GERMS SOUTH AFRICA

Annual Report 2014

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

The GERMS-SA Annual Report 2014 was compiled by the National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.

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Cover photograph: GERMS-SA Principal Investigators Meeting, Johannesburg, October 2014.

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Introduction

The GERMS-SA 2014 Annual Report summarises the findings from national surveillance, including the 34 enhanced surveillance (ESS) hospital sites in all 9 provinces, for the year. General laboratory surveillance includes enteric organisms but enhanced surveillance for these organisms stopped for 2014 and are thus not included in this report. Laboratory information system change-over from DISA*Lab to TrakCare Lab continued in 2014 resulting in ongoing challenges of mapping of data onto the Corporate Data Warehouse, which is vital in our audit process for total case numbers. Austerity measures and challenges with staffing at diagnostic laboratories have impacted on the numbers of isolates sent to, as well as the percentage of viable isolates received by the NICD reference laboratories. The GERMS surveillance system has 11 years of surveillance data and continues to monitor the impact of programmes, like the Expanded Programme on Immunisations and the Comprehensive Care, Management and Treatment Programme for HIV/AIDS, on the South African population.

Clinic surveillance started for drug resistance in TB and HIV, as well as STI surveillance. Only the clinic visits are documented in this report. For an update on clinic surveillance see NICD Communicable Disease Surveillance Bulletin, vol 13 no 2, June 2015 (1).

GERMS-SA surveillance officer meeting, Johannesburg, March 2014.

Methods

In 2014, diseases under surveillance included:

1. Opportunistic infections associated with HIV, e.g. cryptococcosis, invasive non-typhoidal *Salmonella enterica* (NTS) disease, invasive pneumococcal disease (IPD) and rifampicin-resistant *Mycobacterium tuberculosis*
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. Hospital infections, e.g. *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Candida* species

The methods utilised by the GERMS-SA surveillance programme have been previously described in detail (2).

In brief, approximately 183 South African clinical microbiology laboratories participated in the surveillance programme in 2014. The population under surveillance in 2014 was estimated at 54 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 to 31 December 2013, 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. In 2014, no laboratories were required to directly report case patients or send isolates to NICD. For these cases of crypto-

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coccosis, data were obtained directly from the NHLS Corporate Data Warehouse (CDW), which stores information from Disa*Lab and TrakCare laboratory information systems. Cryptococcal isolates, obtained from patients at ESS, continued to be characterised by phenotypic and genotypic tests through 2013, but were not available in 2014. From July 2010 through August 2012, 7 sentinel sites reported cases of *S. aureus* bacteraemia to GERMS-SA. From September 2012 through 2013, laboratory-based bacteraemic *S. aureus* surveillance continued at 3 Gauteng sites only, and in 2014, 2 additional sites in the Western Cape were included. From January 2012, 7 sentinel sites in Gauteng and Western Cape provinces reported cases of candidaemia to GERMS-SA, increasing to 12 sites in 2013. In 2014, candidaemia surveillance changed to 18 new sites in the remaining seven provinces. At ESS, surveillance officers completed clinical case report forms electronically on mobile phones for patients with seven laboratory-confirmed diseases (cryptococcosis [for January through March only, except at 6 cryptococcal screening sites], candidaemia, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, bacteraemic *S. aureus* disease [at 5 sites] and rifampicin-resistant tuberculosis [at 7 sites]), by case patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status, and patient outcome. Case patients were followed up only for the duration of the hospital admission. Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on a Microsoft Access database. A surveillance audit was performed 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 2013 and 2014 from Statistics South Africa (Table 1) (3). Incidence in the HIV-infected and AIDS populations was calculated for 2013 and 2014, 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 (4). All reported incidence is expressed as cases per 100,000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test and p values <0.05 were considered significant throughout. Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (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 (5U2GPS001328).

Table 1. Population denominators used to calculate incidence rates, 2013 and 2014

Province	General population*		HIV-infected population**		AIDS population**	
	2013	2014	2013	2014	2013	2014
Eastern Cape	6,620,137	**6,786,880**	756,979	**777,096**	69,948	**75,325**
Free State	2,753,142	**2,786,757**	359,406	**363,254**	37,490	**39,323**
Gauteng	12,728,438	**12,914,817**	1,227,020	**1,229,076**	139,348	**146,240**
KwaZulu-Natal	10,456,907	**10,694,434**	1,628,536	**1,654,551**	168,173	**177,961**
Limpopo	5,517,968	**5,630,464**	436,918	**449,748**	39,672	**43,143**
Mpumalanga	4,127,970	**4,229,323**	502,186	**511,625**	49,513	**52,712**
Northern Cape	1,162,914	**1,166,680**	80,225	**81,550**	8,293	**8,896**
North West	3,597,589	**3,676,274**	441,816	**446,737**	47,342	**49,611**
Western Cape	6,016,926	**6,116,324**	283,550	**287,163**	30,323	**32,721**
South Africa	52,981,991	**54,001,953**	5,786,603	**5,880,382**	591,116	**629,183**

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

Operational Report

Site visits

Table 2 documents the 59 site visits done by NICD staff to NHLS and private laboratories, hospitals and clinics to meet with stakeholders and surveillance officers and initiate, feedback or train on surveillance projects. Meeting with the people on the ground and feeding back is a core function of the programme and maintains buy-in.

Coordination of meetings

Surveillance officer (SO) meeting, 13-14 March 2014: This meeting, convened at the Genesis Suites and Conferencing in Johannesburg, was attended by all surveillance officers from 9 provinces. The meeting focused on feedback on studies from the project leads, a review of changes within the surveillance system, updates on the GERMS-SA Electronic Data Collection Information System (GEDI) and discussing GERMS-SA future plans.

Surveillance officer meeting, 7-8 August 2014: This meeting was convened in Johannesburg and the main focus was quality data collection via case report form (CRF) training exercises and presentations.

Surveillance officer meeting, 3-5 December 2014: This additional meeting was held in Johannesburg to reinforce the use of technology in data capture, and to improve performance and productivity through improved computer skills by providing surveillance officers with hands-on training in Microsoft applications. Following project updates, a half-day team building session was held at Gold Reef City.

Principal Investigator (PI) meeting, 14-15 October 2014: 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. Plans for the expanded GERMS-SA platform were discussed, including integrated TB/HIV surveillance (including drug resistance), STI clinic surveillance and the role of GERMS-SA provincial epidemiologists. Current surveillance and research activities were reviewed, including preliminary results from the PCV case-control study.

Surveillance audit

A total of 11,437 surveillance cases were detected by GERMS-SA in 2014. Excluding the cases of cryptococcosis (n=5,772), which are all detected by audit as isolates are no longer required to be sent to the NICD, and cases of rifampicin-resistant TB (n=807), for which no audits are performed, 21% (1,009/4,858) of cases were not reported to the NICD by the clinical microbiology laboratories, but were detected by audit of the NHLS Corporate Data Warehouse (Table 3). 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

Surveillance organisms have changed in 2014, making it less comparable to previous years. Enhanced surveillance was not conducted on the enteric pathogens *Salmonella* and *Shigella*. The proportion of completed CRFs in 2014 was similar to that in 2013; the addition of pathogens that cause more severe illness (candidaemia and *S. aureus*) make it more difficult to follow-up patients (Table 4 and 5): 84% (3,410/4,070) of cases had a case report form (CRF) completed (target = 90%). The interview rate continues to improve over the years [2,811 (82%) of the CRFs were completed by patient interview (target = 70%)]. Since 2007, enhanced surveillance site operational reports (ESSOR) have been provided to the site coordinators, laboratory staff and surveillance officers to enable the site team to regularly review site performance, in comparison with set targets. The main objective of these reports is to provide information regarding the overall functioning of the surveillance site, by providing indicators of laboratory participation (submission of isolates), and indicators of surveillance officer performance (completion of CRFs). By reviewing these indicators, problems with data collection can be targeted, and recommendations are provided to improve the site performance. In 2014, these reports were provided quarterly.

Enhanced surveillance site quality monitoring

In 2014, surveillance officers (SO) were audited in terms of quality of work. CRFs from a fixed time period were randomly selected for each surveillance officer so that there were 6 CRFs (one for each organism) to audit per SO. The medical record files were drawn and the GERMS-coordinating staff filled in a modified clean CRF from the original source data and compared their CRF with the original SO CRF. A scoring system was set up and, although the scores varied widely amongst SOs, many of the errors were ones of omission and overlooking information rather than entry of incorrect data.

Table 2. GERMS-SA surveillance site visits between 1 January and 31 December 2014

Date	Province	Laboratory (NHLS or Private)	Hospital/ Clinic
8 January	GA	-	Chris Hani Baragwanath Hospital & SOs
8 January	KZ	NHLS Inkosi Albert Luthuli	-
4 February	KZ	NHLS King Edward VIII	King Edward VIII Hospital & SOs
5 February	KZ	NHLS Addington	Addington Hospital & SOs
6-7 February	WC	NHLS Groote Schuur	Groote Schuur Hospital & SOs
11 February	NW	NHLS Klerksdorp/ Tshepong	Klerksdorp/ Tshepong Hospital & SOs
17 & 24 March	GA	Lancet Richmond	-
26 March	NW	-	Klerksdorp/ Tshepong Hospital SOs
28 March	MP	-	Nelspruit Hospital SOs
2 April	FS	-	Universitas/ Pelonomi Hospital SOs
7 April	GA	-	Tambo Memorial Hospital & SOs
10 April	GA	-	Chris Hani Baragwanath Hospital & SOs
5 May	GA	NHLS Natalspruit	-
6 May	GA	-	Natalspruit Hospital & SOs
6 June	KZ	NHLS Northdale	Northdale Hospital & SOs
17 June	KZ	NHLS Edendale	Edendale Hospital & SOs
20 June	GA	-	Chris Hani Baragwanath Hospital SOs
23 June	FS	NHLS Welkom	-
24 June	KZ	-	Edendale Hospital & SARI SOs
25 June	WC	-	Red Cross Hospital SOs
2-4 July	KZ	NHLS Inkosi Albert Luthuli	Inkosi Albert Luthuli Hospital & SOs
2-4 July	KZ	NHLS King Edward VIII	King Edward VIII Hospital & SOs
2-4 July	KZ	NHLS Addington	Addington Hospital & SOs
2-4 July	KZ	NHLS RK Khan	RK Khan Hospital & SOs
8 July	FS	NHLS Universitas/ Pelonomi	Universitas/ Pelonomi Hospital & SOs
13 July	NC	NHLS Kimberley	Kimberley Hospital & SOs
28 July	NW	-	Klerksdorp/ Tshepong Hospital SOs
7 August	KZ	NHLS Northdale	Surrounding clinics
12 August	GA	NHLS Helen Joseph	Helen Joseph Hospital & SOs
22 August	NW	-	Klerksdorp/ Tshepong Hospital SOs
27-29 August	EC	-	Nelson Mandela Academic Hospital & SOs
1-3 September	LP	NHLS Polokwane/ Mankweng	Polokwane/ Mankweng Hospital & SOs
2-4 September	MP	-	Hluvukani Clinic
9 September	FS	NHLS Bongani	Bongani Hospital & SOs
10 September	NW	NHLS Tshepong	-
10-12 September	NC	-	Kimberley Hospital & SOs
25 September	WC	NHLS Groote Schuur	Groote Schuur Hospital
29 September	NW	-	Jouberton CHC
30 September	GA	-	Chiawelo Clinic
1-2 October	LP	-	Polokwane/ Mankweng Hospital & SOs
1-3 October	KZ	NHLS Mahatma Ghandi	-
1-3 October	KZ	NHLS Port Shepstone	-
1-3 October	KZ	NHLS Stanger	-
1-3 October	KZ	NHLS Ngwelezane	-
3 October	NW	-	Klerksdorp/ Tshepong Hospital SOs
6-9 October	MP	-	Hluvukani Clinic

Table 2 cont. GERMS-SA surveillance site visits between 1 January and 31 December 2014

Date	Province	Laboratory (NHLS or Private)	Hospital/ Clinic
7 October	GA	NHLS Tambo Memorial	Tambo Memorial Hospital & SOs
10 October	KZ	NHLS King Edward VIII	King Edward VIII Hospital & SOs
30 October	EC	NHLS Port Elizabeth	Livingstone Hospital
30 October	EC	Ampath & Pathcare	Livingstone Hospital
31 October	GA	-	Steve Biko Pretoria Academic Hospital SOs
31 October	GA	-	Dr George Mukhari Hospital SOs
5 November	GA	NHLS South Rand	South Rand Hospital & SOs
5 November	WC	-	Tygerberg Hospital SOs
7 November	NW	-	Klerksdorp/ Tshepong Hospital
21 November	NC	-	Kimberley Hospital
28 November	GA	-	Rahima Moosa Mother & Child Hospital SOs
11-12 December	FS	-	Hani Park Clinic
11-12 December	FS	-	Bongani Hospital

SOs: Surveillance Officers

Table 3. Cases detected by surveillance audit by province, 2014

Surveillance case		Percentage of cases detected by audit* n_1/n_2 (%)	Number of cases detected by audit									
			EC	FS	GA	KZ	LP	MP	NC	NW	WC	SA
Invasive	Cryptococcosis**	5772/5772 (100%)	744	236	1417	1564	237	364	43	305	862	**5772**
	Candidaemia	71/435 (16%)	5	18	3	27	10	3	0	5	N/A	**71**
	Meningococcal disease	29/193 (15%)	4	2	13	3	0	0	0	1	6	**29**
	Haemophilus influenzae disease	98/317 (31%)	16	7	35	20	0	8	1	2	9	**98**
	Pneumococcal disease	608/2734 (22%)	66	42	174	181	9	44	12	33	47	**608**
	Staphylococcus aureus disease (BC only)	110/774 (14%)	N/A	N/A	76	N/A	N/A	N/A	N/A	N/A	34	**110**
	Pseudomonas aeruginosa (BC only)	93/405 (23%)	N/A	16	44	0	N/A	N/A	N/A	N/A	33	**93**
Non-invasive	Rifampicin-resistant tuberculosis***	0/807 (N/A)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total**		**1,009/4,858 (21%)**	**91**	**85**	**345**	**231**	**19**	**55**	**13**	**41**	**129**	**1009**

*Percentage of cases detected by audit = number of cases detected on audit (n_1)/total number of cases detected by GERMS-SA (n_2) x 100; **All cryptococcal cases are detected on audit and no isolates are received, therefore this organism is excluded from the total; ***Audits are not performed on TB cases, therefore this organism is excluded from the total; EC: Eastern Cape; FS: Free State; GA: Gauteng; KZ: KwaZulu-Natal; LP: Limpopo; MP: Mpumalanga; NC: Northern Cape; NW: North West; WC: Western Cape; SA: South Africa; BC: Blood culture.

Table 4. Enhanced surveillance site performance indicators, 2014

Enhanced surveillance site*	Case patients, n	Completed case report forms**, n (%)***	Case report forms completed by interview, n (%)†
Addington [1,5]	54	54 (100)	43 (80)
Bertha Gxowa [3]	37	16 (43)	11 (69)
Charlotte Maxeke Johannesburg Academic [1,2,5]	395	389 (98)	346 (89)
Chris Hani Baragwanath [1,4,5]	476	406 (85)	308 (76)
Dr George Mukhari [1,5]	213	197 (92)	174 (88)
Edendale/ Grey's/ Northdale [1,4,5]	299	277 (93)	257 (93)
Far East Rand[3]	48	0 (0)	0 (0)
Groote Schuur/ Red Cross [1,2,5]	307	284 (93)	242 (85)
Helen Joseph/ Rahima Moosa Mother & Child [1,2,5]	250	183 (73)	141 (77)
Kalafong [5]	8	7 (88)	7 (100)
Kimberley [1,4,5]	112	95 (85)	74 (78)
King Edward VIII [1,5]	97	88 (91)	52 (59)
Klerksdorp/ Tshepong [1,4,5]	303	228 (75)	186 (82)
Mankweng/ Polokwane/ Seshego [1,4,5]	99	24 (24)	19 (79)
Natalspruit [5]	96	53 (55)	30 (57)
Nelson Mandela Academic/ Umtata General [1,4,5]	177	126 (71)	105 (83)
Pelonomi/ Universitas [1,5]	174	168 (97)	112 (67)
Pholosong [3]	35	16 (46)	9 (56)
RK Khan [1,5]	94	84 (89)	73 (87)
Rob Ferreira/ Themba [1,4,5]	290	243 (84)	220 (91)
Steve Biko Pretoria Academic/ Tshwane District [1,2,5]	152	150 (99)	145 (97)
Tambo Memorial [3]	70	41 (59)	30 (73)
Tygerberg [1,2,5]	284	281 (99)	227 (81)
TOTAL	**4,070**	**3,410 (84)**	**2,811 (82)**

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; Cryptococcal surveillance was only enhanced for the first quarter of 2014; *There were 5 surveillance officers at Chris Hani Baragwanath, 3 at Helen Joseph/Rahima Moosa Mother and Child Hospital, 3 at Groote Schuur/ Red Cross, 2.5 at Charlotte Maxeke Johannesburg Academic, 2 at Tygerberg, 1.5 at Dr George Mukhari, Steve Biko Academic Hospital and Edendale/Grey's; 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 = 70%; [1]Sites doing candidaemia surveillance; [2]Sites doing *S. aureus* enhanced surveillance (bacteraemia only); [3]Sites doing only cryptococcal surveillance; [4]Sites doing rifampicin-resistant TB surveillance: excludes CRFs where no medical record was found and no interview was done; [5]IPD case-control study sites.

Surveillance reports

Enhanced surveillance site project

In 2014, of 11,437 surveillance case patients detected by GERMS-SA, 4,070 (36%) were diagnosed at enhanced surveillance sites. Of case patients with recorded HIV status, 60% (1,735/2,880) 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 (99%) and rifampicin-resistant TB (84%) were HIV-infected; HIV infection amongst patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 60%, and just over one quarter (27%) 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, 2014**

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[†]	853	595	(70)	570	(96)	562	(99)
Candida species	435	379	(87)	292	(77)	67	(23)
Neisseria meningitidis	58	56	(97)	48	(86)	13	(27)
Streptococcus pneumoniae	985	919	(93)	788	(86)	472	(60)
Haemophilus influenzae	158	146	(92)	115	(77)	38	(33)
Staphylococcus aureus	774	744	(96)	512	(69)	117	(23)
Rifampicin-resistant TB	807	571	(71)	555	(97)	466	(84)
Total	**4,070**	**3,410**	**(84)**	**2,880**	**(85)**	**1,735**	**(60)**

*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. [†] For cryptococcal disease, case report forms were completed for the first quarter of 2014 at all GERMS enhanced surveillance sites and throughout the year at 6 enhanced surveillance sites linked to the Gauteng screen and treat evaluation.

Cryptococcus species

Results

During 2014, 5,772 case patients with laboratory-confirmed, incident cryptococcal disease were reported. The incidence of cryptococcal disease in the HIV-infected population decreased overall and in most provinces, except the Eastern Cape, Limpopo, North West and Western Cape where the incidence increased (Table 6). When cases of cryptococcal antigenaemia (with no concurrent laboratory evidence of cryptococcal meningitis or fungaemia) were excluded, the incidence still decreased overall, remained stable in the Eastern Cape, still increased in Limpopo, North West and the Western Cape and decreased in all other provinces [data not shown]. The highest incidence was recorded among patients aged 35-39 years (Figure 1). One hundred and twenty one (2.5%) children younger than 15 years had laboratory-confirmed cryptococcosis; 54 (45%) of these were younger than 5 years of age. Where sex was known, 55% (3,163/5,703) of patients were male. Most patients (85%) with incident disease were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 13% were diagnosed with fungaemia/ antigenaemia (Table 7). One hundred and thirty one patients were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. In 2014, isolates from cases diagnosed at enhanced surveillance sites (ESS) were no longer submitted to NICD. Clinical case data were collected from patients at ESS for the first quarter of the year and at 6 additional ESS in Gauteng linked to the cryptococcal disease screen & treat evaluation for the entire year. Completed case report forms were available for 70% (595/853) of patients (Table 4). Of 570 patients with known HIV status and a first episode of cryptococcal disease, 562 were known to be HIV-infected (Table 5). In 2014, 56% of HIV-infected patients with known antiretroviral treatment (ART) status (312/556) were on ART at the time of diagnosis of cryptococcal disease or had previously received ART [vs. 52% (935/1,793) in 2013; p=0.09). Among 444 HIV-infected patients who had a CD4+ T-lymphocyte (CD4) count test result recorded close to the time of diagnosis, 390 (88%) had a CD4 count <200 cells/µl; the median CD4 count was 44 cells/µl (interquartile range, 14 – 110). The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease did not change significantly between 2013 and 2014 [689/2,028 (34%) vs. 174/568 (31%); p=0.1].

Discussion

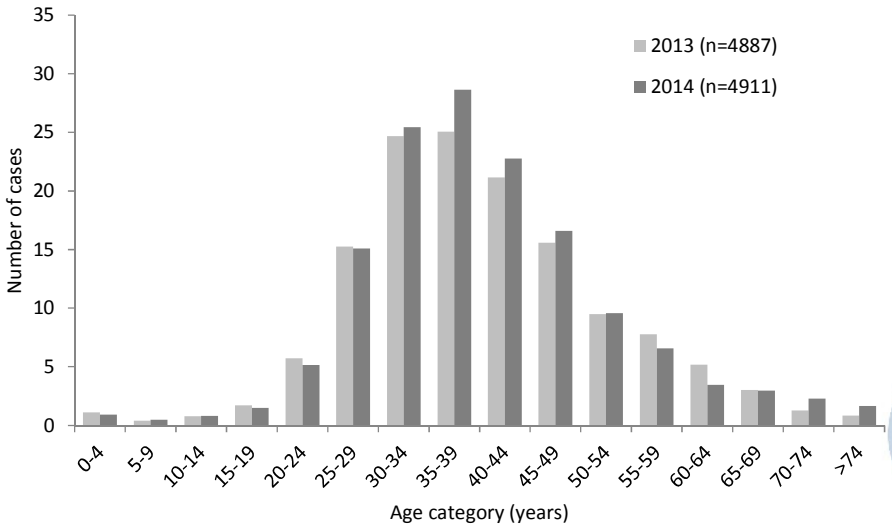
The burden of laboratory-confirmed cryptococcal disease decreased again in 2014 with an overall incidence of 100 cases per 100,000 HIV-infected persons. The incidence climbed in the Eastern Cape, Limpopo, North West and Western Cape. Since the case numbers include patients with cryptococcal antigenaemia diagnosed at NHLS microbiology laboratories (i.e. through provider-initiated screening of cryptococcal disease), this may partly reflect improved case detection in these provinces. Given the large proportion of patients who were on concurrent ART or had previously received ART, more cases may also be diagnosed among ART-experienced persons who have discontinued or failed ART (5). The demographic and clinical profile of patients with cryptococcosis remained largely unchanged and the in-hospital case-fatality ratio remained high.

Table 6. Number of cases and incidence of cryptococcal disease detected by GERMS-SA by province, South Africa, 2013 and 2014, n=12,025

Province	2013		2014	
	n*	Incidence**	n*	Incidence**
Eastern Cape	710	94	744	96
Free State	250	70	236	65
Gauteng	2,119	173	1,417	115
KwaZulu-Natal	1,716	105	1,564	95
Limpopo	153	35	237	53
Mpumalanga	370	74	364	71
Northern Cape	56	70	43	53
North West	259	59	305	68
Western Cape	620	219	862	300
South Africa	**6,253**	**109**	**5,772**	**100**

*These case numbers include patients who had blood specimens submitted to an NHLS microbiology laboratory for early detection of cryptococcal disease and who tested positive for cryptococcal antigenaemia. Case numbers may differ slightly from the previous GERMS-SA Annual Report due to data cleaning.
**Incidence was calculated using HIV-infected population denominators determined by the Actuarial Society of South Africa (ASSA -2008) model and are expressed as cases per 100,000 population.

Figure 1. Incidence* of laboratory-confirmed cryptococcal disease reported to GERMS-SA by age category, South Africa, 2013 and 2014, n=9,798 (age unknown for 1366 cases in 2013 and 861 cases in 2014)



*Incidence was calculated using population denominators from Statistics South Africa and has been expressed as cases per 100,000 persons in the general population; Note: due to the large number of cases with unknown age in 2013 and 2014, incidence is under-estimated.

Table 7. Number and percentage of cases of cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2013 and 2014, n=12,025

Site of specimen	2013		2014	
	n	(%)	n	(%)
Cerebrospinal fluid	5,501	(88)	4,925	(85)
Blood culture	295	(5)	230	(4)
Blood (for CrAg test*)	394	(6)	486	(9)
Other	63	(1)	131	(2)
Total	**6,253**		**5,772**	

Candida species

Results

In 2014, 435 cases of candidaemia were detected from 16 new ESS in 8 provinces (Table 8). The vast majority of cases occurred among children aged 0-4 years and 40% (173/435) of all cases occurred among neonates (≤28 days of age) (Figure 2). Where sex was known, 50% (212/423) of patients were male. Clinical data were collected for 379 (87%) patients. The overall crude case-fatality ratio was high (138/379; 36%). HIV infection is not an independent risk factor for candidaemia; however, 23% (67/293) of patients with candidaemia were also HIV-infected. At least one viable isolate was available for 315 (72%) cases of candidaemia. Overall, *Candida albicans* was the most common species followed by *Candida parapsilosis* (Table 9). While *Candida krusei* was the third most common species, the vast majority of these cases were diagnosed at a single hospital in Gauteng where an outbreak had occurred. All *Candida* isolates had an amphotericin B minimum inhibitory concentration (MIC) ≤1 µg/ml (apart from 5 *C. krusei* isolates and 1 *Candida haemulonii* isolate). Susceptibility results for five common *Candida* species and three antifungal agents are summarised in Table 10; anidulafungin MICs are presented as a proxy for susceptibility to the echinocandin class.

Discussion

Most cases of candidaemia diagnosed at 16 public-sector hospitals in 8 provinces were diagnosed among young children, predominantly neonates. More than a third of patients died in hospital. The epidemiology varied by province. A large outbreak of candidaemia caused by *C. krusei* occurred in a neonatal intensive care unit at a single Gauteng hospital (6). In the Free State, North West and KwaZulu-Natal, *C. parapsilosis* was the dominant pathogen following *C. albicans*. In contrast, *C. glabrata* and *C. parapsilosis* were the two commonest species in Mpumalanga after *C. albicans*. The other provinces reported fewer than ten cases. Knowledge of local hospital or hospital unit epidemiology should guide empiric treatment choices. Conventional amphotericin B remains the empiric drug of choice for candidaemia in the public-sector because of the high prevalence of azole-resistant *C. parapsilosis* isolates. Caspofungin or anidulafungin are also good choices for empiric treatment in all settings where these agents are available.

Table 8. Number of cases of candidaemia detected by GERMS-SA by enhanced surveillance site, 2014, n=435

Enhanced surveillance site	2014
Addington	4
Dr George Mukhari	114
Edendale	45
Grey's	39
Kimberley	10
King Edward VIII	32
Mankweng	9
Nelson Mandela Academic/ Mthatha Provincial	13
Northdale	2
Pelonomi	29
Polokwane	5
RK Khan	8
Rob Ferreira	19
Themba	4
Klerksdorp/ Tshepong	30
Universitas	72
Total	**435**

Figure 2. Number of cases of laboratory-confirmed candidaemia reported to GERMS-SA from 16 new enhanced surveillance sites by age category, 2014, n=426 (age unknown for 9 cases).

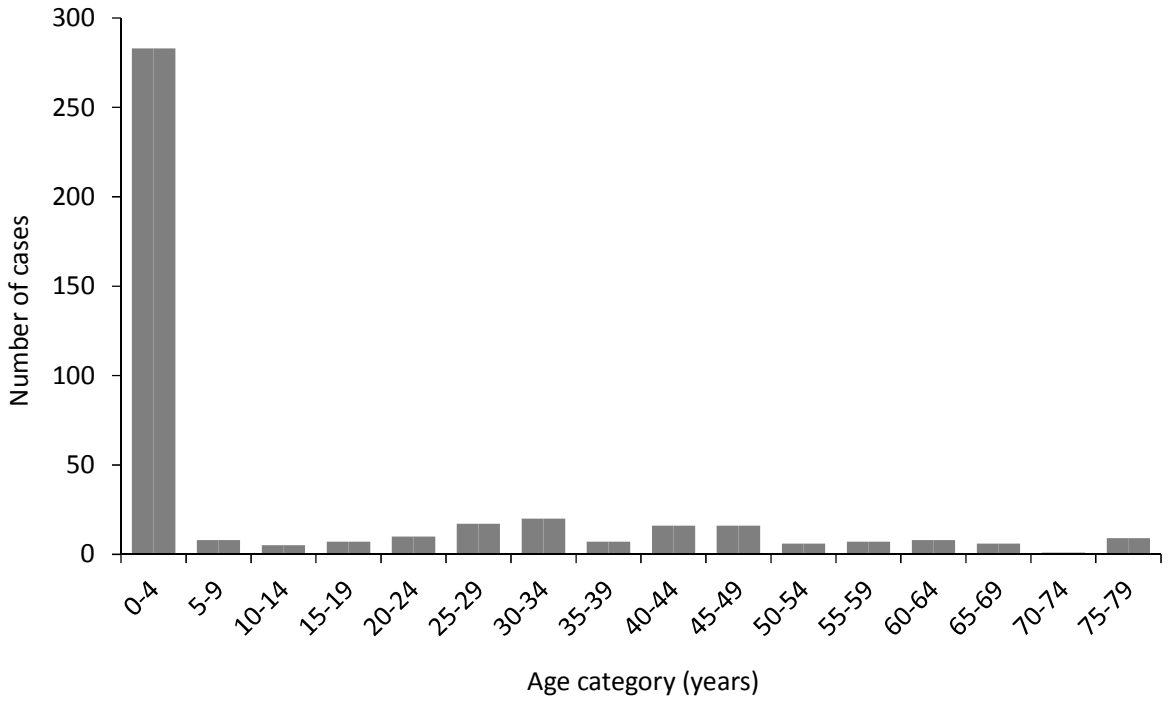


Table 9. *Candida* species distribution for cases of candidaemia with a viable bloodstream isolate by province, 2014, n=315

Species	n (%)								
	EC	FS	GA*	KZ	LP	MP	NC	NW	Overall
Candida albicans	2 (50)	34 (44)	33 (33)	32 (37)	1 (33)	11 (69)	2 (22)	10 (56)	125 (40)
Candida parapsilosis	1 (25)	26 (34)	8 (8)	30 (34)	2 (67)	2 (13)	5 (56)	6 (33)	80 (25)
Candida glabrata	1 (25)	10 (13)	7 (7)	10 (11)	0 (0)	2 (13)	0 (0)	1 (6)	31 (10)
Candida tropicalis	0 (0)	2 (3)	1 (1)	7 (8)	0 (0)	1 (5)	1 (11)	0 (0)	12 (4)
Candida krusei	0 (0)	1 (1)	49 (49)	5 (6)	0 (0)	0 (0)	0 (0)	0 (0)	55 (17)
Other *Candida* species	0 (0)	4 (5)	3 (2)	3 (4)	0 (0)	0 (0)	1 (11)	1 (5)	12 (4)
Total	**4**	**77**	**101**	**87**	**3**	**16**	**9**	**18**	**315**

*All cases from Dr George Mukhari hospital – outbreak of *Candida krusei* in 2014; EC: Eastern Cape, FS: Free State, GA: Gauteng, KZ: KwaZulu-Natal, LP: Limpopo, MP: Mpumalanga, NC: Northern Cape, NW: North West

Table 10. Number and percentage of *Candida* bloodstream isolates (five commonest species only) susceptible* to fluconazole, voriconazole and anidulafungin by broth microdilution testing, 2014, n=303

Susceptible to Antifungal agent	*C. albicans* n/N (%)	*C. parapsilosis* n/N (%)	*C. glabrata* n/N (%)	*C. tropicalis* n/N (%)	*C. krusei* n/N (%)
Fluconazole	125/125 (100)	36†/80 (45)	N/A**	12/12 (100)	N/A
Voriconazole	125/125 (100)	60†/80 (75)	N/A	12/12 (100)	55/55 (100)
Anidulafungin	125/125 (100)	79†/80 (99)	31/31 (100)	12/12 (100)	55/55 (100)

*Based on CLSI M27-S4 species-specific breakpoints for full susceptibility; **Only 2 isolates with MICs ≥64 µg/ml (resistant category); †Isolates with MICs in the intermediate, susceptible dose-dependent or resistant categories confirmed by Etest

Neisseria meningitidis

Results

In 2014, 164 cases of meningococcal disease were reported, and an additional 29 cases were identified on audit: a total of 193 cases of laboratory-confirmed meningococcal disease were identified by the surveillance system during the year (Table 11). Overall incidence was slightly lower than 2013 (0,36 vs 0,44 cases per 100,000 population). The number of cases reported was greatest during the winter and spring months (Figure 3). Of all cases reported, cerebrospinal fluid (CSF) was the most common specimen yielding meningococci (Table 12); the number of cases diagnosed on blood culture was not significantly different in 2014 compared to 2013 (p=0.6). Serogroup W was the most predominant in South Africa (61/156, 39%) (Table 13), as was noted in 2013 (97/190, 51%; p=0.24). Minor year-on-year fluctuations of disease by province were noted. Rates of disease were highest in the Western and Eastern Cape (Table 11). In Gauteng, the incidence of meningococcal disease was estimated at 0.44/100 000, and most of that disease was due to serogroup W (25/42, 60%). In Western Cape, serogroup B was the most common meningococcal serogroup (25/57, 44%). 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 two most common serogroups (Figure 4). Preliminary analysis of case-fatality ratios, as calculated at enhanced surveillance sites where in-hospital outcome is specifically looked for, was 8/58 (14%) in 2014, compared to 8/56 (14%) in 2013 (p=0.9). Of the viable isolates tested for antimicrobial resistance, 13% (11/85) of isolates had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and would be considered non-susceptible. This is higher than what was seen in 2013 (7/116, 6%, p=0.09).

Discussion

Incidence of meningococcal disease remained low in 2014 with serogroup W disease as 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 previous years. The prevalence of non-susceptibility to penicillin has increased compared to 2013. 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 3. Number of laboratory-confirmed, invasive, meningococcal cases reported to GERMS-SA, by month and year, South Africa, 2013-2014, n=426

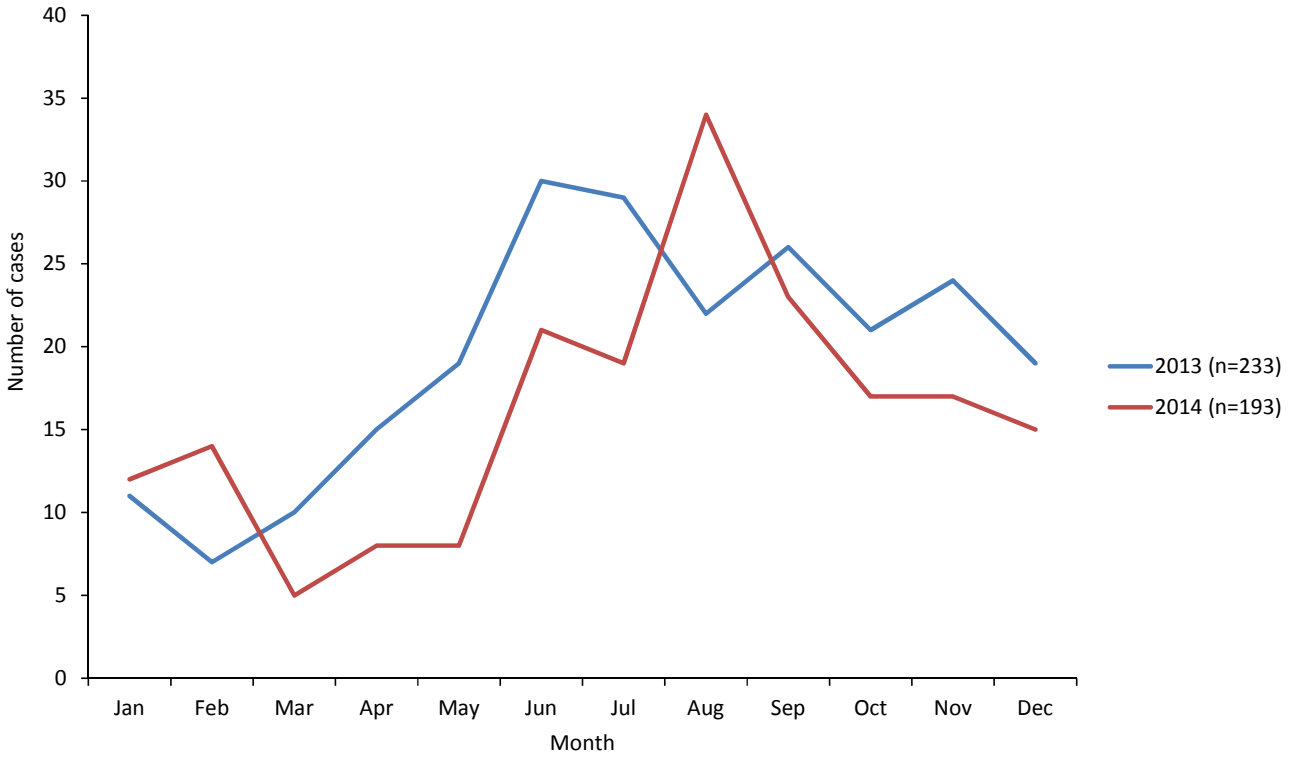


Table 11. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2013 and 2014, n=426 (including audit cases)

Province	2013		2014	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	47	0.71	36	0.53
Free State	14	0.51	5	0.18
Gauteng	69	0.54	57	0.44
KwaZulu-Natal	39	0.37	25	0.23
Limpopo	1	0.02	0	0.00
Mpumalanga	4	0.10	2	0.05
Northern Cape	2	0.17	0	0.00
North West	7	0.19	2	0.05
Western Cape	50	0.83	66	1.08
South Africa	**233**	**0.44**	**193**	**0.36**

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

Table 12. Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2013 and 2014, n=426

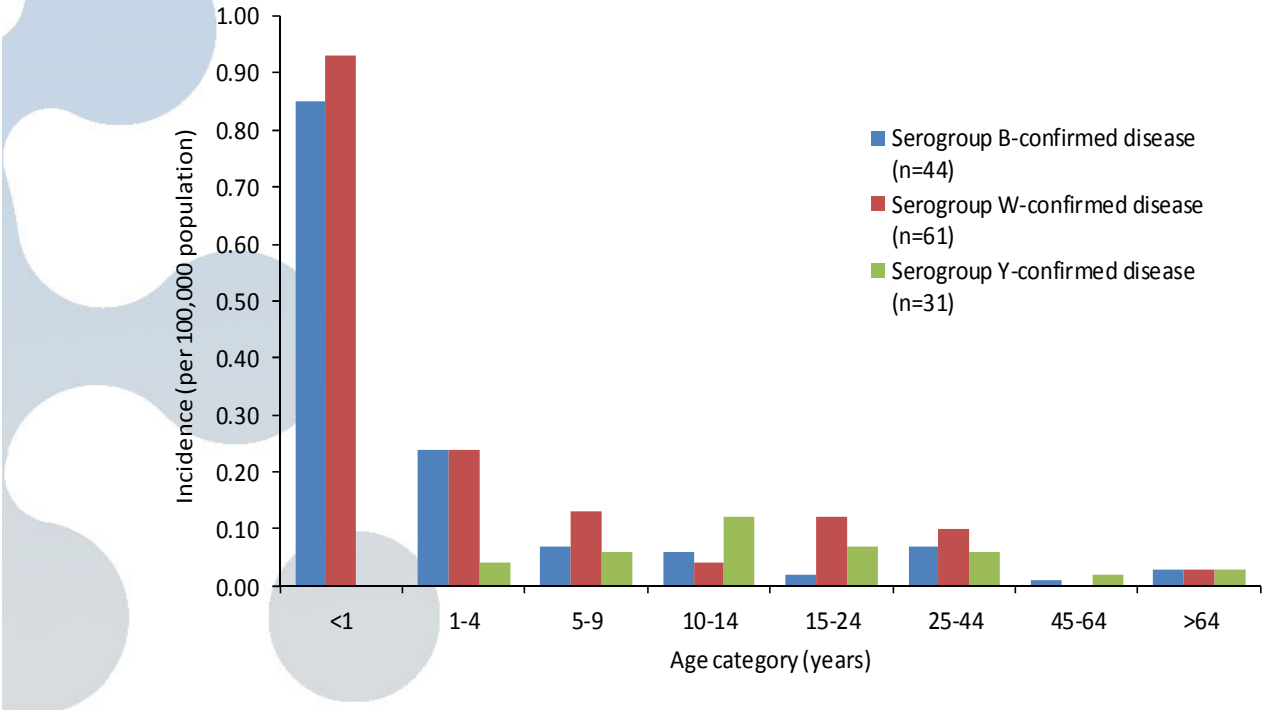
Site of specimen	2013		2014	
	n	(%)	n	(%)
CSF	167	(72)	145	(75)
Blood	63	(27)	47	(24)
Other	3	(1.3)	1	(0.5)
Total	**233**		**193**	

Table 13. Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2014, n=193*

Province	Serogroup								
	Serogroup not available	A	B	C	W	X	Y	NG**	Total
Eastern Cape	4	0	7	6	11	1	7	0	36
Free State	3	0	1	0	0	0	1	0	5
Gauteng	15	0	8	4	25	0	5	0	57
KwaZulu-Natal	5	0	3	2	10	0	5	0	25
Limpopo	0	0	0	0	0	0	0	0	0
Mpumalanga	0	0	0	0	2	0	0	0	2
Northern Cape	0	0	0	0	0	0	0	0	0
North West	1	0	0	0	0	0	1	0	2
Western Cape	9	0	25	6	13	0	12	1	66
South Africa	**37**	**0**	**44**	**18**	**61**	**1**	**31**	**1**	**193**

*156 (81%) with viable isolates or specimens available for serogrouping; ** NG: Non-groupable

Figure 4. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases by serogroup B, W and Y, South Africa, 2014, n=193 (age unknown for n=6; specimens or viable isolates unavailable for serogrouping n=37)**



*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 C, n=18; serogroup X, n=1; non-groupable, n=1

Haemophilus influenzae

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2014 was 219; while an additional 98 cases were identified during the national audit (total number of cases available for analysis was 317). Of these, 192 (61%) had isolates or specimens available for serotyping, and 49/192 (26%) were confirmed as serotype b (Table 14). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (25/49, 51% vs. 7/107, 7%, p<0.001) (Table 15). In 2014, a total of 30 cases of *H. influenzae* serotype b (Hib) were reported amongst children <5 years (Figure 5). Serotype b is no longer the commonest serotype of *H. influenzae* causing disease amongst infants (Figure 6). Rates of Hib disease as recorded by our surveillance network amongst infants <1 year of age decreased from 2010 to 2013 (p<0.001, chi-squared test for trend) and then stabilised between 2013 and 2014 (p=0.77) (Figure 7). Fourteen percent (7/49) of serotype b strains were non-susceptible to ampicillin (MIC>1mg/L, all but one producing beta lactamase), while 9% (10/107) of non-typeable strains were non-susceptible (p=0.4).

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 (7). 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. Rates of Hib in children <1 year, have stabilised in the last year, following a rapid decrease in the preceding 3 years. This change was less marked in the 1-4 year old age group. Non-typeable disease in children <5 years has fluctuated over the last few years. The booster Hib dose may have improved long-term protection against disease and impacted on ongoing Hib transmission in the community (8); however a number of other factors, such as improved prevention and treatment of HIV in infants or changes in diagnosis and reporting of cases, may have also contributed to observed disease changes. 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*.

Table 14. Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2014, n=317*

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	19	1	5	0	0	1	0	5	31
Free State	9	2	3	1	1	0	0	2	18
Gauteng	43	4	19	0	1	0	2	28	97
KwaZulu-Natal	24	3	5	1	0	1	1	13	48
Limpopo	0	0	0	0	0	0	0	0	0
Mpumalanga	11	0	3	0	1	1	1	3	20
Northern Cape	1	0	1	0	0	0	1	2	5
North West	6	2	0	0	0	0	0	0	8
Western Cape	12	5	13	0	1	0	5	54	90
South Africa	**125**	**17**	**49**	**2**	**4**	**3**	**10**	**107**	**317**

*192 (61%) with specimens or viable isolates available for serotyping.

Table 15. Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2014, n=317

Site of specimen	No serotype		Serotype b		Serotypes		Non-typeable	
	n	(%)	n	(%)	n	(%)	n	(%)
CSF	37	(30)	25	(51)	16	(44)	7	(7)
Blood	57	(46)	21	(43)	18	(50)	75	(70)
Other	31	(25)	3	(6)	2	(6)	25	(23)
Total	**125**		**49**		**36**		**107**	

Figure 5. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2014, n=317 (age unknown for n=15; specimens or viable isolates unavailable for serotyping for n=123)

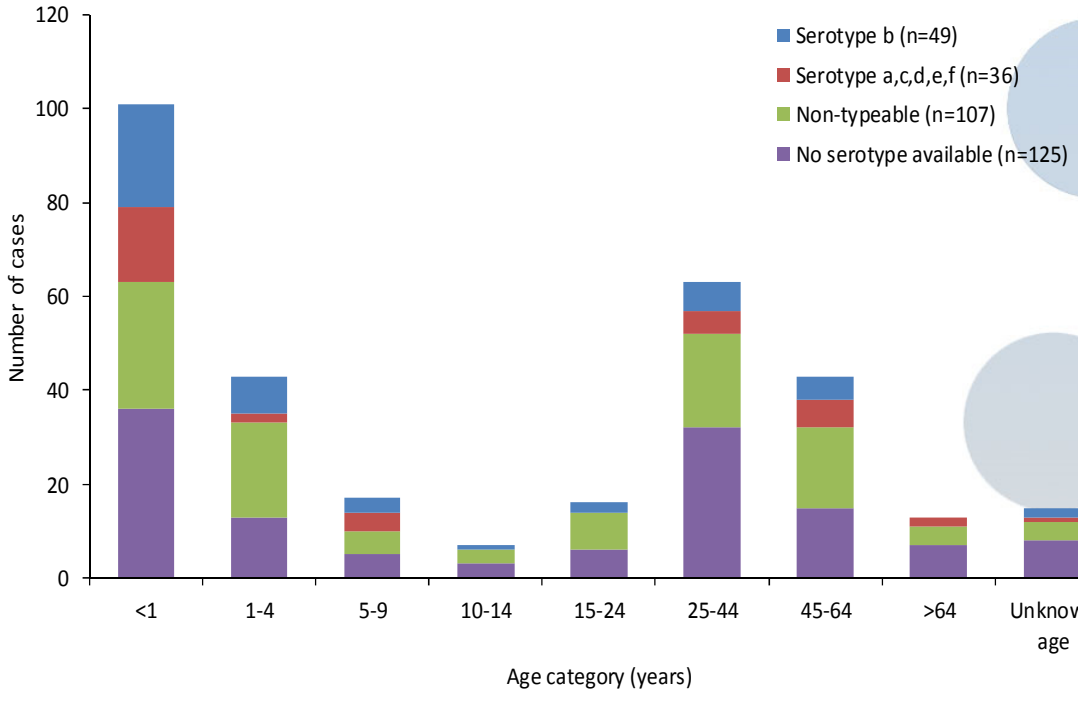
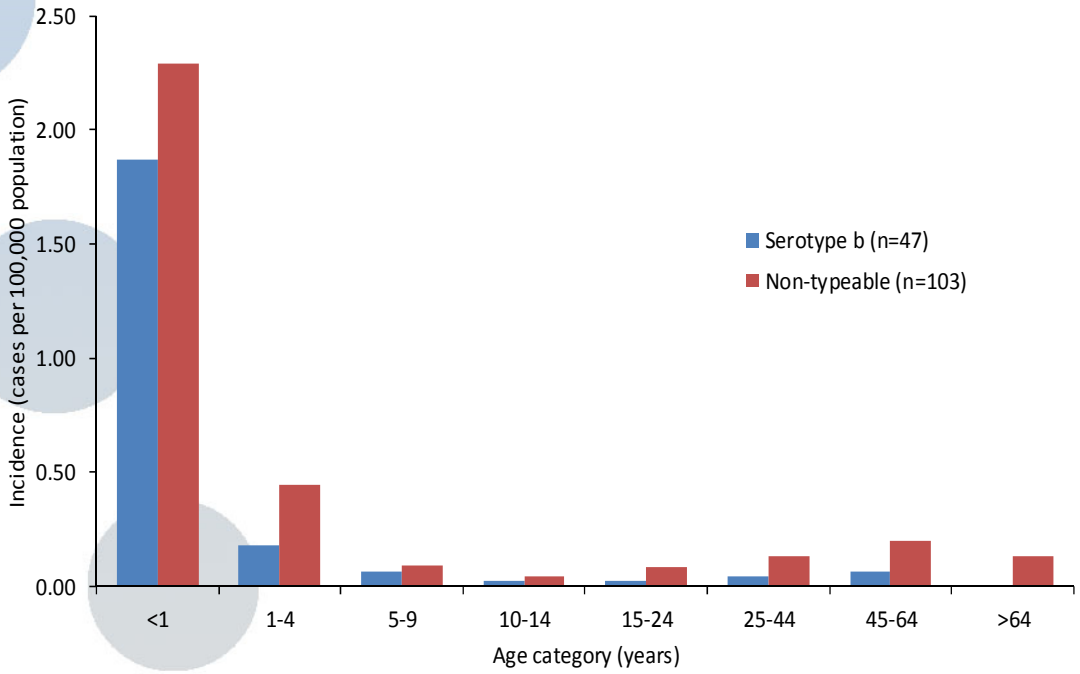
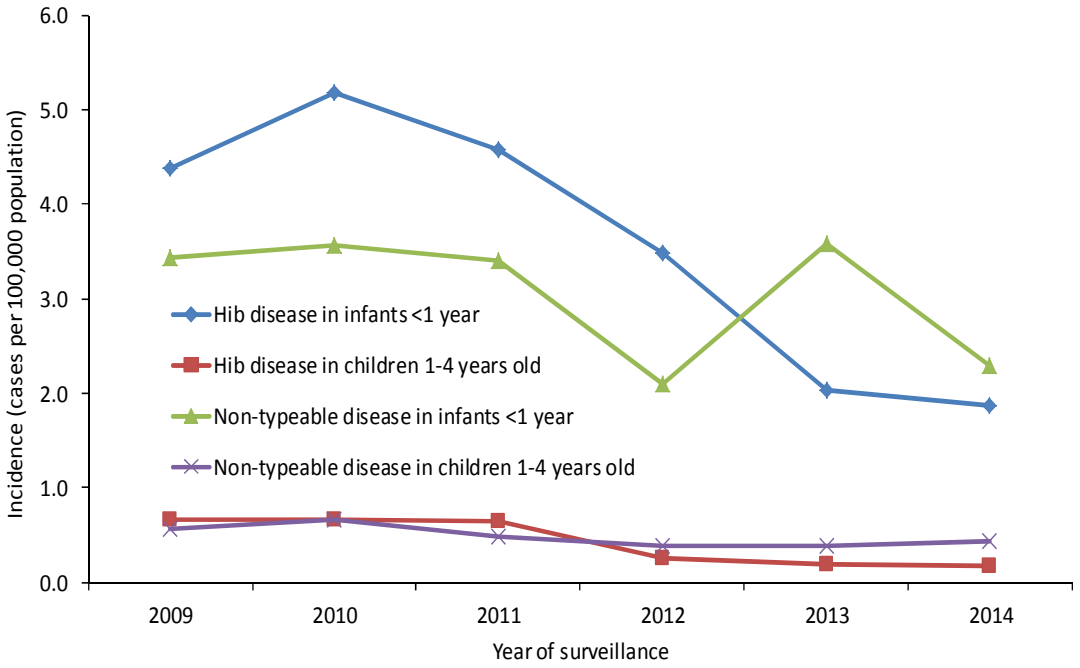


Figure 6. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2014, n=317 (age unknown for n=15; specimens or viable isolates unavailable for serotyping for n=123; other serotypes from cases with known age, n=35)



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

Figure 7. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2014



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

Streptococcus pneumoniae

Results

The 7-valent polysaccharide-protein conjugate pneumococcal vaccine (PCV-7) was introduced into the Expanded Programme on Immunisation (EPI) in South Africa from 1 April 2009. In June 2011, this vaccine was replaced by the 13-valent formulation (PCV-13). Incidence of reported invasive pneumococcal disease (IPD) varied widely by province (Table 16). The age group at highest risk of disease in South Africa was infants <1 year of age, although disease decreased significant from 2009 ($p<0.001$ chi-squared test for trend) (Figure 8). The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 17). Prevalence of non-susceptible strains ranged from 12% to 36% in different provinces (Table 18). Penicillin non-susceptible isolates were most common amongst children 1-4 and 10-14 years of age (Figure 9). Ceftriaxone non-susceptibility was detected amongst 6% (97/1751) of all IPD cases; and no reduction was seen from 2013 (5%, 90/1933). Amongst isolates from CSF specimens, 4% (26/580) were non-susceptible. The number of cases reported amongst children less than 5 years of age due to common serotypes for the period 2009-2014 is shown in Figure 10. The percentage of disease in 2014 amongst children less than 5 years of age due to PCV-7 and newer valency vaccine formulations are shown in Table 19. The number of isolates available for serotyping in this age group has decreased since 2009: (1,009/1,337 [75%] in 2009; 649/909 [71%] in 2010; 465/696 [67%] in 2011; 353/509 [69%] in 2012; 322/498 [65%] in 2013 and 300/464 [64%] in 2014).

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 <5 years of age after the introduction of PCV have been substantial (9). In 2014, as vaccine serotypes continue to decrease, increases have been noted in non-vaccine serotypes. 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 impacted on this opportunistic disease. 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. Ongoing surveillance will assist in evaluating pneumococcal disease in our country at this time of multiple interventions.

Table 16. Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2013 and 2014, n=5,600

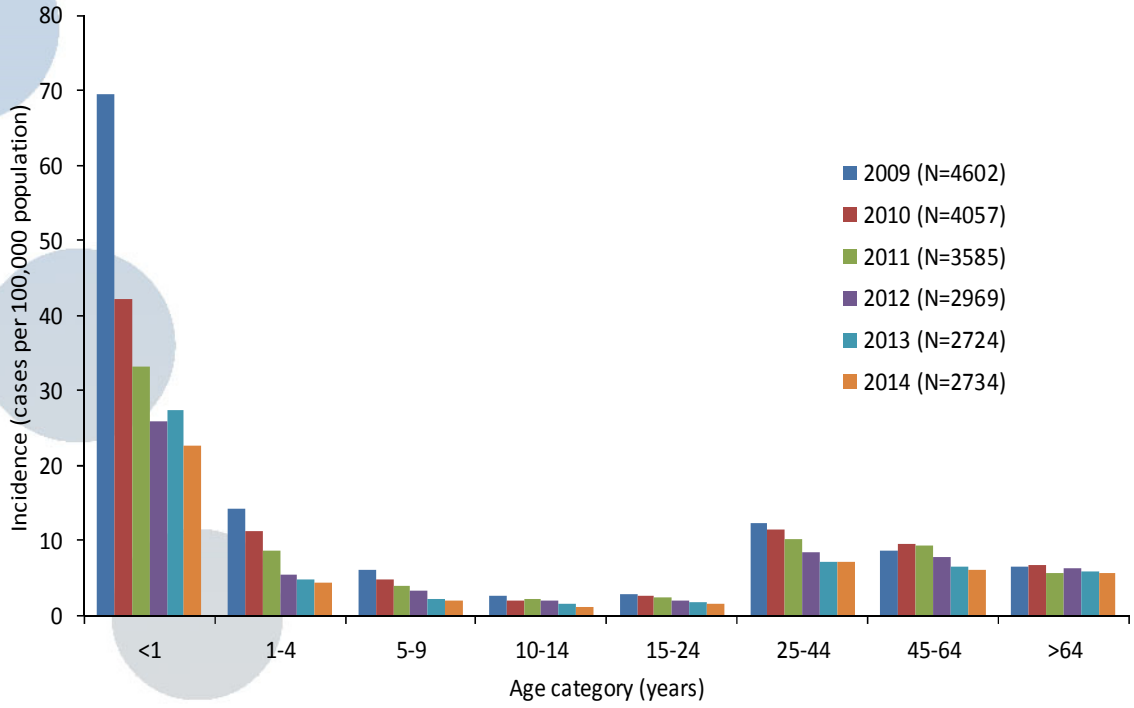
Province	2013		2014	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	301	4.55	229	3.37
Free State	193	7.01	188	6.75
Gauteng	976	7.67	959	7.43
KwaZulu-Natal	496	4.74	499	4.67
Limpopo	62	1.12	41	0.73
Mpumalanga	143	3.46	134	3.17
Northern Cape	81	6.97	42	3.60
North West	136	3.78	111	3.02
Western Cape	478	7.94	531	8.68
South Africa	**2,866**	**5.41**	**2,734**	**5.06**

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

Table 17. Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2013 and 2014, n=5,600

Site of specimen	2013		2014	
	n	(%)	n	(%)
CSF	1144	(40)	1060	(38)
Blood	1439	(50)	1439	(53)
Other	283	(10)	235	(9)
Total	**2,866**		**2,734**	

Figure 8. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2014



2009: N=4,765, age unknown for n=163; 2010: N=4,199, age unknown for n=142; 2011: N=3,804, age unknown for n=219; 2012: N=3,222, age unknown for n=253; 2013: N=2,866, age unknown for n=142; 2014: N=2,734, age unknown for n=162.

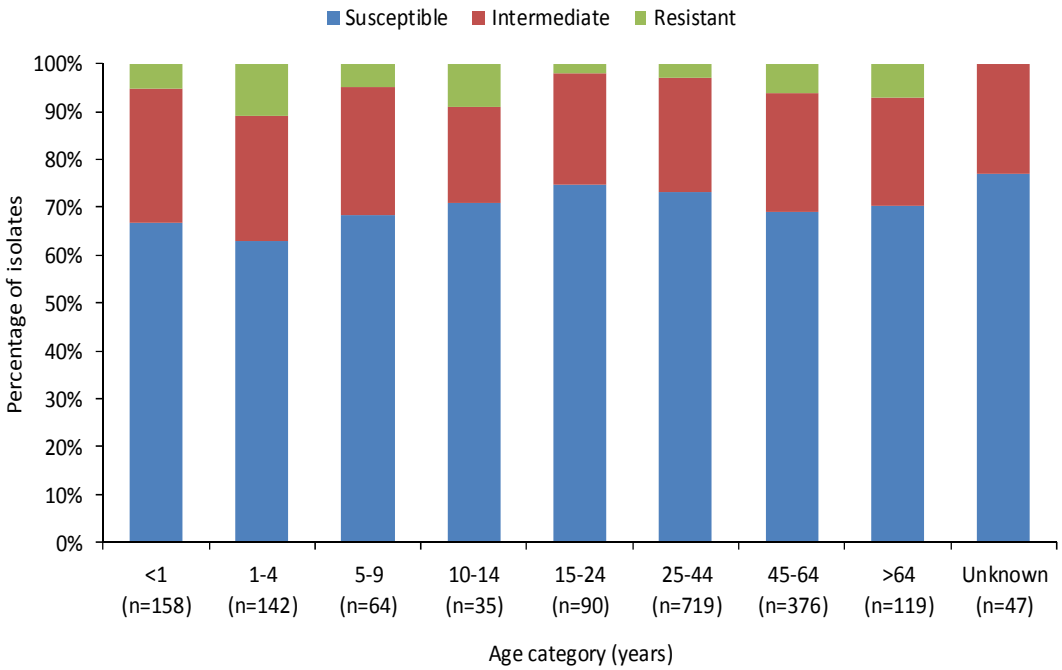
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

Table 18. Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2014, n=2,734

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	(%)	n	(%)	n	(%)
Eastern Cape	109	77	(64)	40	(33)	3	(3)
Free State	57	94	(72)	35	(27)	2	(2)
Gauteng	327	445	(70)	151	(24)	36	(6)
KwaZulu-Natal	240	178	(69)	70	(27)	11	(4)
Limpopo	15	23	(88)	3	(12)	0	(0)
Mpumalanga	61	53	(73)	18	(25)	2	(3)
Northern Cape	13	24	(83)	5	(17)	0	(0)
North West	63	39	(81)	8	(17)	1	(2)
Western Cape	98	307	(71)	99	(23)	27	(6)
South Africa	**983**	**1,240**	**(71)**	**429**	**(25)**	**82**	**(4)**

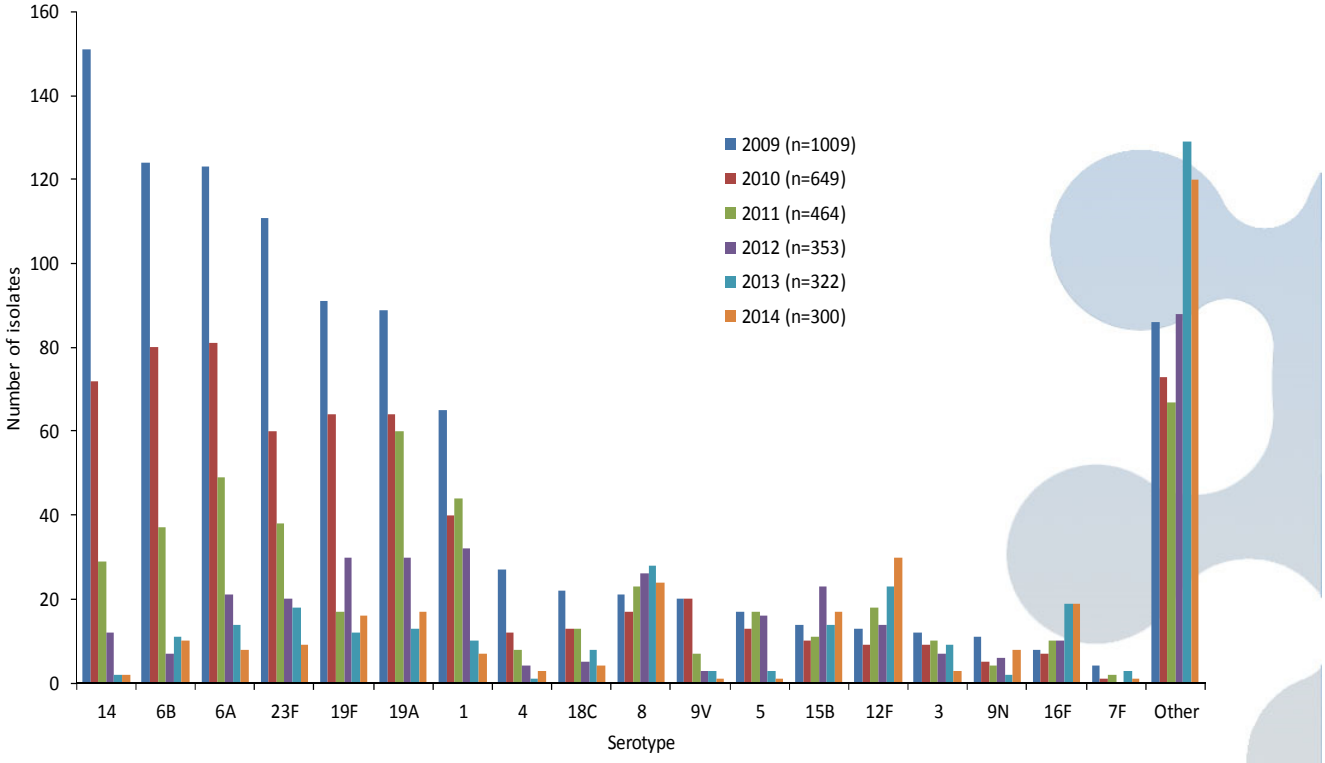
*2013 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Figure 9. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2014, n=2,734 (n=1,750 with viable isolates).



2013 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Figure 10. Pneumococcal serotypes, in descending order, causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2014



2009: N=1337, n=1,009 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; 2013: N=498, n=322 with viable isolates; 2014: N=464, n=300 with viable isolates.

Table 19. 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, 2014, n=464 (n=300 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	14	6	(43)	0	(0)	6	(43)	6	(43)
Free State	13	1	(8)	0	(0)	4	(31)	5	(38)
Gauteng	134	19	(14)	5	(4)	22	(16)	37	(28)
KwaZulu-Natal	51	7	(14)	3	(6)	7	(14)	14	(27)
Limpopo	4	1	(25)	0	(0)	1	(25)	1	(25)
Mpumalanga	9	1	(11)	0	(0)	2	(22)	2	(22)
Northern Cape	7	0	(0)	0	(0)	1	(14)	2	(29)
North West	3	0	(0)	0	(0)	0	(0)	0	(0)
Western Cape	65	10	(15)	0	(0)	11	(17)	15	(23)
South Africa	**300**	**45**	**(15)**	**8**	**(3)**	**54**	**(18)**	**82**	**(27)**

*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 (10).

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

South Africa introduced the 7-valent pneumococcal conjugate vaccine (PCV-7) in April 2009, and PCV-13 replaced PCV-7 in June 2011. A case-control study to assess the effectiveness of PCV against invasive pneumococcal disease (IPD) was started in March 2010. The results for the PCV-7 component of the study were published in Clinical Infectious Diseases in June 2014 (11).

Case enrollment for the PCV-13 component of the study ended in December 2014; while control enrollment continued until the end of March 2015. A total of 719 cases, eligible to receive PCV through the EPI programme, were enrolled in the IPD case control study; 410 in the pre-PCV13 era and 309 in the PCV13 period. The case-control sets for the PCV13 study, with known HIV-status, consisted of 236 HIV-uninfected cases with 1093 controls and 73 HIV-infected cases with 260 controls. Overall, HIV-uninfected cases had a higher average number of controls per case (4.6 controls) than HIV-infected cases (3.6 controls). The numbers of HIV-infected cases enrolled into the PCV-13 component of the study were lower than projected despite the addition of new case enrolment sites to try and address this issue. This was likely due to the success of the Prevention-of-Mother-to-Child-Transmission (PMTCT) programme and increased access to antiretroviral treatment for children. Complete results from the PCV13 study should be available in the second half of 2015.

Staphylococcus aureus

Results

There were 774 cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA from January through December 2014 from Gauteng and Western Cape Province. Of these, the majority of cases were detected from sentinel sites in Johannesburg and Pretoria, Gauteng (54.65%), and Cape Town, Western Cape (45.35%) (Table 20). The numbers of cases were almost equally distributed throughout the whole year, though there was a decline during the summer season, which picked up in the autumn and winter months (Figure 11). Resistance to oxacillin (MRSA) was determined in 189 (31%) isolates (Table 21). We analysed the trend in oxacillin resistance in Gauteng Province which showed a mild increase in 2014: 94 cases (32%) compared to 63 cases in 2013, (29%) (Figure 12). On *mec*A-confirmed *S. aureus* isolates, SCCmec typing was performed and showed predominance of type III in Gauteng Province (31%) (Figure 13). From a total of 602 viable *S. aureus* isolates, 174 (29%) were non-susceptible to clindamycin (Table 21); in addition, 112 (19%) isolates expressed positive D-zone test. Four (1%) non-susceptible vancomycin isolates were noted in 2014. A total of 580 (96%) isolates were susceptible to mupirocin and 599 (99%) to daptomycin (Table 21).

Discussion

Prior hospital admission data were available for 30% (234/774) of patients. Molecular tests indicating community vs. hospital acquired MRSA were performed on 150 MRSA isolates; SCCmec type III was the most predominant amongst the two provinces. Thirty-two percent of *S. aureus* isolates submitted to the AMRL were confirmed as MRSA; a slight increase compared to 2013 (29%). Positive HIV status (13%) was not recorded as the predominant condition for MRSA blood stream infections. Clindamycin-resistant *S. aureus* isolates occurred at high rates (29%); additionally, 19% of isolates presented with clindamycin D-zone test positivity. Five vancomycin non-susceptible isolates that were identified have not yet been confirmed with the reference method. We noted three isolates (1%) were non-susceptible to daptomycin.

Table 20. Number of *Staphylococcus aureus* cases reported to GERMS-SA sentinel sites by province, South Africa, 2014, n=774 (including audit cases)

Province	n	%
Gauteng	423	55
Western Cape	351	45
Total	**774**	**100**

Figure 11. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia cases reported to GERMS-SA sentinel sites by month, 2014, and trend line analysis, n=774

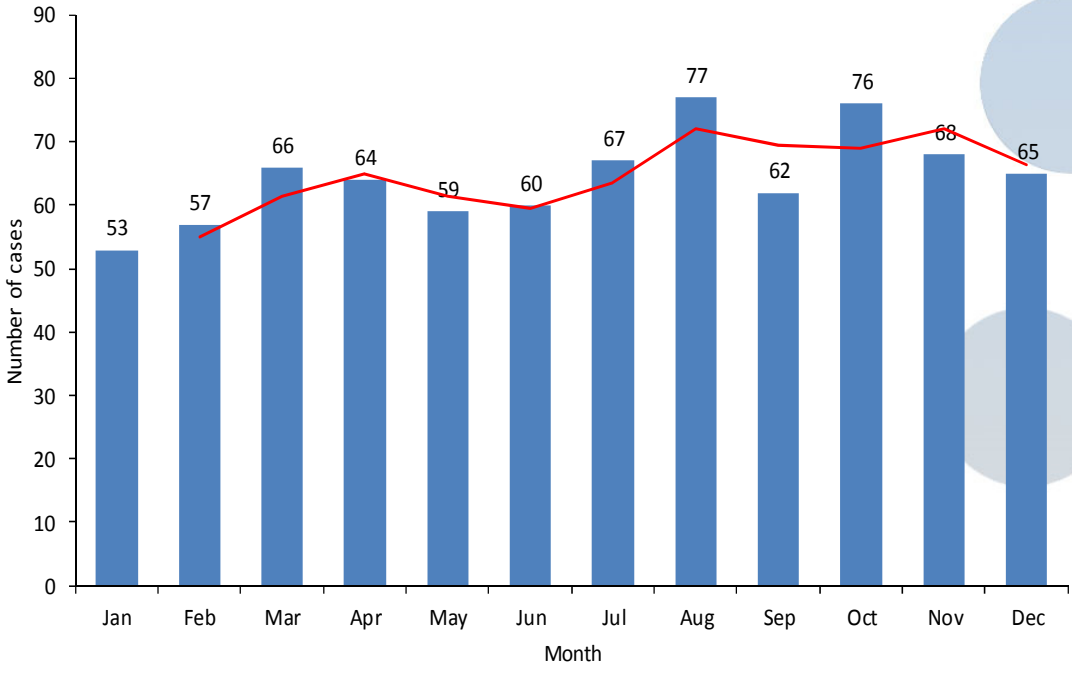


Table 21. Number of viable, laboratory-confirmed *Staphylococcus aureus* reported by GERMS-SA sentinel sites, with reported susceptibility testing to clindamycin (n=602), vancomycin (n=602), mupirocin (n=602), daptomycin (n=602) and oxacillin (n=602), 2014

Province	Antimicrobial agents									
	Oxacillin		Clindamycin		Vancomycin		Mupirocin		Daptomycin	
	S*	NS**	S	NS	S	NS	S	NS	S	NS
Gauteng	201 (68)	94 (32)	204 (69)	91 (31)	293 (98)	2 (1)	288 (98)	7 (2)	294 (99)	1 (1)
Western Cape	212 (69)	95 (31)	224 (73)	83 (27)	305 (99)	2 (1)	292 (95)	15 (5)	305 (99)	2 (1)
Total	**413 (69)**	**189 (31)**	**428 (71)**	**174 (29)**	**598 (99)**	**4 (1)**	**580 (96)**	**22 (4)**	**599 (99)**	**3 (1)**

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

Figure 12. Percentages of susceptibility patterns of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported by GERMS-SA sentinel sites in Gauteng, and trend analysis, 2013 and 2014

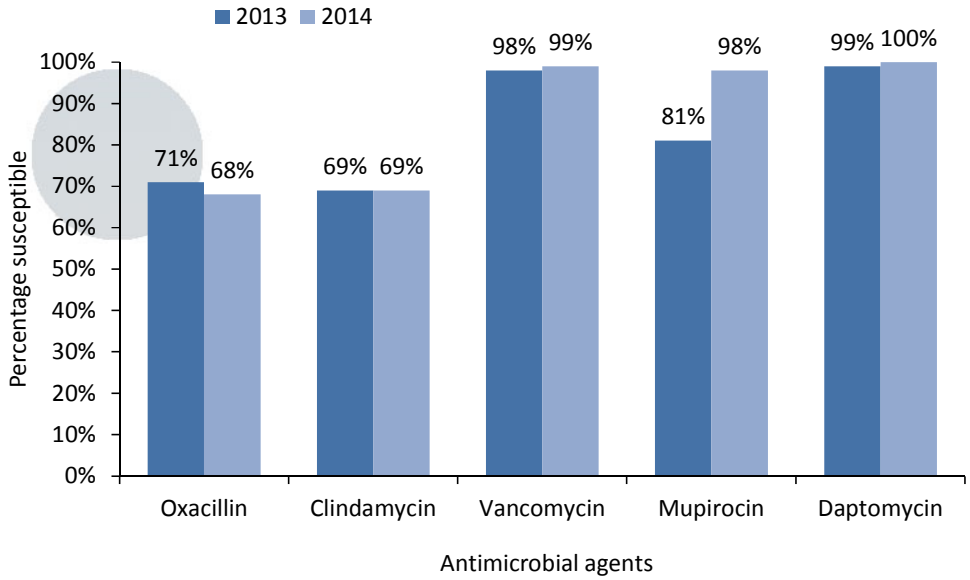
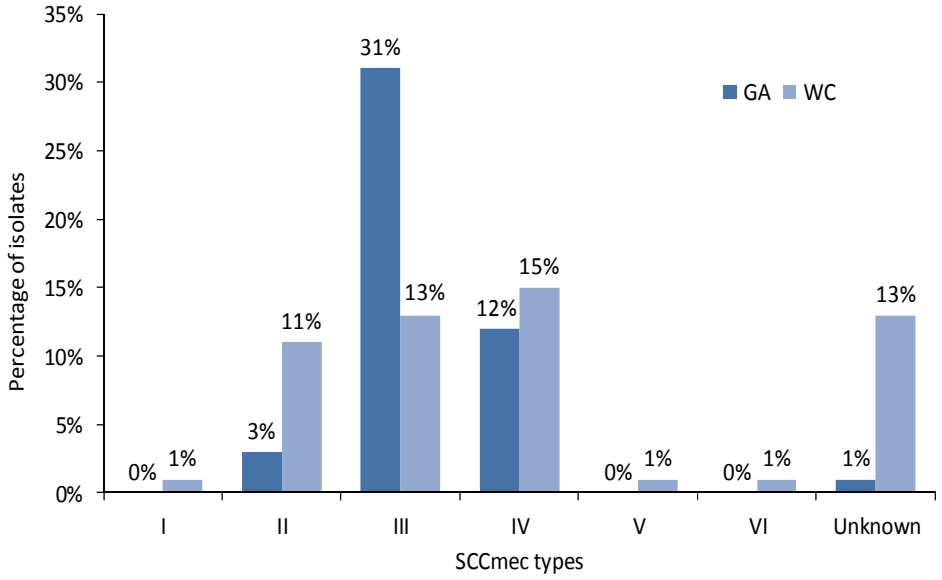


Figure 13. Distribution of SCCmec types of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported by GERMS-SA sentinel sites per province, 2014



Pseudomonas aeruginosa

Results

There were 405 cases of *Pseudomonas aeruginosa* bacteraemia reported to GERMS-SA from January through December 2014 (Table 22), including Gauteng, Free State, KwaZulu-Natal and Western Cape Provinces. The highest number of the cases with *P. aueruginosa* was noted during the winter months (Figure 14). Resistance to *Pseudomonas* antimicrobial agents was recorded for piperacillin/tazobactam (25%), imipenem (29%), colistin (2.5%), ciprofloxacin (27%) and ceftazidime (21%) (Table 23).

Discussion

On average, 25% of *P. aeruginosa* isolates were resistant to recommended agents, the most important of which was the high resistance to imipenem, ciprofloxacin, piperacillin/ tazobactam and ceftazidime. Resistance to colistin was low.

Table 22. Number of *Pseudomonas aeruginosa* cases reported to GERMS-SA sentinel sites by province, South Africa, 2014, n=405 (including audit cases)

Province	n	%
Free State	27	7
Gauteng	187	46
KwaZulu-Natal	25	6
Western Cape	166	41
Total	**405**	**100**

Figure 14. Number of cases of laboratory-confirmed *Pseudomonas aeruginosa* bacteraemia cases reported to GERMS-SA sentinel sites by month, 2014, and trend line analysis, n=405

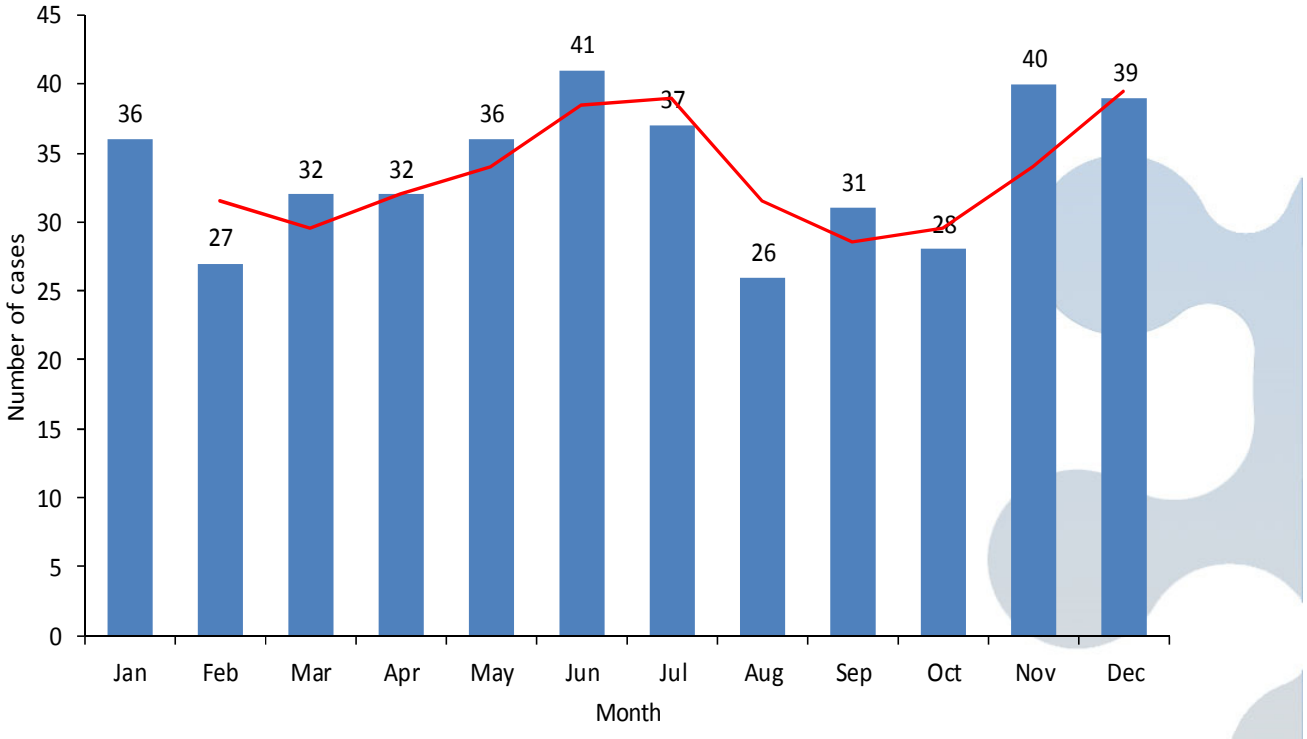


Table 23. Number of viable, laboratory-confirmed *Pseudomonas aeruginosa* reported by GERMS-SA sentinel sites, with reported susceptibility testing to piperacillin/tazobactam (n=303), imipenem (n=303), colistin (n=240), ciprofloxacin (303) and Ceftazidime (n=303), 2014

Province	Antimicrobial agents									
	Piperacillin/ Tazobactam		Imipenem		Colistin		Ciprofloxacin		Ceftazidime	
	S*	NS**	S	NS	S	NS	S	NS	S	NS
Free State	6 (55)	5 (45)	7 (64)	4 (36)	7 (100)	0 (0)	6 (54)	5 (46)	7 (64)	4 (36)
Gauteng	112 (79)	29 (21)	102 (72)	39 (28)	111 (98)	2 (2)	109 (77)	32 (23)	110 (78)	31(22)
KwaZulu-Natal	19 (67)	6(33)	19 (76)	6 (24)	22 (100)	0 (0)	18 (72)	7 (28)	21 (84)	4 (16)
Western Cape	91 (72)	35 (28)	88 (70)	38 (30)	94 (96)	4 (4)	87 (69)	39 (31)	101 (80)	25 (20)
Total	**228 (75)**	**75 (25)**	**216 (71)**	**87 (29)**	**234 (98)**	**6 (3)**	**220 (73)**	**83 (27)**	**239 (79)**	**64 (21)**

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

Rifampicin-resistant Tuberculosis

Results

During 2014, a total of 807 cases of rifampicin-resistant tuberculosis were eligible for inclusion into the surveillance, of which 571 (71%) were successfully enrolled and Case Report Forms (CRF) completed. Of those with completed CRFs, 97% knew their HIV status and of these, 84% were HIV positive. The HIV positive group included 49% females and 51% males with a median age of 35 ± 11years (range 7-74 years). The HIV negative group had a median age of 39 ± 19 years, comprising 65% males and 35% females. Limited risk factor analysis was done for three provinces (Table 24). The results of the initial genotypic analysis of 82 culture positive specimens collected in North West province and 37 culture positive specimens collected in KwaZulu -Natal are shown in Figure 15.

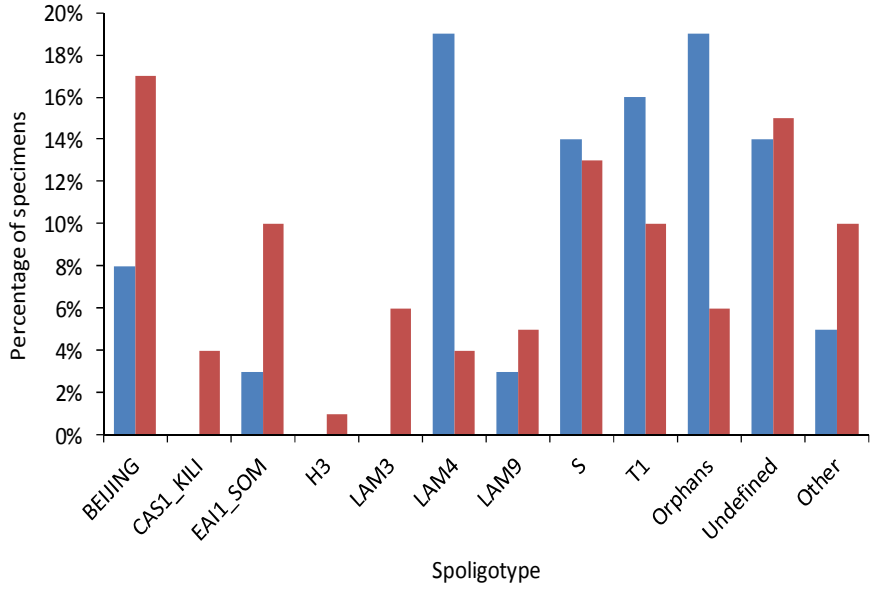
Discussion

The high percentage of HIV positive patients among rifampicin-resistant cases supports the recommendations to start ART in this group of patients irrespective of CD4+ count. As previously noted, only approximately 40% of participants reported previous TB treatment; implying that transmission is playing a role in drug resistant TB in these provinces. Furthermore, a high percentage (28-36%) also reported household contacts with TB. The majority of patients (>85%) had not stayed outside of South Africa in the last six months. Less than 5% gave a history of working in a clinic or laboratory, but this may reflect different referral patterns. As expected, a higher number of cases from participants enrolled in North West province worked in the mines. While numbers are still small, preliminary genotyping results show differences between North West and KwaZulu-Natal provinces, with Beijing family predominating in North West while LAM 4 were more common in KwaZulu-Natal. Collection of an additional sputum specimen for DST and genotyping will add valuable information to the programme.

Table 24. Selected risk factors for rifampicin-resistant TB for Gauteng, North West and Mpumalanga provinces, 2014

Risk Factor	Mpumalanga N=133	Gauteng N=130	North West N=127
HIV status			
Yes	166	114	97
No	14	11	29
Unknown	3	5	1
HIV + % of known status	89%	91%	77%
Previous TB treatment			
Yes	55 (42%)	57 (44.5%)	52 (41%)
No	75 (57%)	55 (43%)	72 (57%)
Unknown	2 (1%)	16 (12.5%)	2 (2%)
Household contact with TB			
Yes	47 (36%)	36 (28%)	43 (34%)
No	80 (62%)	58 (46%)	75 (60%)
Unknown	3 (2%)	33 (26%)	7 (6%)
Stayed in SA in last 6 months			
Yes	122 (92%)	110 (85%)	124 (98%)
No	7 (5%)	0	2 (2%)
Unknown	4 (3%)	20 (15%)	1 (1%)
Previous imprisonment in last 10 years			
Yes	11 (8%)	0	15 (12%)
No	117 (89%)	108 (84%)	104 (82%)
Unknown	4 (3%)	20 (16%)	8 (6%)
Worked in mines/quarry			
Yes	2 (1.5%)	0	26 (21%)
No	127 (95.5%)	109 (84.5%)	92 (72%)
Unknown	4 (3%)	20 (15.5%)	9 (7%)
Worked in hospital/clinic/lab			
Yes	6 (5%)	0	3 (2%)
No	122 (92%)	109 (85%)	115 (91%)
Unknown	4 (3%)	20 (15%)	9 (7%)

Figure 15. Tuberculosis spoligotypes of culture positive specimens by province for North West province (N=82) and KwaZulu-Natal (N=37), 2014



Discussion

The GERMS-SA laboratory-based surveillance continues to be useful in reporting trends in pathogen-specific data. Although the Laboratory Information System changing from DISA*Lab to TrakCare Lab with the challenges of mapping data onto the Corporate Data Warehouse continues, and NHLS laboratories have been under austerity measures, the methodology of GERMS-SA remains the same. For enhanced surveillance our number of surveillance officers has increased to >30 nurses doing record review and interviews. Happily, the percentage of case report forms done on interview is over 80% and we have also been doing audits of our SO data quality to continually improve that aspect.

Patients with opportunistic infections of *Cryptococcus* and rifampicin-resistant TB show 99% and 84% respectively to be HIV-infected. This supports the recommendation that ART should be started in this group of TB patients. Transmission of drug-resistant TB is high and one third of patients report a household contact with TB. Preliminary genotyping results show differences between North West and KwaZulu-Natal provinces, with Beijing family predominating in North West while LAM 4 were more common in KwaZulu-Natal. Overall incidence of cryptococcosis decreased in 2014 but increased in EC, LP, NW and WC which may reflect an improvement in provider-initiated cryptococcal screening. More than 50% of patients with cryptococcosis were on concurrent ART or previous treatment but the in-hospital case fatality ratio remained high at 31%.

The 2014 data continues to monitor the trends in vaccine-preventable diseases of IPD and Hib post-EPI vaccine introduction of PCV13 and the Hib booster. It shows a continued decrease in IPD as well as a stabilisation of Hib disease in children <1 year. Non-vaccine-type disease for *Haemophilus influenzae* and IPD needs to be monitored.

Epidemic-prone diseases: The incidence of meningococcal disease remains low. The prevalence of non-susceptibility to penicillin has increased compared to 2013. 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.

Hospital infections: The majority of candidaemia was in young children and neonates with a high case fatality rate. The epidemiology of candidaemia differed by province and knowledge of local hospital epidemiology should guide empiric treatment. Conventional amphotericin B remains the empiric drug of choice for candidaemia in the public-sector because of the high prevalence of azole-resistant C. *parapsilosis* isolates. *Staphylococcus aureus* surveillance is ongoing in Gauteng and the Western Cape. One third of isolates received were confirmed as MRSA. One third of *S. aureus* isolates were resistant to clindamycin. Only selected sites do *Pseudomonas aeruginosa* surveillance and one quarter of *P. aeruginosa* isolates was resistant to recommended agents.

We encourage you to read the publications from the GERMS-SA group which are based on your laboratory and patient data. Without the isolate submissions from your laboratories, details of serotypes, serogroups, susceptibility testing and molecular testing is impossible. We urge all laboratories to continue to send isolates for GERMS-SA surveillance. Thank you once again for your ongoing participation. Together, with other stakeholders and collaborators, we are able to inform policy and make changes to the health of all South Africans.

Publications

Peer-reviewed publications:

1. **Cohen C, von Mollendorf C, de Gouveia L, Naidoo N, Meiring S, Quan V, Nokeri V, Fortuin-de Smidt M, Malope-Kgokong B, Moore D, Reubenson G, Moshe M, Madhi SA, Eley B, Hallbauer U, Kularatne R, Conklin L, O'Brien KL, Zell ER, Klugman K, Whitney CG, von Gottberg A.** Effectiveness of 7-Valent Pneumococcal Conjugate Vaccine Against Invasive Pneumococcal Disease in HIV-Infected and -Uninfected Children in South Africa: A Matched Case-Control Study. *Clin Infect Dis* 2014, 59:808 -18.
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