NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

*Volume 15. Issue 2 - August 2017*

# PUBLIC HEALTH SURVEILLANCE BULLETIN

# FOREWORD

Measles is a leading cause of vaccine-preventable deaths in Africa. Measles incidence in South Africa in 2016 was sporadic and outbreak thresholds were not exceeded. A review of South Africa's vaccination strategy in light of incidence in 2016 and the measles elimination agenda for Africa is given in this issue, as is a review of lung cancer incidence trends and smoking prevalence in South Africa from 1997 to 2012. Although the overall incidence of lung cancer decreased in South Africa during this period, it increased amongst females congruent with an increase in smoking prevalence in this group.

Cases of paediatric haemolytic uraemic syndrome (HUS) are rare in South Africa. Four paediatric HUS cases occurred in the Western Cape Province in January and February 2017, triggering an outbreak investigation, the details of which are described in this issue.

Human papillomavirus (HPV) is the commonest sexually transmitted infection. The prevalence of HPV in a cohort of sexually-active young females enrolled from primary healthcare centres in four South African provinces during 2015 and 2016 is described in this issue, which also includes the 2016 GERMS South Africa report for invasive meningococcal, pneumococcal and *Haemophilus influenzae* disease. The epidemiology of these diseases and the impact of the pneumococcal and *H. influenzae* serotype b conjugate vaccines on invasive disease incidence in South Africa is described.

Lastly, this issue includes an update of incidence statistics for diseases and syndromes under surveillance in South Africa, covering the period January to December 2015 and 2016. In addition, readers may have noticed the Bulletin's name-change from Communicable Diseases Surveillance Bulletin to Public Health Surveillance Bulletin. This change reflects the broadened scope of the Bulletin to include contributions from the National Cancer Registry.
All contributors and reviewers are thanked for their inputs, and we trust you will find these reports useful and interesting.

Basil Brooke,
Editor

# GERMS-SA Annual surveillance report for laboratory-confirmed invasive meningococcal, pneumococcal and *Haemophilus influenzae* disease, South Africa, 2016

Susan Meiring[1], Jackie Kleynhans[2,3], Linda de Gouveia[3], Vanessa Quan[1], Penny Crowther-Gibson[1], Cheryl Cohen[3], Anne von Gottberg[3]

[1]Division of Public Health Surveillance and Response, National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg
[2]South African Field Epidemiology Training Programme, National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg
[3]Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg

## Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) in collaboration with the Group for Enteric, Respiratory, and Meningeal Disease Surveillance for South Africa (GERMS-SA) performs 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.

## Methods

Approximately 181 South African clinical microbiology laboratories participated in the GERMS-SA surveillance programme in 2016, including 26 enhanced surveillance sites (ESS). The population under surveillance in 2016 was estimated at 55.9 million.[1] Diagnostic laboratories reported case patients to the NICD 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 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 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 2015 and 2016 from Statistics South Africa.[1] 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.

## *Neisseria meningitidis*

*Results*

In 2016, a total of 131 cases of laboratory-confirmed meningococcal disease was identified by the surveillance system. Of these,10 (8%) were detected through audit and 63 (48%) viable isolates were received (Table 1). The overall disease incidence was slightly lower than 2015 (0.23 vs 0.28 cases per 100 000 population). The highest rates were reported in the Western Cape Province (0.86/100 000) and Gauteng Province (0.27/100 000), with increases seen in Western Cape, North West and Mpumalanga provinces since 2015. The number of cases reported was greatest from June to October (Figure 1). Cerebrospinal fluid (CSF) was the most common specimen (92/131, 70%) yielding meningococci (Table 2). Serogroup B was the predominant serogroup in South Africa in 2016 (47/113, 42%) (Table 3). Incidence of disease was greatest amongst children <5 years-of-age and peaked in the 15-24 year age group before tapering off in the older age categories. Age and serogroup-specific incidence rates show that infants had the highest incidence of disease for the three most common serogroups (Figure 2). Of the viable isolates tested for antimicrobial susceptibility, 11% (7/63) had penicillin minimum inhibitory concentrations (MICs) >0.06 µg/ml, and were considered non-susceptible. This penicillin non-susceptibility is similar compared with 2014 (13%, 11/85; p=0.7) and 2015 (9%, 7/80; p=0.7).

Only 43/131 (33%) cases were reported from enhanced sites and thus had additional clinical information. Cases were admitted for a median of 11 days (interquartile range [IQR]: 7-13). The case-fatality ratio was 12% (5/43) and all deaths occurred within 2 days of admission. Similar proportions of patients with meningitis (3/33, 9%) and bacteraemia (1/7, 14%) died (p=0.7). In 2016, fewer meningococcal cases with known HIV status were HIV infected, compared to 2015 (15%, 5/34 in 2016 vs 39%, 20/51 in 2015; p= 0.02). Besides HIV infection, only 1 other case reported an immunocompromising condition which could have predisposed them to this disease. In those who survived to discharge from hospital, 13% (5/38) suffered sequelae. These included 2 with new-onset seizures, 2 with neurological fallout and one with skin scarring from necrotic lesions.

*Discussion*

The incidence of meningococcal disease in South Africa remained low in 2016 and serogroup B disease predominated, similar to 2015.[2] Higher incidence of meningococcal disease in the Western Cape Province reflects the persistence of serogroup B, as well as a small increase in all other serogroups, in this province. The prevalence of penicillin non-susceptibility was 11%. However, high-dose penicillin is still recommended as the drug of choice for confirmed meningococcal disease. Meningococcal disease predominantly affects healthy, young persons, with a high case fatality ratio and high rate of sequelae.

## *Haemophilus influenzae*

*Results*

In 2016, 285 invasive *H. influenzae* cases were identified through the surveillance system. Eighty-six (30%) cases were detected through audit and 179 (63%) had either isolates or specimens available for serotyping. Serotype b (Hib) accounted for 25% (44/179) of cases and non-typeable (HNT) disease was found in 58% (104/179) (Table 4). Serotype b isolates were more likely to be isolated from CSF than non-typeable *H. influenzae* (17/44, 39% vs. 8/104, 8%; p<0.001) (Table 5). Although fewer isolates of serotypes a, c, d, e and f were cultured from CSF in 2016 compared with 2015, this decrease was not significant (14/33, 42% in 2015 vs. 7/31, 23% in 2016, p<0.11). In 2016, a total of 26 cases of Hib was reported amongst children <5 years (Figure 3). Since 2013, HNT disease is the most common serotype of *H. influenzae* causing invasive disease amongst children <5 years, with 37% (15/41) of cases in infants and 90% (9/10) of cases in neonates (Figure 4). Rates of Hib disease amongst children <1 year of age have decreased overall from 2010 to 2016 (p<0.001, chi-squared test for trend), with the increase in the incidence of Hib disease in infants from 1.08 cases per 100 000 in 2015 (13 cases) to 1.66 cases per 100 000 in 2016 (16 cases) not being statistically significant (Figure 5). Twenty-nine percent (8/28) of serotype b strains and 9% (6/69) of non-typeable strains were non-susceptible to ampicillin (MIC>1mg/L). Of the 44 Hib cases, 29 occurred in children <15 years old and Hib vaccination histories were available for 13 (45%) of these children. Only 4/13 (31%) children had received 2 or more doses of Hib vaccine prior to disease onset and were assessed as possible vaccine failures.

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

*Discussion*

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

***Streptococcus pneumoniae***

*Results*

The 7-valent polysaccharide-protein conjugate pneumococcal vaccine (PCV-7) was introduced into the Expanded Programme on Immunisation (EPI) in South Africa from 1 April 2009 and was replaced by PCV-13 from May/June 2011. In 2016, the incidence of reported invasive pneumococcal disease (IPD) varied by province, with the Western Cape and Gauteng provinces reporting the highest disease rates (9.6 cases per 100 000 population and 6.3 cases per 100 000 population, respectively) (Table 6). The highest incidence of disease in South Africa was in infants <1 year, although disease decreased significantly from 2009 ($p<0.001$ chi-squared test for trend) (Figure 6). The majority of cases (1379/2432, 57%) reported to GERMS-SA were diagnosed from positive blood-culture specimens (Table 7). Prevalence of penicillin non-susceptible (minimum inhibitory concentration [MIC] >0.06 µg/ml) strains varied widely by province, from 5% (2/37) of cases in the Northern Cape Province to 38% (11/29) of cases in the North West Province ($p=0.007$, Table 8). Penicillin non-susceptible isolates were most common amongst children 1-4 years (Figure 7). Ceftriaxone non-susceptibility (MIC >0.5µg/ml) was detected amongst 6% (87/1577) of all IPD cases with viable isolates – not significantly different from 2015 (4%, 69/1701). Amongst isolates from CSF specimens, 5% (24/464) were non-susceptible to ceftriaxone. The increase in incidence of IPD in children <5 years of age from 2015 (Figure 6), was not statistically significant and was due to a variety of serotypes (Figure 8). Serotype 8 was the most predominant serotype causing IPD in all age groups in 2016. PCV-13 serotypes that showed non-significant increases included serotypes 4, 14, 19F and 19A. Non-vaccine serotypes in children <5 years of age that showed increases were 6C and 35B. Disease due to serotype 35B increased from 16 in 2015 to 22 in 2016 ($p=0.4$), and 7 cases due to serotype 6C were identified in 2016, while none were seen in 2015 ($p=0.01$). In individuals older than 14 years, serotype 6C (n=17 in 2015 and n=33 in 2016) and serotype 8 (n=159 in 2015 and n=171 in 2016) showed the greatest increases. Twenty-three percent (54/233) of IPD amongst children <5 years was caused by serotypes present in PCV13 (Table 9). The number of isolates available for serotyping in this age group has decreased since 2009 (Figure 9).

Only 927/2432 (38%) of cases were reported from ESS where additional clinical information was collected. Cases were admitted for a median of 7 days (IQR: 2-13 days) and deaths usually occurred at a median of 2 days (IQR: 1-13 days) after admission. In older individuals (≥5 years), 27% (208/757) had underlying conditions - the most common were diabetes mellitus (40/757, 5%) and chronic lung, heart, renal or liver disorders (60/757, 8%). In children <5 years, underlying medical conditions were less common (11/170, 6%). However, 12% (21/170) had preceding prematurity. Of the 692 patients of known HIV status, 493 (71%) were HIV infected (283/493 [57%]; 25-44 years of age) and 197/493 (40%) were using antiretroviral therapy. In children <5 years (n=170), only 124 (73%) children older than 6 weeks had known vaccination status, and of these only 62% (n=77) had received the appropriate number of PCV vaccine doses for age at time of admission.

***Discussion***

Overall IPD incidence continued to decrease in South Africa in 2016. IPD incidence was highest in children <1 year with a further peak seen in adults 25 years and older. HIV infection is still an important risk factor for IPD with 71% of IPD cases co-infected with HIV. Sixty-two percent of IPD cases in children <5 years were vaccinated appropriately with PCV. Clinicians are encouraged to check PCV vaccination histories and ensure that appropriate catch-up doses are given. The proportion of viable pneumococcal isolates received from children <5 years has decreased from 76% to 58% since the vaccine was introduced in 2009. Clinicians are urged to continue taking relevant specimens when pneumococcal disease is suspected and laboratorians should to refer all pneumococci isolated from normally sterile-site specimens so that the ongoing trends in IPD serotypes can be monitored.

## References


1. Statistics South Africa. Mid-year population estimates, South Africa, 2016. STATS-SA 2016.
2. GERMS-SA. Annual report. Johannesburg: National Institute for Communicable Diseases, 2015. Available from: http://www.nicd.ac.za/assets/files/2015%20GERMS-SA%20AR.pdf.

**Table 1.** Numbers of cases and incidence rates of meningococcal disease reported to GERMS-SA by province, South Africa, 2015 and 2016, n=287 (including audit cases).

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

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

**Table 2.** Numbers and percentages of cases of meningococcal disease reported to GERMS-SA by specimen type, South Africa, 2015 and 2016, n=287.

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

**Table 3.** Numbers of cases of invasive meningococcal disease reported to GERMS-SA by serogroup and province, South Africa, 2016, n=131*.

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

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

**Table 4.** Numbers of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by serotype and province, South Africa, 2016, n=285*.

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

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

**Table 5.** Numbers and percentages of cases of invasive *Haemophilus influenzae* disease reported to GERMS-SA by specimen type, South Africa, 2016, n=285.

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

**Table 6.** Numbers of cases and incidence rates of invasive pneumococcal disease reported to GERMS-SA by province, South Africa, 2015 and 2016, n=5070 (including audit cases).

| Province | 2015 | | 2016 | |
|---|---|---|---|---|
| | n | Incidence rate* | n | Incidence rate* |
| Eastern Cape | 232 | 3.35 | 208 | 2.95 |
| Free State | 131 | 4.65 | 147 | 5.14 |
| Gauteng | 970 | 7.35 | 854 | 6.33 |
| KwaZulu-Natal | 354 | 3.24 | 320 | 2.89 |
| Limpopo | 99 | 1.73 | 84 | 1.45 |
| Mpumalanga | 86 | 2.01 | 102 | 2.36 |
| Northern Cape | 27 | 2.28 | 42 | 3.52 |
| North West | 108 | 2.91 | 73 | 1.93 |
| Western Cape | 631 | 10.18 | 602 | 9.57 |
| **South Africa** | **2638** | **4.80** | **2432** | **4.35** |

*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, 2015 and 2016, n=5070.

| Site of specimen | 2015 | | 2016 | |
|---|---|---|---|---|
| | n | % | n | % |
| Cerebrospinal fluid | 980 | 37 | 859 | 35 |
| Blood | 1395 | 53 | 1379 | 57 |
| Other | 263 | 10 | 194 | 8 |
| **Total** | **2638** | | **2432** | |

**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, 2016, n=2432.

| Province | Isolate not available | Susceptible* | | Intermediate* | | Resistant* | |
|---|---|---|---|---|---|---|---|
| | n | n | % | n | % | n | % |
| Eastern Cape | 93 | 86 | 74 | 22 | 19 | 8 | 7 |
| Free State | 41 | 78 | 74 | 26 | 25 | 2 | 2 |
| Gauteng | 340 | 356 | 71 | 109 | 22 | 34 | 7 |
| KwaZulu-Natal | 183 | 98 | 72 | 32 | 23 | 7 | 5 |
| Limpopo | 36 | 39 | 72 | 13 | 24 | 2 | 4 |
| Mpumalanga | 36 | 49 | 72 | 19 | 28 | 0 | 0 |
| Northern Cape | 7 | 35 | 95 | 2 | 5 | 0 | 0 |
| North West | 50 | 18 | 62 | 9 | 31 | 2 | 7 |
| Western Cape | 69 | 398 | 75 | 106 | 20 | 27 | 5 |
| **South Africa** | **855** | **1157** | **73** | **338** | **21** | **82** | **5** |

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

**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, 2016, n=401 (n=233 with viable isolates).

| Province | Total isolates available for serotyping | 7-valent serotypes* | | Serotype 6A# | | 10-valent serotypes** | | 13-valent serotypes*** | |
|---|---|---|---|---|---|---|---|---|---|
| | | n | % | n | % | n | % | n | % |
| Eastern Cape | 11 | 2 | 18 | 0 | 0 | 2 | 18 | 4 | 36 |
| Free State | 14 | 1 | 7 | 0 | 0 | 1 | 7 | 3 | 21 |
| Gauteng | 105 | 14 | 13 | 2 | 2 | 15 | 14 | 22 | 21 |
| KwaZulu-Natal | 17 | 1 | 6 | 0 | 0 | 1 | 6 | 1 | 6 |
| Limpopo | 9 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 22 |
| Mpumalanga | 7 | 1 | 14 | 0 | 0 | 1 | 14 | 1 | 14 |
| Northern Cape | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 33 |
| North West | 4 | 1 | 25 | 0 | 0 | 2 | 50 | 2 | 50 |
| Western Cape | 63 | 10 | 16 | 0 | 0 | 10 | 16 | 18 | 29 |
| **South Africa** | **233** | **30** | **13** | **2** | **1** | **32** | **14** | **54** | **23** |

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

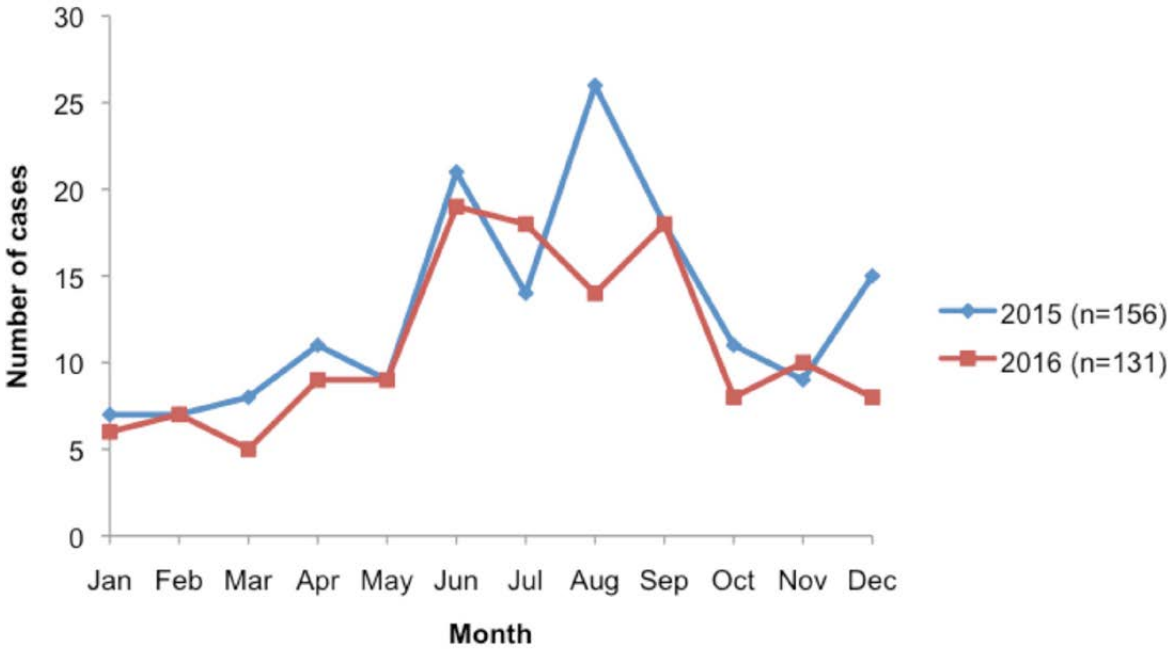
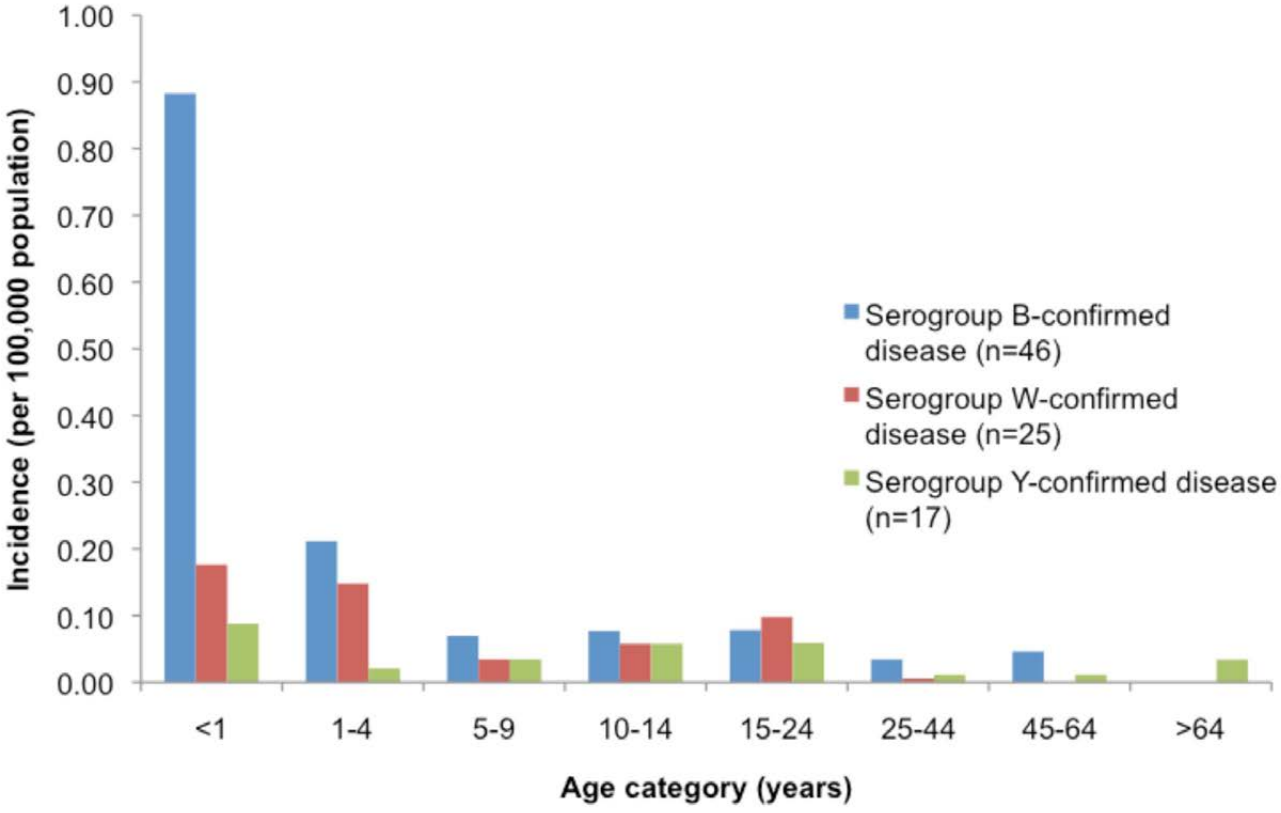



**Figure 1.** Numbers of laboratory-confirmed, invasive, meningococcal cases, reported to GERMS-SA, by month and year, South Africa, 2015-2016, n=287.

**Figure 2.** Age-specific incidence rates* for laboratory-confirmed, invasive, meningococcal cases, by serogroup B, W and Y, South Africa, 2016, n=131 (age unknown for n=7; specimens or viable isolates unavailable for serogrouping n=18).




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

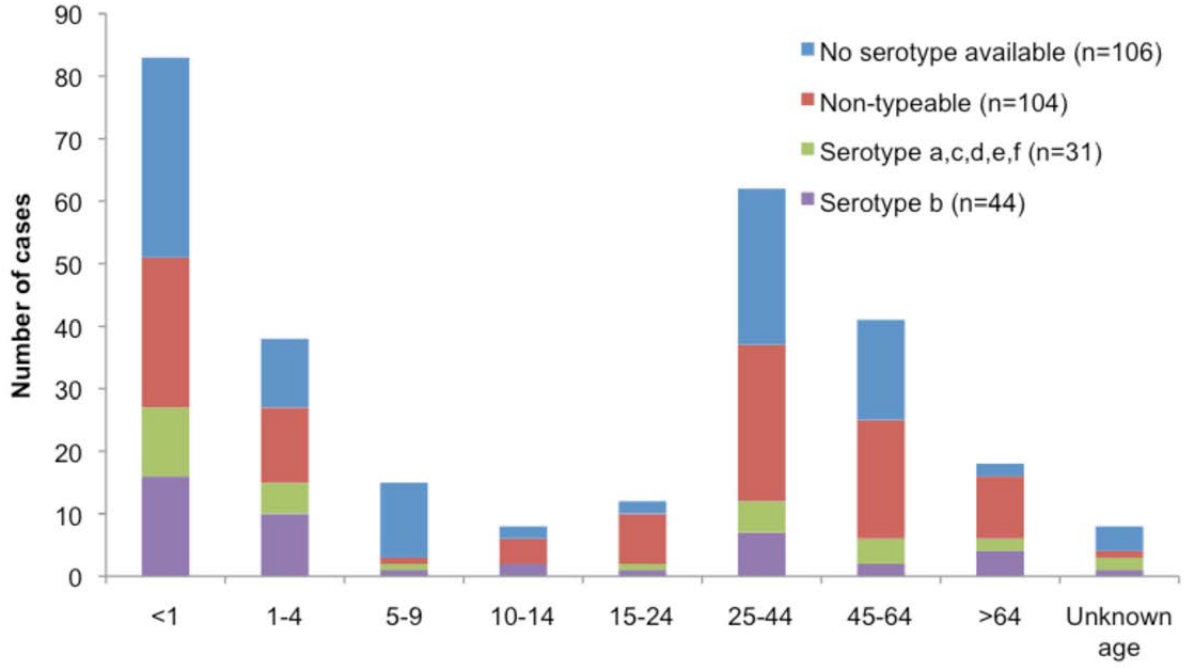
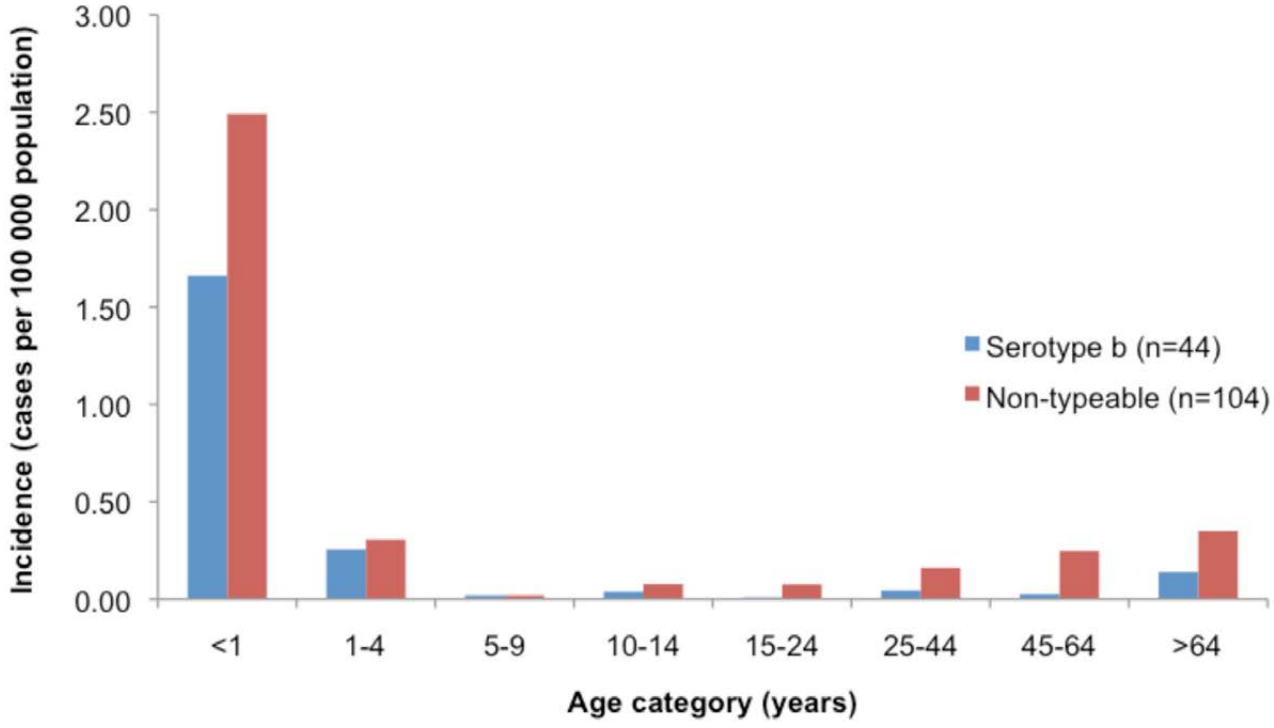


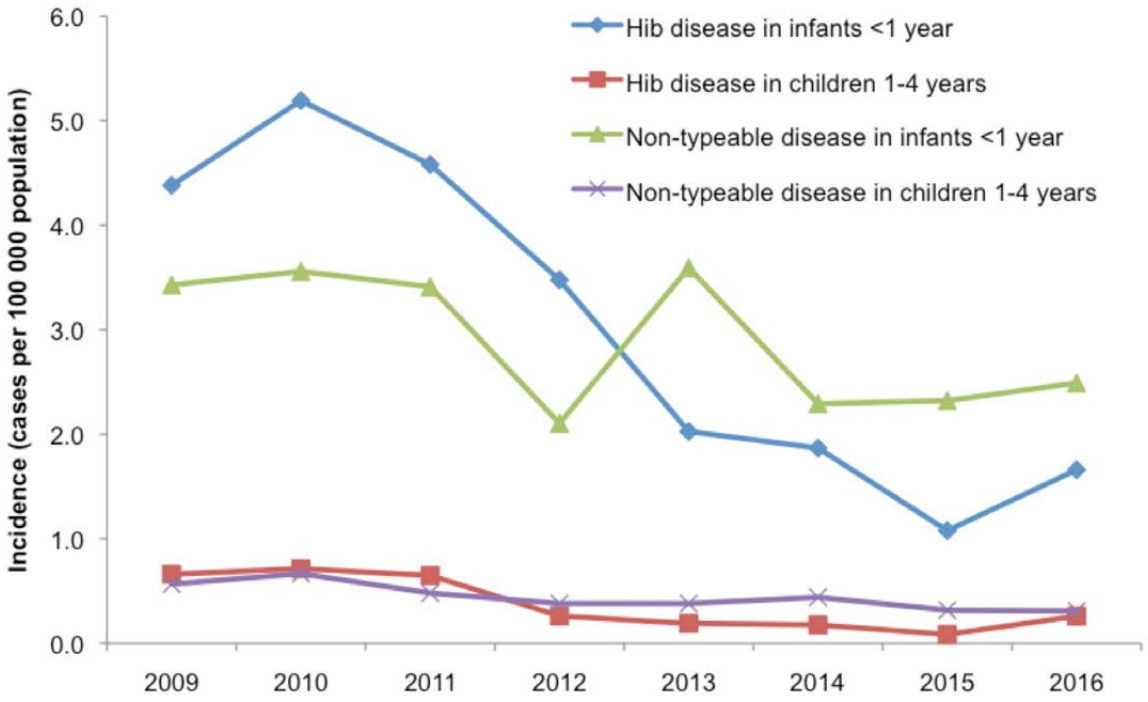

**Figure 3.** Numbers of laboratory-confirmed, invasive, *Haemophilus influenzae* cases, reported to GERMS-SA, by serotype and age group, South Africa, 2016, n=285 (age unknown for n=8; specimens or viable isolates unavailable for serotyping for n=106).

**Figure 4.** Age-specific incidence rates* for laboratory-confirmed, invasive *Haemophilus influenzae* disease, reported to GERMS-SA, by serotype b and non-typeable, South Africa, 2016, n=285 (age unknown, n=8; viable isolates unavailable for serotyping, n=106; other serotypes from cases with known age, n=31).



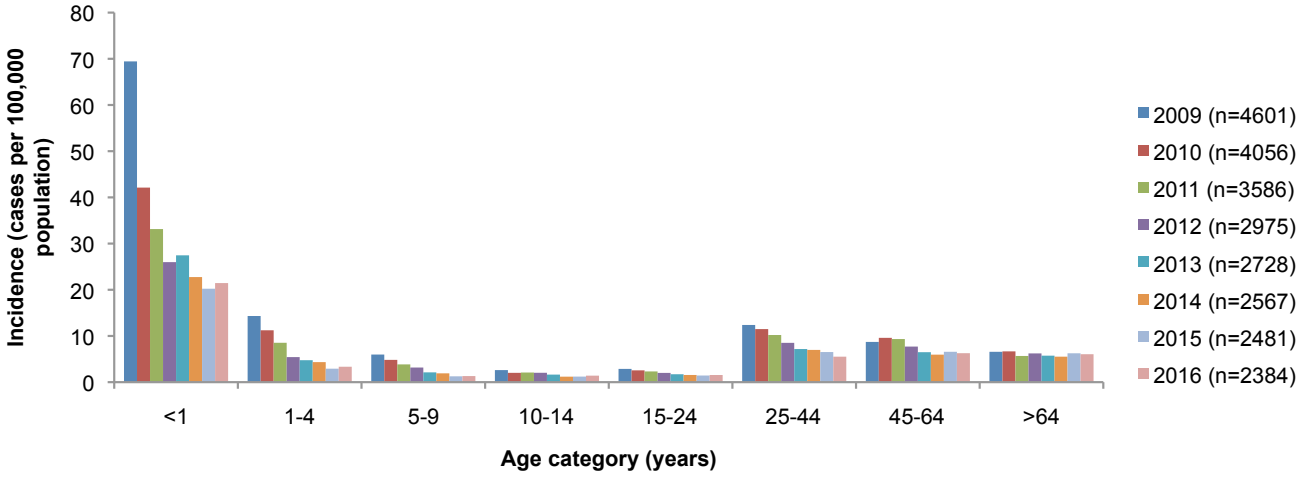

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

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



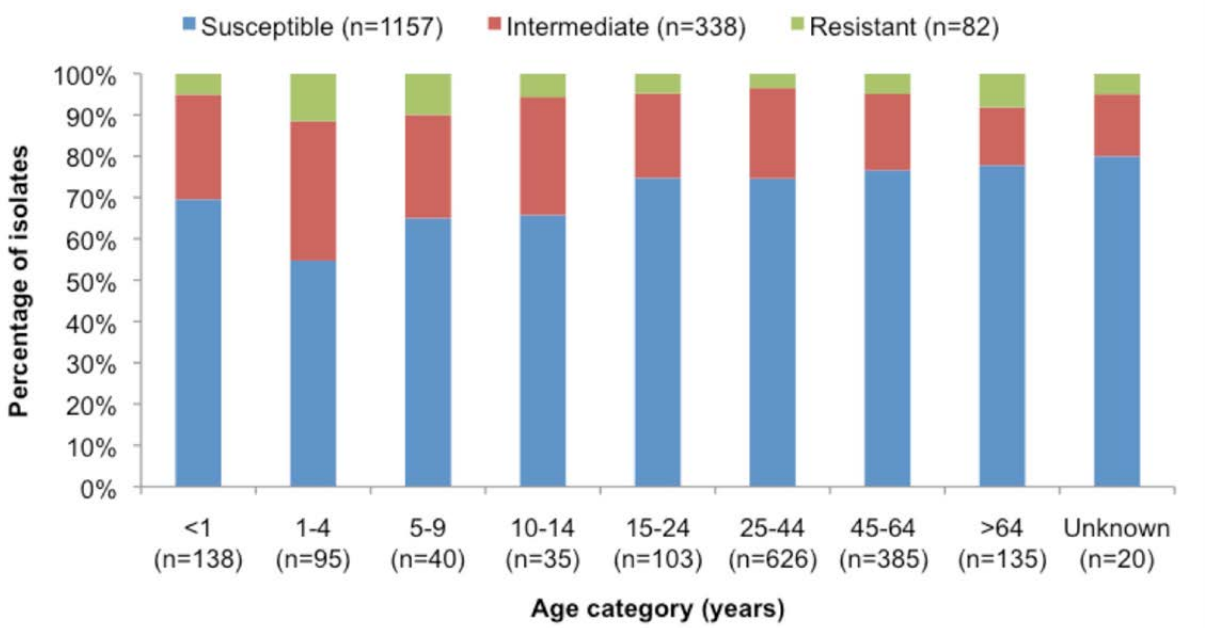

*Incidence rates were calculated based on population denominators provided by Statistics South Africa, and are expressed as cases per 100,000 population.

**Figure 6.** Age-specific incidence rates* for laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, South Africa, 2009 through 2016.



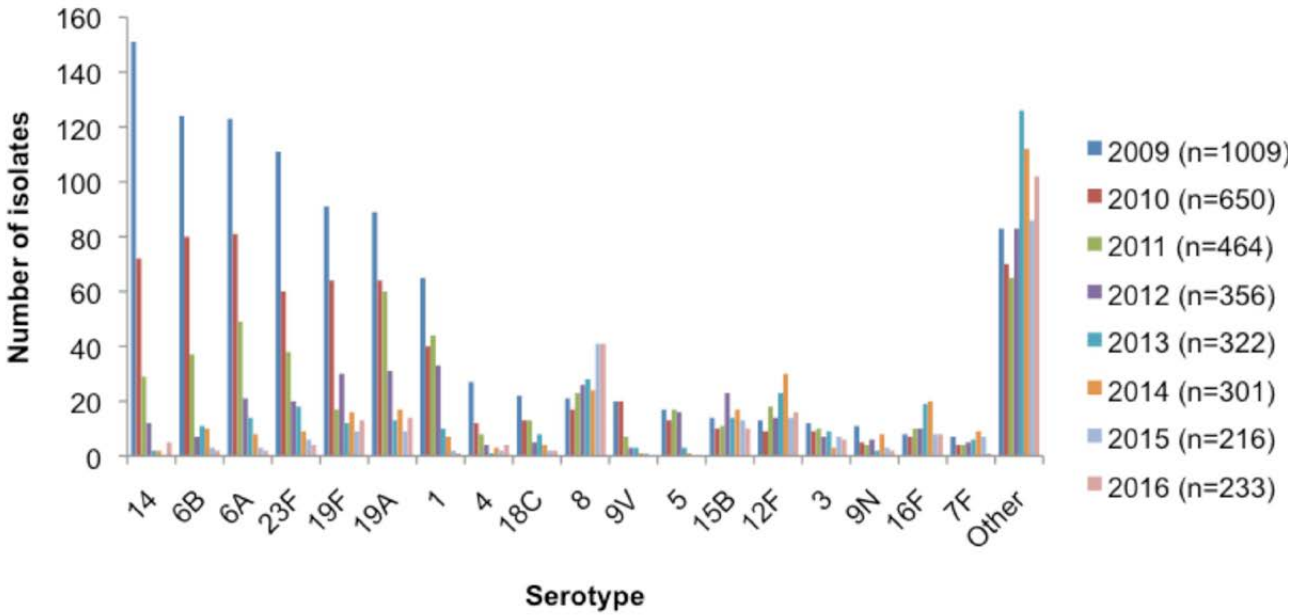

2009: N=4 762, age unknown for n=161; 2010: N=4 197, age unknown for n=141; 2011: N=3 804, age unknown for n=218; 2012: N=3 223, age unknown for n=248; 2013: N=2 866, age unknown for n=138; 2014: N=2 732, age unknown for n=165; 2015: N=2 638, age unknown for n=157; 2016: N=2 432, age unknown for n=48.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

**Figure 7.** Numbers of laboratory-confirmed, invasive pneumococcal disease cases, reported to GERMS-SA, by age group and penicillin susceptibility, South Africa, 2016, n=2,432 (n=1,577 with viable isolates).




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

**Figure 8.** Commonest pneumoccocal serotypes causing laboratory-confirmed, invasive pneumococcal disease, reported to GERMS-SA, in children <5 years, South Africa, 2009-2016.




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.

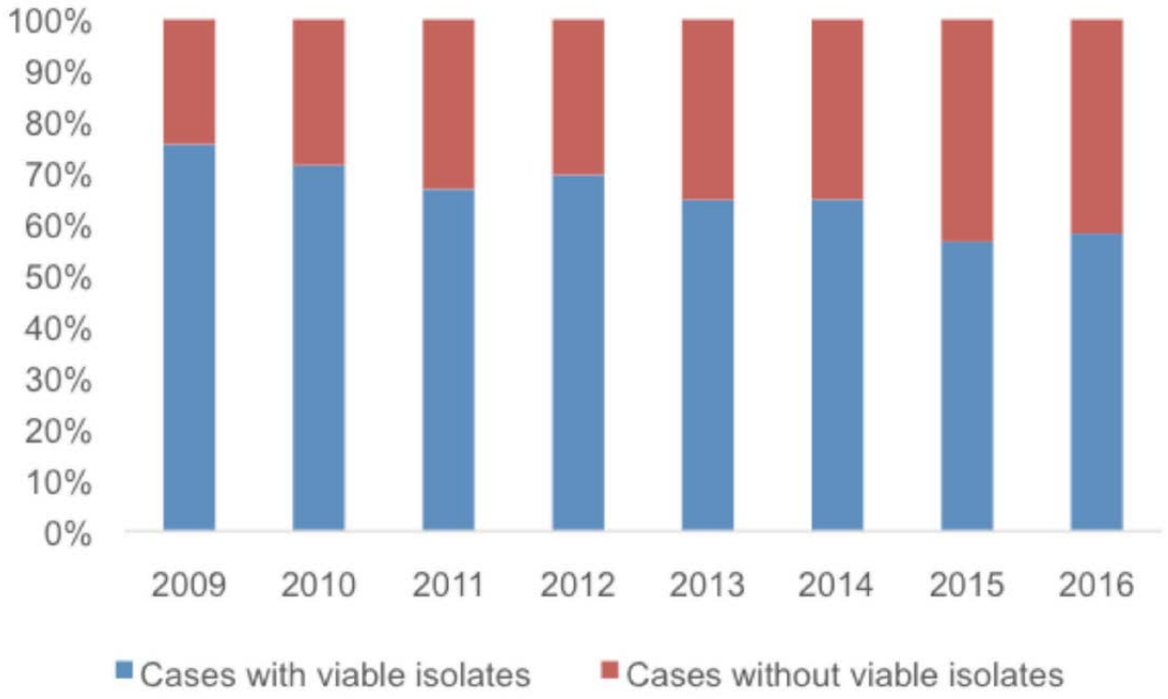



**Figure 9.** Percentage invasive pneumococcal disease cases with viable isolates reported to GERMS-SA, in children <5 years, South Africa, 2009-2016.

# Outbreak report: cluster of haemolytic uraemic syndrome cases among children, Western Cape Province, South Africa, February 2017

Jackie Kleynhans,[1,2] Bosco Kalule,[3] Charlene Lawrence,[4] Mignon McCulloch,[5] Ashton Coetzee,[5] Peter Nourse,[5] Kerrigan McCarthy[6] and Karen Keddy[7]

[1]Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, National Health Laboratory Service
[2]South African Field Epidemiology Training Programme, National Institute for Communicable Diseases, National Health Laboratory Service
[3]Faculty of Health Sciences, University of Cape Town
[4]Communicable Disease Control, Western Cape Department of Health
[5]Paediatric Nephrology Department, Red Cross Children's Hospital, University of Cape Town
[6]Division of Public Health, Surveillance and Response, National Institute for Communicable Diseases, National Health Laboratory Service
[7]Centre for Enteric Diseases Bacteriology, National Institute for Communicable Diseases, National Health Laboratory Service

## Executive summary

The Western Cape Province typically identifies one case of paediatric haemolytic uraemic syndrome (HUS) annually (M. McCulloch, *personal communication*). Four cases of HUS in the Western Cape Province were identified between 31 January and 13 February 2017, triggering an outbreak investigation. All cases were female aged between eight months and five and a half years. Three of the four cases resided in Cape Town; the fourth resided on a farm outside Ceres, but had visited Cape Town prior to symptom onset. All cases initially presented with abdominal cramps, vomiting and diarrhoea, progressing to HUS 3 – 5 days after initial symptom onset. Laboratory culture of a stool specimen from one case led to the isolation of *Escherichia coli* serotype O26:H11, and the presence of the Shiga toxin 2 gene ($stx_2$) was confirmed on polymerase chain reaction (PCR). $Stx_2$ was confirmed on PCR on a stool specimen from a second case, but no pathogen was cultured. Cases were exposed to multiple possible transmission vehicles, including dried beef meat products (biltong and droëwors), fruits, and vegetables. Food samples were collected but no causative organism could be isolated from them. By the end of the investigation all cases had recovered and were discharged from hospital. They will, however, need close long-term follow-up to check for progression to renal failure or recurrence of HUS.

## Background

A clinician at Red Cross War Memorial Children's Hospital (RXCH) contacted the Western Cape provincial health team reporting four cases of haemolytic uraemic syndrome (HUS) between 31 January – 13 February 2017. Cases of HUS are rarely seen, and it was unusual to see four cases in one month. The cases all presented to private hospitals, were all females and were between the ages of eight months and five and a half years. All cases were discussed with the paediatric renal team at RXCH and three, two of whom needed renal dialysis, were admitted to RXCH.

Treating physicians suspected biltong and droëwors as the possible vehicles of transmission. Stool and urine samples collected were negative for campylobacter, salmonella, shigella, cryptosporidium, rotavirus and adenovirus. There were no family histories suggesting evidence of genetic or atypical HUS.

Haemolytic uraemic syndrome manifests as a triad of microangiopathic haemolytic anaemia, thrombocytopenia and acute renal failure. It typically follows diarrhoea and is frequently caused by Shiga toxin-producing *Escherichia coli* (STEC), serotype O157:H7.[1] However, in recent years, more non-O157 STEC have been reported in STEC outbreaks. The main virulence factors for Shiga toxin-producing *E. coli* are $stx_1$ and $stx_2$. In South Africa, *E. coli* serotypes O4, O5, O21, O26, O84, and O111 were found to contain the genes that code for Shiga toxin ($stx_1$ and $stx_2$), although it is not known if these types have a causal relationship with HUS.[2]

The incubation period after ingestion of STEC is 1 – 12 days and symptoms can be similar to infection with other enteric pathogens,[1] making diagnosis difficult without the collection of clinical specimens. Clinical manifestations can range from mild, watery diarrhoea to bloody diarrhoea (dysentery), and in some cases can lead to HUS as a complication, and even death.[1] Other symptoms may include abdominal pain, vomiting and fever.[1] Approximately 70% of cases infected with STEC serotype O157 present with bloody diarrhoea[1] and only approximately 14% of cases develop HUS.[1] The identification of HUS cases may therefore point to a larger, unrecognised outbreak of STEC. Studies have shown that children under five years are at greater risk for developing HUS.[3]

The digestive tracts of cattle and other ruminants are the main reservoirs for STEC and outbreaks have been associated with the consumption of undercooked minced meat, and also dried meats, unpasteurized milk, apple cider, fruits, vegetables and contaminated water.[3] The organism can also be spread directly between individuals.[3] The aetiological agent and vehicle of transmission for HUS may remain unidentified in many cases and outbreaks.

The aim of this investigation was to confirm the number of cases, review hospital medical records of the cases, identify the aetiological agent and to investigate possible sources of the infection.

## Methods

The tertiary institution that admitted three of the cases and the private hospital where the other case was admitted, were visited in order to review the medical records and to collect clinical data. Parents were interviewed, using a standardised case investigation form, to collect data on symptoms, travel, contact histories and other exposures.

A stool specimen from the first case was collected during the investigation and stool specimens from the last two cases from prior to the investigation were available. Western Cape Province environmental health practitioners collected food specimens from various retail and commercial outlets from which the cases had consumed food prior to the onset of symptoms. Stool and food samples were tested at the clinical microbiology laboratory, Faculty of Health Sciences, University of Cape Town. Samples underwent an enrichment step before detection of *stx* genes or identification as *E. coli* by real-time PCR. Isolates found to carry *stx* genes were serotyped at the Centre for Enteric Diseases, NICD. O-antigen serotype was determined by employing antisera from Statens Serum Institute (Copenhagen, Denmark) and H-antigen serotype was determined by whole genome sequencing (WGS).

## Results

All cases were female and aged less than 6 years (Table 1). The onset of symptoms and hospital admission dates of the four cases are shown in Figure 1. Case residential and day-care/school locations showed a broad distribution across Western Cape Province. Case 1, 2 and 4 resided in Cape Town, while case 3 resided in Ceres. Case 3 and her family visited Cape Town a week prior to the onset of symptoms. Case 4 was visiting a holiday home near George at the time of symptom onset. As no cases of dysentery were recorded in the day-care/schools attended by the patients these institutions were not visited during the investigation.

All cases experienced abdominal cramps, vomiting and diarrhoea (two bloody, two non-bloody). Only one case did not present with fever (Table 2). Based on family reports, only cases 3 and 4 received antibiotic treatment upon initial presentation at their general practitioners during the diarrhoeal episodes, and no use of antimotility medication was reported or identified from medical record review. Parents could not recall the name of antibiotic prescribed and this information was not included in the hospital medical records. All 4 cases recovered and were discharged from hospital by the end of the investigation.

No significant animal contact was reported in any of the cases. Three of the four cases were exposed to dried meat products. Case 1 consumed biltong over the course of the week prior to symptom onset. Case 3 (age 8 months) was just starting to consume solid foods when symptoms presented. The only food consumed, besides formula and baby porridge, was droëwors (dried sausage), three and four days before symptom onset, and a mixture of rice, pumpkin and mince prepared by caregivers in the four days prior to symptom onset. These foods were not consumed by anyone other than the case. When symptoms

initially started they were thought to be due to teething; the same was thought for case 4. Case 4 consumed biltong two days before showing symptoms, but the same product was consumed by a contact (2 years old) who did not present with any symptoms. Case 1, 2 and 4 regularly consumed fruits. Although some foodstuffs consumed are similar between cases, these were all purchased from different stores and restaurants. The exact amount consumed was not investigated. No *stx* genes could be detected in any of the food samples collected.

Shiga toxin-producing *Escherichia coli* serotype O26:H11 was isolated from case 4, and the organism contained the following genes: *hlyA, stx*$_2$ and *eae*. The *stx*$_2$ gene was also detected on polymerase chain reaction in the stool from case 1 but STEC could not be cultured.

***Discussion***

Investigators were unable to definitively identify the aetiological agent responsible for this cluster of HUS cases. It was confirmed that Shiga toxin 2 (*stx*$_2$) produced by *Escherichia coli* O26:H11 was responsible for the HUS experienced by case 4 and that case 1 potentially had a similar exposure, as the *stx*$_2$ gene was identified in her stool.

In South Africa, serotype O26 has been identified in enteric disease surveillance,[2] and has also been detected in uncooked beef products.[4] Serotype O26 is one of the most frequently non-O157 STEC serotypes reported in Europe and the United States,[1] and STEC O26:H11 has been associated with outbreaks and implicated as a cause of HUS in children.[1,5] In an outbreak in Denmark fermented beef sausage was the source of infection.[5] Similar to this investigation, STEC O26:H11 has been associated with both bloody and non-bloody diarrhoea.[1] A study comparing O157 and non-O157 found that disease caused by O26 is more likely to progress to HUS than disease caused by O157.[1]

This organism could not be linked to the other cases due to the absence of laboratory specimens and strong epidemiological connections. The inability to culture STEC from the specimen from case 3 is most likely due to the commencement of antibiotic treatment one day prior to sample collection. Although the *stx*$_2$ gene was detected in case 1, the sample was collected 3 weeks after the episode, which likely limited possible detection of the organism. The lack of adequate specimens limited the investigation and thus concrete interventions could not be implemented. HUS is not a notifiable medical condition in South Africa, although nationally notifiable in other countries like Australia and USA. If the condition was notifiable, the Western Cape Department of Health would have been able to investigate sooner, and could possibly have enabled identification of the source of infection so as to prevent additional cases.

Although dried meat products were suspected by initial treating physicians to be the vehicle of transmission, laboratory results could not confirm this. Some of the actual foods consumed by case 3 (rice, pumpkin and beef minced meat mix, frozen after preparation) and case 4 (frozen biltong) were tested and all were negative for STEC. For the other cases, corresponding foodstuffs were sampled days/weeks after purchase and consumption. These food samples may have come from different batches and were unlikely to contain the culprit contaminant.

No strong epidemiological links could be established between the four cases, although it was not confirmed whether all suspected foods consumed had been delivered to the respective retail outlets from a centralised distribution point. Since infection with STEC does not always lead to HUS or severe diarrhoea that warrants medical care, it is also possible that there could have been a much larger STEC outbreak that occurred in the area that was not detected by this investigation. Lastly, it is also possible that these cases may have been sporadic with no epidemiological link despite the unusual clustering in time and place.

Although all four cases recovered fully and were discharged from hospital by the end of the investigation, they will need close long-term follow-up of blood pressure and urinalysis to check for the possibility of progression to renal failure or recurrence of HUS, which would suggest an atypical/genetic form.

**Recommendations**

- It is important that stool specimens are collected from cases presenting with severe diarrhoea before the administration of any antibiotics.
- Haemolytic uraemic syndrome (HUS) should be made a notifiable medical condition in South Africa.

**Authors' note**

Since the finalization of this report, whole genome sequencing was performed on a DNA extract of the stool specimen for case 1, from which $stx_2$ was identified, but STEC could not be cultured. This new analysis identified STEC O26:H11 in the stool, with identical molecular characteristics as the STEC isolate cultured from case 4. This confirms this was in fact an outbreak of STEC O26:H11 (two cases related in time and place), and not just a cluster of HUS cases.

**Acknowledgements**

Staff of the Provincial Department of Health CDC office and the Eastern Health Sub-District (Heinrich Fritz, Phillip Bosman), Cape Winelands District Municipality (Hein Boock, Theresa Davids) and Western District Maitland (Landile Bele) environmental health practitioner officers, are thanked for the collection of the food samples. Thanks also to the case families for their willingness to assist in the investigation.

## References

1. Johnson KE, Thorpe CM, Sears CL. The emerging clinical importance of non-O157 shiga toxin-producing *Escherichia coli*. Clin. Infect. Dis. 2006;43(12):1587-95.
2. Smith AM, Tau NP, Sooka A, Keddy KH, Group for Enteric Respiratory Meningeal Disease Surveillance in South Africa. Surveillance for enterohaemorrhagic *Escherichia coli* associated with human diarrhoea in South Africa, 2006–2009. J. Med. Microbiol. 2011;60(5):681-3.
3. Pennington H. *Escherichia coli* O157. The Lancet. 2010;376(9750):1428-35.
4. Charimba G, Hugo C, Hugo A. The incidence of diarrhoeagenic *Escherichia coli* in minced beef and boerewors. Food Res. Int. 2012;47(2):353-8.
5. Ethelberg S, Smith B, Torpdahl M, Lisby M, Boel J, Jensen T, et al. Outbreak of non-O157 shiga toxin-producing *Escherichia coli* infection from consumption of beef sausage. Clin. Infect. Dis. 2009;48(8):e78-e81.

**Table 1.** Summary of a cluster of paediatric haemolytic uraemic syndrome (HUS) cases and possible sources of aetiological exposures, Western Cape Province, South Africa, 31 January - 13 February 2017.

| Case | Sex | Age | Location | Hospital presented to | Possible exposures |
|---|---|---|---|---|---|
| 1 | F | 5y5m | Pinelands | Vincent Palotti | Biltong, fruit, pizza, chicken nuggets prepared at home |
| 2 | F | 4y1m | Milnerton | Blaauwberg Netcare | Burger, fruit, ham |
| 3 | F | 8m8d | Ceres | Worcester Mediclinic | Droëwors and a rice, pumpkin, mince mix |
| 4 | F | 2y2m | Brackenfell | Panorama | Biltong, pizza, seafood from restaurant, chicken nuggets bought prepared from store, fruit, multiple restaurant meals |

**Table 2.** Summary of major signs and symptoms experienced by a cluster of paediatric haemolytic uraemic syndrome (HUS) cases, Western Cape Province, South Africa, 31 January - 13 February 2017.

| | Non-bloody diarrhoea | Bloody diarrhoea | Vomiting | Bloody vomitus | Fever | Abdominal cramps | Loss of appetite | Muscle pain | Lethargy | Pallor | Jaundice | Rash | Low urine output | Haemolytic uraemic syndrome |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | + | - | + | + | + | + | + | + | + | + | - | - | + | + |
| 2 | - | + | + | - | + | + | + | - | + | + | - | + | - | + |
| 3 | - | + | + | - | + | + | | - | + | + | + | + | - | + |
| 4 | + | - | + | - | - | + | + | - | + | + | - | - | + | + |

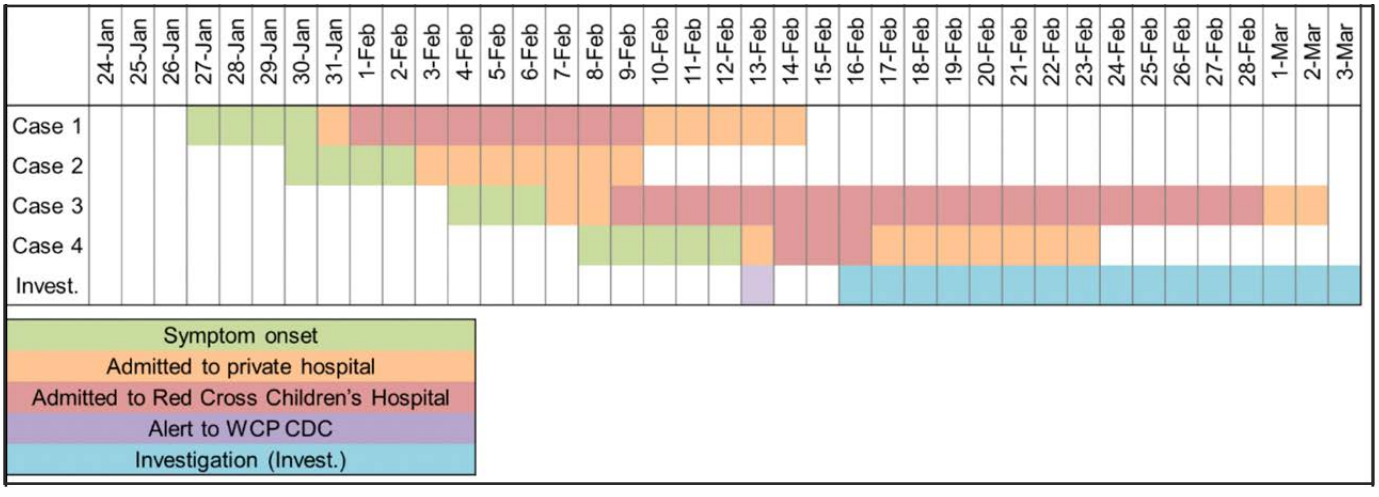



**Figure 1.** Dates of symptom onset and admission to private and public tertiary hospitals of four paediatric haemolytic uraemic syndrome cases in Western Cape Province, South Africa, February 2017. Alert indicates the time at which the National Institute for Communicable Diseases was informed of the cases.

# Annual measles and rubella surveillance review, South Africa, 2016

Nkengafac Villyen Motaze[1,2], Phindile Mabaso[3], Jack Manamela[1], Sheilagh Smit[1], Tshepo Motsamai[1], Melinda Suchard[1,4]

[1]Centre for Vaccines and Immunology, National Institute for Communicable Diseases, National Health Laboratory Service
[2]Department of Global Health, Faculty of Medicine and Health Sciences, Stellenbosch University
[3]Expanded Programme on Immunization, National Department of Health, Pretoria
[4]School of Pathology, Faculty of Health Sciences, University of the Witwatersrand

## Executive summary

Measles is a driver of mortality in under-five children globally and is a leading cause of vaccine-preventable deaths in Africa. This disease is targeted for elimination in the African region by 2020. The public vaccination schedule in South Africa includes measles vaccines at ages 6 and 12 months. Rubella (German measles) vaccination is not currently part of the expanded programme on immunisation in South Africa. The National Institute for Communicable Diseases tests for measles and rubella using sera from suspected measles cases in South Africa. Additionally, a sentinel site surveillance programme collects data on laboratory-confirmed congenital rubella syndrome cases. During 2016, there were 17 confirmed measles cases in South Africa, 817 circulating rubella cases diagnosed at NICD and eight laboratory-confirmed cases of congenital rubella syndrome diagnosed by sentinel site surveillance. All of South Africa's provinces met the target of identifying and collecting specimens from at least 2 suspected rash cases per 100 000 population. Measles incidence was sporadic and outbreak thresholds were not exceeded. The incidence of laboratory-confirmed measles was 0.31 per 1 000 000 for 2016 nationally, which is substantially below the pre-elimination target for measles incidence of <5 per million population, according to the World Health Organization's global measles and rubella strategic plan, 2012-2020.

## Background

Measles and rubella (German measles) are communicable viral diseases that are mainly transmitted through droplets expelled into the air from the respiratory tract of an infected individual. Clinically, measles presents as 'flu-like symptoms with fever, coryza, cough and conjunctivitis. This is followed by a generalised maculopapular rash, which is usually the indicator symptom for suspicion of infection. Measles complications include pneumonia, blindness, encephalitis and dehydration, resulting in high morbidity and mortality, especially in children. A late, fatal complication is subacute sclerosing panencephalitis, which can occur decades after measles infection. Rubella also presents with 'flu-like symptoms that are generally milder than measles. However, congenital rubella syndrome, a teratogenic, often fatal infection, can occur in early pregnancy.

Measles and rubella are vaccine-preventable diseases. Two doses of measles vaccine have been included in the Expanded Programme on Immunization (EPI) in South Africa since 1995. Since January 2016, the first dose is administered at 6 months and the second at one year of age. Rubella-containing vaccines (RCV) are not currently included in the EPI in South Africa but are available in the private health sector.[1]

The WHO African Region aims to eliminate measles by 2020, despite frequent outbreaks.[2] The last large outbreak in South Africa was in 2009-2010 with over 18,000 laboratory-confirmed cases.[3] A smaller outbreak occurred in December 2014 – January 2015 in Northern Cape Province with 31 laboratory-confirmed measles cases. A suspected measles outbreak is defined as the occurrence of five or more suspected cases per 100,000 population in a given geographic area and a confirmed measles outbreak is defined as 3 or more laboratory-confirmed cases in a district within a one month period.[4] The total number of laboratory-confirmed measles cases in South Africa was 68 in 2014 and only 15 in 2015.

There is no target set for rubella elimination in Africa. Rubella is endemic in South Africa and most people become immune during childhood through natural infection. Introduction of RCV into routine vaccination schedules is only recommended by WHO once measles vaccine coverage reaches 95%.[5]

## Methods

Measles surveillance in South Africa consists of identification of suspected measles cases by health care providers, followed by collection of blood for laboratory confirmation. A suspected case is defined as an individual in whom a clinician suspects measles, or a patient with fever and maculopapular rash and either cough, runny nose (coryza) or red eyes (conjunctivitis). Additionally, laboratory test requests received by the National Health Laboratory Service for measles (NHLS) are incorporated into the database of suspected cases. All NHLS laboratories refer measles and rubella immunoglobulin M (IgM) test requests to the Centre for Vaccines and Immunology, NICD. Case definitions used are targeted towards measles but laboratory testing is performed for both measles and rubella. Bi-monthly situational report (SITREP) meetings are held, with representation from the NICD, NDoH and WHO, for purposes of case classification (Table 1).

**Table 1.** Classification system for laboratory-confirmed measles cases, South Africa.

| Classification | Comments |
|---|---|
| **Interim Classification** | |
| **1. IgM+ve measles** | |
| IgM+ve measles, unclassified | |
| IgM+ve measles, vaccine associated | Within 30 days of vaccination of case |
| IgM+ve measles, presumed wild-type | |
| **2. PCR+ve measles** | |
| PCR+ve measles, wild-type strain | |
| PCR+ve measles, vaccine strain | |
| PCR+ve measles, unclassified | Awaiting genotype or unable to genotype |
| **3. Compatible measles case** | |
| **4. Confirmed measles case, epidemiologically-linked** | Onset of both cases within 30 days of each other |
| Final classification | |
| **1. Discarded** | IgM negative or vaccine-associated |
| **2. Compatible measles case** | Not epidemiologically linked, no blood specimen |
| **3. Confirmed measles cases** | IgM+ve or PCR+ve or epidemiologically linked |

IgM: Immunoglobulin M; PCR: polymerase chain reaction; +ve: positive. Vaccine-associated cases are those occurring within 30 days of vaccination. Vaccine virus may cause a mild, non-transmissible 'flu-like illness with rash. The rash and positive IgM response are indication of the vaccine generating a strong immune response and the condition is relevant only as a cause of false-positive IgM results.

## Results & Discussion

*Circulating Measles*

From 1 January to 31 December 2016, 2822 serum samples were tested at NICD, yielding 35 (1.2%) measles IgM-positive cases from eight provinces. There was an increase in number of samples tested as well the number of positive measles and rubella IgM results (Figure 1). Seventeen were classified as confirmed measles cases and individuals above 15 years of age were most affected, with slightly more females than males (Figure 3). There were 17 discarded cases and one case was denotified. An alert was issued in September 2016 when an increase in the number of measles IgM-positive cases was noticed between July and September. However, the threshold of 3 cases within one district within one month was not exceeded and no clusters were

identified. The confirmed measles case rate for South Africa for 2016 was 0.31 per million (Table 2), which is within the pre-elimination target set by WHO.[2]

The number of samples received for testing increased during the last months of the year. This coincided with an increase in the number of rubella cases, which suggests a seasonal pattern that has been previously observed in a 13-year time series of rubella in South Africa. There is currently no similar time series for measles in South Africa but previous outbreaks indicate a seasonal pattern. There is no genotyping available for measles samples from 2016.

*Circulating rubella*

Of the suspected measles cases, 817 (28.8%) tested positive for rubella IgM, most of whom were from Gauteng Province and aged between two and nine years (Figures 3 & 4). There were 11 cases aged under one year and 25 cases aged 15 years and above. These figures likely reflect a reporting bias based on suspicion for suspected measles cases. There was a similar distribution of cases between males and females. No information regarding pregnancy is currently recorded on case investigation forms. Gauteng Province recorded the highest number of rubella cases and Free State Province had the lowest number of cases. There is no genotyping information available for rubella cases from 2016.

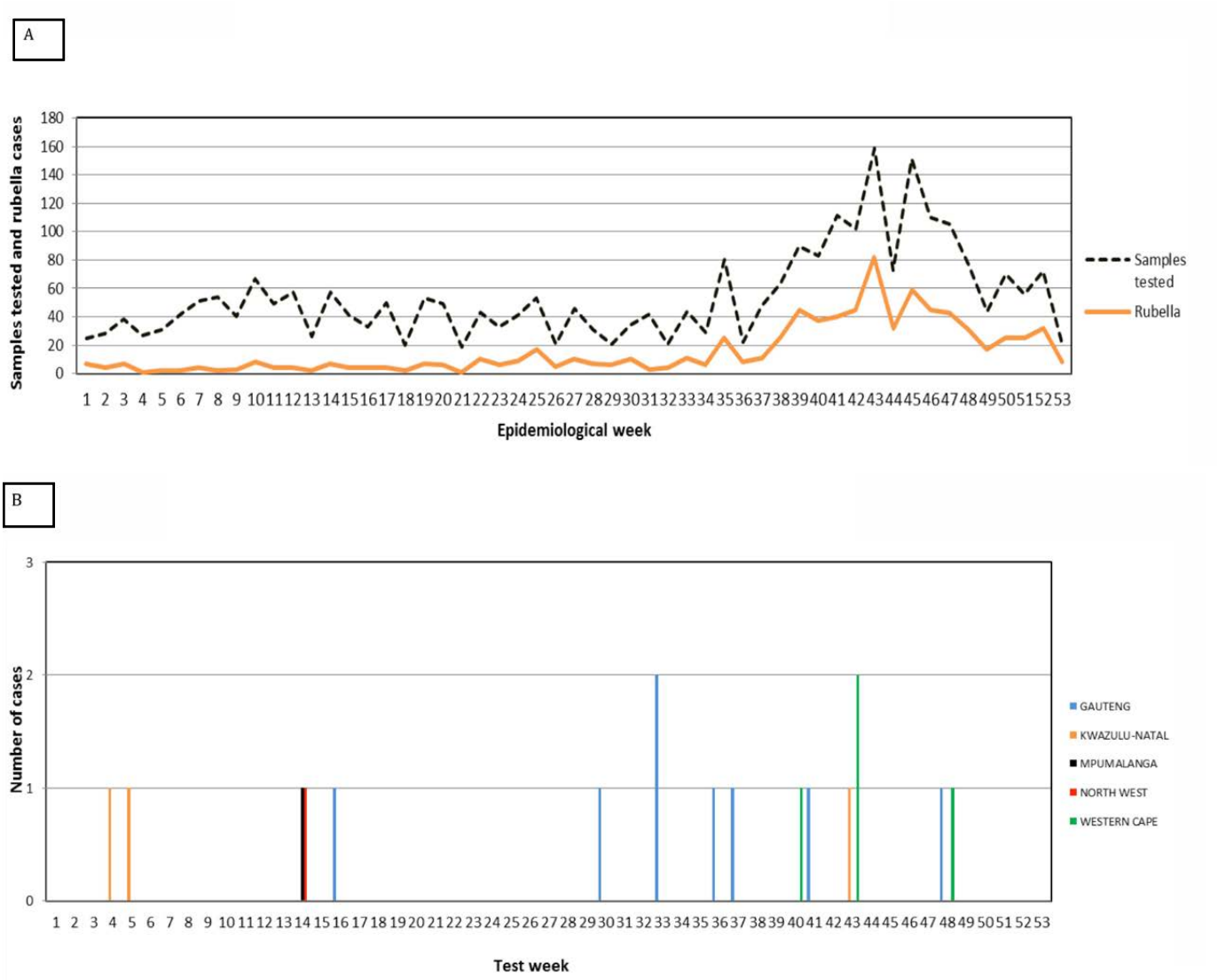



**Figure 1.** Suspected measles cases 1 January – 31 December 2016, South Africa. **A**: Seasonal pattern of suspected measles cases from rash-based surveillance tested at NICD (n=2822), corresponding with seasonal patterns in number of confirmed rubella cases (n=817 rubella IgM positive). **B**: Epidemiological curve of confirmed measles cases for the same period (n=17), showing provincial distribution.

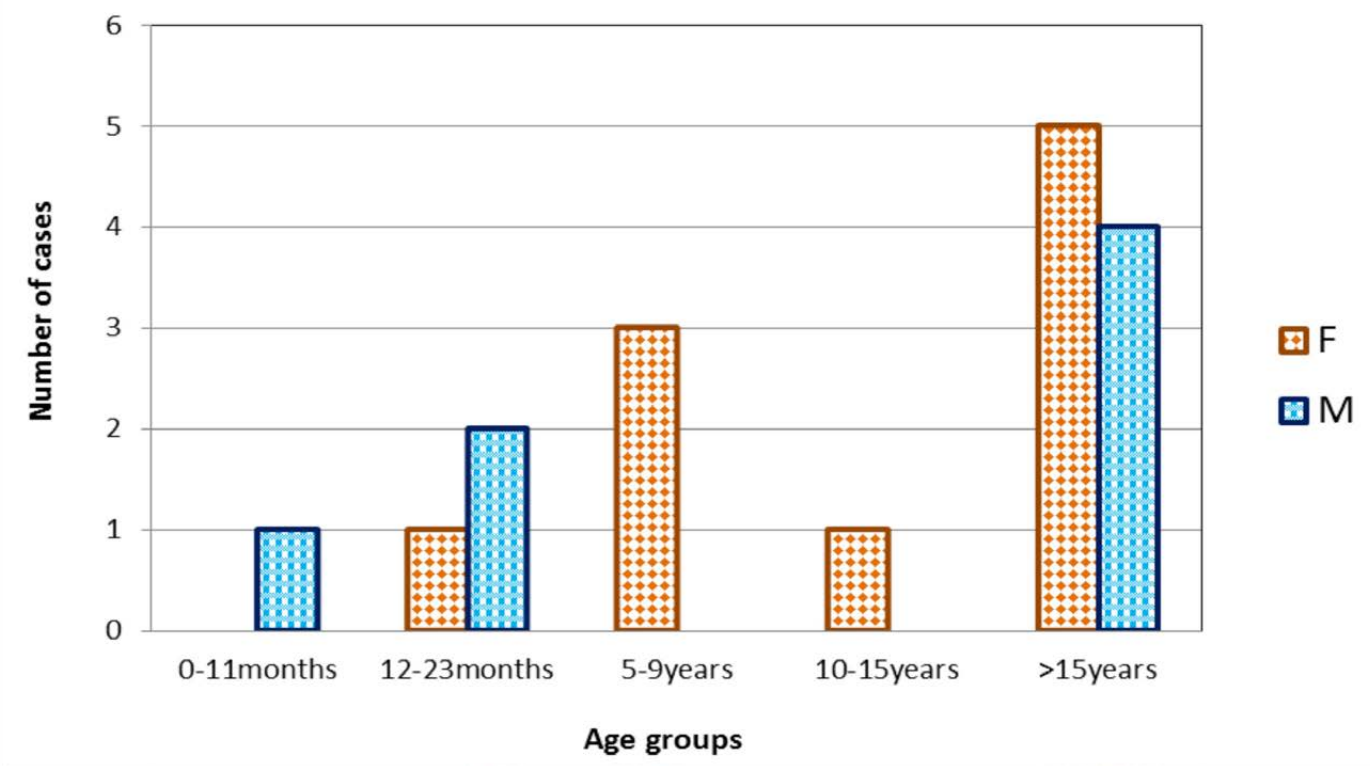



**Figure 2.** Age and gender of confirmed measles cases, 1 January – 31 December, 2016, South Africa (n=17, females=10 and males=7).

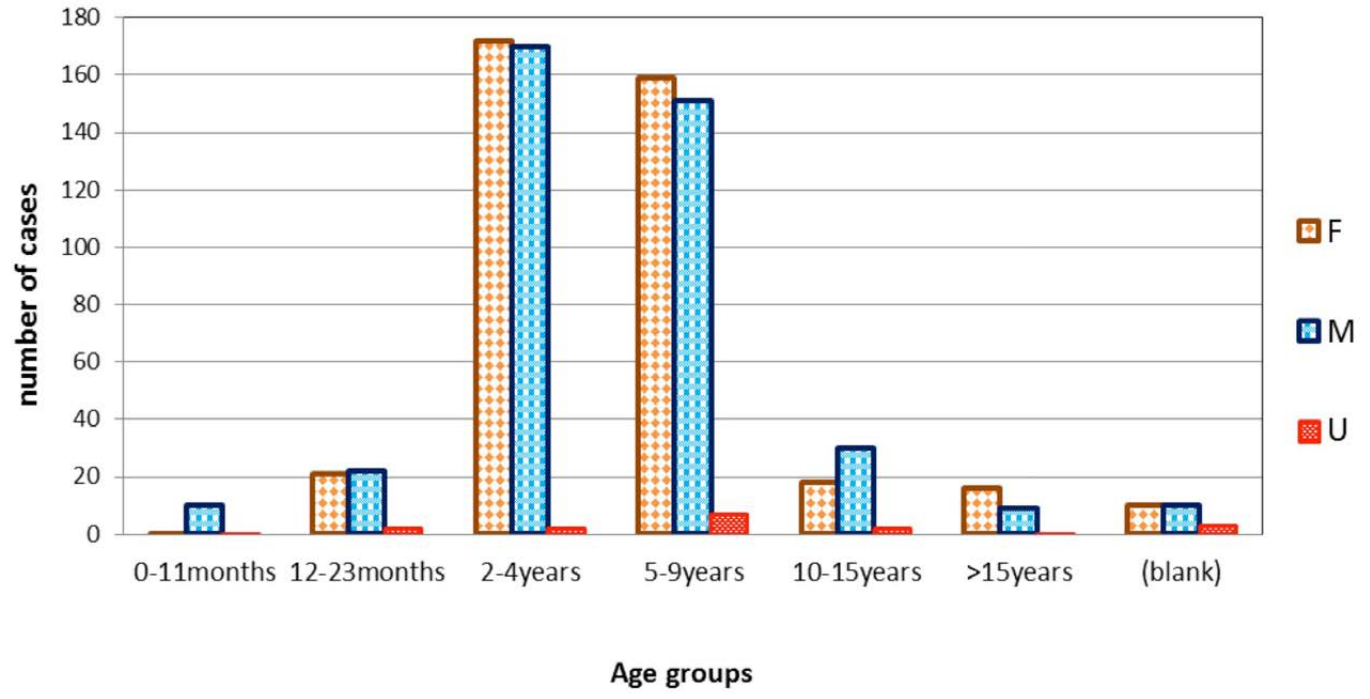



**Figure 3.** Age and gender of laboratory-confirmed rubella cases, 1 January – 31 December, 2016, South Africa, (n= 817, females=397 and males=402, unknown age=18).

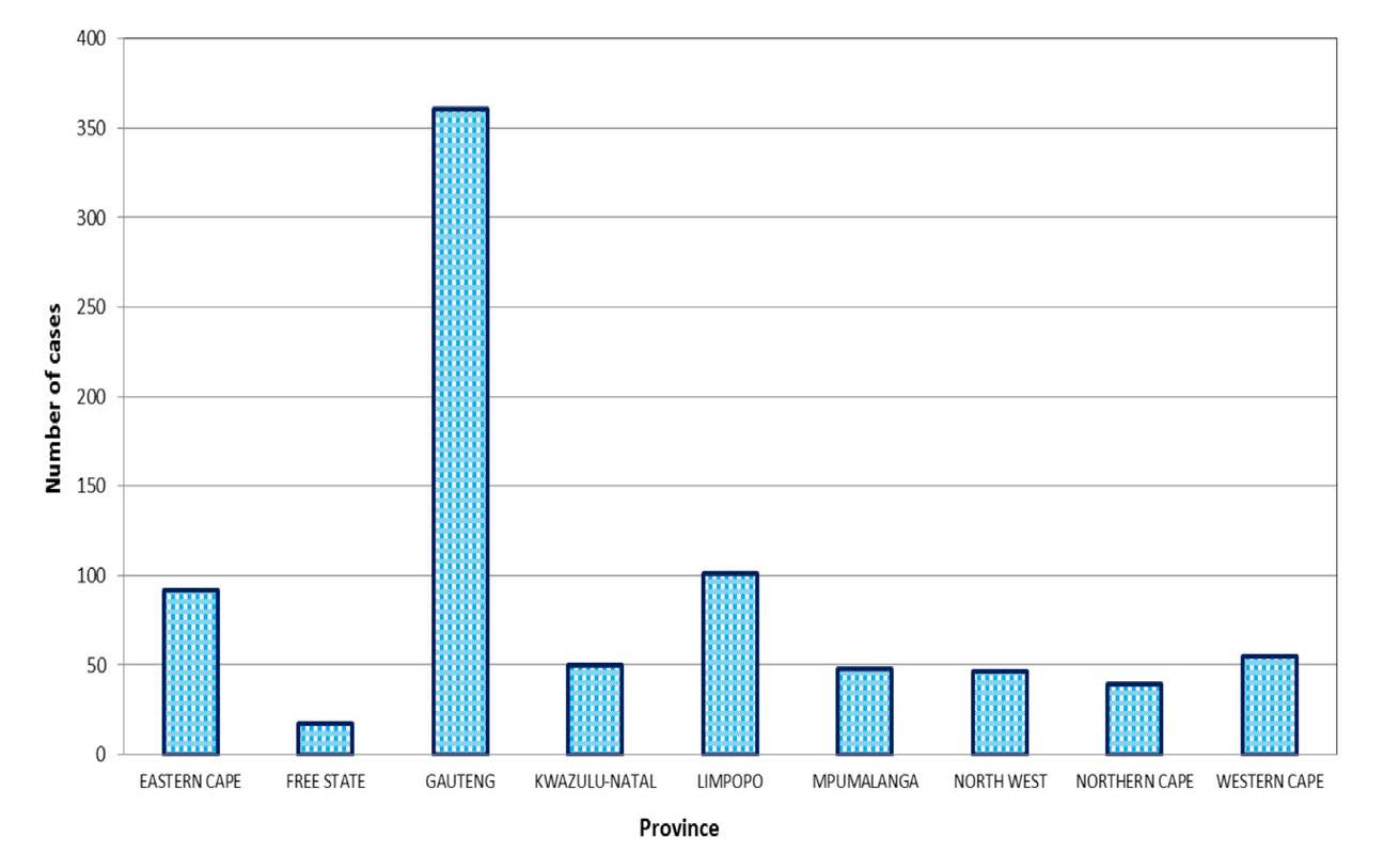



**Figure 4.** Provincial distribution of laboratory-confirmed rubella cases, 1 January – 31 December, 2016, South Africa.

***Congenital rubella syndrome surveillance***

The Centre for Vaccines and Immunology established a sentinel site surveillance program for congenital rubella syndrome (CRS) in 2015. The aim is to obtain baseline data on the burden of CRS in South Arica prior to the introduction of the rubella vaccine in the national Expanded Program for Immunisation and to monitor the impact of the vaccine thereafter. 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. This case definition was adapted from that used by the Centers for Disease Control (CDC).

There were 28 clinical sites and 6 laboratory sites involved in the surveillance program. Tertiary referral hospitals in major cities of each province were selected as study sites and the pediatricians, neonatologists or pediatric infectious disease specialists at these hospitals were invited to be focal persons. Participating laboratories were the National Health Laboratory Service (NHLS) virology departments at participating hospitals. The laboratories reported any positive rubella serology or molecular tests in patients aged 12 months or less. The clinicians who requested the tests were contacted in order to verify cases of confirmed CRS and to complete the case investigation form (CIF).

During the period 1 January – 31 December, 2016, there were eight laboratory-confirmed CRS cases from six sentinel sites. Maternal age ranged from 14 to 38 years (median, 21 years). The commonest birth defects were congenital heart disease, cataracts and microcephaly.

## Surveillance Adequacy Indicators

***Field surveillance indicators for suspected rash cases***

All provinces exceeded the target of 2/100 000 for detection of non-measles, febrile, rash-based illness cases (Table 2). The City of Johannesburg Metro (446) and City of Tshwane Metro (317) provided the highest number of samples.

**Table 2.** Field surveillance adequacy and confirmed measles case rate by province, January – December 2016, South Africa.

| 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 | 304 | 0 | 6 731 182 | 4.52 | 0 |
| FSP | 68 | 0 | 2 768 642 | 2.46 | 0 |
| GAP | 1081 | 9 | 13 543 183 | 7.98 | 0.7 |
| KZN | 265 | 3 | 10 806 536 | 2.45 | 0.28 |
| LMP | 271 | 0 | 5 724 444 | 4.73 | 0.00 |
| MPP | 262 | 1 | 4 290 009 | 6.11 | 0.23 |
| NWP | 181 | 1 | 3 757 770 | 4.82 | 0.27 |
| NCP | 138 | 0 | 1 191 997 | 11.58 | 0.00 |
| WCP | 246 | 3 | 6 362 256 | 3.87 | 0.47 |
| **Total SA** | **2816** | **17** | **55 176 019** | **5.10** | **0.31** |

Figures supplied by National Department of Health. Target for non-measles, febrile, rash illness rate is more than 2 per 100 000. All provinces exceeded the target. Pre-elimination target for confirmed measles cases is less than 5 cases per million population. Denominators from DHIS 2016 midyear estimates projected by Statistics SA based on 2011 census. ECP= Eastern Cape Province, FSP = Free State Province, GAP = Gauteng Province, KZN = KwaZulu-Natal Province, LMP = Limpopo Province, MPP = Mpumalanga Province, NWP = North West Province, NCP = Northern Cape Province, WCP = Western Cape Province, SA = South Africa.

***Laboratory surveillance indicators for suspected rash cases***

a. 91% of results were reported within seven days of receipt in the laboratory, exceeding the target of 80%.
b. Only 1938/2857 (68%) samples were received within 3 days, indicating logistic difficulties with sample transport to referral laboratory.
c. NICD does not require serum samples to be received on ice as live virus is not isolated. Sample transport on ice is usually recommended by WHO.
d. Percentage of samples accompanied by case investigation forms - for measles IgM-positive cases: 57% (20/35) prior to follow-up; 77% (27/35) after follow-up with district and provincial health departments.

***Congenital rubella syndrome surveillance response rate***

The proportion of responses to monthly e-mails obtained from focal clinicians, (including monthly zero reporting), varied between clinicians and ranged from 0% to 100% for this period, with a median of 30%.

## Regional reference laboratory function

The Centre for Vaccines and Immunology, NICD, serves as a regional reference laboratory for measles and rubella for the World Health Organization African Region. For the period January – December 2016, the laboratory performed quality assurance testing for 408 serum samples from other national labs from the southern block of African countries. Using NICD results as a gold standard, discordance for measles IgM was 0.25% and for rubella IgM was 2.6%.

## Conclusion

In 2016 all nine of South Africa's provinces met the target for identifying and collecting specimens from suspected measles cases. The national confirmed measles case rate was 0.31 per million, which is within the pre-elimination target set by WHO.


## Acknowledgements

The contributions of Thobile Johnson and Thulasiswe Buthelezi from the National Department of Health are acknowledged.


## References


1. Motaze NV, Suchard M, Cohen C, Baker L, Blumberg L, (eds). *Vaccine Information for Parents & Caregivers*. Johannesburg: Ideas Wise and Wonderful for National Institute for Communicable Diseases; 2016 [cited 2017 Apr 10]. Available from: http://nicd.ac.za/assets/files/NICD%20Vaccine%20Booklet%20D132%20FINAL.pdf
2. World Health Organization. *Global measles and rubella strategic plan*: 2012-2020. [Internet]. 2012 [cited 2017 Jan 23]. Available from: http://apps.who.int/iris/bitstream/10665/44855/1/9789241503396%5Feng.pdf
3. Ntshoe GM, McAnerney JM, Archer BN, Smit SB, Harris BN, Tempia S, et al. Measles outbreak in South Africa: epidemiology of laboratory-confirmed measles cases and assessment of intervention, 2009–2011. *PLoS ONE*. 2013; 8(2): e55682.
4. National EPI Team, UNICEF South Africa, WHO South Africa, Provincial EPI Coordinators, Provincial Cold Chain Coordinators, editors. *EPI Diseases Surveillance Guide*. The National Department of Health, South Africa; 2015.
5. World Health Organization, Expanded Programme on Immunization, World Health Organization, Department of Immunization *Vaccines and Biologicals*. *Introducing rubella vaccine into national immunization programmes*: a step-by-step guide [Internet]. 2015 [cited 2017 Jan 22]. Available from: http://apps.who.int/iris/bitstream/10665/184174/1/9789241549370_eng.pdf

# Review: The impact of smoking on lung cancer incidence in South Africa. The role of smoking policy

Lactatia Motsuku[1], Mazvita Sengayi[1,2], Wenlong Carl Chen[1,3,4], Elvira Singh[1,2]

[1]National Cancer Registry, National Health Laboratory Service, Johannesburg
[2]School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg
[3]Sydney Brenner Institute for Molecular Bioscience, University of the Witwatersrand, Johannesburg
[4]Division of Human Genetics, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg

## Executive Summary

There is limited information regarding the impact of the South African tobacco smoking control act on lung cancer incidence locally. An analysis of lung cancer incidence trends from the National Cancer Registry and smoking prevalence from literature, using Jointpoint regression software to calculate average annual percentage change (AAPC), was conducted. Lung cancer incidence for males and females combined decreased significantly by an AAPC of 6.25% from 1997 to 2006 and by 3.07% from 2006 to 2012. However, there was a rise in lung cancer incidence by 0.15% from 2005 to 2010 and by 7.23% from 2010 to 2012 in females. Smoking prevalence in females also increased by 2.78% from 2005 to 2010. Overall, the lung cancer incidence trends followed the smoking prevalence pattern throughout the study period. Exploratory studies are necessary to address the rise in smoking prevalence in females.

## Introduction

According to the South African National Cancer Registry (NCR), lung cancer is ranked the 2nd and 5th most common cancer amongst men and women respectively. In South Africa, the age-standardized incidence rate (ASIR) of lung cancer was 10.78 and 3.56 per 100 000 persons for men and women respectively, in 2012. Tobacco smoke has long been identified as a carcinogenic agent for lung cancer and the pathophysiology for development of lung cancer has been widely studied.[1,2] The South African government has committed to reducing tobacco use in the country through the Tobacco Products Control Act of 1993. This act introduced interventions such as labeling tobacco packages with health warnings, a ban on tobacco advertising, restricting sales to persons under 18 years, increasing tobacco tax, regulating smoking in public places, introducing designated smoking areas, displaying of smoking hazards at point of sales and regulating the required standards for manufacturing and reduced ignition propensity in tobacco products. Due in large part to these interventions, smoking prevalence amongst adults decreased from 34% in 1995 to 25% in 2003.[3] Amongst men, smoking prevalence decreased from 40% in 1995 to 22% in 2010. However, the prevalence among women has remained constant at 9% with a slight increase after 2008.[4]

The aim of this study was to explore the relationship between smoking prevalence and incidence trends of lung cancer among adults, and to better understand the impact that tobacco smoking and the introduction of tobacco legislation has had on lung cancer incidence in South Africa.

## Methods

Incidence data for adult lung cancer cases from 1997-2012 were sourced from the National Cancer Registry of South Africa and smoking prevalence data (current smokers) were sourced from work conducted by Winkler *et al.*[5] Data on smoking prevalence were available up to 2010. Both lung cancer incidence and smoking prevalence data were imported into Joinpoint regression software for analysis of annual average percentage (AAPC) change in trends. Calculations of crude rates and age-standardized incidence rates (ASIR) were conducted using the mid-year South African population, as reported by Statistics South Africa, as the denominator and the Segi World Standard Population for standardisation.

The trends in lung cancer incidence rates were plotted alongside smoking prevalence trends to assess if changes in smoking prevalence over time may have affected trends in lung cancer incidence.

## Results

For males and females combined, there was a statistically significant decrease in lung cancer ASIR with an annual average percentage change of 6.25%, from 10.7/100 000 in 1997 to 6.1/100 000 persons in 2006 (Figure 1). The decrease was followed by a non-statistically significant AAPC increase of 3.07%, from 6.1 per 100 000 persons in 2006 to 7.2 per 100 000 persons in 2012. The ASIR was higher among coloured (30.59/100 000) and white persons (23.06/100 000) than in other population groups.

Lung cancer ASIR (per 100 000) and smoking prevalence (%) in men and women are shown in Figure 2. Among males, lung cancer ASIR decreased significantly from 1997- 2000 and 2000 - 2006 by AAPC of 10.24 % and 4.58% respectively, followed by a non-significant decrease between 2006 and 2010 of 1.12 %. However, between 2010 and 2012 there was a significant AAPC increase amongst men of 12.54%. Similarly, smoking prevalence decreased by an AAPC of 4.8% and 5.99 % for 1997 to 2002 and 2002 to 2007 respectively. However, from 2007 to 2010 smoking prevalence among males increased by an AAPC of 0.23%.

In females, ASIR decreased significantly from 5.26 /100 000 persons in 1997 to 3.62 /100 000 persons in 2000 (AAPC -11.17%) and further decreased in 2005 to 2.82 /100 000 persons (AAPC -3.38%). However, ASIR rose to 3.11/100 000 persons in 2010 (AAPC +0.15%) and further to 3.56 /100 000 persons in 2012 (AAPC +7.23%). Over the study period smoking prevalence decreased significantly by an AAPC of 2.99% between 1997 and 2002 for females and another further non-significant decrease by an AAPC of 0.43% between 2002 and 2005. As of 2005, smoking prevalence among females increased by an AAPC of 2.78% for the period 2005 to 2010 (Figure 2).

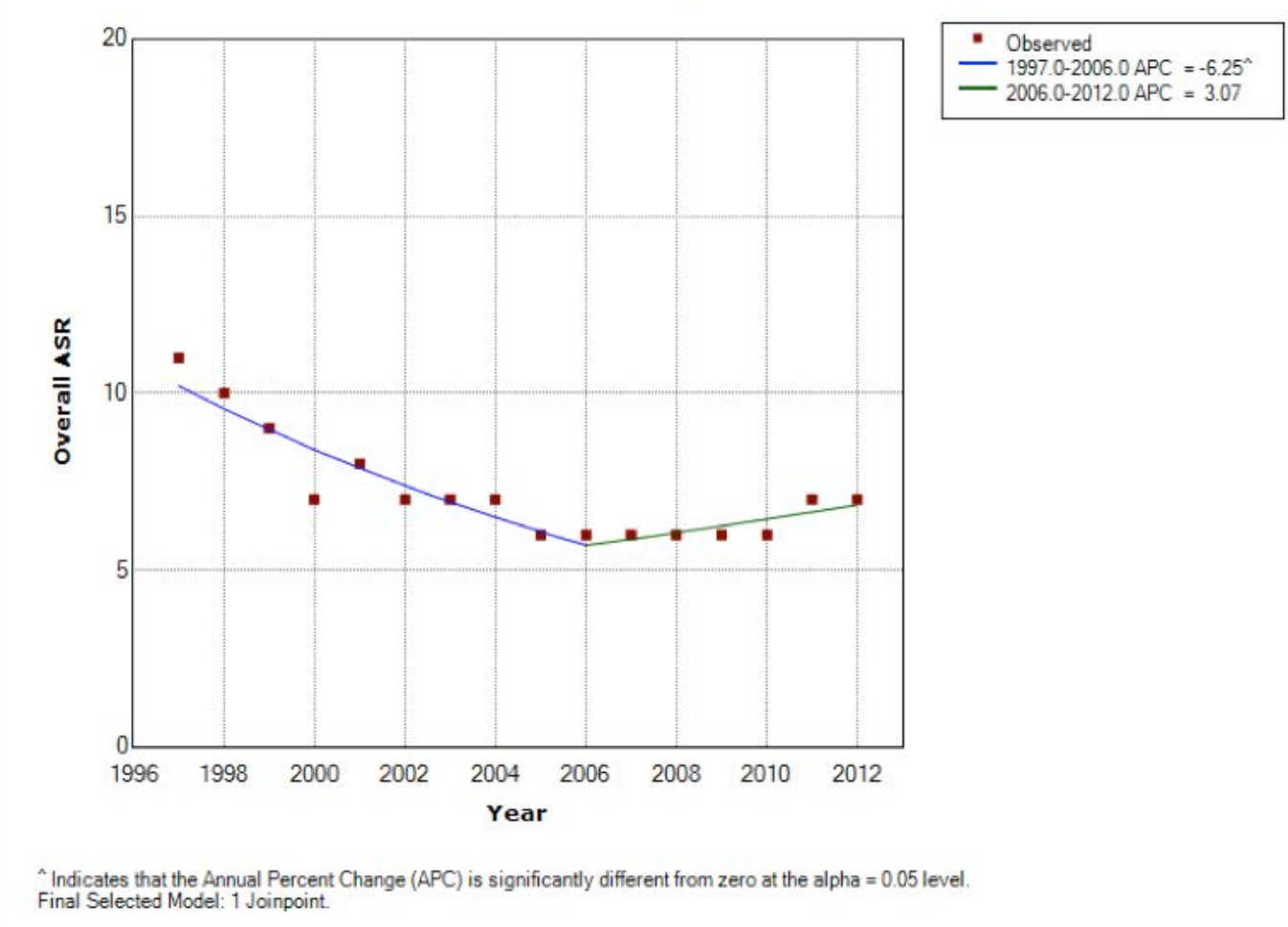
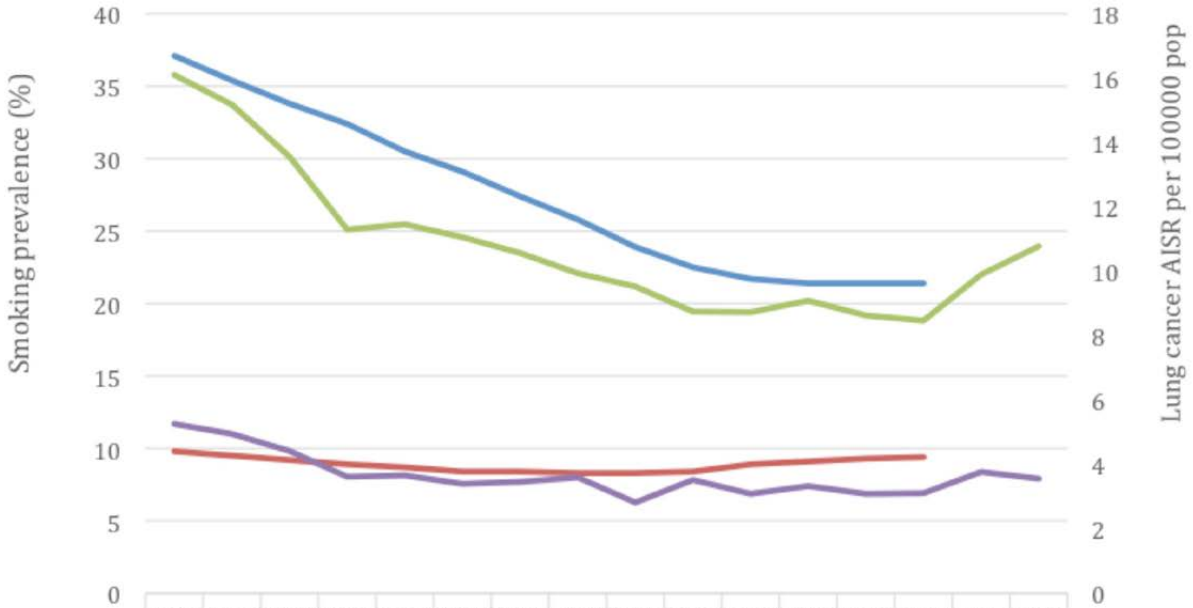



**Figure 1.** Overall lung cancer age standardized incidence rates (ASR), South Africa, 1997 - 2012.




| | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Smoking Male | 37.1 | 35.4 | 33.8 | 32.4 | 30.5 | 29.1 | 27.4 | 25.8 | 23.9 | 22.5 | 21.7 | 21.4 | 21.4 | 21.4 | | |
| Smoking Female | 9.8 | 9.5 | 9.2 | 8.9 | 8.7 | 8.4 | 8.4 | 8.3 | 8.3 | 8.4 | 8.9 | 9.1 | 9.3 | 9.4 | | |
| ASR Male | 16.1 | 15.18 | 13.56 | 11.3 | 11.46 | 11.06 | 10.57 | 9.94 | 9.53 | 8.75 | 8.73 | 9.09 | 8.63 | 8.47 | 9.9 | 10.78 |
| ASR Female | 5.26 | 4.95 | 4.42 | 3.62 | 3.66 | 3.4 | 3.46 | 3.6 | 2.82 | 3.52 | 3.09 | 3.33 | 3.09 | 3.11 | 3.77 | 3.56 |

**Figure 2.** Lung cancer age standardized incidence rates (ASR) and smoking prevalence among South African adults by gender,1997-2012.

## Conclusions

Overall, a reduction in lung cancer incidence was observed as smoking prevalence decreased. Of concern, however, is the increase in smoking prevalence in women and the consequent potential for an increase in lung cancer incidence. The increase in lung cancer incidence in 2011 and 2012 can be partially explained by the introduction of new cancer regulations which made cancer reporting to the NCR mandatory. Therefore, complete reporting of cancer cases diagnosed in private laboratories was achieved by the NCR for the first time in 2011 and 2012. Exploratory studies are needed to understand the factors influencing the increase in smoking prevalence in women.

## Acknowledgements

National Cancer Registry staff of the National Institute for Communicable Diseases are thanked for their inputs.

## References


1. IARC International Agency for Research on Cancer. List of classifications by cancer sites with sufficient or limited evidence in humans, Volumes 1 to 118 [Internet]. International Agency for Research on Cancer. 2017 [cited 2017 Jun 24]. Available from: http://monographs.iarc.fr/ENG/Classification/Table4.pdf%0A
2. Sato M, Shames DS, Gazdar AF, Minna JD. A Translational View of the Molecular Pathogenesis of Lung Cancer. J Thorac Oncol [Internet]. 2007 [cited 2017 Jun 24];2:327–43. Available from: http://www.jto.org/article/S1556-0864(15)30079-4/pdf
3. N, Bradshaw D, Laubscher R, Steyn K. S Afr Med J [Internet]. Vol. 99 Medical Association of South Africa; 1932 [cited 2017 Jul 3]. 744-749 p. Available from: http://www.scielo.org.za/scielo.php?script=sci_arttext&pid=S0256-95742009001000018
4. Shisana O, Labadarios D, Rehle T, Simbayi L, Zuma K, Dhansay A, et al. *South African National Health and Nutrition Examination Survey* (SANHANES-1) [Internet]. Igarss 2014. 2013. Available from: http://www.hsrc.ac.za/uploads/pageNews/72/SANHANES-launch edition (online version).pdf
5. Ng M, Freeman MK, Fleming TD, Robinson M, Dwyer-Lindgren L, Thomson B, et al. Smoking Prevalence and Cigarette Consumption in 187 Countries, 1980-2012. JAMA [Internet]. 2014 Jan 8 [cited 2017 Jul 5];311(2):183. Available from: http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.2013.284692

# Sentinel surveillance of human papillomavirus genotypes among patients attending public healthcare facilities in South Africa, 2015-2016

Zizipho Mbulawa[1,2,3,4], Ranmini Kularatne[2,3], Tendesayi Kufa-Chakezha[2,5], Anna-Lise Williamson[1,4,6,7]

[1]Institute of Infectious Disease and Molecular Medicine, University of Cape Town
[2]Center for HIV and STIs, National Institute for Communicable Diseases, National Health Laboratory Service
[3]Department of Clinical Microbiology & Infectious Diseases, University of the Witwatersrand
[4]Division of Medical Virology, Department of Pathology, University of Cape Town
[5]School of Public Health, University of the Witwatersrand
[6]UCT-MRC Clinical Gynaecological Cancer Research Centre, University of Cape Town
[7]National Health Laboratory Service, Groote Schuur Hospital, Cape Town

## Executive Summary

Human papillomavirus (HPV) is the commonest sexually transmitted infection (STI). Its prevalence in women peaks during adolescence soon after sexual debut, and decreases with age. Specific 'high-risk' HPV genotypes are the cause of cervical cancer. Women co-infected with HIV are at substantially increased risk of HPV infection and HPV-associated cancers. The vaccination strategy in South Africa requires baseline data on HPV in adolescents and young women so that the long-term impact of vaccines on circulating genotypes can be assessed. As part of NICD GERMS STI surveillance, 437 sexually-active young females aged 18-20 years were enrolled from primary healthcare centres in four provinces for testing and genotyping during the period 2015 - 2016. The overall prevalence of HPV infection was 58.4% (255/437). Prevalence of HPV types targeted by available vaccines was as follows: for the bivalent vaccine 12.6% (55/437); the quadrivalent vaccine 18.5% (81/437); and the nanovalent vaccine 30.9% (135/437). HIV infection was significantly associated with HPV infection including multiple genotypes.

## Background

Human papillomavirus (HPV) infection, in particular infection with specific high-risk genotypes, is the cause of cervical cancer. According to the National Cancer Registry, cervical cancer is the second most common cancer among all South African women, and the commonest among black South African women, with age standardized incidence of 21.67 cases per 100 000 (95% CI: 21.06-22.27) in 2011. There are currently three prophylactic HPV vaccines that are being rolled out internationally: Cervarix, Gardasil and Gardasil-9. Cervarix protects against two high-risk HPV types - HPV-16 and -18; Gardasil protects against two low-risk (LR) and two HR-HPV types - HPV-6, -11, -16 and -18; while Gardasil-9 protects against five more types in addition to those targeted by Gardasil - HPV-31, -33, -45, -52 and -58. Both Cervarix and Gardasil demonstrated cross-protective efficacy against phylogenetically related HPV-16 and -18 types, such as HPV-31, -33, -45 and -51. However, the duration of protection is not yet known. The efficacy, safety and immunogenicity of these vaccines have been recognized in surveillance cohorts.[1]

South Africa introduced a school-based national HPV vaccination program in 2014, at which time girls aged 9-10 years were vaccinated with Cervarix given in two doses at least six months apart (to fit into the academic calendar). In order to monitor the impact of vaccination, it is necessary to collect baseline data on HPV genotype prevalence and distribution in unvaccinated populations. Therefore, the aim of this surveillance programme was to determine the baseline prevalence of HPV infection and identify individual HPV genotypes among young sexually-active women in South Africa.

## Methods

***Participant recruitment (inclusion criteria and sentinel sites)***

Study participants between the ages of 18-20 years were enrolled at six primary healthcare clinics in Gauteng (Alexandra clinic),

Mpumalanga (Hluvukani and Kabokweni clinics), KwaZulu-Natal (Phoenix and East Boom clinics) and North West (Jouberton clinic) provinces, during the period 2015 - 2016.

***Participant data and specimen collection***

Following informed consent and enrolment procedures, a questionnaire was administered by surveillance nurses to record demographic, sexual behavioural and clinical information. Endocervical swabs were collected during speculum examination for HPV testing. Among women with genital ulcers and/or vaginal discharge on examination, additional ulcer and/ or vaginal swabs were collected to enable testing for sexually-transmitted pathogens.

***HPV testing and genotyping***

The Linear Array (LA) HPV Genotyping Test (Roche Molecular Systems, Inc., Branchburg, NJ, USA) was used to determine the HPV genotype distribution among all patients. The LA test amplifies the target HPV DNA of 37 different HPV genotypes including high-risk (HPV–16, –18, –31, –33, –35, –39, –45, –51, –52, –56, –58 and –59), probable or possible high-risk (HPV–26, –53, –66, –67, –68, –70, –73 and –82) and low-risk types ((HPV-6, –11, –40, 42, –54, –55, –61, –62, –64, –69, –71, –72, –81, –83, –84, –89 (HPV-CP6108) and –IS39)). HPV-52 was recorded positive only in the absence of HPV types 33, 35 and 58 due to the combined probe used for these 4 types. The β-globin gene was amplified as a control for cell adequacy, extraction and amplification. Samples with a negative β-globin result and a positive HPV DNA result were considered valid and adequate for analysis.

***Data management and analysis***

Descriptive statistics (proportions) were used to determine the prevalence of any HPV infection as well as specific HPV genotypes, and were also used to describe the demographic, behavioural and clinical characteristics of the enrolled population. Univariable and multivariable logistic regressions were used to determine the factors associated with prevalent HPV infection.

## Results

***Description of surveillance population***

A total of 460 women was enrolled of which 437 were included in the analysis for HPV genotypes. Twenty women were excluded for the following reasons: 13 were enrolled outside the surveillance period, seven were duplicate enrolments and three had invalid HPV test results. Demographic, clinical and behavioural data was available for 423 participants (Table 1). Almost all participants were black Africans with median age 19 years (IQR 18-20 years) and median age at sexual debut was 17 years (IQR 16-18 years). One hundred and eighty-one women (42.5%) reported using a condom during their last sexual encounter. Approximately one-fifth (18.9%) presented with concomitant vaginal discharge syndrome (n=74) or genital ulcer disease (n=12). The commonest cause of vaginal discharge was bacterial vaginosis (n=34, 46%) followed by vaginal candidiasis (n=20, 27%). Thirty-four of 74 women (45.9%) with vaginal discharge syndrome were infected with one or more of the STI discharge pathogens, most commonly *Chlamydia trachomatis* (n=19, 55.9%) and *Neisseria gonorrhoeae* (n=13, 38.2%).

***Overall HPV prevalence***

The overall prevalence of HPV infection was 58.4% (255/437). A higher proportion of women had infection with multiple (2-14) HPV types than single HPV infections (32.5% (142/437); 25.9% (113/437) respectively, p=0.04) (Figure 1). The median number of genotypes detected among those with multiple infections was 3 (IQR 2-5). The five most frequently detected HR-HPV types were HPV-59 (12.4%), HPV-58 (8.2%), HPV-16 (7.8%), HPV-45, (6.6%) and HPV-51 (6.6%, Figure 2).

***Prevalence of HPV types targeted by current vaccines and non HR-HPV vaccines types***

The prevalence of HPV types targeted by available vaccines was as follows: bivalent 12.6% (55/437); quadrivalent 18.5% (81/437); and nanovalent 30.9% (135/437) (Figure 3). Some women, 15.1% (66/437), were infected with HR-HPV types that are not targeted by current vaccines and cross-protective HR-HPV types (Figure 1).

***Association of HPV and HIV infection***

Table 2 shows the association of HPV infection with demographic, behavioural and clinical factors. In the univariable analysis, HPV infection was significantly associated with HIV infection (81.8% (54/66) in HIV-infected vs. 53.5% (191/357) in HIV-uninfected women; p<0.001). The prevalence of multiple HPV infection was significantly higher among HIV-positive women than HIV-negative women (72.7% (48/66); 27.2% (97/357) respectively, p<0.001). Similarly, women with positive HSV-2 serology, indicative of pre-existing HSV-2 infection, were significantly more likely to be HPV-infected. In a multivariable logistic regression model adjusting for the effects of age, HIV infection, HSV-2 seropositivity, *Neisseria gonorrhoeae* infection and bacterial vaginosis, HIV-infected young women were almost four times more likely to be HPV-infected [adjusted odds ratio (aOR) 3. 86 (95% CI 1.97-7.57) p<0.001] compared to HIV-uninfected participants, while those who were HSV-2 seropositive were three times more likely to have HPV infection [ aOR 3.22 (95% CI 1.08- 9.56), p=0.04].

## Discussion and conclusion

Over 50% of the young women in this surveillance study were infected with HPV. The association between HIV and HPV is well documented, with HPV infection increasing the risk of HIV acquisition, and HIV infection increasing the risk of HPV acquisition and persistence.[2] The high HPV prevalence in HIV-negative young women (53.5%) increases their risk of HIV acquisition.[3] HIV-infected adolescents are at high risk for abnormal cervical cytology and are more likely to have persistent HPV infections, increasing their risk of cervical cancer.[4]

The current HPV vaccines are prophylactic and are not effective in women who are already infected. Therefore, cancer screening programs are essential to reduce cervical cancer incidence through early detection of precancerous lesions in women who are already HPV infected, unvaccinated or partially vaccinated, and those infected with HPV types not targeted by current vaccines. The high prevalence (32.5%) of HPV types targeted by Gardasil-9 in this population encourages the introduction of this vaccine. HPV 51 has been reported in 2.1% and HPV-35 in 9.7% of African cervical cancers.[5] The high prevalence of HR-HPV types in this population that are not targeted by current vaccines (15.1%), specifically HPV-51 (6.6%) and HPV-35 (5.0%), is also of concern.

These HPV genotype prevalence data in adolescent girls and young women will be used as a baseline for comparison with future surveillance, and will better enable monitoring of vaccine impact over the coming years.


## Acknowledgements

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

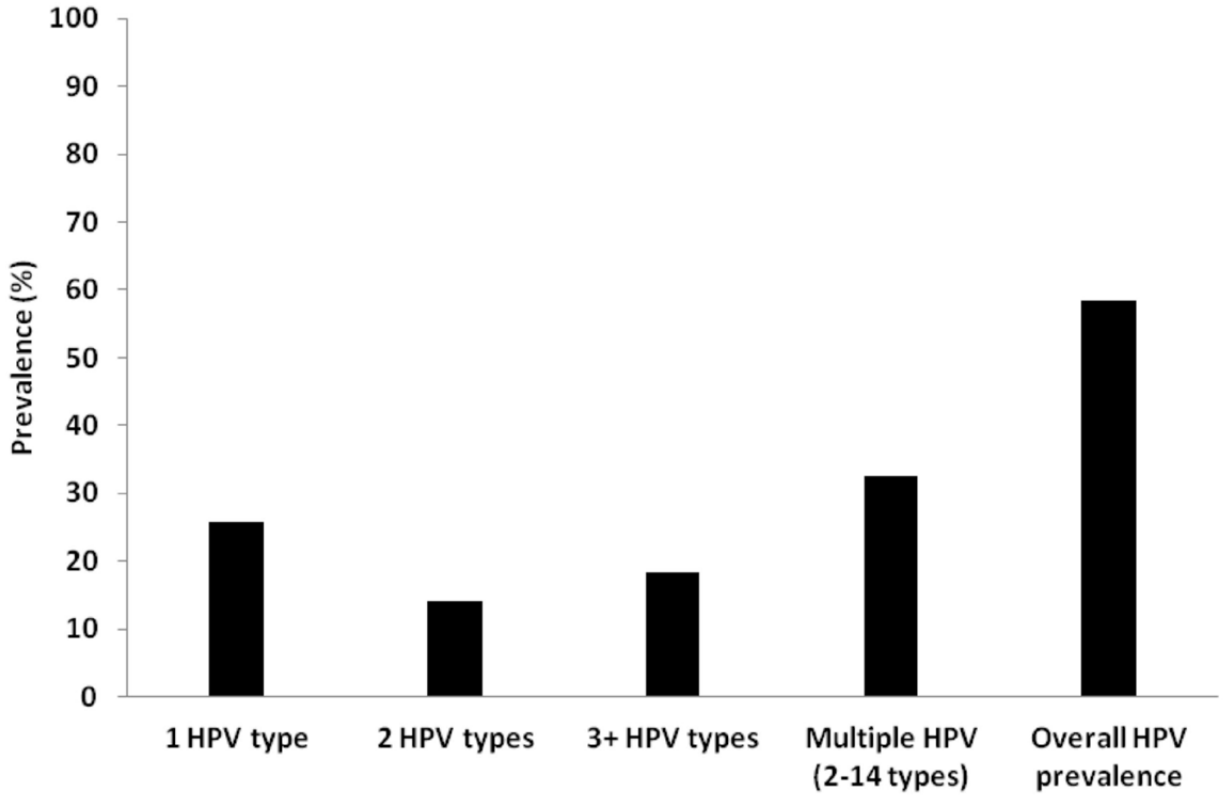
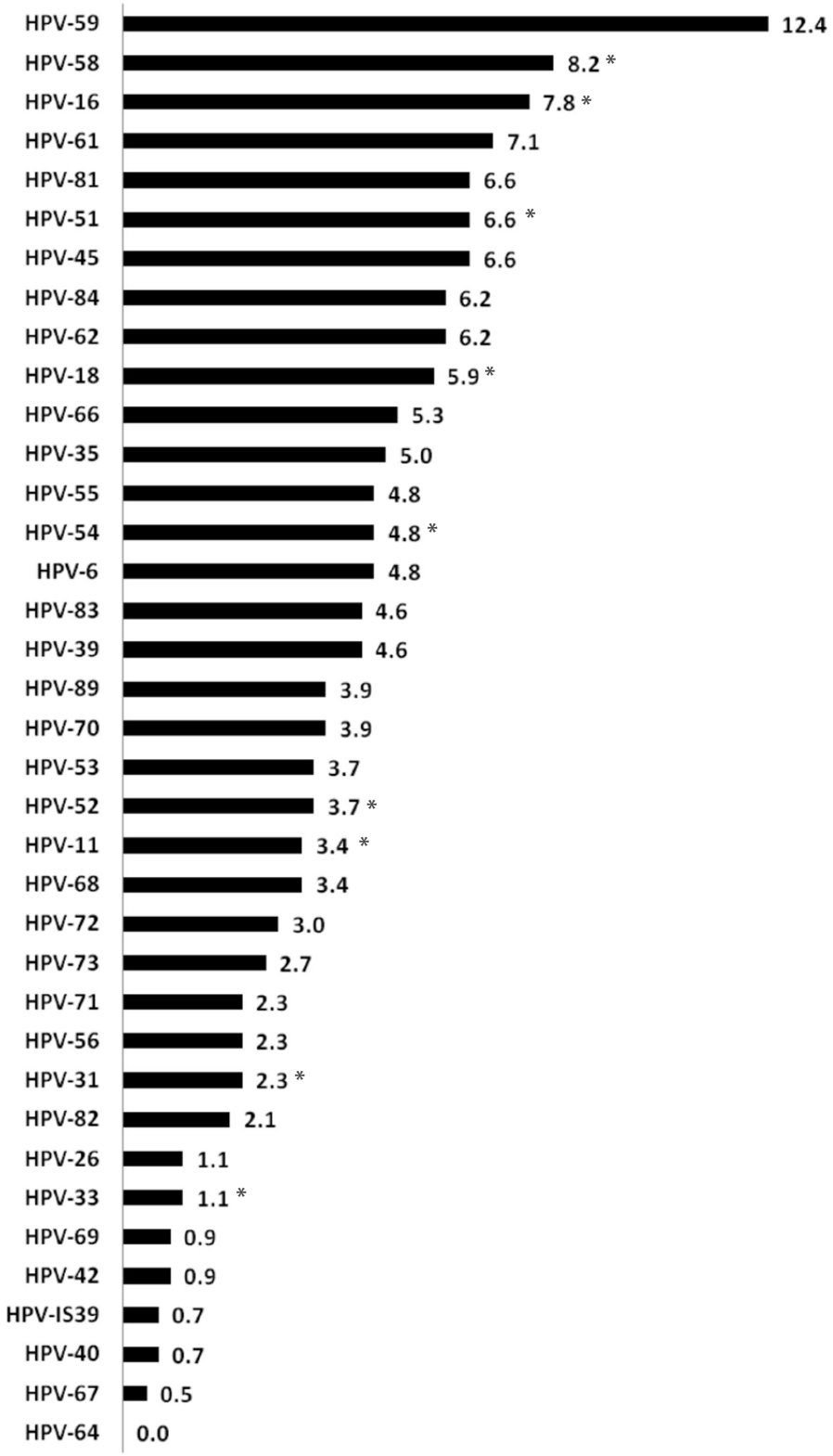



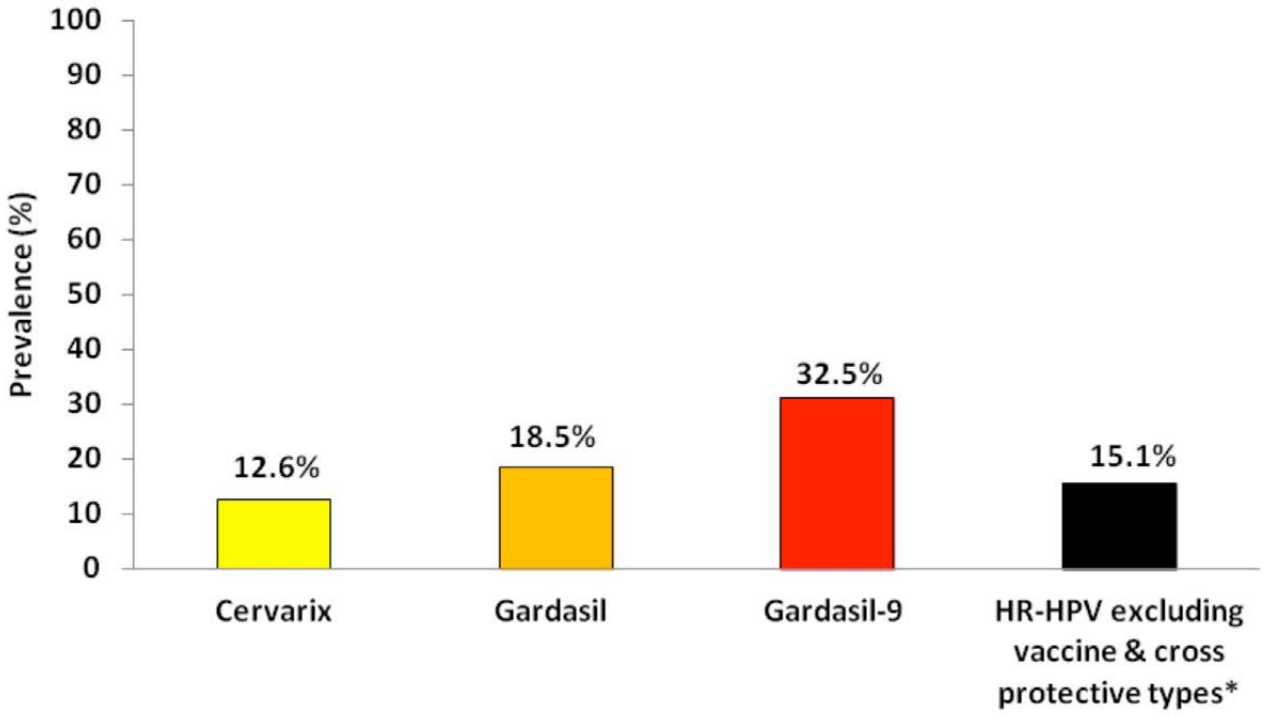

**Figure 1.** Prevalence of overall human papillomavirus (HPV), single infection and multiple infections, from sentinel sites in South Africa, 2015-2016.




*HPV types targeted by three current vaccines

**Figure 2.** Prevalence of different human papillomavirus (HPV) genotypes detected from sentinel sites in South Africa, 2015 – 2016.

**Figure 3.** Prevalence of human papillomavirus (HPV) types targeted by current vaccines and non-vaccine types detected from sentinel sites in South Africa, 2015 – 2016.




Cervarix HPV vaccine (HPV16/18); Gardasil HPV vaccine (HPV6/11/16/18); Gardasil-9 HPV vaccine (HPV6/11/16/18/31/33/45/52/58); HR-HPV excluding vaccine & cross protective types (HPV-35/39/56/59)

**Table 1.** Demographic, behavioural and clinical characteristics of women enrolled for human papillomavirus (HPV) prevalence surveillance (N=423) at sentinel sites in South Africa, 2015-2016.

| Characteristic | N(%) |
|---|---|
| Age (median, IQR ) | 19 years (18 - 20 years) |
| Age at first sex (median, IQR ) | 17 years (16 - 18 years) |
| African ethnicity | 419 (99.1) |
| Province | |
| • Gauteng | 179 (42.3) |
| • KwaZulu-Natal | 10 (2.4) |
| • Mpumalanga | 146 (34.5) |
| • North West | 88 (20.8) |
| Heterosexual orientation | 421 (99.5) |
| History of previous STI syndromes | 47 (11.1) |
| Reported condom use at last sex | 180 (42.5) |
| Reported having sex with someone living in another province in the last 3 months | 45 (10.7) |
| Reported having sex with someone living in another country in the last 3 months | 25 (6.0) |
| STI syndrome(s) diagnosed during clinic visit | |
| Vaginal discharge and/or genital ulcer disease | 80 (18.9) |
| Vaginal discharge | 74 (17.5) |
| Genital ulcer | 12 (2.8) |
| Lower abdominal pain | 68 (16.1) |
| Genital warts | 1 (0.2) |
| None | 278 (65.7) |
| Vaginal discharge pathogens detected in the laboratory (n=74) | |
| Any discharge pathogen | 60 (81.1) |
| Any STI pathogens | 34 (45.9) |
| • *Neisseria gonorrhoeae** | 13 (38.2) |
| • *Chlamydia trachomatis** | 19 (55.9) |
| • *Trichomonas vaginalis** | 7 (20.6) |
| • *Mycoplasma genitalium** | 9 (26.5) |
| Bacterial vaginosis | 34 (45.9) |
| Vaginal candidiasis | 20 (27.0) |
| **HIV infection** | **66 (15.6)** |

**Table 2.** Behavioural and clinical factors associated with human papillomavirus (HPV) infection (≥1 genotypes detected) at sentinel sites in South Africa, 2015-2016.

| Characteristic | % HPV infection | Univariable OR | p-value | Multivariable PRR | p-value |
|---|---|---|---|---|---|
| Age <= 19 years | | | | | |
| No | 105/187 (56.2) | 1 | | 1 | |
| Yes | 141/236 (59.8) | 1.16 (0.79- 1.71) | **0.457** | 1.39 (0.92- 2.08) | **0.118** |
| Province | | | | | |
| KZN, MP, NW | 145/244 (59.4) | 1 | | | |
| Gauteng | 101/179 (56.4) | 0.88 (0.52- 1.31) | 0.536 | | |
| Condom use at last sex | | | | | |
| No | 140/243 (57.6) | 1 | | | |
| Yes | 106/180 (58.9) | 1.05 (0.71- 1.56) | 0.793 | | |
| Previous STI syndrome | | | | | |
| No | 219/376 (58.2) | 1 | | | |
| Yes | 27/47 (57.5) | 0.97 (0.52- 1.77) | 0.917 | | |
| Any discharge STI at enrolment | | | | | |
| No | 226/389 (58.1) | 1 | | | |
| Yes | 20/34 (58.8) | 1.03 (0.56 -2.10) | 0.934 | | |
| *Neisseria gonorrhoeae* | | | | | |
| Negative | 236/410 (57.5) | 1 | | 1 | |
| Positive | 10/13 (76.9) | 2.45 (0.67- 9.06) | **0.177** | 1.41 (0.33- 6.05) | 0.646 |
| *Chlamydia trachomatis* | | | | | |
| Negative | 237/404 (58.7) | 1 | | | |
| Positive | 9/19 (47.7) | 0.63 (0.25- 1.59) | 0.333 | | |
| Bacterial vaginosis | | | | | |
| Negative | 222/389 (57.1) | 1 | | 1 | |
| Positive | 24/34 (70.6) | 1.81 (0.84 – 3.88) | **0.130** | 0.92 (0.35- 2.44) | 0.868 |
| HSV-2 serology | | | | | |
| Negative | 218/389 (56.0) | 1 | | 1 | |
| Positive | 28/34 (82.4) | 3.66 (1.48- 9.04) | **0.005** | 3.22 (1.08- 9.56) | **0.035** |
| HIV | | | | | |
| Negative | 192/357 (53.8) | | | 1 | |
| Positive | 54/66 (81.8) | 3.87 (2.00- 7.48) | **<0.001** | 3.86 (1.97- 7.57) | **<0.001** |

KZN = KwaZulu-Natal Province, MP = Mpumalanga Province, NW = North West Province; STI = sexually transmitted infection; HSV-2 = herpes simplex virus type 2

## Diseases/syndromes under surveillance, South Africa, 2015/2016

**Table 1.** Provisional number of laboratory confirmed cases of diseases under surveillance reported to the NICD - South Africa, corresponding periods 1 January - 31 December 2015/2016*

| Disease/Organism | 1 January to 31 December, year | EC | FS | GA | KZ | LP |
|---|---|---|---|---|---|---|
| Anthrax | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Botulism | 2015 | 0 | 0 | 1 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| *Cryptococcus spp.* | 2015 | 1417 | 376 | 2421 | 3548 | 701 |
| | 2016 | 1093 | 297 | 2308 | 3311 | 510 |
| *Haemophilus influenzae*, invasive disease, all serotypes | 2015 | 27 | 9 | 111 | 37 | 7 |
| | 2016 | 23 | 12 | 101 | 34 | 6 |
| *Haemophilus influenzae*, invasive disease, < 5 years | | | | | | |
| Serotype b | 2015 | 2 | 1 | 5 | 2 | 1 |
| | 2016 | 3 | 2 | 6 | 3 | 2 |
| Serotypes a,c,d,e,f | 2015 | 2 | 0 | 7 | 2 | 1 |
| | 2016 | 2 | 1 | 9 | 1 | 0 |
| Non-typeable (unencapsulated) | 2015 | 1 | 0 | 21 | 3 | 1 |
| | 2016 | 1 | 0 | 15 | 6 | 1 |
| No isolate available for serotyping | 2015 | 3 | 2 | 21 | 4 | 1 |
| | 2016 | 5 | 3 | 24 | 5 | 0 |
| Measles | 2015 | 0 | 0 | 1 | 2 | 0 |
| | 2016 | 2 | 0 | 50 | 3 | 3 |
| *Neisseria meningitidis*, invasive disease | 2015 | 27 | 9 | 46 | 23 | 1 |
| | 2016 | 15 | 2 | 36 | 11 | 1 |
| Novel influenza A virus infections | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Plague | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Rabies | 2015 | 3 | 1 | 0 | 1 | 3 |
| | 2016 | 0 | 1 | 0 | 1 | 0 |
| *Salmonella typhi* | 2015 | 4 | 1 | 29 | 9 | 1 |
| | 2016 | 1 | 1 | 57 | 9 | 5 |
| *Streptococcus pneumoniae*, invasive disease, all ages | 2015 | 232 | 131 | 970 | 354 | 99 |
| | 2016 | 208 | 147 | 856 | 320 | 84 |
| *Streptococcus pneumoniae*, invasive disease, < 5 years | 2015 | 27 | 12 | 169 | 59 | 18 |
| | 2016 | 26 | 19 | 206 | 46 | 16 |
| *Vibrio cholerae* O1 | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Viral haemorrhagic fever (VHF) | | | | | | |
| Crimean Congo haemorrhagic fever (CCHF) | 2015 | 0 | 1 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Other VHF (not CCHF) | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |

*Numbers are for cases of all ages unless otherwise specified. Data presented are provisional cases reported to date and are updated from figures reported in previous bulletins.
Provinces of South Africa: EC – Eastern Cape, FS – Free State, GA – Gauteng, KZ – KwaZulu-Natal, LP – Limpopo, MP – Mpumalanga, NC – Northern Cape, NW – North West, WC – Western Cape
0 = no cases reported

**Table 1.** Continued...

| Disease/Organism | 1 January to 31 December, year | MP | NC | NW | WC | South Africa |
|---|---|---|---|---|---|---|
| Anthrax | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Botulism | 2015 | 0 | 0 | 0 | 0 | 1 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| *Cryptococcus spp.* | 2015 | 876 | 114 | 828 | 754 | 11035 |
| | 2016 | 601 | 58 | 643 | 437 | 9258 |
| *Haemophilus influenzae*, invasive disease, all serotypes | 2015 | 10 | 1 | 3 | 118 | 323 |
| | 2016 | 8 | 6 | 6 | 89 | 285 |
| *Haemophilus influenzae*, invasive disease, < 5 years | | | | | | |
| Serotype b | 2015 | 0 | 0 | 1 | 6 | 18 |
| | 2016 | 2 | 2 | 1 | 5 | 26 |
| Serotypes a,c,d,e,f | 2015 | 0 | 0 | 0 | 10 | 22 |
| | 2016 | 1 | 0 | 0 | 2 | 16 |
| Non-typeable (unencapsulated) | 2015 | 1 | 0 | 0 | 19 | 46 |
| | 2016 | 0 | 0 | 0 | 14 | 37 |
| No isolate available for serotyping | 2015 | 3 | 0 | 1 | 7 | 42 |
| | 2016 | 1 | 0 | 2 | 7 | 47 |
| Measles | 2015 | 1 | 0 | 1 | 0 | 5 |
| | 2016 | 1 | 0 | 6 | 30 | 95 |
| *Neisseria meningitidis*, invasive disease | 2015 | 3 | 2 | 3 | 42 | 156 |
| | 2016 | 5 | 2 | 5 | 54 | 131 |
| Novel influenza A virus infections | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Plague | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Rabies | 2015 | 0 | 0 | 0 | 0 | 8 |
| | 2016 | 0 | 0 | 0 | 0 | 2 |
| *Salmonella typhi* | 2015 | 12 | 0 | 1 | 20 | 77 |
| | 2016 | 9 | 1 | 4 | 40 | 127 |
| *Streptococcus pneumoniae*, invasive disease, all ages | 2015 | 86 | 27 | 108 | 631 | 2638 |
| | 2016 | 102 | 42 | 73 | 602 | 2434 |
| *Streptococcus pneumoniae*, invasive disease, < 5 years | 2015 | 16 | 5 | 27 | 65 | 398 |
| | 2016 | 15 | 3 | 10 | 79 | 420 |
| *Vibrio cholerae* O1 | 2015 | 0 | 0 | 0 | 0 | 0 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Viral haemorrhagic fever (VHF) | | | | | | |
| Crimean Congo haemorrhagic fever (CCHF) | 2015 | 0 | 0 | 0 | 0 | 1 |
| | 2016 | 0 | 0 | 0 | 0 | 0 |
| Other VHF (not CCHF) | 2015 | 0 | 0 | 0 | 0 | 0 |
| | | 0 | 0 | 0 | 0 | 0 |

**Table 2:** Provisional laboratory indicators for NHLS and NICD, South Africa, corresponding periods 1 January - 31 December 2015/2016*

| Programme and Indicator | 1 January to 31 December, year | EC | FS | GA | KZ | LP | MP | NC | NW | WC | South Africa |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Acute Flaccid Paralysis Surveillance** | | | | | | | | | | | |
| Cases <15 years of age from whom specimens received | 2015 | 22 | 11 | 46 | 44 | 20 | 34 | 2 | 13 | 16 | 208 |
| | 2016 | 16 | 16 | 59 | 43 | 46 | 32 | 8 | 7 | 10 | 237 |

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

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

# PUBLIC HEALTH SURVEILLANCE BULLETIN

The Communicable Diseases Surveilance Bulletin is published by the National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service (NHLS),

Private Bag X4,
Sandringham,
2131,
Johannesburg
South Africa

Suggested Citation: [Authors' names or National Institute for Communicable Diseases (if no author)]. [Article title].

Request for e-mail subscription are invited - please send requests to Mrs Sinenhlanhla Jimoh: **SinenhlanhlaJ@nicd.zc.za**

**This bulletin is available on the NICD website: http:\\www.nicd.ac.za**