GERMS SOUTH AFRICA

Annual Report 2010

NATIONAL HEALTH LABORATORY SERVICE

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES

The GERMS-SA Annual Report 2010 was compiled by the National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa.

Editors

Nelesh Govender	Mycology Reference Unit
Vanessa Quan	National Microbiology Surveillance Unit

Contributing authors

Penny Crowther	Epidemiology and Surveillance Unit
Desiree du Plessis	Parasitology Reference Unit
Nelesh Govender	Mycology Reference Unit
Karen Keddy	Enteric Diseases Reference Unit
Olga Perovic	Antimicrobial Resistance Reference Unit
Vanessa Quan	National Microbiology Surveillance Unit
Anne von Gottberg	Respiratory and Meningeal Pathogens Reference Unit

Editorial assistant: Gugu Moyo

Suggested citation:
Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa. GERMS-SA Annual Report 2010. Available from http://nicd.ac.za/?page=germs-sa&id=97

Cover photograph: GERMS-SA Surveillance Officer Meeting, 21-23 September 2010, Cape Town

Contact details
National Institute for Communicable Diseases, a Division of the National Health Laboratory Service
1 Modderfontein Road
Sandringham
2131
South Africa

Switchboard: +27 11 386 6400
www.nhls.ac.za

Table of Contents

Introduction

As in previous years, the 2010 GERMS-SA Annual Report includes a summary of key data from national surveillance, including clinical data from enhanced surveillance sites (ESS) for the year. The surveillance methodology did not change in 2010 and audit cases were not detected from NHLS laboratories in KwaZulu-Natal. Two new pathogens (bacteraemic *Staphylococcus aureus* and *Klebsiella* species) were included under the GERMS-SA umbrella in July 2010 and the interim reports are included. The new, scaled-up HIV/AIDS prevention and treatment plan was launched in April 2010 with the objective to reduce the rate of infection by 50% by 2011 and to provide antiretroviral (ARV) treatment to 80% of those who need to be on treatment (1). GERMS-SA, as a mature surveillance system, is well positioned to monitor the impact of national interventions such as vaccines and the Comprehensive Care, Management and Treatment Programme for HIV/AIDS.

Methods

In 2010, diseases under surveillance included:

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

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

In brief, approximately 200 South African clinical microbiology laboratories participated in the surveillance programme in 2010. The population under surveillance in 2010 was estimated at 50 million. Diagnostic laboratories reported case patients to the NICD using laboratory case report forms, according to standard case definitions. If available, isolates from case patients were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. From 1 July 2008, surveillance methodology for the cryptococcal project was changed, so that only ESS (25 hospitals in 9 provinces), NHLS laboratories in KwaZulu-Natal, and laboratories in the private, mining, and military sectors were required to directly report case patients to NICD. For other cases of cryptococcosis, data were obtained directly from the NHLS Central Data Warehouse (CDW), which obtains information from Disa*Lab laboratory information system. Cryptococcal isolates, obtained from patients at ESS, continued to be characterised by phenotypic and genotypic tests. From July 2010, 7 ESS reported cases of *S. aureus* and *K. pneumoniae* bacteraemia to GERMS-SA.

At ESS, surveillance officers completed clinical case report forms for patients with 7 laboratory confirmed diseases (cryptococcosis, *Pneumocystis jirovecii* pneumonia (PCP), invasive salmonellosis, invasive pneumococcal disease, invasive shigellosis, invasive meningococcal disease, invasive *Haemophilus influenzae* disease), by case patient interview or hospital medical record review, to obtain additional clinical details, including antimicrobial use, vaccination history, HIV status, and patient outcome. Case patients were followed up only for the duration of the hospital admission.

Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on an Epi Info version 6.04d database (Centers for Disease Control and

(Continued from page 4)

Prevention (CDC), Atlanta, USA) or on a Microsoft Access database. A surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) between 1 January and 31 December 2010, 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 also designed to obtain data, from case patients, which were no longer reported to NICD by NHLS laboratories in 8 provinces. Data from case patients, detected by audit, were included on the surveillance database, and have been included in this report. Incidence was calculated using mid-year population estimates for 2009 and 2010 from Statistics South Africa (Table 1) (3). Incidence in the HIV-infected and AIDS populations was calculated for 2009 and 2010, using estimated population denominators from the Actuarial Society of South Africa (ASSA) 2003 model (Table 1), assuming that the HIV/AIDS prevalence amongst cases with known status was similar to those with unknown status (4). All reported incidence rates are expressed as cases per 100 000 population, unless otherwise stated. Reported p-values were calculated using the Mantel-Haenszel chi-squared test and p-values < 0.05 were considered significant throughout.

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

Table 1: Population denominators used to calculate incidence, 2009 and 2010.

Province	General population*		HIV-infected population**		AIDS population**	
	2009	2010	2009	2010	2009	2010
Eastern Cape	6 648 601	6 743 823	757 818	785 217	79 705	84 991
Free State	2 902 518	2 824 570	395 344	396 068	50 111	51 196
Gauteng	10 531 308	11 192 029	1 454 006	1 455 350	166 078	171 132
KwaZulu-Natal	10 449 141	10 645 508	1 567 048	1 572 457	206 294	209 638
Limpopo	5 227 503	5 439 552	451 553	468 659	47 390	50 275
Mpumalanga	3 606 572	3 617 513	459 051	462 687	59 336	60 107
Northern Cape	1 147 137	1 103 918	69 595	71 434	7 458	8 093
North West	3 450 517	3 200 649	501 066	504 224	62 634	64 916
Western Cape	5 356 844	5 223 908	309 102	318 115	28 391	31 338
South Africa	**49 320 141**	**49 991 470**	**5 964 583**	**6 034 211**	**707 397**	**731 686**

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

Operational report

Site visits

In 2010, NICD staff members undertook 58 visits to 41 surveillance sites in all 9 provinces of South Africa (Table 2). This provided the opportunity to engage with staff at many laboratories and hospitals participating in the surveillance programme.

Table 2: GERMS-SA surveillance site visits between 1 January and 31 December 2010.

Date	Province	Laboratory	Hospital
6-7 May 2010	Eastern Cape	NHLS Port Elizabeth, NHLS Grahamstown Pathcare (Port Elizabeth) Ampath (Port Elizabeth)	Livingstone Hospital Settlers Hospital
27-28 May 2010	Eastern Cape	NHLS East London, NHLS Mthatha Ampath (East London) Pathcare (East London) Lancet (East London)	Frere Hospital Nelson Mandela Academic Complex
18 March 2010	Free State	NHLS Universitas, NHLS Pelonomi	Universitas Hospital Pelonomi Hospital
13 January 2010	Gauteng	NHLS CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
18 January 2010	Gauteng	NHLS CHBH	Chris Hani Baragwanath Hospital
27 January 2010	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
9 February 2010	Gauteng	Lancet (Pretoria)	
16 February 2010	Gauteng	NHLS CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
22 February 2010	Gauteng	NHLS SBPAH	Steve Biko Pretoria Academic Hospital
26 February 2010	Gauteng	NHLS CHBH	Chris Hani Baragwanath Hospital
2 March 2010	Gauteng	NHLS CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
12 March 2010	Gauteng	NHLS SBPAH	Steve Biko Pretoria Academic Hospital Kalafong Hospital
21-22 April 2010	Gauteng	NHLS Kalafong (Training)	
28 April 2010	Gauteng	NHLS Natalspruit	Natalspruit Hospital
12 May 2010	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
2 June 2010	Gauteng	NHLS Tembisa	Tembisa Hospital
16 July 2010	Gauteng		Rahima Moosa Mother and Child Hospital
20 October 2010	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
10 November 2010	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital

Cont...

7 December 2010	Gauteng	NHLS Helen Joseph	Helen Joseph Hospital
3-4 March 2010	KwaZulu Natal	NHLS Addington /NHLS RK Khan / NHLS KEH/NHLS Greys'/NHLS Edendale	Addington Hospital RK Khan Hospital King Edward VIII Grey's Hospital Edendale Hospital
20-21 May 2010	KwaZulu Natal	NHLS Prince Street (Training – 6 labs)	-
10-11 June 2010	KwaZulu Natal	NHLS Addington NHLS RK Khan NHLS KEH	Addington Hospital RK Khan Hospital King Edward VIII
6 December 2010	KwaZulu Natal	NHLS Addington NHLS RK Khan NHLS KEH	Addington Hospital RK Khan Hospital King Edward VIII
26 May 2010	Limpopo	NHLS Polokwane	Polokwane Hospital
13-14 October	Limpopo	NHLS Mankweng (Training – 6 labs)	-
15 October 2010	Limpopo	NHLS Tshilidzini NHLS Elim	Tshilidzini Hospital Elim Hospital
16 November 2010	Limpopo	NHLS Polokwane NHLS Mankweng	Polokwane Hospital Mankweng Hospital
26-28 April 2010	Mpumalanga	NHLS Rob Ferreira NHLS Themba	Rob Ferreira Hospital Themba Hospital
26 March 2010	Northern Cape	NHLS Kimberley	Kimberley Hospital
24 February 2010	North West	NHLS Klerksdorp	Klerksdorp Hospital
28 June 2010	North West	NHLS Rustenburg	Job Shimankana Tabane Hospital
27 July 2010	North West	NHLS Carletonville	Carletonville Hospital
8 March 2010	Western Cape	NHLS Groote Schuur	Groote Schuur Hospital
8 March 2010	Western Cape	-	Red Cross Children's Hospital
9 March 2010	Western Cape	NHLS Tygerberg	Tygerberg Hospital
21 April 2010	Western Cape	NHLS Tygerberg	Tygerberg Hospital

Surveillance audit

Of the 18 385 surveillance cases on the GERMS-SA database, 7099 (39%) were detected by audit of the NHLS CDW (Table 3). This percentage has been artificially inflated by the audit for cases of cryptococcosis – the number of audit cases include 4680 cryptococcal cases from non-enhanced surveillance sites that since July 2008 were not required to report these cases to GERMS-SA. Only 18% (311/1761) of cases of cryptococcosis were not reported to the surveillance programme by ESS which are required to report cases. Therefore, the corrected percentage of non-reported cases detected by audit would be 18% (2730/15 466). Overall, GERMS-SA constantly strives to reduce the number of cases detected on audit by raising awareness of the surveillance programme; this is important because GERMS-SA is unable to perform additional microbiological characterisation for these cases.

(Continued on page 8)

(Continued from page 7)

Enhanced surveillance site performance indicators

The performance of ESS improved with respect to meeting performance targets in 2010 (Table 4): 82% (3513/4307) of cases had a case report form completed (target = 90%) and 2124 (60%) of the case report forms were completed by patient interview (target = 60%); quality indicators also improved. Since 2007, ESS operational reports (ESSOR) have been provided to the site coordinators, laboratory staff and surveillance officers to enable the site team to regularly review site performance, in comparison with set targets. The main objective of these reports is to provide information regarding the overall functioning of the surveillance site, by providing indicators of laboratory participation (submission of isolates), and indicators of surveillance officer performance (completion of case report forms). By reviewing these indicators, problems with data collection can be targeted, and recommendations are provided to improve the site performance. In 2010, these reports were provided quarterly.

Coordination meetings

Surveillance officer meeting, 1-3 February 2010: This meeting, convened at the NICD in Johannesburg, was attended by 23 surveillance officers from 9 provinces and paediatricians involved in the invasive pneumococcal disease case-control (IPD CC) study. The meeting focused on the objectives of the IPD CC study and the methodology and practicalities of a matched CC study.

Principal Investigator (PI) meeting, 31 August – 2 September: Convened at the NICD, this meeting was attended by over 50 local, national and international delegates, including representatives from the Department of Health and CDC. Surveillance and research activities were reviewed, and new NICD projects which could impact on the GERMS-SA network were discussed. The meeting was an opportunity to share information on the early operations of the IPD CC study, raise proposals for new studies such as candidaemia surveillance and Group B *Streptococcus* surveillance and discuss GERMS-SA's links with other surveillance systems, e.g. SARI and rotavirus surveillance.

Steering Committee meeting, 2 September: Convened at the NICD after the PI meeting, this was attended by 11 committee members and 9 invited observers. The meeting covered evaluation of current pathogens under surveillance and inclusion of new projects. It was decided to stop surveillance for PCP through GERMS-SA surveillance as syndromic surveillance methods would be better suited to this disease; the majority of PCP cases are diagnosed clinically.

Surveillance officer meeting, 21-23 September: This meeting was convened at Lagoon Beach Hotel, Cape Town and included three days of training and discussion of ESS performance indicators. The meeting focused on issues around public health programmes such as the expanded programme on immunisation (EPI), the prevention of mother to child HIV transmission programme and the paediatric antiretroviral treatment programme.

Table 3: Cases detected by surveillance audit by province, 2010.

Surveillance case		Percentage of cases detected by audit* n_1/n_2 (%)	Number of cases detected by audit									
			EC	FS	GA	KZ	LP	MP	NC	NW	WC	SA
Invasive	Typhoid fever**	0/58 (0)	0	0	0	0	0	0	0	0	0	**0**
	Non-typhoidal salmonellosis†	71/674 (11)	16	2	37	0	0	1	0	7	8	**71**
	Shigellosis	3/49 (6)	2	0	1	0	0	0	0	0	0	**3**
	Cryptococcosis†††	4991/7371 (68)	1201	374	1384	113	468	592	15	460	384	**4991**
	Meningococcal disease	38/366 (10)	1	5	19	0	5	3	1	0	4	**38**
	Haemophilus influenzae disease	91/313 (29)	28	8	26	0	1	4	1	2	21	**91**
	Pneumococcal disease	828/4206 (20)	130	74	349	0	29	97	9	67	73	**828**
	Pneumocystis jirovecii pneumonia	12/298 (4)	0	0	5	0	0	6	0	0	1	**12**
	Klebsiella pneumoniae disease	451/971 (46)	0	35	370	0	0	0	0	0	46	**451**
	Staphylococcus aureus disease	280/787 (36)	0	15	237	0	0	0	0	0	28	**280**
Non-invasive	*Salmonella* Typhi**	2/18 (11)	1	0	0	0	0	1	0	0	0	**2**
	Non-typhoidal salmonellosis†	171/1570 (11)	22	11	79	0	14	19	3	11	12	**171**
	Shigellosis	161/1704 (9)	26	1	71	0	9	9	3	19	23	**161**
	Total	**7099/18 385 (39)**	**1427**	**525**	**2578**	**113**	**526**	**732**	**32**	**566**	**600**	**7099**

*Percentage of cases detected by audit = number of cases detected on audit (n_1)/total number of cases detected by GERMS-SA (n_2) x 100; **Only *Salmonella enterica* serotype Typhi; †Including *Salmonella enterica* serotype Paratyphi; †††Cryptococcal cases detected by audit = number of cases not reported by enhanced surveillance sites + cases from all non-enhanced surveillance sites not required to report cases since July 2008; EC: Eastern Cape; FS: Free State; GA: Gauteng; KZ: KwaZulu-Natal; LP: Limpopo; MP: Mpumalanga; NC: Northern Cape; NW: North West; WC: Western Cape; SA: South Africa.

Table 4: Enhanced surveillance site performance indicators, 2010.

Enhanced surveillance site*	Case patients, n	Completed case report forms**, n (%)***	Case report forms completed by interview, n (%)†	Completion of select data fields for interviewed patients††, %
Addington	182	180 (99)	103 (57)	97
R K Khan	198	185 (93)	127 (69)	99
Chris Hani Baragwanath	1003	781 (78)	410 (52)	97
Dr George Mukhari	258	83 (32)	40 (48)	95
Edendale/ Grey's	236	227 (96)	158 (96)	100
Groote Schuur/ Red Cross/ Victoria	369	351 (95)	165 (47)	98
Charlotte Maxeke Johannesburg Academic	516	497 (96)	355 (71)	99
Tygerberg	193	160 (83)	62 (39)	100
Kimberley	168	154 (92)	112 (73)	98
King Edward	151	107 (71)	58 (54)	100
Mankweng/ Polokwane	112	90 (80)	78 (87)	100
Nelson Mandela Academic/ Mthatha Provincial	190	147 (77)	91 (62)	99
Pelonomi/ Universitas	158	138 (87)	84 (61)	100
Steve Biko Pretoria Academic/ Tshwane District	209	159 (76)	65 (41)	96
Rob Ferreira/ Themba	237	225 (95)	127 (56)	98
Rustenburg	127	119 (94)	89 (75)	100
TOTAL	**4307**	**3513 (82)**	**2124 (60)**	**99**

Note - The percentage (in brackets) in each cell was calculated using the numerator from that cell and the corresponding denominator from the cell to the left; *There were 6 surveillance officers at Chris Hani Baragwanath, 3 at Charlotte Maxeke Johannesburg Academic, 2 at GSH/RXH/Victoria and 2 at Greys'/Edendale for most of 2010, 2 at KEH for the latter half of 2010; one surveillance officer was present at all other sites; **Low case report form completion rates at certain sites are due to the turnover of surveillance staff – if other reasons for low completion of case report forms were detected, these were addressed at those sites. ***Target = 90%; †Target = 60%; ††This was calculated by subtracting the number of "unknown" answers from a particular field on the case report form, which could easily have been answered by a patient interviewed.

Surveillance reports

Enhanced surveillance site project

In 2010, of 18 385 surveillance case patients detected by GERMS-SA, 4307 (23%) were diagnosed at ESS. Of case patients with recorded HIV status, 82% (2578/3140) were HIV-infected (Table 5). The proportion of case patients with confirmed HIV infection varied by surveillance disease: unsurprisingly, a very high proportion of patients with AIDS defining infections like cryptococcosis (99%) and PCP (83%) were HIV-infected; HIV infection

(Continued on page 11)

(Continued from page 10)

amongst patients with invasive pneumococcal disease and non-typhoidal salmonellosis, for which HIV is a known risk factor, were both 74%, and less than one third (29%) of patients with invasive meningococcal disease were HIV-infected.

Table 5: Number and percentage* of patients, diagnosed with laboratory-confirmed disease at GERMS-SA enhanced surveillance sites, with confirmed HIV-1 infection, South Africa, 2010, n=4307.**

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	1761	1468 (83)	1373 (94)	1359 (99)
Pneumocystis jirovecii	120	90 (75)	84 (93)	70 (83)
Neisseria meningitidis	173	158 (91)	132 (84)	38 (29)
Streptococcus pneumoniae	1723	1454 (84)	1183 (81)	871 (74)
Haemophilus influenzae	192	150 (78)	129 (86)	66 (51)
Salmonella species†	318	267 (84)	224(84)	166 (74)
Shigella species†	20	16 (80)	15 (94)	8 (53)
Total	**4307**	**3603 (84)**	**3140 (87)**	**2578 (82)**

*The percentage (in brackets) in each cell was calculated using the numerator from that cell and the corresponding denominator from the cell to the left; **HIV infection was confirmed by an age-appropriate laboratory test and recorded by surveillance officers at enhanced surveillance sites; †Invasive.

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

Results

Salmonella Typhi isolation by month shows the effect of a foodborne outbreak in Pretoria (Tshwane) in May and June (Figure 1) (5), in press). *Salmonella* Typhi isolates from both invasive and non-invasive sites are reported in Table 6. A single isolate of *Salmonella* Paratyphi B L (+) tartrate (+) (*Salmonella* Paratyphi B var. Java) was received from a stool specimen of a 37 year-old male in Gauteng. A second isolate of *Salmonella* Paratyphi B L (-) tartrate (-) was received from a 10 month old infant in KwaZulu Natal (Figure 1). No isolates of *Salmonella* Paratyphi A or of *Salmonella* Paratyphi C were received. The number of isolates within each age group is reported in Table 7, indicating that most isolates are from patients in the 5 – 34 year age group, although infection is seen among both older and younger age groups. The occurrence of the typhoid fever outbreak in May and June contributed to the extended age range in comparison with the past years (5).

No isolates of *Salmonella* Typhi received in 2010 were resistant to ciprofloxacin, the treatment of choice, but resistance to nalidixic acid remains cause for concern (Table 8). The *Salmonella* Paratyphi B isolates were fully susceptible to all antimicrobials tested.

(Continued on page 12)

(Continued from page 11)

Discussion

Salmonella Typhi isolates from both invasive and non-invasive sites are included in these analyses, as both add to burden of infection in South Africa and thus represent a public health risk, although data may not reflect actual burden of disease. This is compounded by the challenges of alternative diagnostic methods for typhoid fever, including both clinical and serological. The number of reported *Salmonella* Typhi isolates was regarded as a substantial underestimate and thus incidence was not calculated. These thus exclude those patients in whom a serological or clinical diagnosis was made without culture. Certain antimicrobials were tested for epidemiological purposes only, and should not be used for treatment of typhoid fever. Nalidixic acid resistance may be used as a marker for quinolone resistance; it is indicative of the potential for an organism to develop fluoroquinolone resistance (6). Response to ciprofloxacin may be poor in the presence of nalidixic acid resistance. The ciprofloxacin E-test is recommended to guide antimicrobial management in such cases (6). Ceftriaxone would be regarded as the alternative therapy of choice in these cases, as well as those typhoid fever cases where the organism is fully resistant to ciprofloxacin.

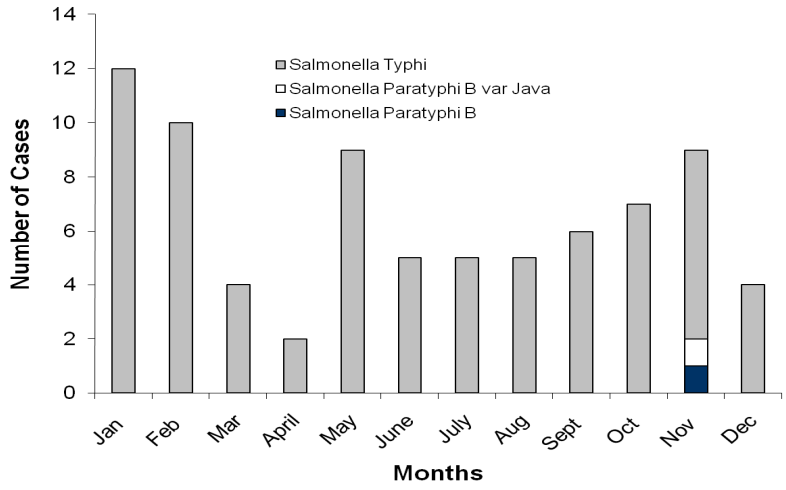


Figure 1. Number of non-invasive and invasive cases of *Salmonella* Typhi and Paratyphi B, reported to GERMS-SA, by month of specimen collection, South Africa, 2010, n=76 (including audit reports).

Table 6: Number of invasive and non-invasive *Salmonella* Typhi cases reported to GERMS-SA, South Africa, 2010, n=76.

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	2	9
Free State	0	2
Gauteng	4	25
KwaZulu-Natal	2	7
Limpopo	1	0
Mpumalanga	2	9
Northern Cape	0	0
North West	0	0
Western Cape	7	6
South Africa	**18**	**58**

Table 7: Number of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2010, n=76.

Age category (years)	*Salmonella* Typhi isolates
0 - 4	10
5 – 14	21
15 – 24	14
25 – 34	16
35 - 44	6
45 - 54	5
55 - 64	1
≥ 65	1
Unknown	2
Total	**76**

Table 8: Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2010, n=74 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)	Intermediate (%)	Resistant (%)
Ampicillin	66 (89.2)	1 (1.4)	7 (9.4)
Trimethoprim	64 (86.5)	0 (0.0)	10 (13.5)
Sulphamethoxazole	46 (62.2)	0 (0.0)	28 (37.8)
Chloramphenicol	63 (85.1)	1 (1.4)	10 (13.5)
Nalidixic acid	63 (85.1)	0 (0.0)	11 (14.9)
Ciprofloxacin	74 (100.0)	0 (0.0)	0 (0.0)
Tetracycline	71 (95.9)	0 (0.0)	3 (4.1)
Streptomycin	67 (90.5)	0 (0.0)	7 (9.5)
Imipenem	74 (100.0)	0 (0.0)	0 (0.0)
Ceftriaxone	74 (100.0)	0 (0.0)	0 (0.0)

Non-typhoidal *Salmonella enterica* (NTS)

Results

Invasive diseases do not appear to have a seasonal prevalence, but increased number of non-invasive disease due to NTS in the earlier months of the year may be a surveillance artefact, due to increased surveillance for foodborne disease prior to FIFA 2010 World Cup (Figure 2). The number of cases of invasive and non-invasive disease, by province, reported to GERMS-SA, is stated in Table 9. The number of cases of invasive and non invasive disease, by age group, is shown in Table 10, but incidence has only been calculated for invasive NTS, due to differences in stool-taking practices in adult and paediatric medical care. Most invasive isolates were identified from blood cultures, although isolates were frequently identified from both blood culture and another site, including stool and other normally-sterile sites (Table 11). Multi-drug resistance remains a challenge, including resistance to first-line antimicrobial agents and the quinolones (Table 12). Of the NTS isolates tested, 153/1976 (7.7%) were extended-spectrum beta-lactamase (ESBL) producers (Table 12). Multi-drug resistant serotypes included primarily *Salmonella* Typhimurium and *Salmonella* Isangi (Table 13).

(Continued on page 14)

(Continued from page 13)

Discussion

Non-typhoidal salmonellosis may be a food-borne disease, for which data are poorly captured in South Africa, and where the patients normally present with gastroenteritis, or may be an AIDS-defining illness, in which case the organism frequently becomes invasive. No marked seasonal prevalence was noted in 2010 for invasive or non invasive isolates. *Salmonella* Infantis appears to be gaining importance as a common serotype in South Africa. Certain antimicrobial agents were tested for epidemiological reasons only, and should not be used for treatment. Antimicrobial resistance remains a cause for concern.

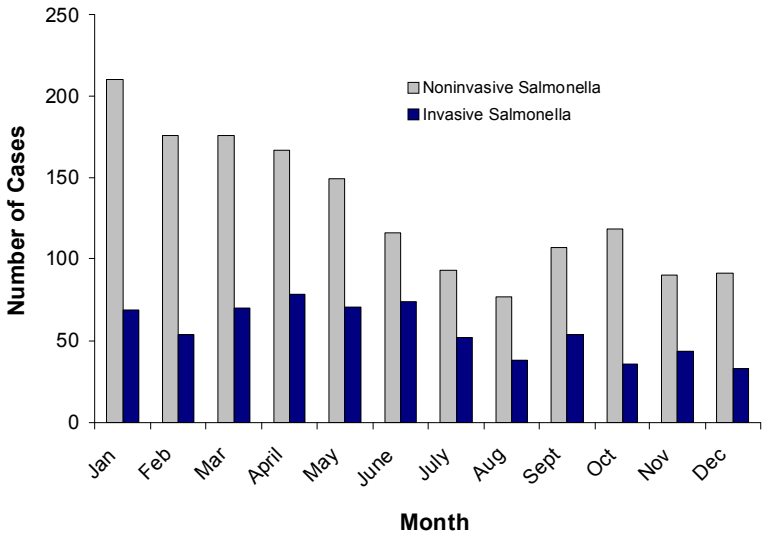


Figure 2. Number of non-invasive and invasive, non-typhoidal *Salmonella* cases, reported to GERMS-SA, by month of specimen collection, South Africa, 2010, n=2244 (including audit reports).

Table 9: Number* of invasive and non-invasive non-typhoidal *Salmonella* cases reported to GERMS-SA, by province, South Africa, 2010, n=2244 (including audit reports).

Province	Non-invasive, non-typhoidal *Salmonella* isolates	Invasive, non-typhoidal *Salmonella* isolates
Eastern Cape	211	55
Free State	54	22
Gauteng	706	381
KwaZulu-Natal	206	79
Limpopo	30	12
Mpumalanga	112	18
Northern Cape	15	15
North West	46	17
Western Cape	190	75
South Africa	**1570**	**674**

*Incidence was not calculated as there may have been regional differences in specimen collection practices

Table 10: Number of cases and incidence for invasive* and non-invasive non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2010, n=2244 (including audit reports).

	Cases		
Age Category (years)	Non-invasive	Invasive	Incidence for invasive disease**
0 - 4	613	184	3.6
5 - 14	167	35	0.3
15 - 24	95	42	0.4
25 - 34	196	140	1.7
35 - 44	160	131	2.2
45 - 54	117	66	1.6
55 - 64	78	34	1.1
≥ 65	75	22	0.9
Unknown	69	20	-
Total	**1570**	**674**	**1.3**

*Incidence for non-invasive non-typhoidal *Salmonella* was 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 is expressed as cases per 100 000 population.

Table 11: Number of non-typhoidal *Salmonella* cases reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2010, n=2244 (including audit reports).

Specimen	n	%
CSF	24	1
Blood culture	598	27
Stool	1329	59
Other	293	13
Total	**2244**	**100**

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

Table 12: Antimicrobial susceptibility test results for all non-typhoidal *Salmonella* isolates received by GERMS-SA, South Africa, 2010, n=1976 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	1630	(82.5)	3	(0.1)	343	(17.4)
Trimethoprim	1647	(83.4)	0	(0.0)	329	(16.6)
Sulphamethoxazole	990	(50.1)	0	(0.0)	986	(49.9)
Chloramphenicol	1666	(84.3)	17	(0.9)	293	(14.8)
Nalidixic acid	1768	(89.5)	0	(0.0)	208	(10.5)
Ciprofloxacin	1965	(99.4)	3	(0.2)	8	(0.4)
Tetracycline	1494	(75.6)	31	(1.6)	451	(22.8)
Streptomycin	1597	(80.8)	0	(0.0)	379	(19.2)
Imipenem	1976	(100.0)	0	(0.0)	0	(0.0)
Ceftriaxone	1823	(92.3)	0	(0.0)	153	(7.7)

Table 13: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2010, n=1384 (excluding audit reports).

	Serotype				
Province	**Enteritidis**	**Heidelberg**	**Infantis**	**Isangi**	**Typhimurium**
Eastern Cape	32	3	1	32	85
Free State	15	0	3	0	32
Gauteng	337	15	27	18	295
KwaZulu-Natal	79	5	4	33	72
Limpopo	7	1	0	7	7
Mpumalanga	21	14	5	0	32
Northern Cape	4	0	0	1	14
North West	14	1	0	1	14
Western Cape	49	6	4	2	92
South Africa	**558**	**45**	**44**	**94**	**643**

Shigella species

Results

Higher isolation rates in January through to May are potentially a surveillance artefact, due to heightened awareness of food and waterborne disease prior to the FIFA 2010 World Cup and increased testing of symptomatic patients. Slightly increased numbers from January to March in 2010 do however suggest seasonality (Figure 3). Although the primary burden of disease due to *Shigella* is non-invasive dysentery or diarrhoea, invasive disease remains an important cause of morbidity in South Africa (Table 14). The predominant burden of disease, including both invasive and non-invasive shigellosis, is in the under-five-year age group (Table 15). Quinolone resistance remains low, but fluoroquinolone resistance appears to be emerging (Table 16). Nine of 1588 (1%) isolates tested were ESBL-producers. Predominant serotypes confirm that *S. flexneri* 2a remains the commonest cause of shigellosis in South Africa. *S. dysenteriae* type 1 was not isolated in 2010 (Table 17).

Discussion

Shigella infection is largely due to water-borne outbreaks in South Africa, although person-to-person transmission may play a role. Certain antimicrobials were tested for surveillance purposes only, and should not be used for treatment. Resistance to the third generation cephalosporins and fluoroquinolones remains low, but should continue to be monitored.

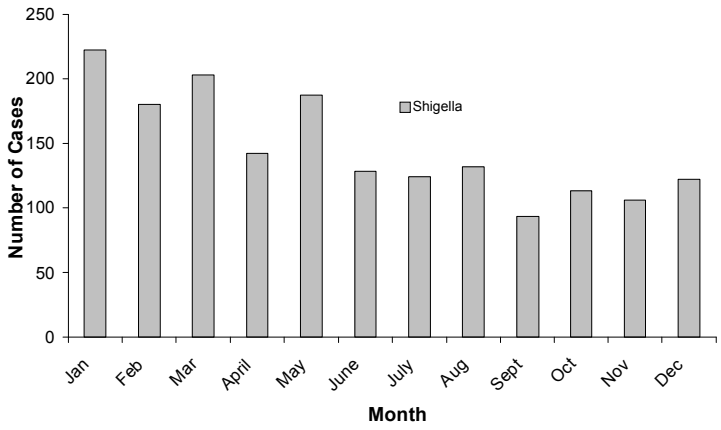


Figure 3. Number of non-invasive and invasive *Shigella* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2010, n=1753 (including audit reports).

Table 14: Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2010, n=1753 (including audit reports).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	264	6
Free State	53	0
Gauteng	692	19
KwaZulu-Natal	133	9
Limpopo	17	1
Mpumalanga	50	2
Northern Cape	35	1
North West	36	1
Western Cape	424	10
South Africa	**1704**	**49**

Table 15: Number of cases* and incidence for *Shigella* (invasive and non-invasive) reported to GERMS-SA by age category, South Africa, 2010, n=1753.**

	Cases		
Age Category (years)	Non-invasive	Invasive	Incidence for invasive disease**
0 - 4	820	16	0.31
5 - 14	247	5	0.05
15 - 24	81	1	0.01
25 - 34	180	5	0.06
35 - 44	115	10	0.17
45 - 54	77	5	0.12
55 - 64	60	0	0.00
≥ 65	54	2	0.08
Unknown	70	5	-
Total	**1704**	**49**	**0.09**

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

Table 16: Antimicrobial susceptibility test results for *Shigella* isolates received by GERMS-SA, South Africa, 2010, n=1588 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	870	(54.8)	1	(0.1)	717	(45.1)
Trimethoprim	132	(8.3)	0	(0.0)	1456	(91.7)
Sulphamethoxazole	271	(17.1)	0	(0.0)	1317	(82.9)
Chloramphenicol	1090	(68.6)	27	(1.7)	471	(29.7)
Nalidixic acid	1571	(98.9)	0	(0.0)	17	(1.1)
Ciprofloxacin	1584	(99.7)	0	(0.0)	4	(0.3)
Tetracycline	619	(39.0)	40	(2.5)	929	(58.5)
Streptomycin	622	(39.2)	0	(0.0)	966	(60.8)
Imipenem	100	(100.0)	0	(0.0)	0	(0.0)
Ceftriaxone	1582	(99.6)	0	(0.0)	6	(0.4)

Table 17: Commonest* invasive and non-invasive *Shigella* serotypes reported to GERMS-SA by province, South Africa, 2010, n=1218 (excluding audit reports, missing isolates, mixed and contaminated cultures).

Province	*S. dysenteriae* type 1	*S. flexneri* type 2a	*S. flexneri* type 3a	*S. flexneri* type 6	*S. sonnei* phase I/II
Eastern Cape	0	93	42	13	45
Free State	0	8	4	5	15
Gauteng	0	154	60	68	237
KwaZulu-Natal	0	56	11	8	34
Limpopo	0	3	1	1	1
Mpumalanga	0	4	4	11	8
Northern Cape	0	7	2	5	2
North West	0	4	1	2	5
Western Cape	0	179	58	15	52
South Africa	**0**	**508**	**183**	**128**	**399**

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

Diarrhoeagenic *Escherichia coli* (DEC)

Results

An increased number of cases in the first half of the year is potentially a surveillance artefact, as discussed above (Figure 4). Enteropathogenic *E. coli* (EPEC) remains the commonest cause of diarrhoea, due to this pathogen, identified in South Africa (Table 18). The predominance of cases among younger children under five years of age may reflect, in part, specimen-taking practices, as well as the burden of diarrhoeal disease in this age group (Table 19). Three patients had mixed infections with three different DEC pathotypes and 23 patients had mixed infections with two different DEC pathotypes. Six isolates of *E. coli* O157 were received, two of these were enterohaemorrhagic *E. coli* (EHEC), and four were enteropathogenic *E. coli* (EPEC). A range of serotypes were associated with Shiga-toxigenic *E. coli* (STEC) and EHEC, including O157 (two isolates), O26 (two isolates), O111, O117, O115 and O5. The commonest serotypes associated with EPEC included O55, O111, O119, O127, O145 and O109. Diverse serotypes were also noted for other enterovirulent *E. coli* isolates. Identification of both EHEC and STEC was incidental (7).

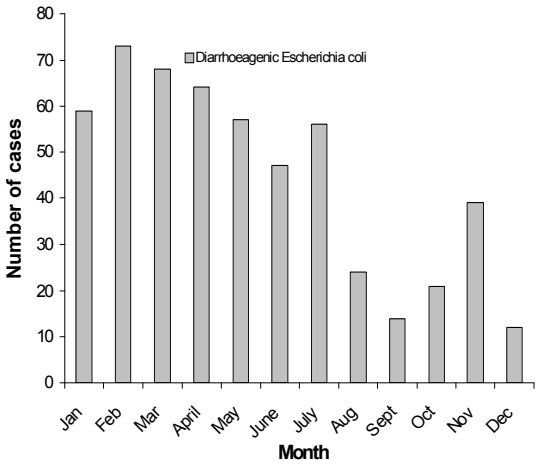


Figure 4. Number of diarrhoeagenic *Escherichia coli* isolates, reported to GERMS-SA, by month of

Discussion

Incidence was not calculated as numbers were not viewed as being fully representative. Actual burden of disease due to diarrhoeagenic *E. coli* is probably greatly underestimated in South Africa, as management is primarily syndromic and centres on rehydration. As a result, clinicians are unlikely to prioritise stool-taking in uncomplicated cases of

(Continued on page 19)

(Continued from page 18)

diarrhoea. Disease in the past appears to have been primarily associated with water-borne outbreaks, due to high level of faecal contamination in water sources, and this trend appears to be continuing. The predominance of isolates received in children under the age of one year may reflect culturing practices; infants are more likely to have stools taken for culture due to the devastating effects of diarrhoea in children of this age. Seasonality graphs may be affected by current specimen-taking and laboratory diagnostic practices may not be optimal to accurately reflect burden of illness in South Africa of disease due to diarrhoeagenic *E. coli*.

Table 18: Number of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by province, South Africa, 2010, n=534.

Province	DAEC	EAggEC	STEC/ EHEC	EIEC	EPEC	ETEC
Eastern Cape	5	18	0	0	37	1
Free State	1	0	0	0	1	0
Gauteng	29	17	7	4	277	5
Kwazulu-Natal	1	0	1	0	4	0
Limpopo	1	1	0	0	2	0
Mpumalanga	50	20	0	3	23	7
Northern Cape	0	2	0	0	4	0
North West	0	0	0	0	8	0
Western Cape	3	0	0	0	2	0
South Africa	**90**	**58**	**8**	**7**	**358**	**13**

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.*

Table 19: Number of diarrhoeagenic *E. coli* isolates reported to GERMS-SA by age category, South Africa, 2010, n=534.

Age category (years)	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC
0 - 4	52	45	7	3	344	9
5 - 14	5	2	0	0	3	1
15 - 24	2	3	0	0	0	0
25 - 34	11	1	0	2	4	2
35 - 44	10	2	1	1	2	0
45 - 54	3	1	0	1	1	0
55 - 64	2	1	0	0	0	1
≥ 65	3	1	0	0	0	0
Unknown	2	2	0	0	4	0
Total	**90**	**58**	**8**	**7**	**358**	**13**

Vibrio cholerae O1

A single case of cholera due to *Vibrio cholerae* O1 Ogawa was reported in 2010 in South Africa. The organism was isolated from the stool of a 37 year-old woman, who presented with profuse watery diarrhoea on returning from a trip to India in June (8). Molecular epidemiological techniques using pulsed field gel electrophoresis (PFGE) confirmed that the isolate was closely related to known Indian strains of *Vibrio cholerae* O1.

Cryptococcus species

Results

During 2010, 7371 case patients, with laboratory-confirmed, incident cryptococcal episodes, were reported. The overall incidence for the general South African population decreased in 2010 (Table 20). Similarly, incidence amongst HIV-infected individuals (140/100 000 in 2009 and 122/100 000 in 2010) and people sick with AIDS (12/1000 in 2009 and 10/1000 in 2010) decreased. Incidence decreased in all provinces except the Western Cape where the incidence remained stable (Table 20). The peak incidence of cryptococcosis was recorded amongst patients aged 35-39 years (Figure 5). Two hundred and twelve children, younger than 15 years, had laboratory-confirmed cryptococcosis; 48/212 (23%) were younger than 1 year-old. Where gender was known (7258/7371, 98%), 53% patients were female. Most patients (6623/7371; 90%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 649/7371 (9%) were diagnosed with fungaemia (Table 21). Ninety two patients were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. At ESS, 1761 patients were diagnosed with cryptococcosis, with viable isolates received from 1296/1761 (73%) patients. Isolates were typed from 1296 cases; 1240 (96%) were identified as *Cryptococcus neoformans* and 51 (4%) were identified as *Cryptococcus gattii.* Of note, both *C. gattii* and *C. neoformans* were isolated from 4 patients. *C. gattii* cases were diagnosed in 8 provinces: Gauteng (n=24), Mpumalanga (n=11), Limpopo (n=5), KwaZulu-Natal (n=5), North West (n=4), Western Cape (n=3), Northern Cape (n=3) and Free State (n=1). The in-hospital case-fatality ratio for patients at enhanced surveillance sites did not significantly change between 2009 and 2010 (591/1812 (33%) vs. 503/1459 (34%)); p=0.2).

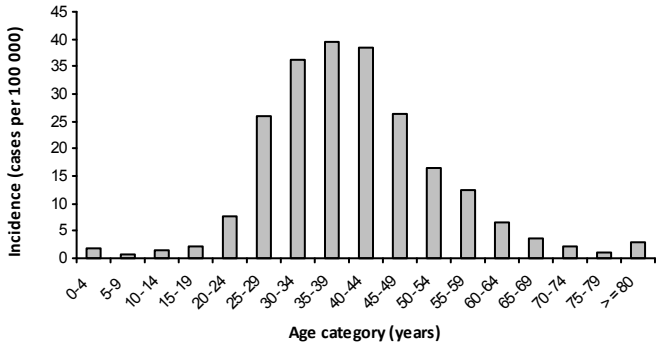


Figure 5. Age-specific incidence for laboratory-confirmed, cryptococcal cases, reported to GERMS-SA, South Africa, 2010, n=7371.

Discussion

In 2010, almost 1000 fewer incident cases were detected by GERMS-SA, compared with 2009. The overall incidence also decreased. This may indicate that the National HIV/AIDS Comprehensive Care, Management and Treatment (CCMT) Programme has made an impact. Most patients continued to be diagnosed with meningitis. The demographic profile of patients with cryptococcosis mirrored the profile of HIV-infected patients in South Africa. Although very few children were diagnosed with cryptococcosis, more than a quarter of paediatric cases were diagnosed amongst infants <1 year-old. In 2010, a low proportion of patients were infected with *C. gattii; C. gattii* cases were diagnosed across the country. The in-hospital mortality of patients with cryptococcosis remained high, and is probably due to patients entering the health care system with advanced cryptococcal disease.

Table 20: Number of cases and incidence of cryptococcal disease reported to GERMS-SA by province, South Africa, 2009 and 2010, n=15701.

	2009*		2010*	
Province	**n**	**Incidence****	**n**	**Incidence****
Eastern Cape	1393	21	1336	20
Free State	483	17	460	16
Gauteng	2125	20	2117	19
KwaZulu-Natal	1455	14	1053	10
Limpopo	682	13	552	10
Mpumalanga	836	23	734	20
Northern Cape	82	7	65	6
North West	738	21	555	17
Western Cape	536	10	499	10
South Africa	**8330**	**17**	**7371**	**15**

*A similar surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) in 2009 and 2010, detecting additional microscopy (India ink), cryptococcal antigen and culture-confirmed cases; **Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100 000

Table 21: Number and percentage of cases of cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2009 and 2010, n=15701.

Site of specimen	2009		2010	
	n	**%**	**n**	**%**
CSF	7676	92	6623	90
Blood	579	7	649	9
Other	75	1	92	1
Unknown	0	0	7	<1
	8330		**7371**	

Pneumocystis jirovecii

Results

In 2010, 298 cases of *P. jirovecii* pneumonia (PCP) were reported (Table 22), with 307 specimens available for analysis. Numbers of *P. jirovecii*-positive specimens peaked in children less than one year of age and in the 20 to 59 year age group (Figure 6). Of cases with known gender, 60% (178/298) were female. Of all reported case patients, 120 (40%) were diagnosed at enhanced surveillance sites and had clinical data available. During admission, 84% (75/89) of patients who tested for HIV, were HIV-infected. Where outcome was known, in-hospital case-fatality ratio was 33% (30/91). In 17% (16/93) of patients, this was their second or later hospitalization for PCP. Of patients who recovered, 95% (57/60) were discharged with a lower respiratory tract infection as the final diagnosis. Most of the patients had concurrent infections, of which clinically-diagnosed candidiasis (30/85) and TB (23/85) were the most common. Restriction fragment length polymorphism (RFLP)

(Continued on page 22)

(Continued from page 21)

analysis was performed on 141 of 307 specimens received for 2010 (Figure 7) to determine prevalent mutations in the DHPS gene. The most frequent observed mutations were the wild type + M1 mix (47/141), followed by wild type + M3 or wild type + M1 + M2 mix (25/141) and wild type (23/141).

Discussion

According to published data, *Pneumocystis* pneumonia (PCP) is the opportunistic infection that patients most often present with when HIV infection is diagnosed for the first time (9). The number of cases reported here does not approximate the true burden of disease in South Africa, and for this reason PCP surveillance through GERMS-SA ended on 31 December 2010. Analysis of the data and specimens collected are ongoing. Currently, the Parasitology Reference Unit is proposing to add PCP as an aetiological agent to the current severe acute respiratory infections (SARI) surveillance study, a prospective, hospital-based sentinel surveillance initiated in 2009. In this surveillance system, persons hospitalised with acute respiratory illness, who meet inclusion criteria have clinical data and specimens obtained for aetiology testing.

In the beginning of 2010 we introduced a restriction fragment length polymorphism (RFLP) test to determine the extent of the two main dihydropteroate synthase (DHPS) gene mutations [M1 at codon 55 and M2 at codon 57 (M3 mutation is a combination of these two)] circulating in the population under surveillance. It is suggested that these mutations are linked to sulfa-drug resistance, and are more likely to occur in patients who have previously been exposed to sulfa drugs (10). Antimicrobial drug resistance has emerged as a possible contributor to failure of patients to respond to PCP therapy, although results correlating resistance markers with clinical outcome have been conflicting (11). We have found a high number of DHPS mutations in specimens processed so far, indicating that mutations are a common occurrence in the surveillance population (12). The relationship between these mutations and treatment failure and patient outcome still needs to be investigated.

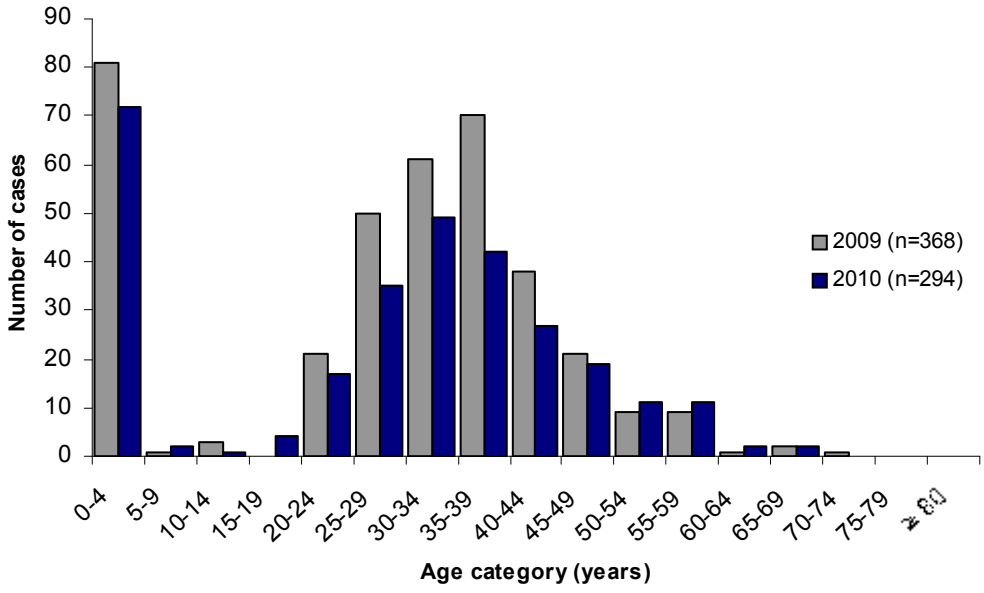
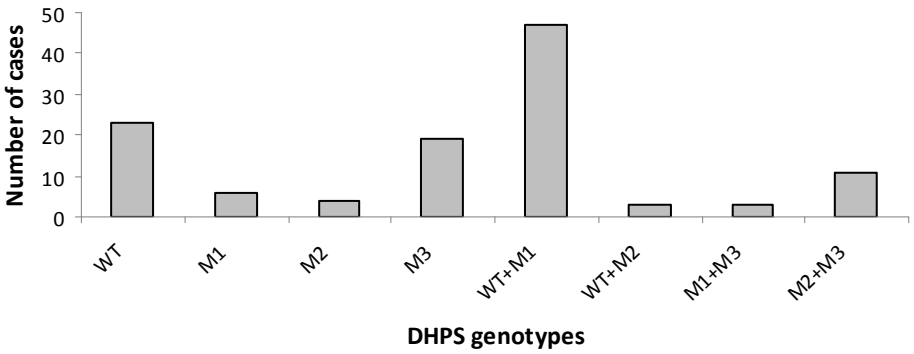


Figure 6. Number of laboratory-confirmed, *Pneumocystis jirovecii* pneumonia (PCP) cases reported to GERMS-SA, by age category, South Africa, 2009-2010, n=677.



WT: wild type genotype; M1: mutation at codon 55; M2: mutation at codon 57; M3: double mutation at codons 55 and 57; WT+M1, WT+M2, WT+M3, WT+M1+M2, M1+M3, M2+M3: genotype mixes

Figure 7. *Pneumocystis jirovecii* DHPS genotypes identified in specimens sent to Parasitology, NICD through the GERMS-SA network, 2010 (n=141)

Table 22: Number of *Pneumocystis jirovecii* pneumonia (PCP) cases reported to GERMS-SA by province, South Africa, 2009-2010, n=669.

Province	2009	2010
Eastern Cape	37	22
Free State	19	10
Gauteng	141	160
KwaZulu-Natal	19	9
Limpopo	0	0
Mpumalanga	6	3
Northern Cape	0	1
North West	44	20
Western Cape	105	73
South Africa	**371**	**298**

Neisseria meningitidis

Results

In 2010, 366 cases of meningococcal disease were reported, and an additional 38 cases were identified on audit: a total of 404 cases of laboratory-confirmed meningococcal disease was identified by the surveillance system during the year (Table 23). The number of cases reported increased during the winter and spring months (Figure 8). Of all cases reported, cerebrospinal fluid (CSF) was the most common specimen yielding meningococci (Table 24), and the number of cases diagnosed on blood culture remained similar in 2010 compared to 2009 (p=0.1). Cases of W135 disease were reported from all provinces, and this serogroup was the most predominant in South Africa (159/334, 48%) (Table 25), but the proportion decreased from 2009 (235/397, 59%; p=0.002). Minor year-on-year fluctuations of disease by province were noted, for example there was a more than 50% reduction of disease incidence in Mpumulanga and a doubling of disease incidence in the Northern Cape. However, for both these provinces, this represented a small number of cases. In Gauteng,

(Continued on page 24)

(Continued from page 23)

the incidence of meningococcal disease was estimated at 1.67 cases per 100 000 population, and most of that disease was due to serogroup W135 (92/161, 57%). The preponderance of serogroup B disease in Western Cape was still noted: 33/61 (54%) of all isolates serogrouped. 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 9). Preliminary analysis of case-fatality ratios, as calculated at ESS where in-hospital outcome is specifically looked for, was 27/158 (17%) in 2010, compared to 24/157 (15%) in 2009 (p=0.7). Of the viable isolates tested for antimicrobial resistance, 4/229 (2%) isolates had penicillin minimum inhibitory concentrations (MICs) >0.06µg/ml, and would be considered intermediately resistant.

Discussion

Overall incidence of disease did not change from 2009 and serogroup W135 disease decreased but remained the predominant serogroup. Changes in meningococcal disease incidence in provinces may reflect improved laboratory confirmation of disease and better reporting to the surveillance network, or may reflect a true increase in incidence. Case-fatality ratios have remained similar compared to 2009. The prevalence of intermediate resistance to penicillin remained low in 2010. 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.

Table 23: Number of cases and incidence of meningococcal disease reported to GERMS-SA by province, South Africa, 2009 and 2010, n=866 (including audit cases).

Province	2009		2010	
	n	Incidence*	n	Incidence *
Eastern Cape	36	0.5	31	0.5
Free State	18	0.6	26	0.9
Gauteng	203	1.9	187	1.7
KwaZulu-Natal	32	0.3	22	0.2
Limpopo	3	0.1	13	0.2
Mpumalanga	67	1.9	28	0.8
Northern Cape	9	0.8	20	1.8
North West	19	0.6	11	0.3
Western Cape	75	1.4	66	1.3
South Africa	**462**	**0.9**	**404**	**0.8**

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

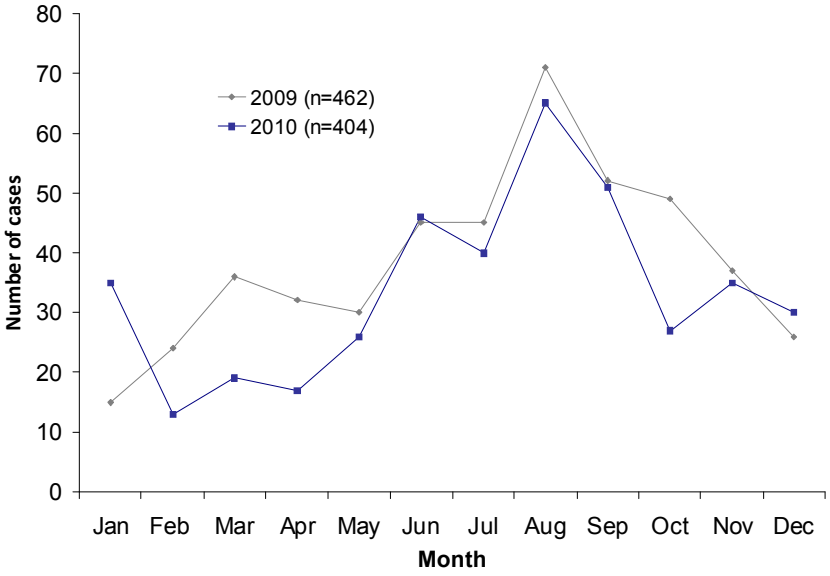


Figure 8. Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2009-2010, n=866.

Table 24: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2009 and 2010, n=866.

Site of specimen	2009		2010	
	n	%	n	%
CSF	336	73	312	77
Blood	124	27	91	23
Other	2	0.4	1	0.2
	462		**404**	

Table 25: Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2010, n=404*.

Province	Serogroup							
	Serogroup not available	A	B	C	W135	X	Y	Total
Eastern Cape	5	0	7	2	15	0	2	31
Free State	10	0	9	1	4	0	2	26
Gauteng	26	3	38	10	92	2	16	187
KwaZulu-Natal	2	0	4	4	8	0	4	22
Limpopo	6	0	1	0	5	0	1	13
Mpumalanga	7	0	3	0	16	0	2	28
Northern Cape	6	0	2	2	3	0	7	20
North West	3	0	3	2	2	0	1	11
Western Cape	5	0	33	4	14	0	10	66
South Africa	70	3	100	25	159	2	45	404

*334 (83%) with specimens or viable isolates available for serogrouping.

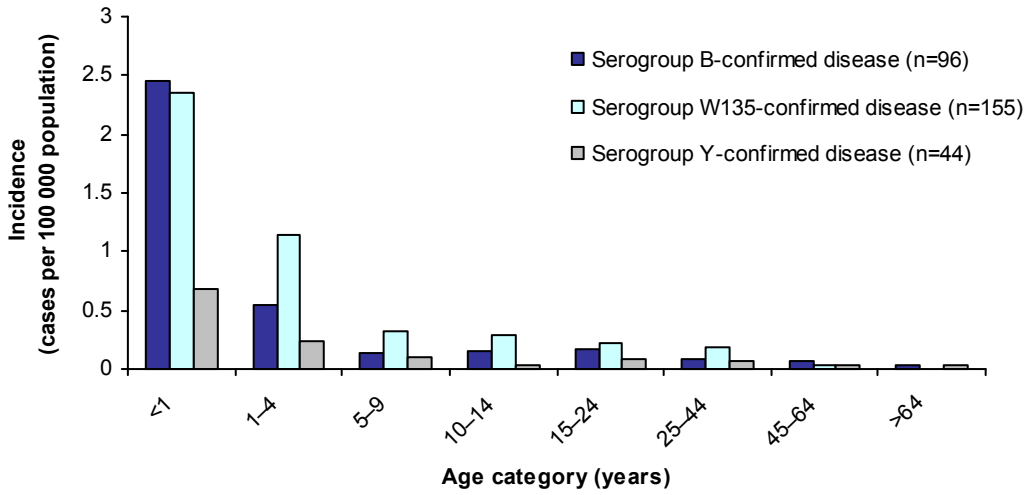


Figure 9. Age-specific incidence rates for laboratory-confirmed, invasive, meningococcal cases, by serogroup, South Africa, 2010, n=404 (age unknown for n=13; specimens or viable isolates unavailable for serogrouping n=70).

Haemophilus influenzae

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2010 was 313, while an additional 91 cases were identified during the national audit (total number of cases available for analysis was 404). Of these, 294 (73%) had isolates or specimens available for serotyping, and 123/294 (42%) were confirmed as serotype b (Table 26). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (81/123, 66% vs. 12/125, 10%, p<0.001) (Table 27). In 2010, a total of 82 cases of *H. influenzae* serotype b (Hib) were reported amongst children <5 years (Figure 10). Serotype b was the more common *H. influenzae* causing disease amongst infants (Figure 11). Rates of Hib disease as recorded by our surveillance network amongst infants <1 year of age were similar in 2010 as compared to 2009 (p=0.8) (Figure 12). Twenty percent of serotype b strains were non-susceptible to ampicillin (MIC>1mg/L, all producing beta lactamase), 17 of 85 isolates tested, while 12% (10/85) of non-typeable strains were non-susceptible (p=0.1).

Discussion

Since the introduction of the Hib conjugate vaccine into the EPI for South Africa in 1999, there has been a reduction in cases reported due to this serotype. Population-based studies in South Africa before the introduction of the conjugate Hib vaccine had demonstrated annual rates of invasive Hib disease of 170 per 100 000 infants below one year of age (13; 14) and any increases noted recently were small in comparison to the substantial decline in disease subsequent to the introduction of the vaccine. Recognising that our surveillance system underestimates disease, reported cases of Hib disease amongst children <1 year are being monitored carefully. In April 2009, the updated infant vaccination programme in South Africa introduced a booster dose of conjugate Hib vaccine given at 18 months as part of a combination vaccine (Pentaxim: diphtheria-tetanus-acellular pertussis-inactivated poliovirus-*Haemophilus influenzae* type-b conjugate). It is hoped that this booster will improve long-term protection against disease and impact on ongoing Hib transmission in the community. However it is too early to comment on the stabilisation of rates of Hib in children <1 year comparing 2010 to 2009, and we urge clinical and laboratory staff to continue reporting all cases of *H. influenzae.*

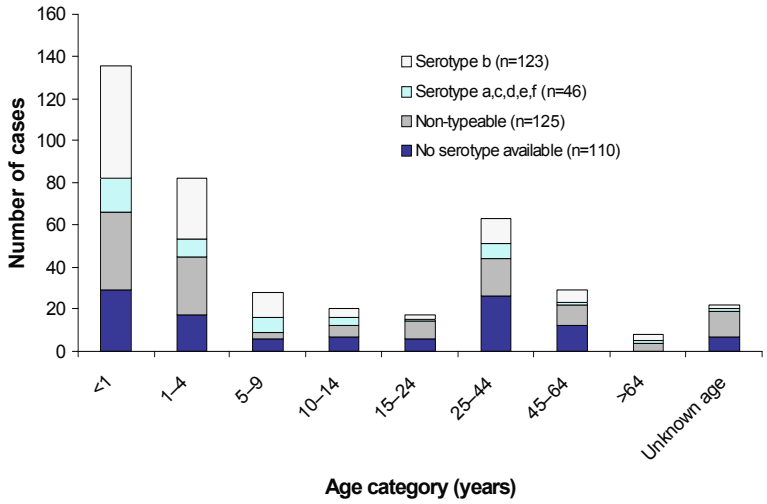


Figure 10. Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2010, n=404 (age unknown for n=22; specimens or viable isolates unavailable for serotyping for n=110).

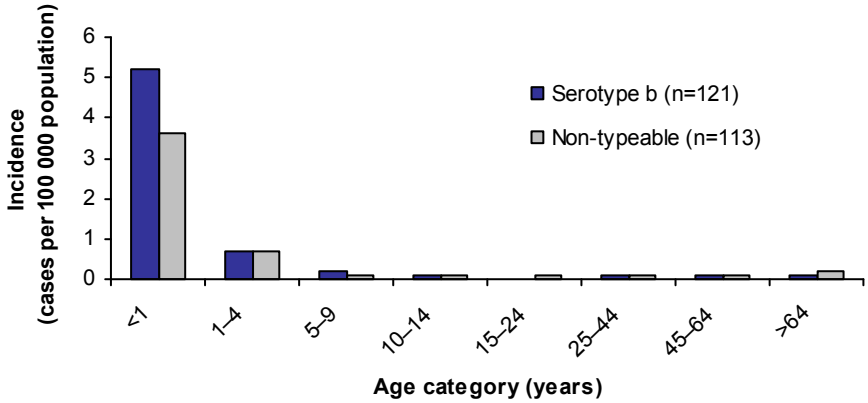


Figure 11. Age-specific incidence for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype, South Africa, 2010, n=404 (age unknown for n=22; viable isolates unavailable for serotyping for n=110).

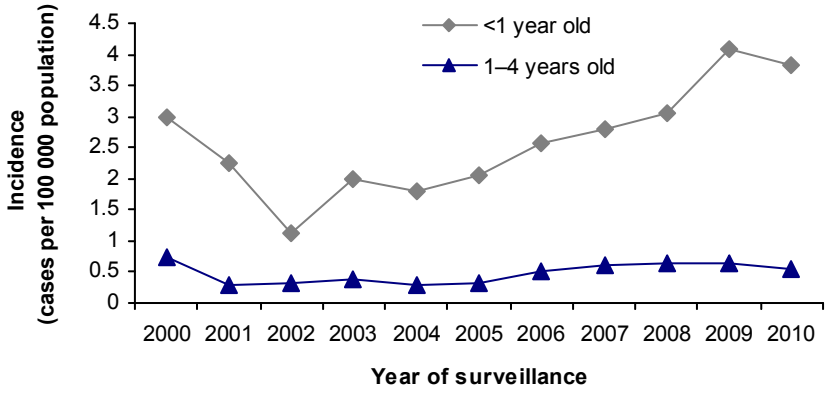


Figure 12. Incidence rates of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2000-2010 (excluding cases identified using polymerase chain reaction (PCR) on specimens which was only done 2007-2010).

Table 26: Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2010, n=404*

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	30	0	10	0	0	0	0	4	44
Free State	9	1	10	0	1	0	1	3	25
Gauteng	33	4	44	1	2	3	9	71	167
KwaZulu-Natal	2	0	18	0	1	1	1	8	31
Limpopo	2	1	4	0	0	0	0	3	10
Mpumalanga	5	1	9	0	0	0	1	0	16
Northern Cape	1	0	7	0	0	1	0	2	11
North West	3	0	3	0	0	0	1	1	8
Western Cape	25	8	18	0	1	1	6	33	92
South Africa	**110**	**15**	**123**	**1**	**5**	**6**	**19**	**125**	**404**

*294 (73%) with specimens or viable isolates available for serotyping.

Table 27: Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2010, n=404.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
CSF	20	18	81	66	13	28	12	10
Blood	46	42	40	33	31	67	96	77
Other	44	40	2	2	2	4	17	14
Total	**110**		**123**		**46**		**125**	

Streptococcus pneumoniae

Results

Incidence of reported invasive pneumococcal disease (IPD) varied widely by province (Table 28). The age group at highest risk of disease in South Africa was infants <1 year of age, and there was an ongoing significant reduction in disease comparing 2010 to 2009, p<0.001 (Figure 13). The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 29). Penicillin non-susceptible isolates (MIC>0.06mg/L), have remained stable (1478/3389, 44% in 2009 compared to 1204/2857, 42% in 2010, p=0.2). Prevalence of non-susceptible strains ranged from 29% to 52% in different provinces (Table 30). Penicillin non-susceptible isolates were common amongst children less than 5 years of age (Figure 14). Ceftriaxone non-susceptibility was detected amongst 8% (225/2855) of all IPD cases, and in 7% (73/1094) of isolates detected from CSF specimens. PREVENAR (7-valent conjugate pneumococcal vaccine, PCV7) was introduced into the EPI in South Africa from 1 April 2009. The number of cases amongst children less than 5 years of age due to common serotypes in 2009 (including the seven serotypes in PCV7: 4, 6B, 9V, 14, 18C, 19F and 23F) are compared with 2009 in Figure 15.

The percentage of disease in 2010 amongst chidren <5 years due to PCV7 and newer valency

(Continued on page 29)

(Continued from page 28)

vaccine formulations are shown in Table 31.

Discussion

Differences in IPD incidence by province have been documented for several years, and are partly due to differences in specimen-taking practices and laboratory reporting, however real differences in disease incidence cannot be excluded. The decrease in incidence of disease in children <1 year of age is most likely due to the introduction of PCV7 in South Africa. Our data for 2010 show similar prevalences of pneumococcal resistance to penicillin and ceftriaxone compared with 2009. The low levels of penicillin non-susceptibility from blood culture specimens still support the use of penicillin as first-line therapy for community-acquired pneumonia. Vancomycin, together with ceftriaxone, should be considered for the empiric treatment of suspected pneumococcal meningitis (CSF specimens positive for Gram-positive cocci or latex agglutination tests positive for *S. pneumoniae*), especially amongst unvaccinated children. As ceftriaxone-resistant isolates are likely to be serotypes contained in PCV7, we anticipate that the number of resistant isolates causing disease will decrease with wider use of the vaccine.

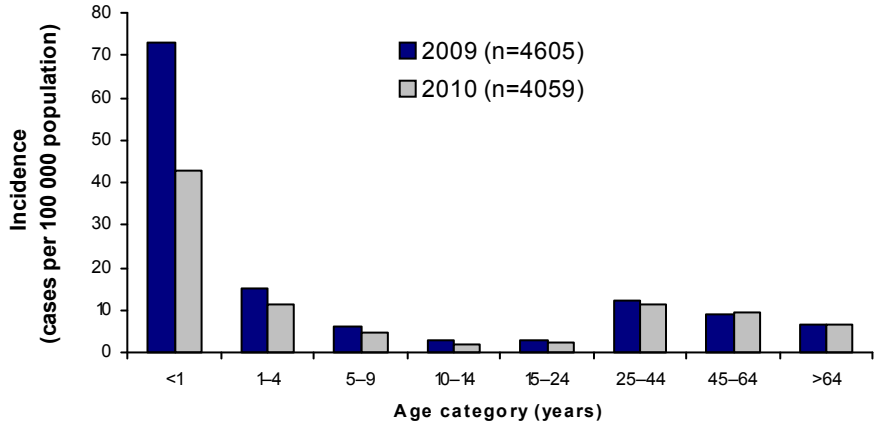
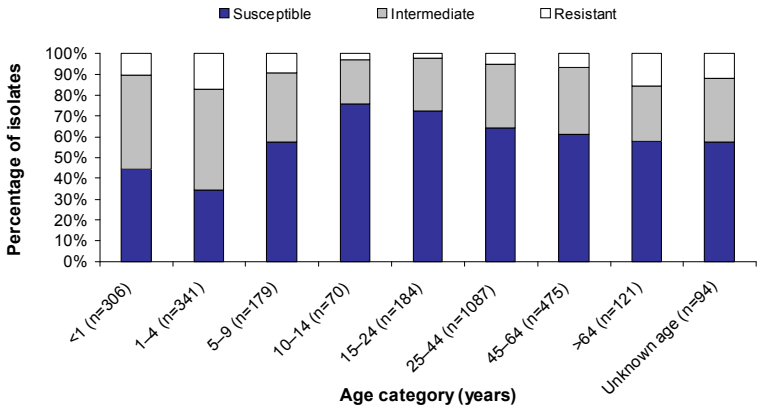


Figure 13. Age-specific incidence rates for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 and 2010 (2009: n=4605; age unknown for n=164; 2010: n=4059; age unknown for n=147).



2009 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Figure 14. Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2010, n=4206 (n=2857 with viable isolates).

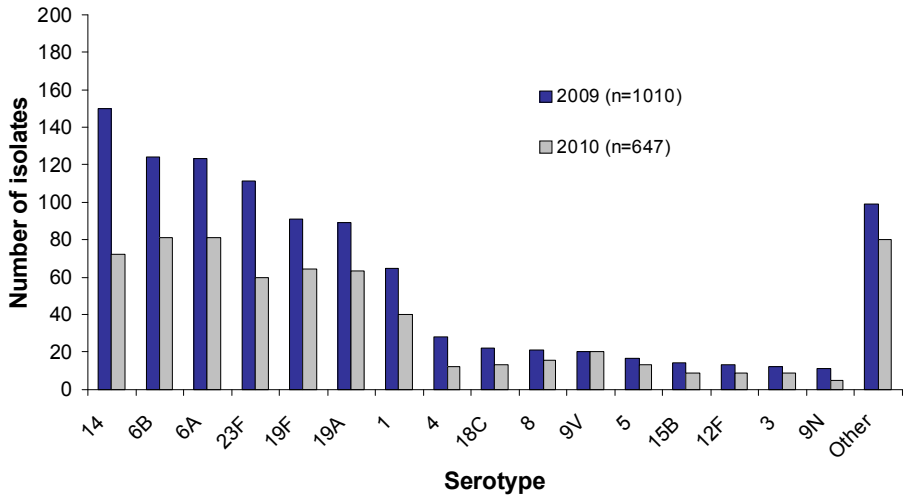


Figure 15. Pneumoccocal serotypes, in descending order, causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2010 (2009: n=1338, n=1010 with viable isolates; 2010: n=907; n=647 with viable isolates).

Table 28: Number of cases and incidence of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2009 and 2010, n=8975.

Province	2009		2010	
	n	Incidence*	n	Incidence*
Eastern Cape	362	5.4	388	5.8
Free State	308	10.6	318	11.3
Gauteng	2256	21.4	1847	16.5
KwaZulu-Natal	529	5.1	426	4.0
Limpopo	111	2.1	109	2.0
Mpumalanga	301	8.4	241	6.7
Northern Cape	88	7.7	105	9.5
North West	175	5.1	183	5.7
Western Cape	639	11.9	589	11.3
South Africa	**4769**	**9.7**	**4206**	**8.4**

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

Table 29: Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2009 and 2010, n=8975.

Site of specimen	2009		2010	
	n	%	n	%
CSF	1800	38	1709	41
Blood	2517	53	2025	48
Other	452	9	472	11
	4769		**4206**	

Table 30: Number and percentage of penicillin non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2010, n=4206.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	164	128	57	84	38	12	5
Free State	107	131	62	72	34	8	4
Gauteng	616	715	58	404	33	112	9
KwaZulu-Natal	68	200	56	133	37	25	7
Limpopo	45	40	63	17	27	7	11
Mpumalanga	128	75	66	34	30	4	4
Northern Cape	23	39	48	31	38	12	15
North West	91	65	71	25	27	2	2
Western Cape	107	260	54	172	36	50	10
South Africa	**1349**	**1653**	**58**	**972**	**34**	**232**	**8**

*2009 CLSI breakpoints for penicillin (oral penicillin V) were used: susceptible, ≤0.06mg/L; intermediately resistant, 0.12-1mg/L; resistant, ≥2mg/L.

Table 31: Number and percentage of 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, 2010, n=907 (n=647 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	45	22	49	6	13	27	60	37	82
Free State	32	19	59	3	9	22	69	27	84
Gauteng	279	135	48	36	13	160	57	227	81
KwaZulu-Natal	96	41	43	10	10	50	52	73	76
Limpopo	12	8	67	0	0	9	75	9	75
Mpumalanga	22	11	50	5	23	11	50	18	82
Northern Cape	32	16	50	3	9	19	59	25	78
North West	15	7	47	3	20	11	73	14	93
Western Cape	114	64	56	15	13	68	60	100	88
South Africa	647	323	50	81	13	377	58	530	82

*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 (15).

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

The invasive pneumococcal disease (IPD) case-control study is a nested matched case-control study to estimate effectiveness of a 7-valent pneumococcal conjugate vaccine (PCV) against IPD in South Africa. The study commenced on the 1 March 2010, and the first case to be enrolled was at Chris Hani Baragwanath Hospital in Johannesburg. The last site (Dr George Mukhari Hospital) started on 5 October 2010. The study is nested in GERMS-SA and the 24 enhanced GERMS-SA hospitals have been combined into 21 IPD sites, which include 2 new non-enhanced sites (Rahima Moosa and Kalafong hospitals). The study population includes all children who are eligible to receive PCV7 through the EPI programme i.e. born after the 15 February 2009. In the Western Cape and Free State the date of birth criteria differ as the roll-out of PCV7 was delayed in these provinces. In 2010, 156 cases of invasive pneumococcal disease were enrolled in the study and to date 372 controls have been accepted as eligible.

Klebsiella pneumoniae

Results

From July through December 2010, 519 cases of *Klebsiella pneumoniae* bloodstream infections were reported, and an additional 452 cases were identified on audit: a total of 971 cases of laboratory-confirmed bacteraemia caused by *K. pneumoniae* were identified (Table 32). The highest number of cases (n=649; 67%) was detected from Gauteng province (Table 32). Most cases of bacteraemia occurred amongst adults (Figure 16).The highest number of cases was detected during December 2010 (Figure 17). Of the viable *K. pneumoniae* isolates tested for antimicrobial resistance, 295/475 (62%) were extended spectrum β-lactamase (ESBL) producers. The percentage of isolates which were ESBL-producing varied by province (Gauteng, 141/248 (57%) vs. Free State, 37/46 (80%)) (Figure 18).

Discussion

Sentinel surveillance for *K. pneumoniae* bacteraemia was initiated in July 2010 through GERMS-SA. Incidence has not been reported. In the start-up phase, over half of the detected cases were only identified through audit; isolates were not submitted for these cases. It is important to recognise that there may have been an inherent selection bias – laboratories may have selectively reported cases with antimicrobial-resistant isolates. Amongst the submitted isolates, almost two-thirds were ESBL producers. Most ESBL-producing isolates were submitted from Free State and Western Cape laboratories.

Table 32: Number of *Klebsiella pneumoniae* cases reported to GERMS-SA sentinel sites by province, South Africa, July-December 2010, n=971 (including audit cases).

Province	*Klebsiella pneumoniae*
Free State	82
Gauteng	649
KwaZulu-Natal	36
Limpopo	13
Western Cape	191
All sentinel sites	**971**

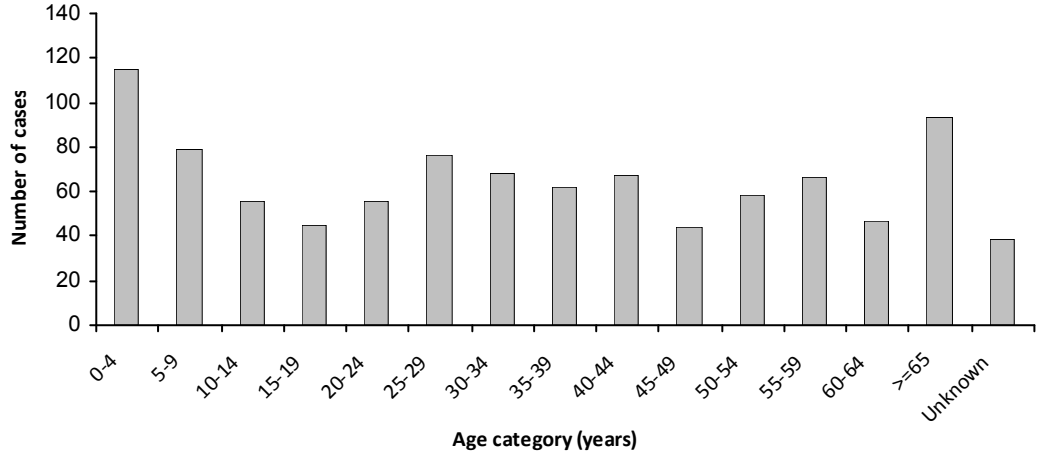


Figure 16. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA sentinel sites by age category, July- December 2010, n=971

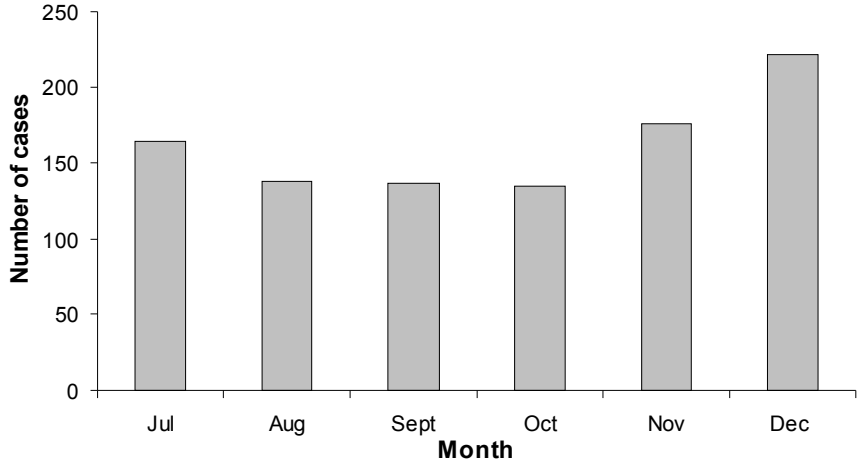
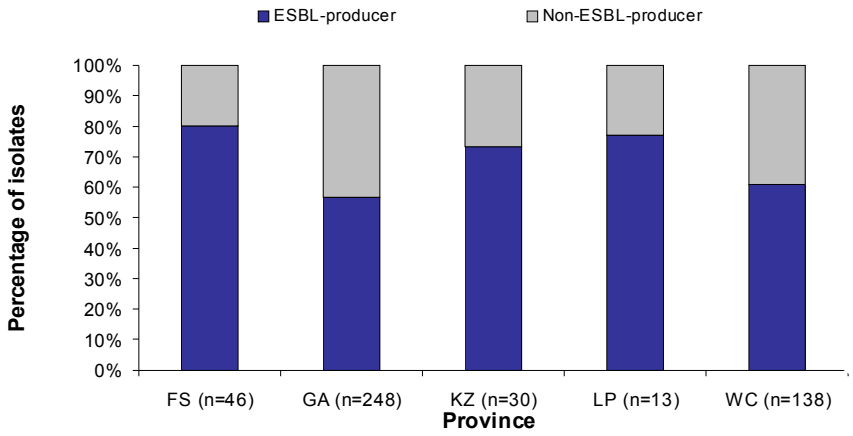


Figure 17. Number of cases of laboratory-confirmed *Klebsiella pneumoniae* bacteraemia reported to GERMS-SA sentinel sites by month, July- December 2010, n=971



*Sentinel sites may have preferentially submitted antimicrobial-resistant isolates

Figure 18. Number of viable, laboratory-confirmed *Klebsiella pneumoniae* isolates reported by GERMS-SA sentinel sites*, by province and ESBL production, July-December 2010, n=478

Staphylococcus aureus

Results

The number of cases of *Staphylococcus aureus* bacteraemia reported to the GERMS-SA from July through December 2010 was 506 while an additional 280 cases (36%) were identified during an audit (total number of cases available for analysis was 786) (Table 33). Of these, the majority of cases were detected from sentinel sites in Gauteng (Table 33). The highest number of cases (n=177) was detected in July 2010 (Figure 19). Most cases (577/786, 73%) occurred amongst patients aged >15 years (Figure 20). Resistance to oxacillin was determined for a subset of isolates (n=348) from 6 sentinel sites; the percentage of isolates which were MRSA: Free State (11//24, 46%), Gauteng (78/182, 43%) and Western Cape (74/179, 41%) (Figure 21).

Discussion

Incidence of *S. aureus* bacteraemia was not calculated. In addition, cases could not be separated into hospital- versus community-acquired categories because only laboratory-based data were available. Most cases of S. *aureus* bacteraemia occurred amongst adult patients. The percentage of *S. aureus* isolates which were MRSA was almost certainly biased by isolate submission practices at some sentinel sites (laboratories may have selectively reported cases with antimicrobial-resistant isolates).

Table 33: Number of *Staphylococcus aureus* cases reported to GERMS-SA sentinel sites by province, South Africa, July-December 2010, n=786 (including audit cases)

Province	*Staphylococcus aureus*
Free State	40
Gauteng	510
KwaZulu-Natal	26
Limpopo	3
Western Cape	207
All sentinel sites	**786**

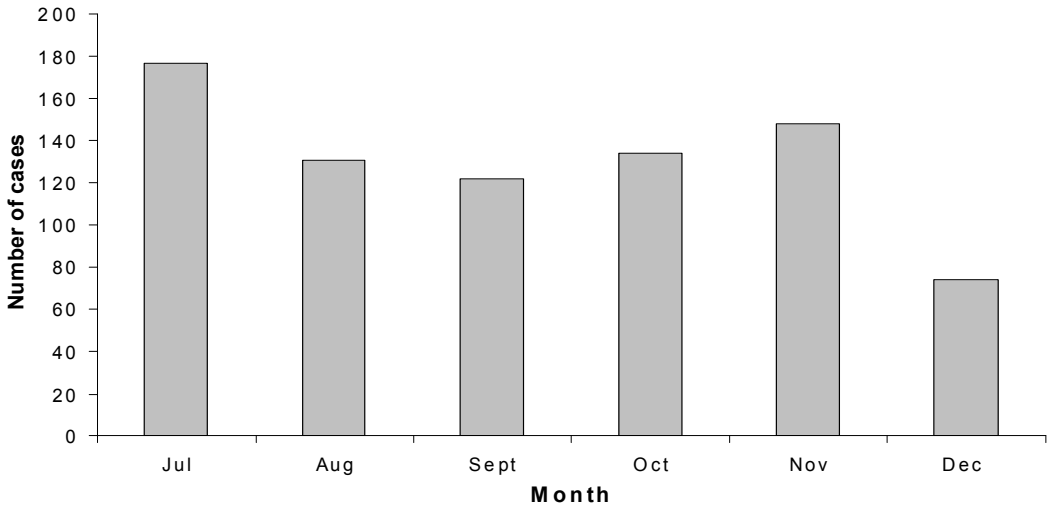


Figure 19. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by month, July- December 2010, n=786

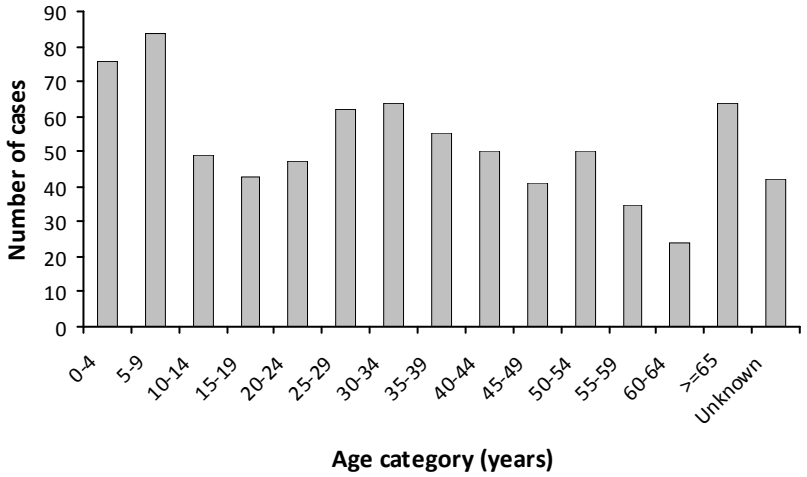
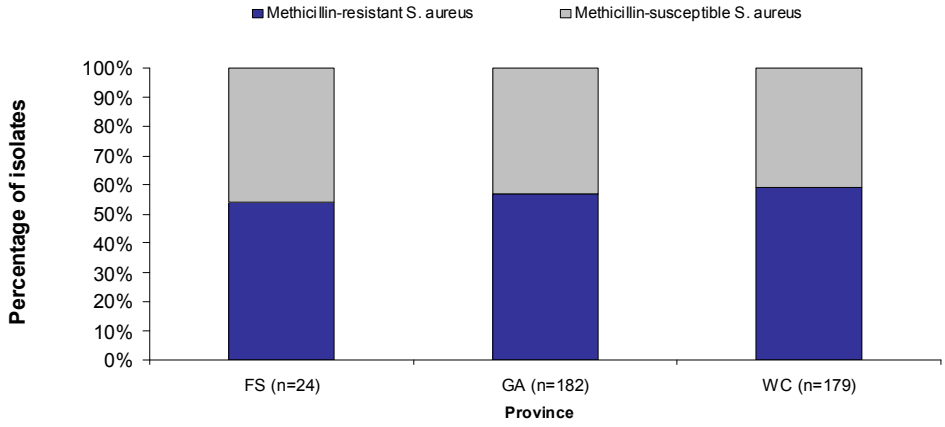


Figure 20. Number of cases of laboratory-confirmed *Staphylococcus aureus* bacteraemia reported to GERMS-SA sentinel sites by age category, July- December 2010, n=786.



*Sentinel sites may have preferentially submitted antimicrobial-resistant isolates

Figure 21. Number of viable, laboratory-confirmed *Staphylococcus aureus* isolates reported by GERMS-SA sentinel sites*, by province and oxacillin resistance, July-December 2010, n=385

Discussion

Leveraging on the strength of its national network of >200 reporting public- and private-sector laboratories, GERMS-SA has largely focused on surveillance of community-acquired diseases of public health importance to date. Surveillance data on epidemic-prone bacterial diseases, AIDS-associated opportunistic infections and vaccine-preventable bacterial diseases have been used to influence public health policy, change clinical management and estimate the effectiveness of public health interventions. In 2010, GERMS-SA has documented remarkable changes to the epidemiology of both cryptococcosis and IPD. The incidence of laboratory-confirmed cryptococcosis has decreased independent of changes to surveillance methods. It is likely that improved care, management and treatment of HIV-infected patients in South Africa has led to this decline. Ongoing surveillance will be able to document if this trend will continue. Unfortunately, the high in-hospital mortality has not changed; other public health measures such as screening to detect disease earlier may impact on outcomes.

(Continued on page 36)

(Continued from page 35)

The decreased incidence of IPD amongst children less than 1 year is also likely a direct result of PCV7. Two other seismic shifts occurred in 2010. The GERMS-SA steering committee agreed that surveillance for PCP was not appropriately housed within a laboratory-based surveillance programme. Although PCP is a common and important AIDS-defining opportunistic infection, GERMS-SA could not accurately estimate the burden of disease - an important objective. PCP surveillance may be re-launched within the SARI programme in 2011. In the era of rapidly emerging antimicrobial resistance and frequent nosocomial outbreaks, GERMS-SA also expanded its surveillance activities to include hospital-acquired infections in mid-2010. Sentinel laboratory-based surveillance for bacteraemic *S. aureus* and *K. pneumoniae* will allow GERMS-SA to detect emerging resistance, characterise nosocomial pathogens more carefully and document local epidemiology.

Publications

Publications in peer-reviewed journals

1. Cohen C, Singh E, Wu HM, Martin S, de Gouveia L, Klugman KP, Meiring S, Govender N, von Gottberg A. Increased incidence of meningococcal disease in HIV-infected individuals associated with higher case-fatality ratios in South Africa. *AIDS* 2010;24:1351-60.
2. du Plessis M, de Gouveia L, Skosana H, Thomas J, Blumberg L, Klugman KP, von Gottberg A. Invasive *Neisseria meningitidis* with decreased susceptibility to fluoroquinolones in South Africa, 2009. *J Antimicrob Chemother* 2010;65:2258-60.
3. Fali A, du Plessis M, Wolter N, Klugman KP, von Gottberg A. Single report of beta-lactam resistance in an invasive *Haemophilus influenzae* isolate from South Africa mediated by mutations in penicil lin-binding protein 3, 2003-2008. *Int J Antimicrob Agents* 2010;36:480-482.
4. Feldman C, Brink AJ, von Gottberg A, Wolter N, de Gouveia L, Perovic O, Klugman KP. Antimicrobial susceptibility of pneumococcal isolates causing bacteraemic pneumococcal pneumonia: analysis using current breakpoints and fluoroquinolone pharmacodynamics. *Int J Antimicrob Agents* 2010;36:95-97.
5. Mothibeli KM, du Plessis M, von Gottberg A, de Gouveia L, Adrian P, Madhi SA, Klugman KP. An unusual pneumococcal sequence type is the predominant cause of serotype 3 invasive disease in South Africa. *J Clin Microbiol* 2010;48:184-91.
6. Smith AM, Govender N, Keddy KH, for the Group for Enteric, Respiratory and Meningeal Disease Surveillance in South Africa (GERMS-SA). 2010. Quinolone-resistant *Salmonella* Typhi in South Af rica, 2003-2007. *Epidemiology and Infection* 138:86-90.
7. Keddy KH, Smith AM, Sooka A, Ismail H, Oliver S. 2010. Fluoroquinolone-resistant typhoid, South Africa. *Emerging Infectious Diseases* 16:879-880.
8. Feasey N, Archer BN, Heyderman RS, Gordon MA, Keddy KH. 2010. Typhoid Fever and invasive Non-Typhoid Salmonellosis, Malawi and South Africa. *Emerging Infectious Diseases* 16:1448-1451.
9. Keddy KH, Sooka A, Ismail H, Smith AM, Weber I, Letsoalo ME, Harris BN. Molecular epidemiological investigation of a typhoid fever outbreak in South Africa, 2005: the relationship to a prior epidemic in 1993. *Epidemiology and Infection.* 2010. (Epub ahead of print).

Publications in non-peer-reviewed journals

1. von Gottberg A. Bacterial meningitis in the era of paediatric vaccination against the encapsulated pathogens. *CME (Continuing Medical Education)* June 2010; 28 (6):198-202.

References

1. South Africa.Info 2010, Zuma to launch new HIV/Aids plan, 23 April 2010, viewed 18 April 2011, http://www.southafrica.info/news/hiv-230410.htm
2. Govender N, Quan V, Prentice E, von GA, Keddy K, McCarthy KM, et al. GERMS-SA: A national South African surveillance network for bacterial and fungal diseases. Johannesburg, South Africa: National Institute for Communicable Diseases; 2006.
3. Statistics South Africa. Mid-year population estimates, South Africa, 2010. P0302. 20 July 2010. Available from: http://www.statssa.gov.za/publications/P0302/P03022010.pdf 2010. Accessed 14 March 2011
4. Actuarial Society of South Africa AIDS Committee. ASSA2003 AIDS and demographic model, 2005. Available from: http://aids.actuarialsociety.org.za/ASSA2003-Model-3165.htm Accessed 14 March 2011
5. Smith AM, Keddy KH, Ismail H, Thomas J, Van Der Gryp R, Manamela M, Huma M, Sooka A, Theobald L, Mennen M, O'Reilly L . International collaboration tracks a typhoid fever outbreak over two continents from South Africa to Australia. J. Me Microbiol (in press).
6. Crump JA, Barrett TJ, Nelson JT, Angulo FJ. Reevaluating fluoroquinolone breakpoints for *Salmonella enterica* serotype Typhi and for non-Typhi salmonellae. Clin Infect Dis 2003 Jul 1;37(1):75-81
7. 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 Feb ; 13 Available from http://www.eurosurveillance.org/edition/v13n09/080228_4.asp. Accessed 25 March 2011
8. NICD. Imported cholera. NICD Communique. http://www.nicd.ac.za/assets/files/NICDCommJune10Vol09_06.pdf Accessed 25 March 2011
9. Morris A, Lundgren JD, Masur H, Walzer PD, Hanson DL, Frederick T, et al. Current epidemiology of *Pneumocystis* pneumonia. Emerg Infect Dis 2004 Oct; 10(10): 1713-20.
10. Huang L, Crothers K, Atzori C, Benfield T, Miller R, Rabodonirina M et al. Dihydropteroate synthase gene mutations in *Pneumocystis* and sulfa resistance. Emerg Infect Dis 2004 October; 10(10): 1721-8.
11. Crothers K, Beard CB, Turner J, Groner G, Fox M, Morris A et al. Severity and outcome of HIV-associated *Pneumocystis* pneumonia containing *Pneumocystis jirovecii* dihydropteroate synthase gene mutations. AIDS 2005 May; 19(8): 801-5.
12. Dini L, du Plessis M, Frean J & Fernandez V. High prevalence of dihydropteroate synthase mutations in *Pneumocystis jirovecii* isolated from patients with *Pneumocystis* pneumonia in South Africa. J Clin Microbiol 2010 June; 48(6): 2016-2021.
13. Madhi SA, Kuwanda L, Saarinen L, Cutland C, Mothupi R, Kayhty H, Klugman KP. Immunogenicity and effectiveness of *Haemophilus influenzae* type b conjugate vaccine in HIV infected and uninfected African children. *Vaccine* 2005;23:5517-25.
14. Hussey G, Hitchcock J, Schaaf H, Coetzee G, Hanslo D, van Schalkwyk E, Pitout J, Clausen J, van der Horst W. Epidemiology of invasive *Haemophilus influenzae* infections in Cape Town, South Africa. *Ann Trop Paediatr* 1994;14:97-103.
15. 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 Oct 28;368(9546):1495-502.

Acknowledgements

GERMS-SA: Sandeep Vasaikar, (Eastern Cape); Eugene Elliot (Free state); Alan Karstaedt, Jeannette Wadula, David Moore, Sharona Seetharam, Charles Feldman, Trusha Nana, Norma Bosman, Maphoshane Nchabeleng, Anwar Hoosen, Bonnie Maloba, Ruth Lekalakala (Gauteng); Yacoob Coovadia, Nomonde Dlamini, Prasha Mahabeer, Yesho Mahabeer, Halima Dawood, Sumayya Haffejee (Kwa-Zulu Natal); Ken Hamese (Limpopo) Greta Hoyland, Jacob Lebudi (Mpumalanga); Stan Harvey, Pieter Jooste (Northern Cape); Andrew Rampe (North west); Elizabeth Wasserman, Preneshni Naicker, Andrew Whitelaw (Western Cape); Juanita Smit, Keshree Pillay, Chetna Govind, Ben Prinsloo (LANCET laboratories); Adrian Brink, Maria Botha, Inge Zietsman, Suzy Budavari, Xoliswa Poswa, Mark Cruz da Silva (AMPATH laboratories); Jennifer Coetzee, Marthinus Senekal (PATHCARE laboratories); Chris van Beneden, Stephanie Schrag, Elizabeth Zell, Anne Schuchat, Tom Chiller, Angela Ahlquist, Fred Angulo, Nancy Rosentein-Messonier, Katherine Robinson (CDC); Victor Fernandez, Leigh Dini (SMI); Keith Klugman, Anne von Gottberg, Linda de Gouveia, Karen Keddy, Arvinda Sooka, Nelesh Govender, Jaymati Patel, Vanessa Quan, Susan Meiring, Melony Fortuin-de Smidt, Taskeen Khan, Claire von Mollendorf, John Frean, Desiree du Plessis, Bhavani Poonsamy, Olga Perovic, Marshagne Smith, Vivian Fensham, Cheryl Cohen, Penny Crowther, Jabulani Ncayiyana

GERMS-SA would like to thank laboratory staff at participating sites throughout South Africa for submitting case report forms and isolates, administrative staff at facilities across the country who have facilitated participation in the surveillance programme, surveillance officers at ESS for their tireless efforts, the patients who participated in surveillance activities, despite their illnesses, NICD staff working on the programme for their dedication and hard work, our international and local collaborators, including the Centers for Disease Control and Prevention (CDC)-South Africa, NICD/ NHLS management for their support of the programme, and Department of Health.

This publication was partly supported by a Cooperative Agreement (Number 5U2GPS001328-02) from the Centers for Disease Control and Prevention (CDC). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of CDC-South Africa.

Contact details

Please contact the NICD unit which coordinates GERMS-SA, the National Microbiology Surveillance Unit (NMSU), for further information:

Physical address:
National Institute for Communicable Diseases, a Division of National Health Laboratory Service
SAVP Building
1 Modderfontein Road
Sandringham
Johannesburg

Postal address:
National Institute for Communicable Diseases, a Division of National Health Laboratory Service
Private Bag X4
Sandringham
2131
South Africa

Telephone: +27 11 386 6234

Facsimile: +27 11 386 6221

The GERMS-SA website can be accessed via the NICD website: **www.nhls.ac.za (follow the NICD link, surveillance and GERMS)**