answers from a particular field on the case report form, which could easily have been answered by a patient on interview.

Surveillance reports

Enhanced Surveillance Report

In 2011, of 17 981 surveillance case patients detected by GERMS-SA, 4074 (23%) were diagnosed at enhanced surveillance sites. Of case patients with recorded HIV status, 82% (2627/3223) 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 69% and 71%, respectively, and less than one third (26%) 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, 2011**

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	1915	1734 (91)	1651 (95)	1620 (98)
Neisseria meningitidis	127	105 (83)	86 (81)	22 (26)
Streptococcus pneumoniae	1457	1276 (88)	1090 (84)	754 (69)
Haemophilus influenzae	214	160 (75)	129 (80)	48 (37)
Salmonella species	327	288 (88)	245 (85)	174 (71)
Shigella species	34	27 (79)	22 (81)	9 (41)
Total	**4074**	**3590 (88)**	**3223 (90)**	**2627 (82)**

*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 serotypes Typhi and Paratyphi

Results

Salmonella Typhi isolates from both invasive and non-invasive sites are reported in Table 6. Cases of enteric fever were higher in January, although there was an unusual peak in June, including a cluster from the Western Cape (Figure 1). No isolates of *Salmonella* Paratyphi C were received. The number of isolates within each age group is reported in Table 7, indicating that most isolates are from patients in the 5 year – 34 year age group, although infection is seen in both older and younger age groups. Eleven (17.5%) *Salmonella* Typhi isolates received in 2011 were intermediately resistant to ciprofloxacin, the treatment of choice (Table 8), following the revised CLSI guidelines (4). Two isolates of *Salmonella* Paratyphi A were received from blood cultures in a 47-year old female (Gauteng) and a 15-year old male (Western Cape) and showed intermediate resistance to ciprofloxacin (4), the remaining six were identified from stool specimens. Three isolates of *Salmonella* Paratyphi B L (+) tartrate (+) (*Salmonella* Paratyphi B var. Java) were received; two from stool specimens from children less than five years (Gauteng and KwaZulu-Natal) and one from a urine specimen from a 62-year old female (KwaZulu-Natal).

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. This is compounded by the challenges of alternative diagnostic methods for typhoid fever, including both clinical and serological. The number of reported *Salmonella* Typhi isolates was regarded as a substantial underestimate and thus incidence rates were not calculated. These results exclude those patients in whom a serological or clinical diagnosis was made without culture. Revised CLSI guidelines for *Salmonella* Typhi and extra-intestinal non-typhoidal *Salmonella* have highlighted the emerging resistance in this pathogen to the fluoroquinolones (4). Ceftriaxone would be regarded as the alternative therapy of choice in these cases, as well as those typhoid fever cases where the organism is fully resistant to ciprofloxacin.

Figure 1. Number of non-invasive and invasive cases of *Salmonella* Typhi (n=72) and Paratyphi (n=11) reported to GERMS-SA, by month of specimen collection, South Africa, 2011 (including audit reports).

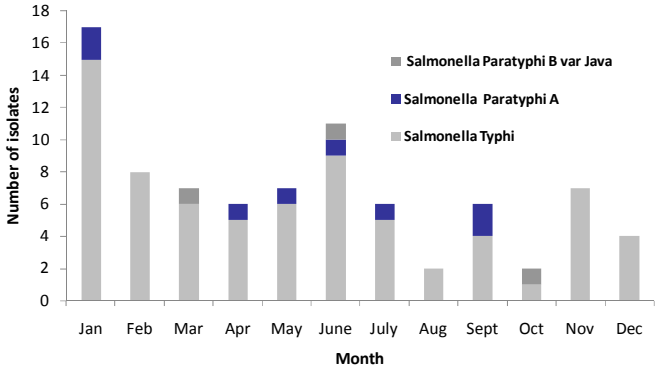


Table 6: Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2011, n=72 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	1	9
Free State	0	2
Gauteng	3	17
KwaZulu-Natal	2	10
Limpopo	0	1
Mpumalanga	1	9
Northern Cape	0	0
North West	0	1
Western Cape	2	14
South Africa	**9**	**63**

Table 7: Number of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2011, n=72 (including audit reports, missing isolates, mixed and contaminated cultures).

Age category (years)	*Salmonella* Typhi isolates
0 - 4	8
5 – 14	21
15 – 24	16
25 – 34	13
35 - 44	6
45 - 54	1
55 - 64	1
≥ 65	0
Unknown	6
Total	**72**

Table 8: Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2011, n=63 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)	Intermediate (%)	Resistant (%)
Ampicillin	48 (76)	0 (0)	15 (24)
Trimethoprim	48 (76)	0 (0)	15 (24)
Sulphamethoxazole	37 (59)	0 (0)	26 (41)
Chloramphenicol	48 (76)	0 (0)	15 (24)
Nalidixic acid	52 (83)	0 (0)	11 (18)
Ciprofloxacin	52 (83)	11 (18)	0 (0)
Streptomycin	48 (76)	0 (0)	15 (24)
Tetracycline	63 (100)	0 (0)	0 (0)
Imipenem	63 (100)	0 (0)	0 (0)
Ceftriaxone	63 (100)	0 (0)	0 (0)

Non-typhoidal *Salmonella enterica* (NTS)

Results

Invasive diseases do not appear to have a seasonal prevalence, but increased numbers of non-invasive disease due to NTS in the earlier months of the year and December reflect seasonality (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, but incidence rates have only been calculated for invasive NTS, due to differences in stool-taking practices in adult and paediatric medical care. 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). Multi-drug resistance remains a challenge, including resistance to first-line antimicrobial agents and the fluoroquinolones (Table 12a and b), as well as ESBL production: 14/475 (3.0%) of invasive NTS and 83/955 (8.7%) of non-invasive NTS produced ESBLs. Fifty-six (67.5%) of 83 non-invasive ESBL-producing isolates were *Salmonella* Isangi (Table 12b and Table 13). *Salmonella* Enteritidis replaced *Salmonella* Typhimurium as the commonest 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. Clusters of food-borne disease were reported (5-11). Seasonal prevalence was noted in 2011 for non-invasive disease. Due to revisions in reporting guidelines for invasive and non-invasive NTS, analysis of antimicrobial resistance has been reported separately. Greater numbers of isolates of invasive NTS received in 2011 appeared intermediately or fully resistant to ciprofloxacin, following the revised CLSI guidelines (Table 12a) (4). Certain antimicrobial agents were tested for epidemiological reasons only, and should not be used for treatment. Antimicrobial resistance remains a cause for concern.

Figure 2. Number of non-invasive (n=1441) and invasive (n=608), non-typhoidal *Salmonella* (NTS) cases, reported to GERMS-SA, by month of specimen collection, South Africa, 2011 (including audit reports).

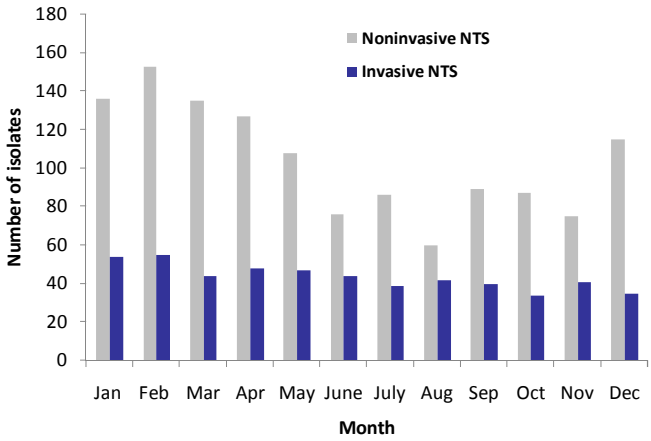


Table 9: Number* of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2011, n= 2049 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive, non-typhoidal *Salmonella* isolates	Invasive, non-typhoidal *Salmonella* isolates
Eastern Cape	162	35
Free State	27	25
Gauteng	575	307
KwaZulu-Natal	270	112
Limpopo	15	6
Mpumalanga	80	44
Northern Cape	24	7
North West	37	12
Western Cape	251	60
South Africa	**1441**	**608**

*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, 2011, n= 2049 (including audit reports, missing isolates, mixed and contaminated cultures).

	Cases		
Age Category (years)	**Non-invasive**	**Invasive**	**Incidence rate for invasive disease****
0 - 4	560	165	3.2
5 - 14	125	29	0.3
15 - 24	103	29	0.3
25 - 34	150	114	1.3
35 - 44	154	105	1.7
45 - 54	107	67	1.6
55 - 64	84	28	0.9
≥ 65	74	26	1.0
Unknown	84	45	-
Total	**1441**	**608**	**1.2**

*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, 2011, n=2049 (including audit reports, missing, mixed and contaminated cultures).

Specimen	**n**	**%**
CSF	14	0.7
Blood culture	531	25.9
Stool	1184	57.8
Other	320	15.6
Total	**2049**	**100.0**

*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 12a: Antimicrobial susceptibility test results for all invasive non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2011, n=475 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	**Susceptible (%)**	**Intermediate (%)**	**Resistant (%)**
Ampicillin	410 (86)	2 (0)	63 (13)
Trimethoprim	411 (87)	0 (0)	64 (14)
Sulphamethoxazole	254 (54)	0 (0)	221 (47)
Chloramphenicol	419 (88)	3 (1)	53 (11)
Nalidixic acid	409 (86)	0 (0)	66 (14)
Ciprofloxacin	403 (85)	66 (14)	6 (1)
Tetracycline	394 (83)	20 (4)	61 (13)
Streptomycin	413 (87)	0 (0)	62 (13)
Imipenem	475 (100)	0 (0)	0 (0)
Ceftriaxone	461 (97)	0 (0)	14 (3)

Table 12b: Antimicrobial susceptibility test results for all non-invasive non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2011, n=955 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)	Intermediate (%)	Resistant (%)
Ampicillin	805 (84)	0 (0)	150 (16)
Trimethoprim	823 (86)	0 (0)	132 (14)
Sulphamethoxazole	422 (44)	0 (0)	533 (56)
Chloramphenicol	791 (83)	11 (1)	153 (16)
Nalidixic acid	846 (89)	0 (0)	109 (11)
Ciprofloxacin	929 (97)	21 (2)	5 (1)
Tetracycline	677 (71)	35 (4)	243 (25)
Streptomycin	791 (83)	0 (0)	164 (17)
Imipenem	955 (100)	0 (0)	0 (0)
Ceftriaxone	871 (91)	1 (0)	83 (9)

Table 13: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2011, n= 1184 (excluding audit reports, missing isolates, mixed and contaminated cultures).

	Serotype				
Province	**Enteritidis**	**Heidelberg**	**Isangi**	**Newport**	**Typhimurium**
Eastern Cape	23	2	23	3	76
Free State	11	0	1	4	20
Gauteng	339	12	12	16	156
KwaZulu-Natal	100	9	15	1	48
Limpopo	4	1	0	0	2
Mpumalanga	26	3	11	1	26
Northern Cape	4	0	0	0	15
North West	9	0	0	1	2
Western Cape	75	8	6	9	110
South Africa	**591**	**35**	**68**	**35**	**455**

Shigella

Results

Increased numbers from January to April 2011 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. flexneri* 2a remains the commonest cause of shigellosis in South Africa. *S. dysenteriae* type 1 was not isolated in 2011 (Table 17). Eight (0.5%) of 1467 *Shigella* isolates were ESBL-producers. Of these, a single *S. flexneri* 2a was from a blood culture and the remainder were from non-invasive specimens.

Discussion

Shigella infection is largely due to water-borne outbreaks in South Africa, although person-to-person transmission may play a role. The importance of systemic shigellosis in young children and women has been evaluated (12). Certain antimicrobials were tested for surveillance purposes only, and should not be used for treatment. Resistance to fluoroquinolones remains low, but should continue to be monitored. ESBL-production is rarely documented, but remains important as ESBL subtypes appear common to those in other nosocomial pathogens (13).

Figure 3. Number of non-invasive and invasive *Shigella* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2011, n=1685 (including audit reports).

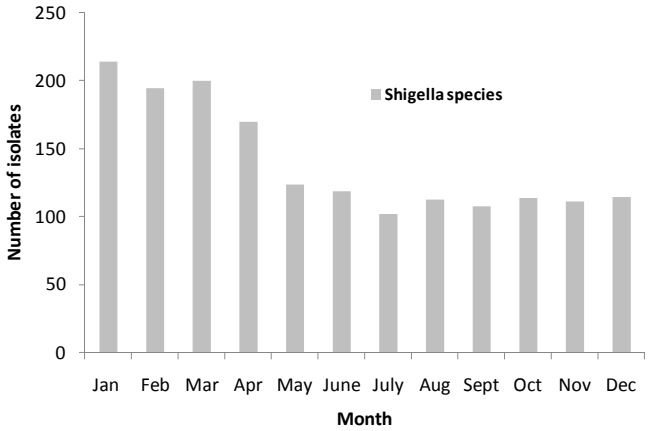


Table 14: Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2011, n=1685 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	217	6
Free State	42	2
Gauteng	619	26
KwaZulu-Natal	187	16
Limpopo	14	0
Mpumalanga	34	2
Northern Cape	36	3
North West	18	0
Western Cape	451	12
South Africa	**1618**	**67**

Table 15: Number of cases* and incidence rates for *Shigella* (invasive and non-invasive) reported to GERMS-SA by age category, South Africa, 2011, n=1685 (including audit reports, missing isolates, mixed and contaminated cultures) .**

	Cases		
Age Category (years)	Non-invasive	Invasive	Incidence rate for invasive disease**
0 - 4	783	33	0.64
5 - 14	235	4	0.04
15 - 24	76	2	0.02
25 - 34	172	13	0.15
35 - 44	109	4	0.06
45 - 54	82	4	0.09
55 - 64	52	1	0.03
≥ 65	56	2	0.08
Unknown	53	4	-
Total	**1618**	**67**	**0.13**

*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, 2011, n=1467 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)	Intermediate (%)	Resistant (%)
Ampicillin	776 (53)	0 (0)	691 (47)
Trimethoprim	128 (9)	0 (0)	1339 (91)
Sulphamethoxazole	247 (17)	0 (0)	1220 (83)
Chloramphenicol	969 (66)	1 (0)	497 (34)
Nalidixic acid	1455 (99)	0 (0)	12 (1)
Ciprofloxacin	1464 (100)	0 (0)	3 (0)
Tetracycline	603 (41)	4 (0)	860 (59)
Streptomycin	589 (40)	0 (0)	878 (60)
Imipenem	1467 (100)	0 (0)	0 (0)
Ceftriaxone	1459 (99)	0 (0)	8 (1)

Table 17: Commonest* invasive and non-invasive *Shigella* serotypes, including *Shigella dysenteriae* type 1, reported to GERMS-SA by province, South Africa, 2011, n=1160 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. dysenteriae* type 1	*S. flexneri* type 2a	*S. sonnei* phase i/ii	*S. flexneri* type 3a	*S. flexneri* type 6
Eastern Cape	0	82	14	31	14
Free State	0	12	6	6	4
Gauteng	0	164	193	56	67
KwaZulu-Natal	0	48	39	19	19
Limpopo	0	3	2	0	0
Mpumalanga	0	9	1	7	5
Northern Cape	0	7	6	2	2
North West	0	1	2	3	1
Western Cape	0	200	56	41	38
South Africa	**0**	**526**	**319**	**165**	**150**

*Including *Shigella dysenteriae* type 1: Although these isolates are currently rare in South Africa, the potential for future epidemics remains while these strains are in circulation.

Diarrhoeagenic *Escherichia coli* (DEC)

Results

An increased number of cases in the first half of the year is potentially a surveillance artefact, as discussed above (Figure 4). Enteropathogenic *E. coli* (EPEC) remains the commonest cause of diarrhoea, due to this pathogen, identified in South Africa (Table 18). 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). Three patients had mixed infections with three different DEC pathotypes and 23 patients had mixed infections with two different DEC pathotypes. Six isolates of *E. coli* O157 were received, two of these were enterohaemorrhagic E. coli (EHEC), and four were enteropathogenic *E. coli* (EPEC). Two isolates of EHEC, including O157 and O26 (two isolates) were identified from infants less than one year of age, from Mpumalanga and Gauteng respectively. The commonest serotypes associated with EPEC included O55, O111, O119 and O127. Diverse serotypes were also noted for other enterovirulent *E. coli* isolates. Identification of EHEC was incidental (14).

Discussion

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 primar-

(Continued on page 17)

(Continued from page 16)

ily associated with water-borne outbreaks, due to high level of faecal contamination in water sources, and this trend appears to be continuing. The predominance of isolates received in children under the age of one year may reflect culturing practices: infants are more likely to have stools taken for culture due to the devastating effects of diarrhoea in children of this age. Seasonality is reflected by greater numbers of cases in the months from January to April.

Figure 4. Number of diarrhoeagenic *Escherichia coli* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2011, n=234

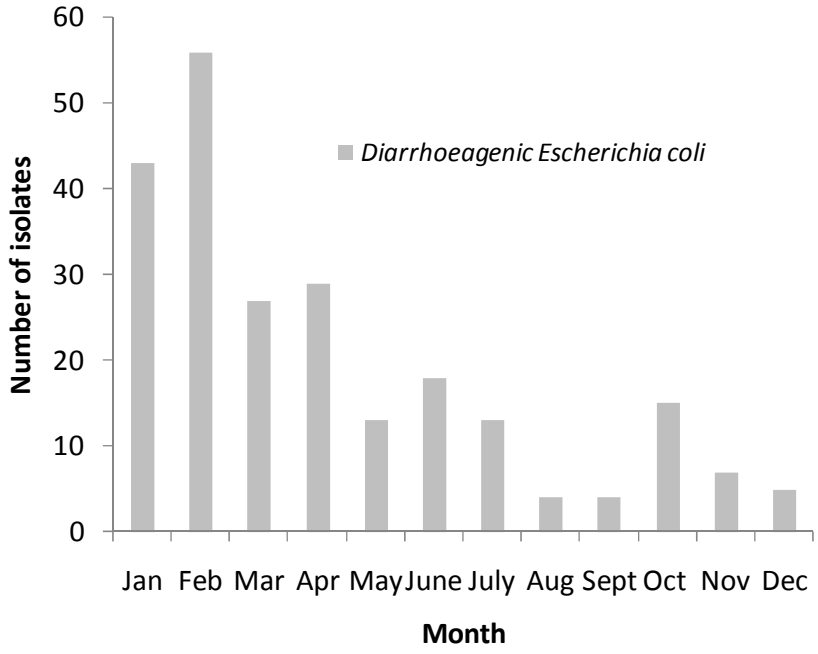


Table 18: Number of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by province, South Africa, 2011, n=234.

Province	DAEC	EAggEC	STEC/ EHEC	EIEC	EPEC	ETEC
Eastern Cape	4	7	0	1	26	0
Free State	0	0	0	0	0	0
Gauteng	6	8	1	0	108	0
Kwazulu-Natal	0	0	0	0	8	0
Limpopo	0	0	0	0	0	0
Mpumalanga	16	10	1	3	19	2
Northern Cape	2	0	0	0	0	0
North West	1	0	0	0	3	0
Western Cape	4	0	0	1	3	0
South Africa	**33**	**25**	**2**	**5**	**167**	**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.*

(Continued on page 18)

Table 19: Number of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by age category, South Africa, 2011,

Age category (years)	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC
0 - 4	14	17	2	1	154	0
5 - 14	2	0	0	1	1	0
15 - 24	4	2	0	1	3	0
25 - 34	2	3	0	1	4	0
35 - 44	5	1	0	0	2	1
45 - 54	4	1	0	0	0	0
55 - 64	2	0	0	0	0	0
≥ 65	0	0	0	1	1	0
Unknown	0	1	0	0	2	1
Total	**33**	**25**	**2**	**5**	**167**	**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.*

Vibrio cholerae O1

A single case of cholera due to *Vibrio cholerae* O1 Ogawa was reported in 2011 in South Africa. The organism was isolated from the stool of a 37 year old woman, who presented to a hospital in Limpopo, from Zimbabwe, with profuse watery diarrhoea in May.

Cryptococcus species

Results

During 2011, 6599 case patients, with laboratory-confirmed, incident cryptococcal episodes, were reported. The overall incidence for the general South African population decreased in 2011 (Table 20). Similarly, incidence amongst HIV-infected individuals (132/100 000 in 2010 and 118/100 000 in 2011) decreased. Incidence decreased or remained stable in all provinces except KwaZulu-Natal where the incidence increased (Table 20). The peak incidence of cryptococcosis was recorded amongst patients aged 35-39 years; incidence decreased between 2010 and 2011 in almost all age categories (Figure 5). One hundred and sixty-nine children, younger than 15 years, had laboratory-confirmed cryptococcosis; 72/169 (43%) were younger than 5 years of age. Where gender was known (6493/6599, 98%), 50% of patients were female. Most patients (5845/6599; 89%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 665/6599 (10%) were diagnosed with fungaemia (specimen data were missing for 26 cases) (Table 21). Sixty-three patients were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. At enhanced surveillance sites, 1915 patients were diagnosed with cryptococcosis, with viable isolates received from 1289/1915 (67%) patients. Isolates were speciated from all these cases; 1235 (96%) were identified as *Cryptococcus neoformans* and 54 (4%) were identified as *Cryptococcus gattii.* Cases of *C. gattii* disease were diagnosed in 7 provinces: Gauteng (n=17), Mpumalanga (n=15), Limpopo (n=9), KwaZulu-Natal (n=4), North West (n=4), Western Cape (n=1) and Northern Cape (n=4). The in-hospital case-fatality ratio for patients at enhanced surveillance sites decreased significantly between 2010 and 2011 (644/1835 (35%) vs. 530/1734 (31%), p=0.003).

Discussion

In 2011, approximately 600 fewer incident cases were detected by GERMS-SA, compared with 2010. The overall incidence also decreased – a slow but steady decline has been noted for several years now. This may indicate that the antiretroviral treatment programme has made an impact on this AIDS-defining opportunistic infection. It is difficult to comment on trends in KwaZulu-Natal because case reporting is not subjected to an audit and an increase in incidence may indicate better reporting. Most patients continued to be diagnosed with meningitis. The demographic profile of patients with cryptococcosis remained unchanged. Although very few children were diagnosed with cryptococcosis, more than one-third of paediatric cases were diagnosed among children <5 years of age. *C. neoformans* was the predominant pathogen causing disease; the small number of patients who were infected with *C. gattii* were diagnosed across the country. The in-hospital mortality of patients with cryptococcosis decreased significantly for the first time and may be related to earlier health-seeking behaviour of patients with meningitis and/or improved in-hospital patient care.

Figure 5. Age-specific incidence rates for laboratory-confirmed, cryptococcal cases, reported to GERMS-SA, South Africa, 2010 and 2011, n=13110 (age unknown for 693 cases)

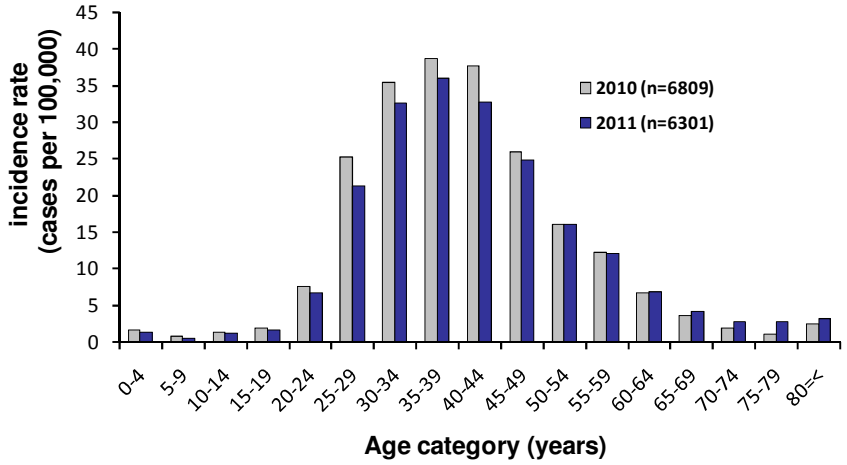


Table 20: Number of cases and incidence of cryptococcal disease reported to GERMS-SA by province, South Africa, 2010 and 2011, n=13803.

	2010*		2011*	
Province	**n**	**Incidence****	**n**	**Incidence****
Eastern Cape	1330	20	1236	18
Free State	457	16	357	13
Gauteng	2099	19	1938	17
KwaZulu-Natal	962	9	1037	10
Limpopo	568	10	417	8
Mpumalanga	703	19	597	16
Northern Cape	63	6	66	6
North West	532	17	453	14
Western Cape	490	9	498	9
South Africa	**7204**	**14**	**6599**	**13**

*A similar surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) in 2010 and 2011, detecting additional microscopy (India ink), cryptococcal antigen and culture-confirmed cases; **Incidence rates were calculated based on population denominators provided by Statistics South Africa, 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, 2010 and 2011, n=13803.

Site of specimen	2010		2011	
	n	%	n	%
CSF	6474	90	5845	89
Blood	631	8	665	10
Other	75	<1	63	<1
Unknown	24	<1	26	<1
	7204		**6599**	

Neisseria meningitidis

Results

In 2011, 289 cases of meningococcal disease were reported, and an additional 36 cases were identified on audit: a total of 325 cases of laboratory-confirmed meningococcal disease were identified by the surveillance system during the year (Table 22). Overall incidence decreased from 2010 (0.83 cases per 100 000 population in 2010 compared to 0.64/100 000 in 2011, p=0.001). The number of cases reported was greatest during the winter and spring months (Figure 6). Of all cases reported, cerebrospinal fluid (CSF) was the most common specimen yielding meningococci (Table 23), and the number of cases diagnosed on blood culture remained similar in 2011 compared to 2010 (p=0.3). Cases of W135 disease were reported from all provinces, and this serogroup remained the most predominant in South Africa in 2011 (137/275, 50%) (Table 24), with a similar proportion to 2010 (159/333, 48%; p=0.6). Minor year-on-year fluctuations of disease by province were noted. In Gauteng, the incidence of meningococcal disease was estimated at 1.19/100 000, and most of that disease was due to serogroup W135 (65/116, 56%). In Western Cape, serogroup B disease decreased by ~40%, from 33 of 61 cases with serogroup data in 2010 to 17 of 51 cases in 2011 (p=0.03). 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 7). Preliminary analysis of case-fatality ratios, as calculated at enhanced surveillance sites where in-hospital outcome is specifically looked for, was 20/105 (19%) in 2011, compared to 27/158 (17%) in 2010 (p=0.7). Of the viable isolates tested for antimicrobial resistance, 3% (5/197) of isolates had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and would be considered intermediately resistant.

Discussion

Overall incidence of disease has declined from 2010. Serogroup W135 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 remained similar compared to 2010. The prevalence of intermediate resistance to penicillin remained low in 2011. 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 6. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2010-2011, n=740.

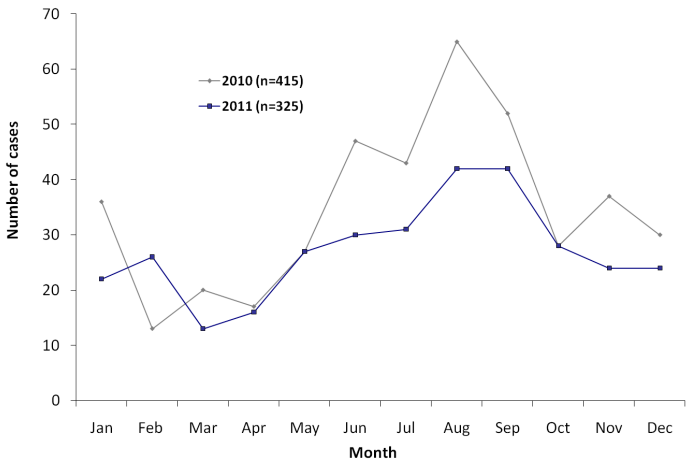
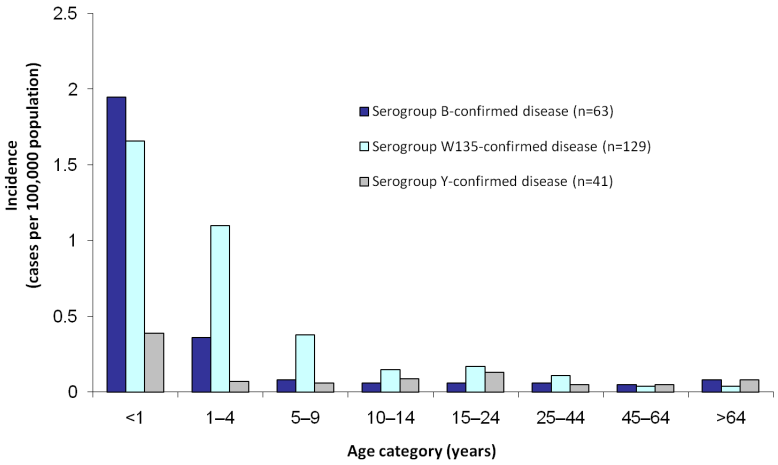


Figure 7. Age-specific incidence rates for laboratory-confirmed, invasive, meningococcal cases, by serogroup, South Africa, 2011, n=325*



*275 (85%) with specimens available for serogrouping, of which 261 had age known; 28 were serogroup C.

Table 22: Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2010 and 2011, n=740 (including audit cases).

Province	2010		2011	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	31	0.46	49	0.73
Free State	26	0.92	25	0.89
Gauteng	187	1.67	133	1.19
KwaZulu-Natal	33	0.31	29	0.27
Limpopo	13	0.24	8	0.15
Mpumalanga	28	0.77	18	0.50
Northern Cape	20	1.81	6	0.54
North West	11	0.34	5	0.16
Western Cape	66	1.26	52	1.00
South Africa	**415**	**0.83**	**325**	**0.64**

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

Table 23: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2010 and 2011, n=740.

Site of specimen	2010		2011	
	n	%	n	%
CSF	323	78	242	74
Blood	91	22	81	25
Other	1	0.2	2	0.6
	415		**325**	

Table 24: Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2011, n=325*.

Province	Serogroup							
	Serogroup not available	A	B	C	W135	X	Y	Total
Eastern Cape	14	0	8	3	21	0	3	49
Free State	6	0	10	2	4	0	3	25
Gauteng	17	0	24	10	65	0	17	133
KwaZulu-Natal	1	0	5	4	13	0	6	29
Limpopo	4	0	1	0	3	0	0	8
Mpumalanga	4	0	1	3	8	0	2	18
Northern Cape	2	0	1	0	1	0	2	6
North West	1	0	0	0	3	0	1	5
Western Cape	1	0	17	8	19	0	7	52
South Africa	**50**	**0**	**67**	**30**	**137**	**0**	**41**	**325**

*275 (85%) with specimens or viable isolates available for serogrouping.

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2011 was 308, while an additional 83 cases were identified during the national audit (total number of cases available for analysis was 391). Of these, 288 (74%) had isolates or specimens available for serotyping, and 111/288 (39%) were confirmed as serotype b (Table 25). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (61/111, 55% vs. 4/137, 3%, p<0.001) (Table 26). In 2011, a total of 75 cases of *H. influenzae* serotype b (Hib) were reported amongst children <5 years (Figure 8), with the highest incidence occurring amongst infants (Figure 9). Rates of Hib disease as recorded by our surveillance network amongst infants <1 year of age were similar over the last 3 years (p=0.3, chi-squared test for trend) (Figure 10). Twenty-three percent (17/73 isolates tested) of serotype b strains were non-susceptible to ampicillin (MIC>1mg/L, all producing beta lactamase), while 12% (13/111) of non-typeable strains were non-susceptible (p=0.3).

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 (15). 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 (16,17) 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 ongoing Hib transmission in the community (18). Rates of Hib in children <1 year have stabilised in the last 3 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 8. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2011, n=391 (age unknown for n=30; specimens or viable isolates unavailable for serotyping for n=103).

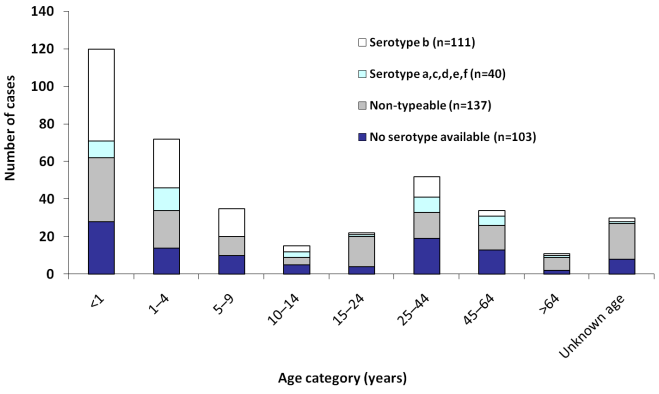


Figure 9. Age-specific incidence rates for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype, South Africa, 2011, n=391*

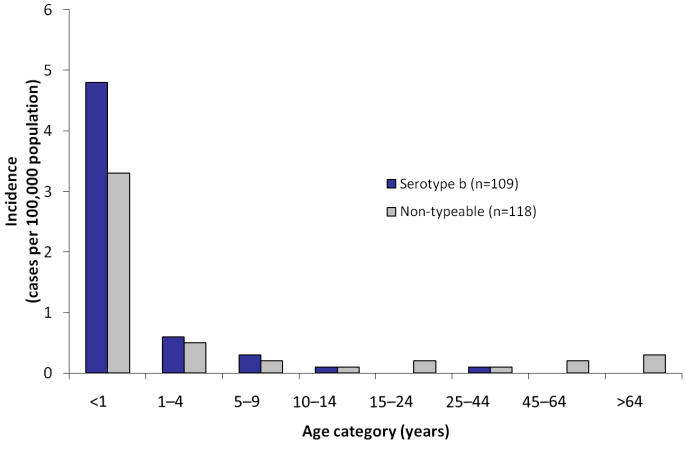


Figure 10. Incidence rates of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2000-2011 (excluding cases identified using polymerase chain reaction (PCR) on specimens which was only done 2007-2011).

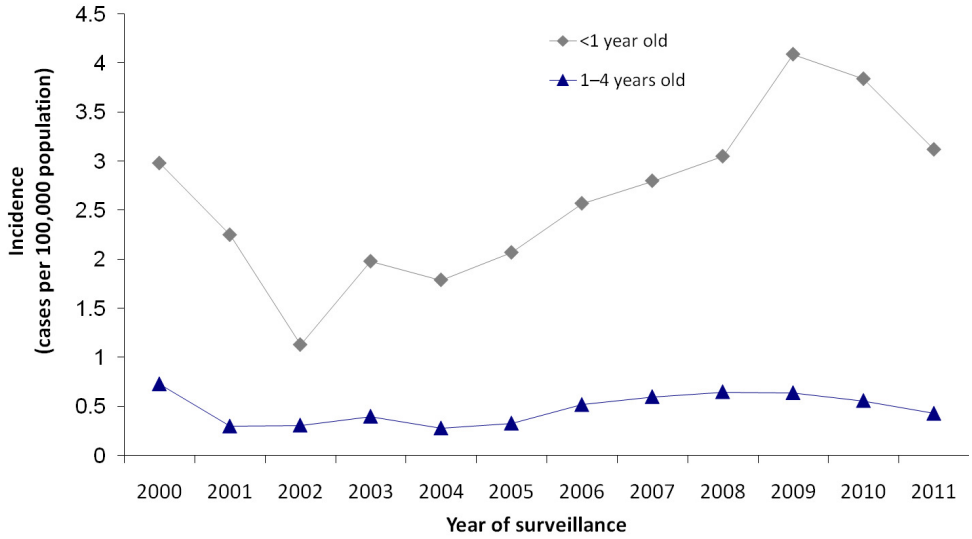


Table 25: Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2011, n=391*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	14	0	10	0	0	1	0	4	29
Free State	10	0	10	0	0	0	1	5	26
Gauteng	41	4	30	1	6	3	7	61	153
KwaZulu-Natal	1	1	17	1	1	1	1	15	38
Limpopo	3	0	2	0	0	0	0	1	6
Mpumalanga	10	1	9	0	0	0	0	1	21
Northern Cape	3	0	8	0	0	0	0	1	12
North West	5	0	3	0	0	0	0	0	8
Western Cape	16	2	22	1	3	0	5	49	98
South Africa	**103**	**8**	**111**	**3**	**10**	**5**	**14**	**137**	**391**

*288 (74%) with specimens or viable isolates available for serotyping.

Table 26: Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2011, n=391.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
CSF	23	22	61	55	9	23	4	3
Blood	44	43	45	41	31	78	104	76
Other	36	35	5	5	0	0	29	21
Total	**103**		**111**		**40**		**137**	

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 27). The age group at highest risk of disease in South Africa was infants <1 year of age, and there was an ongoing significant reduction in disease since 2009 (p<0.001 chi-squared test for trend) (Figure 11). The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 28). Penicillin non-susceptible isolates (MIC>0.06mg/L) in all age groups have decreased (1210/2872, 42% in 2010 compared to 823/2410, 34% in 2011, p<0.001). Prevalence of non-susceptible strains (intermediate and resistant) ranged from 25% to 43% in different provinces (Table 29). Penicillin non-susceptible isolates were common amongst children less than 5 years of age (Figure 12), but numbers in this age group have decreased compared with last year (393/649, 61% in 2010 compared to 208/468, 44% in 2011, p<0.001). A smaller reduction in penicillin non-susceptibility was seen in individuals 5 years and older (778/2134, 36% in 2010 compared with 589/1878, 31% in 2011, p=0.001). Ceftriaxone non-susceptibility was detected amongst 5% (126/2410) of all IPD cases, a reduction from 2010 (8%, 223/2862, p<0.001), and in 2011 was less likely to be detected in cases with pneumococci isolated from CSF (4%, 35/866, compared to 6%, 91/1544, of isolates from all other specimens, p=0.05). The number of cases amongst children less than 5 years of age due to common serotypes for the period 2009-2011 are shown in Figure 13. The percentage of disease in 2011 amongst children less than 5 years of age due to PCV7 and newer valency vaccine formulations are shown in Table 30. The number of isolates in this age group available for serotyping has decreased in the last three years (1009/1337, 75%, in 2009, 649/909, 71%, in 2010 and 468/680, 69%, in 2011, p=0.001)

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-coinfection, 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 (20,21). Reductions in antimicrobial non-susceptibility can also be attributed to reductions in the least susceptible serotypes: paediatric and PCV-7 serotypes. The low level of penicillin non-susceptibility from blood culture specimens still supports the use of penicillin as first-line therapy for community-acquired pneumonia. Vancomycin, together with ceftriaxone, should be considered for the empiric treatment of suspected pneumococcal meningitis (CSF specimens positive for Gram-positive cocci or latex agglutination tests positive for *S. pneumoniae*) that may be due to ceftriaxone-resistant pneumococci, especially amongst unvaccinated children (22). As ceftriaxone-resistant isolates are likely to be serotypes contained in PCV-7 and PCV-13, we anticipate that the number of resistant isolates causing disease will continue to decrease with wider use of the vaccine. We urge clinicians to continue taking relevant specimens when pneumococcal disease is suspected and laboratorians to submit all pneumococci isolated from normally sterile site specimens. Ongoing surveillance will assist in evaluating pneumococcal disease in our country at this time of multiple interventions.

Figure 11. Age-specific incidence rates for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2011

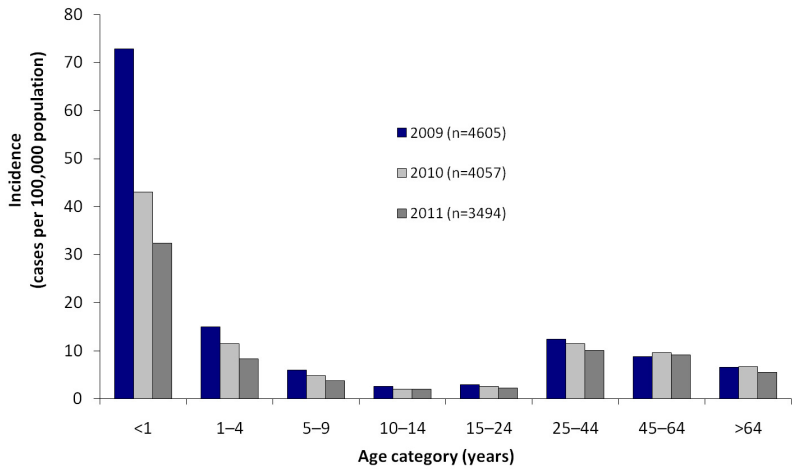
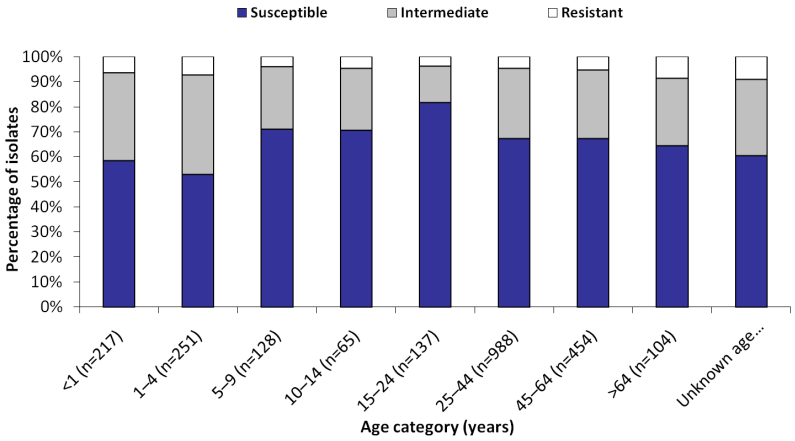


Table 27: Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2010 and 2011, n=7807.

Province	2010		2011	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	390	5.78	344	5.04
Free State	318	11.26	230	8.33
Gauteng	1845	16.48	1593	14.06
KwaZulu-Natal	426	4.00	356	3.29
Limpopo	109	2.00	61	1.10
Mpumalanga	240	6.63	204	5.58
Northern Cape	105	9.51	67	6.11
North West	182	5.69	190	5.84
Western Cape	584	11.18	563	10.65
South Africa	4199	8.40	3608	7.13

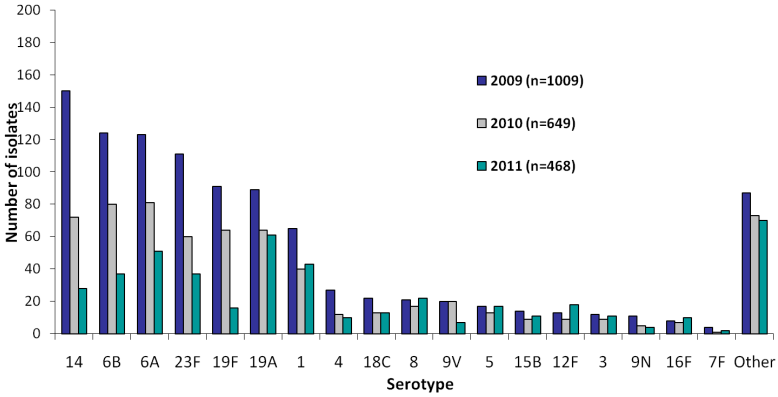
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000 population.

Figure 12. Number and percentage of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2011, n=3608 (n=2410 with viable isolates).



2011 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L

Figure 13. Pneumoccocal serotypes, in descending order, causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2011*



*2009: n=1337, n=1009 (75%) with viable isolates; 2010: n=909; n=649 (71%) with viable isolates; 2011: n=680, n=468 (69%) with viable isolates

Table 28: Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2010 and 2011, n=7807.

Site of specimen	2010		2011	
	n	%	n	%
CSF	1707	41	1440	40
Blood	2024	48	1739	48
Other	468	11	429	12
	4199		**3608**	

Table 29: Number and percentage of penicillin non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2011, n=3608.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	181	99	61	59	36	5	3
Free State	91	98	71	35	25	6	4
Gauteng	515	731	68	282	26	65	6
KwaZulu-Natal	48	176	57	115	37	17	6
Limpopo	45	12	75	3	19	1	6
Mpumalanga	98	78	74	25	24	3	3
Northern Cape	18	30	61	16	33	3	6
North West	102	64	73	20	23	4	5
Western Cape	100	299	65	139	30	25	5
South Africa	**1198**	**1587**	**66**	**694**	**29**	**129**	**5**

*2011 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Table 30: 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, 2011, n=680 (n=468 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	20	4	20	2	10	11	55	14	70
Free State	30	12	40	6	20	14	47	18	60
Gauteng	214	58	27	21	10	90	42	122	57
KwaZulu-Natal	56	15	27	7	13	24	43	31	55
Limpopo	5	2	40	0	0	3	60	4	80
Mpumalanga	22	12	55	1	5	14	64	18	82
Northern Cape	18	9	50	0	0	11	61	13	72
North West	12	3	25	1	8	7	58	7	58
Western Cape	91	33	36	13	14	36	40	55	60
South Africa	468	148	32	51	11	210	45	282	60

*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 [(19) Whitney 2006].

Case-control study to estimate effectiveness of a 7-valent pneumococcal conjugate vaccine against invasive pneumococcal disease (IPD) in South Africa

South Africa introduced PCV7 in April 2009 using a three-dose schedule (6 and 14 weeks and 9 months) with no catch-up. Preliminary analysis of the effectiveness of ≥2 PCV7 doses against vaccine-serotype invasive pneumococcal disease (IPD) and all IPD in HIV-infected and -uninfected children was conducted end of 2011. Invasive disease (pneumococcus isolated from a sterile site) was identified in children aged ≥ 16 weeks through GERMS-SA. Isolates were serotyped by Quellung or PCR. Four hospitalised controls, matched for age, HIV-status and hospital were selected for each case. We calculated effectiveness as 1 minus matched odds ratio for vaccination. We enrolled 133 HIV-uninfected cases and 535 controls and 83 HIV-infected cases and 254 controls from March 2010 through September 2011. Coverage with ≥2 doses was 65% (346/535 [71/346, 21% received ≥3 doses]) in HIV-uninfected and 67% (170/254 [52/170, 31% ≥3 doses) in HIV-infected controls. Effectiveness of ≥2 doses against vaccine serotypes was 68% (95% CI:4,89) in HIV-uninfected and -18% (95% CI: -303,65) in HIV-infected children. Effectiveness against all IPD was 46% (95% CI: -2,71) in HIV-uninfected and 26% (95% CI: -62,66) in HIV-infected children. In the subgroup aged 16-40 weeks, effectiveness against vaccine serotypes was 79% (95% CI: 5,95) in HIV-uninfected and 51% (-440,96) in HIV-infected children and remained unchanged for all IPD. Preliminary results indicate that PCV7 is protecting HIV-uninfected children in South Africa. A schedule including three primary doses efficacious among HIV-infected children in an earlier South African trial, may be needed for HIV-infected children. These children should then also receive a fourth dose (booster dose) at 9 months. These data were presented at the 8th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), March 12-15, 2012, Iguaçu, Brazil (23).

Klebsiella pneumoniae

In 2011 almost equal numbers of *Klebsiella pneumoniae* (KP) and Staphylococcus *aureus* (SA) isolates were recorded through GERMS-SA surveillance (Figure 14).

Results

From January through December 2011, 1601 cases of *Klebsiella pneumoniae* bloodstream infections were reported (Table 31). The highest number of cases (n=1038; 65%) was detected from Gauteng province (Table 31). Most cases of bacteraemia occurred amongst adults (Figure 15).The lowest numbers of cases were detected during winter (June-September) though distribution was high throughout the year (Figure 16). Of the viable *K. pneumoniae* isolates tested for antimicrobial resistance, 684/996 (69%) were extended spectrum β-lactamase (ESBL) producers. A total of 561 (56%) of isolates were susceptible to ciprofloxacin and 92% to tigecycline. Most of ciprofloxacin resistant isolates (n=434) were ESBL producers (63%) (Figure 17). ESBL production was common among *K. pneumoniae* isolates all four provinces (Figure 18).

Discussion

Sentinel surveillance for *K. pneumoniae* bacteraemia was initiated in July 2010 through GERMS-SA. Incidence has not been reported. In 2011, over 70% of all 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 and mostly amongst adult patients in all four provinces.

Figure 14. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* (1601) and *Staphylococcus aureus* (1649) bacteraemia reported to GERMS-SA sentinel sites by provinces, January - December 2011.

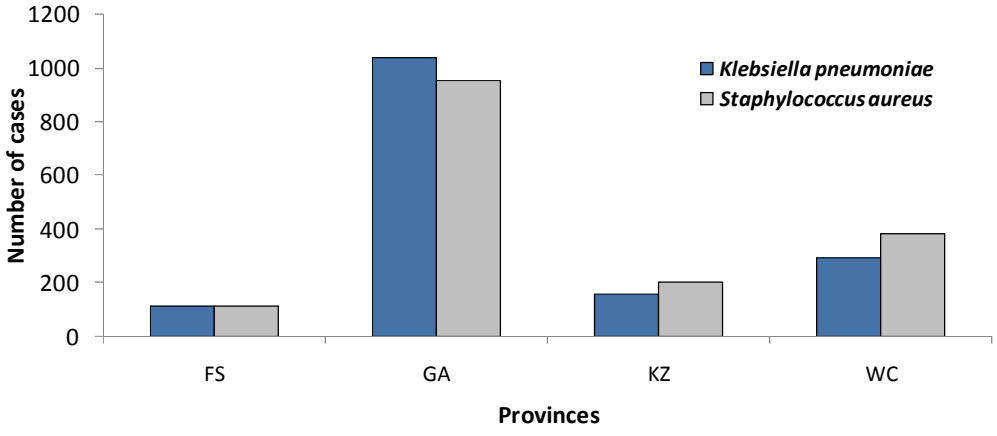


Table 31: Number of *Klebsiella pneumoniae* cases reported to GERMS-SA sentinel sites by province, South Africa, January-December 2011, n=1601 (including audit cases).

Province	*Klebsiella pneumoniae*	
	n	%
Free State	113	7
Gauteng	1038	65
KwaZulu-Ntal	157	10
Western Cape	293	18
All sentinel sites	**1601**	**100**

Figure 15. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA sentinel sites by age category, January- December 2011, n=1440.

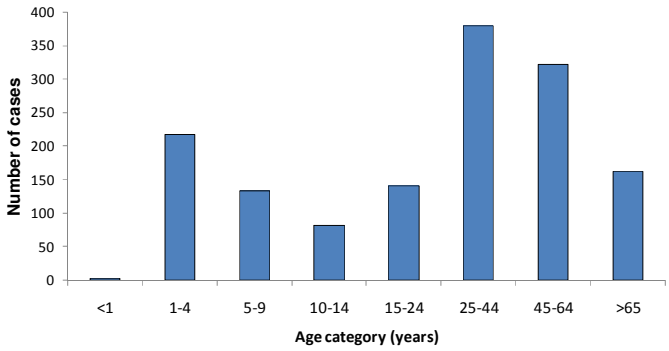


Figure 16. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA from sentinel sites by month, January - December 2011, n=1599.

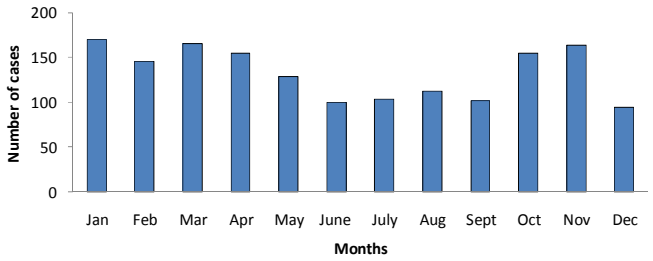


Figure 17. Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites, by ESBL production and susceptibility to ciprofloxacin and tigecycline, January-December 2011, n=996.

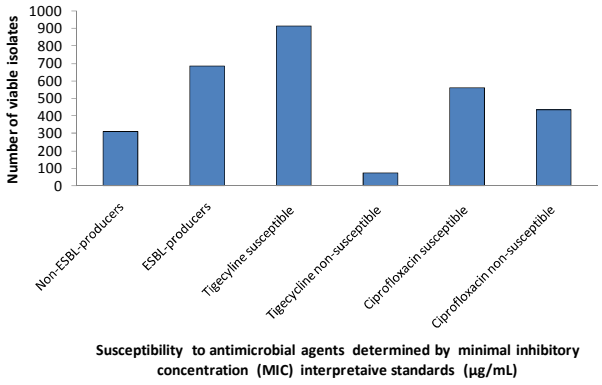
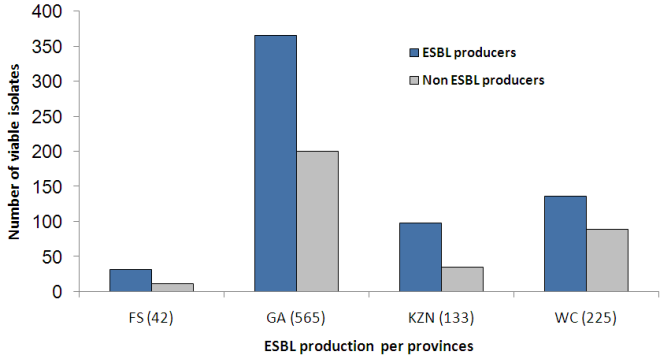


Figure 18. Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites, by province and ESBL production, January-December 2011, n=996.



Staphylococcus aureus

Results

The number of cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA from January through December 2011 was 1649 (Figure 14). Of these, the majority of cases were detected from sentinel sites in Gauteng (58%) followed by Western Cape (23%) (Table 32). The numbers of cases were equally distributed throughout the whole year (Figure 19). Most cases occurred amongst patients aged 25 years to 65 years (Figure 20). The percentage of isolates that were susceptible to mupirocin was 73%; 22% exhibited low-level resistance and 5% high-level resistance (Figure 21). Resis-

(Continued on page 29)

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tance to oxacillin (MRSA) was determined for 451 (45%) isolates overall; percentage of MRSA isolates from Free State was 53%, Gauteng 50%, KZN 42% and Western Cape 34% (Figure 22).

Discussion

Incidence of *S. aureus* bacteraemia was not calculated. In addition, cases could not be separated into hospital- versus community-acquired categories because only laboratory-based data were available. The majority of cases of *S. aureus* bacteraemia occurred amongst adult patients. The percentage of *S. aureus* isolates that were methicillin-resistant was almost half of the total number submitted to the AMRRU.

Figure 19. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by month, January - December 2011, n=1635.

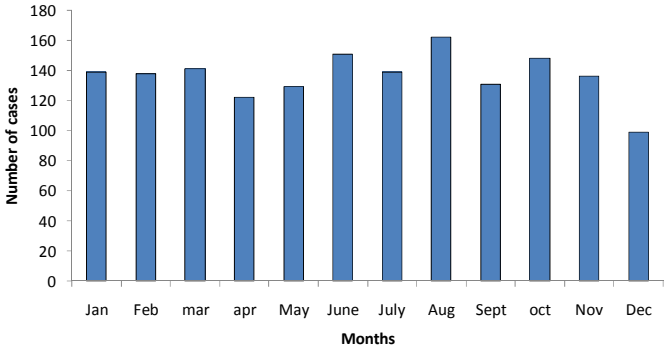

Figure 20. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA from sentinel sites by age category, January - December 2011, n=1448.

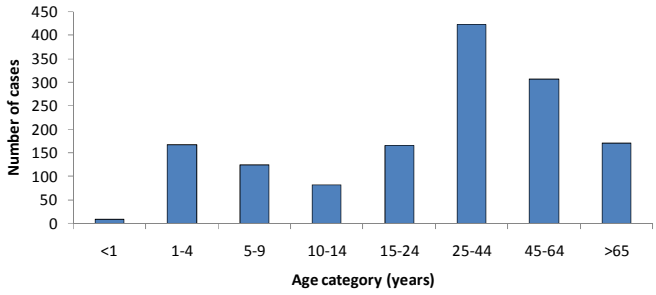

Figure 21. Number of viable, laboratory-confirmed *Staphylococcus aureus* isolates reported by GERMS-SA sentinel sites, with susceptibility to oxacillin and mupirocin, January - December 2011, n=1003.

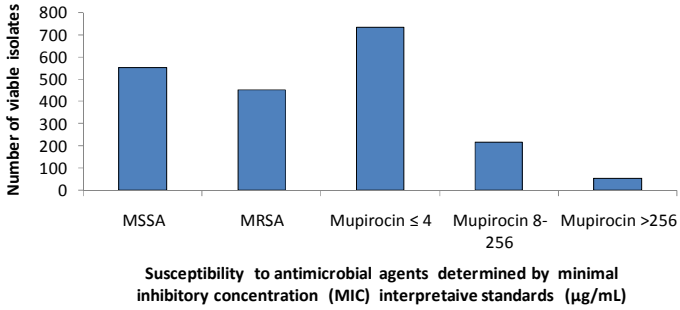

Figure 22. Number of viable, laboratory-confirmed *Staphylococcus aureus* isolates reported by GERMS-SA sentinel sites, by province and oxacillin resistance, January-December 2011, n=1003.

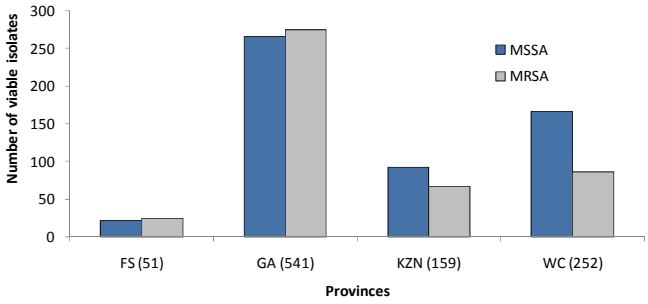

Table 32: Number of *Staphylococcus aureus* cases reported to GERMS-SA sentinel sites by province, South Africa, January-December 2011, n=1649 (including audit cases).

Province	*Staphylococcus aureus*	
	n	%
Free State	113	7
Gauteng	954	58
Kwa Zulu Natal	200	12
Western Cape	381	23
All sentinel sites	**1648**	**100**

Discussion

In summary some of the highlights in this report include: the emerging resistance to fluoroquinolones in *Salmonella* Typhi isolates and the increase in invasive non-typhoidal *Salmonellae* which are inter-mediately or fully-resistant to ciprofloxacin. A slow but steady decline of incident cases of cryptococcosis has been noted for several years now. In 2011 there were approximately 600 fewer cases reported by GERMS-SA, compared with 2010. This may indicate that the antiretroviral treatment programme has made an impact on this AIDS-defining opportunistic infection. The in-hospital mortality of patients with cryptococcosis decreased significantly for the first time and may be related to earlier health-seeking behaviour of patients with meningitis and/or improved in-hospital patient care. Rates of *Haemophilus influenzae* type b (Hib) in children <1 year have stabilised in the last 3 years and invasive pneumococcal disease incidence has decreased in children <1 year of age. These are partly due to the introduction of Hib booster vaccine and PCV7 in South Africa respectively as well as the impact of improvements to HIV prevention and treatment programmes. Hospital-acquired infection surveillance data has also showed that methicillin resistant *Staphylococcus aureus* (MRSA) makes up 50% of isolates submitted to the surveillance programme.

Surveillance data on epidemic-prone bacterial diseases, AIDS-associated opportunistic infections and vaccine-preventable bacterial diseases has significantly contributed to the development of clinical guidelines for pneumonia, meningococcal disease, cholera, cryptococcosis and typhoid fever; and to changes to the Expanded Programme on Immunisations with the introduction of pneumococcal conjugate vaccine as well as the Hib booster dose. More recently data emanating from the GERMS-SA activities has contributed to the Department of Health acting decisively in responding to a proposed cryptococcal antigen screening program which will facilitate the early diagnosis of cryptococcal meningitis.

A great strength of the GERMS-SA surveillance programme is its existing infrastructure of ~200 reporting public- and private-sector laboratories nationally and on their reporting and sending of isolates matching the GERMS-SA case-definitions. GERMS-SA surveillance is as strong as its participating laboratories. We thank all laboratory staff for their unyielding participation in national surveillance and urge clinicians to continue taking specimens and laboratory staff to send isolates.

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Publications in Peer reviewed Journals

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(Continued on page 32)

(Continued from page 31)

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