

GROUP FOR ENTERIC, RESPIRATORY, AND MENINGEAL DISEASE SURVEILLANCE FOR SOUTH AFRICA (GERMS-SA) REPORT FOR 2012

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Introduction

The 2012 Annual GERMS-SA Report summarizes the findings from national surveillance, including the enhanced surveillance sites (ESS) at 25 hospitals covering all nine of South Africa's provinces. As usual audits were conducted through the NHLS Central Data Warehouse (CDW) and KwaZulu-Natal NHLS laboratories were included in the audits for the first time.

Candidaemia/bacteraemia surveillance was added to the surveillance pathogens in 2012 while *Staphylococcus aureus* enhanced surveillance and rifampicin-resistant tuberculosis surveillance began in September 2012. Only *S. aureus* ESS data for the period September to December 2012 are included in this report. *Klebsiella pneumoniae* surveillance ended in July 2012.

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

Diseases under surveillance in 2012 included:

- Opportunistic infections associated with HIV, e.g. cryptococcosis, invasive non-typhoidal *Salmonella enterica* (NTS) disease and invasive pneumococcal disease (IPD)
- Epidemic-prone diseases, e.g. *Neisseria meningitidis*, *Salmonella enterica* serotype Typhi, *Shigella* species, *Vibrio cholerae*, diarrhoeagenic *Escherichia coli* and rifampicin-resistant

Mycobacterium tuberculosis

- Vaccine-preventable diseases, e.g. *Haemophilus influenzae* type b (Hib), and *Streptococcus pneumoniae*
- Nosocomial infections, e.g. *Staphylococcus aureus*, *Klebsiella* species and *Candida* species

Methods

The methods utilised by the GERMS-SA surveillance programme have previously been described in detail.¹ In brief, approximately 200 South African clinical microbiology laboratories participated in the surveillance programme in 2012. The population under surveillance in 2012 was estimated at 52.3 million (table 1). Diagnostic laboratories reported case patients to the National Institute for Communicable Diseases (NICD) using laboratory case report forms, according to standard case definitions. If available, isolates from case patients were submitted to the NICD for further phenotypic and genotypic characterisation.

From 1 July 2008, surveillance methodology for the cryptococcal project was changed, so that only enhanced surveillance sites, NHLS laboratories in KZN, and laboratories in the private, mining, and military sectors were required to directly report case patients to the NICD. For other cases of cryptococcosis, data were obtained directly from the CDW, which obtains information from the Disa*Lab and TrakCare laboratory information systems. Cryptococcal isolates, obtained from patients at ESS, continued to be characterised by phenotypic and genotypic tests. From July 2010, seven sentinel sites reported cases of *S. aureus* and *Klebsiella*

pneumoniae bacteraemia and, from January 2012, nine sentinel sites reported cases of candidaemia to GERMS-SA. *Klebsiella pneumoniae* surveillance ended in July 2012. Laboratory bacteraemic *S. aureus* surveillance continues at three Gauteng sites only.

Surveillance officers at ESS completed clinical case report forms for patients with laboratory-confirmed diseases including cryptococcosis, invasive salmonellosis, invasive pneumococcal disease, invasive shigellosis, invasive meningococcal disease, invasive *Haemophilus influenzae* disease and candidaemia (from September 2012 *S. aureus* was included at three sites and rifampicin-resistant tuberculosis included at four sites). Report forms were completed by case patient interview or hospital medical record review in order 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 where laboratory, clinical and demographic data from case patients were recorded on a Microsoft Access database. For all diseases under surveillance, except cryptococcosis, the NHLS CDW 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 in the surveillance database and have been included in this report. However, the change-over process from the DISA*lab to TrakCare Lab system proved problematic for auditing purposes and all case numbers may not be reflected.

Disease incidences were calculated using mid-year population estimates for 2011 and 2012 from Statistics South Africa (table 1).² Incidences in the HIV-infected

and AIDS populations were calculated for 2011 and 2012 using estimated population denominators from the Actuarial Society of South Africa (ASSA) 2008 model (table 1), assuming that the HIV/AIDS prevalence amongst cases with known status was similar to that of unknown status.³ All reported incidences are expressed as cases per 100 000 population unless otherwise stated. p-Values were calculated using the Mantel-Haenszel chi-squared test and p values < 0.05 were considered significant throughout.

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

Table 1: Population denominators used to calculate disease incidence rates for 2011 and 2012.

Province	General population*		HIV-infected population**		AIDS population**	
	2011	2012	2011	2012	2011	2012
Eastern Cape	6553889	6586307	715736	736404	60525	64849
Free State	2744120	2748506	351746	355466	35390	36010
Gauteng	12202306	12463886	1215856	1222605	126240	132375
KwaZulu-Natal	10236872	10345539	1576025	1602236	149621	158413
Limpopo	5388120	5452206	409161	423400	32285	36035
Mpumalanga	4022088	4074763	482288	492287	44827	46712
Northern Cape	1143254	1153090	76966	78711	6868	7617
North West	3496855	3546631	431576	436670	44230	45384
Western Cape	5792096	5904017	273114	278889	24533	27595
South Africa	51579600	52274945	5532468	5626668	524519	554990

Data source: *Statistics South Africa; **Actuarial Society of South Africa (ASSA 2008)

References

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2. Statistics South Africa. Mid-year population estimates, South Africa, 2013. P0302. 14 May 2013. Available from: <http://www.statssa.gov.za/publications/P0302/P03022013.pdf> Accessed 20 May 2013
3. Actuarial Society of South Africa AIDS Committee. ASSA2008 AIDS and Demographic Model, March 2011. Available from: <http://aids.actuarialsociety.org.za/ASSA2008-Model-3480.htm> Accessed 20 May 2013

SALMONELLA ENTERICA SEROTYPE TYPHI AND S. ENTERICA SEROTYPES PARATYPHI A, PARATYPHI B AND PARATYPHI C

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Results

Salmonella Typhi isolates from both invasive and non-invasive sites are reported for 2012 in table 2. Cases of enteric fever were highest in October, although there was an unusual peak in July (figure 1). The number of isolates within each age group is shown in table 3. Most isolates were from patients in the 5 – 34 year age group, although infection was also seen in older and younger age groups, including children younger than five years. Ciprofloxacin resistance remained a problem, but azithromycin resistance was

not recorded based on European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines (table 4).¹ One isolate each of *Salmonella* Paratyphi A and of *Salmonella* Paratyphi B var Java was received from the Western Cape Province. These were obtained from a blood culture and a stool culture respectively. Both patients were adult females. Both isolates were susceptible to first and second line antimicrobials. No isolates of *Salmonella* Paratyphi C were received in 2012.

Table 2: Numbers of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA by province, South Africa, 2012. n=63 (including audit reports, missing isolates, mixed and contaminated cultures).

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

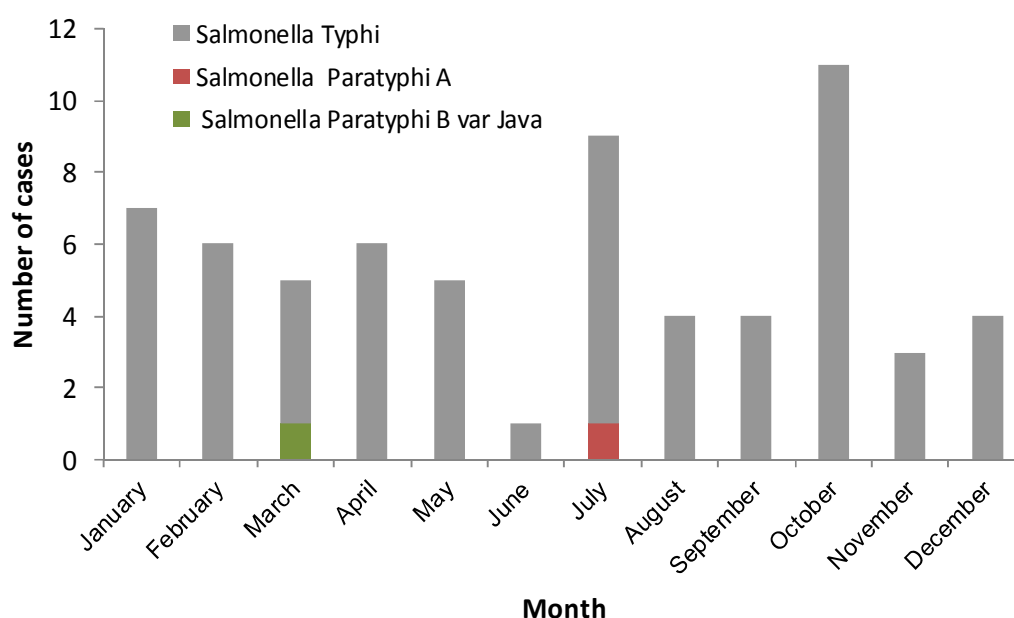


Figure 1: Numbers of non-invasive and invasive cases of *Salmonella* Typhi (n=63) and Paratyphi (n=2) reported to GERMS-SA, by month of specimen collection, South Africa, 2012 (including audit reports).

Table 3: Numbers of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2012. n=63 (including audit reports, missing isolates, mixed and contaminated cultures).

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

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

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

Discussion

Salmonella Typhi isolates from both invasive and non-invasive sites are included in these analyses as both contribute to the burden of infection in South Africa and thus represent a public health risk. However, these data may not reflect the actual burden of disease. Strict seasonality was not observed in 2012, but this may be an artefact of low case numbers. Case detection is compounded by the challenges of alternative diagnostic methods for typhoid fever, which include clinical and

serological techniques. These data thus exclude those patients in whom an alternative diagnosis was made. The number of reported *Salmonella* Typhi isolates should therefore be regarded as an underestimate which precludes the calculation of incidence rates.

EUCAST guidelines for *Salmonella* Typhi provide break points for azithromycin - an alternative treatment option - as ciprofloxacin resistance emerges.¹ Ceftriaxone may also be used as an alternative therapy in these cases.

Reference

1. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 3.1, 2013. <http://www.eucast.org>. Accessed 30 April 2013.

NON-TYPHOIDAL *SALMONELLA* ENTERICA (NTS)

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Results

Invasive disease tends not to have a seasonal prevalence, but increased numbers of non-invasive disease due to NTS in the earlier months of 2012 and again in December reflect seasonality, although a lower peak occurred in the mid-year winter months (figure 2).

The numbers of cases of invasive and non-invasive disease reported to GERMS-SA by province are shown in table 5.

The numbers of cases of invasive and non-invasive disease by age group are shown in table 6.

Most invasive isolates were identified from blood cultures, although isolates were frequently identified from both blood culture and another site such as stool and other normally-sterile sites (table 7). Resistance to first-line antimicrobial agents and to the fluoroquinolones was noted (table 8), as well as extended spectrum beta-lactamase (ESBL) production (119/1721=6.9% of all NTS). *Salmonella enteritidis* was the most common NTS isolated (table 9).

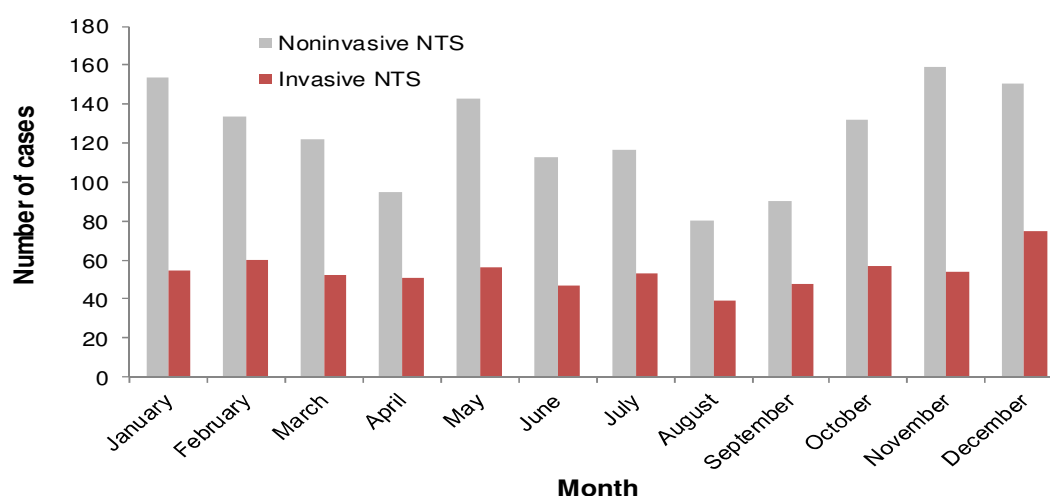


Figure 2: Numbers of non-invasive (n=1490) and invasive (n=647), non-typhoidal *Salmonella* (NTS) cases reported to GERMS-SA by month of specimen collection, South Africa, 2012 (including audit reports).

Table 5: Numbers* of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA by province, SA 2012. n= 2137 (including audit reports, missing isolates, mixed and contaminated cultures).

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

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

Table 6: Numbers of cases and incidence rates for invasive* and non-invasive*, non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2012. n= 2137 (including audit reports, missing isolates, mixed and contaminated cultures).

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

*Incidence rates for non-invasive non-typhoidal *Salmonella* were not calculated because specimens may not have been submitted for culture from all patients with gastroenteritis due to non-typhoidal *Salmonella* in clinical practice;

**Incidence rates are expressed as cases per 100000 population.

Table 7: Numbers of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2012. n=2137 (including audit reports, missing, mixed and contaminated cultures).

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

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

Table 8: Antimicrobial susceptibility test results for all non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2012. n=1721 (excluding audit reports, missing isolates, mixed and contaminated cultures). Clinically relevant antimicrobials for non-invasive and invasive strains are reported.

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

Table 9: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2012. n=1303 (excluding audit reports, missing isolates, mixed and contaminated cultures).

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

Discussion

Non-typhoidal salmonellosis may be a food-borne disease, for which data are poorly captured in South Africa, and where the patients normally present with gastroenteritis, or it may be an AIDS-defining illness, in which case the organism frequently becomes invasive. Seasonal prevalence was noted in 2012 for non-invasive disease. However, an unusual peak in case numbers between May and July in non-invasive

isolates reflects a nosocomial outbreak of *Salmonella* gastroenteritis in the Eastern Cape, rather than seasonality.¹ Incidence rates have only been calculated for invasive NTS due to differences in stool-taking practices in adult and paediatric medical care. Antimicrobial resistance remains a cause for concern in invasive and non-invasive cases. *Salmonella enteritidis* was the commonest serotype, as also noted in 2011.²

References

1. Smith AM, Mthanti MA, Haumann C, Tyalisi N, Sooka A, Keddy KH. GERMS-SA Surveillance Network. Nosocomial outbreak of *Salmonella typhimurium* primarily affecting a paediatric ward, South Africa, 2012 (manuscript in preparation).
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SHIGELLA SPECIES

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Results

Slightly increased numbers of *Shigella* isolates from January to April 2012 suggest seasonality (figure 3). Although the primary burden of disease due to *Shigella* is non-invasive dysentery or diarrhoea, invasive disease remains an important cause of morbidity in South Africa (table 10). The predominant burden of disease, including both invasive and non-invasive shigellosis, is in the under-five-year age group (table 11). Quinolone resistance remains low, but fluoroquinolone resistance appears to be emerging (table 12). Extended spectrum

beta-lactamase (ESBL) production is rarely documented but remains important. Four (0.3%) of 1433 *Shigella* isolates were ESBL-producers. Of these, a single *S. flexneri* 6 was from a blood culture in an adult; the remainder were from non-invasive specimens from children less than five years of age. Predominant serotypes confirm that *S. sonnei* remains the most common cause of shigellosis in South Africa (table 13). *Shigella dysenteriae* type 1 was not isolated in 2012 (data not shown).

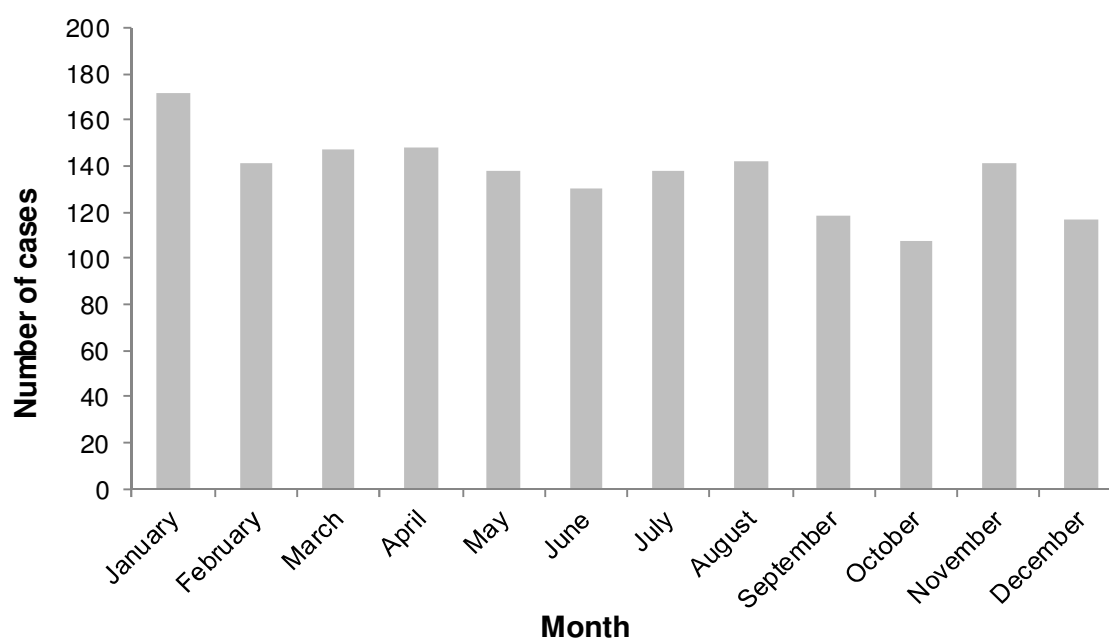


Figure 3: Numbers of *Shigella* isolates reported to GERMS-SA by month of specimen collection, South Africa, 2012. n=1639 (including audit reports).

Table 10: Numbers of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2012. n=1639 (including audit reports, missing isolates, mixed and contaminated cultures).

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

Table 11: Numbers of cases* and incidence rates for *Shigella* (invasive and non-invasive)** reported to GERMS-SA by age category, South Africa, 2012. n=1639 (including audit reports, missing isolates, mixed and contaminated cultures).

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

*Cases may be under-reported due to local clinical practices: no mixed infections were identified.

**Incidence rates are expressed as cases per 100 000 population.

Table 12: Antimicrobial susceptibility test results for *Shigella* isolates received by GERMS-SA, South Africa, 2012. n=1433 (excluding audit reports, missing isolates, mixed and contaminated cultures). Clinically relevant antimicrobials for non-invasive and invasive strains are reported.

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

Table 13: Commonest invasive and non-invasive *Shigella* serotypes reported to GERMS-SA by province, South Africa, 2012. n=1476 (excluding audit reports, missing isolates, mixed and contaminated cultures).

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

Discussion

Shigella infections are primarily associated with water-borne outbreaks in South Africa, although person-to-person transmission may also play a role.

Resistance to fluoroquinolones remains low, but should be monitored continually. ESBL-production is rarely documented but must also be continually monitored as

ESBL-producing subtypes appear common to those identified in other nosocomial pathogens.¹ Although *S. dysenteriae* type 1 isolates were not reported in South Africa in 2012, the potential for future epidemics remains in those instances where there is an absence of safe water and adequate sanitation, and because a vaccine is not available.

Reference

1. Tau NP, Smith AM, Sooka A, Keddy KH for GERMS-SA. Molecular characterization of extended-spectrum beta-lactamase-producing *Shigella* isolates from humans in South Africa, 2003-2009. *J Med Microbiol.* 2012 61 (Pt 1):162-4.

DIARRHOEAGENIC *ESCHERICHIA COLI* (DEC)

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Results

An increased number of *Escherichia coli* cases were identified in October and November 2012 (figure 4). Enteropathogenic *E. coli* (EPEC) remains the commonest cause of diarrhoea in South Africa (table 14). Most

cases were identified in children less than 5 years of age (table 15). No specific serotypes predominated. Among the enterohaemorrhagic or Shiga-toxicogenic *E. coli* (EHEC/STEC) isolates, two sorbitol-negative *E. coli* O157 were received (data not shown).

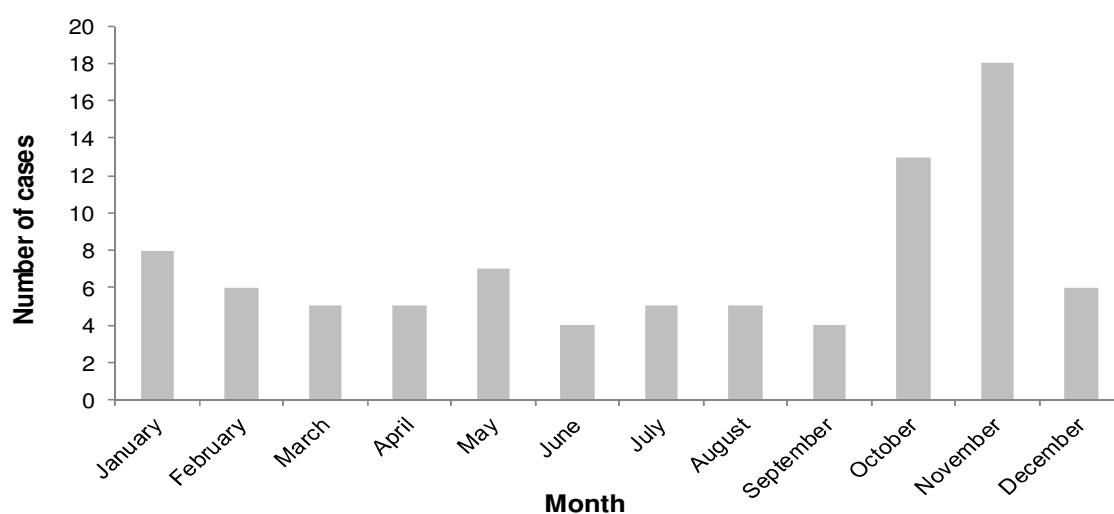


Figure 4: Numbers of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by month of specimen collection, South Africa, 2012. n=86.

Table 14: Numbers of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by province, South Africa, 2012. n=86.

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

DAEC=diffusely-adherent *E. coli*; EAggEC=enteroaggregative *E. coli*; STEC/EHEC=Shiga-toxigenic *E. coli* or enterohaemorrhagic *E. coli*; EIEC=enteroinvasive *E. coli*; EPEC=enteropathogenic *E. coli*; ETEC= enterotoxigenic *E. coli*.

*Mixed pathotype: contained virulence genes from more than one pathotype.

Table 15: Numbers of diarrhoeagenic *E. coli* isolates reported to GERMS-SA by age category, South Africa, 2012. n=86.

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

DAEC=diffusely-adherent *E. coli*; EAggEC=enteroaggregative *E. coli*; STEC/EHEC=Shiga-toxigenic *E. coli* or enterohaemorrhagic *E. coli*; EIEC=enteroinvasive *E. coli*; EPEC=enteropathogenic *E. coli*; ETEC= enterotoxigenic *E. coli*.

*Mixed pathotype: contained virulence genes from more than one pathotype.

Discussion

Fewer isolates were received in 2012 than in previous years, possibly due to financial constraints within the health care system,¹ but there is a suggestion of seasonality with increased case numbers in the last quarter of 2012. The predominance of cases in children under five years of age may reflect, in part, specimen-taking practices, as well as the burden of diarrhoeal disease in this age group. Incidence rates were not calculated as numbers of cases were not considered to be fully representative. The actual burden of disease

due to diarrhoeagenic *E. coli* is probably greatly underestimated in South Africa because management is primarily syndromic and centres on rehydration. As a consequence, clinicians are unlikely to prioritise stool-taking in uncomplicated cases of diarrhoea.

Disease in the past appears to have been primarily water-borne due to high levels of faecal contamination in water sources, and this trend appears to be continuing. The identification of EHEC/STEC was primarily incidental, as there are currently no useful biochemical markers in sorbitol-positive isolates.²

References

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2. Werber D, Frank C, Wadl M, Karch H, Fruth A, Stark K. Looking for tips to find icebergs - surveillance of haemolytic uraemic syndrome to detect outbreaks of Shiga toxin-producing *E. coli* infection. 2008. Available from http://www.eurosurveillance.org/edition/v13n09/080228_4.asp. Accessed 25 March 2010.

VIBRIO CHOLERAЕ O1

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

CRYPTOCOCCUS SPECIES

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Results

During 2012, 6817 case patients with laboratory-confirmed cryptococcal episodes were reported. The incidence of cryptococcal disease in the HIV-infected population has decreased in the Eastern Cape, Free State, Limpopo, Mpumalanga and North West provinces and has increased in Gauteng, Northern Cape and Western Cape provinces (table 16). The highest incidence was recorded amongst patients aged 35-39 years: 31 cases per 100 000 persons in the general population (figure 5). One hundred and fifty-five children younger than 15 years had laboratory-confirmed cryptococcosis; 72/155 (46%) were younger than 5 years of

age. Where gender was recorded (6748/6817, 99%), 47% of patients were female. Most patients (89%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 9% were diagnosed with fungaemia (table 17). Ninety-six patients were diagnosed using cultures of urine, sputum, pleural fluid and other specimen types. At enhanced surveillance sites, 1920 patients were diagnosed with cryptococcosis, with viable isolates received from 1177 (61%) patients. Isolates were speciated from all these cases; 1131 (96%) were identified as *Cryptococcus neoformans* and 46 (4%) were identified as *C. gattii*. Cases of *C. gattii* disease were diagnosed in seven

provinces: Gauteng (n=18), Mpumalanga (n=14), Kwa-Zulu-Natal (n=5), North West (n=4), Limpopo (n=2), Free State (n=2) and Western Cape (n=1). The in-hospital case-fatality ratio for patients at enhanced surveillance

sites did not change significantly between 2011 and 2012 [463/1476 (31%) vs. 529/1639 (32%) respectively, P=0.6].

Table 16: Numbers of cases and incidence of cryptococcal disease detected by GERMS-SA by province, South Africa, 2011 and 2012. n=13 367.

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

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

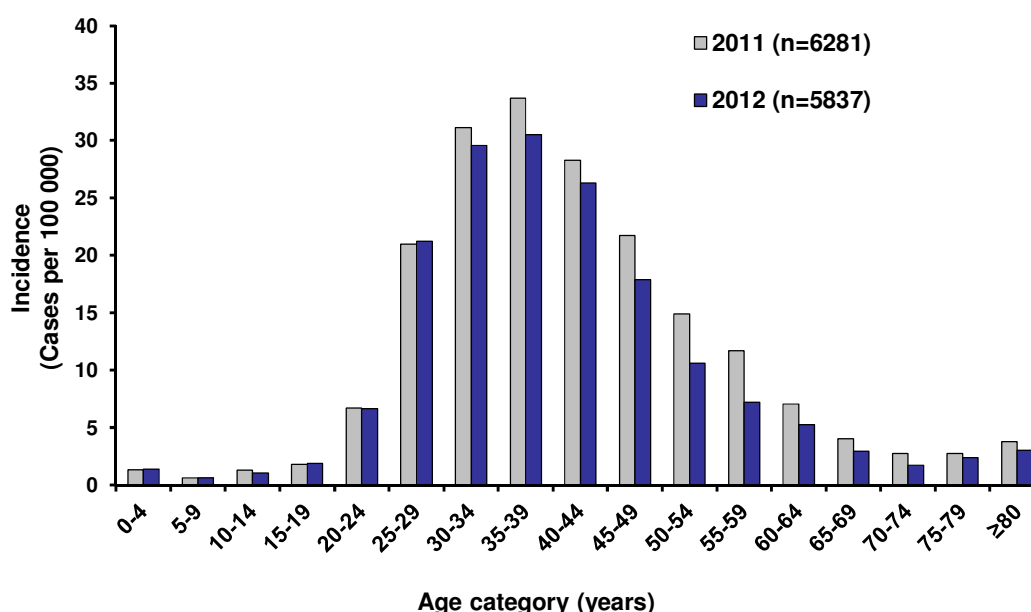


Figure 5: Incidence of laboratory-confirmed cryptococcal disease reported to GERMS-SA by age category, South Africa, 2011 and 2012. n=12 118 (age unknown for 1249 cases).

Table 17: Numbers and percentages of cases of cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012. n=13 367.

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

Discussion

The burden of laboratory-confirmed cryptococcal disease was again high in 2012 with an overall incidence of 119 cases per 100 000 HIV-infected persons. Approximately 300 more cases were detected by GERMS-SA in 2012 compared with 2011. This increase was largely due to improved surveillance case detection in 2012 which included NHLS laboratories in KwaZulu-Natal for the first time. However, the surveillance audit may not have detected all cases in KwaZulu-Natal because some laboratories there do not use an electronic laboratory information system. Furthermore, during the changeover from DISA*Lab to TrakCare Lab some cases may not have been detected by the central data warehouse (CDW). Hence the decrease in cryptococcosis incidence may not be a true reflection of disease burden but rather an artefact of the laboratory information system.

The GERMS-SA programme now undertakes annual national audits of all public-sector laboratories. Most patients continued to be diagnosed with meningitis. More men were diagnosed with cryptococcal disease than women. This may reflect a lower *Anti-Retroviral Therapy* (ART) coverage and initiation of ART at low CD4+ T-lymphocyte counts among South African men. *Cryptococcus neoformans* was the predominant pathogen causing disease and the small number of patients who were infected with *C. gattii* were diagnosed from across the country. The in-hospital case-fatality ratio remained high and unchanged. Implementation of cryptococcal screening to detect disease earlier could potentially change the epidemiology of disease and reduce mortality.

CANDIDA SPECIES

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Results

In 2012, 532 cases of candidaemia were detected from nine sentinel hospitals (table 18). The vast majority of cases occurred among children aged 0-4 years and 146 (29%) of all cases occurred among neonates (≤ 28 days of age) (figure 6). Where gender was known, 54% (282/519) of patients were male. Clinical data were collected for 351 (66%) patients. The overall crude case-fatality ratio was high (145/347; 42%).

Although HIV infection is not an independent risk factor for candidaemia, 19% (46/247) of patients who were diagnosed with candidaemia were also HIV-infected. In total, 528 viable isolates were processed in the reference laboratory and at least one viable isolate was available for 410 (77%) cases of candidaemia.

Overall, *Candida albicans* was the most common species followed by *C. parapsilosis* and *C. glabrata*. Species distribution differed significantly between Gauteng and Western Cape provinces (table 19). All *Candida* isolates had an amphotericin B minimum inhibitory concentration (MIC) ≤ 1 $\mu\text{g/ml}$ (apart from two *C. krusei* isolates with an MIC of 2 $\mu\text{g/ml}$). Susceptibility results for five common *Candida* species and three antifungal drugs are summarised in table 20. The percentage of *C. parapsilosis* isolates that were susceptible to fluconazole ((27/130 (21%) vs. 7/11 (64%); $P=0.001$)) and voriconazole ((38/130 (30%) vs. 10/11 (91%); $P<0.001$)) differed significantly between Gauteng and the Western Cape respectively.

Table 18: Numbers of cases of candidaemia detected by GERMS-SA by enhanced surveillance site, Gauteng and Western Cape provinces, South Africa, 2012. n=532.

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

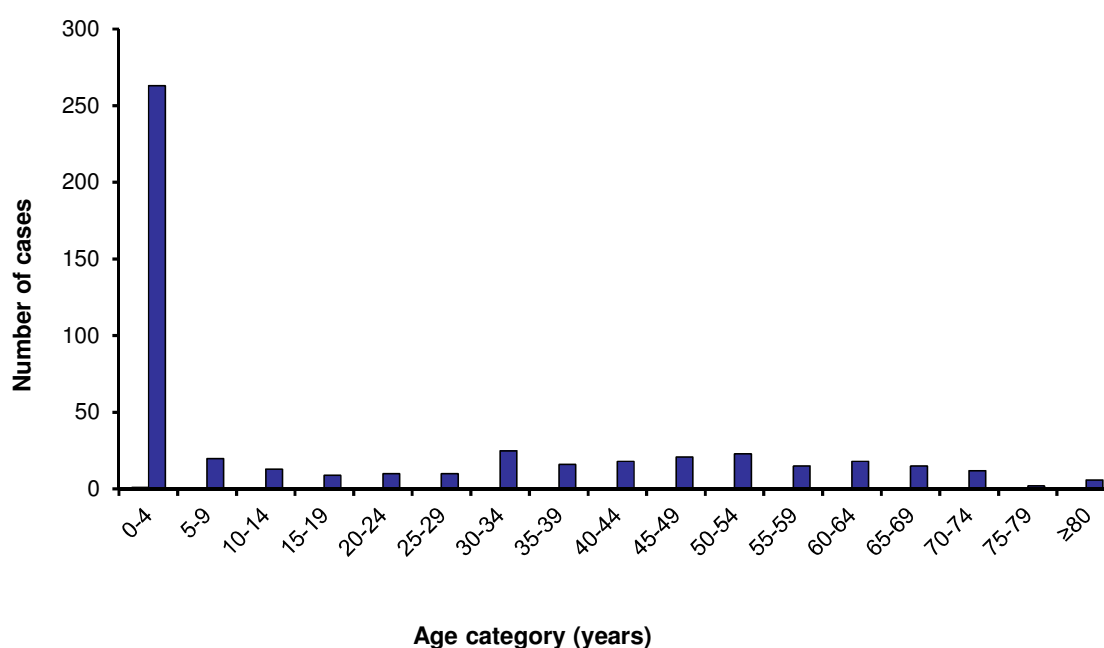


Figure 6: Numbers of cases of laboratory-confirmed candidaemia reported to GERMS-SA by age category, Gauteng and Western Cape provinces, South Africa, 2012. n=496 (age unknown for 36 cases).

Table 19: *Candida* species distribution by candidaemia cases with a viable bloodstream isolate, Gauteng and Western Cape provinces, South Africa, 2012. n=410.

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

Table 20: Numbers and percentages* of *Candida* bloodstream isolates (five commonest species only) susceptible to fluconazole, voriconazole and caspofungin by broth microdilution testing, Gauteng and Western Cape provinces, South Africa, 2012. n=391.

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

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

Discussion

Culture-confirmed candidaemia represents the tip of the iceberg for this common hospital-associated infection because blood culture is an insensitive means of diagnosis. Despite this limitation, enhanced surveillance has provided insight into the clinical epidemiology of candidaemia diagnosed at mostly public-sector hospitals in two provinces. Overall, most cases of candidaemia were diagnosed among young children, predominantly neonates, and almost half of patients died in hospital.

The epidemiology of candidaemia is clearly different between Gauteng and Western Cape. In Gauteng, *C.*

albicans and *C. parapsilosis* were detected in equal proportions whereas *C. albicans* and *C. glabrata* were the two most common species in the Western Cape. Knowledge of local hospital or hospital unit epidemiology should guide empiric treatment choices. In Gauteng, amphotericin B remains the empiric drug of choice for candidaemia because of the high prevalence of azole-resistant *C. parapsilosis* isolates. Caspofungin is also a reasonable choice in settings where this drug is available. In the Western Cape, high-dose fluconazole or amphotericin B are both reasonable choices for empiric treatment of candidaemia.

NEISSERIA MENINGITIDIS

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Results

In 2012, 191 cases of meningococcal disease were reported and an additional 39 cases were identified on audit, giving a total of 230 cases of laboratory-confirmed meningococcal disease identified by the surveillance system through the year in South Africa (table 21). Overall incidence decreased from that of 2011 (0.66 cases per 100,000 population in 2011 compared to 0.44/100,000 in 2012, $P < 0.001$). The number of cases reported was greatest during the winter and spring months (figure 7). Of all cases reported, cerebrospinal fluid (CSF) was the most common specimen yielding

meningococci (table 22), and the number of cases diagnosed on blood culture was similar in 2012 compared to that of 2011 ($P = 0.3$). Meningococcal Serogroup W was the most predominant in South Africa (72/176, 41%) (table 23), and the proportion of cases recorded in 2012 was similar to that of 2011 (137/275, 50%; $P = 0.08$). Minor year-on-year fluctuations of disease by province were noted. Rates of disease were highest in the Western and Eastern Cape (table 21). In Gauteng, the incidence of meningococcal disease was estimated at 0.62/100 000, and most cases were

attributed to serogroup W (29/56, 52%). In the Western Cape, serogroup B was the most common (21/45, 47%). Risk of disease was greatest amongst children less than five years of age. Age and serogroup-specific incidence rates show that infants were at greatest risk of disease for the three most common serogroups (figure 8). Preliminary analysis of case-fatality ratios, as calculated

at enhanced surveillance sites where in-hospital outcome was specifically recorded, was 7/76 (9%) in 2012, which is lower but not significantly different from the 19/105 (18%) recorded in 2011 (P=0.1). Of the viable isolates tested for antimicrobial resistance, 5% (6/129) had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and are considered non-susceptible.

Table 21: Numbers of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2011 and 2012. n=570 (including audit cases).

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

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

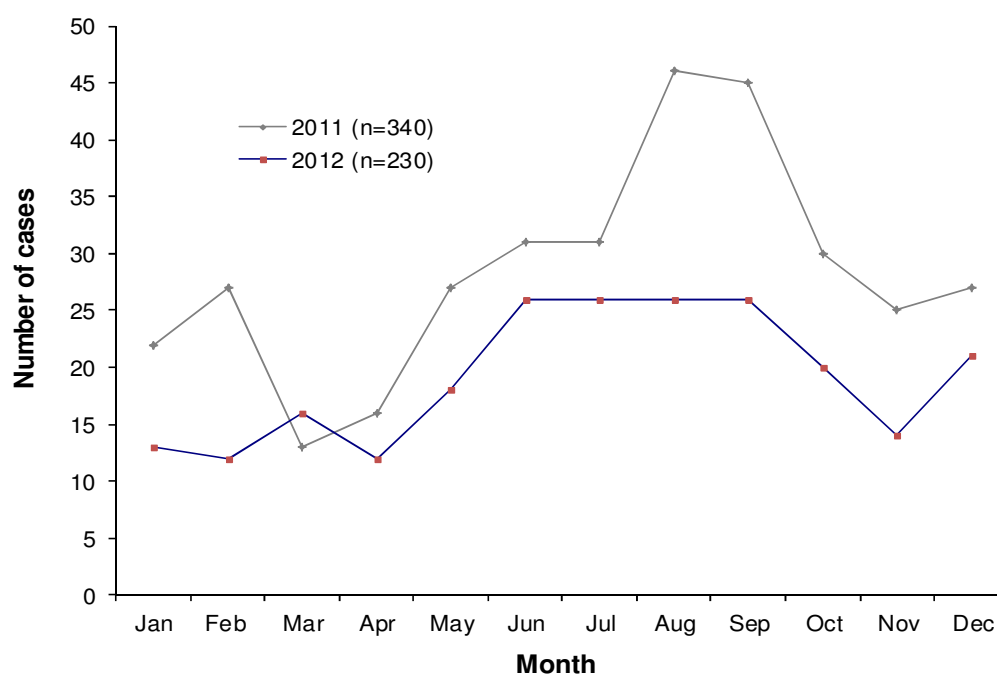


Figure 7: Numbers of laboratory-confirmed, invasive, meningococcal cases reported to GERMS-SA by month and year, South Africa, 2011-2012. n=570.

Table 22: Numbers and percentages of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012. n=570.

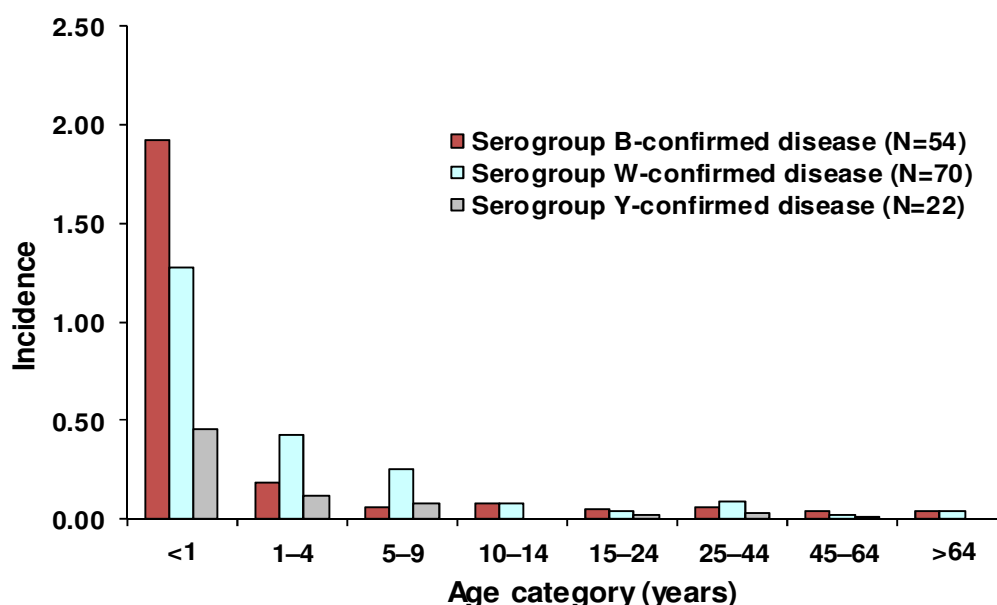
Site of specimen	2011		2012	
	n	%	n	%
CSF	254	75	162	70
Blood	84	25	67	29
Other	2	0.6	1	0.4
	340		230	

Table 23: Numbers of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2012. n=230*.

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

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

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



Incidence was calculated using population denominators from Statistics South Africa and is expressed as cases per 100 000 persons in the general population. *Other serogroups: serogroup A, n=2; serogroup C, n=21; non-groupable, n=2.

Discussion

The incidence of meningococcal disease continues to decline in all provinces except the Western and Eastern Cape. Serogroup W disease remained the predominant serogroup. Changes in meningococcal disease incidences in the provinces may reflect changes in the capability to confirm disease in the laboratory as well as changes in reporting to the surveillance network, or may reflect true changes in incidence.

Case-fatality ratios have not changed significantly compared with those of 2011. The prevalence of non-susceptibility to penicillin remained low in 2012. The clinical relevance of increased MICs is unclear, and penicillin is, at present, still being recommended as the drug of choice for therapy for confirmed meningococcal disease.

Haemophilus influenzae

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Results

A total of 229 cases of *Haemophilus influenzae* invasive disease was reported in 2012. An additional 98 cases were identified during the national audit giving a total of 327 cases for analysis. Of these, 192 (59%) isolates or specimens were available for serotyping, and 69/192 (36%) were confirmed as serotype b (table 24). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (43/69, 62% vs. 6/88, 7%, $P < 0.001$) (table 25). In 2012, a total of 49 cases of *H. influenzae* serotype b (Hib) was reported

amongst children <5 years (figure 9). Serotype b was the commonest serotype of *H. influenzae* causing disease amongst infants (figure 10). Rates of Hib disease as recorded by the surveillance network amongst infants <1 year of age were similar over the period 2009 to 2012 (chi-squared test for trend, $P = 0.2$) (figure 11). Twenty-three percent (11/47 isolates tested) of serotype b strains were non-susceptible to ampicillin (MIC > 1 mg/L, all producing beta lactamase), and 9% (7/75) of non-typeable strains were non-susceptible.

Table 24: Numbers of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2012. n=327*.

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

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

Table 25: Numbers and percentages of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2012. n=327.

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

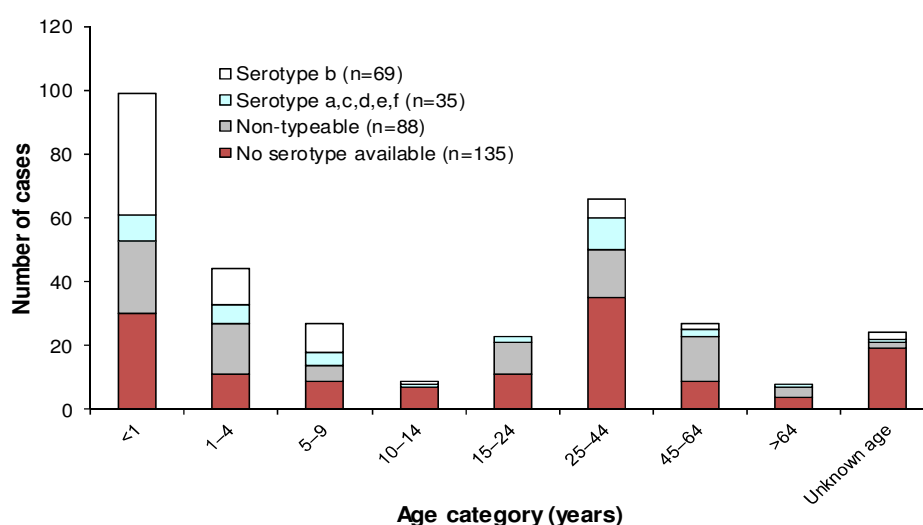
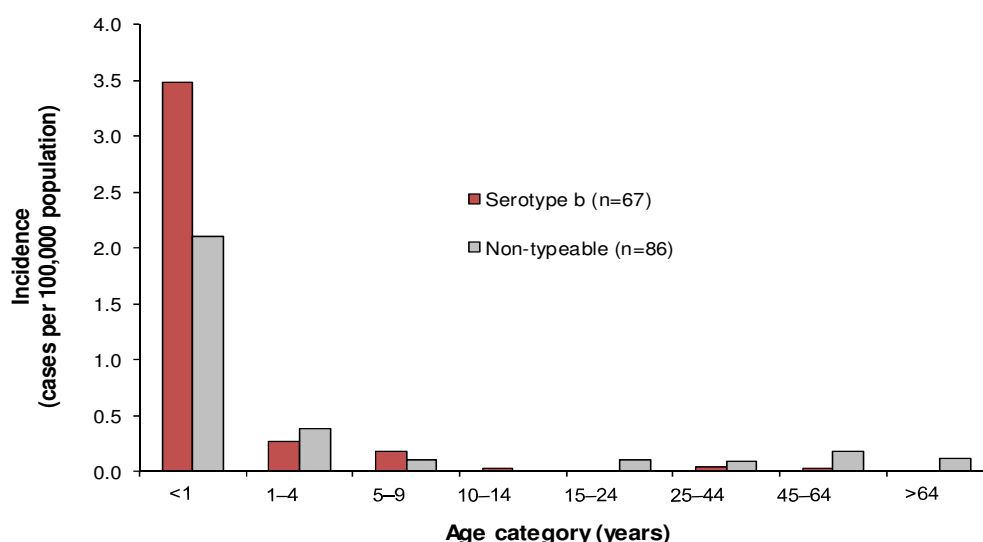


Figure 9: Numbers of laboratory-confirmed, invasive *Haemophilus influenzae* cases reported to GERMS-SA by serotype and age group, South Africa, 2012. n=327 (age unknown n=24; specimens or viable isolates unavailable for serotyping n=135).

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



*Other serotypes from cases with age known, n=34.

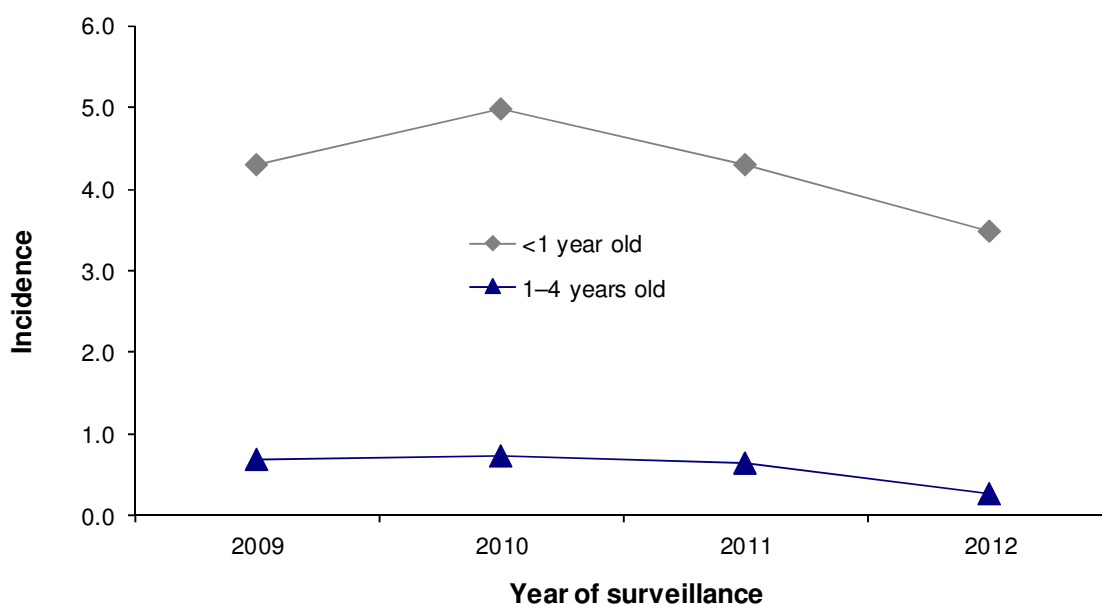


Figure 11: Incidence rates of laboratory-confirmed *Haemophilus influenzae* serotype b disease reported to GERMS-SA in children <5 years old, South Africa, 2009-2012. Incidence was calculated using population denominators from Statistics South Africa and has been expressed as cases per 100 000 persons in the general population.

Discussion

Since the introduction of the Hib conjugate vaccine into the Expanded Programme on Immunisation (EPI) for South Africa in 1999 there has been a reduction in cases reported due to this serotype.¹ Population-based studies in South Africa prior to the introduction of the conjugate Hib vaccine showed annual rates of invasive Hib disease of 170 per 100 000 infants below one year of age,^{2,3} and any increases noted recently were small in comparison to the substantial decline in disease subsequent to the introduction of the vaccine. Recognising that the surveillance system underestimates disease, reported cases of Hib disease amongst children <1 year are being monitored carefully.

In April 2009 the updated infant vaccination programme in South Africa introduced a booster dose of conjugate Hib vaccine given at 18 months as part of a combination

vaccine (Pentaxim: diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*Haemophilus influenzae* type-b conjugate). The first children to benefit from this would have received a dose in November 2010. It is hoped that this booster will improve long-term protection against disease and exert an impact on ongoing Hib transmission.⁴

Rates of Hib in children <1 year have stabilised during the last four years. This could be related to interventions such as improved prevention and treatment of HIV in infants, the introduction of the booster dose of Hib vaccine, or changes in diagnosis and reporting of cases. More data are needed to evaluate the relative contribution of each of these factors and we urge clinical and laboratory staff to continue reporting all cases of *H. influenzae*.

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STREPTOCOCCUS PNEUMONIA

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Results

The 7-valent polysaccharide-protein conjugate pneumococcal vaccine (PCV-7) was introduced into the Expanded Programme on Immunisations (EPI) in South Africa from 1 April 2009. In April 2010, this vaccine was replaced by the 13-valent formulation (PCV-13).

The incidence of reported invasive pneumococcal disease (IPD) varied widely by province (table 26). The age group at highest risk of disease in South Africa was infants <1 year of age. There has been an ongoing significant reduction in disease since 2009 (chi-squared test for trend, $P < 0.001$) (figure 12).

The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (table 27). The prevalence of non-susceptible strains ranged from 22% to 36% in different provinces (table 28). Penicillin non-susceptible isolates were most common amongst children less than 5 years of age (Figure 13).

Ceftriaxone non-susceptibility was detected amongst 5% (117/2160) of all IPD cases, and no reduction was seen since 2011 (5%, 126/2409). Amongst isolates from CSF specimens, 4% (31/834) were non-susceptible.

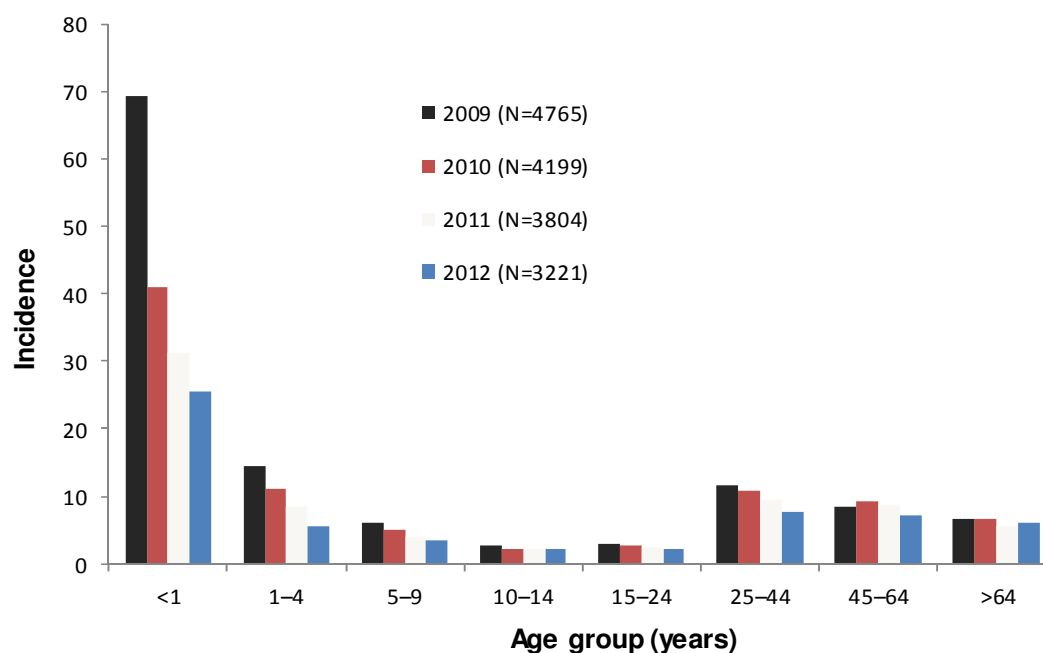
The numbers of cases amongst children less than 5 years of age due to common serotypes for the period 2009-2012 are shown in Figure 14. The percentages of disease in 2012 amongst children less than 5 years of age due to PCV7 and newer valency vaccine formulations are shown in table 29. The number of isolates in this age group available for serotyping has decreased in over the last four years (1009/1337 [75%] in 2009, 649/909 [71%] in 2010, 468/680 [69%] in 2011 and 353/509 [69%] in 2012).

Table 26: Numbers of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2011 and 2012. n=7025.

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

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100000 population.

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



2009: age unknown n=163; 2010: age unknown n=142; 2011: age unknown n=219; 2012: age unknown n=256. Incidence was calculated using population denominators from Statistics South Africa and has been expressed as cases per 100 000 persons in the general population.

Table 27: Numbers and percentages of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2011 and 2012. n=7025.

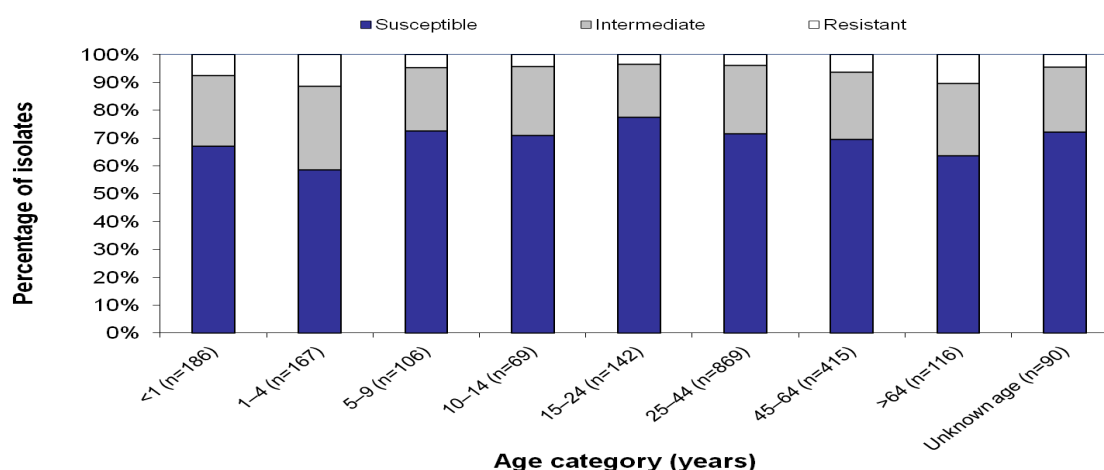
Site of specimen	2011		2012	
	n	%	n	%
CSF	1580	42	1383	43
Blood	1785	47	1501	47
Other	439	11	337	10
	3804		3221	

Table 28: Numbers and percentages of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2012. n=3221.

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

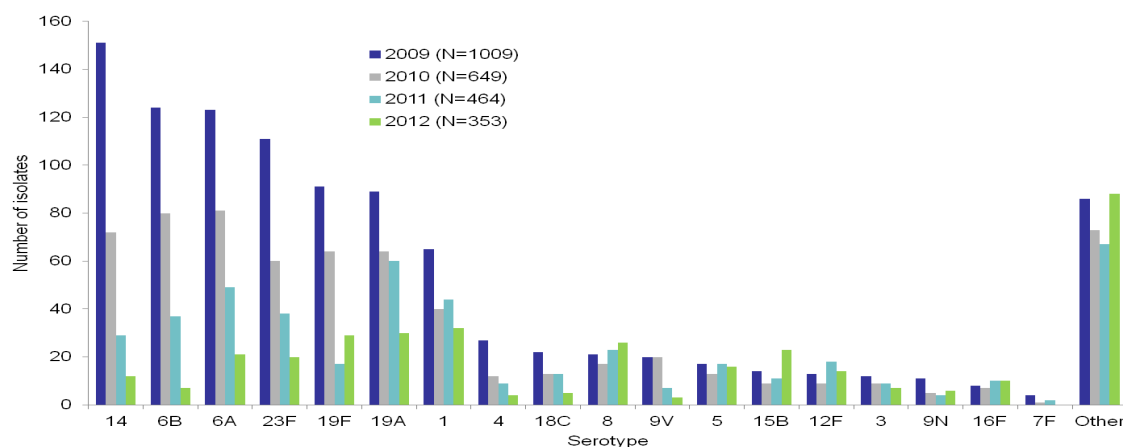
*2012 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤ 0.06 mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥ 2 mg/L.

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



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

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



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

Table 29: Numbers and percentages of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2012. n=508 (n=353 with viable isolates).

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

*7-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F; 10-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F; 13-valent serotypes: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A.

Cross-protection with 6B has been demonstrated.¹

Discussion

Differences in invasive pneumococcal disease incidence by province have been documented for several years, and are partly due to differences in specimen-taking practices and laboratory reporting. However, real differences in disease incidence cannot be excluded. The decreases in incidence of disease in children <1 year of age are partly due to the introduction of PCV7 in South Africa.

When surveillance data are analysed by HIV-coinfection, vaccine and non-vaccine serotypes have

decreased in HIV-infected infants, suggesting that HIV prevention and treatment improvements have also substantially impacted on this opportunistic disease.²

Clinicians are urged to continue taking relevant specimens when pneumococcal disease is suspected and laboratorians are urged to send all pneumococci isolated from normally sterile site specimens. Ongoing surveillance will assist in evaluating pneumococcal disease in South Africa at this time of multiple interventions.

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1. Whitney CG, Pilishvili T, Farley MM, Schaffner W, Craig AS, Lynfield R, et al. Effectiveness of seven-valent pneumococcal conjugate vaccine against invasive pneumococcal disease: a matched case-control study. *Lancet* 2006; 368(9546):1495-502.
2. Nunes MC, von Gottberg A, de Gouveia L, Cohen C, Moore DP, Klugman KP, Madhi SA. The impact of antiretroviral treatment on the burden of invasive pneumococcal disease in South African children: a time series analysis. *AIDS* 2011; 25:453-62.

CASE-CONTROL STUDY TO ESTIMATE EFFECTIVENESS OF A PNEUMOCOCCAL CONJUGATE VACCINE (PCV) AGAINST INVASIVE PNEUMOCOCCAL DISEASE (IPD) IN SOUTH AFRICA

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A case-control study to assess the effectiveness of the 7-valent pneumococcal conjugate vaccine (PCV-7) against invasive pneumococcal disease (IPD) was conducted from March 2010 through November 2012. Preliminary results were described in the 2011 GERMS-SA annual report.¹

PCV-13 replaced PCV-7 in June 2011. Since this time a study designed to evaluate the effectiveness of PCV-13 against laboratory confirmed vaccine-serotype IPD compared to no vaccination among HIV-infected and -uninfected children eligible to receive PCV through the routine vaccination programme in South Africa has been conducted. Up to 12 June 2013 for the PCV-13 study, 178 children <5 years of age were screened and all were age-eligible. Of the age-eligible cases, 117 have completed enrolment of cases and controls. These case-control sets consist of 98 HIV-uninfected cases with

518 controls, and 19 HIV-infected cases with 82 controls. Overall, HIV-uninfected cases have a higher average number of controls per case (5.3 controls) than HIV-infected cases (4.3 controls).

The numbers of HIV-infected cases enrolled into the PCV-13 component of the study was lower than projected. This decrease in HIV-infected IPD cases is possibly due to the improved Prevention-of-Mother-to-Child-Transmission (PMTCT) programme and increased access to antiretroviral treatment for children. New case enrolment sites have been added in order to try and address the decrease in numbers of HIV-infected cases. The enrolment of HIV-infected controls has also proved challenging for the above reasons, but has improved significantly with the inclusion of HIV clinics as a source of controls.

Reference

1. Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa. GERMS-SA Annual Report 2011. Available from: <http://www.nicd.ac.za/units/germs/germs.htm>. Accessed 30 April 2013.

KLEBSIELLA PNEUMONIAE

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Results

In 2012 higher numbers of *Klebsiella pneumoniae* (KP) were recorded through GERMS-SA surveillance than *Staphylococcus aureus* (SA) isolates, particularly in Gauteng province (figure 15). From January through July 2012, 1426 cases of *K. pneumoniae* bloodstream infections were reported (table 30). The highest number of cases (n=843; 59%) was detected from Gauteng province (table 30). The lowest numbers of cases were

detected during winter (June-July) although distribution was high throughout the year (figure 16). Of the viable *K. pneumoniae* isolates tested for antimicrobial resistance, 239 (75%) were extended spectrum β -lactamase (ESBL) producers (figure 17). A total of 160 (50%) isolates was susceptible to ciprofloxacin, 292 (92%) to tigecycline, 297 (94%) to ertapenem and 202 (65%) to piperacilli/tazobactam (table 31).

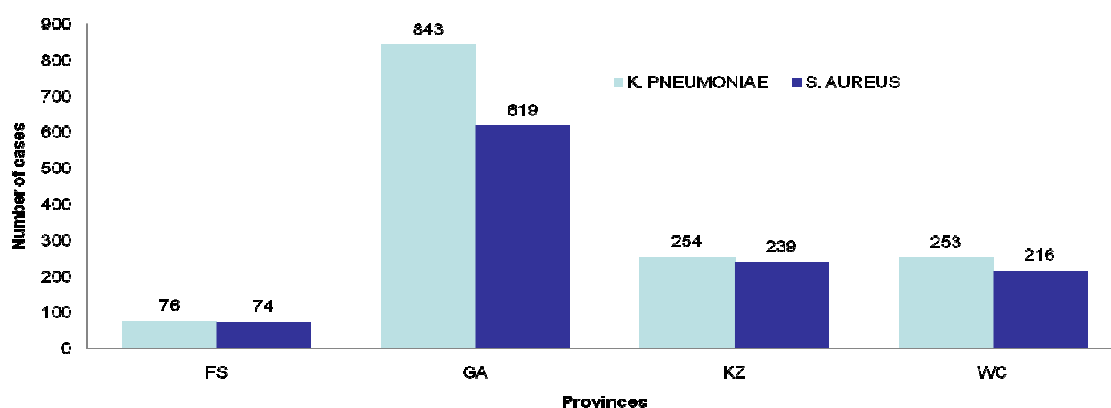


Figure 15: Numbers of cases of laboratory-confirmed *Klebsiella pneumoniae* (1426) and *Staphylococcus aureus* (1148) bacteraemia reported to GERMS-SA sentinel sites by province, South Africa, January - July 2012. FS=Free State, GA=Gauteng, KZ=Kwazulu-Natal, WC=Western Cape.

Table 30: Number of *Klebsiella pneumoniae* cases reported to GERMS-SA sentinel sites by province, South Africa, January-July 2012. n=1426 (including audit cases).

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

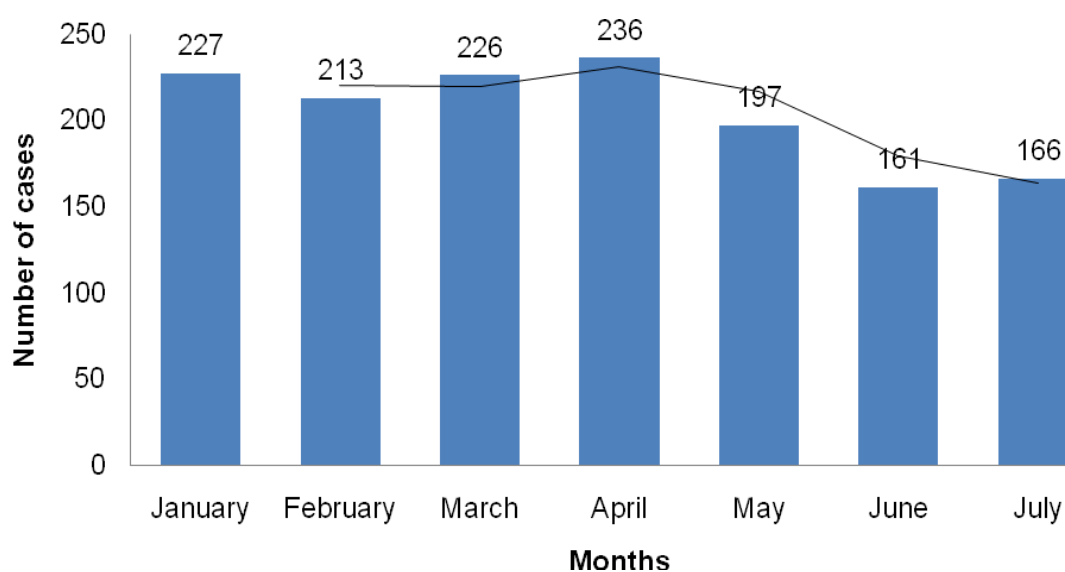


Figure 16: Numbers and trend line of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA from sentinel sites by month, January - July 2012. n=1426.

Table 31: Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites by antimicrobial susceptibility and province, South Africa, January-July 2012. n=317.

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

S= susceptible to antimicrobial agents; NS = non susceptible.

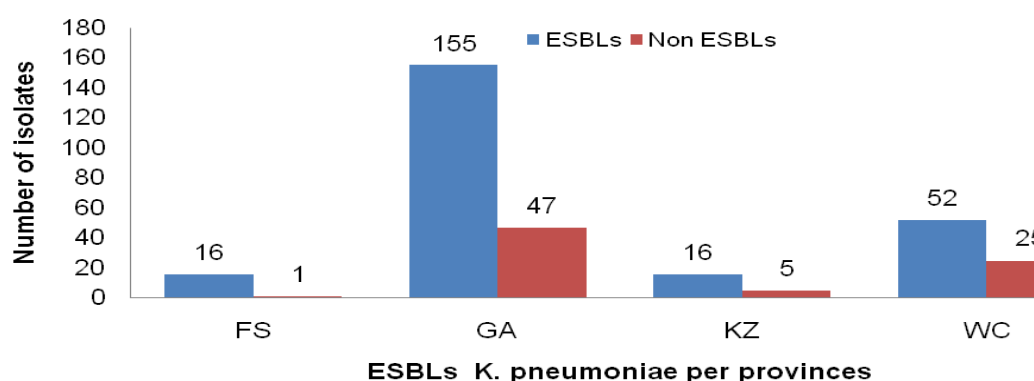


Figure 17: Numbers of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites, by extended spectrum β -lactamase (ESBL) production, January-July 2012. n=317. FS=Free State, GA=Gauteng, KZ=Kwazulu-Natal, WC=Western Cape.

Discussion

Sentinel surveillance for *K. pneumoniae* bacteraemia was initiated in July 2010 through GERMS-SA. In 2012, over 70% of the isolates were submitted to the reference laboratory. Amongst these, two-thirds were ESBL

producers. *Klebsiella pneumoniae* isolates were distributed almost equally throughout the year with a decline in trend during the winter months in all four provinces.

STAPHYLOCOCCUS AUREUS

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Results

The number of cases of *Staphylococcus aureus* bacteraemia reported to GERMS-SA from January through July 2012 was 1148 (table 32). Of these, the majority were detected from sentinel sites in Gauteng (54%), followed by KwaZulu-Natal (21%) and Western Cape provinces (19%) (table 32). The numbers of cases were equally distributed throughout the year, although there

was a decline during autumn which then increased through the winter months (figure 4). Resistance to oxacillin (MRSA) was detected in 289 (44%) isolates. *Staphylococcus aureus* was susceptible to vancomycin in 99.4% of isolates and clindamycin in 82% of isolates. Three non-susceptible vancomycin isolates were noted in 2012. Ninety-six percent of isolates were susceptible to mupirocin (table 33).

Table 32: Numbers of *Staphylococcus aureus* cases reported to GERMS-SA sentinel sites by province, South Africa, January - July 2012. n=1148 (including audit cases).

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

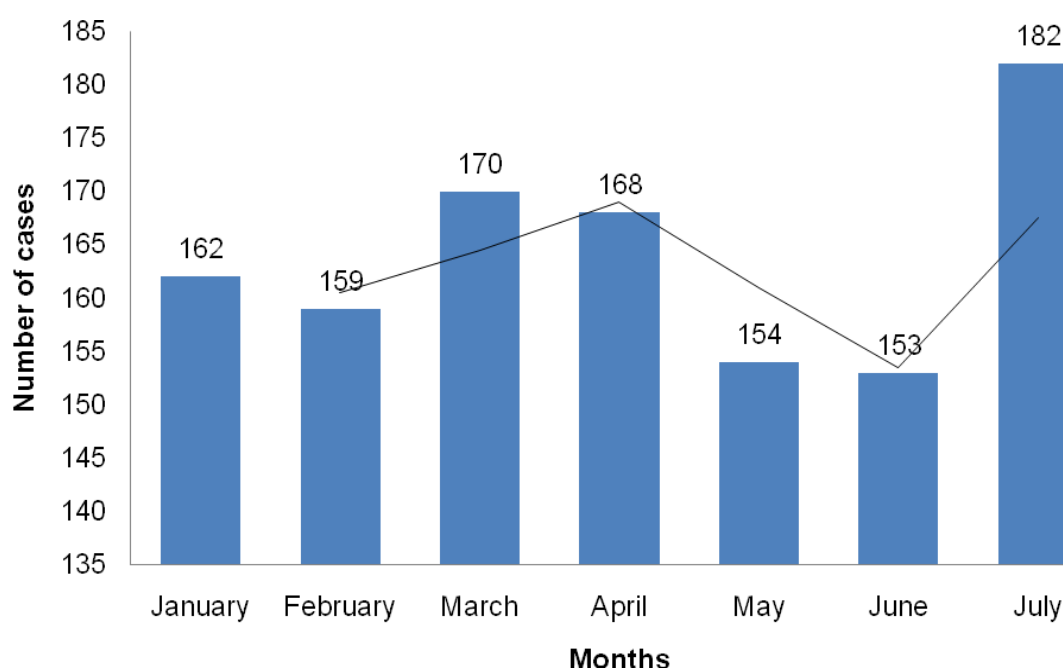


Figure 18: Numbers of cases and trend line of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by month, South Africa, January - July 2012. n=1148.

Table 33: Numbers of viable, laboratory-confirmed *Staphylococcus aureus* reported by GERMS-SA sentinel sites, by antimicrobial susceptibility and province, South Africa, January - July 2012.

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

S= susceptible to antimicrobial agents; NS = non susceptible.

Discussion

The incidence of *S. aureus* bacteraemia was not calculated and cases could not be separated into hospital-versus community-acquired categories because only laboratory-based data were available.

The percentage of *S. aureus* isolates which were methicillin-resistant was as high as 44% of the total number submitted to the NICD. Clindamycin resistant *S. aureus* isolates occurred at a high rate of 18% and three vancomycin non-susceptible isolates were identified but not confirmed using the reference method.

RIFAMPICIN-RESISTANT TUBERCULOSIS

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South Africa has a high incidence of tuberculosis (TB) including a high incidence of drug-resistant cases.¹ In 2012, a phased nationwide implementation of Xpert MTB/RIF rapid diagnostic testing for TB suspects was initiated. To date, over 1 million tests have been performed, with a national average of 14.55% *Mycobacterium tuberculosis* (MTB) positivity of which 7.14% showed rifampicin resistance.

Through GERMS-SA, the Centre for Tuberculosis, NICD, has initiated a sentinel surveillance system for rifampicin-resistant TB in South Africa. The aim of this system is to estimate the sensitivity and specificity of rifampicin resistance as a predictor of Multi-Drug-

Resistant TB so as to estimate the burden of resistance to other TB drugs. The surveillance system also aims to identify the prevalent rifampicin-resistant strains and to determine the impact of the implementation of the Xpert MTB/RIF rapid diagnostic test on the epidemiology of rifampicin-resistant TB over time.

Four GERMS-SA enhanced TB surveillance sites have been established in the Gauteng, Mpumalanga, Northern Cape and Eastern Cape provinces. Surveillance activities at the pilot site in Gauteng are currently being evaluated in order to optimise processes and outputs. Ultimately, TB surveillance will include one enhanced surveillance site per province.

Reference

1. World Health Organisation. Global tuberculosis Report 2012. www.who.int/tb Accessed 5 May 2013.

DISCUSSION – GERMS-SA 2012

Susan Meiring

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In 2012 the GERMS-SA laboratory-based surveillance programme continued to provide robust data for public health action, reporting on 17 733 cases of laboratory-confirmed disease. In addition to the usual opportunistic, epidemic-prone and vaccine-preventable diseases

under surveillance, three new priority diseases were added to the enhanced surveillance repertoire namely: *Candida* spp., *Staphylococcus aureus* and rifampicin-resistant tuberculosis (TB).

The enhanced surveillance data for candidaemia have already shown very high in-hospital mortalities, with a substantial difference in antifungal susceptibility profiles between isolates from the Gauteng and Western Cape provinces. The last quarter of 2012 saw enhanced surveillance for *Staphylococcus aureus* bacteraemia and rifampicin-resistant tuberculosis initiated at selected sites. The former aims to describe epidemiological differences between hospital-associated and community-associated methicillin-resistant *Staphylococcus aureus*, while the latter will attempt to describe the outcomes and clinical differences between patients with rifampicin mono-resistant TB and multidrug-resistant TB.

Although three-quarters of patients presenting at enhanced surveillance sites with a GERMS-SA listed infection were co-infected with HIV, there are several other factors that may also have affected the epidemiology of the diseases under surveillance. These are water quality and sanitation, overcrowding and housing, vaccine availability and uptake, antiretroviral therapy rollout, and prevention of mother to child transmission programmes. The effects of these factors on the surveillance data are apparent in the continued downward trend of invasive pneumococcal disease in the vaccinated and unvaccinated populations, the stabilisation of *Haemophilus influenzae* type b disease in infants, the outbreak of non-typhoidal salmonellosis in the Eastern Cape and the change in gender profile for cryptococcosis.

Monitoring the susceptibility of pathogens to antimicrobial empiric therapy continued through 2012. Concerns were raised over the ongoing increase in ciprofloxacin resistance in *Salmonella* Typhi. Fortunately, azithromycin and ceftriaxone can still be used as effective alternative therapies. Penicillin continues to be the drug of choice for meningococcal disease. Ceftriaxone in adequately high doses is still effective for the empiric treatment of pneumococcal meningitis but vancomycin should be added if high level resistance (MIC ≥ 1 $\mu\text{g/ml}$) is confirmed or if there is a poor clinical response 48 hours post treatment.

The strength of the GERMS-SA surveillance programme is attributable to the ongoing participation of public and private sector laboratories. This is because the NICD reference laboratories require the submission of isolates for serotyping/serogrouping, antimicrobial susceptibility testing and molecular analysis of pathogen strains. This information is then communicated to stakeholders in order to improve the health of all South Africans. All partner laboratories are thanked for their participation in the GERMS-SA programme and are encouraged to continue their participation in future.

Table 1: Provisional number of laboratory confirmed cases of diseases under surveillance reported to the NICD - South Africa, corresponding periods 1 January - 30 June 2012/2013*

Disease/Organism	1 Jan to 30 Jun, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Anthrax	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Botulism	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
<i>Cryptococcus spp.</i>	2012	634	176	1037	1026	95	209	38	170	343	3728
	2013	388	118	1077	906	68	172	24	121	321	3195
<i>Haemophilus influenzae</i> , invasive disease, all sero- types	2012	18	8	50	18	1	6	2	4	35	142
	2013	16	11	56	26	2	4	4	1	63	183
<i>Haemophilus influenzae</i> , invasive disease, < 5 years											
	Serotype b	2012	1	2	10	1	1	3	1	1	7
	2013	1	0	5	2	0	0	0	0	4	12
Serotypes a,c,d,e,f	2012	1	0	3	0	0	0	0	0	4	8
	2013	0	1	2	0	0	0	0	1	4	8
Non-typeable (unencapsulated)	2012	0	1	10	1	0	0	0	0	2	14
	2013	0	1	6	0	1	0	1	0	2	11
No isolate available for serotyping	2012	4	1	6	2	0	2	1	1	1	18
	2013	3	4	16	5	0	3	1	0	16	48
Measles	2012	0	1	7	6	1	0	0	1	1	17
	2013	1	0	1	0	0	0	0	0	0	2
<i>Neisseria meningitidis</i> , invasive disease	2012	13	0	38	12	2	1	0	4	27	97
	2013	23	6	17	18	1	1	1	3	23	93
Novel Influenza A virus infections	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Plague	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
Rabies	2012	0	0	0	3	3	0	0	0	0	6
	2013	0	2	0	1	1	1	0	0	0	5
<i>Salmonella spp.</i> (not typhi), invasive disease	2012	14	7	127	42	3	18	5	3	38	257
	2013	10	7	89	40	2	16	1	2	53	220
<i>Salmonella spp.</i> (not typhi), isolate from non-sterile site	2012	71	5	244	94	1	33	5	3	154	610
	2013	56	26	270	107	4	31	5	15	187	701
<i>Salmonella typhi</i>	2012	1	0	10	9	0	2	0	0	5	27
	2013	1	1	18	8	0	9	0	0	8	45
<i>Shigella dysenteriae 1</i>	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0
<i>Shigella spp.</i> (Non Sd1)	2012	122	23	310	84	0	6	12	0	209	766
	2013	128	43	357	117	4	28	6	16	131	830
<i>Streptococcus pneumoniae</i> , invasive disease, all ages	2012	156	109	587	272	27	70	8	55	209	1493
	2013	146	96	416	214	23	51	27	48	238	1259
<i>Streptococcus pneumoniae</i> , invasive disease, < 5 years	2012	32	14	122	49	2	10	2	8	26	265
	2013	23	20	99	23	5	2	2	16	38	228
<i>Vibrio cholerae</i> O1	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	1	0	0	0	0	1
Viral Haemorrhagic Fever (VHF)											
	Crimean Congo Haemorrhagic Fever (CCHF)	2012	0	0	0	0	0	0	0	0	0
	2013	0	2	0	0	0	0	0	1	0	3
Other VHF (not CCHF)	2012	0	0	0	0	0	0	0	0	0	0
	2013	0	0	0	0	0	0	0	0	0	0

Footnotes

*Numbers are for cases of all ages unless otherwise specified. Data presented are provisional cases reported to date and are updated from figures reported in previous bulletins.

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

0 = no cases reported

Table 2: Provisional laboratory indicators for NHLS and NICD, South Africa, corresponding periods 1 January - 31 March 2012/2013*

Programme and Indicator	1 January to 30 June, year	EC	FS	GA	KZ	LP	MP	NC	NW	WC	South Africa
Acute Flaccid Paralysis Surveillance											
Cases < 15 years of age from whom specimens received	2012	35	15	28	43	13	22	0	11	13	180
	2013	27	9	28	28	16	17	1	10	17	153

Footnotes

*Numbers are for all ages unless otherwise specified. Data presented are provisional numbers reported to date and are updated from figures reported in previous bulletins.

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

0 = no cases reported

Monitoring for the presence of polio in a country is based on AFP (acute flaccid paralysis) surveillance – the hallmark clinical expression of paralytic poliomyelitis. The clinical case definition of AFP is an acute onset of flaccid paralysis or paresis in any child under 15 years of age. AFP is a statutory notifiable disease and requires that 2 adequate stool specimens are taken as soon as possible, 24 to 48 hours apart, but within 14 days after onset of paralysis, for isolation and characterisation of polio virus. The differential diagnosis of AFP is wide, the most common cause of which is Guillain-Barre Syndrome. The incidence of AFP in a population has been studied in a number of developing countries and WHO have determined, as a result of these studies, that the criterion for adequate surveillance of AFP is 2 cases per 100 000 population of children less than 15 years of age (it was formerly 1 per 100,000 but this was thought to be inadequately sensitive).

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