GERMS

SOUTH AFRICA

Annual Report 2016

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

Division of the National Health Laboratory Service

The GERMS-SA Annual Report 2016 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 Surveillance Officers' Meeting 1-3 November 2016.

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Introduction

For 2016 the idea was to have all NICD Centres reporting their Centre work (including GERMS-SA) in the NICD Surveillance Bulletin. For GERMS-SA it makes better sense to have a consolidated report, hence the delay for the 2016 report.

Challenges with staffing at National Health Laboratory Service (NHLS) diagnostic laboratories continues to impact the numbers of isolates sent to National Institute for Communicable Diseases (NICD) reference laboratories. The annual percentage of viable isolates received continues to fall. This means that we have fewer isolates for antimicrobial susceptibility testing and serotyping/serogrouping but the surveillance continues to be useful in reporting trends in pathogen-specific data.

For the first time this report will include all GERMS projects using our platform. These include STI, HIV drug resistance, rotavirus/diarrhoeal aetiological surveillance and zoonosis surveillance. These projects differ from the laboratory-based surveillance in that some are syndromic surveillance and specimens are taken from patients.

We encourage all laboratory staff to continue participating in the NICD surveillance programmes. We thank you for your ongoing service to the health of all South Africans.

Surveillance Officers' Meeting 1-3 November 2016

Methods

In 2016, diseases under surveillance included:

1. Opportunistic infections associated with HIV, e.g. cryptococcosis, 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), *Streptococcus pneumoniae* and rotavirus
4. Hospital infections, e.g. *Staphylococcus aureus*, Carbapenem resistant Enterobacteriaceae and *Candida* species

The methods utilised by the GERMS-SA surveillance programme have been previously described in detail (1).
In brief, approximately 222 South African clinical microbiology laboratories participated in the surveillance programme in 2016. The population under surveillance in 2016 was estimated at 55.9 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) (29 hospitals in 9 provinces), NHLS laboratories in KZN, and laboratories in the private, mining, and military sectors were required to directly report case patients to NICD. In 2015 and 2016, no laboratories were required to directly report case patients or send isolates to NICD. For these

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cases of cryptococcosis, 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. 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, 2015 and 2016, 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. Candidaemia surveillance changed to 18 new sites in the remaining seven provinces in 2014, with an additional 2 in 2015. All laboratories were asked to send candidaemia isolates in 2016. Carbapenam Resistant Enterobacteriaceae (CRE) surveillance started in July 2015 in four provinces and these organisms were requested to be sent: *Klebsiella* spp., *Enterobacter* spp., *Citrobacter* spp., *Serratia* spp., *E. coli*., *Providentia* spp., *Proteus* spp., *Salmonella* spp., *Morganella* spp. and *Acinetobacter baumannii* .

Enhanced surveillance was not conducted on any of the enteric pathogens in 2015 but restarted for *Salmonella* Typhi only in 2016. At ESS, surveillance officers completed clinical case report forms electronically using the Mobenzi application on mobile phones for patients with nine laboratory-confirmed diseases (cryptococcosis [for January through March only], candidaemia, invasive pneumococcal disease, invasive meningococcal disease, invasive *Haemophilus influenzae* disease, invasive *Salmonella* Typhi disease, bacteraemic *S. aureus* disease [at 5 sites], rifampicin-resistant tuberculosis [at 8 sites] and rifampicin-susceptible TB [3 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 for NHLS laboratories in all provinces using the NHLS CDW. 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; Incidence was calculated using mid-year population estimates for 2015 and 2016 from Statistics South Africa (Table 1) (2). Incidence in the HIV-infected and AIDS populations was calculated for 2015 and 2016, using the Thembisa model (Table 1) (3). All reported incidence is expressed as cases per 100,000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test and p values <0.05 were considered significant throughout. Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M140159 (previously M08-11-17) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/NHLS.

Table 1. Population denominators used to calculate incidence rates, South Africa, 2015 and 2016

Province	General population*		HIV-infected population**	
	2015	**2016**	2015	**2016**
Eastern Cape	6,916,185	**7,061,717**	772,491	**785,770**
Free State	2,817,941	**2,861,618**	367,495	**368,479**
Gauteng	13,200,349	**13,498,151**	1,811,921	**1,855,046**
KwaZulu-Natal	10,919,077	**11,079,717**	1,913,446	**1,934,126**
Limpopo	5,726,792	**5,803,941**	453,830	**461,355**
Mpumalanga	4,283,888	**4,328,256**	660,569	**675,414**
Northern Cape	1,185,628	**1,191,651**	74,860	**75,332**
North West	3,706,962	**3,790,614**	464,491	**467,974**
Western Cape	6,200,098	**6,293,200**	417,098	**430,491**
South Africa	54,956,920	**55,908,865**	6,980,332	**7,104,796**

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

Operational Report

Site visits

In 2016, NICD staff members did 37 site visits to feedback, train and trouble-shoot at laboratories, hospitals and clinics linked to GERMS surveillance (Table 2). Feedback is important to maintain or improve surveillance participation.

Coordination of meetings

Surveillance officer meeting, 1-3 November 2016: the aims of this meeting were to understand GERMS-SA's different surveillance programmes and to discuss the challenges of quality data collection in GERMS-SA projects.

GERMS-SA NICD Surveillance Review: due to financial constraints it was decided to hold this meeting every second year.

Surveillance audit

A total of 18,836 surveillance cases were detected by GERMS-SA in 2016. Excluding the cases of cryptococcosis (n=6,964), 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=1,291), for which no audits are performed, 17% (1,836/10,581) 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

The proportion of completed CRFs in 2016 was similar to that in 2015; the addition of pathogens that cause more severe illness (candidaemia and *S. aureus*) make it more difficult to follow-up patients (Tables 4 and 5): 93% (4,931/5,328) of cases had a case report form (CRF) completed (target = 90%). The interview rate was poorer than previous years partly due to the hospital setting challenges and sicker patients with candidaemia and *S. aureus* [3,736 (76%) 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 2016, these reports were provided quarterly.

Enhanced surveillance site quality monitoring

In 2016, surveillance officers (SOs) were audited in terms of quality of work. CRFs from a fixed time period were randomly selected for each surveillance officer so that there were 7 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. Data training was done regularly to overcome these errors.

Table 2: GERMS-SA surveillance laboratory, hospital and clinic site visits and DOH meetings between January and December 2016

Date	Province	Laboratory (NHLS or private)	Clinics	Hospital	Database training
12-January	Gauteng	Dr. George Mukhari NHLS	-	-	SOs
22 January	Mpumalanga	-	Hluvukani CHC	-	-
27 January	Gauteng	Chris Hani Baragwanath NHLS	-	-	SOs
27-28 January	Eastern Cape	Port Elizabeth Provincial NHLS	Zwide CHC	-	-
29 January	Kwa-Zulu Natal	Northdale NHLS	Surrounding Clinics	-	-
04 February	Kwa-Zulu Natal	Northdale NHLS	Surrounding Clinic	-	-
09 February	Gauteng	Chris Hani Baragwanath NHLS	-	CHBAH	-

Date	Province	Laboratory (NHLS or private)	Clinics	Hospital	Database training
16-17 February	Kwa-Zulu Natal	Edendale NHLS	Eastboom CHC	Edendale Laboratory	
22-24 February	Mpumalanga	-	Hluvukani CHC	-	-
25 February	Eastern cape	Dora Nginza NHLS	-	Dora Nginza Hospital	-
25-26 February	Northern Cape	Kimberley NHLS	-	-	SOs
7-10 March	Kwa-Zulu Natal	-	Eastboom CHC	-	-
08 March	North West	-	Jouberton CHC	Tshepong Hospital	-
10 March	Northern Cape	-	-	Kimberley Hospital	-
16-17 March	Eastern Cape	PE Provincial NHLS	-	Dora Nginza Hospital	-
5-7 April	Mpumalanga	-	Hluvukani CHC	-	-
14 April	Gauteng	Chris Hani Baragwanath NHLS	Chiawelo CHC	Chris Hani Baragwanath Hospital	-
19-21 April	Eastern Cape	Port Elizabeth NHLS	Zwide CHC, New Brighton CHC	Jose Pearson Hospital, Empilisweni Hospital	-
3-5 May	Mpumalanga	Rob Ferreira NHLS	Kabokweni CHC, Hluvukani CHC	Barberton Hospital, Bongani Hospital	-
13 May	Gauteng	Steve Biko/ DGM NHLS	-	Steve Biko/ DGM Hospital	SOs-
09 June	Gauteng	CHBAH NHLS			
19 June	Northern Cape	Kimberley NHLS	-	Kimberley Hospital	
20-21 June	Northern Cape	Tshepong NHLS	-	Klerksdorp Hospital	
22-23 June	Free State	Universitas NHLS	-	Universitas Hospital, Pelonomi Hospital	-
23-24 June	Kwa-Zulu Natal	Addington / KEH NHLS	-	-	SOs
27 June	Kwa-Zulu Natal	Northdale NHLS	Eastboom CHC	-	-
12-13 July	Mpumalanga	-	Hluvukani CHC	-	-
20 July	Gauteng	Charlotte Maxeke NHLS	-	-	-
05 August	Western Cape	George NHLS	-	-	-
10-12 August	Limpopo	Mankweng/ Seshego NHLS	-	Mankweng/ Seshego Hospitals	-
29 August	Kwa-Zulu Natal	RK Khan NHLS	Phoenix Clinic	RK Khan Hospital	-
07 September	North West	Tshepong NHLS	Jouberton Clinic	Tshepong Hospital	-
24 September	North West	Tshepong NHLS	Jouberton Clinic	Tshepong Hospital	-
26 September	Free State	Universitas NHLS	-	Universitas Hospital	-
05 October	Gauteng	Helen Joseph NHLS	-	Helen Joseph Hospital	-
07 November	Free State	Universitas NHLS	-	Universitas Hospital	-
24 November	North West	Tshepong/ Klerksdorp NHLS	Jouberton Clinic	Tshepong/ Klerksdorp Hospitals	-

SOs = surveillance officers

Table 3. Cases detected by surveillance audit by province, 2016

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**	6,964/6,964 (100%)	854	257	1905	1994	446	568	50	469	421	6,964
	Candidaemia	157/1,760 (9%)	11	0	102	19	2	1	1	3	18	157
	Salmonella Typhi	0/95 (0%)	0	0	0	0	0	0	0	0	0	0
	Non-typhoidal salmonellosis†	120/638 (19%)	12	1	48	34	7	2	5	1	10	120
	Shigellosis	11/26 (42%)	0	0	2	0	0	0	0	9	0	11
	Meningococcal disease	10/131 (8%)	0	0	3	4	0	3	0	0	0	10
	Haemophilus influenzae disease	86/285 (30%)	15	2	38	13	1	1	1	3	12	86
	Pneumococcal disease	605/2,432 (25%)	77	28	221	167	19	24	3	37	29	605
	Staphylococcus aureus disease (BC only)	114/955 (12%)	N/A	N/A	82	N/A	N/A	N/A	N/A	N/A	32	114
	Carbapenem resistant Enterobacteriaceae (BC only)	76/440 (17%)	N/A	2	45	16	N/A	N/A	N/A	N/A	13	76
Non-invasive	*Salmonella* Typhi	0/28 (0%)	0	0	0	0	0	0	0	0	0	0
	Non-typhoidal salmonellosis†	373/2,504 (15%)	47	7	86	150	16	13	11	17	26	373
	Shigellosis	284/1,287 (22%)	17	6	76	86	12	4	2	37	44	284
	Cholera††	0/0 (N/A)	0	0	0	0	0	0	0	0	0	0
	Rifampicin-resistant tuberculosis***	0/1,291 (N/A)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total		**1,836/10,581 (17%)**	**179**	**46**	**703**	**489**	**57**	**48**	**23**	**107**	**184**	**1,836**

*Percentage of cases detected by audit = number of cases detected on audit (n1)/total number of cases detected by GERMS-SA (n2) x 100; **All 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; †Excluding Salmonella enterica serotype Paratyphi; ††Only Vibrio cholerae O1; 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, 2016.

Enhanced surveillance site	Case patients, n	Completed case report forms*, n (%)**	Case report forms completed by interview, n (%)***
Addington [1]	44	40 (91)	31 (78)
Charlotte Maxeke Johannesburg Academic [2]	542	530 (98)	391 (74)
Chris Hani Baragwanath/ Zola-Jabulani District [3]	863	789 (91)	460 (58)
Dr George Mukhari [1]	159	149 (94)	131 (88)
Edendale/ Greys'/ Northdale [1,3]	305	301 (99)	277 (92)
Groote Schuur/ Red Cross [2]	319	283 (89)	246 (87)
Helen Joseph/ Rahima Moosa Mother & Child [2]	431	416 (97)	314 (75)
Kimberley [1,3]	156	155 (99)	106 (68)
King Edward VIII/ Inkosi Albert Luthuli Central Hospital [1]	132	116 (88)	72 (82)
Klerksdorp/ Tshepong [1,3]	224	219 (98)	172 (79)
Mankweng/ Polokwane/ Seshego [1,3]	127	113 (89)	78 (69)
Netcare Milpark[1]	87	81 (93)	39 (53)
Pelonomi/ Universitas [1,3]	247	234 (95)	188 (80)
Port Elizabeth/ Dora Nginza/ Livingstone [1,3]	684	546 (80)	448 (82)
RK Khan [1]	73	66 (90)	61 (92)
Rob Ferreira/ Themba [1,3]	205	203 (99)	175 (86)
Steve Biko Pretoria Academic/ Tshwane District [2]	353	345 (98)	289 (84)
Tygerberg [2]	377	345 (92)	258 (75)
Total†	**5,328**	**4,931 (93)**	**3,736 (76)**

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 2016; *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 rifampicin-resistant TB surveillance.

Surveillance reports

Enhanced surveillance site project

In 2016, of 18,836 surveillance case patients detected by GERMS-SA, 5,328 (28%) were diagnosed at enhanced surveillance sites (Table 4). Of case patients with recorded HIV status, 79% (1,015/1,290) 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 (97%) were HIV-infected; HIV infection amongst patients with invasive pneumococcal disease, for which HIV is a known risk factor, was 71%.

Table 5. Numbers and percentage* of patients diagnosed with laboratory-confirmed invasive disease at GERMS-SA enhanced surveillance sites, with confirmed HIV-1 infection **, South Africa, 2016

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†	595	592	(99)	497	(84)	482	(97)
Neisseria meningitidis	43	43	(100)	34	(79)	5	(15)
Streptococcus pneumoniae	928	874	(94)	692	(79)	493	(71)
Haemophilus influenzae	119	119	(100)	77	(64)	35	(45)
Total	**1,685**	**1,628**	**(97)**	**1,290**	**(79)**	**1,015**	**(79)**

*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 2016 at all GERMS enhanced surveillance sites.

Cryptococcus species

Results

During 2016, 6,964 case patients with laboratory-confirmed incident cryptococcal disease (including meningitis, fungaemia and culture-positive disease at other sites but excluding cryptococcal antigenaemia) were reported (Table 6). A total of 2,260 cases of cryptococcal antigenaemia (with no concurrent recorded cryptococcal meningitis or fungaemia) were detected at NHLS microbiology laboratories. After excluding the latter cases, the incidence remained stable across all provinces between 2015 and 2016 (overlapping 95% confidence intervals). In 2016, the highest incidence was recorded among males aged 40-44 years; the peak incidence among females was in the group aged 30-34 years (Figure 1). Two hundred and seven children younger than 15 years had laboratory-confirmed cryptococcosis; 105 (51%) were younger than 5 years of age.

Most patients (93%) with incident disease were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species) and 4% with fungaemia (Table 7). In 2016, 194 patients were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. Clinical case data were collected from patients at ESS for the first quarter of 2015 and 2016. For these 2 years, completed case report forms were available for 7% (901/13,540) of patients. Of 833 patients with known HIV status, 807 (97%) were HIV-infected. Of 786 HIV-infected patients with known antiretroviral treatment (ART) status, 448 (57%) were on ART at the time of diagnosis of cryptococcal disease or had previously received ART. Among 645 HIV-infected patients who had a CD4+ T-lymphocyte (CD4) count test result recorded close to the time of diagnosis, 614 (95%) had a CD4 count <200 cells/µl; the median CD4 count was 37 cells/µl (interquartile range, 15 – 89). The in-hospital case-fatality ratio for patients at ESS with a first episode of cryptococcal disease was 37% (328/549), with no significant difference between 2015 and 2016 (p=0.83).

Discussion

Following inclusion of a cryptococcal antigen (CrAg) screen-and-treat intervention in the 2015 national consolidated HIV guidelines, cases of antigenaemia have been diagnosed through both provider-initiated and reflex laboratory screening. Cases of antigenaemia diagnosed by provider-initiated screening in a microbiology/ clinical pathology lab are detected by GERMS-SA surveillance. In October 2016, national reflex CrAg screening was implemented at all NHLS CD4 laboratories; however, these cases are tracked through a separate surveillance system (NICD CrAg dashboard). For this reason, cases of cryptococcal antigenaemia diagnosed by provider-initiated screening were excluded from this report. The epidemiology of cryptococcal meningitis or culture-confirmed cryptococcal disease has remained largely unchanged between 2015 and 2016.

Table 6: Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA by province, South Africa, 2015-2016, n=13,540

Province	2015		2016	
	n*	Incidence (95% CI)†	n*	Incidence (95% CI)†
Eastern Cape	777	101 (94-108)	854	109 (101-116)
Free State	266	72 (64-81)	257	70 (61-78)
Gauteng	1794	99 (94-104)	1905	103 (98-107)
KwaZulu-Natal	1809	95 (90-99)	1994	103 (99-108)
Limpopo	396	87 (79-96)	446	97 (88-106)
Mpumalanga	536	81 (74-88)	568	84 (77-91)
Northern Cape	52	69 (51-88)	50	66 (48-85)
North West	483	104 (95-113)	469	100 (91-109)
Western Cape	463	111 (101-121)	421	98 (88-107)
South Africa	**6,576**	**94 (92-96)**	**6,964**	**98 (96-100)**

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

Figure 1. Number of cases and incidence of cryptococcal meningitis or culture-positive cryptococcal disease detected by GERMS-SA, by gender and age group, South Africa, 2016, n=6,236.

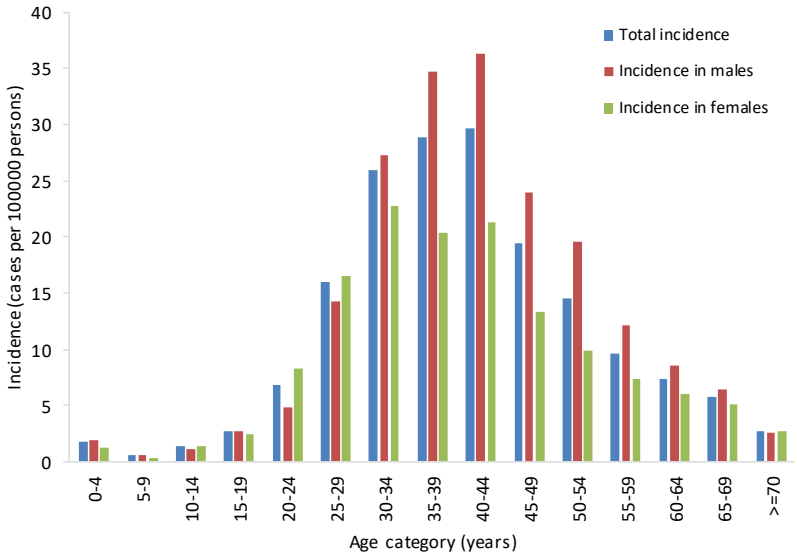


Table 7: Number and percentage of cases of cryptococcal meningitis or culture-positive cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2015-2016, n=13,540

Site of specimen	2015		2016	
	n*	%	n*	%
Cerebro-spinal fluid	6148	93	6498	93
Blood	248	4	272	4
Other	180	3	194	3
Total	6,576		6,964	

*These case numbers exclude patients who tested positive for cryptococcal antigenaemia.

National and enhanced sentinel surveillance for candidaemia

Results

In 2016, 1,760 cases of candidaemia were detected, 1,127 (64%) of which were diagnosed in Gauteng province. Of all cases, 473 (27%) were reported from the private sector. The age of cases was significantly lower in the public- vs. the private sector (median, 3 years [IQR, 7 months to 46 years] vs. median, 56 years [IQR, 37 to 68 years]; p<0.001). Where sex was known, 54% (939/1732) of patients were male. Clinical case report forms were completed for 979 (55%) patients, including 75 cases at 3 private facilities in Gauteng province. The overall crude case-fatality ratio was high (408/964; 42%) and varied significantly by species (*C. albicans*, 49%; *C. parapsilosis*, 35%; *C. glabrata*, 48%; *C. tropicalis*, 33% and *C. auris*, 48%; p=0.02) and age category (infants <1 year, 36%; children 1-17 years, 27%; adults 18-44 years, 50%; adults 45-64 years, 54% and adults ≥65 years, 69%; p<0.001). HIV infection is not an independent risk factor for candidaemia; however, 23% (127/542) of patients were HIV-infected, all but 3 in the public-sector. A significantly higher proportion of patients was admitted to an intensive care unit in the private- vs. public-sector (68/74 [92%] vs. 633/875 [72%]; p<0.001). At least one viable isolate was identified to species level for 1,408 (80%) cases of candidaemia. Overall, *C. parapsilosis* was the most common species followed by *C. albicans;* the species distribution differed significantly by sector (p<0.001) (Table 8; Figure 2).Of particular concern, *C. auris* accounted for 9% (126/1,372) of cases and was the second commonest species in the private-sector and the fourth commonest in the public-sector. All *Candida* isolates had an amphotericin B minimum inhibitory concentration (MIC) ≤ 2 µg/ml (apart from 4 *C. krusei*, 2 *C. parapsilosis* and 1 *C. albicans* isolate).

Susceptibility results for five commonest *Candida* species, including *C. auris*, and three antifungal agents are summarised in Table 9; anidulafungin MICs are presented as a proxy for susceptibility to the echinocandin class.

Discussion

The epidemiology of culture-confirmed candidaemia has changed since a national survey was last conducted in 2009 and 2010, with the emergence of *C. auris* as a major pathogen. There continue to be differences in epidemiology between the public- and private-sector, with some variation by province. In 2016, candidaemia was diagnosed far more commonly among young children, predominantly neonates, in the public sector and among older adults in the private sector. Overall more than a third of patients with candidaemia, many of whom were critically ill, died in hospital. A large majority of bloodstream *C. parapsilosis* isolates were resistant to fluconazole. *C. auris*, an emerging pathogen, is also fluconazole resistant, with very few exceptions. Azole-resistant strains of *C. parapsilosis* and *C. auris* now dominate in the private sector, particularly in Gauteng province. Fluconazole prophylaxis should thus be discouraged in this setting, even in high-incidence hospital units. Knowledge of local hospital or hospital unit epidemiology should guide empiric treatment choices. Conventional amphotericin B remains the empiric antifungal agent of choice for candidaemia in the public-sector because of the high prevalence of azole-resistant *C. parapsilosis* isolates. Caspofungin, micafungin or anidulafungin are also good choices for empiric treatment in all settings where these agents are available.

Table 8: *Candida* species distribution for cases of candidaemia with a viable bloodstream isolate by health sector and province, 2016, n=1,366

Species	n (%):									
	EC	FS	GA	KZ	LP	MP	NC	NW	WC	Overall
Public-sector facilities										
Candida albicans	21 (46)	34 (37)	165 (33)	49 (42)	12 (55)	7 (70)	7 (54)	5 (38)	56 (46)	356 (38)
Candida parapsilosis	8 (17)	47 (51)	188 (38)	37 (32)	1 (5)	0 (0)	4 (31)	4 (31)	24 (20)	313 (34)
Candida auris	0 (0)	0 (0)	32 (6)	0 (0)	2 (9)	0 (0)	0 (0)	0 (0)	1 (1)	35 (4)
Candida glabrata	11 (24)	7 (7)	56 (11)	15 (13)	4 (18)	2 (20)	2 (15)	3 (23)	29 (24)	129 (14)
Candida tropicalis	3 (7)	0 (0)	11 (2)	10 (9)	0 (0)	0 (0)	0 (0)	1 (8)	6 (5)	31 (3)
Other *Candida species*	3 (7)	4 (4)	42 (9)	6 (5)	3 (14)	1 (10)	0 (0)	0 (0)	7 (6)	15 (2)
Sub-total	46	92	494	117	22	10	13	13	123	930
Private-sector facilities										
Candida albicans	0 (0)	0 (0)	48 (13)	2 (22)	1 (100)	3 (19)	0 (0)	2 (33)	4 (13)	60 (14)
Candida parapsilosis	0 (0)	0 (0)	192 (52)	5 (56)	0 (0)	9 (56)	0 (0)	1 (17)	20 (61)	227 (52)
Candida auris	0 (0)	1 (100)	83 (22)	2 (22)	0 (0)	4 (25)	0 (0)	0 (0)	1 (3)	91 (21)
Candida glabrata	2 (100)	0 (0)	35 (10)	0 (0)	0 (0)	0 (0)	0 (0)	3 (50)	4 (12)	44 (10)
Candida tropicalis	0 (0)	0 (0)	3 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (1)
Other *Candida species*	0 (0)	0 (0)	7 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (12)	11 (3)
Sub-total	2	1	368	9	1	16	0	6	33	436
Total	**48**	**93**	**862**	**126**	**23**	**26**	**13**	**19**	**156**	**1,366**

EC: Eastern Cape, FS: Free State, GA: Gauteng, KZ: KwaZulu-Natal, LP: Limpopo, MP: Mpumalanga, NC: Northern Cape, NW: North West , WC: Western Cape

Figure 2. Species distribution for cases of candidaemia with a viable bloodstream isolate by health sector, South Africa, 2016, n=1,366

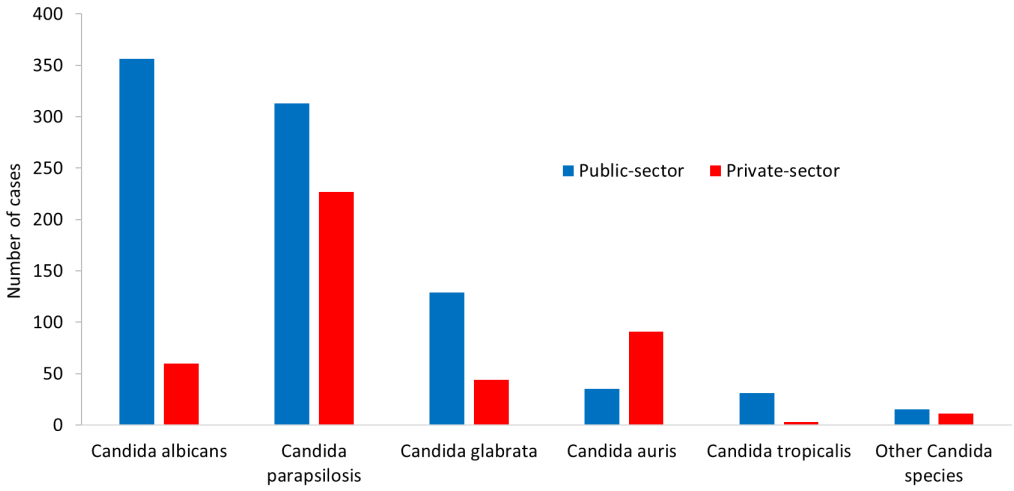


Table 9: Number and percentage of *Candida* bloodstream isolates (five commonest species only) susceptible to fluconazole, voriconazole and anidulafungin by sector, 2016, n=1,288

Antifungal agent	Number (%) of isolates susceptible to:				
	C. albicans	***C. parapsilosis***	***C. glabrata***	***C. tropicalis***	***C. auris***
Public-sector facilities	n=354	n=316	n=130	n=31	n=33
Fluconazole	345 (97)	101 (32)	0 (0)	30 (97)	No breakpoints or ECV[b]
Voriconazole	349 (99)	170 (54)	No breakpoints	27 (87)	No breakpoints or ECV[c]
Anidulafungin	354 (100)	316 (100)	128 (98)	30 (97)	No breakpoints or ECV[d]
Private-sector facilities	n=60	n=227	n=44	n=3	n=90
Fluconazole	60 (100)	31 (14)	0 (0)	3 (100)	No breakpoints or ECV[b]
Voriconazole	60 (100)	68 (30)	No breakpoints	3 (100)	No breakpoints or ECV[c]
Anidulafungin	60 (100)	227 (100)	43 (98)	3 (100)	No breakpoints or ECV[d]

[*]Based on CLSI M27-S4 species-specific breakpoints for susceptibility; [b]98% of isolates with an MIC ≥8 mg/L; [c]44% of isolates with an MIC ≥1 mg/L; [d]3 isolates with an MIC ≥1 mg/L; ECV: epidemiologic cut-off value

Enhanced sentinel surveillance for *S. aureus* bacteraemia in Gauteng and the Western Cape

Results

In 2016, 955 cases of *S. aureus* bacteraemia were detected (Table 10). The majority of cases were detected from sentinel sites in Johannesburg and Pretoria (560; 59%). 586 (61%) patients were male. Adults aged ≥18 years accounted for 548 (57%) cases. *S. aureus* isolates were available for 78% (746/955) of case patients. The proportion of MRSA cases decreased from 32% (242/748) in 2015 to 25% (188/746) in 2016 (p=0.002) (Figure 3). SCC*mec* typing was performed for 187 *mec*A-positive *S. aureus* isolates in 2016. There was a predominance of type III SCC*mec* in Gauteng (73/187; 39%) and type IV in the Western Cape (38/187; 20%) (Figure 4). Among 746 viable *S. aureus* isolates, 200 (73%) were non-susceptible to clindamycin. All isolates were susceptible to vancomycin and daptomycin in 2016. A total of 731 (95%) isolates were susceptible to mupirocin (Figure 3). Among 955 patients, 273 (29%) died.

Discussion

There was a significant decrease in the proportion of cases of MRSA bacteraemia in 2016, compared to 2015. Overall, SCC*mec* type III predominated and was more common in Gauteng; type IV was dominant in the Western Cape. A similar proportion of isolates was resistant to clindamycin and oxacillin. As expected, no vancomycin or daptomycin non-susceptible isolates were identified. Other than a reduction in MRSA cases, there was no change in the susceptibility pattern of bloodstream *S. aureus* isolates over the reporting period.

Table 10: Number and percentages of cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by province, South Africa, 2015 (n=927) and 2016 (n=955) (including audit cases)

Province	2015		2016		Total	
	n	%	n	%	n	%
Gauteng	516	56	560	59	1076	57
Western Cape	395	44	395	41	806	43
Total	**927**	**100**	**955**	**100**	**1,882**	**100**

Figure 3. Proportion of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia with isolates susceptible to various antimicrobial agents reported to GERMS-SA in Gauteng, 2015 and 2016, n=1,494

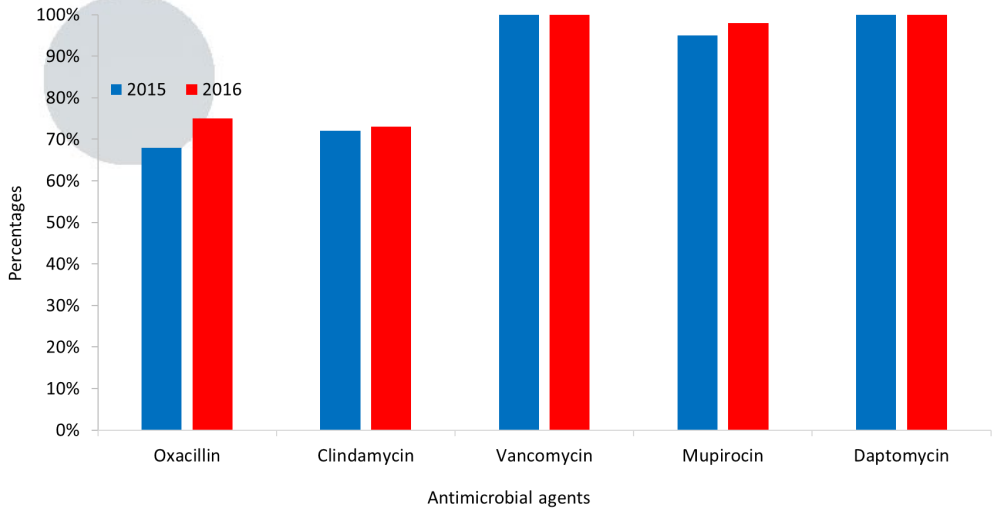
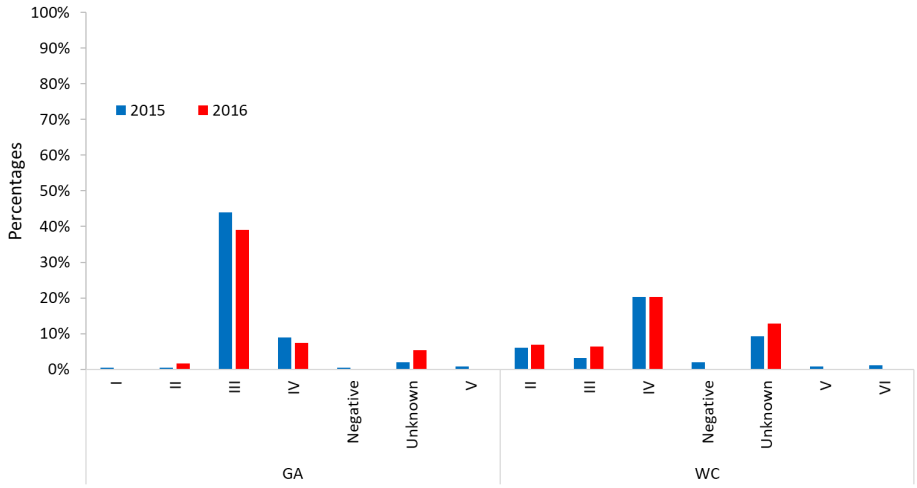


Figure 4. SCC*mec* distribution for laboratory-confirmed cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA by province, 2015 and 2016, n=433



Enhanced sentinel surveillance for CRE bacteraemia in four provinces

Results

There were 440 cases of CRE bacteraemia (as detected by a diagnostic laboratory) reported to GERMS-SA from July 2015 through to December 2016 (Table 11). Half (n=220) were male and the majority (233; 53%) were adults aged 16-55 years. The majority of cases were detected from sentinel sites in Gauteng (298; 68%) followed by KwaZulu-Natal (105; 24%) (Table 11).

CRE isolates were available for 67% (294/440) of patients and submitted to NICD for antimicrobial susceptibility testing (Table 12). *Klebsiella pneumoniae* was the commonest organism (217; 74% of cases) followed by *Enterobacter cloacae* (28; 10%), *Serratia* (19; 7%) and *Escherichia coli* (17; 6%) (Figure 5). Most cases occurred in adult medical wards (Figure 6). Among all isolates, 87% (256) were non-susceptible to ertapenem, 57% (168) non-susceptible to imipenem and 58% (171) non-susceptible to meropenem and doripenem (Figure 7). We confirmed carbapenemase genes in 81% (238/294) of isolates including NDM (109/238; 45%) and OXA-48 or variants (111/238; 47%) (Figure 8). 23 (8%) isolates were susceptible to ertapenem with an MIC ≤ 0.5 mg/L but were OXA-48 positive. Over the surveillance period, there was a shift towards CRE mediated by OXA-48 & variants (Figure 8). Among viable isolates, 76% were susceptible to tigecycline (Table 12). Of all patients with CRE bacteraemia, 158 (36%) died.

Discussion

The number of CRE bacteraemia cases detected over the surveillance period is relatively small but these highly-resistant organisms have an impact on the public-sector health system in terms of patient outcomes and healthcare costs. Most cases were detected in Gauteng and KwaZulu-Natal. We noted a shift to CPE mediated by OXA-48 & variants; these enzymes are not easily detected in the laboratory. In addition, the OXA genes are located on a very efficient transposon with the potential for point mutations.

Table 11: Number of cases of carbapenem-resistant Enterobacteriaceae (CRE) bacteraemia reported to GERMS-SA by province, July 2015 to December 2016, n=440 (including audit cases)

Province	2015		2016		Total	
	n	%	n	%	n	%
Free State	1	1	3	1	4	1
Gauteng	80	68	218	67	298	68
KwaZulu-Natal	32	27	73	23	105	24
Western Cape	4	4	29	9	33	7
Total	**117**	**100**	**323**	**100**	**440**	**100**

Figure 5. Species distribution of Enterobacteriaceae submitted for CRE bacteraemia surveillance to GERMS-SA, n=294

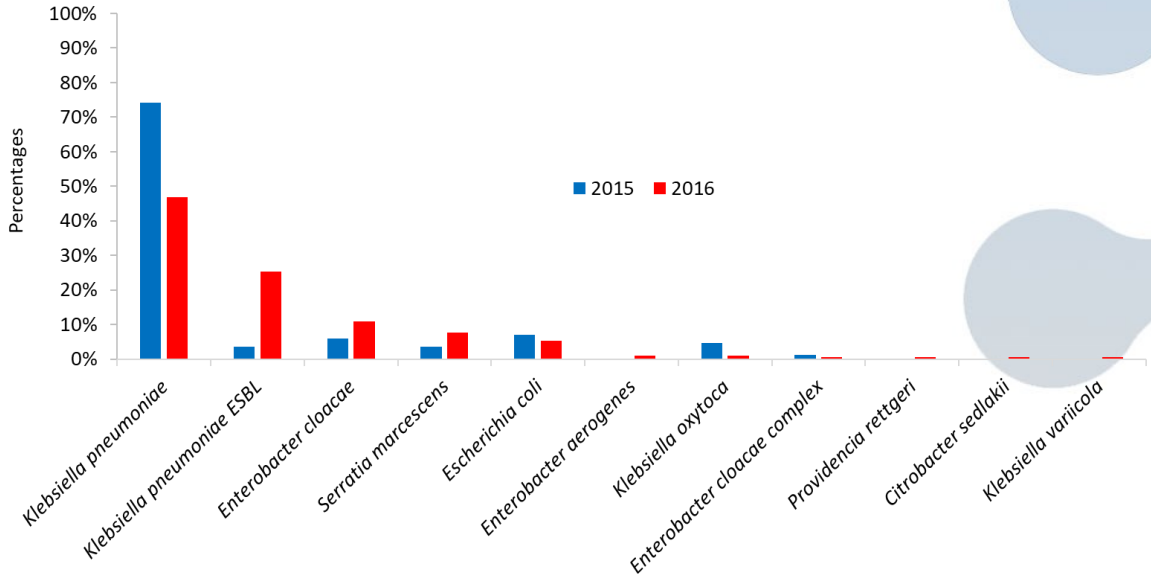


Figure 6. Distribution of cases of CRE bacteraemia by ward type, n=440

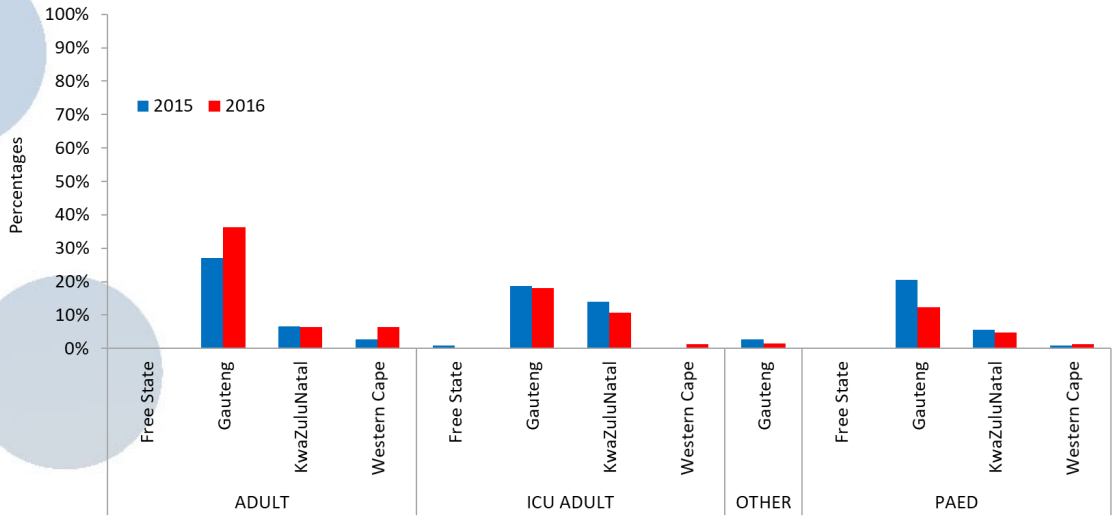


Figure 7. Antimicrobial susceptibility results for Enterobacteriaceae bloodstream isolates, n=294

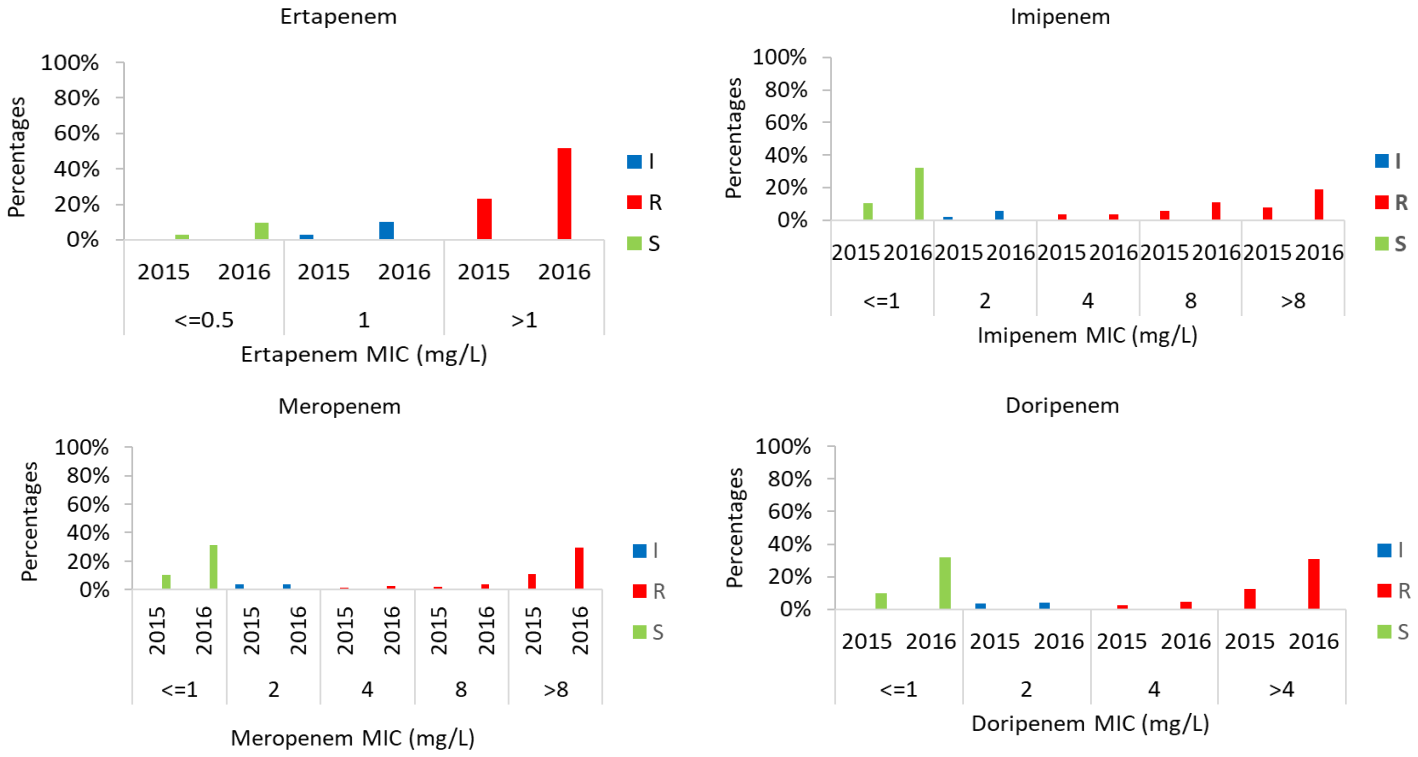


Figure 8. Carbapenemase gene detection in 238 (81%) of 294 Enterobacteriaceae bloodstream isolates

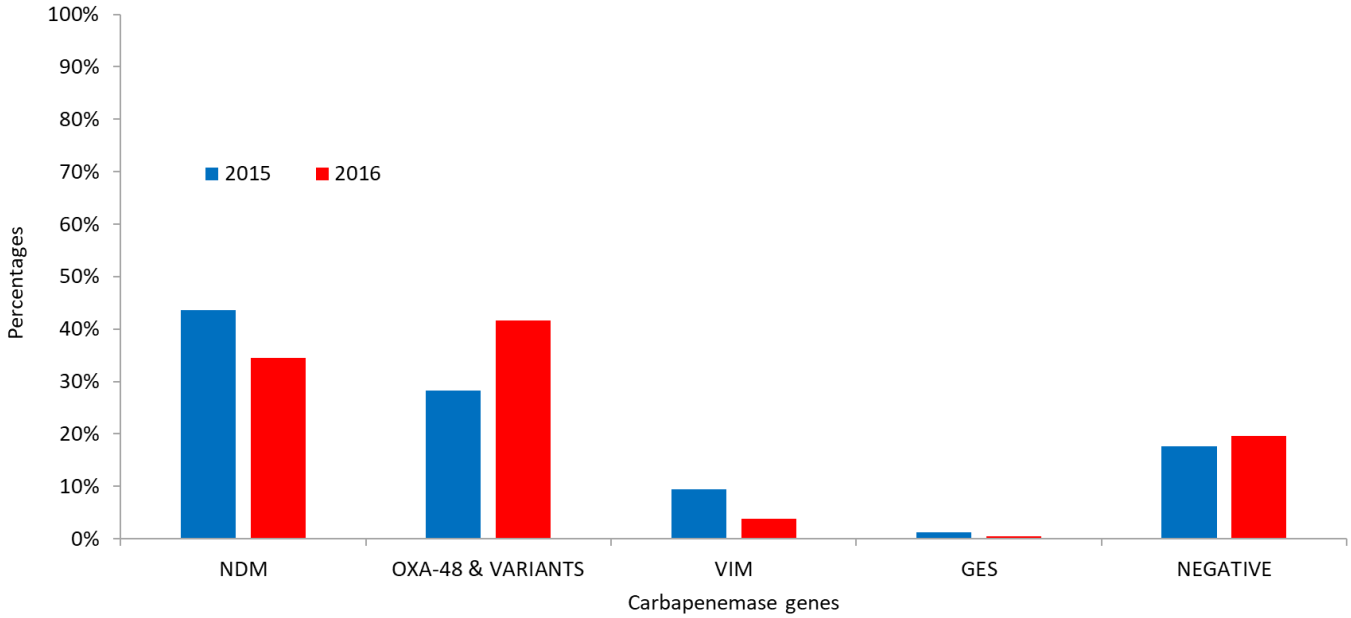


Table 12: Number and percentages of carbapenem-resistant Enterobacteriaceae (CRE) bloodstream isolates reported to GERMS-SA susceptible to antimicrobial agents per province, 2015-2016, n=294

Province	Tigecycline	Ceftazidime	Ciprofloxacin	Doripenem
	n (%)	n (%)	n (%)	n (%)
Free State	2 (1)	0 (0)	0 (0)	1 (1)
Gauteng	149 (67)	21 (95)	25 (76)	112 (90)
KwaZulu-Natal	60 (27)	1 (5)	6 (18)	4 (3)
Western Cape	12 (5)	0 (0)	2 (6)	7 (6)
Total susceptible	**223 (100)**	**22 (100)**	**33 (100)**	**124 (100)**

Neisseria meningitidis

Results

In 2016, a total of 131 cases of laboratory-confirmed meningococcal disease were identified by the surveillance system, of these 10 (8%) were detected through audit and 63 (48%) viable isolates were received (Table 13). The overall disease incidence was slightly lower than 2015 (0.23 vs 0.28 cases per 100 000 population). The highest rates were reported in the Western Cape (0.86/100 000) and Gauteng Province (0.27/100 000), with increases seen in Western Cape, North West and Mpumalanga provinces since 2015. The number of cases reported was greatest from June to October (Figure 9). Cerebrospinal fluid (CSF) was the most common specimen (92/131, 70%) yielding meningococci (Table 14). Serogroup B was the predominant serogroup in South Africa in 2016 (47/113, 42%) (Table 15). Incidence of disease was greatest amongst children <5 years-of-age and peaked in the 15-24 year age group before tapering off in the older age categories. Age and serogroup-specific incidence rates show that infants had the highest incidence of disease for the three most common serogroups (Figure 10). Of the viable isolates tested for antimicrobial susceptibility, 11% (7/63) of isolates had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and would be considered non-susceptible. This penicillin non-susceptibility is similar when compared with 2014 (13%, 11/85; p=0.7) and 2015 (9%, 7/80; p=0.7). Only 43/131 (33%) cases were reported from enhanced sites and thus had additional clinical information. Cases were admitted for a median of 11 days (interquartile range [IQR]: 7-13). Case-fatality ratio was 12% (5/43) and all deaths occurred within 2 days of admission. Similar proportions of patients with meningitis (3/33, 9%) and bacteraemia (1/7, 14%) died (p=0.7). In 2016, fewer meningococcal cases with known HIV status were HIV infected compared to 2015 (15%, 5/34 in 2016 vs 39%, 20/51 in 2015; p= 0.02). Besides HIV infection, only 1 other case reported an immunocompromising condition which could have predisposed them to this disease. In those who survived to discharge from hospital, 13% (5/38) suffered sequelae following their disease. These included 2 with new-onset seizures, 2 with neurological fallout and one with skin scarring from necrotic lesions.

Discussion

Incidence of meningococcal disease remains low in 2016 and serogroup B disease was the predominant serogroup, similar to 2015. Higher incidence of meningococcal disease in the Western Cape reflects the persistence of serogroup B disease, as well as a small increase in all other serogroups, in this province. The prevalence of penicillin non-susceptibility was 11%, however high-dose penicillin is still recommended as the drug of choice for confirmed meningococcal disease. Meningococcal disease predominantly affects healthy, young persons, with a high case fatality ratio and high rate of sequelae.

Table 13: Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2015 and 2016, n=287 (including audit cases)

Province	2015		2016	
	n	Incidence rate*	N	Incidence rate*
Eastern Cape	27	0.39	15	0.21
Free State	9	0.32	2	0.07
Gauteng	46	0.35	36	0.27
KwaZulu-Natal	23	0.21	11	0.10
Limpopo	1	0.02	1	0.02
Mpumalanga	3	0.07	5	0.12
Northern Cape	2	0.17	2	0.17
North West	4	0.11	5	0.13
Western Cape	41	0.66	54	0.86
South Africa	**156**	**0.28**	**131**	**0.23**

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

Figure 9: Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2015-2016, n=287

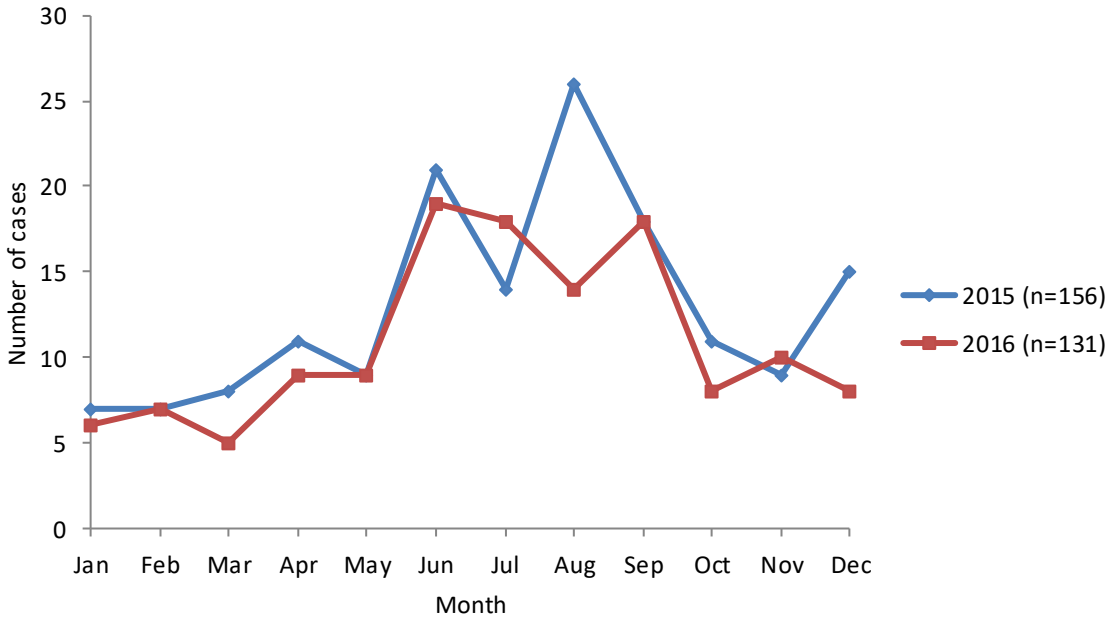


Table 14: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2015 and 2016, n=287

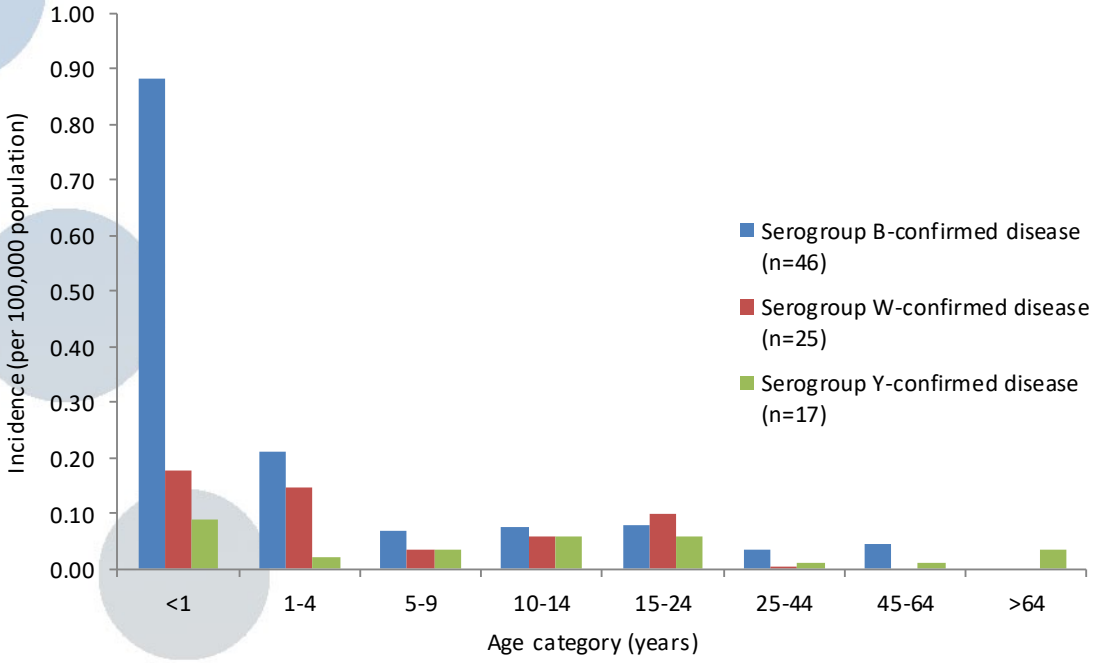
Site of specimen	2015		2016	
	n	%	n	%
Cerebrospinal fluid	112	72	92	70
Blood	44	28	38	29
Other	0	0	1	1
Total	**156**		**131**	

Table 15: Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2016, n=131*

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	NG**	Total
Eastern Cape	0	0	5	7	1	2	0	0	15
Free State	0	0	2	0	0	0	0	0	2
Gauteng	6	0	13	1	14	1	0	1	36
KwaZulu-Natal	5	0	2	1	0	3	0	0	11
Limpopo	0	0	0	0	0	1	0	0	1
Mpumalanga	3	0	2	0	0	0	0	0	5
Northern Cape	1	0	0	0	1	0	0	0	2
North West	1	0	1	1	1	1	0	0	5
Western Cape	2	0	22	5	12	10	1	2	54
South Africa	**18**	**0**	**47**	**15**	**29**	**18**	**1**	**3**	**131**

*113 (86%) with viable isolates or specimens available for serogrouping/genogrouping; ** NG: Non-groupable (including 2 that were negative for genogroups A, B, C, W, Y, X by polymerase chain reaction)

Figure 10: Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, W and Y, South Africa, 2016, n=131 (age unknown for n=7; specimens or viable isolates unavailable for serogrouping n=18).**



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

Haemophilus influenzae

Results

In 2016, 285 invasive *Haemophilus influenzae* cases were identified through the surveillance system. Eighty-six (30%) cases were detected through audit and 179 (63%) had either isolates or specimens available for serotyping. Serotype b (Hib) accounted for 25% (44/179) of cases and non-typeable (HNT) disease was found in 58% (104/179) (Table 16). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (17/44, 39%% vs. 8/104, 8%; p<0.001) (Table 17). Although less serotype a, c, d, e and f disease was isolated from CSF in 2016 compared with 2015, this decrease was not significant (14/33, 42% in 2015 vs. 7/31, 23% in 2016, p<0.11).

In 2016, a total of 26 cases of Hib were reported amongst children <5 years (Figure 11). Since 2013, HNT disease is the most common serotype of *H. influenzae* causing invasive disease amongst children <5 years with 37% (15/41) of cases in infants and 90% (9/10) of cases in neonates due to HNT (Figure 12). Rates of Hib disease amongst children <1 year-of-age have decreased overall from 2010 to 2016 (p<0.001, chi-squared test for trend), with the increase in the incidence of Hib disease in infants from 1.08 cases per 100,000 in 2015 (13 cases) to 1.66 cases per 100,000 in 2016 (16 cases) not being statistically significant (Figure 13). Twenty-nine percent (8/28) of serotype b strains and 9% (6/69) of non-typeable strains were non-susceptible to ampicillin (MIC>1mg/L). Of the 44 Hib cases, 29 occurred in children <15 years old and Hib vaccination histories were available for 13 (45%) of these children. Only 4/13 (31%) children had received 2 or more doses of Hib vaccine prior to disease onset and were assessed as possible vaccine failures.

Additional clinical information was available only from enhanced surveillance sites which accounted for 119/285 (42%) cases. Patients were admitted for a median of 9 days (IQR: 3-15 days). Case-fatality ratio was 34% (40/119) and median time to death was 1 day from admission (IQR: 0-9 days). Forty-four percent (24/54) of cases with HNT disease died compared to 25% (4/16) of cases with Hib disease (p=0.18). Conditions (other than HIV) predisposing individuals to *H. influenzae* invasive disease were reported in 51/112 (46%) patients – these included cardiac, lung, or renal disease; previous head injury; malignancy; prematurity; malnutrition; previous stroke; history of smoking or excessive alcohol use. Of the 77 patients who had known HIV status, 35 (45%) were HIV infected and 54% (19/35) of these reported receiving antiretroviral therapy.

Discussion

Incidence rates for Hib disease remain low. Infants have the highest incidence of both invasive Hib and HNT disease. The majority of cases of Hib in children <15 years of age were unvaccinated, highlighting the importance of Hib vaccination in this young population. Ampicillin non-susceptibility remains high amongst invasive Hib isolates (27% in 2015 and 29% in 2016). HIV co-infection and other co-morbidities were present amongst almost half of the cases and case-fatality from invasive *H. influenzae* disease remains high (26% in 2015 and 34% in 2016).

Table 16: Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2016, n=285*

Province	Serotype								
	Sero-type not availa-ble	a	b	c	d	e	f	Non-type-able	Total
Eastern Cape	15	1	3	0	0	1	0	3	23
Free State	5	1	4	0	0	0	0	2	12
Gauteng	47	7	9	2	1	2	3	30	101
KwaZulu-Natal	15	0	3	0	0	1	1	14	34
Limpopo	1	0	4	0	0	0	0	1	6
Mpumalanga	2	1	3	0	0	0	0	2	8
Northern Cape	1	0	2	0	0	0	0	3	6
North West	4	0	2	0	0	0	0	0	6
Western Cape	16	4	14	0	1	1	4	49	89
South Africa	**106**	**14**	**44**	**2**	**2**	**5**	**8**	**104**	**285**

*179 (63%) with specimens or viable isolates available for serotyping.

Table 17: Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2016, n=285

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	26	25	17	39	7	23	8	8
Blood	54	51	26	59	23	74	71	68
Other	26	25	1	2	1	3	25	24
Total	**106**		**44**		**31**		**104**	

Figure 11: Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2016, n=285 (age unknown for n=8; specimens or viable isolates unavailable for serotyping for n=106).

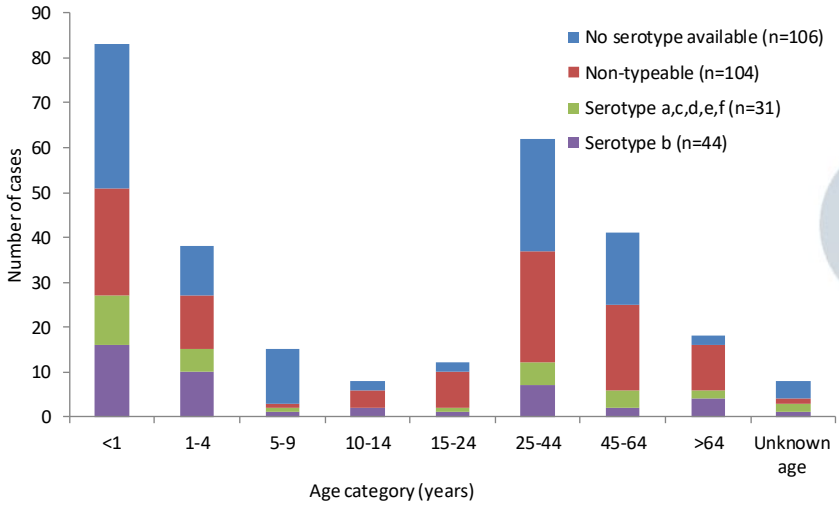


Figure 12: Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2016, n=285 (age unknown, n=8; viable isolates unavailable for serotyping, n=106; other serotypes from cases with known age, n=31).

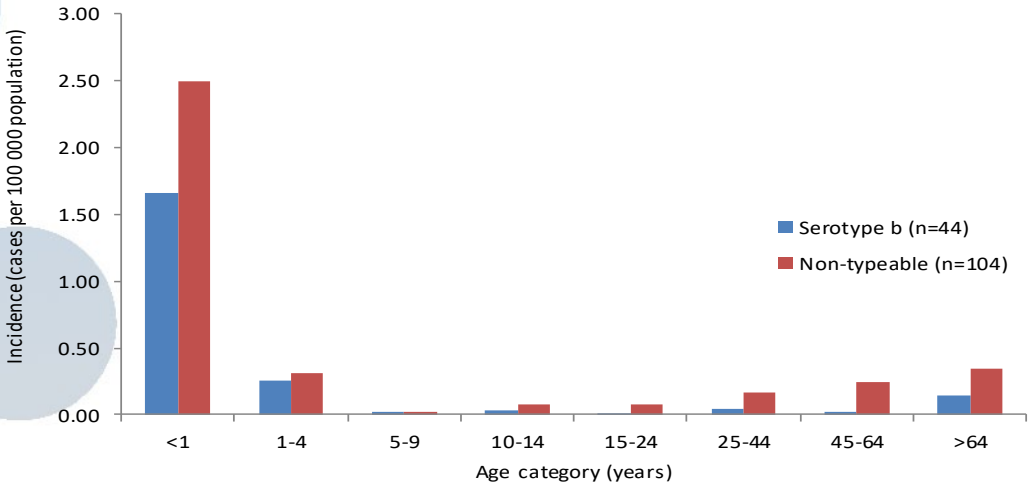
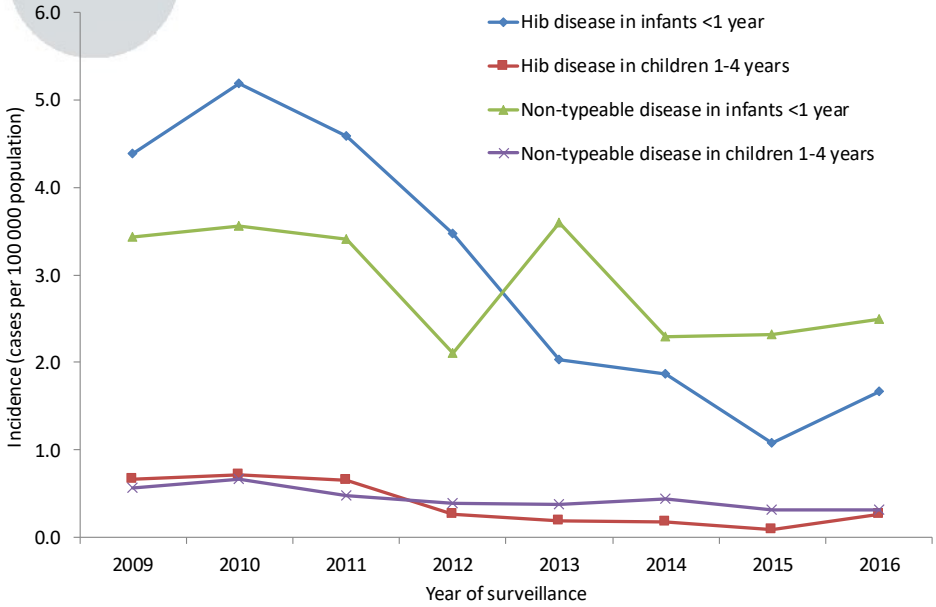


Figure 13: Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2009-2016.



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 and was replaced by PCV-13 from May/June 2011. In 2016, incidence of reported invasive pneumococcal disease (IPD) varied by province, with the Western Cape and Gauteng Provinces reporting the highest disease rates (9.6 cases per 100,000 population and 6.3 cases per 100,000 population, respectively) (Table 18). The highest incidence of disease in South Africa was in infants <1 year-of-age, although disease decreased significantly from 2009 (p<0.001 chi-squared test for trend) (Figure 14). The majority of cases (1,379/2,432, 57%) reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 19). Prevalence of penicillin non-susceptible (minimum inhibitory concentration [MIC] >0.06µg/ml) strains varied widely by province, from 5% (2/37) of cases in the Northern Cape to 38% (11/29) of cases in the North West (p=0.007) (Table 20). Penicillin non-susceptible isolates were most common amongst children 1-4 years-of-age (Figure 15). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 6% (87/1577) of all IPD cases with viable isolates – not significantly different from 2015 (4%, 69/1,701). Amongst isolates from CSF specimens, 5% (24/464) were non-susceptible to ceftriaxone.

The increase in incidence of IPD in children <5 years-of-age from 2015 (Figure 14), was not statistically significant and was due to a variety of serotypes (Figure 16). Serotype 8 was the most predominant serotype causing IPD in all age groups in 2016. PCV-13 serotypes that showed non-significant increases included serotypes 4, 14, 19F and 19A. Non-vaccine serotypes in children <5 years-of-age that showed increases were 6C and 35B. Disease due to serotype 35B increased from 16 in 2015 to 22 in 2016 (p=0.4), and 7 cases due to serotype 6C were identified in 2016, while none were seen in 2015 (p=0.01). In individuals older than 14 years, serotype 6C (n=17 in 2015 and n=33 in 2016) and serotype 8 (n=159 in 2015 and n=171 in 2016) increased the most. Twenty-three percent (54/233) of IPD amongst children <5 years of age was caused by serotypes present in PCV13 (Table 21). The number of isolates available for serotyping in this age group has decreased since 2009 (Figure 17). Only 927/2432 (38%) of cases were reported from ESS where additional clinical information was collected. Cases were admitted for a median of 7 days (IQR: 2-13 days) and deaths usually occurred a median of 2 days (IQR: 1-13 days) after admission. In older individuals (≥5 years), 27% (208/757) had underlying conditions - the most common were diabetes mellitus (40/757, 5%) and chronic lung, heart, renal or liver disorders (60/757, 8%).

In children <5 years, underlying medical conditions were less common (11/170, 6%), however 12% (21/170) had preceding prematurity. Of the 692 patients who had known HIV status, 493 (71%) were HIV infected (283/493 [57%] of whom were 25-44 years-of-age) and 197/493 (40%) were using antiretroviral therapy. In children <5 years-of-age (n=170), only 124 (73%) children older than 6 weeks had known vaccination status and of these children only 62% (n=77) had received the appropriate number of PCV vaccine doses for age at time of admission.

Discussion

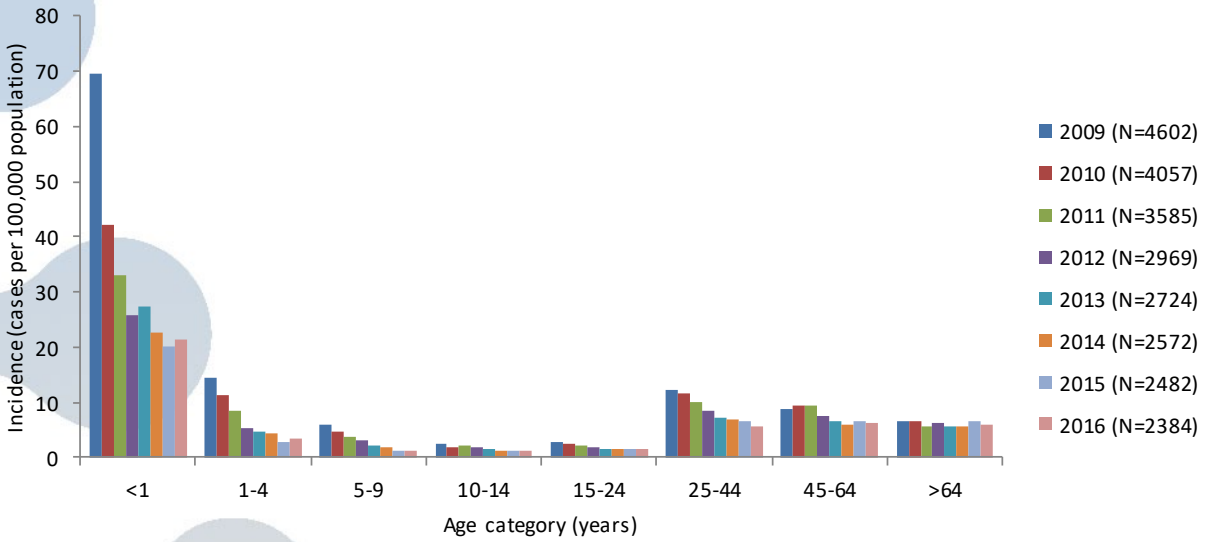
Overall IPD incidence continued to decrease in South Africa. IPD incidence is highest in children <1 year-of-age with a further peak seen in adults 25 years and older. HIV infection is still an important risk factor for IPD with 71% of IPD cases co-infected with HIV. Sixty-two percent of IPD cases in children <5 years were vaccinated appropriately with PCV and clinicians are encouraged to check PCV vaccination histories and ensure that appropriate catch-up doses are given. The percent of viable pneumococcal isolates received from children <5 years has decreased from 76% to 58% since the vaccine was introduced in 2009. 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 so that the ongoing trends in IPD serotypes can be monitored.

Table 18: Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2015 and 2016, n=5,070 (including audit cases)

Province	2015		2016	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	232	3.35	208	2.95
Free State	131	4.65	147	5.14
Gauteng	970	7.35	854	6.33
KwaZulu-Natal	354	3.24	320	2.89
Limpopo	99	1.73	84	1.45
Mpumalanga	86	2.01	102	2.36
Northern Cape	27	2.28	42	3.52
North West	108	2.91	73	1.93
Western Cape	631	10.18	602	9.57
South Africa	2,638	4.80	2,432	4.35

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

Figure 14: Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2016.



2009: N=4,762, age unknown for n=161; 2010: N=4,197, age unknown for n=141; 2011: N=3,804, age unknown for n=218; 2012: N=3,223, age unknown for n=248; 2013: N=2,866, age unknown for n=138; 2014: N=2,732, age unknown for n=165; 2015: N=2,638, age unknown for n=157; 2016: N=2,432, age unknown for n=48.
*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

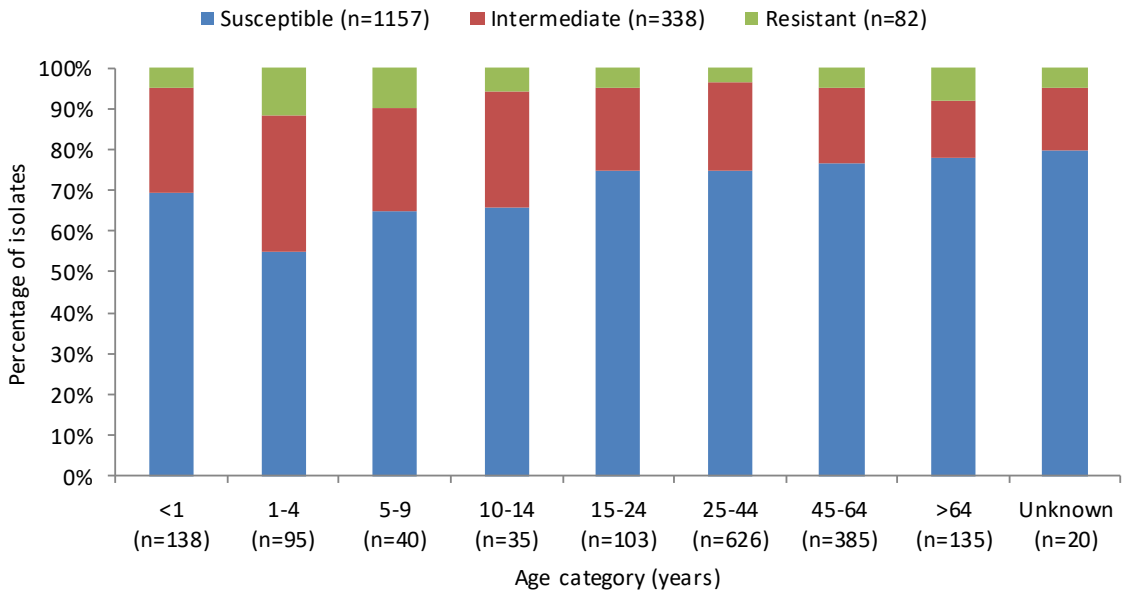
Table 19: Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2015 and 2016, n=5,070

Site of specimen	2015		2016	
	n	%	n	%
Cerebrospinal fluid	980	37	859	35
Blood	1395	53	1379	57
Other	263	10	194	8
Total	**2,638**		**2,432**	

Table 20: Number and percentage of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2016, n=2,432

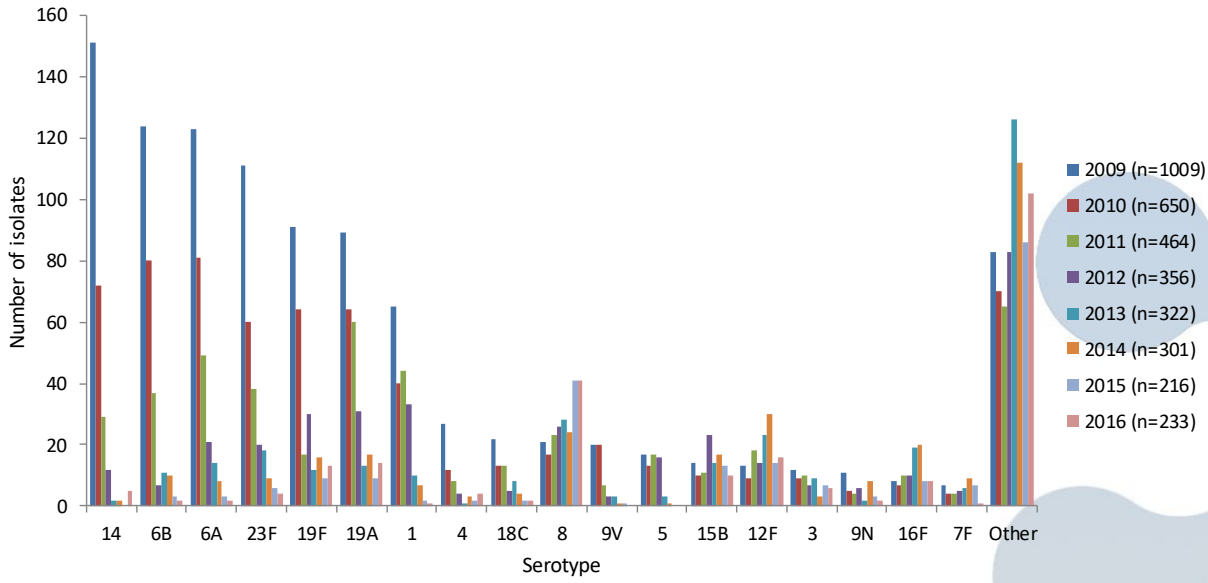
Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	93	86	74	22	19	8	7
Free State	41	78	74	26	25	2	2
Gauteng	340	356	71	109	22	34	7
KwaZulu-Natal	183	98	72	32	23	7	5
Limpopo	36	39	72	13	24	2	4
Mpumalanga	36	49	72	19	28	0	0
Northern Cape	7	35	95	2	5	0	0
North West	50	18	62	9	31	2	7
Western Cape	69	398	75	106	20	27	5
South Africa	**855**	**1,157**	**73**	**338**	**21**	**82**	**5**

Figure 15: Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2016, n=2,432 (n=1,577 with viable isolates).



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

Figure 16: Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2016.



2009: N=1,336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable.

Table 21: 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, 2016, n=401 (n=233 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	11	2	18	0	0	2	18	4	36
Free State	14	1	7	0	0	1	7	3	21
Gauteng	105	14	13	2	2	15	14	22	21
KwaZulu-Natal	17	1	6	0	0	1	6	1	6
Limpopo	9	0	0	0	0	0	0	2	22
Mpumalanga	7	1	14	0	0	1	14	1	14
Northern Cape	3	0	0	0	0	0	0	1	33
North West	4	1	25	0	0	2	50	2	50
Western Cape	63	10	16	0	0	10	16	18	29
South Africa	**233**	**30**	**13**	**2**	**1**	**32**	**14**	**54**	**23**

All serotypes included in each of the categories:

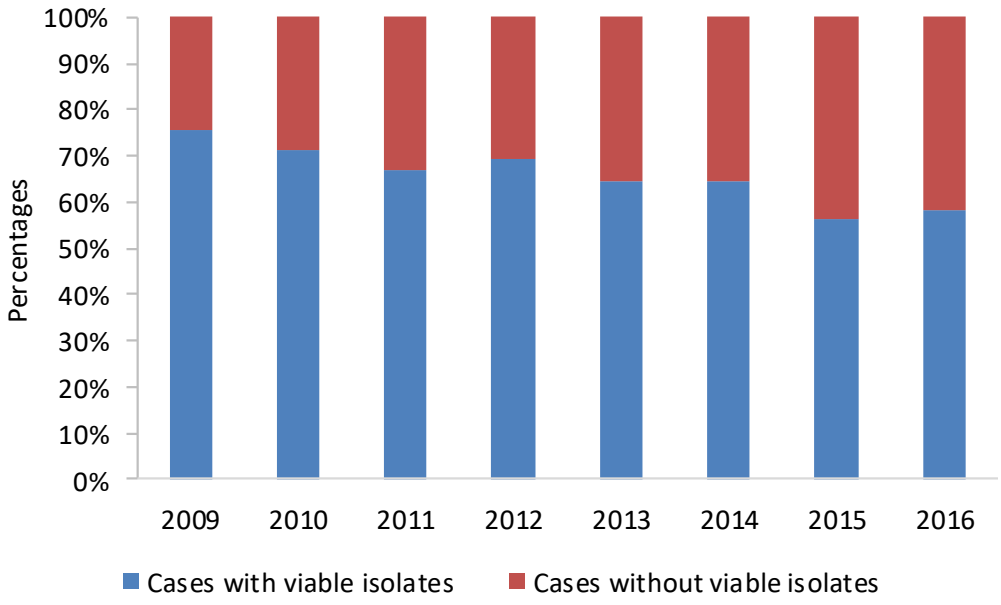
7-valent serotypes*: 4, 6B, 9V, 14, 18C, 19F, 23F

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

Figure 17: Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, in children <5 years, South Africa, 2009-2016.



2009: N=1,336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates.

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

Results

Salmonella Typhi isolates from both invasive and non-invasive sites are reported in Table 22. Cases of enteric fever were highest in January, although there was no marked seasonality (Figure 18). The number of isolates within each age group is reported in Table 23, indicating that most isolates are from patients in the 5 to 14 year and 25 to 34 year age groups, although infection is seen in both older and younger age groups, including younger children (less than five years). Ciprofloxacin resistance is problematic, although azithromycin remains susceptible (Table 24), following CLSI guidelines (4). Seven isolates of *Salmonella* Paratyphi A and six isolates of *Salmonella* Paratyphi B were identified, but no *Salmonella* Paratyphi C isolates were identified. No antimicrobial susceptibility testing was conducted on *Salmonella* Paratyphi A or *Salmonella* Paratyphi B isolates.

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, numbers were comparable with previous non-outbreak years (5). This is compounded by the challenges of alternative diagnostic methods for typhoid fever, including both clinical and serological. These data thus exclude those patients in whom alternative diagnostic methods were used, without culture confirmation. Although strict seasonality is not observed, the greatest number of cases were seen during January and February. Greater numbers reported from Gauteng and Western Cape provinces may reflect healthcare seeking behavior and specimen collection practices. The number of reported *Salmonella* Typhi isolates was regarded as an underestimate and thus incidence rates were not calculated. Susceptibility testing was undertaken against limited numbers of antimicrobials due to resource constraints. *Salmonella* Typhi should routinely be tested against azithromycin, which is an alternative treatment option, as ciprofloxacin resistance emerges (4). Continual monitoring of resistance to these two antimicrobials has become mandatory (6). Ceftriaxone may also be used as an alternative therapy. Paratyphoid fever remains rare in South Africa (7).

Table 22: Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2016, n=123 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	0	1
Free State	1	0
Gauteng	9	47
KwaZulu-Natal	2	6
Limpopo	0	5
Mpumalanga	2	7
Northern Cape	0	1
North West	1	2
Western Cape	13	26
South Africa	28	95

Figure 18. Number of non-invasive and invasive cases of *Salmonella* Typhi (n=126) and Paratyphi (n=13) reported to GERMS-SA, by month of specimen collection, South Africa, 2016 (including audit reports). Note: *Salmonella* Paratyphi C was not identified in 2016.

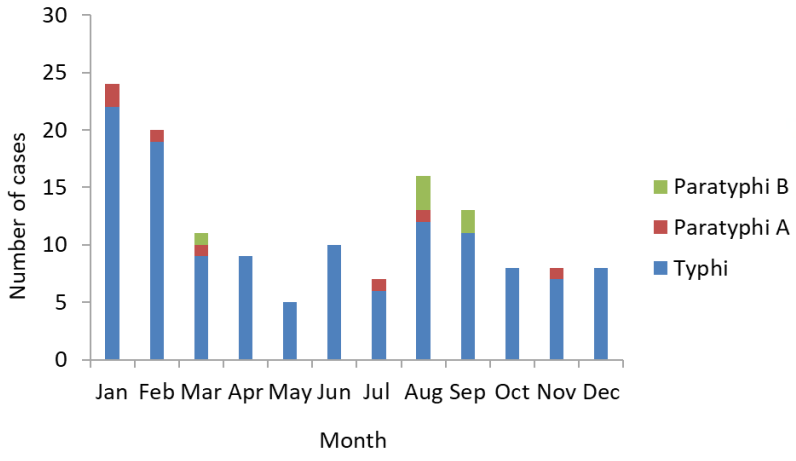


Table 23: Number of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2016, n=123 (including audit reports, missing isolates, mixed and contaminated cultures).

Age category (years)	*Salmonella* Typhi isolates
0 - 4	14
5 - 14	41
15 - 24	19
25 - 34	26
35 - 44	10
45 - 54	6
55 - 64	2
≥ 65	4
Unknown	1
Total	123

Table 24: Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2016, ciprofloxacin, n=112 and azithromycin, n=112 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)		Resistant (%)	
Ciprofloxacin	95	(85%)	17	(15%)
Azithromycin	112	(100%)	0	(0%)

Non-typhoidal *Salmonella enterica* (NTS)

Results

Invasive disease does not appear to have a seasonal prevalence; increased numbers of non-invasive disease in the earlier months of the year and a lower incidence in the winter months reflect seasonality (Figure 19). The number of cases of invasive and non-invasive disease, by province, reported to GERMS-SA, is stated in Table 25. The number of cases of invasive and non-invasive disease, by age group, is shown in Table 26. Most invasive isolates were identified from blood cultures (18%), although isolates were frequently identified from both blood culture and another site, including stool and other normally-sterile sites (Table 27). Resistance to the fluoroquinolones was noted (Table 28), and limited azithromycin resistance was noted (4). *Salmonella* Enteritidis was the commonest NTS isolated (Table 29).

Discussion

Non-typhoidal salmonellosis may be foodborne, in which case patients normally present with gastroenteritis, or may be associated with HIV-infection, in which case the organism frequently becomes invasive. Invasive *Salmonella* Typhimurium ST313, has been documented to occur in South Africa in association with HIV (8). Seasonal prevalence was noted in 2016 for non-invasive disease. Antimicrobial resistance remains a cause for concern in both invasive and non-invasive cases, including emerging resistance to azithromycin. *Salmonella* Enteritidis has replaced *Salmonella* Typhimurium as the commonest serotype, as noted in 2011, 2012, 2013 and 2015 (9, 10, 11, 12).

Figure 19. Number of non-invasive (n=2,504) and invasive (n=638) cases of non-typhoidal *Salmonella* reported to GERMS-SA, by month of specimen collection, South Africa, 2016 (including audit reports).

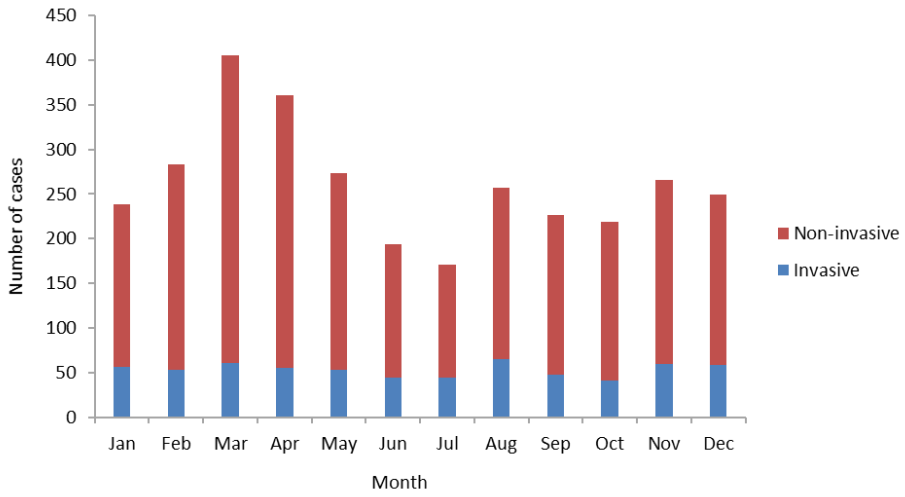


Table 25: Number of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2016, n= 3,142 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive, non-typhoidal *Salmonella isolates*	Invasive, non-typhoidal *Salmonella isolates*
Eastern Cape	217	62
Free State	61	21
Gauteng	1 139	240
KwaZulu-Natal	355	67
Limpopo	86	27
Mpumalanga	149	36
Northern Cape	1	0
North West	26	20
Western Cape	91	8
Unknown	379	157
South Africa	2,504	638

Table 26: Number* of cases of invasive and non-invasive non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2016, n=3,142 (including audit reports, missing isolates, mixed and contaminated cultures).

Age Category (years)	Cases	
	Non-invasive	Invasive
0 - 4	855	113
5 - 14	164	39
15 - 24	273	120
25 - 34	288	124
35 - 44	227	100
45 - 54	244	21
55 - 64	174	39
≥ 65	210	46
Unknown	69	36
Total	2,504	638

*Incidence rates 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.

Table 27: Number of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2016, n=3 142 (including audit reports, missing, mixed and contaminated cultures).

Specimen	n	%
CSF	15	0.5
Blood culture	569	18
Stool	2 148	68.5
Other	410	13
Total	3,142	100

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

Table 28: Antimicrobial susceptibility test results for all non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2016, ciprofloxacin, n=211 and azithromycin, n=168 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)	Resistant (%)
Ciprofloxacin	161 (76%)	50 (24%)
Azithromycin	165 (98%)	3 (2%)

Table 29: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2016, n=1,091 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	Serotype				
	Enteritidis	Infantis	Isangi	Typhimurium	Virchow
Eastern Cape	31	2	8	76	0
Free State	12	0	0	23	0
Gauteng	293	9	10	163	8
KwaZulu-Natal	43	1	0	30	3
Limpopo	12	1	7	8	0
Mpumalanga	42	0	2	22	2
Northern Cape	5	0	0	19	1
North West	12	0	1	11	0
Western Cape	80	5	0	148	1
South Africa	530	18	28	500	15

Shigella species

Results

Slightly increased numbers from March through May 2016 are in contrast with the pattern observed during 2015, when increased cases from January through March, and again from October through December suggested seasonality (Figure 20). The primary burden of disease due to *Shigella* is non-invasive dysentery or diarrhoea, although invasive disease cases continue to occur (Table 30). The predominant burden of disease, including both invasive and non-invasive shigellosis, is in the under-five-year age group (Table 31). No fluoroquinolone resistance was detected in isolates tested, but one isolate was shown to be resistant to azithromycin (Table 32). Predominant serotypes confirm that *S. flexneri* 2a remains the commonest cause of shigellosis in South Africa (Table 33). *S. dysenteriae* type 1 was not isolated in 2016.

Discussion

Shigella infection is associated with waterborne outbreaks in South Africa, although person-to-person transmission plays an important role. Invasive disease appears to be decreasing (9, 10, 11, 12). Resistance to fluoroquinolones and azithromycin remains low, but should continue to be monitored. ESBL-production is rarely documented. *S. dysenteriae* type 1 isolates are not reported and appear to be rare as there were no isolates in South Africa in 2016 or preceding years, when systematic surveillance was conducted (9, 10, 11, 12).

Figure 20. Number of non-invasive and invasive *Shigella* isolates reported to GERMS-SA, by month of specimen collection, South Africa, 2016, n=1,313 (including audit reports).

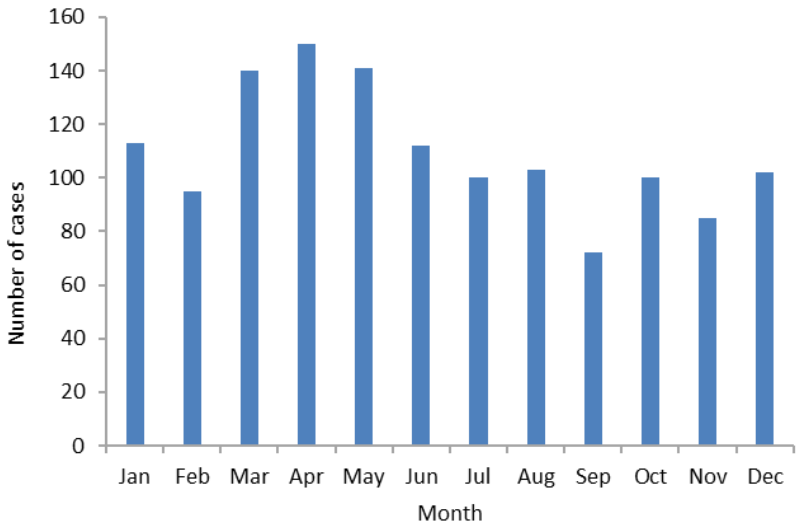


Table 30: Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2016, n=1,313 (including audit reports, missing isolates, mixed and contaminated cultures).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	129	0
Free State	71	1
Gauteng	495	8
KwaZulu-Natal	159	3
Limpopo	10	1
Mpumalanga	43	2
Northern Cape	6	0
North West	34	1
Western Cape	340	10
South Africa	1,287	26

Table 31: Number* of invasive and non-invasive *Shigella* cases reported to GERMS-SA by age category, South Africa, 2016, n=1,313 (including audit reports, missing isolates, mixed and contaminated cultures).

Age Category (years)	Cases	
	Non-invasive	Invasive
0 - 4	577	7
5 - 14	218	0
15 - 24	55	0
25 - 34	126	2
35 - 44	78	4
45 - 54	60	6
55 - 64	50	3
≥ 65	66	2
Unknown	57	2
Total	1,287	26

*Incidence rates were not calculated because specimens may not have been submitted for culture from all patients with gastro-enteritis due to *Shigella* in clinical practice.

Table 32: Antimicrobial susceptibility test results for *Shigella* isolates received by GERMS-SA, South Africa, 2016, ciprofloxacin, n=130 and azithromycin, n=127 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible	(%)	Resistant	(%)
Ciprofloxacin	130	(100)	0	(0)
Azithromycin	126	(99)	1	(0)

Table 33: Commonest invasive and non-invasive *Shigella* serotypes reported to GERMS-SA by province, South Africa, 2016, n=1,266 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. flexneri* type 2a	*S. flexneri* type 3a	*S. flexneri* type 4	*S. flexneri* type 6	*S. sonnei*
Eastern Cape	42	15	9	2	30
Free State	21	10	0	8	25
Gauteng	116	49	18	42	207
KwaZulu-Natal	53	10	8	14	32
Limpopo	2	1	1	1	3
Mpumalanga	12	7	0	2	12
Northern Cape	4	0	0	0	1
North West	5	4	2	5	15
Western Cape	135	40	16	23	69
South Africa	390	136	54	97	394

Vibrio cholerae O1

Results

No cases of *Vibrio cholerae* O1 were identified in 2016.

Discussion

The lack of outbreaks of cholera in 2016 supports the importance of heightened awareness and rapid responses in years past in the event of disease being identified (9, 10, 11, 12).

Rifampicin-resistant Tuberculosis

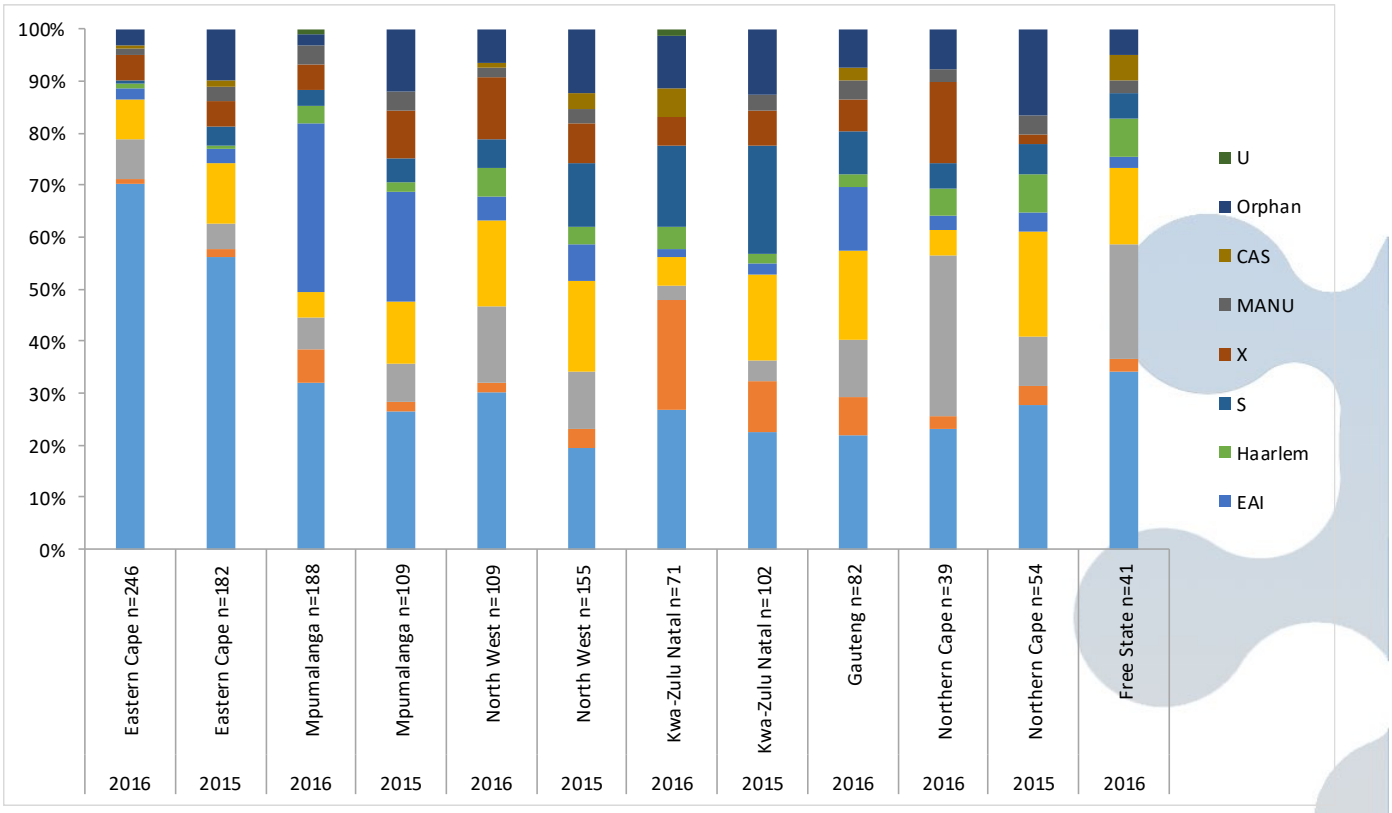
Results

In 2016, Gauteng and Free State were added into the Rifampicin resistant surveillance program. A total of 1,115 sputum samples were received for the year and valid typing results were available for 698 isolates. The median age of patients enrolled in the surveillance was 37yrs (IQR 30-48); 54% were male. There was no association between strain type and age group or gender. The majority of samples processed were smear positive (71%) indicating infectiousness and risk of transmission to close contacts. Gauteng and Free State had the highest proportion of smear positive cases, 84% and 81% respectively. Rifampicin mono resistant cases were most common in Northern Cape and North West provinces. The rest of the provinces had predominantly MDR TB cases. Ninety-one isolates (13%) had more than one strain type, most occurred in Eastern Cape (26/91) and Mpumalanga (30/91). There was a strong association between strain type and province ($p<0.01$). Figure 21 below shows a comparison between 2015 and 2016 of strain types in the provinces.

Discussion

Beijing is still the dominant lineage among most provinces, most notably in the Eastern Cape (70% for 2016). This lineage is known to be associated with greater transmissibility and increased ability to acquire drug resistance. In Mpumalanga, both Beijing and East African Indian (EAI) lineages were equally common for 2016, and was similar to 2015. Compared to the Beijing lineage, the EAI lineage is reported to have a reduced potential tor transmissibility, which is a possible reason for the lineage not being prominent in other provinces however the higher relative proportion of this strain type in MP and the increase observed between 2015 and 2016 suggest that it may have adapted in this area. Interestingly, in the Northern Cape the LAM family was the predominant type for 2016, this is in contrast to 2015 where Beijing was the predominant lineage. Furthermore, the T lineage has markedly decreased from 2015, which places a question on the fitness of this lineage. Whilst the LAM 4 lineage is present in all provinces, the highest proportion occurred in KZN, this has been consistent for 2015 and 2016. The LAM4 lineage in KZN is known to be predominant among MDR TB and XDR TB cases, and was the same lineage that caused the Tugela Ferry outbreak associated with high mortality. It is also interesting to note that all the strain types found belonged to modern lineages rather than ancestral ones.

Figure 21: Tuberculosis spoligotypes of culture positive specimens by province (South Africa) for 2015 and 2016



Rifampicin-susceptible Tuberculosis

Results

In 2016, 267 enrolled rifampicin susceptible cases had a case report form completed. Data from three provinces (Eastern Cape, Gauteng and North West) were analyzed. More than 50% of the patients were HIV positive. The North West Province had the highest proportion of TB/HIV co-infection cases (63%), followed by Gauteng (60%) and Eastern Cape (44%). Forty percent of patient were on anti-retroviral therapy (ART) and less than 5% had received Isoniazid Preventative Therapy (IPT). A further 20% of cases were however being screened at interview for enrollment to start ARTs. The Eastern Cape had the highest proportion of previously treated TB cases (36%). Smoking (65%) and alcohol (44%) use was also more prevalent among patients in the Eastern Cape. Close to 50% of patients from the North west Province reported to have someone in household diagnosed with TB in the last two years. Table 34 shows the comparison of factors by province. A total of 265 (99%) had a sample tested and 59% of cases were smear positive. Cultures were negative in 19% (50/265) precluding further analysis. Drug susceptibility results were successfully performed for 175 samples and of these 6 were isoniazid mono resistant (IMR), with the majority from Gauteng (5/6). The overall prevalence was 3.4% and for Gauteng it was 9.6%. There was no association with age or gender and IMR nor with other factors. However, there was a strong association between smear and IMR (p=0.049).

Discussion

The majority of TB cases were co-infected with HIV highlighting its continued importance in controlling the TB epidemic. Anti-retroviral treatment has been previously shown to reduce TB incidence and having less than half the cohort of TB patients on ART highlights an important gap that needs to be addressed. The policy recommending test and treat for HIV will likely change this over time. Previous treatment exposure was low in Gauteng compared to the other provinces and is suggestive of primary transmission rather than reactivation. It is also interesting to note the strong association between IMR and smear positivity indicative of transmission as well as Gauteng having a relatively higher proportion of IMR cases. Previous household contact with a TB patient was very common in Eastern Cape with half having been exposed and the need for improved contact management of index cases is critical. The high prevalence of smoking, which is a known risk factor for TB is an important health issue that is often overlooked leading to poor lung health and increased long term susceptibility to TB and other infections. Alcohol use which can impact on treatment adherence and drug levels was also observed to be relatively common and should be taken into consideration when managing patients. The findings of this surveillance has important public health importance however as the surveillance was conducted only at a few sites the generalizability of these findings is limited.

Table 34 shows the comparison of factors by province

Risk Factor	EC=162	GP=70	NW=35	TOTAL=267
Previous treatment for TB				
unknown	1	8	4	13
no	102	54	21	177
yes	59	8	10	77
Proportion with previous TB treatment exposure	**36%**	**11%**	**29%**	**29%**
Household contact previously diagnosed with TB in the past 2 years				
unknown	14	10	5	29
no	103	48	13	164
yes	45	12	17	74
Proportion with a previous household TB contact	**28%**	**17%**	**49%**	**28%**
Highest level of education completed				
unknown	1	8	4	13
no formal	0	0	2	2
primary	29	10	8	47
secondary	116	51	19	186
tertiary	16	1	2	19
Proportion who have completed secondary education among positive respondents	**82%**	**84%**	**68%**	**81%**

Risk Factor	EC=162	GP=70	NW=35	TOTAL=267
History of Imprisonment				
unknown	1	8	4	13
no	151	61	27	239
yes	10	1	4	15
Proportion who have been previously imprisoned	**6%**	**1%**	**11%**	**6%**
Alcohol history				
unknown	**1**	**8**	**4**	**13**
no	**90**	**49**	**19**	**158**
yes	**71**	**13**	**12**	**96**
Proportion who have used alcohol	**44%**	**19%**	**34%**	**36%**
Previous work at a mine				
unknown	5	49	7	61
no	153	17	24	194
yes	4	4	4	12
Proportion with prior mining work exposure	**2%**	**6%**	**11%**	**4%**
Previous hospital admissions in the past year				
unknown	15	8	4	27
no	125	57	22	204
yes	22	5	9	36
Proportion who have previously been admitted to hospital	**14%**	**7%**	**26%**	**13%**
Smoking history				
unknown	1	8	4	13
no	56	32	12	100
yes	105	30	19	154
Proportion with a positive smoking history	**65%**	**43%**	**54%**	**58%**
HIV status				
unknown	6	13	5	24
negative	84	15	8	107
positive	72	42	22	136
Proportion with HIV among those with a known status	**46%**	**74%**	**73%**	**56%**
History of IPT exposure among HIV positive patients				
unknown	4	0	3	7
no	65	40	19	124
yes	3	2	0	5
Proportion of HIV positive patients who have received IPT treatment	**4%**	**5%**	**0**	**4%**
History of prior anti-retroviral treatment among HIV positive patients				
no	25	23	5	53
screened for initiation	16	2	9	27
yes	31	17	8	56
Proportion of HIV positive patients who have had prior ART exposure	**43%**	**40%**	**36%**	**41%**

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Polokwane NHLS laboratory site visit, 11 August 2016

Diarrhoeal surveillance

Introduction

Diarrhoeal diseases remain an important cause of morbidity and mortality in the South African population especially in young children and infants. In order to decrease the burden of diarrhoeal diseases, the rotavirus vaccine was introduced into the national immunizations program in August 2009. The oral monovalent vaccine administered to children at 6 and 14 weeks of age protects them against rotavirus, the most important cause of severe diarrhoea and death in children <5 years. Subsequent impact studies have shown a decrease in both rotavirus -specific (54-58% reduction in children < 5 years) and all-cause diarrhoea (45-65% reduction in children <12 months and 40-50% reduction in children 13-24 months) in South Africa. Continuous monitoring of diarrhoea and rotavirus in children <5 years is, however, required to ensure the vaccine formulation and program are functioning properly and to identify rotavirus strains that may escape protection, if any.

Methods

In 2016 diarrhoea surveillance was conducted at 11 sites, roughly one in each province with Gauteng and Mpumalanga each having two. Some of the sites did not conduct surveillance for a full 12 months in 2016 so the surveillance months have been indicated where applicable. The surveillance sites included: Chris Hani Baragwanath Academic Hospital (CHBAH, Gauteng Province), Dr George Mukhari Hospital (DGM, Gauteng/ North West Province border), Mapulaneng Hospital (MPH, Mpumalanga Province (MP)), Matikwane Hospital (MKH, MP), Edendale Hospital (EGH, Kwa-Zulu Natal Province), Red Cross Children's Hospital (Western Cape Province; January-February), Kimberley Hospital (KBH, Northern Cape Province), Pelonomi Hospital (PNH, Free State Province), Polokwane Hospital (PKH, Limpopo Province; January-April), Dora Nginza Hospital (DNH, Eastern Cape Province; March-December) and Klerksdorp Hospital (KDH, North West Province; April-December).

All children <5 years admitted to a sentinel hospital for the treatment of acute diarrhoea (WHO definition; seven days or less) were approached for enrolment. Enrolment was conducted systematically from Monday to Friday (8am-5pm), after informed consent was obtained from a parent or guardian, and demographic, clinical and outcome data were collected in a structured questionnaire by dedicated surveillance officers. Stool specimens were collected for rotavirus and enteric pathogen screening.

Specimens were screened at the MRC-Diarrhoeal Pathogens Research Unit laboratory at Sefako Makgatho Health Sciences University or at the Centre for Enteric Diseases, NICD for rotavirus (commercial EIA and standardized characterization protocols) and other enteric pathogens (Taqman array card).

The enteric Taqman array card utilized quantitative PCR with primers and probes for the following targets:

- Viruses: Rotavirus, adenovirus, astrovirus, enterovirus, norovirus GI, norovirus GII, sapovirus, oral poliovirus type 1, 2 and 3
- Bacteria: *Escherichia coli* (Enteroaggregative *E. coli* (EAEC targets: aaiC, aatA, aar, aggR), Enteropathogenic *E. coli* (EPEC targets: eae, bfpA), Enterotoxigenic *E. coli* (ETEC targets: LT, STh, STp), Shiga-toxin producing *E. coli* (STEC targets: stx1, stx2)), *Aeromonas* spp., *Bacteroides fragilis*, *Campylobacter* spp. (with *C. jejuni/coli* detection), *Clostridium difficile*, *Helicobacter pylori*, *Mycobacterium tuberculosis*, *Salmonella* spp., *Shigella/*Enteroinvasive *E.coli (*EIEC), *Vibrio cholerae*
- Parasites: *Encephalitozoon intestinalis*, *Enterocytozoon bieneusi*, *Cryptosporidium* spp. (with *hominis/parvum* detection), *Entamoeba histolytica*, *Giardia* spp. (with assemblage A/B detection), *Cyclospora cayetanensis*, *Cystoisospora belli*, *Ancyclostoma duodenale*, *Necator americanus*, *Ascaris lumbricoides*, *Strongyloides stercoralis*, *Trichuris trichiura*
- Controls: MS2 (RNA), PhHV (DNA), bacterial 16S

The Ct values associated with clinically relevant enteric infections were based on value calculated from the Global Enteric Multisite study (GEMS) and were as follows: Rotavirus – Ct=33; *Cryptosporidium* – Ct=28; *Shigella*/EIEC – Ct=28; Enterovirus – Ct=34; Adenovirus – Ct=30; *Campylobacter* spp. – Ct=35; *Giardia* spp. – Ct=32; *B. fragilis* – Ct=35; Sapovirus – Ct=32; *Isospora* – Ct=35. Enteric pathogens detected at these Ct values or lower were considered positive while pathogens detected at Ct values higher than the specified limits were considered associated with asymptomatic infections or shedding and were not included in the prevalence calculations. For assignment as EAEC positive, at least three gene targets had to have a Ct<35 while for EPEC both gene targets had to have Ct<35.

The start of the rotavirus season was defined as a rotavirus detection rate of above 20% for two consecutive weeks. The end of the season was defined as a rotavirus detection rate of below 20% for two consecutive weeks.

10 *C. hominis/C. parvum* dual infections). In addition, 68% (46/68) of *Campylobacter* spp. were identified as *C. jejuni* or *C. coli.* There were differences in the prevalence of enteric pathogens at the different sites and at Dora Nginza Hospital, higher levels of EPEC and *Cystoisospora belli* were detected compared to the rest of the sites.

investigations and provided information on all the enteric pathogens associated with moderate-to-severe diarrhoea in children <5 years in the sentinel sites under surveillance. The cards highlighted the importance of *Cryptosporidium* and *Shigella*/EIEC in diarrhoea in children <5 years, identified enteric pathogen with regional importance (EPEC and *Cystoisospora belli* in the Eastern Cape) and suggested future avenues of research into enterovirus, adenovirus and *B. fragilis.*

Results

A total of 752 stool specimens were screened in 2016 (Table 1) with 17% (132/752) positive for rotavirus. The RCCH site was not included in the tables below as they only contributed 10 specimens for 2016, collected in January and February with one rotavirus positive. The rotavirus season began in week 28 (11 July) and ended in week 36 (11 September; Figure 1). The maximum detection rate (65%; 17/26) was in week 29 (31 July; Figure 1). A total of 110 rotavirus positive strains were genotyped with G3P [8] (24%; 26/110) and G3P[4] (23%; 25) predominant and other strains detected at lower levels (G2P[4], G9P[8], G1P[8], G2P[6], G8P[8], G9P[6], G8P[4], G3P[6] and mixed strain infections).
A total of 75% (574/752) of the specimens collected in 2016 were screened using the enteric Taqman array card. Only three specimens were negative for all the pathogens targeted on the array card. The most common pathogens detected by site are summarized (Table 2). Rotavirus was the most common pathogen detected in 23% of cases followed by EAEC, *Cryptosporidium* and *Shigella*/EIEC. A total of 84% (84/101) of the *Cryptosporidium* strains were typed (59 *C. hominis*, 15 *C. parvum* and 10 *C. hominis/C. parvum* dual infections). In addition, 68% (46/68) of *Campylobacter* spp. were identified as *C. jejuni* or *C. coli.* There were differences in the prevalence of enteric pathogens at the different sites and at Dora Nginza Hospital, higher levels of EPEC and *Cystoisospora belli* were detected compared to the rest of the sites.

Table 1. Summary of the stool specimens collected per site per month in 2016 and the number and percentage of specimens positive for rotavirus.

	Site										
Month	CHBAH	MPH	MKH	DGM	EDH	KBH	PKH	PNH	DNH	KDH	Total
January	16	4	0	3	2	7	4	13	0	0	49
February	23	5	4	12	10	16	0	21	0	0	91
March	21	7	3	3	6	15	4	36	11	0	106
April	15	2	2	6	4	10	1	14	5	7	66
May	2	3	1	9	2	2	0	15	7	6	47
June	11	0	3	2	4	0	0	11	13	6	50
July	25	3	3	12	9	0	0	5	6	9	72
August	13	10	17	20	14	2	0	9	2	1	88
September	9	3	8	9	4	6	0	11	1	2	53
October	8	1	4	6	3	3	0	9	0	4	38
November	9	5	3	15	12	2	0	3	3	0	52
December	5	0	4	4	3	9	0	11	3	1	40
Total screened	**157**	**43**	**52**	**101**	**73**	**72**	**9**	**158**	**51**	**36**	**752**
Rotavirus positive	28	13	17	17	16	12	0	16	9	4	132
Percentage rotavirus positive	18	30	33	17	22	17	0	10	18	0	17

Site names are abbreviated as follows: CHBAH-Chris Hani Baragwanath Academic Hospital, MPH-Mapulaneng Hospital, MKH-Matikwane Hospital, DGM-Dr George Mukhari Hospital, EDH-Edendale Hospital, KBH-Kimberley Hospital, PKH-Polokwane Hospital, PNH-Pelonomi Hospital, DNH-Dora Nginza Hospital, KDH-Klerksdorp Hospital.

Figure 1. Number of stool specimens and percentage rotavirus positive per week in 2016.

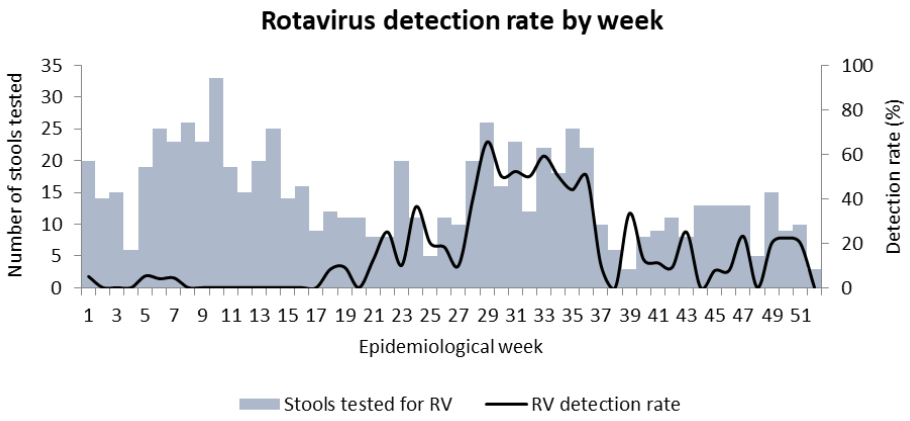


Table 2. Summary of enteric pathogens detected by site in 2016. The results are reported as percentages.

	Site								
Pathogen	CHBAH	MPH/MKH	EDH	KBH	PKH	PNH	DNH	KDH	Total
Rotavirus	23	38	35	14	0	16	23	9	23
EAEC	13	32	10	30	38	26	19	14	21
Cryptosporidium spp.	12	10	10	32	13	29	9	23	18
Shigella/EIEC	24	17	15	14	13	13	13	20	18
Enterovirus	10	14	12	20	0	25	19	6	16
Adenovirus	17	18	17	18	25	13	13	9	16
Campylobacter spp.	10	11	13	14	13	12	11	14	12
Giardia spp.	4	10	3	14	13	15	11	6	9
B. fragilis	5	5	10	13	13	10	4	6	8
EPEC	7	2	8	11	0	4	21	3	7
Sapovirus	3	3	3	7	13	6	4	6	7
C. belli	0	0	3	0	0	4	13	3	2
Total specimens screened	145	87	60	56	8	126	47	35	574

Site names are abbreviated as follows: CHBAH-Chris Hani Baragwanath Academic Hospital, MPH-Mapulaneng Hospital, MKH-Matikwane Hospital, DGM-Dr George Mukhari Hospital, EDH-Edendale Hospital, KBH-Kimberley Hospital, PKH-Polokwane Hospital, PNH-Pelonomi Hospital, DNH-Dora Nginza Hospital, KDH-Klerksdorp Hospital.

Discussion

The rotavirus detection rate (17%) was lower than seen in the pre-vaccine era and the number of hospitalized children at the sentinel sites under surveillance treated for diarrhoea also dropped dramatically compared to the pre-vaccine era. The 23% rotavirus detection rate seen in the Taqman card screening is not unusual as the method is more sensitive than the EIA used for surveillance. The G3P[8]/G3P[4] strains were uncommon as this genotype has not circulated in South Africa since 2005. However, the G3s were not associated with increased severity and simply reflect the changing and unpredictable nature of rotavirus genotype circulation globally. The use of the enteric Taqman array cards for screening of stool specimens was easy and rapid to perform, suitable for diarrhoeal outbreak investigations and provided information on all the enteric pathogens associated with moderate-to-severe diarrhoea in children <5 years in the sentinel sites under surveillance. The cards highlighted the importance of *Cryptosporidium* and *Shigella*/EIEC in diarrhoea in children <5 years, identified enteric pathogen with regional importance (EPEC and *Cystoisospora belli* in the Eastern Cape) and suggested future avenues of research into enterovirus, adenovirus and *B. fragilis.*

Prospective Sentinel Surveillance of Human Immunodeficiency Virus in South Africa and Related Drug Resistance, 2015-2016

Introduction

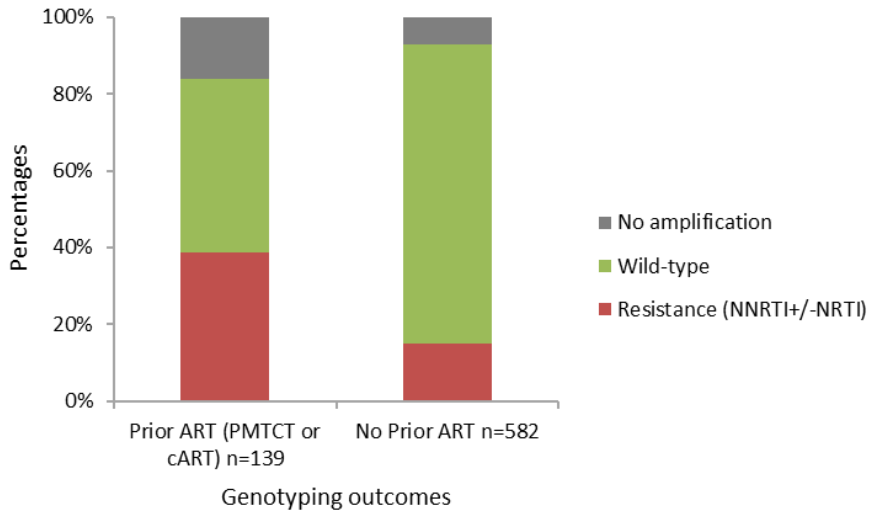
South Africa (SA) is afflicted with dual epidemics of Tuberculosis (TB) and Human Immunodeficiency Virus (HIV). The country has the world's largest antiretroviral (ARV) program, with approximately 3.5 million people ever started ARV therapy (ART) by 2016. The National Department of Health adopted a public health approach by using standardised combinations of ARVs: first line ART consists of tenofovir (TDF) or zidovudine (AZT) and lamivudine (3TC) or emitricitabine (FTC) with either efavirenz (EFV) or nevirapine (NVP). As of April 2015, all patients with CD4 cell count < 500cells/ml, advanced WHO staging and TB-HIV co-infection were eligible for life-long ART. Clinical and laboratory monitoring recommends that CD4 and HIV viral load testing be performed at 6 and 12 months, and viral loads repeated every 12 months thereafter. Routine testing for HIV drug resistance (HIVDR) is not performed at ART initiation or NNRTI-based regimen failure - patients failing on these regimens are switched to a standardised protease inhibitor-containing 2nd line regimen after intensified adherence counselling. HIVDR testing is available for PI regimen failure and is a prerequisite for access to 3rd-line regimen selection.

The NICD Centre for HIV and STIs established an integrated TB-HIV surveillance study in 2014/15 by building on the GERMS-SA hospital-based enhanced surveillance platform. The study introduced surveillance for rifampicin and other drug-resistance in persons initiating TB treatment and /or HIVDR surveillance in persons initiating ART in the same clinic. A single primary health clinic in each province has been selected on the basis of convenience from clinics with high TB and HIV case loads. By 2016, enrolment had started in the Eastern Cape (EC, Feb 2015), North West (NW, Jan 2015), Mpumulanga (MP, Oct 2014) and Gauteng (GP, February 2016) provinces. At each clinic, a dedicated surveillance officer (SO) identifies and enrols eligible patients (i.e. patients initiating TB therapy or ART according to routine clinic procedures). Where consent is obtained, SOs interview the participants using a standard questionnaire and available medical records to collect relevant clinical and epidemiological data, and collect sputum or whole blood specimens from the participants. Here, we report on HIVDR data in patients initiating ART and enrolled in the GERMS HIVDR surveillance study during 2015 and 2016. All sites keep enrolling until a pre-defined sample size has been achieved.

Results

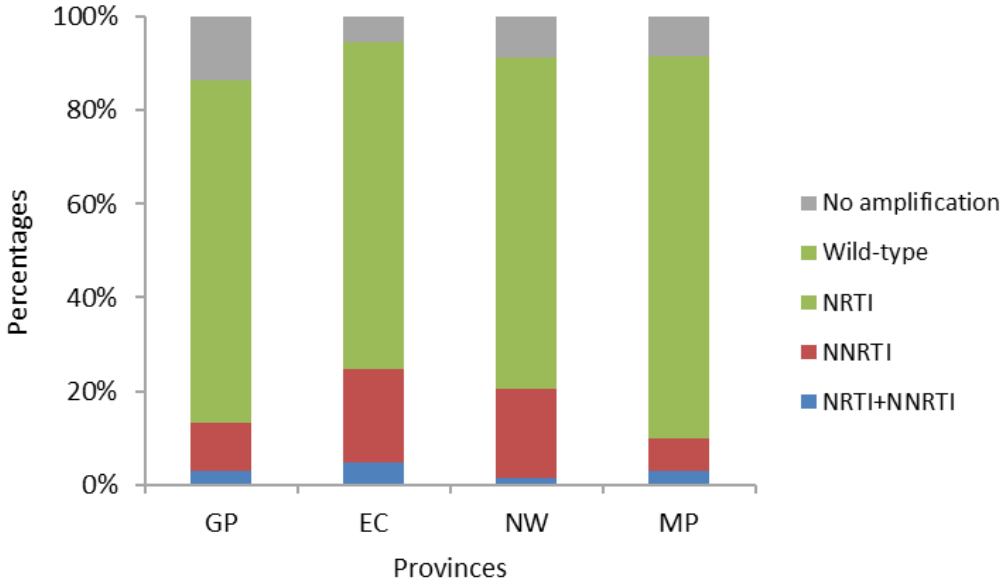
During 2015 and 2016, 721 specimens were collected for HIVDR testing, 193 (27%) from GP, 252 (35%) from EC, 196 (27%) from NW and 80 (11%) from MP. The GP, EC and NW clinics were located in urban/peri-urban areas, whereas the MP clinic was located in a rural community. Sixty six percent of all enrolled participants were female, and the average age was 35 years (IQR 29 -44 years). Sixty five percent (65%) of participants were unemployed and 21% are smokers. Six percent (6%) had received a tertiary education, and 76% had completed secondary school. Median CD4 count at time of ART initiation was 303 cells/µl (IQR 167 – 497 cells/µl). Thirteen percent have ever been diagnosed with TB. Two thirds were currently experiencing clinical markers of HIV infection, including HIV wasting, oral candidiasis, rash and Kaposi sarcoma at time of treatment initiation. Prior exposure to ART (as PMTCT and/or previous ART) was reported in 139 (19%) participants: 58 of these reported receiving PMTCT (as single-dose nevirapine, Option A or Option B), and 81 had previously received combination ART for clinical management.

Figure 1: HIV drug-resistance genotyping outcomes amongst 721 participants enrolled in NICD HIVDR surveillance during 2015 and 2016, according to participants' prior exposure to antiretroviral therapy.



HIVDR testing was successful in 91% of specimens, with amplification failure primarily due to viral loads <1000 copies/ml. NNRTI resistance was detected in 19% of specimens, of which 3% harboured dual NRTI/NNRTI drug resistance. The K103N mutation, which confers high-level resistance to efavirenz and nevirapine, was most commonly detected. When analysed according to prior ART exposure, HIVDR was present in 39% of participants with any prior ART vs 15% of those with no reported prior ART (Figure 1.) . Rates of resistance varied between 10% and 25%, with highest rates being detected in EC (Figure 2).

Figure 2: HIV drug-resistance genotyping outcomes amongst 721 participants enrolled in NICD HIVDR surveillance during 2015 and 2016, according to province of origin.



Conclusion

The data show high proportions of patients are re-initiating ART (19%), and high proportions of NNRTI HIVDR (19%) are present, which may compromise the effectiveness of the NNRTI drug in the standardised first line regimens.

Sentinel site surveillance, while not population-based and therefore not necessarily generalizable to all clinics, does provide good assessments of prevalence and trend data. In addition, prior exposure to ART recording may not be accurate, due to recall bias and absence of data in medical files. The extent to which the facilities surveyed herein are similar to facilities elsewhere and to what extent the patients enrolled are similar to those in the national program needs to be determined in order to ascertain the representivity of this data. However, surveillance through the GERMS platform allows for valuable, consistent and intensified data collection over longer periods of time. Different rates of resistance detected across provinces may reflect patterns specific to the clinic in which the research was conducted and do not necessarily reflect provincial patterns.

Aetiological surveillance of Sexually Transmitted Infection Syndromes at sentinel sites: GERMS SA 2014-2016

Executive Summary

Sentinel aetiological surveillance of STI syndromes was conducted at primary healthcare facilities in four South African provinces in the period 2014-2016. *Neisseria gonorrhoeae* was the predominant cause of MUS; and syndromic management with dual antimicrobial therapy, which also covers *Chlamydia trachomatis*, the second most common pathogen, is rational. Herpes simplex virus was the commonest detectable cause of genital ulceration, supporting the continued use of acyclovir in syndromic management. The syndromic management of VDS remains complex: the commonest causes, bacterial vaginosis and candidiasis, are not considered as STIs; however, a significant proportion of patients with either condition were co-infected with STI pathogens. The HIV seroprevalence among STI patients was high, underlining the importance of linkage to universal HIV counselling and testing in primary healthcare settings.

Background

In South Africa, STIs are managed principally at primary healthcare facilities (PHCs) using standard syndromic management guidelines (1). National clinical STI syndrome surveillance is conducted by NDoH at 270 surveillance sites across the country. Clinical surveillance data on the distribution of STI syndromes in Gauteng Province PHCs (2000 – 2007) have revealed that male urethritis syndrome (MUS), vaginal discharge syndrome (VDS) and genital ulcer syndrome (GUS) together comprise nearly 80% of all syndromes seen (2).

Periodic aetiological surveillance of the three main STI syndromes is critical in validating the existing treatment algorithms. In 2014-2016 STI aetiological surveillance was conducted in the following provinces: Gauteng (Alexandra Health Centre); Mpumalanga (Kabokweni and Hluvukani Clinics); North-West (Jouberton Clinic); KZN (Eastboom Community Health Centre in Pietermaritzburg and Phoenix Clinic in Durban); and Eastern Cape (Gqebera Clinic).

Objectives

The primary objectives of surveillance were to determine the aetiologies of the three major STI syndromes (MUS, GUS, VDS) and the susceptibility profiles of *Neisseria gonorrhoeae* isolates. Secondary objectives were to determine co-infections (e.g. HIV) among patients presenting with STI Syndromes.

Methods

Consecutive consenting patients presenting with MUS, VDS or GUS at the selected PHCs between January 2014 and December 2016 were included in the surveillance. Inclusion criteria were STI patients aged 18 years and above with a new episode of clinically confirmed MUS, VDS and/ or GUS. The target sample size per site was as follows: 100 cases each of MUS and GUS and approximately 150-200 cases of MUS (in order to obtain at least 100 viable gonococcal isolates from each site). Following eligibility and informed consent procedures, a nurse-administered questionnaire was used to document demographic and clinical information. Swabs were used for the sampling of genital discharge (vaginal, endocervical, urethral) and genital ulcers. Additionally, a 10ml specimen of venous blood was collected from each participant.

Results

Patient demographic and clinical characteristics

Of 1,824 participants, 962 (52.7%) were male (Table 1). Median age of participants was 27 years (IQR 23-32 years) and the majority were of black African ethnicity (99.4%) and of heterosexual orientation (98.9%). With respect to high risk sexual behaviours: median age at sexual debut was 17 years (IQR 16-19 years), and self-reported condom use at last sexual encounter was low (17.6%). Almost one-third of participants (28.7%) had been diagnosed with an STI syndrome within the preceding 12-month period.

Table 1: Demographic and clinical characteristics of participants

Variable	All (N = 1,824)
Male (n, %)	962 (52.7)
Current age Median(IQR)	27 (23- 32)
Black Africans (n,%)	1,813 (99.4)
Age at first sex Median(IQR)	17 (16- 19)
Condom use (n,%)	322 (17.6)
Sex with someone outside province (n,%)	292 (16.0)
Sex with someone outside country (n,%)	214 (11.7)
STI syndrome diagnosed in the past 12 months (n,%)	523 (28.7)
Heterosexual orientation (n,%)	1,803 (98.9)
Main syndrome diagnosed	
MUS	808 (44.3)
VDS	757 (41.5)
GUD	366 (20.1)
>=2 syndromes	107 (5.9)

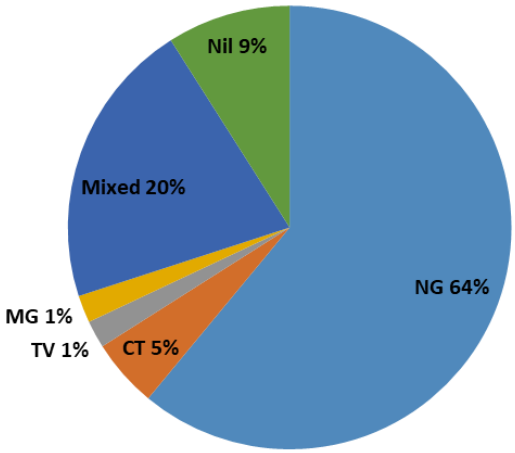
Laboratory results

STI Syndrome aetiologies

MUS

Among 808 patients presenting with MUS, *Neisseria gonorrhoeae* was the commonest cause (666, 82.4%; 95% CI 79.6 – 84.9), followed by *Chlamydia trachomatis* (178, 22.0%; 95% CI 19.3 - 25) (Figure 1). The majority of patients (578, 71.5%; 95% CI 68.3 – 74.5) had infections caused by single agents. *Trichomonas vaginalis* and *Mycoplasma genitalium* accounted for less than 5% of MUS. Multiple pathogens were detected in approximately 20% (161; 95% CI 17.3 – 22.8): the majority of these mixed infections (150, 93.2%) were caused by *Neisseria gonorrhoeae* together with one or more STI pathogens, mostly *Chlamydia trachomatis* (123, 76.4%). An STI pathogen was detected in approximately 91% of specimens (739; 95%CI 89.3-93.2); less than 10% of specimens (69; 95% CI 6.8 – 10.7) had no identifiable STI aetiology.

Figure 1: Relative prevalence of STI pathogens in MUS (N = 808)



Mixed aetiology (n = 161):
Mostly NG + CT (76%)
Overall prevalence (single + mixed infections)
- **NG: 82%**
- **CT: 22%**
- **TV: 4%**
- **MG: 4%**

Key: *Neisseria gonorrhoeae* (NG); *Chlamydia trachomatis* (CT); *Trichomonas vaginalis* (TV); *Mycoplasma genitalium* (MG)

VDS

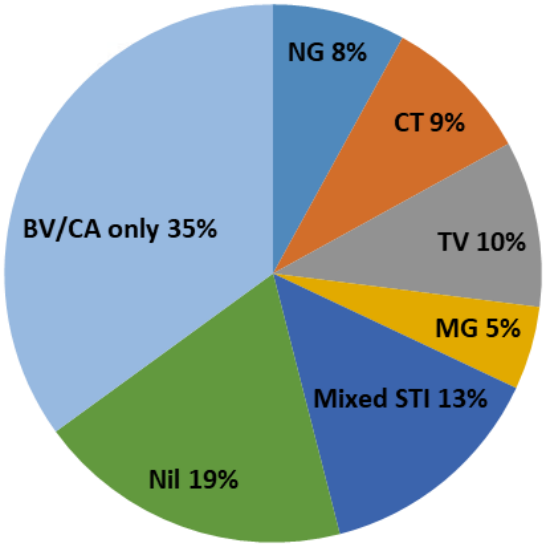
Among 756 women with VDS (Figure 2), less than 50% had a detectable STI pathogen in single or mixed infections (330; 95% CI 40.1 – 47.1). The commonest STI aetiology was *Neisseria gonorrhoeae* (140, 18.5%; 95%CI 15.9 – 21.4), followed by *Chlamydia trachomatis* (134, 17.7%; 95% CI 15.2 – 20.6). *Trichomonas vaginalis* accounted for less than 15% of infections, and *Mycoplasma genitalium* for less than 10%.

Overall, single STI pathogens were detected in 234 VDS cases (31%; 95% CI 27.7 – 34.3); and mixed infections with multiple (two or more) STI pathogens in 96 (13%; 95% CI 10.5 – 15.3).

Most VDS cases were attributed to conditions that are not traditionally considered to be STIs: bacterial vaginosis (BV) was identified in 427/752 (56%; 95% CI 52.8 – 59.9), and vulvovaginal candidiasis (CA) accounted for 167 (22%; 95% CI 19.2 – 25.1). An identifiable pathogen or cause was not found for 144 (19%; 95% CI = 16.4 - 22) of VDS cases.

A significant proportion of VDS patients had co-infection with STI and non-STI aetiologies. Only 98/752 (13%) of VDS cases tested for all causes had a sole STI aetiology; the rest (232/752, 31%) had an STI plus BV and/or CA. Overall 205 VDS cases (27%) had BV-STI co-infections, and sixty-five VDS cases (8.5%) had CA-STI co-infections. Therefore 205/427 patients with BV (48%; 95% CI 43.3 – 52.8) and 65/167 patients with CA (39%; 95% CI 31.8 – 46.6) had STI co-infections.

Figure 2: Relative prevalence of VDS aetiologies (N = 752)



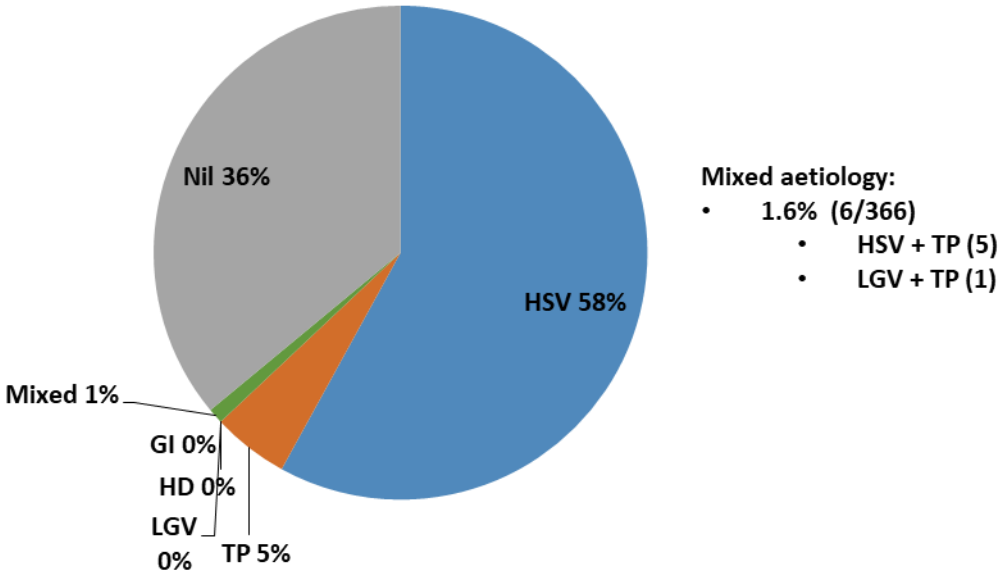
Any STI pathogen (single/ mixed infections): 44% (330/756)
Overall prevalence
NG : 18%
CT : 18%
TV : 14%
MG : 9%
STI only: 13% (98/752)
BV: 57% (427/752)
Overall BV with STI: 27%
Of those with BV: 48% had STI(205/427)
CA: 22% (167/752)
Overall CA with STI: 9% (65/752)
Of those with CA: 39% had STI (65/167)

Key: *Neisseria gonorrhoeae* (NG); *Chlamydia trachomatis* (CT); *Trichomonas vaginalis* (TV); *Mycoplasma genitalium* (MG); bacterial vaginosis (BV); vulvovaginal candidiasis (CA)

GUS

Among 366 GUS cases (Figure 3), the major cause was herpes simplex virus (HSV) in 59.3% (217/366; 95% CI 54 - 64); followed by *Treponema pallidum* (TP) in 6.0% (22/366; 95% CI 4 - 9). Type-specific PCR revealed that 99.0% (215/217) HSV infections were caused by HSV-2. Most pathogen-detectable cases had a single aetiology (228/366, 62.3%). Only 6 cases had mixed aetiology: all were co-infected with HSV and one other pathogen, namely TP (5), HD and LGV (1). An ulcer-derived pathogen was not identified in 36.1% GUS cases (132; 95% CI 31.3 – 41.1).

Figure 3: Relative prevalence of STI pathogens in GUS



Key: herpes simplex virus (HSV); *Treponema pallidum* (TP); lymphogranuloma venereum (LGV); granuloma inguinale (GI)

Serological results

HIV co-infection rates were as follows: 57.3% (208/363; 95% CI 52.1 – 62.3) in GUS; 47.2% (350/742; 95% CI 43.6 – 50.8) in VDS and 26.6% (211/794; 95% CI 23.6 – 29.8) in MUS. There was a significant association between HIV seropositivity and all STI syndromes (p<0.001).

Discussion and Conclusions

This surveillance study provides a snapshot of STI Syndrome aetiologies across several South African provinces in 2014-2016. Overall the study found that the majority of participants enrolled with STI syndromes were young and reported high risk sexual behaviour, such as young age at sexual debut and unprotected sex at last sexual encounter. *Neisseria gonorrhoeae* was the predominant cause of male urethritis syndrome. Based on our data, syndromic management for MUS in the South African public health sector should include cover for the two leading causes, *Neisseria gonorrhoeae* and *Chlamydia trachomatis*.

Bacterial vaginosis was the leading cause of VDS, and prevalent in over 50% of females. A significant proportion of women with BV were co-infected with one or more STI pathogens. These findings suggest that BV is associated with risk factors for traditional STI infections, and that the management algorithm for VDS should be reconfigured to increase the predictive value of the algorithm for STI pathogens.

Herpes simplex virus-2 remains the leading cause of pathogen-detectable GUD in Gauteng, and this supports the use of antiviral therapy in the syndromic management guidelines

The HIV prevalence among patients presenting with STI syndromes is significantly higher than the UNAIDS 2015 estimated prevalence of 19.1% for adults aged 15-49 years in the general South African population. This underscores the importance of linkage to universal HIV testing and treatment for STI patients; and support the recently adopted national policy of early ARV initiation for those who are HIV-infected.

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Zoonotic aetiologies in febrile adults in the Mnisi Community, Mpumalanga Province, South Africa, 2014-2016

Introduction

The Mnisi area is a malaria endemic area in rural Mpumalanga and is bordered by the Kruger National Park. Contact between wildlife, livestock and humans is frequent. Zoonoses cause infectious diseases in humans who interact with livestock, domestic animals and vectors. A high prevalence of zoonotic infections was observed in a previous study at 3 public health clinics in Mnisi. A single sentinel site was established at the community health clinic in Mnisi for the NICD surveillance programme in 2014.

The goal of the study was to investigate selected zoonotic diseases in an agropastoral rural community in South Africa.

Methods

From September 2014 to December 2016, consenting adult volunteers presenting to the clinic with fever (>37.5 °C) or a history of fever, and on whom a malaria rapid test was done, were enrolled and a questionnaire administered. Acute and convalescent blood samples were collected for a panel of laboratory tests for leptospirosis, Q fever, bartonellosis, brucellosis, arboviruses and rickettsiae (Table 1).

Results

70 adult patients were enrolled during the reporting period. 46% (32/70) did not return for follow up blood samples. The median age was 34 years (IQR 26-46 years) and 60% were female. The median duration of illness was 2 days (IQR 1-3 days). Sixty percent (40/67) received an antibiotic at the clinic and 11% (8/70) were referred to the hospital. Twenty-four percent (17/70) of patients had no systemic symptoms, 59% (31/53) presented with only one symptom: muscle pain (67%) and respiratory symptoms (39%) were most common.

On laboratory testing, 79% (55/70) of patients showed evidence of a recent or past infection/exposure for at least one of the zoonotic diseases tested for in this study (Table2).

Conclusions

Two thirds of patients had previous tick bite fever. Few patients tested positive for brucellosis; there is a good animal *Brucella* spp vaccination programme in this area.

Table 1. Panel of tests performed

Test	Test particulars	Samples tested	Interpretation of results
Rickettsiosis IgG and IgM IFA*	*Rickettsia conorii IgG and IgM IFA kits, Vircell, Spain*	IgG and IgM: all participants	IgG: titer of 1:40 deemed positive IgM: titer of 1:192 or greater deemed positive, or fourfold rise in titer
Q fever IgG ELISA**	Panbio® *Coxiella burnetii (Q fever) IgG ELISA (Standard Diagnostics Inc., Republic of Korea)*	Convalescent serum samples, or acute samples where convalescent samples not available	As per manufacturer's recommendations Index values calculated using run-based cut-off values. As per manufacturer's recommendations
Chikungunya, Rift Valley fever, Sindbis fever and West Nile fever HAI***	In-house assay	Serum samples from all participants	Titres higher than 1:20 were deemed positive
Chikungunya, Rift Valley fever, Sindbis fever and West Nile fever IgM capture ELISA	In-house assay	Serum samples that tested positive per arbovirus HAI	Percentage positivity values higher than the calculated run-based or population based cut-off values
Leptospira IgM ELISA	Panbio® *Leptospira IgM ELISA (Standard Diagnostics Inc., Republic of Korea).*	Convalescent serum samples, or acute samples where convalescent samples not available	Index values calculated using run-based cut-off values. As per manufacturer's recommendations
*Bartonella PCR****	*Bartonella spp. 16S/23S rRNA internal transcribed spacer (ITS) region (in house) and sequencing*	Acute whole blood samples from all participants. All positive amplicons were sequenced	Fragment sizes variable depending on species approximately 640 – 788 bp for outer primers and 481 – 573 bp for inner primers
Brucella serology (total antibodies)	Brucellacapt® assay (Vircell S.L., Spain)	Acute serum samples from all participants	Titres higher than 1:320 were deemed positive

*IFA: indirect immunofluorescence assay; **ELISA: enzyme-linked immunosorbent assay; *** HAI: haemagglutination inhibition assay; **** PCR: polymerase chain reaction

Table 2. Laboratory test results

Laboratory test positive	Number of patients positive /	% positive
Rickettsiosis IgG	42/67	62.7
Rickettsiosis IgM	11/67	16.4
Q fever IgG	13/70	18.6
Arboviruses	3/70	4.2
Leptospira IgM	1/70	1.4
Bartonella spp PCR	0/44	0
Brucella serology	0/66	0

SUMMARY OF GERMS-SA SURVEILLANCE

The GERMS-SA laboratory-based surveillance continues to be useful in reporting trends in pathogen-specific data. For enhanced sentinel surveillance, the percentage of case report forms done on interview was 76% (still reaching the target of 70%) and ongoing training and auditing of our surveillance officer data quality is done to continually improve that aspect.

Opportunistic infections: For *Cryptococcus* spp, incidence remained stable across provinces for 2015 and 2016. The peak incidence in men was in the 40-44 year old age group; in women it was in the 30-34 year old age group. Where we had HIV information, 97% were infected with HIV and only 57% were on ART (either previously or at the time of diagnosis). Patients still come into hospital with a low CD4 count and the in-hospital case fatality rate continues to be high (37%).

Rifampicin-resistant TB surveillance was done in seven provinces in 2016. Three quarters of the samples processed were smear -positive indicating infectiousness and risk of transmission to close contacts. Rifampicin mono-resistance was found mostly in NC and NW provinces. The other provinces had predominantly MDR TB cases. Beijing is still the dominant lineage in all provinces but shares dominance with East African Indian lineage in MP and LAM in NC. LAM4 (predominant in MDR and XDR TB cases in KZN) was the same lineage which caused the Tugela Ferry outbreak and is present in all provinces.

Rifampicin-susceptible TB surveillance looks at risk factors for TB as well as INH mono-resistance. From 3 provinces data showed a high rate of HIV infection and low ART use (40%) and only 5% isoniazid preventive therapy, high smoking and alcohol consumption. INH mono-resistance is <10%.

Vaccine-preventable diseases: The 2016 data continues to monitor the trends in vaccine-preventable diseases of IPD and Hib post-EPI vaccine introduction of PCV13 and the Hib booster. Hib disease remains low, infants being the most affected with Hib and non-typeable disease. Please remember that *Hib is a notifiable medical condition.*

There is a continued decrease in IPD; HIV is still an important risk factor for IPD. Only two thirds of IPD cases in children <5 years were vaccinated appropriately. Clinicians should remember to check the vaccine status of children and remember to give catch-up doses.

Epidemic-prone diseases: The incidence of meningococcal disease continues to decrease; WC having the highest rate and serogroup B being the predominant serogroup (47/113, 42%). High-dose penicillin is still being recommended as the drug of choice for therapy for confirmed meningococcal disease, although penicillin non-susceptibility was 11%.

For enteric organisms there is a great underestimation of enteric disease because of health-care seeking behaviour, specimen-collection practices, the challenges of alternative diagnostic methods for typhoid fever etc. For *Salmonella* Typhi, azithromycin is an alternative treatment option since the emergence of ciprofloxacin resistance. Paratyphoid fever remains rare in South Africa. For non-typhoidal salmonellosis, *Salmonella* Enteritidis has replaced *S.* Typhimurium as the commonest serotype. Antimicrobial resistance is a concern including emerging resistance to azithromycin. For shigellosis, fluoroquinolone and azithromycin resistance remains low but monitoring should be continued. *Shigella flexneri* 2a remains the commonest serotype. *S. dysenteriae* type 1 has not been isolated in the last few years. No cases of *Vibrio cholerae* O1 were identified.

Hospital infections: The 2016 candidaemia surveillance covered all provinces; one third of cases came from private sector laboratories. The age of patients were significantly lower in public– vs. the private sector. Overall crude case-fatality ratio was high (42%). Overall *C. parapsilosis* was the most common species followed by *C. albicans.* Particularly worrying was *C. auris* (9% [126/1372]) emerging as the second commonest species in the private-sector and fourth commonest in the public-sector. Resistance to fluconazole was high. Azole-resistant strains of *C. parapsilosis* and *C. auris* now dominate in the private-sector, particularly in Gauteng, and fluconazole prophylaxis should thus be discouraged in this setting. Conventional amphotericin B remains the empiric drug of choice for candidaemia in the public-sector because of the high prevalence of azole-resistant isolates. Caspofungin, micafungin or anidulafungin are good choices of empiric treatment where available.

Staphylococcus aureus surveillance is ongoing in Gauteng and the Western Cape. Twenty-five percent of isolates received were confirmed as MRSA. SCC mec type III was more common in Gauteng and SCC mec IV in the Western Cape, same as for 2015. All isolates were susceptible to vancomycin and daptomycin.
CRE surveillance in four provinces showed that *Klebsiella pneumoniae* was the commonest organism (74% of 440 cases). There was a shift to CPE mediated by OXA-48 and variants.

Information from our enhanced surveillance show that at least one third of patients die in hospital and the majority of deaths occur early on in admission, suggesting that access to healthcare is late. The percentage of patients infected with HIV is high although only about half were on antiretroviral treatment.

For the first time we report the additional surveillance projects using the GERMS-SA platform in this consolidated report.

Diarrhoeal surveillance: rotavirus was identified in 17% of 752 stool isolates (lower than pre-vaccine era). The Taqman cards highlighted the importance of *Cryptosporidium* and *Shigella/* EIEC in diarrhoea in children <5 years.

HIV Drug resistance in patients initiating ART: high proportions of patients are re-initiating ART (19%) and high proportions of NNRTI HIVDR (19%) are present which may compromise the effectiveness of the NNRTI drug in standardised first-line regimens.

STI surveillance: *Neisseria gonorrhoeae* was the predominant cause of MUS; and syndromic management with dual antimicrobial therapy, which also covers *Chlamydia trachomatis*, the second most common pathogen, is rational. Herpes simplex virus was the commonest detectable cause of genital ulceration, supporting the continued use of acyclovir in syndromic management. The syndromic management of VDS remains complex: the commonest causes, bacterial vaginosis and candidiasis, are not considered as STIs; however, a significant proportion of patients with either condition were co-infected with STI pathogens. The HIV seroprevalence among STI patients was high, underlining the importance of linkage to universal HIV counselling and testing in primary healthcare settings.

Zoonosis in febrile adults: acute febrile study in adults attending one rural Mpumalanga clinic bordered by the Kruger National Park and where the populations of human, livestock, domestic animals and wildlife are in frequent contact, showed a high seroprevalence of tick bite fever. There was no brucellosis in patients but this area has a good animal brucellosis vaccine programme.

The GERMS-SA publications and effects on policy are as a result of the isolates that your participating laboratories submit. We encourage all laboratory staff to continue participating in the NICD surveillance programmes. We thank the laboratories and clinic staff (and patients) for their ongoing service to the health of all South Africans.

Chris Hani Baragwanath Academic Hospital NHLS laboratory site visit, 9 June 2016

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