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FOREWORD

There were three measles outbreaks in 2017 in South Africa, specifically in the Western Cape, Gauteng and KwaZulu-Natal provinces. These outbreaks caused the national measles incidence rate to increase significantly. Details of these outbreaks are given in this issue, which also contains the invasive meningococcal, *Haemophilus influenzae* and pneumococcal disease surveillance report for 2017. The epidemiology of disease caused by *Neisseria meningitidis*, *H. influenzae* type b (Hib) and *Streptococcus pneumoniae* in South Africa is described, with the results highlighting the ongoing importance of adequate vaccine doses in children to protect them from serious illness.

Human papillomavirus (HPV) is a common sexually transmitted infection that is also associated with a number of cancers. As part of the HPV vaccination strategy in South Africa, it is important to have baseline data on HPV in adolescent girls and young women. Women between the ages of 18 and 20 years were therefore recruited to participate in HPV surveillance in 2017 as described in this issue. Lastly, this issue presents an assessment of the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), a particularly common cause of bacteraemia, in four of South Africa's provinces. *Staphylococcus aureus* resistance to antimicrobial agents was fortunately low during 2016 and 2017, suggesting that no specific evolution of MRSA clonal types is occurring in South Africa.

All contributors are thanked for their inputs, and we trust you will find these reports useful and interesting.

Basil Brooke

Editor

ANNUAL MEASLES AND RUBELLA SURVEILLANCE REVIEW, SOUTH AFRICA, 2017

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Executive summary

Despite the availability of a safe and effective vaccine, measles remains a significant cause of childhood morbidity and mortality in humans globally. In 2017, there were three measles outbreaks in South Africa, specifically in the Western Cape, Gauteng and KwaZulu-Natal provinces. These outbreaks largely occurred in communities who were unvaccinated or had low vaccination coverage. Of 6256 suspected measles cases, 210 were laboratory-confirmed. Rubella infection was identified in 2 512 of the suspected measles cases, indicating a high level of circulating rubella in South Africa. Only seven of South Africa's provinces met the national measles surveillance target of at least two suspected rash cases per 100 000 population. Due to the three measles outbreaks, the national measles incidence rate per million increased from 0.3 in 2016 to 3.7 in 2017, exceeding the World Health Organisation's (WHO) elimination target of less than 1 per million population. This data highlights the fact that there are measles vaccination coverage gaps among young children and adults, and emphasises the urgent need to improve measles vaccine awareness and coverage in order to meet WHO elimination targets.

Background

Measles is a highly contagious, severe viral infection caused by a paramyxovirus, *Morbillivirus*. Airborne transmission occurs via aerosolized droplet nuclei from the nose, throat and mouth of an infected person. Up to 90% of exposed susceptible persons develop measles. Clinically, the incubation period from exposure to prodrome averages 10 to 12 days, and 14 days from exposure to rash. The measles prodrome classically presents with fever (>38°C), any of the three C's (cough, coryza, and conjunctivitis) and Koplik spots (which are considered pathognomonic for measles). Thereafter, a generalized non-vesicular maculopapular rash begins on the face and upper neck, and becomes confluent on the upper body. Complications such as diarrhoea, otitis media, pneumonia, dysentery and/or death can occur in about 30% of measles cases, particularly in young children under the age of five years or in older adults.[1] Before the development of a safe and effective vaccine in 1963, measles infection was nearly universal during childhood and was responsible for an estimated 2.6 million deaths each year.[2]

Rubella (German measles) is a Togavirus within the *Rubivirus* genus. It is a contagious viral infection that is spread through direct or droplet contact with the respiratory secretions of an infected person.[3] The incubation period is 14 days and symptoms are often mild or subclinical. Prodome is rare in young children, but in older children and adults there may be low-grade fever, malaise and lymphadenopathy. A maculopapular rash occurs 14 to 17 days after exposure, first appearing on the face and progressing from head to foot, and lasting about 3 days. Complications of rubella are rare and generally occur more often in adults than in children. The most serious complication of rubella infection is congenital rubella syndrome (CRS), which occurs when the rubella virus infects a developing foetus. CRS in the first trimester of pregnancy is teratogenic and can lead to miscarriage or serious birth defects such as deafness, eye defects, heart defects, and mental retardation in as many as 85% of infected infants.

The best protection against measles and rubella is through vaccination. In South Africa, single-dose measles vaccination began in 1975 as part of the Expanded Programme on Immunization (EPI). Thereafter in 1995, a 2-dose strategy at 9 and 18 months was adopted, with supplemental vaccination campaigns occurring every three to four years. In 2016, the two-dose measles vaccine schedule changed to 6 and 12 months. Administration of the first dose at 6 months aims to prevent the high morbidity and mortality associated with the disease in young infants. Unlike measles, rubella is not part of the current South African EPI, although rubella vaccine is available in the private sector. Historically, the omission of rubella vaccine from EPI was based on the understanding that natural rubella infection in childhood should render most women of childbearing age immune and therefore prevent CRS. In addition, under conditions of imperfect vaccine coverage, the addition of a rubella-containing vaccine (RCV) could increase the susceptibility of adult women by slowing, but not interrupting, rubella transmission. This may theoretically be increasing the age of primary rubella infections and therefore increase the number of CRS cases.[4-7] For this reason, the introduction of a RCV into the EPI should be carefully considered and meticulously implemented to avoid increasing the risk of CRS.

To prevent measles outbreaks, it is estimated that population immunity rates should be approximately 95%.[8] In 2016, the World Health Organisation (WHO) estimated that globally only 85% of children have received the first dose of measles vaccine by their first birthday through routine health services, and 64% a second dose.[9] These coverage levels remain short of the level required to achieve the African regional 2020 measles elimination goal. Over the years South Africa has had several measles outbreaks: between 2003 and 2005 there were 1 676 laboratory-confirmed case-patients and in 2009 to 2011 there were more than 18 000 laboratory-confirmed measles case-patients.[10] From 2012 to 2016, annual numbers for measles IgM positive case-patients were relatively low, with only 17 laboratory-confirmed case reported in 2016.[11] However, in 2017 there were measles outbreaks in the Western Cape (n=31), Gauteng (n=96) and Kwazulu-Natal (n=59) provinces.

This report documents the annual measles and rubella surveillance collated at the Centre for Vaccines and Immunology (CVI), National Institute for Communicable Diseases (NICD) for the period 1 January to 31 December, 2017.

Methods

Sample collection and laboratory testing

As part of the National Department of Health (NDoH) programme to eliminate measles and in line with WHO strategy, all patients throughout South Africa presenting with rash, fever and any one of the three C's (coryza, conjunctivitis or

cough), or any person in whom a clinician suspects measles, are advised to have a blood specimen submitted to the CVI for measles IgM and rubella IgM antibody testing.

For the period 1 January 1 to 31 December, a total of 6435 serum specimens and 68 throat swabs were received for testing. For measles IgM and rubella IgM, commercial ELISA kits (Siemens Enzygnost: Behring, Germany and/or EUROIMMUN: Luebeck, Germany) were used according to the manufacturer's instructions. If a sample was equivocal for measles IgM antibody, a second blood specimen was requested for repeat testing. Throat swab specimens and measles IgM reactive samples, i.e. positive and equivocal, were also tested using real-time reverse transcription-PCR (RT-PCR) to detect viral RNA. Positive samples (measles virus RNA detected) were then tested by conventional RT-PCR to amplify the 3'region of the nucleoprotein gene for subsequent sequencing and phylogenetic analysis. Based on the serology and/or PCR results, each suspected measles case was provisionally classified as measles IgM positive, measles PCR positive, compatible with measles, or epidemiologically-linked (Table 1). Thereafter, the WHO definition was used to define the measles outbreak: A confirmed measles outbreak = the occurrence of 3 or more confirmed measles cases in a health facility/district/sub-district in a month.[12]

Measles cases were classified at bi-monthly situational report (SITREP) meetings with representation from the NICD, NDoH and WHO. All suspected measles cases were allocated a final classification as discarded, compatible or confirmed (Table 1).

Table 1. Measles case classifications for laboratory-confirmed cases in South Africa.

Interim measles classification		**Comment**
IgM positive	Unclassified Vaccine associated Presumed wild-type	Case is within 30 days of receiving a measles vaccination
PCR positive	Unclassified Vaccine strain Presumed wild-type	Awaiting genotyping or unable to genotype sample Sequencing results indicate the presence of vaccine-derived RNA
Compatible		Case meets the clinical case definition, is not epidemiologically linked, awaiting blood specimen, or blood specimen is equivocal
Epidemiologically-linked		Case meets the clinical case definition and is linked to a laboratory-confirmed case within 30 days of each other
Final measles classification		**Comment**
Discarded		Case that does not meet the clinical or laboratory definition (IgM -ve or vaccine-associated/vaccine strain present)
Compatible		Case meets the clinical case definition, not epidemiologically linked, but no blood specimen received, or blood specimen is equivocal
Confirmed		Case meets the clinical case definition and is laboratory-confirmed IgM +ve and/or PCR +ve and/or epidemiologically-linked

IgM=Immunoglobulin M; **PCR=**polymerase chain reaction; **+ve**: positive; **-ve**: negative. Vaccine-associated cases were cases occurring within 30 days of a measles vaccination, as vaccine virus may cause a mild, non-transmissible 'flu-like' illness with a rash. The rash and positive IgM results are an indication of the vaccine generating an immune response, which can cause a false-positive IgM result.

Congenital rubella syndrome (CRS) surveillance

In 2015, a sentinel site surveillance programme was set up to establish baseline data on the burden of CRS in South Africa. Tertiary referral hospitals in major cities of each of South Africa's provinces were selected as study sites. Paediatricians, neonatologists or paediatric infectious disease specialists at these hospitals served as focal persons. Virology departments from the National Health Laboratory Service (NHLS) were asked to share any positive rubella tests in patients aged ≤12 months. Clinicians requesting the tests were also contacted. Currently, 28 clinical sites and 6 laboratory sites are involved in the surveillance programme.

A case definition adapted from the Centres for Disease Control & Prevention (CDC) was used in the surveillance. A laboratory-confirmed CRS case was defined as any child under 12 months of age with a positive rubella test (serology or PCR) and who presents with at least one of the following: cataracts, congenital glaucoma, congenital heart disease, hearing impairment, pigmentary retinopathy, purpura, hepatosplenomegaly, jaundice, microcephaly, developmental delay, meningoencephalitis or radiolucent bone disease.

Data analysis

Descriptive analyses were performed using Excel 2016. Results are reported as frequencies for categorical variables or as median values with ranges for continuous variables.

Results

Circulating measles

From 1 January to 31 December 2017, 6 256 samples were received for serology and molecular testing (Figure 1A and 1B). In total there were 210 laboratory-confirmed measles cases from eight provinces. There were districts in the Western Cape, Gauteng and KwaZulu-Natal provinces that exceeded the outbreak threshold of more than 3 laboratory confirmed cases per month. Laboratory-confirmed rubella cases were identified in 2512 of the referred samples and 23 had simultaneous acute infection with measles and rubella. Seven measles IgM-positive cases were discarded - two were denotified and five were classified as vaccine-associated.

Febrile rash samples received for testing increased over the last quarter of the year, which coincided with the seasonal distribution of rubella as observed in 2016 (Figure 1A). Measles was detected throughout the year and did not appear to have a seasonal distribution. Nationally, laboratory-confirmed measles cases were equally present in males and females (53% vs. 47%, respectively). The majority of measles cases occurred in the 20-44 year old age group (Figure 2A and 2B), which is outside the age group targeted by the national measles vaccination campaign (children aged between 6 months and 5 years). In the 15-19 year old age group, there were a greater number of measles cases in males (n=18) compared to females (n=4). This can be explained by the fact that the first measles outbreak occurred in a boys' high school in the Western Cape.

Concerning process indicators for the 210 laboratory-confirmed measles cases (Table 2), 42% had a case investigation form (CIF), 43% had a unique epidemiological (EPID) number, and 31% had both a CIF and EPID. Measles vaccination was reported in 17% of all cases, compared with the national average of 75% (using the national immunization coverage data[13]), indicating that people who caught measles were less likely to have been vaccinated than the general population.

Figure 1. Suspected measles cases with febrile rash (n=6256), and laboratory-confirmed measles (n=210) and rubella (n=2512) cases in South Africa, 1 January to 31 December, 2017. **A**: Suspected and laboratory-confirmed measles and rubella cases by month, South Africa, 2017. **B**: Laboratory-confirmed measles and rubella cases by province, South Africa, 2017.

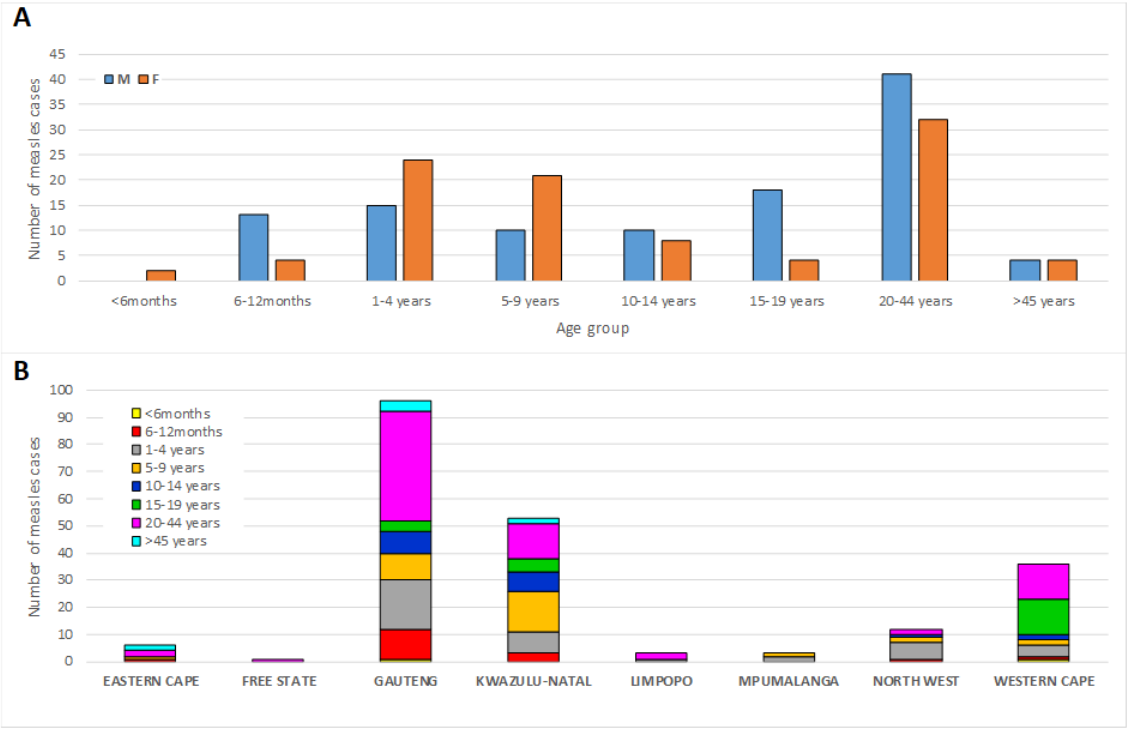

Figure 2. A: Age and gender distribution (males, n=111 and females, n=99) of laboratory-confirmed measles cases in South Africa, 1 January to 31 December 2017 **B**: Laboratory-confirmed measles cases stratified into age groups by province.

Table 2. Surveillance data for laboratory-confirmed measles cases in South Africa for the period 1 January to 31 December, 2017 (n=210).

Category	N (%)
Laboratory-confirmed measles cases	210
Measles cases with a case investigation form (CIF) received	89 (42.4)
Measles cases with an epidemiological (EPID) number	90 (42.9)
Measles cases with a CIF and EPID number	65 (31.0)
Measles cases where vaccination status was recorded on CIF or through correspondence	36 (17.1)
Number of vaccine doses received when vaccination status was recorded	
1	6 (2.9)
2	14 (6.7)
More than 2	2 (1.0)
Unknown	14 (6.7)

Provincial measles outbreaks

Western Cape Province: The first laboratory-confirmed measles case from the Western Cape Province was identified from a specimen collected on 27 January 2017 from the Cape Winelands District (Figure 3A,B). The case was a 16-year-old male learner at Stellenbosch High School whose vaccination status was unknown. Within the next two weeks, an additional five cases were laboratory-confirmed. A provincial vaccination campaign was initiated targeting children under 15 years of age in the affected sub-districts and children under 5 years of age in the rest of the province. More than 450 000 learners and staff members were vaccinated by March 2017. In total, 36 laboratory-confirmed cases were identified, with the majority having an epidemiological link with the school where the index case was detected. In this outbreak, 36% of cases occurred in the 15-19 year age group (13 out of 36) with an incidence rate of 27.8 per million population (Table 3).

Gauteng Province: From January to March, 2017, several measles cases were detected in the City of Johannesburg, Ekurhuleni and City of Tshwane (Figure 3A,C). A measles outbreak was consequently declared in March. A total of 16 laboratory-confirmed measles cases was identified within a 30-day period. Ten cases were linked to a single family and most cases were unvaccinated primary school children with vaccine-hesitant parents. By 24 November 2017, the last case was reported in Gauteng, totalling 96 laboratory-confirmed cases. Measles cases were most common in the 22-44 year age group (40/96, 42%), but the incidence rate was highest in the <1-4 year age group (23 per million population) (Table 3). In response to the outbreak, officials initiated a province-wide vaccination campaign from May to June 2017 that targeted children up to the age of 15 years in the affected sub-districts and up to 5 years of age in the rest of the province.

KwaZulu-Natal province: In August 2017, a third measles outbreak was declared in KwaZulu-Natal Province following an increase in measles cases in the Ethekwini and Umgungundlovu districts (Figure 3A,D). By 31 December 2017, there were 53 measles cases of which 52 were laboratory confirmed and 1 epidemiologically linked. Measles frequency was

highest in the 5-9 year age group (28.3% - 15/53, incidence rate of 12.6 per million population, Table 3). The majority of measles cases occurred within communities that were hesitant to accept vaccination for religious and other social reasons. Outbreak response activities including contact tracing and measles vaccinations were carried out in schools, health facilities and households. Community mobilisation activities, including face-to-face meetings and radio interviews, were carried out in collaboration with local community representatives and the Islamic Medical Association in order to encourage vaccine uptake during immunisation campaigns.

While the outbreaks in the Western Cape and Gauteng provinces were contained through vigorous vaccination campaigns and were declared over within 2017, the outbreak in KwaZulu-Natal continued into 2018 with six additional measles cases occurring at the end of January. The outbreak in KwaZulu-Natal Province was declared over on 20th February 2018. In total there were 62 laboratory-confirmed cases and a single epidemiologically-linked case. This outbreak primarily affected the 5-9 year old age group (n=17 cases at the end of the outbreak).

Sporadic measles cases

Aside from the provincial measles outbreaks mentioned, 25 other laboratory-confirmed measles cases were intermittently detected in other provinces as follows: Eastern Cape (n=6), Free State (n=1), Limpopo (n=3), Mpumalanga (n=3) and North West (n=12) (Figure 3A).

Measles molecular typing

A total of 366 specimens (68 throat swabs and 298 sera) was tested using real-time RT-PCR. Of these, 154 (42.1%) were positive of which 75 (48.7%) were positive on the conventional RT-PCR. Seventy-one sequences were obtained and all were identified as D8 genotype wild-type measles virus. Phylogenetic analysis showed two monophyletic clusters of sequences: a Western Cape cluster and a cluster containing sequences from Gauteng, KwaZulu-Natal and North West provinces, suggesting that there were at least two separate importation events of closely-related genotype D8 viruses.

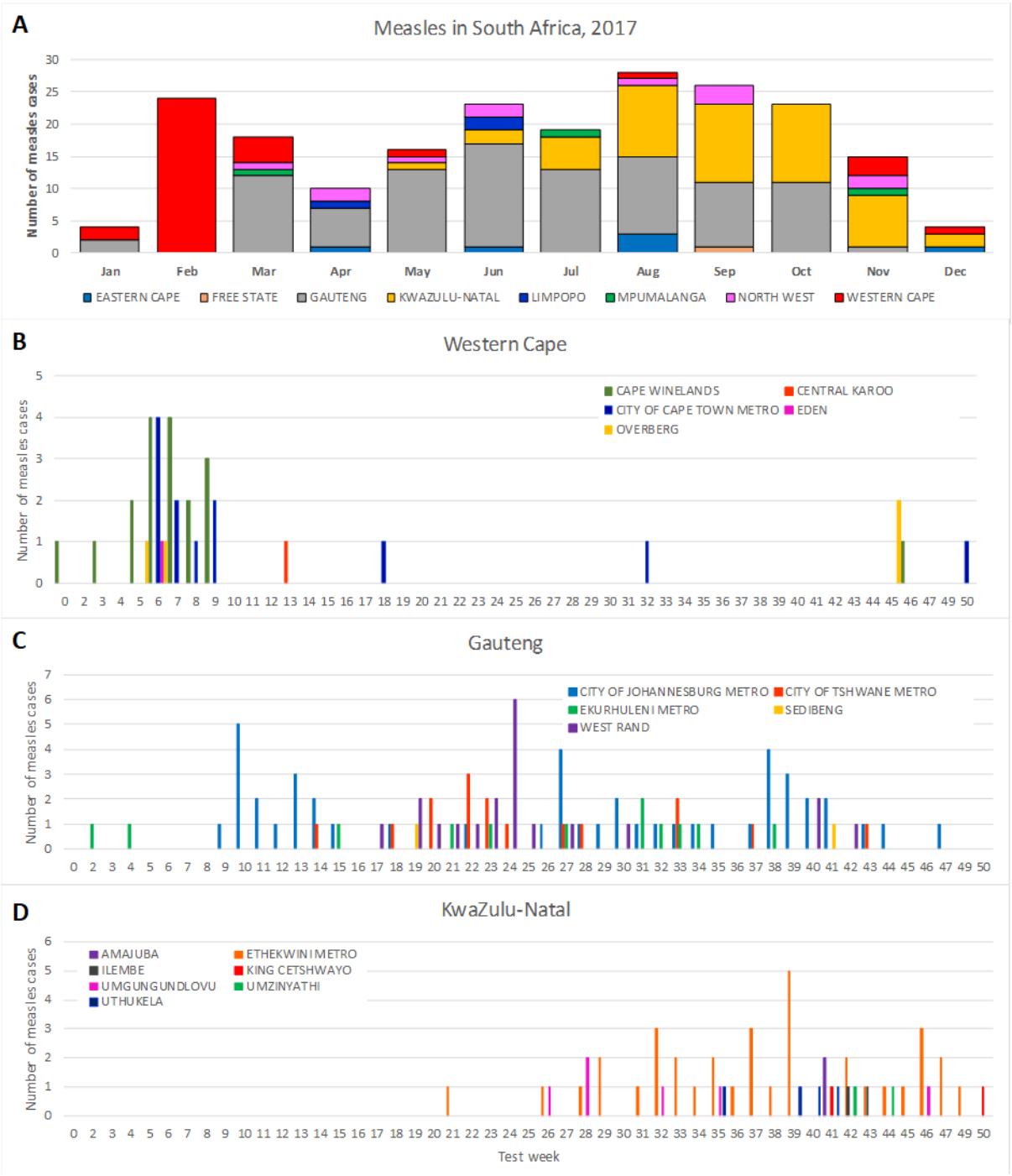

Figure 3. Laboratory-confirmed measles cases in South Africa for the period 1 January to 31 December, 2017.

A: Monthly distribution of laboratory-confirmed measles cases stratified by province **B**: Epidemiological curve of the measles outbreak in Western Cape Province by district **C**: Epidemiological curve of the measles outbreak in Gauteng Province by municipality **D**: Epidemiological curve of the measles outbreak in KwaZulu-Natal Province by district.

Table 3. Incidence rate per million by age group of laboratory-confirmed measles cases by those provinces that experienced outbreaks, South Africa 1 January to 31 December, 2017.

Province	Category (N)	Age group (years)					
		0 – 4	5 – 9	10 – 14	15 – 19	20 – 44	>45
WCP	Confirmed Measles case	6	2	2	13	13	0
	Total population per age group	566 838	596 462	503 672	467 474	2 778 231	1 597 635
	Confirmed measles case incidence per 1 000 000	10.6	3.4	4.0	27.8	4.7	0.0
GP	Confirmed Measles case	30	10	8	4	40	4
	Total population per age group	1 304 143	1 189 820	1 022 519	970 823	6 659 725	3 131640
	Confirmed measles case incidence per 1 000 000	23.0	8.4	7.8	4.1	6.0	1.3
KZN	Confirmed Measles case	11	15	7	5	13	2
	Total population per age group	1 231 052	1 194 286	1 111 398	1 007 111	4 488 097	2 042 840
	Confirmed measles case incidence per 1 000 000	8.9	12.6	6.3	5.0	2.9	1.0
National	Confirmed Measles case	58	31	18	22	73	8
	Total population per age group	5 866 631	5 764 612	5 093 740	4 591 979	23 439 180	11 765 806
	Confirmed measles case incidence per 1 000 000	9.9	5.4	3.5	4.8	3.1	0.7

Total population figures were supplied by Statistics South Africa mid-year population estimates 2017.[15] **WCP**= Western Cape Province; **GP**= Gauteng Province; **KZN**= KwaZulu-Natal Province

Circulating rubella

From January to December, 2017, a total of 2512 rubella cases was identified in South Africa. Monthly distribution indicates that rubella was circulating throughout the year but peaked in spring (September, October and November) with case numbers exceeding 350 (Figure 1A). Overall, KwaZulu-Natal Province had the highest number of laboratory-confirmed cases followed by Gauteng Province (Figure 1B). This represents more than double the number of rubella cases detected in 2016 (n=817) from rash-based surveillance specimens. Rubella was equally distributed amongst males and females and was predominant in the 1-4 and the 5-9 year old age groups (Figure 4A and 4B), which corresponded with the high rubella incidence rates in those age groups (Table 4). Importantly, in the 15 to 44 year old age group, 56% of the rubella cases were detected amongst females.

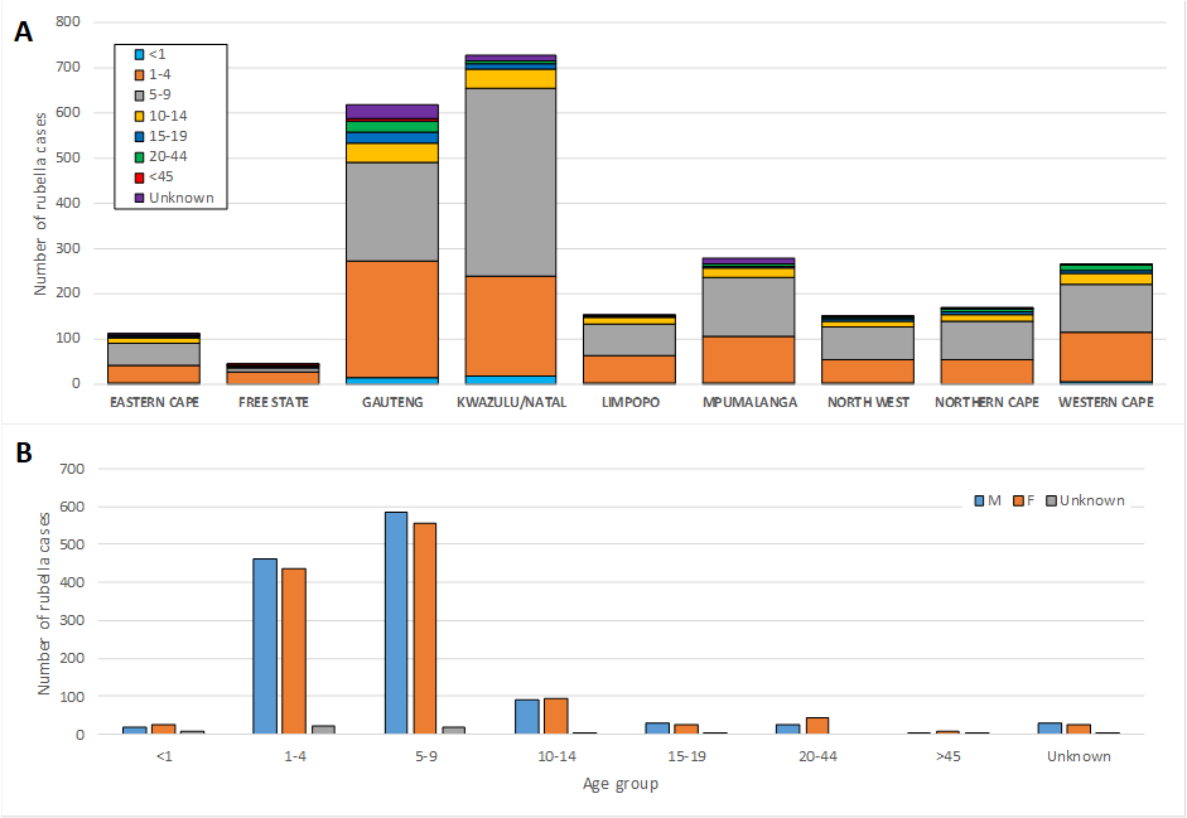

Figure 4. Rubella cases in South Africa for the period 1 January to 31 December, 2017. **A:** provincial distribution of laboratory-confirmed rubella cases (n=2512) stratified by age group **B**: Age and gender of laboratory-confirmed rubella cases (males, n=1239; females, n=1214; Unknown, n=59).

Table 4. Rubella incidence rate per million by age group in laboratory-confirmed rubella cases in the provinces with measles outbreaks for the period 1 January to 31 December, 2017.

Province	Category	Age group					
		0 – 4	**5 – 9**	**10 – 14**	**15 – 19**	**20 – 44**	**>45**
WC	**Confirmed rubella case**	115	107	23	6	12	0
	Total population per age group	566 838	596 462	503 672	467 474	2 778 231	1 597 635
	Confirmed rubella case incidence per 1000 000	202.9	179.4	45.7	12.8	4.3	0.0
GP	**Confirmed rubella case**	272	219	42	23	26	6
	Total population per age group	1 304 143	1 189 820	1 022 519	970 823	6 659 725	3 131 640
	Confirmed rubella case incidence per 1000 000	208.6	184.1	41.1	23.7	3.9	1.9
KZN	**Confirmed rubella case**	240	414	42	11	8	0
	Total population per age group	1 231 052	1 194 286	1 111 398	1 007 111	4 488 097	2 042 840
	Confirmed rubella case incidence per 1000 000	195.0	346.7	37.8	10.9	1.8	0.0
National	**Confirmed rubella case**	971	1159	186	55	69	10
	Total population per age group	5 866 631	5 764 612	5 093 740	4 591 979	23 439 180	11 765 806
	Confirmed rubella case incidence per 1000 000	165.5	201.1	36.5	12.0	2.9	0.8

Total population figures were supplied by Statistics South Africa Mid-year population estimates 2017.[14] **WC**= Western Cape Province; **GP**= Gauteng Province; **KZN**= KwaZulu-Natal Province.

Congenital rubella syndrome (CRS) surveillance

In 2017, there were eight laboratory-confirmed cases of CRS from three provinces (Figure 5). Gender distribution was similar amongst the cases and was comparable to the number of CRS cases reported in 2016 (n=8). Median maternal age was 26 years (range: 15 - 38 years), median parity was 2 (range: 1 - 4), and median gestation was 36.5 weeks (range: 32 - 41 weeks) with half the infants preterm at birth. Hepatosplenomegaly (88%) and congenital heart disease (63%) were the most common complications reported. As rubella vaccination is not yet part of the EPI, 38% of mothers said they were not vaccinated and 63% did not know their status. Further details on CRS surveillance in South Africa are in submission.[16]

Responses to monthly e-mails sent to clinicians at study sites varied from 0% (eight sites in 2016 and nine sites in 2017) to 100% (three sites in 2016 one site in 2017). Telephonic follow-up was conducted for sites with zero reporting to confirm absence of detected cases.

Field and laboratory surveillance indicators for suspected rash cases

Only seven provinces exceeded the target of 2 per 100 000 for detection of non-measles, febrile, rash-based illness cases, which decreased the national rate from 5.1 in 2016 to 4.4 in 2017 (Table 5). Given the measles outbreaks in the Western Cape, Gauteng and KwaZulu-Natal provinces, the national incidence rate for confirmed measles cases per million population increased from 0.3 in 2016 to 3.7 in 2017. In particular, Gauteng and Western Cape provinces had the highest measles incidence rates of 7.0 and 5.6 respectively. Concerning laboratory surveillance indicators in 2017, 97% of results were reported within seven days of receipt in the laboratory, exceeding the target of 80%, and representing an improvement from the 91% reporting rate in 2016.

Regional references laboratory function

A total of 479 serum samples was received from the national laboratories of countries in southern Africa and were retested for measles and rubella IgM as part of the WHO quality control system.

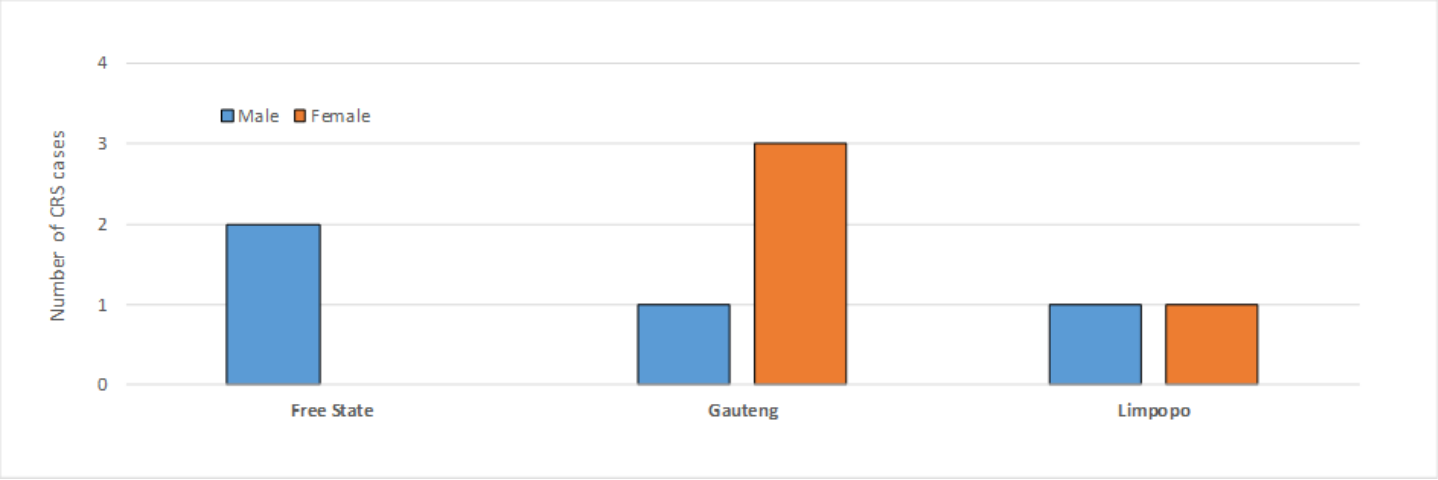

Figure 5. Distribution of laboratory-confirmed congenital rubella syndrome (CRS) cases by province and gender, South Africa, 1 January to 31 December 2017.

Table 5. Field surveillance adequacy and the confirmed measles case rate by province, South Africa, 1 January to 31 December 2017. (WHO targets for non-measles, febrile, rash illness surveillance = > 2 per 100 000, WHO elimination target for confirmed measles cases= <1 case per million population).

Province	Non-measles, febrile, rash illness cases	Confirmed measles cases	Total population	Non-measles, febrile, rash illness rate per 100 000	Confirmed measles case incidence rate per 1 000 000
ECP	112	6	7 139 336	1.6	0.8
FSP	43	1	2 881 998	1.5	0.3
GP	617	96	13 773 639	4.5	7.0
KZN	725	53	11 229 961	6.5	4.7
LMP	153	3	5 877 930	2.6	0.5
MPP	277	3	4 388 269	6.3	0.7
NCP	152	12	1 200 703	4.0	3.1
NWP	168	0	3 847 629	14.0	0.0
WCP	265	36	6 393 555	4.1	5.6
Total SA	2 512	210	56 733 020	4.4	3.7

Total population figures were supplied by the National Department of Health using the District Health Information Software (DHIS) 2017 midyear estimates.[17] **ECP** = Eastern Cape Province; **FSP** = Free State Province; **GP** = Gauteng Province; **KZN** = KwaZulu -Natal Province; **LMP** = Limpopo Province; **MPP** = Mpumalanga Province; **NCP** = Northern Cape Province; **NWP** = North West Province; **WCP** = Western Cape Province.

Discussion and conclusion

In 2017, three measles outbreaks occurred in South Africa resulting in a national incidence rate of 3.7 per million population, 12-fold higher than the national incidence rate reported in 2016. Outbreak investigations and surveillance data analysis showed that the majority of measles cases were in vaccine-hesitant communities or were in patients who had received fewer than the two recommended doses. For this reason, and to better understand and address the issues raised by vaccine-hesitant communities, outbreak mobilisation activities including face-to-face meetings and radio interviews were carried out in collaboration with local community representatives and the Islamic Medical Association. Similarly, given that the national immunization coverage is less than the recommended 95%, both national and provincial supplementary immunisation activities (SIAs) were arranged, targeting all children from 6 months to 5 years of age in public and private sectors, including those whose vaccinations were up-to-date. SIAs are an effective strategy for delivering vaccination to children otherwise missed by routine services (e.g. the hard-to-reach and underserved groups/ communities) and are an integral part of the measles elimination campaign. SIAs should therefore be scheduled every 2-3 years prior to an outbreak. The last SIAs occurred in 2010 during the 2009-2011 measles outbreak.[10]

The incidence of circulating rubella was 3-fold higher in 2017 as compared to 2016, which corresponded to the increase in rash-based surveillance across the country due to the high index of suspicion and an increase in specimen collection. While rubella was predominant in the younger age groups, a high proportion of females of child-bearing age were also infected. These findings may indicate an underreporting of CRS and emphasises an urgent need to understand the burden of CRS.

In conclusion, continuous surveillance is an important public health measure for the control and elimination of measles, with the aim of reaching the 2020 WHO elimination goal for the African region. Inadequacies in aspects of the surveillance data highlight the importance of meticulously and timeously investigating each suspected measles case before an outbreak occurs. The three measles outbreaks that occurred in 2017 are a stark reminder that South Africa remains vulnerable to such events. The fact that these outbreaks largely occurred in communities who were unvaccinated or had low vaccination coverage highlights the urgent need to improve vaccine awareness and vaccine coverage in these communities.

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GERMS-SA ANNUAL SURVEILLANCE REPORT FOR LABORATORY-CONFIRMED INVASIVE MENINGOCOCCAL, *HAEMOPHILUS INFLUENZAE* AND PNEUMOCOCCAL DISEASE, SOUTH AFRICA, 2017

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Executive summary

The NICD and GERMS-SA conducts national laboratory-based surveillance for *Neisseria meningitidis*, *Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*, describing the epidemiology of these diseases and monitoring the impact of the pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. Participating laboratories reported case patients to the NICD using laboratory case report forms. Isolates from case patients, if available, were submitted to the NICD for phenotypic and genotypic characterisation. A surveillance audit was additionally performed for NHLS laboratories in all provinces using the NHLS Central Data Warehouse. 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. *Neisseria meningitidis* invasive disease incidence remained low for 2017, with Serogroup B predominating. Penicillin non-susceptibility was below 10%. The overall incidence of *H. influenzae* also remained low in 2017, and non-typeable disease accounted for the majority of cases. The majority of children <15 years of age with *H. influenzae* serotype b (Hib) had not been fully vaccinated, highlighting the importance of Hib vaccinations in children under 2 years. The incidence of invasive pneumococcal disease (IPD) in 2017 was similar to that in 2016, remaining low with marked reductions seen amongst all age categories post introduction of pneumococcal conjugate vaccine (PCV) into the expanded programme on immunization (EPI). Penicillin and ceftriaxone susceptibility of IPD isolates remained unchanged in 2017. HIV infection and infant HIV exposure are continued risk factors for disease. Residual disease in children <5 years was largely due to non-vaccine serotypes, and the majority of vaccine-type disease occurred in children who have not received adequate doses of PCV-13.

Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) in collaboration with GERMS-SA (a nationwide network of clinical microbiology laboratories that participate in an active surveillance programme for pathogens of public health importance) conducts national laboratory-based surveillance for *Neisseria meningitidis, Haemophilus influenzae* type b (Hib) and *Streptococcus pneumoniae*. The surveillance aims to describe the epidemiology of these diseases and monitor the impact of the pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease in South Africa. This report summarises the findings for 2017.

Methods

Approximately 181 South African clinical microbiology laboratories participated in the GERMS-SA surveillance programme in 2017, including 26 enhanced surveillance sites (ESS).[1] The population under surveillance in 2017 was estimated at 56.5 million.[2] Diagnostic laboratories reported case patients to the NICD using laboratory case report forms according to a standard case definition: the isolation of the organism under surveillance from any normally sterile site. If available, isolates from case patients were submitted on Dorset transport media to the NICD for further phenotypic and genotypic characterisation. Culture negative cases with a positive supplementary test e.g. Gram stain and/or antigen detection, were also reported and their samples were submitted for molecular detection of the 3 pathogens. At ESS, surveillance officers completed clinical case report forms electronically using the Mobenzi application on mobile phones for patients with laboratory-confirmed invasive meningococcal disease, invasive *H. influenzae* disease and invasive pneumococcal 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 for the duration of their hospital admission. Data management was centralised at the NICD. Laboratory, clinical and demographic data from case patients were recorded on a Microsoft Access database. A surveillance audit was performed for NHLS laboratories in all provinces using the NHLS Central Data Warehouse (CDW). 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; these cases are included in this report. Incidence was calculated using mid-year population estimates for 2016 and 2017 from Statistics South Africa.[2] Ethics approval for the on-going activities of the surveillance programme was obtained from the Human Research Ethics Committee (Medical), University of Witwatersrand (clearance number M08-11-17) and from relevant University and Provincial Ethics Committees for other enhanced surveillance sites. Surveillance activities were funded by the NICD/ NHLS.

Results and Discussion

Neisseria meningitidis

In 2017, 136 cases of laboratory-confirmed invasive meningococcal disease (IMD) were identified through the surveillance system, of which 70 (51%) were viable isolates received and 9 (7%) were detected on audit. The overall disease incidence was 0.24 cases per 100 000 population, similar to that in 2016 (0.23/100 000). Incidence was highest in the Western Cape Province (0.75/100 000) followed by Gauteng (0.29/100 000), Eastern Cape (0.29/100 000) and Free State provinces (0.21/100 000) (Table 1). Disease peaked in the winter and spring months (June to October) with a further peak in December (Figure 1). No outbreaks of meningococcal disease were detected in 2017. Cerebrospinal fluid was the most common specimen from which meningococci were identified (94/136, 69%) (Table 2). Serogroup B (45/108, 42%) was the most common serogroup causing disease, followed by W (27/108, 25%) and Y (21/108, 19%) (Table 3; Figure 2). IMD occurred more frequently in males (73/133, 55%) than females. Incidence was highest in children <5 years with a small increase in the 15-24 year age category. Infants had the highest incidence of IMD for all serogroups (Figure 10). Of the viable isolates tested for antimicrobial susceptibility, 6% (4/70) were non-susceptible to penicillin with minimum inhibitory concentrations (MICs) >0.06µg/ml, all were susceptible to 3rd generation cephalosporin and ciprofloxacin.

Thirty-nine (29%) IMD patients presented to the enhanced surveillance sites and 35/39 (90%) had additional clinical information available. The median time for each admission was 7 days (interquartile range 5-10 days). The case-fatality ratio was 17% (6/35); 3 of these patients died on the day of admission, 2 died after 6 days and 1 after 8 days. Twenty-eight percent of patients with HIV status available were HIV-coinfected (8/29). For those who survived to discharge from hospital, 6/29 (21%) suffered sequelae following IMD. These included 1 patient requiring amputation of the toes, 1 with skin scarring following necrotic lesions, 1 developed hydrocephalus, 2 experienced new onset of seizures, and 1 with loss of vision and new onset of seizures.

Invasive meningococcal disease incidence remained low for 2017. Serogroup B predominated once again, particularly in the Western Cape Province, driving up the incidence in that province. Penicillin non-susceptibility was below 10%, justifying the continued recommendation of high-dose penicillin as the first-line therapy for confirmed IMD. Although uncommon, meningococcal disease in South Africa is a devastating illness largely affecting young children and has an in-hospital case fatality of 17%, with 21% of patients suffering sequelae post-discharge from hospital.

Table 1. Number of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2016 and 2017, n=267 (including audit cases).

Province	2016		2017	
	n	Incidence rate*	N	Incidence rate*
Eastern Cape	15	0.21	19	0.29
Free State	2	0.07	6	0.21
Gauteng	36	0.27	41	0.29
KwaZulu-Natal	11	0.10	8	0.07
Limpopo	1	0.02	3	0.05
Mpumalanga	5	0.12	4	0.09
Northern Cape	2	0.17	1	0.08
North West	5	0.13	5	0.13
Western Cape	54	0.86	49	0.75
South Africa	**131**	**0.23**	**136**	0.24

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

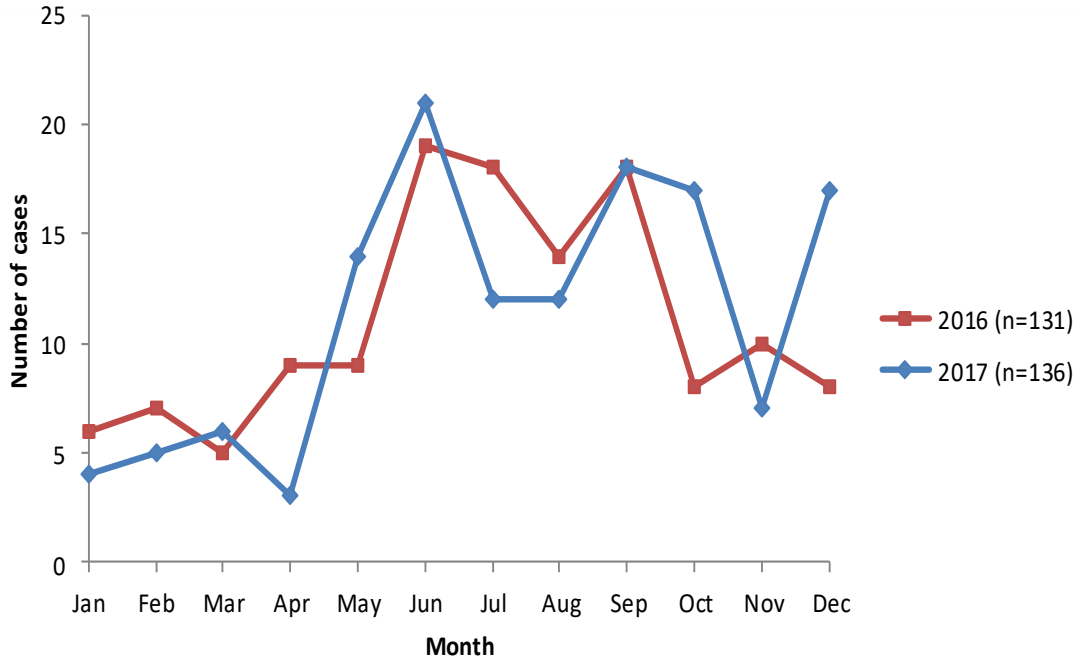

Figure 1. Numbers of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2016-2017, n=267.

Table 2. Number and percentages of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2016 and 2017, n=267.

Site of specimen	2016		2017	
	n	%	n	%
Cerebrospinal fluid	92	70	94	69
Blood	38	29	42	31
Other	1	1	0	0
Total	**131**		**136**	

Table 3. Numbers of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2017, n=136*.

Province	Serogroup								
	Serogroup not available	A	B	C	W	Y	Z	NG**	Total
Eastern Cape	2	0	6	5	3	3	0	0	19
Free State	0	0	3		2	1	0	0	6
Gauteng	7	0	11	6	8	9	0	0	41
KwaZulu-Natal	3	0	3	0	0	2	0	0	8
Limpopo	3	0	0	0	0	0	0	0	3
Mpumalanga	3	0	0	1	0	0	0	0	4
Northern Cape	1	0	0	0	0	0	0	0	1
North West	4	0	0	0	1	0	0	0	5
Western Cape	5	0	22	2	13	6	0	1	49
South Africa	**28**	**0**	**45**	**14**	**27**	**21**	**0**	**1**	**136**

*108 (79%) with viable isolates or specimens available for serogrouping/genogrouping; ** NG: Non-groupable (including 1 that was negative for genogroups A, B, C, W, Y, X by polymerase chain reaction)

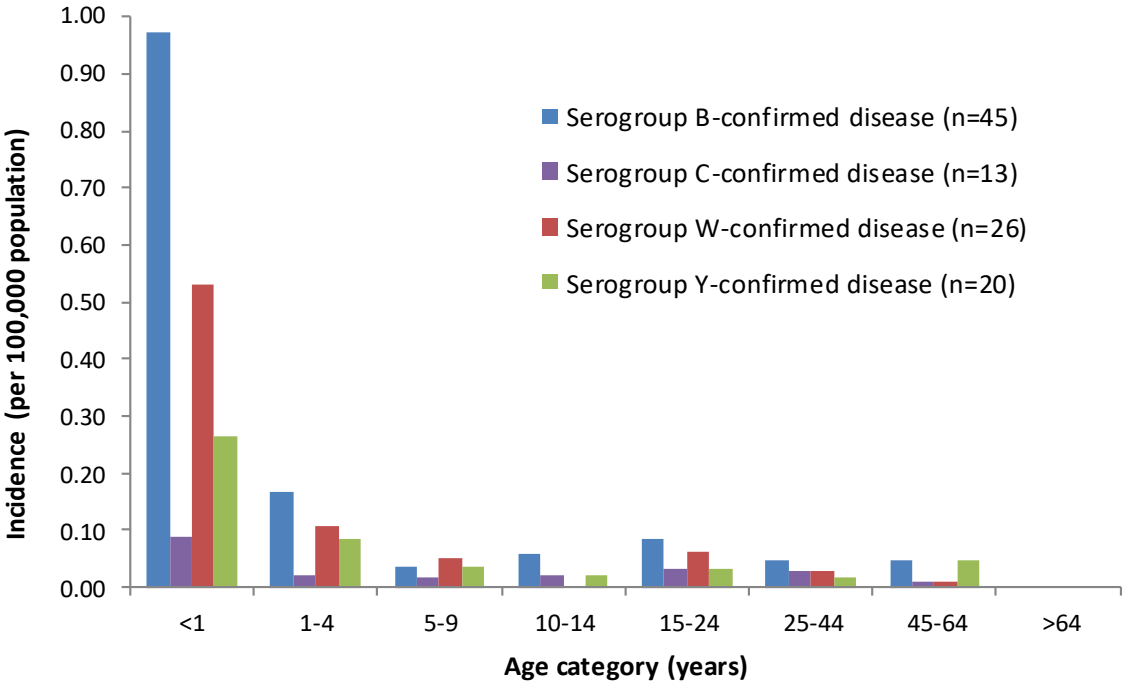

Figure 2. Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, C, W and Y, South Africa, 2017, n=136** (**age unknown for n=3; specimens or viable isolates unavailable for serogrouping n=28; one Non-groupable specimen).

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

Haemophilus influenzae

There were 313 cases of invasive *H. influenzae* (HI) disease identified through the surveillance programme in 2017, of which 33% (103) were detected on audit and 59% (184) had either viable isolates (118) or specimens (66) available for serotyping (Table 4). Ten cases were co-infected with invasive *S. pneumoniae.* Western Cape Province (112/313, 36%) reported the highest number of cases, followed by Gauteng Province (84/313, 27%) (Table 4). Twenty-two percent of cases (41/184) were serotype b (Hib) and non-typeable (HNT) disease was found in 64% (118/184) (Table 4). Most cases were isolated from blood, however Hib isolates were more likely than HNT isolates to be found in CSF (19/41, 46% versus 11/118, 9%, p<0.001) (Table 5). Children <5 years had the highest burden of all types of invasive HI, followed by a second peak in the 25-44 year age group (Figure 3). Incidence of Hib in infants was 1.6 per 100 000, decreasing to 0.08 per 100 000 in 1-4 year olds, similar to that of 2016 (Figure 4 and 5). HNT incidence was also highest in infants (2.3 per 100 000) and peaked again in 45-64 year age group (0.3 per 100 000). Since 2010, Hib incidence in children <1 year has decreased significantly from 5.2 to 1.6 cases per 100 000 (p<0.001); and remained below 0.3 per 100 000 in 1-4 year olds, since 2012 (Figure 5). Seventeen percent (4/23) of Hib isolates and 7% (5/76) of HNT isolates were non-susceptible to ampicillin (MIC>1mg/L). Twenty-four cases of Hib disease occurred in children <15 years of age and vaccine history was available for 54% (13/24). Thirty-eight percent (5/13) of these children with invasive Hib had received appropriate doses of Hib vaccine for their age, and were possible vaccine failures, whilst 54% (7/13) had not received appropriate Hib vaccine doses for their age. The remaining child only had a verbal history of having received childhood vaccinations.

Clinical information was available for 87% (129/149) of cases presenting to the enhanced surveillance sites (ESS). Patients were admitted for a median of 9 days (interquartile range (IQR) 2-21). Case fatality was 29% (36/126) and median time to death was within one day of admission (IQR 0-9). Case fatality appeared to be lower amongst those with Hib than with HNT disease, but this did not reach statistical significance (13% (2/15) vs. 29% (14/49), p=0.3). Amongst those with known HIV status, 33% (30/92) were HIV infected. Conditions other than HIV predisposing to HI disease were reported in 71/129 (55%) patients – the most common conditions included chronic lung disease, underlying cardiac disease, malignancy, prematurity and history of smoking. Of 20 patients at ESS with HI on CSF: 25% (4/20) died during their hospitalization, and 25% (4/16) who survived to discharge suffered sequelae – these included 2 with new onset seizures, 1 with hydrocephalus and 1 with weakness of the limbs.

Overall incidence of HI remained low and HNT accounted for the majority of cases. The highest rates of disease were seen in infants for both Hib and HNT, with HNT incidence increasing with age. Case-fatality ratios were high (29%) and long-term sequelae following meningitis occurred in 25% of cases. The majority of children <15 years of age with Hib had not been fully vaccinated, highlighting the importance of Hib vaccinations in children under 2 years.

Table 4. Numbers of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2017, n=313*.

Province	Serotype								
	Serotype not available	a	b	c	d	e	f	Non-typeable	Total
Eastern Cape	20	1	2	0	0	0	2	8	33
Free State	3	1	0	0	0	0	0	9	13
Gauteng	45	1	15	0	0	1	2	20	84
KwaZulu-Natal	22	1	3	1	1	0	2	11	41
Limpopo	3	0	5	0	0	0	0	1	9
Mpumalanga	6	0	0	1	0	0	0	1	8
Northern Cape	2	0	0	0	0	0	0	3	5
North West	4	0	2	0	0	0	1	1	8
Western Cape	24	5	14	2	0	0	3	64	112
South Africa	**129**	**9**	**41**	**4**	**1**	**1**	**10**	**118**	**313**

*184 (59%) with specimens or viable isolates available for serotyping.

Table 5. Numbers and percentages of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2017, n=313.

Site of specimen	No serotype available		Serotype b		Serotypes a, c, d, e, f		Non-typeable	
	n	%	n	%	n	%	n	%
Cerebrospinal fluid	28	22	19	46	9	36	11	9
Blood	62	48	21	51	15	60	72	61
Other	39	30	1	2	1	4	35	30
Total	**129**		**41**		**25**		**118**	

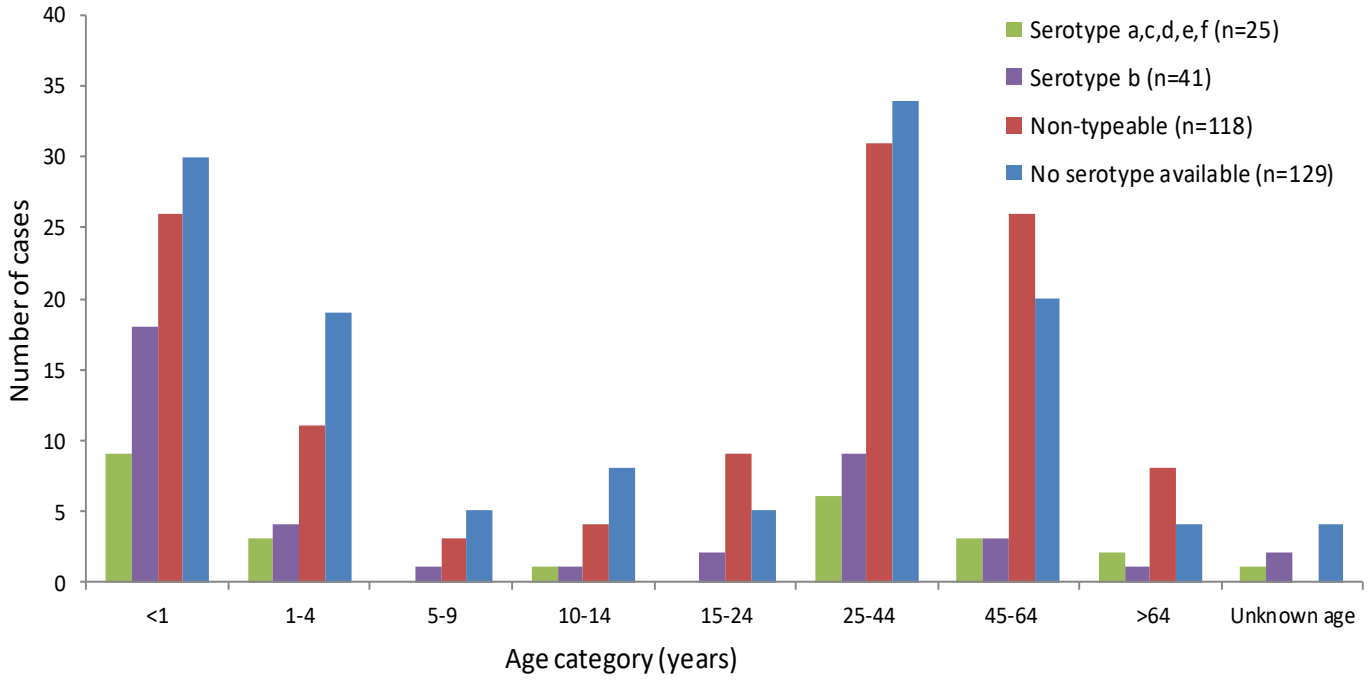

Figure 3. Numbers of laboratory-confirmed, invasive, *Haemophilus influenzae* cases reported to GERMS-SA by serotype and age group, South Africa, 2017, n=313 (age unknown for n=7; specimens or viable isolates unavailable for serotyping for n=129).

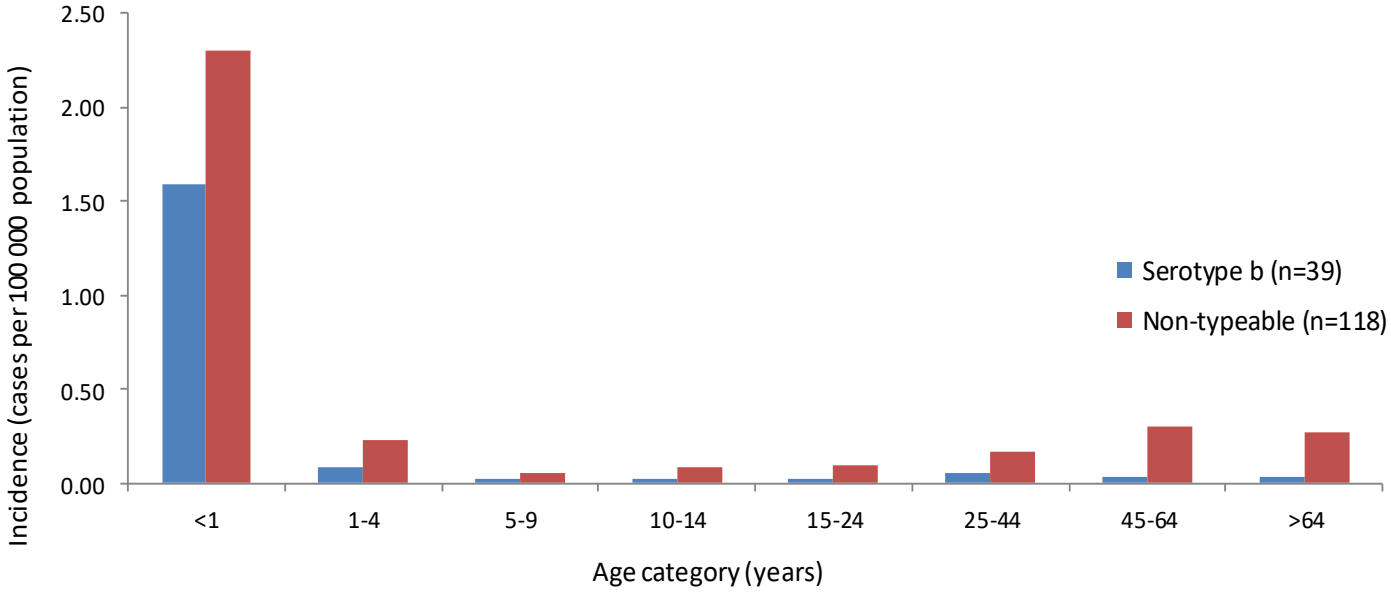

Figure 4. Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype b and non-typeable, South Africa, 2017, n=313 (age unknown, n=3; viable isolates unavailable for serotyping, n=129; other serotypes from cases with known age, n=24).

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

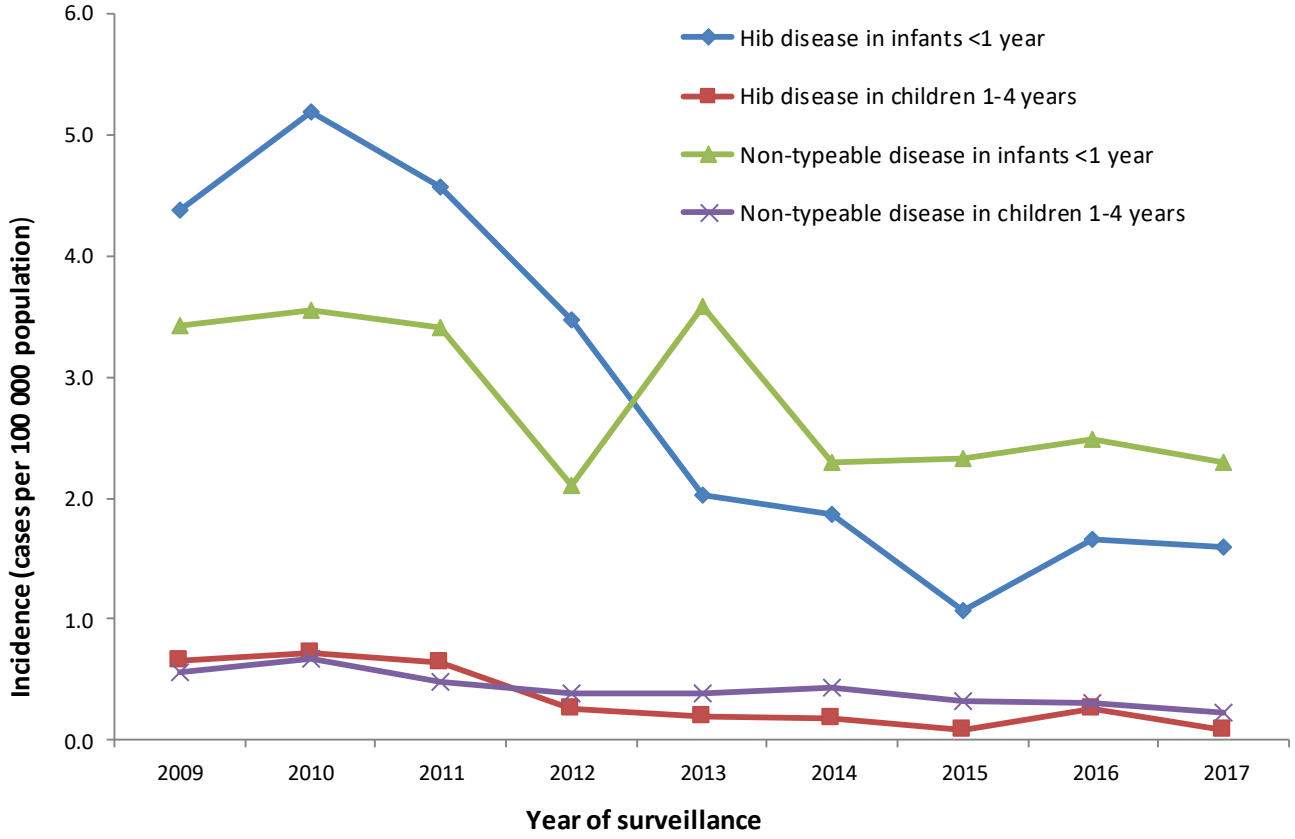

Figure 5. Incidence rates* of laboratory-confirmed, *Haemophilus influenzae* serotype b disease reported to GERMS-SA in children <5 years old, South Africa, 2009-2017.

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

Streptococcus pneumoniae

The incidence of invasive pneumococcal disease (IPD) in 2017 was similar to that in 2016 (4.3 vs 4.4 per 100 000 population, p=0.9) (Table 6). IPD incidence varied by province with the highest incidence seen in the Western Cape (10.4 per 100 000 population) followed by Gauteng Province (6.1 per 100 000 population) (Table 6).

Since the introduction of the pneumococcal conjugate vaccine (PCV-7) into the Expanded Programme on Immunisation (EPI) in 2009, and the replacement of PCV-7 with PCV-13 in 2011, there was a 79% reduction in IPD in children <5 years (from 30 per 100 000 population in 2005 to 6 per 100 000 population in 2017, p<0.001). There was also a 46% reduction in IPD in those aged five years and older (from 7 per 100 000 population in 2005 to 4 per 100 000 population in 2017). In 2017, the highest burden of IPD was still in infants (20 per 100 000 population), followed by the 45-64 year age group (7 per 100 000 population) (Figure 6). Ten patients with IPD were co-infected with invasive *H. influenzae*. The majority of cases were isolated from blood culture specimens (61%, 1480/2441) (Table 7). Penicillin non-susceptibility (minimum inhibitory concentration (MIC) >0.06µg/ml) was detected in 29% (439/1531) of IPD isolates, the highest proportion being in children 1-4 years of age (44%) (Table 8, Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 7% (114/1531) of isolates from all specimens, and amongst 5% (19/388) of IPD isolated from CSF. Serogroups 8, 12F, 19A, 3 and 19F were the most predominant serogroups causing IPD in 2017. Amongst children <5 years, serogroup 8 (35/201) caused the bulk of disease followed by serogroups 15A (14/201) and 19A (13/201) (Figure 8).

Unfortunately, only 55% (207/374) of IPD isolates from children <5 years-of-age were sent to the NICD for serotyping (Figure 9). Of these, 20% (41/207) were serotypes containing PCV-13 (Table 9).

Thirty-nine percent (952/2441) of IPD patients presented to the enhanced surveillance sites (ESS), and 871/952 (91%) had additional clinical information available. Patients were admitted for a median hospital stay of 8 days (interquartile range (IQR) 2-15) and most deaths occurred within 2 days of admission (IQR 1-7). Overall case fatality was 32% (274/846). HIV-coinfection was present in 64% (437/681) of IPD patients, and 37% (29/78) of infants, with maternal HIV-status available, were HIV exposed (6 HIV-infected and 23 HIV-uninfected infants). Forty-nine percent (406/825) of patients had an underlying medical condition (excluding HIV infection) predisposing them to IPD.

Of 236 patients at ESS with pneumococcus on CSF, 40% (94/236) died during their hospitalization, and 33% (47/142) who survived to discharge suffered at least one sequelae – these included new onset seizures (15), limb weakness/ paralysis (12), hearing loss (10), hydrocephalus (5), and loss of vision (4). Twenty-four episodes of IPD caused by serotypes present in the PCV-13 vaccine occurred in children <10 years-of-age at ESS. Vaccine history was available for 67% (16/24). Eighty-one percent (13/16) of these children had not received adequate PCV-13 doses for their age and 2 neonates were too young to receive vaccine. Only one child who received 3 PCV-13 doses could possibly be considered a vaccine failure.

IPD incidence remained low in 2017, with marked reductions seen amongst all age categories post introduction of PCV into the expanded programme on immunization. Children <1 year-of-age had the highest incidence of disease followed by a peak in the 45-64 year age category (a shift from the 25-44 year age category peak seen in previous years). Penicillin and ceftriaxone susceptibility of IPD isolates remain unchanged. HIV infection and infant HIV exposure remain risk factors for disease. Pneumococcal meningitis has high mortality and morbidity. Residual disease in children <5 years was largely due to non-vaccine serotypes, and the majority of vaccine-type disease occured in children who have not received adequate doses of PCV-13. Clinicians should ensure that all children (and adults with risk factors for IPD) receive adequate vaccine doses to protect them from this serious illness. The number of viable isolates submitted to the NICD for serotyping is still low, and participating laboratories are urged to remember to forward pneumococci from normally sterile sites to the NICD.

Table 6. Numbers of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2016 and 2017, n=4873 (including audit cases).

Province	2016		2017	
	n	Incidence rate*	n	Incidence rate*
Eastern Cape	208	2.95	208	3.20
Free State	147	5.14	117	4.08
Gauteng	854	6.33	868	6.08
KwaZulu-Natal	320	2.89	269	2.43
Limpopo	84	1.45	74	1.28
Mpumalanga	102	2.36	105	2.36
Northern Cape	42	3.52	53	4.37
North West	73	1.93	72	1.87
Western Cape	602	9.57	675	10.37
South Africa	2432	4.35	2441	4.32

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

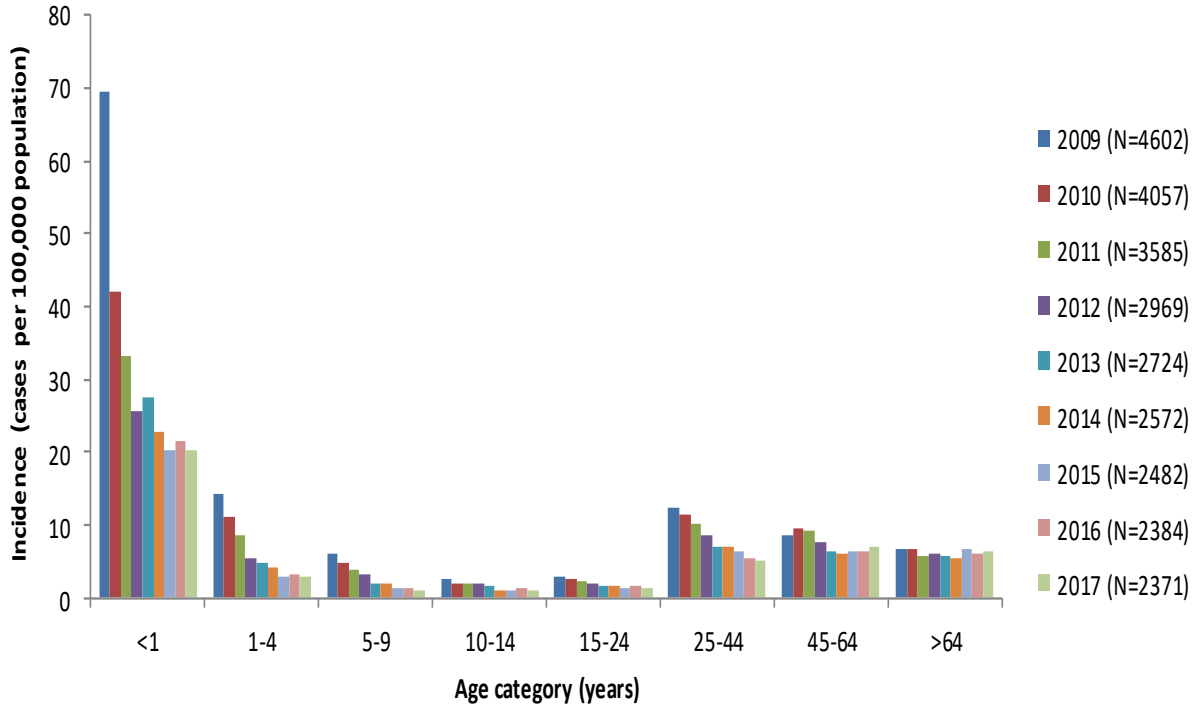

Figure 6. Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease reported to GERMS-SA South Africa, 2009 through 2017.

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

Table 7. Numbers and percentages of cases of invasive pneumococcal disease reported to GERMS-SA by specimen type, South Africa, 2016 and 2017, n=4873.

Site of specimen	2016		2017	
	n	%	n	%
Cerebrospinal fluid	859	35	792	32
Blood	1379	57	1480	61
Other	194	8	169	7
Total	**2432**		**2441**	

Table 8. Numbers and percentages of penicillin susceptible and non-susceptible isolates from invasive pneumococcal disease cases reported to GERMS-SA by province, South Africa, 2017, n=2441.

Province	Isolate not available	Susceptible*		Intermediate*		Resistant*	
	n	n	%	n	%	n	%
Eastern Cape	115	70	75	17	18	6	6
Free State	45	52	72	18	25	2	3
Gauteng	363	358	71	107	21	40	8
KwaZulu-Natal	152	70	60	38	32	9	8
Limpopo	32	31	74	10	24	1	2
Mpumalanga	40	39	60	20	31	6	9
Northern Cape	12	31	76	7	17	3	7
North West	37	28	80	5	14	2	6
Western Cape	114	413	74	109	19	39	7
South Africa	**910**	**1092**	71	**331**	22	**108**	7

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

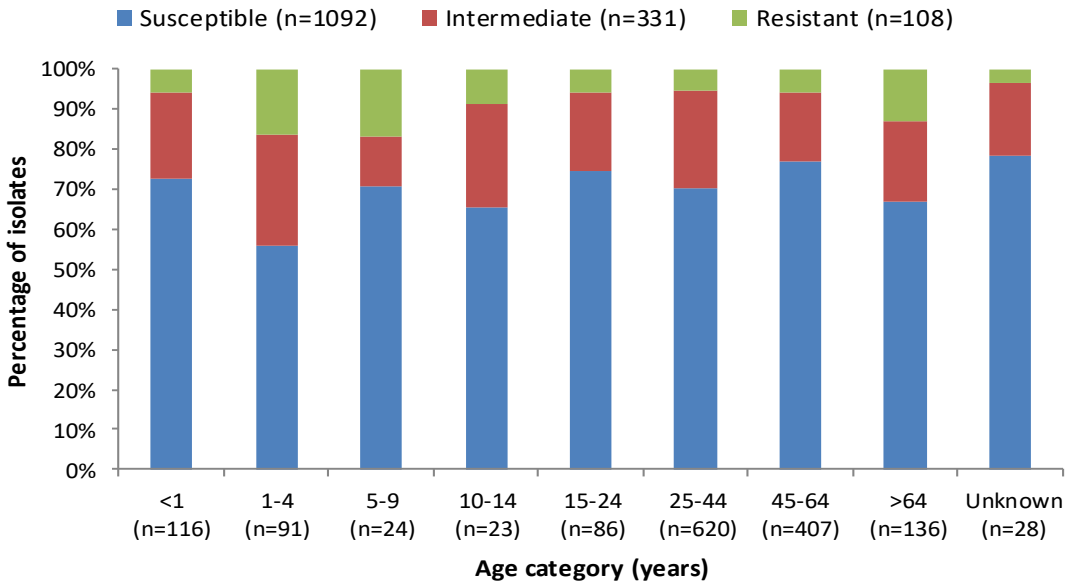

Figure 7. Numbers of laboratory-confirmed, invasive pneumococcal disease cases reported to GERMS-SA by age group and penicillin susceptibility, South Africa, 2017, n=2441 (n=1531 with viable isolates).

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

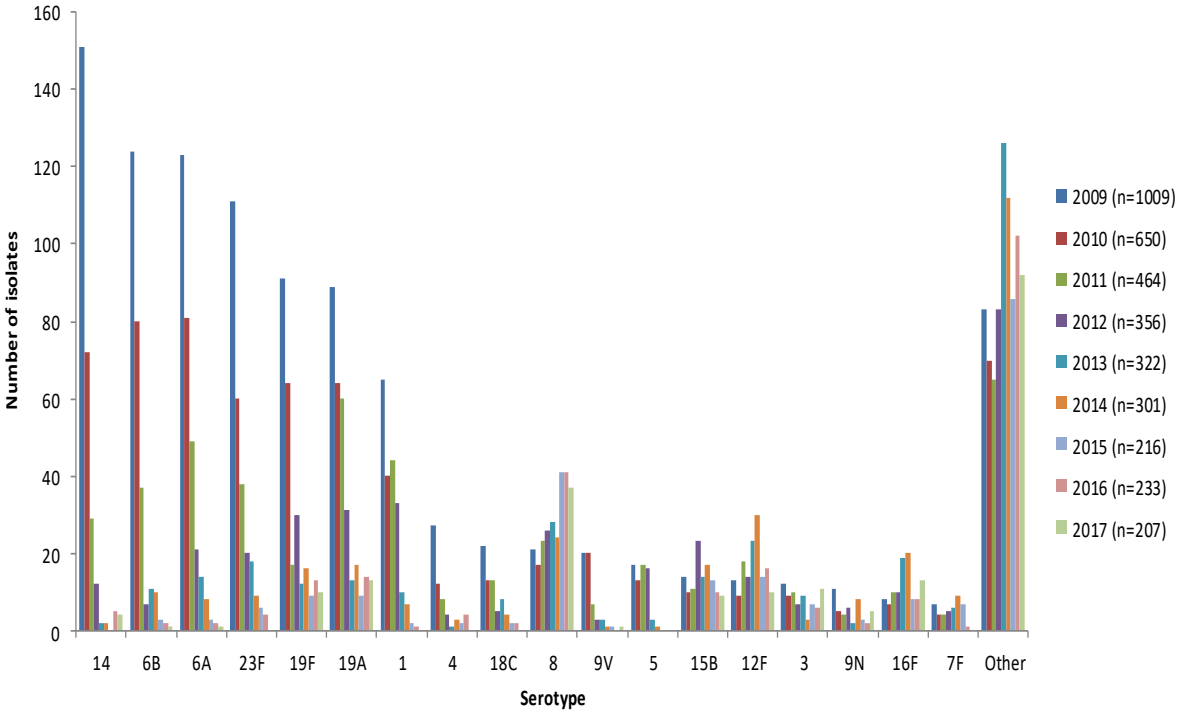

Figure 8. Most common pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA in children <5 years, South Africa, 2009-2017.

2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates; 2017: N=374, n=167 without viable isolates.

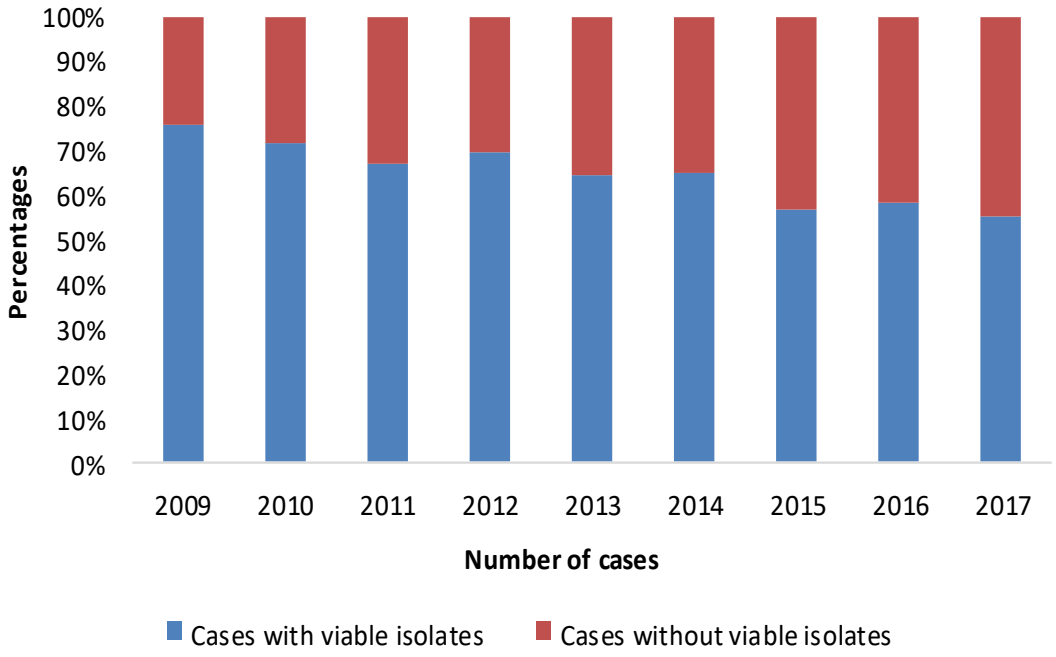

Figure 9. Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA in children <5 years, South Africa, 2009-2017.

2009: N=1336, n=327 without viable isolates; 2010: N=910; n=260 without viable isolates; 2011: N=695, n=231 without viable isolates; 2012: N=512, n=156 without viable isolates; 2013: N=498, n=176 without viable isolates; 2014: N=465, n=164 without viable isolates; 2015: N=382, n=166 without viable isolates; 2016: N=401, n=168 without viable isolates; 2017: N=374, n=167 without viable isolates.

Table 9. Numbers and percentages of invasive pneumococcal cases reported amongst children less than 5 years of age caused by the serotypes contained in the 7-valent, 10-valent and 13-valent pneumococcal conjugate vaccines, South Africa, 2017, n=374 (n=207 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	7	2	29	0	0	2	29	2	29
Free State	7	1	14	0	0	1	14	5	71
Gauteng	91	6	7	0	0	6	7	15	16
KwaZulu-Natal	15	2	13	1	7	2	13	5	33
Limpopo	11	0	0	0	0	0	0		0
Mpumalanga	7	0	0	0	0	0	0	3	43
Northern Cape	1	0	0	0	0	0	0		0
North West	5	1	20	0	0	1	20	2	40
Western Cape	63	4	6	0	0	4	6	9	14
South Africa	**207**	**16**	**8**	**1**	**0.5**	**16**	**8**	**41**	**20**

All serotypes included in each of the categories: 7-valent serotypes*: 4, 6B, 9V, 14, 18C, 19F, 23F
10-valent serotypes**: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F
13-valent serotypes***: 4, 6B, 9V, 14, 18C, 19F, 23F, 1, 5, 7F, 19A, 3, 6A

Acknowledgments

We would like to thank all clinical and laboratory staff throughout South Africa for submitting case reports and isolates for the GERMS-SA national surveillance programme, as well as all the patients who agreed to provide further clinical details. We would also like to acknowledge the epidemiologists, scientists, technologists, nursing and administration staff of CRDM and GERMS-SA for their contribution to the programme. The surveillance programme was financially supported by the National Institute for Communicable Diseases, a division of the National Health Laboratory Service.

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SENTINEL SURVEILLANCE OF HUMAN PAPILLOMAVIRUS GENOTYPES AMONG YOUNG WOMEN ATTENDING PUBLIC HEALTHCARE FACILITIES IN SOUTH AFRICA, 2017

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Executive summary

Human papillomavirus (HPV), a sexually transmitted virus, is associated with a number of cancers, with cervical cancer being the most important. HPV vaccination should occur prior to exposure to HPV infection as the current HPV vaccines are prophylactic. As part of the HPV vaccination strategy in South Africa it is important to have baseline data on HPV in adolescent girls and young women so that the impact of vaccination can be assessed. Therefore, women between the ages of 18 and 20 years attending public healthcare facilities in South Africa during 2017 were recruited to participate in HPV surveillance. Cervical swabs were taken for HPV genotyping. The overall HPV prevalence was 64.4% (181/281). HPV-16 (11.7%, 33/281) was the most commonly detected HPV type. When compared with HIV-negative women, HIV-positive women not on antiretroviral treatment were found to have a higher risk of HPV infection (RR: 1.32, 95% CI: 1.10-1.58, p=0.003), but this was not observed among those on antiretroviral treatment (RR: 1.10, 95% CI: 0.78-1.57, p=0.585). HPV types targeted by the Cervarix® HPV vaccine, (HPV-16/18, currently used in the South African school-based HPV vaccination program), were detected in 16.7% (47/281) of women, while those found in the Gardasil (HPV-6/11/16/18) were detected in 23.8% (67/281) of women; and those in the Gardasil® 9 (HPV-6/11/16/18/31/33/45/52/58) were detected in 35.9% (101/281) of women. The high prevalence of HPV types targeted by Gardasil® 4 and Gardasil® 9 HPV encourages the introduction of vaccines targeting a higher number of HPV types in South Africa.

Introduction

In 2014, South Africa introduced a school-based vaccination with Cervarix® against human papillomavirus (HPV)16/18 in public schools. Cervarix® vaccination is given in two doses (six-months apart) within the academic calendar. The school-based HPV vaccination program currently targets girls aged 9 or older in grade 4. HPV is sexually transmitted and HPV vaccination should therefore be given prior to sexual debut. The median age of sexual debut among South African women ranges between 16 and 19 years.[1-4] HPV vaccination coverage of up to 93% has been observed within the HPV school-based vaccination program.[5]

The aim of HPV vaccination is to reduce the incidence of infection that will result in a reduction of HPV-associated cancers, including those of the cervix, anus, vulva, vagina, penis and oropharynx. Cervical cancer is the most common cancer in South African women between the ages of 15 and 44 years with an age standardized rate (ASR) of 30.2 per 100 000 population. HPV16 (50.7%), HPV18 (13.5%), HPV33 (7.3%), HPV35 (6.0%) and HPV45 (5.6%) are the most common high-risk (HR) HPV types observed in cervical cancer cases in South Africa.[5]

HPV typing data in an unvaccinated population is important to inform vaccination campaigns as well as to establish a baseline to monitor the impact on prevalence of HR-HPV types after vaccination. This report is an update of previous study by Mbulawa et al.[6], and reports on overall HPV prevalence, prevalence of HPV genotypes and prevalence of HPV types targeted by current HPV vaccines, namely, Cervarix®, Gardasil® and Gardasil® 9, among young women attending public healthcare facilities in South Africa during 2017. Factors associated with HPV infection, particularly HIV infection and associated ART use, were also investigated.

Methods

Participant recruitment, data and specimen collection. A total of 286 sexually active young women between the ages of 18 -20 years was recruited from the family planning units of primary healthcare clinics (PHCs) in four provinces namely, Gauteng (Alexandra community health centre), Free State (Heidedal clinic), Western Cape (Site C Youth Clinic, Khayelitsha) and Eastern Cape (Zwide clinic) during 2017. During the informed consent process, a detailed description of study procedures was discussed with each of the participants. A questionnaire designed to record demographic, behavioural and clinical data was administered by surveillance nurses. An endocervical swab for HPV testing was collected by a surveillance nurse during speculum examination. Endocervical swabs were transported at 2-8°C to the Centre for HIV and STIs of the National Institute for Communicable Diseases (NICD) laboratories in Johannesburg and Cape Town where HPV testing was performed.

HPV testing and genotyping. DNA from endocervical swabs was extracted by a MagNA Pure Compact (Roche) using the MagNA Pure Compact Nucleic Acid Isolation Kit (Roche). DNA was stored at -80°C until processing. HPV genotyping was performed on extracted DNA using the Roche Linear Array HPV genotyping test which identifies 37 different HPV genotypes; HR-HPV types included HPV-16, -18, -31, -33, -35, -39, -45, -51, -52, -56, -58 and -59; probable or possible HR-HPV types included HPV-26, -53, -66, -67, -68, -70, -73 and -82; and low-risk (LR) HPV types included HPV-6, -11, -40, 42, -54, -55, -61, -62, -64, -69, -71, -72, -81, -83, -84, -89 (HPV-CP6108) and HPV-82. HPV-52 was recorded positive only in the absence of HPV-33, -35 and -58 due to the combined probe used for these four types. The Roche Linear Array HPV genotyping test also amplifies the β-globin gene as an internal control for cell adequacy, extraction and amplification in each specimen. Samples with negative β-globin results were considered invalid and excluded from the analysis.

Data management and statistical analysis. Completed questionnaires were couriered to the data centre at the NICD, entered into an Access database and exported into Stata® 14.2 [Stata Corporation, College Station, Texas, United States] for analysis. Descriptive statistics were used to describe demographic, behavioural and clinical characteristics of enrolled participants as well as HPV prevalence. Binomial univariable and multivariable regression was used to determine factors associated with the detection of any HPV genotypes. Variables with p-values < 0.2 in univariable

analyses were included in the multivariable analysis. The target sample size per site was 100 participants, estimated using the Wald test, assuming a prevalence of any HPV infection between 58% and 70% power of 80% and α-level of 0.05. Assuming a power of 80% and α-level of 0.05, a sample size of 286 was required to measure a prevalence of any HPV genotype of 64% +/- 4% across all the sites.

Results

Description of surveillance population. A total of 286 women between the ages of 18 and 20 years (median 19 years) participated in HPV surveillance. The majority were enrolled at the Western Cape site – 80(28%), followed by the Gauteng Province site - 77 (26.9%), the Eastern Cape site – 69 (24.1%) and the Free State site - 60 (21%). The median age at first sex was 17 years (IQR 16-17 years). The majority of women self-reported heterosexual activity (99.3%, 280/282). Only 32.2% (92/194) reported the use of a condom at last sexual encounter. Vaginal sex was the most common sex act reported by participants (97.9%, 278/284), followed by oral sex (11.3%, 32/284) and receptive anal sex (2.5%, 7/284). At least one in five participants - 21.2% (50/236) - was HIV-positive; with 16 of the 50 (32%) reporting that they were taking antiretroviral treatment (ART).

HPV prevalence and impact of HIV status. Of the 286 women enrolled, 281 (98.3%) had a valid HPV genotype result. The overall HPV prevalence was 64.4% (181/281). Infection with multiple (2-10) HPV types was more common ((42.0% (118/281)) than single HPV infections (22.4%, 63/281, p<0.001, Figure 1). HPV-16 (11.7%, 33/281) was the most commonly detected HPV type (Figure 2). HIV-positive women not on ART had a higher risk of HPV infection compared to HIV-negative women (RR: 1.32, 95% CI: 1.10-1.58, p=0.003). A slightly increased but statistically insignificant risk of HPV infection was also observed among HIV-positive women who reported taking ART compared to HIV negative women (RR: 1.10, 95% CI: 0.78-1.57, p=0.585, Table 1).

Prevalence of HPV types targeted by bivalent, quadrivalent and nonavalent HPV vaccines. HPV types targeted by the bivalent HPV vaccine (HPV-16/18) were detected in 16.7% (47/281) of women, while those found in the quadrivalent vaccine (HPV-6/11/16/18) were detected in 23.8% (67/281) of women, and those in the nonavalent vaccine (HPV-6/11/16/18/31/33/45/52/58) were detected in 35.9% (101/281) of women (Figure 3). The bivalent HPV vaccine (Cervarix®) is currently being used in school-based vaccination in South Africa. HR-HPV types that are not targeted by bivalent, quadrivalent or nonavalent HPV vaccines, and not cross-protective, were observed in 18.9% (53/281) of the women (HPV-35/39/56/59, Figure 3).

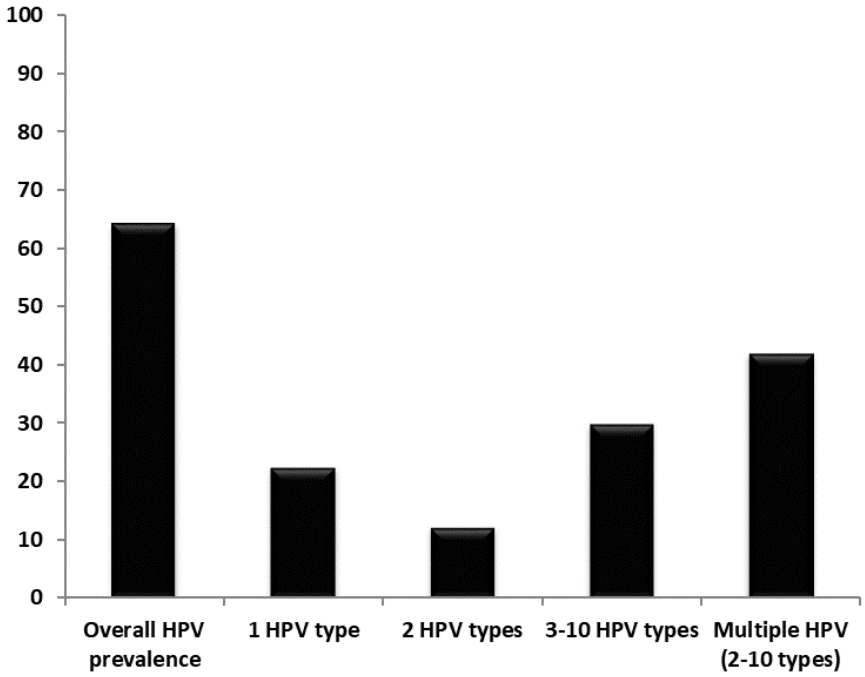

Figure 1. Prevalence of overall human papillomavirus (HPV), single infection and multiple infections among young women attending GERMS sentinel sites in South Africa, 2017.

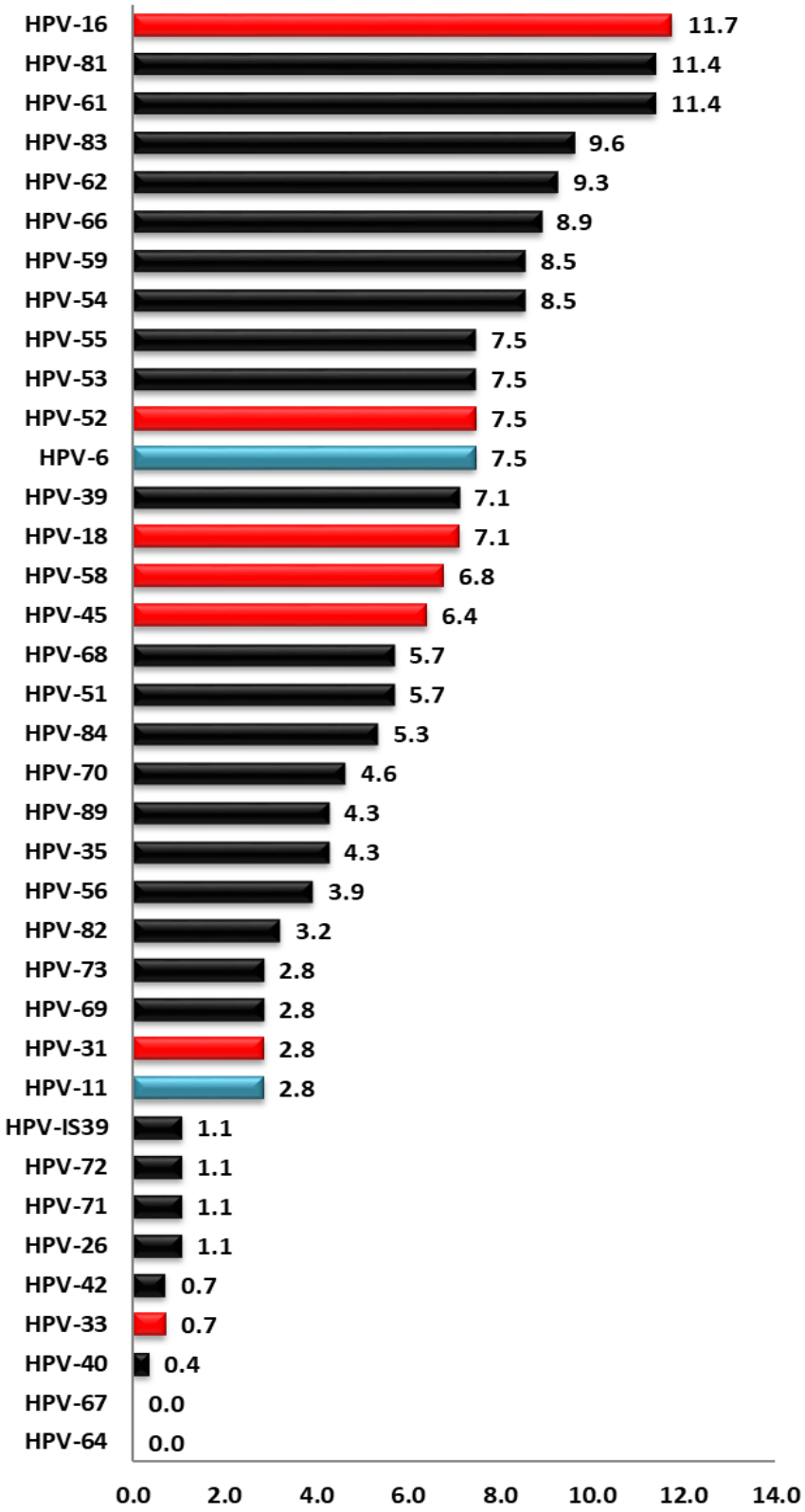

Figure 2. Prevalence of different human papillomavirus (HPV) genotypes detected among young women attending GERMS sentinel sites in South Africa, 2017. HPV types targeted by three current HPV vaccines are indicated by red bars (HR-HPV-16, -18, -31, -33, -45, -52 and 58) and blue bars (LR: HPV-6 and -11).

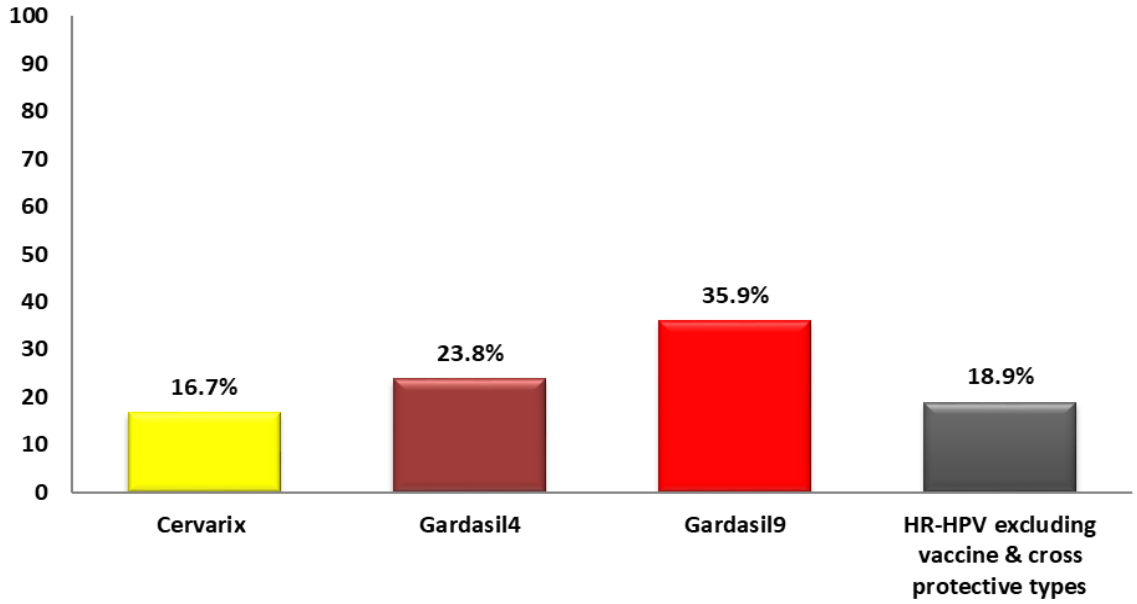

Figure 3. Prevalence of human papillomavirus (HPV) types targeted by current HPV vaccines and HR-HPV non-vaccine types detected among young women attending GERMS sentinel sites in South Africa, 2017.

Table 1. Factors associated with the prevalence of any human papillomavirus (HPV) genotype among enrolled women (N= 281), South Africa, 2017.

Factor	HPV n/N	%HPV infection	Univariable RR (95% CI)	p-value	Multivariable RR (95% CI)	p-value
Age						
18 years	46/74	58.2	0.96 (0.77- 1.19)	0.692		
19 years	57/87	65.5	1.01 (0.82- 1.23)	0.938		
20 years	78/120	65.0	reference			
HIV status						
Negative	141/231	61.0	reference		reference	
Positive, on ARVs	11/16	68.8	1.13 (0.80- 1.59)	0.500	1.10 (0.78 - 1.57)	0.585
Positive, not on ARVs	29/34	85.3	1.38 (1.17- 1.66)	**<0.001**	1.32 (1.10- 1.58)	**0.003**
Condom use						
Yes	129/190	67.9	reference		reference	
No	52/91	57.1	0.84 (0.69- 1.03)	0.096	0.90 (0.73- 1.10)	0.321
Age at first sex						
17-20 years	91/139	65.5	reference			
≤16 years	87/134	64.9	0.99 (0.83- 1.18)	0.925		
missing	3/8	37.5	0.57 (0.23- 1.51)	0.226		
Sex Act						
Vaginal only	158/240	65.8	reference			
Vaginal &/receptive anal & /oral	20/34	58.8	0.89 (0.66- 1.20)	0.455		
missing/none	3/7	42.9	0.65 (0.28- 1.54)	0.328		
Study site						
Inland Provinces (GP/FS)	80/135	59.3	reference		reference	
Cape Provinces (EC/WC)	101/146	69.2	1.17 (0.98- 1.39)	0.086	1.11 (0.93- 1.32)	0.25

ARVs=Antiretrovirals. GP=Gauteng Province. FS=Free State Province. EC=Eastern Cape Province. WC=Western Cape Province

Discussion and conclusions

High overall HPV prevalence (64.4%) was observed among young women attending family planning services at primary healthcare clinics. The prevalence of the most common HPV type in HPV-associated cancers, HPV-16, was 11.7%. It is well documented that HIV infection increases the risk of HPV acquisition and persistence. In this study, HIV-infected women not on ART were found to have higher risk of HPV infection compared to HIV-negative women, but this was not observed among those women on ART. A systematic review by Kelly et al.[7] reported that HIV infected women on ART had lower prevalence of HR-HPV than those not on ART. This may be as a consequence of early ART initiation and sustained adherence which results in functional mucosal immune reconstitution and HPV clearance. All HIV positive young women should be initiated on ART as early as possible to reduce direct morbidity and mortality from HIV infection and also to promote HPV clearance and prevent progression of HPV infection to cervical intraepithelial neoplasia and cancer of the cervix.

The study was conducted at a few surveillance sites in four provinces, limiting the generalisability of the current study findings to other settings and provinces. Even though none of the facilities met their target sample size of 100 participants per site, a reasonable sample size was achieved overall. Strengths of this study include the fact that participants were recruited from geographically diverse locations, and the availability of risk factor data. HPV-16/18 targeted by Cervarix® were detected in 16.7% women, while HPV-6/11/16/18/31/33/45/52/58 targeted by Gardasil® 9 were detected in 35.9% of women. The high prevalence of HPV types targeted by Gardasil® 9 was previously observed in NICD GERMS-SA HPV surveillance that was conducted in young among women accessing family planning services in Gauteng, Mpumalanga, KwaZulu-Natal and North West provinces between 2015 and 2016.[6] These observations encourage the introduction of vaccine targeting high numbers of HPV types such as Gardasil® 9 in South Africa.

In conclusion, this surveillance programme provides useful HPV baseline prevalence data for assessing the effectiveness of HPV vaccination, i.e. by enabling comparisons over time to detect significant changes in the prevalence of HR-HPV types (both vaccine and phenotypically related non-vaccine HPV genotypes). It also enables monitoring for genotype replacement and guides the formulation of enhanced HPV vaccination strategies, including catch-up HPV vaccination programmes.

Acknowledgements

We thank the all the young women who kindly participated in the surveillance, the clinical staff at the sentinel sites and the NICD GERMS-SA surveillance team who recruited participants and collected specimens. This surveillance was supported by grants from South African Research Chairs Initiative of the Department of Science and Technology and funding from the National Department of Health.

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CHARACTERISATION OF *STAPHYLOCOCCUS AUREUS* BLOODSTREAM ISOLATES FROM GAUTENG AND WESTERN CAPE PROVINCES, SOUTH AFRICA, 2016 AND 2017

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Executive summary

Staphylococcus aureus bacteraemia is one of the most prevalent bacterial infections in South African healthcare settings and according to international literature, it is the second most frequent pathogen isolated from patients with bacteraemia.[1] Of concern is the presence of methicillin-resistant *Staphylococcus aureus* (MRSA). The prevalence of MRSA differs globally; a surveillance study conducted in four South African provinces showed a MRSA prevalence of 40% in 2012. This decreased from 53% in 2010.[2] In the current study, a total of 374 (24%) MRSA isolates collected as part of a national surveillance programme from two provinces in South Africa were characterised phenotypically. Typing methods such as SCC*mec* and *spa*-typing provide important information about circulating clones of MRSA. All isolates were screened for methicillin resistance using real-time PCR and then typed using conventional typing methods to identify the *mec* element types and *spa*-types. Overall, resistance to antimicrobial agents was low - approximately 0-32% on average - and the MIC_{50} and MIC_{90} did not change for most of the antimicrobial agents over the two-year period except for the MIC_{90}s of rifampicin, which decreased from >2 in 2016 to <=0.5 in 2017 and vancomycin, which increased from 1 in 2016 to 2 in 2017. The most common SCC*mec* type was SCC*mec* type III (45%). The most common spa type was t037 (45%).

Introduction

Staphylococcus aureus infections are a significant cause of morbidity and mortality globally within healthcare settings and in the community.[3] Estimates of mortality of *S. aureus* bacteraemia from 15 studies conducted in Europe, the United States and Asia ranged from 5% to 64%.[4] A recent prospective observational study of patients over 13 years of age with *S. aureus* bacteraemia admitted to one referral hospital in South Africa showed a mortality of 47%.[5] The organism's ability to cause disease such as skin and soft tissue infections, bacteraemia, infective endocarditis, osteomyelitis and necrotising pneumonia is elevated by its ability to develop resistance to frequently-used antibiotics, e.g. methicillin, as well as virulence factors, e.g. those encoded by the staphylococcal cassette chromosome *mec* (SCC*mec*).[3,6]

Methicillin resistance is conferred by the exogenous gene *mecA* or its homologue *mecC*. These genes are located within a mobile genetic element, SCC*mec*[7], which is a large heterologous element consisting of a *mec* complex and a recombinase complex (*ccr*). The *mec* complex contains *mecA/mecC* and its regulators *mecI* and *mecRI*. The *ccr*

complex encodes a site-specific recombinase aiding in the mobility of the element.[8] Several SCC*mec* types exist (I, II, III, IVa, IVb, IVc, IVd, V, VI, VII, VIIII, IX, X and XI) depending on the combination of the class of the *mec* gene complex and the *ccr* allotype (http://www.sccmec.org/). Hospital-associated methicillin-resistant *S. aureus* (MRSA) infections are usually associated with SCC*mec* types I, II or III whereas community-associated MRSA infections are linked to smaller SCC*mec* types IV, V, VI or VII[6] although this may not strictly be the case; epidemiological data are required to make this conclusion.

Spa-typing is a single-locus typing technique that investigates DNA sequence of the protein A gene variable repeat region. This technique rapidly and accurately discriminates *S. aureus* strains[9] and investigates evolutionary relationships among isolates by studying routes of transmission to assess the source of infection. The aim of this study was to identify the common methicillin resistance determinant, SCC*mec* types and *spa*-types in South African MRSA isolates.

Materials and Methods

Bacterial Strains. Blood culture isolates from a surveillance study for the period 1 January 2016 to 31 December 2017 from sentinel centres in South Africa were analysed. Sites represented the Gauteng (n=841) and Western Cape (n=702) provinces. Ethical clearance was obtained from the University of the Witwatersrand's Human Research Committee.

All *S. aureus* blood culture positive isolates were submitted. Any isolate received from the same patient within a 21-day period was considered a duplicate and was rejected. A new/recurrent case was accepted after the 21-day period. Based on the case definition, we received 1543 *S. aureus* isolates submitted on Dorset transport media (Diagnostic Media Products, National Health Laboratory Service). Each isolate was plated onto a 5% blood agar plate (Diagnostic Media Products, National Health Laboratory Service) followed by organism identification and antimicrobial susceptibility testing using automated systems. Organism identification was done using VITEK II (bioMèrieux, Marcy-l'Etoile France) and MALDI-TOF MS (Microflex, Bruker Daltonics, MA, USA) and antimicrobial susceptibility testing using the MicroScan Walkaway system (Siemens, Sacramento, CA, USA). Interpretation of susceptibility was performed according to the Clinical and Laboratory Standards Institute (CLSI) guidelines.[10]

Polymerase chain reaction (PCR) screening for *mecA* and *mecC* in MRSA isolates. DNA was extracted and used in the genotypic assays. The LightCycler 480 II (Roche Applied Science, Penzberg, Germany) instrument was used for the real-time PCR of *mecA* using the LightCycler 480 Probes Master kit (Roche Diagnostics, IN, USA) with previously published primers and probes.[11] The G-Storm (Somerton Biotechnology Centre, Somerton, UK) thermal cycler was used for the conventional PCR of *mecC* using the Qiagen Multiplex PCR kit (Qiagen, Nordrhein-Westfalen, Germany) with previously published primers.[12]

SCC*mec* Typing. All 374 *mecA*-positive MRSA isolates were typed by multiplex PCR using the Qiagen Multiplex PCR kit and previously published primers[13] to identify the current prevalent *mec* element types.

***Spa*-typing.** *Spa*-typing was performed on all 374 MRSA isolates. The *spa* gene was amplified using previously published primers[14] and the Amplitaq Gold DNA Polymerase kit (Applied Biosystems, CA, USA). Purified PCR products

(Qiagen Purification kit; Qiagen, Nordrhein-Westfalen, Germany) were sequenced. Sequences were assembled using CLC Bio main workbench (Qiagen, Hilden, Germany) and analysed using the Ridom StaphType software (Ridom GmbH, Würzburg, Germany).

Statistical analysis. Data analyses were performed using Stata version 14 (StataCorp LP, College Station, Texas, USA).

Results

Phenotypic. A total of 1543 isolates was received for the period 1 January 2016 to 31 December 2017. Of these 374 (24%) were MRSA. A majority of the isolates were received from the Gauteng Province (n=841, 55 %) followed by the Western Cape Province (n=702, 46%). Nine-hundred and fifty cases were males (62%). The gender for one case was unknown. Susceptibility to the following antimicrobial agents was high over the 2-year period: mupirocin, daptomycin, linezolid, teicoplanin, vancomycin, rifampicin, fosfomycin and fusidic acid ranged from 88% to 100% susceptible. The remaining agents showed relatively low resistance levels (ranging from 19% to 32% resistance) (Figure 1). The antimicrobial susceptibility profiles for most antibiotics were comparable for 2016 and 2017, with the exception of ciprofloxacin (p=0.012), tetracycline (p=0.04) and rifampicin (p=0.001), which showed significant increases in susceptibility in 2017. Overall, the MIC_{50} and MIC_{90} did not change for antimicrobial agents during the study period except for the MIC_{90}s for rifampicin and vancomycin (Table 1).

PCR Screening for *mecA* and *mecC* in MRSA isolates. All 374 phenotypically - and genotypically - confirmed MRSA isolates harboured the *mecA* gene. No isolate harboured the *mecC* gene.

SCCmec typing. The most common SCC*mec* type identified was SCC*mec* type III (n=168, 45%) followed by types IV (n=110, 29%), II (n=32, 9%) and one each for types V and VI (0.3%). Unidentified banding patterns were obtained for 62 isolates (17%) (Figure 2). No type I SCC*mec* element was observed. Most of the isolates representing SCC*mec* type II (n=25, 7%) and type IV (n=79, 21%) were from Western Cape Province and most of the type III isolates were from Gauteng Province (n= 141, 38%). Forty-two (11%) of the unidentified banding patterns were seen in Western Cape Province. One isolate (0.3%) each of types V and VI were from Gauteng Province.

***Spa*-typing.** *Spa*-typing of 374 of the isolates revealed 40 different *spa*-types, seven of which were novel and have not as yet been assigned. One isolate was nontypeable as it produced no *spa*-type. The five most common *spa*-types were t037 (n=168, 45%), t1257 (n=61, 16%), t045 (n=41, 11%), t012 (n=2, 8%) and t01971 (n=14, 4%) which accounted for 83% of the isolates tested (Figure 3). The remaining *spa*-types represented a minimum of one to a maximum of seven isolates. Of the five most common *spa*-types, the majority of the t1257 (n=36, 10%), t045 (n=31, 8%), t012 (n=19, 5%) and t01971 (n=14, 4%) *spa*-types were seen in Western Cape Province and t037 (n=137, 37%) was observed in Gauteng Province.

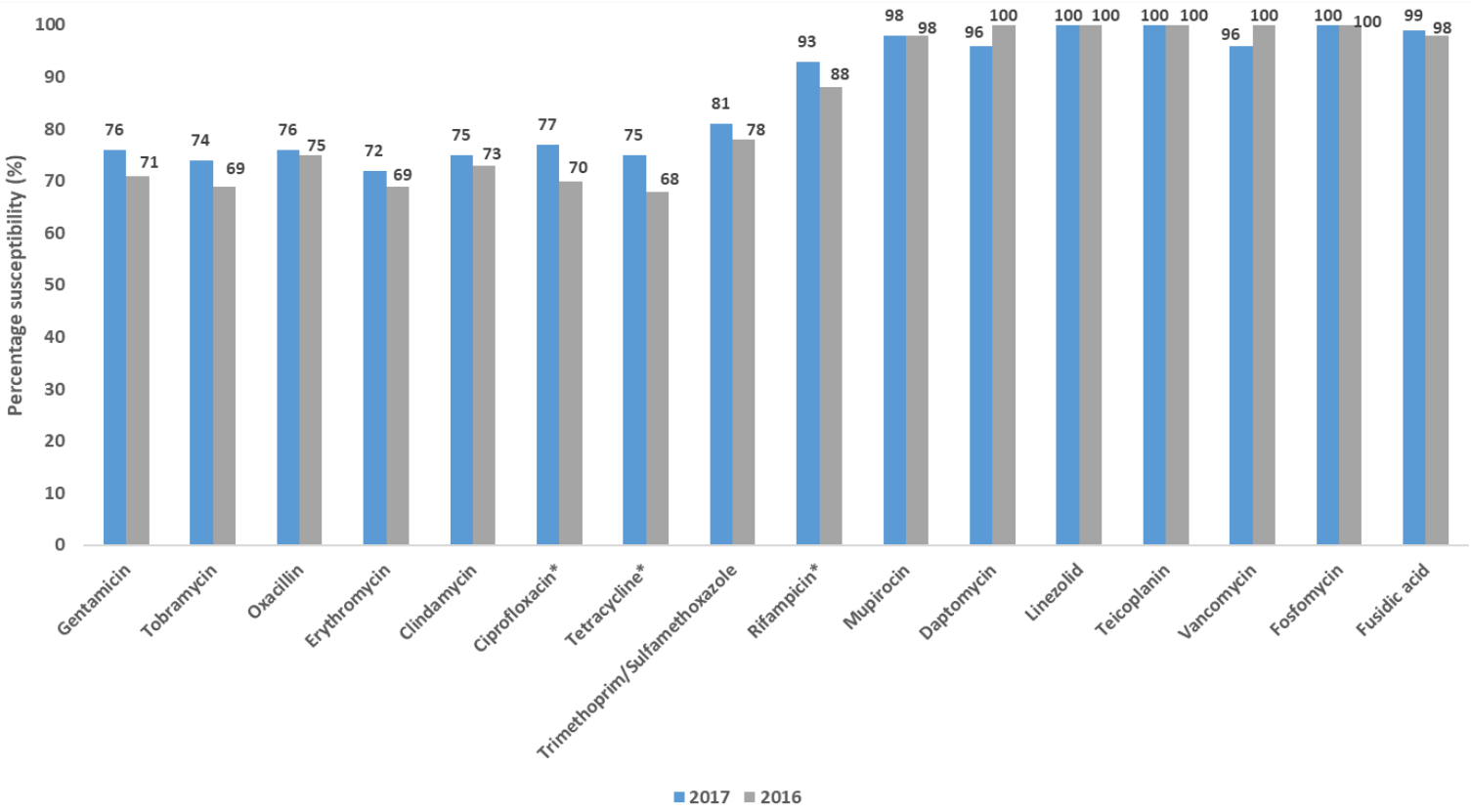

Figure 1. *Staphylococcus aureus* percentage susceptibilities to antimicrobial agents from Gauteng and Western Cape provinces, South Africa, 2016-2017 (n=1543).

* The antimicrobial susceptibility profiles for ciprofloxacin (p=0.012), tetracycline (p=0.04) and rifampicin (p=0.001) showed significant increases in susceptibility in 2017.

Table 1. *Staphylococcus aureus* minimum inhibitory concentrations (MIC_{50} and MIC_{90}) by antimicrobial agent using the Microscan breakpoint panel (PM33), South Africa 2016 and 2017.

Antibiotic	MIC_{50}		MIC_{90}		MIC interpretive breakpoints (µg/ml) based on CLSI guidelines (2017)	
	2016	2017	2016	2017	S	R
Gentamicin	<=1	<=1	>8	>8	<=4	>=16
Tobramycin	<=1	<=1	>8	>8	<=4	>=16
Oxacillin	<=0.25	<=0.25	>2	>2	<=2	>=4
Erythromycin	<=0.5	<=0.5	>4	>4	<=0.5	>=8
Clindamycin	<=0.25	<=0.25	<=0.25	<=0.25	<=0.5	>=4
Ciprofloxacin	<=1	<=1	>2	>2	<=1	>=4
Tetracycline	<=1	<=1	>8	>8	<=4	>=16
Trimethoprim/Sulfamethoxazole	<=2/38	<=2/38	>4/76	>4/76	<=2/38	>4/76
Rifampicin	<=0.5	<=0.5	>2	<=0.5	<=1	>=4
Mupirocin	<=256	<=256	<=256	<=256	<=4	>=256
Daptomycin	<=1	<=1	<=1	<=1	<=1	_
Linezolid	2	2	2	2	<=4	>=8
Teicoplanin	<=1	<=1	<=1	<=1	<=8	>=32
Vancomycin	1	1	1	2	<=2	>=16
Fosfomycin*	<=32	<=32	<=32	<=32	<=32	>=32
Fusidic acid**	<=2	<=2	<=2	<=2	<=2	>=32

MIC_{50} - minimal inhibitory concentration needed to inhibit 50% organism growth

MIC_{90} - minimal inhibitory concentration needed to inhibit 90% organism growth

S - susceptible

R - resistant

*Based on European Committee on Antimicrobial Susceptibility Testing (EUCAST) guidelines.

**Based on Comite de Antibiogramme de la Societe Francaise de Microbiologie (CA-SFM, 2008).

For 2017, results for linezolid were missing for 3 isolates and results for vancomycin were missing for 1 isolate.

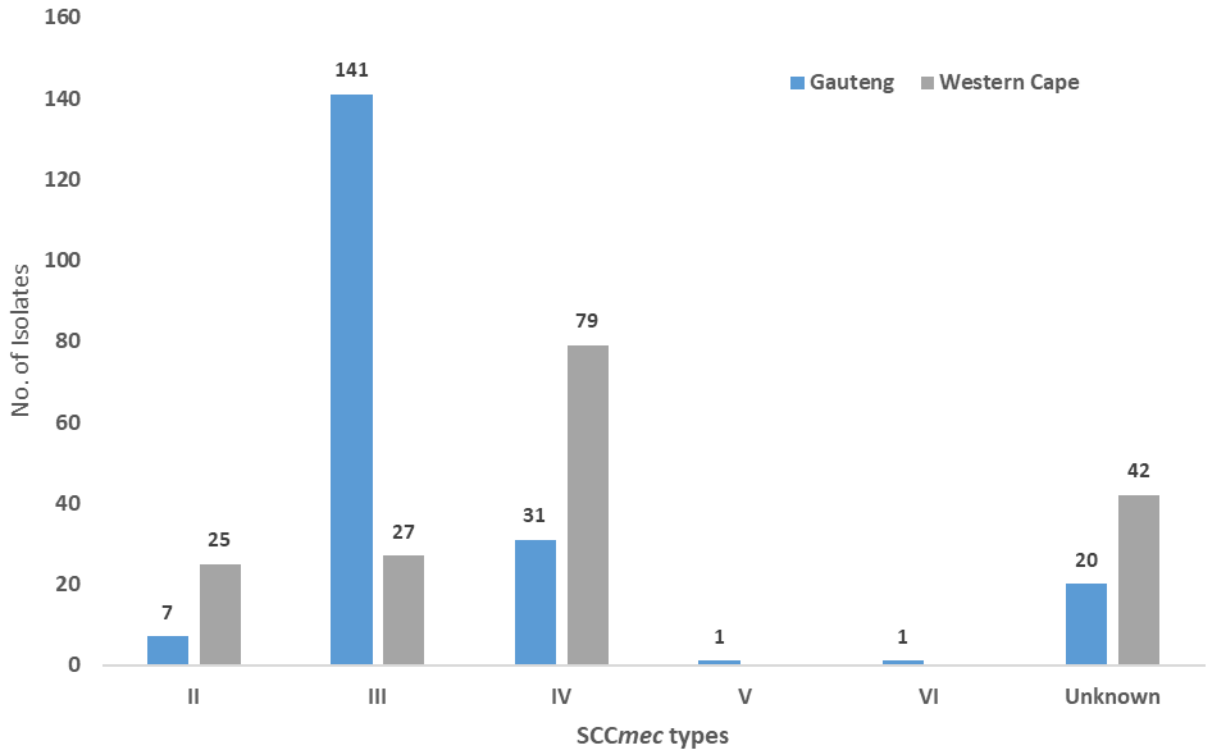

Figure 2. SCC*mec* type elements for 374 methicillin-resistant *Staphylococcus aureus* isolates by province, South Africa, 2016 and 2017.

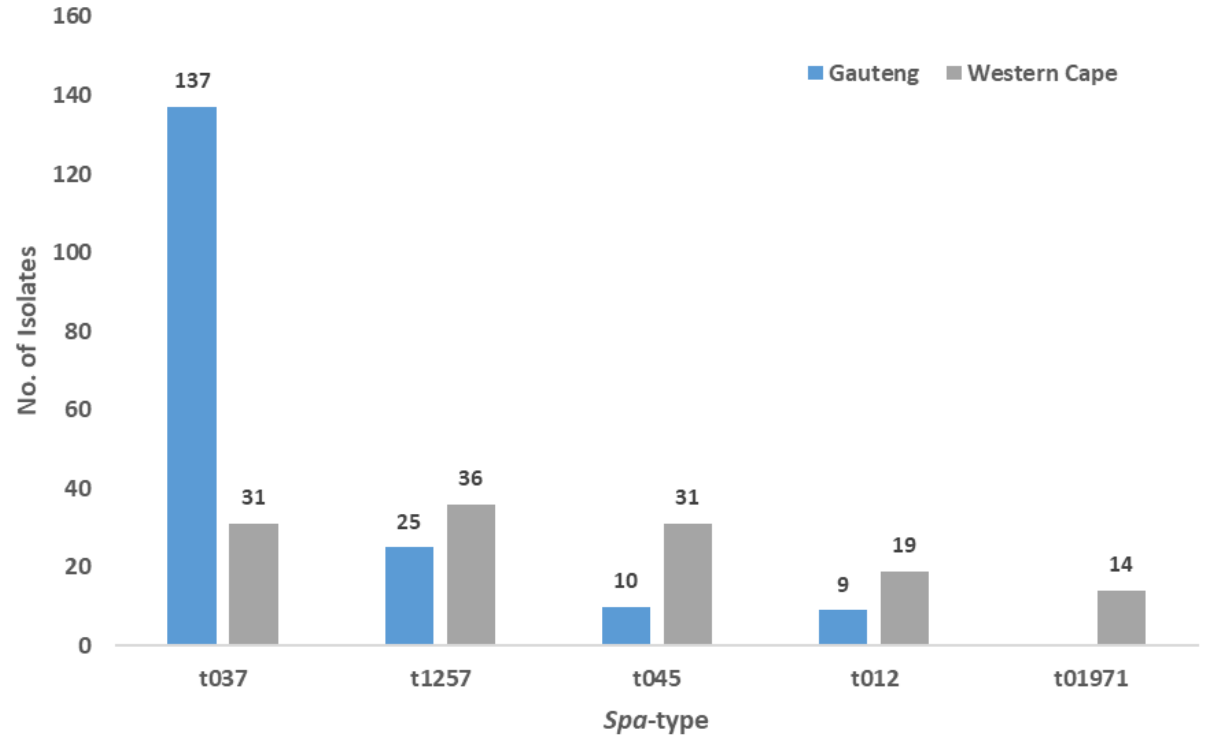

Figure 3. *Spa*-types for 312 methicillin-resistant *Staphylococcus aureus* isolates by province, South Africa, 2016 and 2017.

Discussion

This study investigated *S. aureus* isolates obtained over a 2-year surveillance study period. Overall resistance levels were low for all antimicrobial agents and the MIC_{50} and MIC_{90} were stable. The population structure of MRSA causing bacteraemia was described in 374 surveillance isolates using a combination of molecular typing methods and confirmed with *mec*A. Strains carrying *mecC* were not present. It should be noted that only human samples were included with no isolates from livestock, which has often been associated with *mecC*. The majority of the isolates were classified as SCC*mec* type III, most of which were from Gauteng Province. Based on conventions[6], it is speculated that the majority of the *S. aureus* bacteraemia infections are hospital-associated but epidemiological data are required to make this conclusion. The most common *spa*-type identified was t1037; this is consistent with previous findings from various studies in South Africa[2,15-17] and indicates that there has not been much evolution of circulating MRSA types. The majority of these were from Gauteng Province. It should be noted that most of the isolates were received from Gauteng. When considering the molecular results more variability was seen in isolates from Western Cape Province as compared to Gauteng Province, perhaps indicating a genetically diverse MRSA population in Western Cape Province and a more conserved MRSA population in Gauteng Province.

In conclusion, this report demonstrates the common and established circulating SCC*mec* element types and *spa*-types in two provinces. When compared to previous South African findings, these have not changed over the past eight years showing no evolution of MRSA clonal types.

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