GERMS SOUTH AFRICA

Annual Report 2009

NHLS

NICD

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Introduction

As in previous years, the 2009 GERMS-SA Annual Report includes a summary of the main findings from national surveillance, including clinical data from enhanced surveillance sites (ESS), for the year. In addition, the operational report summarises the many activities conducted in support of the GERMS-SA programme. A new section has also been added to summarise the progress made on studies nested within GERMS-SA. This report indicates that GERMS-SA has entered a new phase. The enhanced surveillance backbone provides robust clinical data each year which is comparable to previous years. The programme is also now able to provide a platform for conducting more in-depth studies to explore key questions generated through surveillance. The objectives of these nested studies fit within the core objectives of GERMS-SA and have public health relevance. Two such studies are described in this annual report: A case-control study to estimate the effectiveness of the PCV against IPD amongst South African infants and a follow-up study to determine the post-discharge outcome of patients with cryptococcosis. GERMS-SA continues to provide strategic information on the burden of HIV-associated opportunistic infections in South Africa. Early in 2010, the Deputy Minister of Health announced a new plan to scale up access to HIV prevention and treatment (1). As South Africa prepares to enter a new era of enhanced access to HIV prevention and care, GERMS-SA is well positioned to monitor the impact of these new interventions in South Africa.

GERMS-SA Surveillance Officer Meeting, 11-13 November 2009

Methods

Diseases which are currently under surveillance by GERMS-SA include:

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

The methods used by GERMS-SA have been previously described in detail (2).

In brief, approximately 200 South African, diagnostic laboratories participated in the surveillance programme in 2009. The South African population under surveillance in 2009 was estimated to be 49.3 million. Diagnostic laboratories reported cases to the National Institute for Communicable Diseases (NICD) in Johannesburg using laboratory case report forms, according to standard case definitions. If available, isolates from case patients were submitted on Dorset transport media to NICD for phenotypic and genotypic characterisation. In 2009, only enhanced surveillance sites (ESS = 25 hospitals in 9 provinces), National Health Laboratory Service (NHLS) laboratories in KwaZulu-Natal, and laboratories in the private, mining, and military sectors were required to directly report cases of cryptococcal disease to NICD. Data from cases of cryptococcosis diagnosed at other NHLS laboratories were obtained directly from the NHLS Corporate Data Warehouse (NHLS CDW). Cryptococcal isolates, obtained from case patients at ESS, were characterised by phenotypic and genotypic tests.

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

Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on Epi Info version 6.04d (Centers for Disease Control and Prevention, Atlanta, USA) or Microsoft Access database. A surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) between 1 January and 31 December 2009, using the NHLS CDW. For all diseases under surveillance except cryptococcosis, the audit was designed to obtain basic demographic and laboratory data from case patients with laboratory-confirmed disease not directly reported to GERMS-SA by participating laboratories. For cryptococcosis, the audit was designed to obtain data from cases which were no longer reported by NHLS laboratories in 8 provinces. In 2009, the audit did not include *P. jirovecii* and diarrhoeagenic *Escherichia coli*. Data from case patients, detected by audit, were included on the surveillance databases, and have been included in this report. Incidence rates were calculated using mid-year population estimates for 2008 and 2009

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Table 1: Population denominators used to calculate incidence rates, 2008 and 2009.

Province	General population*		HIV-infected population**		AIDS population**	
	2008	2009	2008	2009	2008	2009
Eastern Cape	6,579,245	6,648,600	728,915	757,818	75,300	79,705
Free State	2,877,694	2,902,400	393,863	395,344	49,656	50,111
Gauteng	10,447,246	10,531,300	1,446,094	1,454,006	165,632	166,078
KwaZulu-Natal	10,105,437	10,449,300	1,560,573	1,567,048	204,976	206,294
Limpopo	5,274,836	5,227,200	433,820	451,553	45,229	47,390
Mpumalanga	3,589,909	3,606,800	455,135	459,051	59,581	59,336
Northern Cape	1,125,881	1,147,600	67,330	69,595	6,787	7,458
North West	3,425,153	3,450,400	496,274	501,066	60,618	62,634
Western Cape	5,261,922	5,356,900	297,669	309,102	25,499	28,391
South Africa	**48,687,323**	**49,320,500**	**5,879,673**	**5,964,583**	**693,278**	**707,397**

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

(Continued from page 5)

from Statistics South Africa (Table 1) (3). Incidence rates in the HIV-infected and AIDS populations were calculated for 2008 and 2009, 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.

In 2009, ethics approval for the ongoing activities of the surveillance programme was renewed by the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and by relevant University and Provincial Ethics Committees for ESS outside Gauteng. 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 were partially funded through an NHLS-CDC Cooperative Agreement (Grant number: 5U2GPS001328-02).

Operational report

Site visits

In 2009, NICD staff members visited 35 surveillance sites in 8 provinces of South Africa (Table 2). This provided the opportunity to engage with personnel at laboratories and hospitals participating in the programme.

Surveillance audit

Of 19,237 surveillance cases detected by GERMS-SA, 7,063 (37%) were detected by audit of the NHLS CDW (Table 3). Reporting of cases ranged from 47% for cases of cholera to 98% for cases of typhoid. The audit included 4,533 cases of cryptococcosis from non-ESS; NHLS laboratories were not required to report these cases to GERMS-SA. The ESS directly reported 1,866/2,135 (88%) cases of cryptococcosis.

Enhanced surveillance site performance indicators

In 2009, overall ESS performance improved (Table 4). Eighty-five percent (4,960/5,854) of cases had a case report form completed (target = 90%) and 2,637 (53%) of the case report forms were completed by interview (target = 60%). 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 was 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 were targeted, and recommendations were made to improve the site performance. In 2009, these reports were provided quarterly.

Coordination meetings

Surveillance officer meeting, 12-13 March 2009: This meeting, convened at the NICD in Johannesburg, was attended by 19 surveillance officers from 8 provinces. The meeting included two days of training, discussion of ESS performance indicators and a session on voluntary counselling and testing for HIV. The focus of the meeting was on improving performance.

Principal Investigator (PI) meeting, 5-6 November 2009: 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 focused on invasive pneumococcal disease (IPD) and a planned case-control study, nested within GERMS-SA, to estimate the effectiveness of a 7-valent pneumococcal conjugate vaccine against invasive pneumococcal disease in South Africa.

Steering Committee meeting, 6 November 2009: Convened at the NICD after the PI meeting, this was attended by 7 committee members and 7 invited observers. The meeting covered topics including sustainability and funding of GERMS-SA, new projects, and the role of GERMS-SA to improve the management of patients with cryptococcosis.

Surveillance officer meeting, 11-13 November 2009: This 3-day meeting, convened at the NICD, was attended by 18 surveillance officers from 9 provinces. Feedback from the PI meeting was provided and surveillance officer performance indicators were discussed. Changes made to the clinical case report form for 2010 were also reviewed. The meeting focused on strategies to optimally capture information related to the new vaccines included as part of the EPI in 2009 and surveillance officers were introduced to the planned IPD case-control study.

Table 2: GERMS-SA surveillance site visits between 1 January and 31 December 2009.

Date	Province	Laboratory	Hospital
15 July 2009	Eastern Cape	NHLS Nelson Mandela Academic Complex	Nelson Mandela Academic Hospital Complex
26 May 2009	Free State	NHLS Makopane	Makopane Hospital
26-28 August 2009	Free State	Ampath	-
		Pathcare	-
		van Rensburg and Partners	-
		NHLS Universitas	Universitas Hospital
		NHLS Pelonomi	Pelonomi Hospital
		NHLS Bongani	Bongani Hospital
		NHLS Manapo	Manapo Hospital
		NHLS Boitumelo	Boitumelo Hospital
		NHLS Dihlabeng	Dihlabeng Hospital
19 January 2009	Gauteng	NHLS CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
		NHLS CHBH	Chris Hani Baragwanath Hospital
2 April 2009	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
8-9 June 2009	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
		NHLS Northern Branch	
27 July 2009	Gauteng	Lancet Richmond	-
5 August 2009	Gauteng	NHLS Germiston	Germiston Hospital
12-13 August 2009	Gauteng	NHLS Steve Biko Academic	Steve Biko Academic Hospital
		NHLS Northern Branch	
24 August 2009	Gauteng	Ampath Pomona	-
27 August 2009	Gauteng	Ampath Metalbox	-
3 September 2009	Gauteng	NHLS Kalafong	Kalafong Hospital
		1 Military	1 Military Hospital
21 October 2009	Gauteng	Ampath Pretoria	-
25 November 2009	Gauteng	NHLS Leratong	Leratong Hospital
11-12 December 2009	Gauteng	NHLS Dr George Mukhari	Dr George Mukhari Hospital
26-27 March 2009	KwaZulu-Natal	NHLS Addington	Addington Hospital
		NHLS RK Khan	RK Khan Hospital
		NHLS Grey's	Grey's Hospital
		NHLS Edendale	Edendale Hospital
			King Edward VIII Hospital
25-26 February 2009	Limpopo	NHLS Mankweng	Mankweng Hospital
13 July 2009	Mpumalanga	NHLS Themba	Themba Hospital
14 January 2009	North West	NHLS Job Shimankana Tabane	Job Shimankana Tabane Hospital
26 October 2009	North West	Westvaal Orkney	AngloGold Ashanti
30 July 2009	Western Cape	NHLS Groote Schuur	Groote Schuur Hospital

Table 3: Cases detected by surveillance audit by province, 2009.

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**	1/58 (2)	1	0	0	0	0	0	0	0	0	1
	Non-typhoidal salmonellosis†	123/763 (15)	23	3	64	0	3	12	0	9	9	123
	Shigellosis	9/68 (13)	0	2	1	0	2	0	0	3	1	9
	Cryptococcosis†††	4802/7965 (60)	1068	357	1208	0	521	672	22	551	403	4802
	Meningococcal disease	39/462 (8)	5	2	18	0	1	5	0	4	4	39
	Haemophilus influenzae disease	95/387 (24)	18	8	40	0	1	16	1	4	7	95
	Pneumococcal disease	846/4768 (18)	130	62	378	0	39	120	12	60	45	846
Non-invasive	*Salmonella* Typhi**	0/8 (0)	0	0	0	0	0	0	0	0	0	0
	Non-typhoidal salmonellosis†	309/1792 (17)	36	14	121	0	32	42	12	29	23	309
	Shigellosis	185/1744 (11)	30	9	74	0	9	22	4	10	27	185
	Cholera††	422***/1222 (53)	1	0	6	0	159	246	0	9	1	422
	Total	**6831/19237 (37)**	**1312**	**457**	**1910**	**0**	**767**	**1135**	**51**	**679**	**520**	**6831**

*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; ††Only *Vibrio cholerae* O1; ***Cholera audit case numbers were not available by province at time of publication of this report; †††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, 2009.

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/ R K Khan	567	502 (89)	333(66)	99
Chris Hani Baragwanath	1,384	1,097 (79)	558 (51)	97
Dr George Mukhari	284	202(71)	64 (32)	80
Edendale/ Grey's	397	378 (95)	237 (63)	100
Groote Schuur/ Red Cross/ Victoria	505	487 (96)	189 (39)	99
Charlotte Maxeke Johannesburg Academic	739	722 (98)	490 (68)	100
Karl Bremmer/ Tygerberg	305	210 (69)	68 (32)	99
Kimberley	171	162 (95)	131 (81)	97
King Edward	227	165 (73)	56 (34)	96
Mankweng/ Polokwane	159	118 (74)	103 (87)	100
Nelson Mandela Academic/ Mthatha Provincial	206	118 (57)	44 (37)	89
Pelonomi/ Universitas	228	209 (92)	128 (61)	100
Steve Biko Pretoria Academic/ Tshwane District	219	202 (92)	101 (50)	95
Rob Ferreira/ Themba	290	238 (82)	46 (19)	95
Rustenburg	173	150 (87)	89 (60)	100
TOTAL	**5854**	**4960 (85)**	**2637 (53)**	**96**

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 5 surveillance officers at Chris Hani Baragwanath and 2 at Charlotte Maxeke Johannesburg Academic in 2009; one surveillance officer was present at all other sites; **Low case report form completion rates at certain sites are due to the turnover of surveillance staff – if other reasons for low completion of case report forms were detected, these were addressed at those sites. ***Target = 90%; †Target = 60%; ††This was calculated by subtracting the number of "unknown" answers from a particular field on the case report form, which could easily have been answered by a patient on interview.

Surveillance Reports

Enhanced surveillance site project

In 2009, of 23199 surveillance case patients detected by GERMS-SA, 5854 (25%) were diagnosed at enhanced surveillance sites. Of case patients with recorded HIV status, 85% (3,368/3,979) were HIV-infected (Table 5). The proportion of case patients with confirmed HIV infection varied by disease: unsurprisingly, a very high proportion of patients with AIDS-defining infections like cryptococcosis (98%) and PCP (88%) were HIV-infected; HIV infection in patients with invasive pneumococcal disease and non-typhoidal salmonellosis, for which HIV is a known risk factor, were 74% and 75% respectively; and just less than half (46%) 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, 2009, n=5,854.

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	2,853	2371 (83)	1927 (81)	1887 (98)
Pneumocystis jirovecii	149	138 (93)	135 (98)	119 (88)
Neisseria meningitidis	170	156 (92)	115 (74)	53 (46)
Streptococcus pneumoniae	2034	1755 (86)	1363 (78)	1012 (74)
Haemophilus influenzae	177	145 (82)	107 (74)	53 (50)
Salmonella species	430	356 (83)	302 (85)	226 (75)
Shigella species	41	39 (95)	30 (77)	18 (60)
Total	**5854**	**4960 (85)**	**3979 (80)**	**3368 (85)**

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

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

Results

Salmonella Typhi isolates from both invasive and non-invasive sites are reported in Table 6. Two isolates of *Salmonella* Paratyphi A were received from Western Cape and two from North West Province, all from adults; a single isolate of *Salmonella* Paratyphi B L (+) tartrate (+) (*Salmonella* Paratyphi B var. Java) was received from a 32 month-old child in the Free State. No isolates of *Salmonella* Paratyphi C were received. The number of isolates within each age group is reported in Table 7, indicating that most isolates were from children in the 5-14 year age group, although infection was also seen in older and younger age groups. *Salmonella* Typhi isolation by month suggested a seasonal pattern in 2009, although numbers are too low to be conclusive (Figure 1). No major outbreaks were detected in 2009. A single isolate of *Salmonella* Typhi was resistant to ciprofloxacin (5). (Table 8), the treatment of choice. Two *Salmonella* Paratyphi A isolates were available for susceptibility testing: both were resistant to nalidixic acid, but susceptible to ampicillin, cotrimoxazole and chloramphenicol. The *Salmonella* Paratyphi B isolate was resistant to ampicillin, chloramphenicol and nalidixic acid.

Discussion

Salmonella Typhi isolates from both invasive and non-invasive sites were included in these analyses, as both added to the burden of infection in South Africa and

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thus represented 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 clinical and serological diagnosis. The number of reported *Salmonella* Typhi isolates was regarded as a substantial underestimate and thus incidence rates were not calculated. These results reflect culture-confirmed cases, and thus excluded 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. 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. The ciprofloxacin E-test is recommended to guide antimicrobial manage-ment in such cases (6).

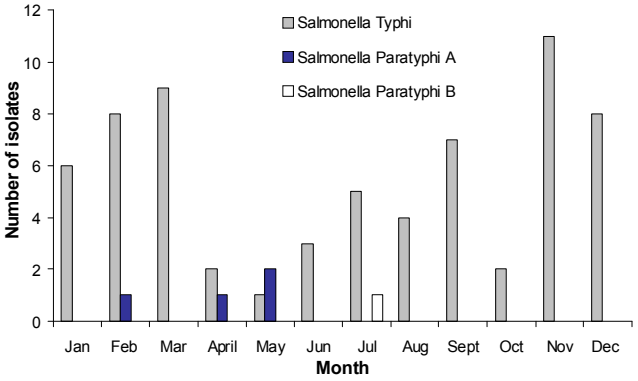

Figure 1: Number of non-invasive and invasive cases of *Salmonella* Typhi and Paratyphi A and B, reported to GERMS-SA, by month of specimen collection, South Africa, 2009, n=71

Table 6: Number of invasive and non-invasive *Salmonella* Typhi isolates reported to GERMS-SA, South Africa, 2009, n=66.

Province	Non-invasive *Salmonella* Typhi	Invasive *Salmonella* Typhi
Eastern Cape	2	10
Free State	1	2
Gauteng	1	25
KwaZulu-Natal	0	4
Limpopo	0	0
Mpumalanga	3	5
Northern Cape	0	1
North West	0	1
Western Cape	1	10
South Africa	**8**	**58**

Table 7: Number of *Salmonella* Typhi isolates reported to GERMS-SA by age category, South Africa, 2009, n=66.

Age category (years)	*Salmonella* Typhi
Neonate	0
< 1	0
1 - 4	7
5 - 14	22
15 - 24	12
25 - 34	5
35 - 44	10
45 - 54	2
55 - 64	3
≥ 65	3
Unknown	2
Total	**66**

Table 8: Antimicrobial susceptibility test results for all *Salmonella* Typhi isolates received by GERMS-SA, South Africa, 2009, n=65 (excluding audit reports).

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	50	(77)	0	(0)	15	(23)
Cotrimoxazole	52	(80)	0	(0)	13	(20)
Chloramphenicol	58	(89)	0	(0)	7	(11)
Nalidixic acid	53	(82)	0	(0)	12	(18)
Ciprofloxacin	64	(98)	0	(0)	1	(2)
Tetracycline	56	(86)	1	(2)	8	(12)
Kanamycin	65	(100)	0	(0)	0	(0)
Streptomycin	53	(82)	0	(0)	12	(18)
Imipenem	65	(100)	0	(0)	0	(0)
Ceftriaxone	65	(100)	0	(0)	0	(0)

Non-typhoidal *Salmonella enterica* (NTS)

Results

Both invasive and non-invasive disease appeared to have a seasonal prevalence in the warmer months (Figure 2). The number of cases of invasive and non-invasive disease, by province, reported to GERMS-SA, is stated in Table 9. The number of cases of invasive and non-invasive disease, by age group, is shown in (Table 10), but incidence rates were only 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 remained a challenge, including resistance to first-line antimicrobial agents and the quinolones (Table 12). Of 2094 NTS isolates tested, 149 (7%) were extended-spectrum beta-lactamase (ESBL) producers (Table 12). Multi-drug resistant serotypes included primarily *Salmonella* Typhimurium and *Salmonella* Isangi (Table 13).

Discussion

Non-typhoidal salmonellosis may be a food-borne disease, for which data are poorly captured in South Africa, and where the patients normally present with gastro enteritis, or may be an AIDS-defining illness, in which case the organism frequently becomes invasive. No marked seasonal prevalence was noted in 2009 for invasive or non-invasive isolates. *Salmonella* Infantis appeared to gain 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 remained a cause for concern.

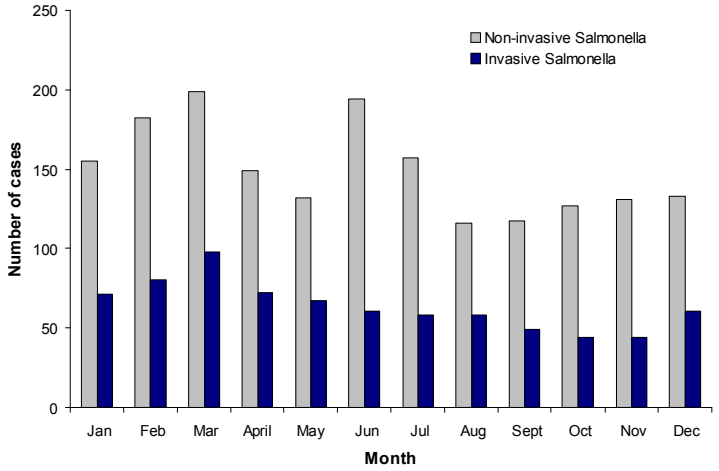

Figure 2: Number of non-invasive and invasive, non-typhoidal *Salmonella* cases, reported to GERMS-SA, by month of specimen collection, South Africa, 2009, n=2555 (including audit reports).

Table 9: Number* of invasive and non-invasive non-typhoidal *Salmonella* isolates reported to GERMS-SA, by province, South Africa, 2009, n=2555 (including audit reports).

Province	Non-invasive, non-typhoidal *Salmonella*	Invasive, non-typhoidal *Salmonella*
Eastern Cape	192	63
Free State	50	30
Gauteng	849	396
KwaZulu-Natal	156	93
Limpopo	37	9
Mpumalanga	161	45
Northern Cape	30	12
North West	78	36
Western Cape	239	79
South Africa	**1792**	**763**

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

Table 10: Number of cases and incidence rates for invasive* non-typhoidal *Salmonella* reported to GERMS-SA by age category, South Africa, 2009, n=2555 (including audit reports).

	Cases		
Age Category (years)	Non-invasive	Invasive	Incidence rate for invasive disease**
0 - 4	711	215	4.24
5 - 14	172	35	0.34
15 - 24	116	58	0.57
25 - 34	213	142	1.71
35 - 44	196	154	2.69
45 - 54	136	85	1.98
55 - 64	90	32	1.09
≥ 65	93	18	0.75
Unknown	65	24	-
Total	**1792**	**763**	**1.55**

*Incidence rates for non-invasive non-typhoidal *Salmonella* were not calculated because specimens may not have been submitted for culture from all patients, with gastroenteritis due to non-typhoidal *Salmonella,* in clinical practice; **Incidence rates are expressed as cases per 100, 000 population.

Table 11: Number of non-typhoidal *Salmonella* isolates reported to GERMS-SA by primary anatomical site of isolation*, South Africa, 2009, n=2555 (including audit reports).

Specimen	n	%
CSF	33	1.29
Blood culture	643	25.17
Stool	1491	58.36
Other	388	15.19
Total	**2555**	**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, 2009, n=2094 (excluding audit reports).

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	1673	(80)	0	(0)	421	(20)
Cotrimoxazole	1686	(81)	0	(0)	408	(19)
Chloramphenicol	1710	(82)	18	(1)	366	(17)
Nalidixic acid	1846	(88)	0	(0)	248	(12)
Ciprofloxacin	2087	(99.7)	4	(0.2)	3	(0.1)
Tetracycline	1365	(65)	212	(10)	517	(25)
Kanamycin	1948	(93)	47	(2)	99	(5)
Streptomycin	1592	(76)	0	(0)	502	(24)
Imipenem	2094	(100)	0	(0)	0	(0)
Ceftriaxone	1944	(93)	1	(0.1)	149	(6.9)

Table 13: Commonest invasive and non-invasive non-typhoidal *Salmonella* serotypes reported to GERMS-SA by province, South Africa, 2009, n=1579 (excluding audit reports).

	Serotype				
Province	Dublin	Enteritidis	Infantis	Isangi	Typhimurium
Eastern Cape	4	15	7	18	118
Free State	2	8	7	0	32
Gauteng	19	223	182	28	326
KwaZulu-Natal	8	53	16	35	86
Limpopo	0	2	1	1	3
Mpumalanga	4	21	12	0	68
Northern Cape	1	6	0	0	13
North West	0	16	3	1	19
Western Cape	10	58	39	6	108
South Africa	**48**	**402**	**267**	**89**	**773**

Shigella species

Results

Higher isolation rates in January to March and increasing numbers from October to December in 2009 suggested seasonality (Figure 3). Although the primary burden of disease due to *Shigella* is non-invasive dysentery or diarrhoea, invasive disease remained an important cause of morbidity in South Africa (Table 14). The predominant burden of disease, including both invasive and non-invasive shigellosis, was in the under-five-year age group (Table 15). Quinolone resistance remained low, but fluoroquinolone resistance appeared to be emerging (Table 16). Three of 1612 (0.2%) isolates tested were ESBL-producers. *S. flexneri* 2a remained the commonest cause of shigellosis in South Africa and *S. dysenteriae* type 1 was rarely isolated (Table 17).

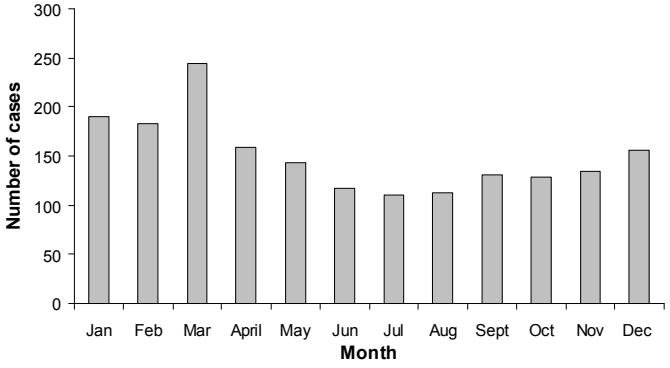

Figure 3: Number of non-invasive and invasive *Shigella* isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2009, n=1812 (including audit reports).

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.

Table 14: Number of invasive and non-invasive *Shigella* isolates reported to GERMS-SA by province, South Africa, 2009, n=1812 (including audit reports).

Province	Non-invasive *Shigella*	Invasive *Shigella*
Eastern Cape	277	3
Free State	80	4
Gauteng	664	21
KwaZulu-Natal	146	9
Limpopo	16	2
Mpumalanga	92	5
Northern Cape	20	0
North West	27	4
Western Cape	422	20
South Africa	**1744**	**68**

Table 15: Number of cases* and incidence rates for *Shigella* (invasive and non-invasive)** reported to GERMS-SA by age category, South Africa, 2009, n=1812.

	Cases		
Age Category (years)	**Non-invasive**	**Invasive**	**Incidence rate for invasive disease****
0 - 4	810	27	0.53
5 - 14	272	5	0.05
15 - 24	94	4	0.04
25 - 34	188	11	0.13
35 - 44	121	5	0.09
45 - 54	76	9	0.21
55 - 64	59	4	0.14
≥ 65	70	1	0.04
Unknown	54	2	-
Total	**1744**	**68**	**0.14**

*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, 2009, n=1612.

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	866	(54)	0	(0)	746	(46)
Cotrimoxazole	259	(16)	0	(0)	1353	(84)
Chloramphenicol	1102	(68)	8	(1)	502	(31)
Nalidixic acid	1594	(99)	0	(0)	18	(1)
Ciprofloxacin	1611	(99.9)	0	(0)	1	(0.1)
Tetracycline	679	(42)	24	(2)	909	(56)
Kanamycin	1604	(99.5)	1	(0.1)	7	(0.4)
Streptomycin	644	(40)	0	(0)	968	(60)
Imipenem	1612	(100)	0	(0)	0	(0)
Ceftriaxone	1609	(99.8)	0	(0)	3	(0.2)

Table 17: Commonest* invasive and non-invasive *Shigella* serotypes reported to GERMS-SA by province, South Africa, 2009, n=1169 (excluding audit reports).

Province	*S.dysenteriae* type 1	*S. flexneri* type 1b	*S. flexneri* type 2a	*S. flexneri* type 6	*S. sonnei* phase I/II
Eastern Cape	0	91	33	17	23
Free State	0	25	8	2	16
Gauteng	1	158	57	70	199
KwaZulu-Natal	0	38	16	13	20
Limpopo	0	2	0	2	1
Mpumalanga	1	14	5	11	21
Northern Cape	0	3	1	7	0
North West	0	2	1	1	8
Western Cape	0	175	64	25	38
South Africa	**2**	**508**	**185**	**148**	**326**

*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

Enteropathogenic *E. coli* (EPEC) remained the commonest cause of diarrhoea, due to this pathogen, identified in South Africa (Table 18). The predominance of cases amongst 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. A range of serotypes were associated with STEC/ EHEC, including O157 (a single isolate), O26 and O111. Serotypes associated with EPEC included O55, O111, O119, O127, O142 and O157. Diverse serotypes were also noted for other enterovirulent *E. coli* isolates. Identification of both EHEC and STEC was incidental (7).

Discussion

Incidence rates were not calculated as numbers were not viewed as being fully representative. Actual burden of disease due to diarrhoeagenic *E. coli* was probably greatly underestimated in South Africa, as management

(Continued on page 17)

Table 18: Number of diarrhoeagenic *Escherichia coli* isolates reported to GERMS-SA by province, South Africa, 2009, n=549*.

Province	DAEC	EAggEC	STEC/ EHEC	EIEC	EPEC	ETEC
Eastern Cape	8	27	0	2	69	15
Free State	1	0	0	0	8	1
Gauteng	25	24	9	1	236	9
Kwazulu-Natal	1	4	1	0	4	0
Limpopo	1	1	0	0	0	0
Mpumalanga	31	16	0	0	15	16
Northern Cape	0	0	0	0	0	0
North West	1	3	0	0	7	0
Western Cape	9	0	0	1	3	0
South Africa	**77**	**75**	**10**	**4**	**342**	**41**

*Representing 520 infectious episodes, including those patients who had more than one pathotype; 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*.

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is primarily syndromic and centres on rehydration. As a result, clinicians were unlikely to prioritise stool-submission in uncomplicated cases of 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 appeared to continue. 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 was not reflected as it is believed that the 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 19: Number of diarrhoeagenic *E. coli* isolates reported to GERMS-SA by age category, South Africa, 2009, n=549.

Age category (years)	DAEC	EAggEC	EHEC/ STEC	EIEC	EPEC	ETEC
Neonate	5	5	0	0	33	3
< 1	19	31	3	0	144	15
1 - 4	21	27	5	2	150	15
5 - 14	5	0	0	0	2	0
15 - 24	3	0	0	0	2	2
25 - 34	8	4	1	1	1	3
35 - 44	4	3	0	1	2	1
45 - 54	6	2	0	0	1	0
55 - 64	2	1	0	0	1	1
≥ 65	4	0	0	0	1	0
Unknown	0	2	1	0	5	1
Total	**77**	**75**	**10**	**4**	**342**	**41**

Vibrio cholerae O1

Results

The number of laboratory-confirmed cases reported to GERMS-SA in 2009 by province is shown in Table 20. This does not reflect the actual number of cases that were identified clinically and a large proportion was identified by audit. Where isolates were received contaminated or were missing, these have been included in the analysis, to improve estimates of duration of the outbreak and age distribution of cases. A number of cases may have been imported from Zimbabwe, but as these cases increase the burden on South African health care facilities as well as the public health risk to the local population, they have been included in the overall count. All age categories were affected (Table 21). Multidrug resistance was increasingly common and was noted with each outbreak cluster. Although resistance profiles differed amongst isolates from different clusters (data not shown), resistance to the quinolones was high (Table 22). Figure 4 shows the temporal clustering of the cholera outbreaks in South Africa in 2009. The case distribution highlights the epidemic that started in November 2008 (following an epidemic in Zimbabwe), and waned over the first half of 2009.

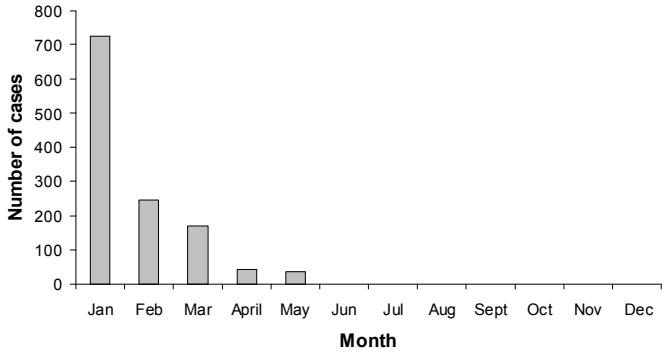

Figure 4: Number of *V. cholerae* O1 isolates, reported to GERMS-SA, by month of specimen collection, South Africa, 2009, n=1222 (including audit reports).

Discussion

Imported cases of cholera add to burden of infection in South Africa and thus represent a public health risk. The organism was multi-drug resistant, but as these resistant patterns were inconsistent, cumulative (for-the-year) resistance patterns could not be used to guide management of severely-dehydrated patients and could not be used to predict treatment for current or future

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outbreaks. Inappropriate usage of antimicrobials may have driven resistance. Antimicrobial treatment has not been shown to alter mortality rates (8). Certain antimicrobials were tested for epidemiological purposes only and are not suitable for treatment.

Table 20: Number of *Vibrio cholerae* O1 isolates reported to GERMS-SA by province, South Africa, 2009, n=575 (excluding audit reports).

Province	*Vibrio cholerae* O1 El Tor Inaba	*Vibrio cholerae* O1 El Tor Ogawa
Eastern Cape	0	0
Free State	0	0
Gauteng	0	37
KwaZulu-Natal	0	0
Limpopo	8	445
Mpumalanga	0	62
Northern Cape	0	0
North West	1	18
Western Cape	0	4
South Africa	**9**	**566**

Table 21: Number of *V. cholerae* O1 cases, reported to GERMS-SA, by age category, South Africa, 2009, n=1222 (including audit reports).

Age category (years)	*V. cholerae* O1 cases
< 1	14
1 - 4	82
5 - 14	119
15 - 24	202
25 - 34	224
35 - 44	150
45 - 54	105
55 - 64	103
≥ 65	130
Unknown	93
Total	**1222**

Table 22: Antimicrobial susceptibility test results for four outbreak clusters of *V. cholerae* O1 reported to GERMS-SA, South Africa, 2009, n=573.

Antimicrobial agent	Susceptible (%)		Intermediate (%)		Resistant (%)	
Ampicillin	556	(97)	0	(0)	17	(3)
Cotrimoxazole	1	(0.1)	0	(0)	572	(99.9)
Chloramphenicol	343	(60)	222	(39)	8	(1)
Nalidixic acid	1	(0.1)	0	(0)	572	(99.9)
Ciprofloxacin	573	(100)	0	(0)	0	(0)
Tetracycline	558	(97)	10	(2)	5	(1)
Kanamycin	557	(97)	9	(2)	7	(1)
Streptomycin	2	(0.3)	0	(0)	571	(99.7)
Imipenem	573	(100)	0	(0)	0	(0)
Ceftriaxone	566	(99)	0	(0)	7	(1)
Erythromycin*	391	(70)	159	(29)	5	(1)

*Where standard CLSI breakpoints do not exist, susceptibility categories were determined according to the methods of Ng *et al* (9). Not all viable isolates received were available for susceptibility testing and only 555 isolates were available for testing against erythromycin.

Cryptococcus species

Results

During 2009, 7965 case patients, with laboratory-confirmed, incident cryptococcal episodes, were reported. The overall incidence for the general South African population remained stable: 15/100,000 in 2008 and 16/100,000 in 2009 (Table 23). Similarly, incidence amongst HIV-infected individuals (128/100,000 in 2008 and 134/100000 in 2009) and people sick with AIDS (11/1,000 in 2008 and 12/1000 in 2009) remained stable. Incidence remained fairly stable in all provinces, except Limpopo and Northern Cape where the incidence increased (Table 23). The absolute number of detected cases decreased in 3 provinces: Western Cape, North West and Free State. The peak incidence of cryptococcosis was recorded amongst patients aged 35-39 years (Figure 5). Two hundred and fifty four children, younger than 15 years, had laboratory-confirmed cryptococcosis; 66/254 (26%) were younger than 1 year-old. Where gender was known (7860/7965, 99%), 51% patients were female. Most patients (7,347/7,965; 92%) were diagnosed with meningitis (laboratory tests on cerebrospinal fluid positive for *Cryptococcus* species), and 5,45/7,965 (7%) were diagnosed with fungaemia (Table 24). The remainder of case patients (n=73) were diagnosed by culture of urine, sputum, pleural fluid and other specimen types. At ESS, 2,135 patients were diagnosed with cryptococcosis, with viable isolates received from 1537/2135 (72%) patients. Of 1,533 isolates which were typed, 1470 (96%) were identified as *Cryptococcus neoformans*; the remaining 63 were identified as *Cryptococcus gattii. C. gattii* cases were diagnosed in 5 provinces: Gauteng (n=25), Mpumalanga (n=13), Limpopo (n=9), KwaZulu-Natal (n=7), North West (n=5), and Western Cape (n=4). The in-hospital case-fatality ratio for patients at enhanced surveillance sites did not significantly change between 2008 and 2009 (566/1,841 (31%) vs. 591/1,812 (33%); p=0.2).

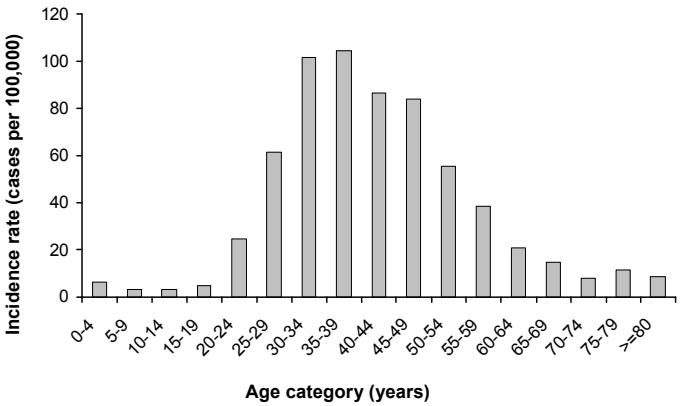

Figure 5: Age-specific incidence rates for laboratory-confirmed, cryptococcal cases, reported to GERMS-SA, South Africa, 2009, n=7965.

Discussion

In 2009, approximately 400 more patients with incident, laboratory-confirmed cryptococcosis were reported, compared with 2008. However, the overall incidence remained stable and fewer cases were detected in 3 provinces. This indicates that the National HIV/AIDS Comprehensive Care, Management and Treatment (CCMT) Programme has made an impact; this will be confirmed with ongoing surveillance data. Although the incidence increased in Limpopo and Northern Cape, this was associated with a relatively small increase in the absolute number of detected cases. Most patients continued to be diagnosed with meningitis. It is likely that clinical syndromes such as pulmonary cryptococcosis were not recognised by clinicians or

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were masked by co-morbid diseases such as pulmonary tuberculosis (10). The demographic profile of patients with cryptococcosis continued to mirror the profile of HIV-infected patients in South Africa. Although very few children were diagnosed with cryptococcosis, more than a quarter of cases were diagnosed amongst infants <1 year-old. In 2009, a small proportion of patients were infected with *C. gattii;* the geographical distribution of *C. gattii* cases was unchanged from 2008. 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 23: Number of cases and incidence rates of cryptococcal disease reported to GERMS-SA by province, South Africa, 2008 and 2009, n=15511.

	2008*†		2009*	
Province	**n**	**Incidence rate****	**n**	**Incidence rate****
Eastern Cape	1218	19	1329	20
Free State	497	17	467	16
Gauteng	2011	19	2049	19
KwaZulu-Natal	1242	12	1271	12
Limpopo	432	8	671	13
Mpumalanga	758	21	805	22
Northern Cape	57	5	87	8
North West	749	22	729	21
Western Cape	582	11	557	10
South Africa	**7546**	**15**	**7965**	**16**

*A similar surveillance audit was performed for NHLS laboratories in 8 provinces (excluding KwaZulu-Natal) in 2008 and 2009, detecting additional microscopy (India ink), cryptococcal antigen and culture-confirmed cases; **Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population; †The number of detected cases in 2008 was updated following data cleaning procedures

Table 24: Number and percentage of cases of cryptococcal disease reported to GERMS-SA by specimen type, South Africa, 2009, n=15511.

Site of specimen	2008		2009	
	n	**%**	**n**	**%**
CSF	7079	94%	7347	92%
Blood	440	6%	545	7%
Other	27	<1%	73	1%
	7546		**7965**	

Pneumocystis jirovecii

Results

In 2009, 371 cases of PCP were reported (Table 25). The number of *P. jirovecii*-positive specimens peaked amongst children less than one year of age and in the 20 to 59 year age group (Figure 6). Of cases with known gender, 62% (227/364) were female. Of all reported case patients, 153 (41%) were diagnosed at ESS and had available clinical data. During admission, 88% (125/142) of patients tested for HIV were HIV-infected. Where outcome was known, the in-hospital case-fatality ratio was 31% (44/144). In 18% (22/120) of patients, the diagnosis of PCP was associated with a second or later hospitalisation for PCP. Of patients who recovered, 96% (95/99) were discharged with a lower respiratory tract infection as a final diagnosis. Most of the case patients had concurrent infections, of which clinically-diagnosed candidiasis (49/153) and tuberculosis (23/153) were the most common (Figure 7).

Discussion

PCP is often the first-diagnosed opportunistic infection (11). The number of cases reported here does not approximate the true burden of disease in South Africa. This is because PCP is usually clinically-diagnosed, and only laboratory-confirmed cases of PCP are reported through GERMS-SA; there are only ten

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laboratories that offer PCP testing in four of the nine provinces in South Africa; PCP testing is expensive and needs well-trained personnel; and the quality of the specimens received by the testing laboratory is often poor which may affect the result. Since 2008, the Parasitology Reference Unit has taken steps to tackle some of these problems. Training was offered to all existing PCP-testing laboratories; five laboratories were trained in 2008 and 2009. In 2009, NHLS Grey's Hospital (KwaZulu-Natal) became a testing site for PCP and was provided with a UV microscope and training. Set-up of PCP testing is now targeted for provinces where no such facilities exist: Eastern Cape, Northern Cape, North West, Limpopo and Mpumalanga. A proficiency testing scheme for the identification of *P. jirovecii* was launched in 2008; 9 laboratories participated in 2009.

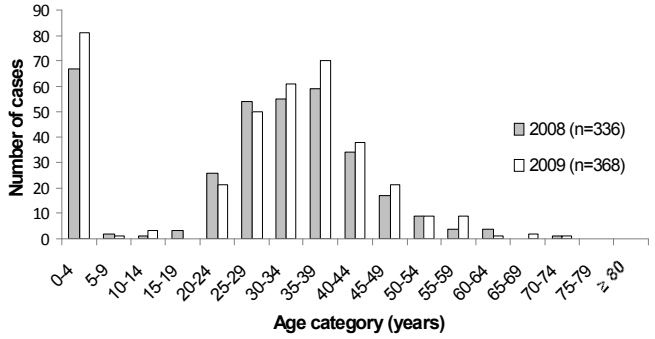

Figure 6: Number of laboratory-confirmed, *Pneumocytis jirovecii* pneumonia (PCP) cases reported to GERMS-SA, by age category, South Africa, 2008-2009, n=734.

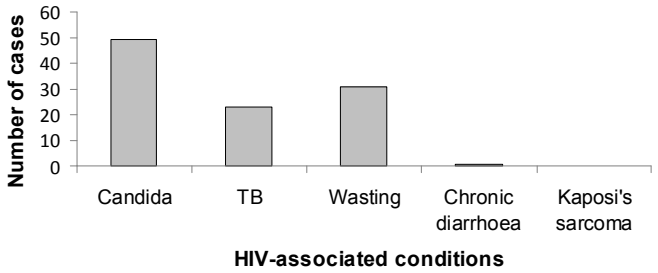

Figure 7: Number of laboratory-confirmed, *Pneumocystis jirovecii* pneumonia (PCP) cases with reported, HIV-associated conditions, South Africa, 2009, n=153*.

Table 25: Number of *Pneumocystis jirovecii* pneumonia (PCP) cases reported to GERMS-SA by province, South Africa, 2008-2009, n=715.

Province	2008	2009
Eastern Cape	30	37
Free State	20	19
Gauteng	163	141
KwaZulu-Natal	23	19
Limpopo	1	0
Mpumalanga	14	6
Northern Cape	3	0
North West	25	44
Western Cape	65	105
South Africa	**344**	**371**

Neisseria meningitidis

Results

In 2009, 425 cases of meningococcal disease were reported, and an additional 37 cases were identified on audit: 462 cases of laboratory-confirmed, meningococcal disease were identified by the surveillance system during the year (Table 26). 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 27), and the number of cases diagnosed on blood culture remained similar in 2009 compared to 2008 (p=0.2). Cases of W135 disease were reported from all provinces, and this serogroup was the most predominant in South Africa (235/397, 59%) (Table 28); the proportion was the same as in 2008 (207/360, 58%; p=0.6). The only increase in disease incidence was noted for Mpumalanga (1.86 cases per 100,000 population in 2009 compared with 1.00 in 2008, p=0.002). The predominant serogroup in Mpumalanga was serogroup W135 (47/60, 78% in 2009 vs. 19/24, 79% in 2008; p=0.9). In Gauteng, the incidence of meningococcal disease was estimated at 1.93 cases per 100,000 population, and most of that disease was due to serogroup

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W135 (111/173, 64%). The preponderance of serogroup B disease in Western Cape was still noted: 35/68 (51%) of all isolates serogrouped. Disease confirmed to be caused by serogroup C decreased in Gauteng, from 21 cases in 2008 to 13 cases in 2009. 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 all serogroups (Figure 9). Preliminary analysis of case-fatality ratios, as calculated at ESS where in-hospital outcome is specifically looked for, was 24/155 (15%) in 2009, compared to 47/178 (26%) in 2008 (p=0.02). Of the viable isolates tested for antimicrobial resistance, 17/319 (5%) 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 2008 and serogroup W135 disease remained stable. Increases of meningococcal disease incidence in Mpumalanga 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 decreased, and correspond more closely with the range 9% to 12% as reported from other settings (12,13,14,15). The prevalence of intermediate resistance to penicillin remained low in 2009, and was within the annual prevalence range (from 3% to 13%) previously reported from South Africa (16). The clinical relevance of increased MICs is unclear, and penicillin is, at present, still being recommended as the drug of choice for therapy for confirmed meningococcal disease.

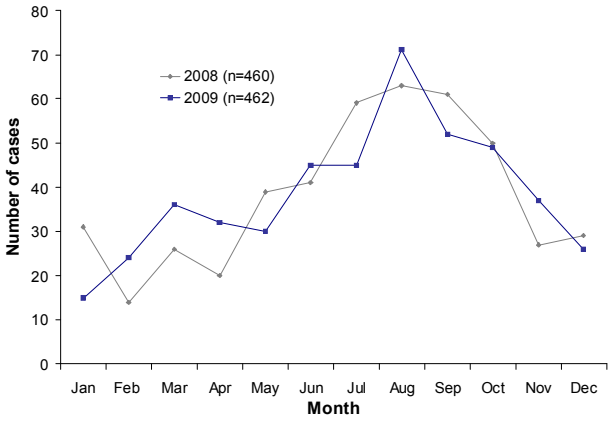

Figure 8: Number of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2008-2009, n=922.

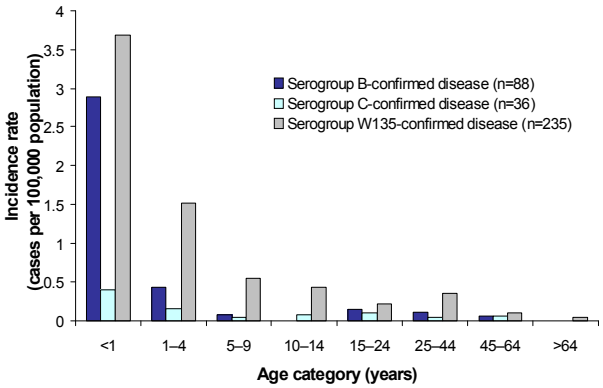

Figure 9: Age-specific incidence rates for laboratory-confirmed, invasive, meningococcal cases, by serogroup, South Africa, 2009, n=462 (age unknown for n=12; specimens or viable isolates unavailable for serogrouping n=65).

Table 26: Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2008 and 2009, n=922 (including audit cases).

Province	2008		2009	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	29	0.44	36	0.54
Free State	21	0.73	18	0.62
Gauteng	224	2.14	203	1.93
KwaZulu-Natal	34	0.34	32	0.31
Limpopo	5	0.09	3	0.06
Mpumalanga	36	1.00	67	1.86
Northern Cape	8	0.71	9	0.78
North West	15	0.44	19	0.55
Western Cape	88	1.67	75	1.40
South Africa	**460**	**0.94**	**462**	**0.94**

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

Table 27: Number and percentage of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2008 and 2009, n=922.

Site of specimen	2008		2009	
	n	%	n	%
CSF	318	69%	336	73%
Blood	136	30%	124	27%
Other	6	1%	2	<1%
	460		**462**	

Table 28: Number of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2009, n=462*.

Province	Serogroup							
	Serogroup not available	A	B	C	W135	X	Y	Total
Eastern Cape	6	0	8	3	16	1	2	36
Free State	3	0	3	6	4	0	2	18
Gauteng	30	2	32	13	111	0	14	203
KwaZulu-Natal	4	0	3	1	22	0	2	32
Limpopo	1	0	1	0	1	0	0	3
Mpumalanga	7	0	1	6	47	1	4	67
Northern Cape	1	0	3	0	4	0	1	9
North West	6	0	2	0	9	0	2	19
Western Cape	7	0	35	7	21	0	4	75
South Africa	**65**	**2**	**88**	**36**	**235**	**2**	**31**	**462**

*397 (86%) with specimens or viable isolates available for serogrouping.

Haemophilus influenzae

Results

The number of cases of *Haemophilus influenzae* invasive disease reported in 2009 was 292, while an additional 95 cases were identified during the surveillance audit (total number of cases available for analysis was 387). Of these, 264 (68%) had isolates or specimens available for serotyping, and 105/264 (40%) were confirmed as serotype b (Table 29). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (56/105, 53% vs. 9/112, 8%, p<0.001) (Table 30). In 2009, a total of 73 cases of *H. influenzae* serotype b (Hib) were reported in children <5 years (Figure 10). Of the non-viable isolates received or culture-negative cases reported, serotyping was identified by polymerase chain reaction (PCR) testing of transport media or specimens wherever possible. Serotype b was the more common *H. influenzae* causing disease in infants (Figure 11). Since 2002, rates of Hib disease as recorded by our surveillance network in infants <1 year of age have increased, and there seems to be a continued increase in 2009 (p<0.001, chi-squared test for trend, 2002 to 2009) (Figure 12). Small increases in numbers of Hib cases confirmed on viable isolates (methodology used since 2000) were seen for four provinces comparing 2008 to 2009 (Eastern Cape, Kwa-Zulu Natal, Northern Cape and Western Cape). Numbers were small for all provinces except Western Cape: increase from 13 viable isolates confirmed as Hib in 2008 to 24 in 2009. Nineteen percent of serotype b strains were resistant to ampicillin (MIC>1mg/L, all producing beta lactamase), 17of 91 isolates tested, while 13% (12/96) of non-typeable strains were resistant (p=0.2).

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 (17). 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 (18,19). and any increases noted recently are still small in comparison to the sub-

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stantial decline in disease subsequent to the introduction of the vaccine. The biggest increase was seen for Western Cape, and this may have been linked to more aggressive laboratory protocols to maintain viability of bacterial isolates. Recognising that our surveillance system underestimates disease, the increases in reported cases of Hib disease in 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.

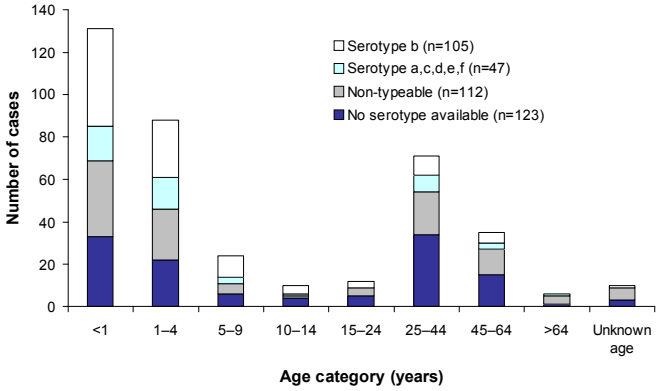

Figure 10: Number of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2009, n=387 (age unknown for n=10; specimens or viable isolates unavailable for serotyping for n=123).

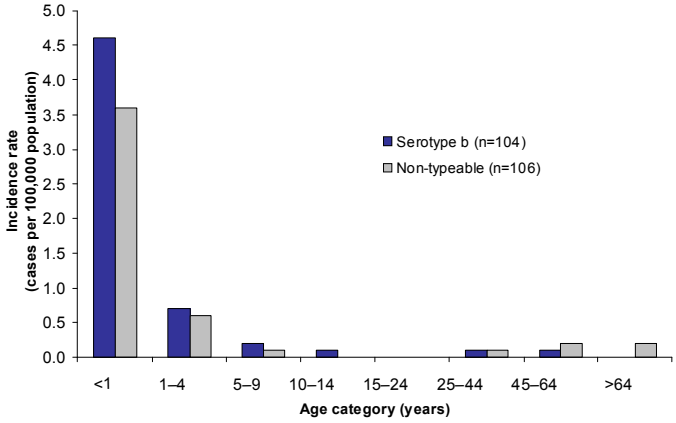

Figure 11: Age-specific incidence rates for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype, South Africa, 2009, n=387 (age unknown for n=10; viable isolates unavailable for serotyping for n=123).

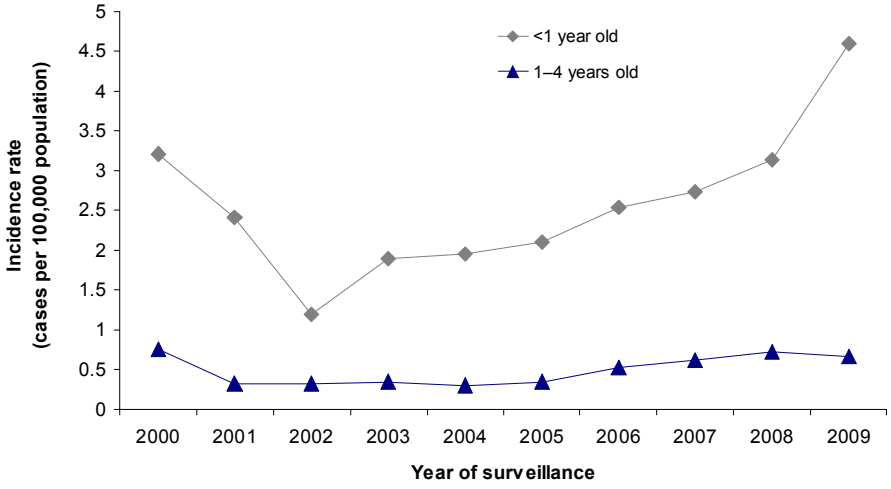

Figure 12: Incidence rates of laboratory-confirmed, *Haemophilus influenzae* serotype b disease, reported to GERMS-SA, in children <5 years old, South Africa, 2000-2009 (excluding cases identified using polymerase chain reaction (PCR) on specimens which was only done 2007-2009).

Table 29: Number of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2009, n=387*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	22	0	13	0	0	1	0	3	39
Free State	8	1	8	0	1	0	0	4	22
Gauteng	54	9	26	2	3	2	11	52	159
KwaZulu-Natal	5	0	18	1	0	1	1	17	43
Limpopo	1	0	2	0	0	0	0	1	4
Mpumalanga	17	0	4	1	0	0	2	3	27
Northern Cape	3	0	4	0	0	0	0	1	8
North West	5	0	4	0	0	1	0	1	11
Western Cape	8	4	26	0	1	1	4	30	74
South Africa	**123**	**14**	**105**	**4**	**5**	**6**	**18**	**112**	**387**

*264 (68%) with specimens or viable isolates available for serotyping.

Table 30: Number and percentage of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2009, n=387.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
CSF	24	20	56	53	19	40	9	8
Blood	68	55	46	44	27	57	90	80
Other	31	25	3	3	1	2	13	12
Total	**123**		**105**		**47**		**112**	

Streptococcus pneumoniae

Results

Incidence of reported invasive pneumococcal disease (IPD) varied widely by province (Table 31). The age group at highest risk of disease in South Africa was infants <1 year of age, and there was a significant reduction in disease comparing 2008 to 2009, p<0.001(Figure 13). The majority of episodes reported to GERMS-SA were diagnosed from positive blood culture specimens (Table 32). Penicillin non-susceptible isolates (2009 CLSI breakpoints for penicillin [oral penicillin V], MIC>0.06mg/L) (20), have increased (1,276/3,326, 38% in 2008 compared to 1,478/3,387, 44% in 2009, p<0.0001). Prevalence of non-susceptible strains ranged from 32% to 52% in different provinces (Table 33). Penicillin non-susceptible isolates were common in children less than 5 years of age (Figure 14). A non-meningitis-causing pneumococcus with a penicillin MIC of ≤2mg/L, according to updated CLSI guidelines (penicillin parenteral, non-meningitis), can be considered susceptible (20). Using this breakpoint, only 3% (70/2,141) of isolates cultured from specimens other than CSF were non-susceptible to penicillin. Ceftriaxone non-susceptibility was detected in 8% (276/3,387) of all IPD cases, and in 8% (102/1,246) of isolates detected from CSF specimens. Ceftriaxone-resistant pneumococci were more common in children <5 years (137/1007, 14% in children <5 years vs. 129/2,267, 6% in individuals ≥5 years of age, p<0.001), and this remained significant if restricted to meningitis. The majority of cetriaxone-resistant isolates were serotypes contained in PCV7 (256/276, 93%). On preliminary univariate analysis, there were no differences by gender, province, enhanced surveillance site, syndrome or in mortality when comparing susceptible to non-susceptible isolates. Prevalence of ceftriaxone resistance as detected by the surveillance system from 2003 through 2008 ranged from 0.4% to 0.9% (data not shown). PREVENAR® (7-valent conjugate pneumococcal vaccine, PCV7) was introduced into the EPI in South Africa from 1 April 2009. The number of cases in children less than 5 years of age due to common se-

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rotypes in 2009 (including the seven serotypes in PCV7: 4, 6B, 9V, 14, 18C, 19F and 23F) are compared with 2008 in Figure 15. The percentage of disease in 2009 in children <5 years due to PCV7 and newer valency vaccine formulations are shown in Table 34.

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 was mostly likely due to the introduction of PCV7 in South Africa. In a preliminary analysis performed within 6 months of PCV7 introduction, we noted a significant decrease of approximately 25% in serotype-specific disease among infants less than 1 year of age, and no changes in other age groups (21). Ongoing surveillance will be essential to document further reduction in disease in infants, and as vaccine coverage increases we hope to see declines in disease in older children. Our data for 2009 show an increase in pneumococcal resistance to penicillin and ceftriaxone. Although a true, sudden increase may be possible, we believe that this increase is due to a change in laboratory methodology that was introduced in 2009. For isolates that are screened non-susceptible by disk diffusion, we changed from using agar dilution or Etest® (bioMérieux, Marcy l'Etoile, France) to Etest® (AB bioMérieux, Solna, Sweden) methodology for MIC determination to broth microdilution methodology (the recommended CLSI method). 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 most of these ceftriaxone-resistant isolates were identified as serotypes contained in PCV7, we anticipate that the number of resistant isolates causing disease will decrease with wider use of the vaccine.

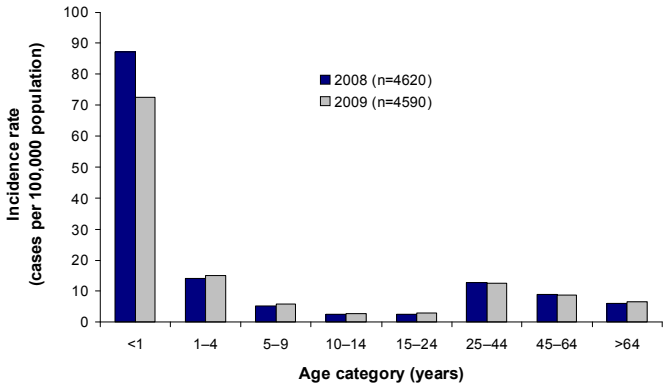

Figure 13: Age-specific incidence rates for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2008 and 2009 (2008: n=4837; age unknown for n=217; 2009: n=4768; age unknown for n=178).

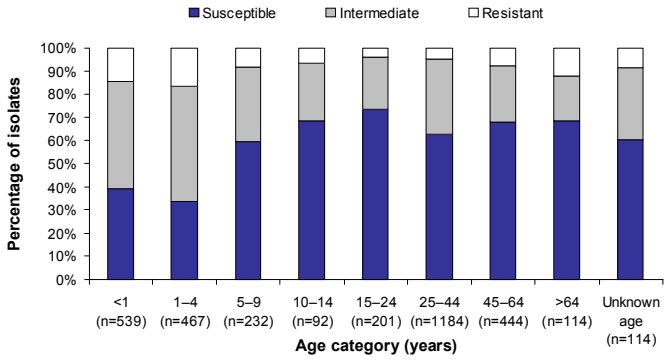

Figure 14: Number of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2009, n=4768 (n=3387 with viable isolates).

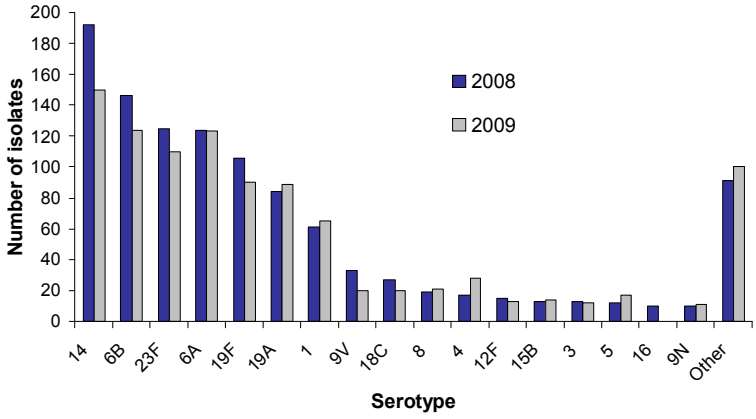

Figure 15: Pneumoccocal serotypes, in descending order, causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2008-2009 (2008: n=1464, n=1098 with viable isolates; 2009: n=1334; n=1007 with viable isolates).

Table 31: Number of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2008 and 2009, n=9605.

Province	2008		2009	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	356	5.41	362	5.44
Free State	320	11.12	309	10.65
Gauteng	2356	22.55	2254	21.40
KwaZulu-Natal	573	5.67	528	5.05
Limpopo	112	2.12	111	2.12
Mpumalanga	257	7.16	302	8.37
Northern Cape	84	7.46	88	7.67
North West	193	5.63	175	5.07
Western Cape	586	11.14	639	11.93
South Africa	**4837**	**9.93**	**4768**	**9.67**

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

Table 32: Number and percentage of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2008 and 2009, n=9605.

Site of specimen	2008		2009	
	n	%	n	%
CSF	1755	36%	1805	38%
Blood	2644	55%	2513	53%
Other	438	9%	450	9%
	4837		**4768**	

Table 33: Number and percentage of penicillin non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2009, n=4768.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	165	95	48	88	45	14	7
Free State	78	143	62	67	29	21	9
Gauteng	698	904	58	487	31	165	11
KwaZulu-Natal	69	233	51	196	43	30	7
Limpopo	48	43	68	18	29	2	3
Mpumalanga	141	98	61	49	30	14	9
Northern Cape	21	39	58	18	27	10	15
North West	83	56	61	31	34	5	5
Western Cape	78	298	53	217	39	46	8
South Africa	**1381**	**1909**	**56**	**1171**	**35**	**307**	**9**

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

Table 34: 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, 2009, n=1007.

Province	Total isolates available for serotyping	7-valent serotypes *		Serotype 6A#		10-valent serotypes*		13-valent serotypes*	
		n	%	n	%	n	%	n	%
Eastern Cape	54	28	52	13	24	28	52	45	83
Free State	50	31	62	4	8	35	70	44	88
Gauteng	462	233	50	55	12	287	62	385	83
KwaZulu-Natal	145	83	57	15	10	90	62	122	84
Limpopo	12	8	67	2	17	8	67	10	83
Mpumalanga	47	18	38	6	13	27	57	37	79
Northern Cape	40	20	50	2	5	25	63	32	80
North West	11	6	55	2	18	7	64	11	100
Western Cape	186	115	62	24	13	121	65	166	89
South Africa	**1007**	**542**	**54**	**123**	**12**	**628**	**62**	**852**	**85**

*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 (22).

Progress report for studies nested within GERMS-SA

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

Principal Investigators: Cheryl Cohen and Anne von Gottberg

Background: In 2009, a case-control study to estimate effectiveness of a 7-valent pneumococcal conjugate vaccine (PCV) against invasive pneumococcal disease in South Africa was planned for start-up in 2010. The study will be a matched, case-control study nested within the GERMS-SA surveillance programme. The study will be conducted at 25 ESS located in all nine provinces. The study population will include children aged ≥ 8 weeks in South Africa who are part of the birth cohort eligible to receive PCV through the Expanded Programme on Immunisation (EPI) (born after 15 February 2009).

Study Objectives: The primary objectives of the study are:

1. To determine the effectiveness of 2 or more doses of pneumococcal conjugate vaccine (PCV) against laboratory- confirmed vaccine-serotype invasive pneumococcal disease (IPD) among HIV- infected and HIV-uninfected children eligible to receive vaccination through the routine vaccination p rogramme in South Africa, compared to no vaccination.
2. To determine the effectiveness of 2 or more doses of PCV against all laboratory-confirmed IPD (all serotypes) among HIV-infected and HIV-uninfected children eligible to receive vaccination, compared to no vaccination.

Secondary objectives include determining the effectiveness of partial (1 or 2 doses) and complete (3 doses) series of PCV, determining the effectiveness against specific serotypes and determining the effectiveness against multidrug-resistant pneumococcus.

Study Progress: A number of study-related activities were conducted in 2009 in preparation for the start-up in 2010. These activities included the following:

1. Securing study funding through a research grant from the Accelerated Vaccine Introduction Initiative (AVI), with additional supplementary funds obtained from Pfizer.
2. Development of a study protocol and submission to relevant university and provincial ethics committees throughout the year.
3. Presentation of the planned study to the Department of Health EPI Task Group, 5-6 August 2009.
4. Conducting a pilot study at Chris Hani Baragwanath Hospital by Dr George Nelson, (Epidemic Intelligence Officer, CDC, USA), 12-23 October 2009.
5. Presentation of the study protocol at the GERMS-SA PI Meeting, 5-6 November 2009 and at the Steering Committee meeting, 6 November 2009.
6. Surveillance officer training, NICD, Sandringham, 11-13 November 2009
7. Recruitment of additional personnel required for the study.

Cryptococcal meningitis in Gauteng Province, South Africa: exploring post-hospital discharge outcomes and uptake of care, 2009

Investigators: Katherine Gaskell, Alison Grant, Kerrigan McCarthy, Olga Perovic, Vanessa Quan and Nelesh Govender

Background: In South Africa, cryptococcal meningitis is associated with high, early mortality. The estimated in-hospital case-fatality ratio for patients diagnosed with cryptococcosis at GERMS-SA ESS has remained consistently high (approximately 30%) over several years. In the pre-HAART era, it was estimated that overall 14-day and 90-day survival for patients identified through surveillance in Gauteng was 68% and 41%, respectively (Park B, *et al.* unpublished).

Study Objective: We undertook to determine post-hospital discharge outcomes and uptake of care amongst a group of patients with cryptococcal meningitis, identified through GERMS-SA surveillance, at a single Johannesburg hospital in the post-HAART era.

Study Methods: We identified patients consecutively diagnosed with incident cryptococcosis at a single Johannesburg hospital, 1 January 2008 through 31 March 2009. A retrospective review of paper-based and electronic records was conducted (including hospital, outpatient HIV clinic, and laboratory and pharmacy records); data were extracted using a standardised case report form. Post-discharge telephonic interviews were also conducted in July 2009 with patients who provided informed consent.

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Study Progress: The study was completed in September 2009. The findings of this study were summarised by Katherine Gaskell in a report submitted in partial fulfilment of the requirements for the degree of MSc in Control of Infectious Diseases at the London School of Hygiene and Tropical Medicine, and were also presented at the GERMS-SA PI meeting, 5-6 November 2009. In summary, 217 patients were included in the study. Sixty (28%) patients died in hospital; 157 patients were discharged alive. At three months, 17 patients were known to have died, 72 were known to be alive and 68 patients were lost to follow-up. Three-month mortality rate was estimated to range from 35% (77/217) if all patients who were lost to follow-up were presumed to have survived to 67% (145/217) if all patients lost to follow-up were presumed to have died.

Discussion

In 2009, the GERMS-SA programme showed its value in several areas. It has become evident that the incidence of cryptococcosis, a useful, sentinel, HIV-associated opportunistic infection, has stabilised. This may be an indication that the antiretroviral treatment programme has reached sufficient people to prevent an escalation in the number of new cases year-on-year. However, the overall incidence of this life-threatening fungal disease still remains high and work needs to be done to ensure that more cases are prevented and new cases are managed optimally. PCV was introduced into the EPI in April 2009. Despite low, estimated coverage of PCV and a high HIV prevalence, GERMS-SA has already demonstrated a significant decrease of serotype-specific, invasive pneumococcal disease amongst South African infants. These early, direct effects are likely to be amplified as vaccine coverage increases. GERMS-SA continues to monitor the impact of the Hib vaccine: although a significant increase in the number of Hib cases has been documented amongst young children, it is anticipated that the addition of a booster dose to the EPI in April 2009 may address this. In addition, GERMS-SA has documented emerging antimicrobial resistance in several pathogens: a rare, single, fluoroquinolone-resistant *S.* Typhi isolate; several fluoroquinolone-resistant NTS isolates; a single, fluoroquinolone-resistant *Shigella* isolate; and significantly increased penicillin and ceftriaxone resistance amongst *S. pneumoniae* isolates predominantly from young children between 2008 and 2009. The emergence of antimicrobial resistance in these important bacterial pathogens will impact on the choice of empiric treatment of common disease syndromes such as sepsis, pneumonia and meningitis.

Publications by GERMS-SA Authors

Publications in peer-reviewed journals

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3. Murphy E, Andrew L, Lee KL, Dilts DA, Nunez L, Fink PS, Ambrose K, Borrow R, Findlow J, Taha MK, Deghmane AE, Kriz P, Musilek M, Kalmusova J, Caugant DA, Alvestad T, Mayer LW, Sacchi CT, Wang X, Martin D, von Gottberg A, du Plessis M, Klugman KP, Anderson AS, Jansen KU, Zlotnick GW, Hoiseth SK. Sequence Diversity of the Factor H Binding Protein Vaccine Candidate in Epidemiologically Relevant Strains of Serogroup B *Neisseria meningitidis*. *J Infect Dis* 2009;200:379-89.
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Publications in non-peer-reviewed journals

Nil

Department of Health reports

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2. Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa. Special Report on Laboratory-confirmed Meningitis, 2005 through 2008. Submitted to Communicable Diseases Cluster, National Department of Health. 27 March 2009.
3. Group for Enteric, Respiratory and Meningeal disease Surveillance in South Africa. Special Report on Treatment of Patients with Incident Cryptococcosis at 25 GERMS-SA Sentinel Hospitals, South Africa, 1 January 2008 to 31 March 2009. Submitted to Communicable Diseases Cluster, National Department of Health. 10 July 2009.
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