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FOREWORD

In the wake of the listeriosis outbreak, this issue contains a general review of foodborne disease (FBD) outbreaks in South Africa for the period 2013 to 2017. This review suggests that although FBD outbreaks are a notifiable medical condition in South Africa, they are likely under-investigated and underreported.

Leprosy still occurs in South Africa, although cases are extremely rare. An investigation into two cases from a tertiary hospital in Limpopo Province's Vhembe district is described in this issue, as is a report on the detection of non-polio acute flaccid paralysis (AFP) in South Africa. This report describes a case of AFP caused by a vaccine-derived poliovirus that was detected in an immunocompromised child in December, 2017.

Dengue virus is not currently in circulation in South Africa, and incidence is restricted to the importation of cases. Nevertheless, the risk of a local outbreak is significant, especially in northern KwaZulu-Natal as discussed in this issue, which also contains the 2017 malaria vector surveillance report. This report shows that several malaria vector species were collected from South Africa's endemic districts, highlighting the need for intensive, sustained control operations.

Lastly, this issue contains the 2017 respiratory pathogens surveillance report for South Africa, showing that the country's 'flu season was predominated initially by influenza A(H3N2) followed by influenza B towards the end of the season, and co-circulation of influenza A(H1N1)pdm09 at low levels.

We hope our readers will find this bumper edition useful and interesting, and thank all contributors and reviewers, especially Prof John Frean, for their inputs.

Basil Brooke,

Editor

A REVIEW OF FOODBORNE DISEASE OUTBREAKS REPORTED TO THE OUTBREAK RESPONSE UNIT, NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES, SOUTH AFRICA, 2013 – 2017

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Executive summary

Foodborne diseases (FBDs) are a major public health concern and an important cause of morbidity and mortality globally. We abstracted secondary data from FBD outbreak reports submitted to Outbreak Response Unit (ORU) from 2013 – 2017, in order to conduct a retrospective descriptive review of the outbreaks. Stool and environmental samples (food and water) were collected and tested for the presence of enteric foodborne pathogens. 327 FBD outbreaks were reported from January 2013 to December 2017, causing illness in 11 155 individuals, with 8 680 hospital visits, 494 hospital admissions and 49 deaths. Most of the outbreaks were reported in warmer months. Most outbreaks were reported from KwaZulu-Natal (141/327, 43.1%), Gauteng (63/327, 19.3%) and Mpumalanga (40/327, 12.2%) Province. Stool and environmental specimens were collected in 239/327 (73.1%) of reported outbreaks. Stool samples were collected in 147/239 (61.5%); food samples in 132/239 (55.2%) and water samples in 33/239 (13.8%). *Salmonella* species was commonly isolated in stool (29/147, 19.7%) and food (15/132, 11.4%) samples. Although FBD outbreaks are a notifiable medical condition in South Africa, they are likely underreported. There is great variability in how FBD outbreaks are reported and investigated throughout the country. The lack of epidemiological data hinders more detailed description of the outbreaks. The failure to obtain food exposure histories in both cases and non-cases, and failure to obtain clinical and environmental samples for appropriate laboratory investigations, are major gaps in FBD outbreak investigations. Limitations of the review include the use of secondary data abstracted from district outbreak investigation reports. This review is based on the FBD outbreaks reported to ORU/NICD, and is not representative of the actual burden of FBD in the country. Strengthening and training of outbreak response teams to improve FBD outbreak investigations, including specimen and epidemiological data collection and report writing is recommended.

Introduction

Foodborne diseases (FBDs) are a major public health concern and an important cause of morbidity and mortality globally. [1] FBDs include a wide range of illnesses resulting from consumption of

foodstuffs contaminated with microorganisms or chemicals, and may be infectious or toxic in nature.[2,3] The main causes of FBDs are pathogenic microorganisms, including bacteria, viruses, parasites, fungi, prions and chemicals (both naturally occurring and man-made). [1,3,4]

Food contamination may occur at any stage of food production to consumption ('farm to fork') and can also be a result of environmental contamination, including water and soil contamination.[3,5] Examples of typically unsafe food include uncooked foods of animal origin, fruits and vegetables contaminated with faeces, and shellfish containing marine biotoxins.[4]

Foodborne pathogens can cause intestinal disease (for example, severe diarrhoea) or extraintestinal infections (such as meningitis). Chemical contamination can lead to acute poisoning or long-term diseases, such as cancer. FBDs may lead to long-lasting disability or death.[3,4] The clinical presentation of FBDs most commonly takes the form of gastrointestinal symptoms. However, other symptoms such as neurological, immunological and gynaecological symptoms may occur.[5] Whilst unsafe food is a global health threat, vulnerable groups (including infants, young children, the elderly, pregnant women and people with underlying illness) are most at risk for severe FBD.[3]

The World Health Organization (WHO) Foodborne Disease Burden Epidemiology Reference Group (FERG) reported the global estimates of burden of FBDs in 2010. The FERG found the global burden of FBDs to be comparable to those caused by major infectious diseases, HIV/AIDS, malaria and tuberculosis.[1,6] Annually, FBDs causes about 600 million illness episodes, 420 000 deaths and 33 million healthy life years lost (disability-adjusted life years, DALYs) globally. Children under 5 years accounted for 125 000 (almost 1/3) of the deaths from FBDs.[1,6]

WHO Africa region had the highest FBDs estimated burden in 2010, with over 91 million people falling ill and 137 000 deaths annually. This represents 1/3 of the global death toll due to FBDs. Diarrhoeal diseases are responsible for 70% of FBDs burden.[1,6,7]

The estimated burden of FBDs in South Africa is not well established due to lack of data. FBD (also termed 'food poisoning') is a notifiable medical condition in South Africa.[8] The Outbreak Response Unit (ORU) of the National Institute for Communicable Diseases (NICD) aims to facilitate epidemiological and laboratory diagnosis requirements during outbreaks through partnership with National Health Laboratory Services (NHLS) diagnostic laboratories and NICD reference laboratories. This article provides a retrospective review and descriptive analysis of FBD outbreaks reported to ORU over a five-year period, (from January 2013 to December 2017).

Methods

FBD outbreak definition and investigations. A FBD outbreak is defined as any FBD/food poisoning incident affecting two or more people that are epidemiologically linked by a common food or beverage source.[9] ORU assists the National Department of Health (NDoH) to collate FBD reports from district and provincial health departments. It also provides technical support for FBD investigation and control, working closely with the Provincial and NDoH communicable disease control (CDC) health authorities.

Epidemiological investigation. Outbreaks are investigated by the local/district health municipality outbreak response team (ORT) comprising CDC, environmental health, surveillance officers, infection prevention and control (IPC) and emergency medical services (EMS) authorities, with support from provincial and NDoH and ORU (NICD) where required. We abstracted secondary data from FBD outbreak reports submitted to ORU. Data was captured and analysed using Excel 2016.

Laboratory investigation. Stool and environmental samples (food and water) were collected during outbreak investigations and tested at the NHLS regional diagnostic laboratories, public health laboratories and Centre for Enteric Diseases (CED) at NICD. The stool and food samples were tested for the presence of foodborne pathogens such as S*almonella* species, *Clostridium perfringens, Bacillus cereus, Shigella* species, *Listeria monocytogenes*, *Staphylococcus aureus*, *Escherichia coli* O157:H7, *Campylobacter* species, *Vibrio cholerae* and *Yersinia enterocolitica,* depending on the test requested and capacity of the testing laboratory (regional diagnostic laboratories vs public health laboratories).

Results

Epidemiological investigation: 327 FBD outbreaks were reported from January 2013 to December 2017, causing illness in 11 155 individuals, with 8 680 hospital visits, 494 hospital admissions and 49 deaths (Table 1). Age and gender were not adequately reported; as a result, these data were not analysed. Most of the outbreaks were reported in warmer months (February 43/327, 13.1%; August 32/327, 9.8%; October 39/327, 11.9% and November 37/327, 11.3%) (Figure 1). KwaZulu-Natal Province reported the most outbreaks (141/327, 43.1%), followed by Gauteng (63/327, 19.3%) and Mpumalanga (40/327, 12.2%) provinces (Figure 2).

Institutional outbreaks were most common (106/327, 32.4%) and were reported from schools, correctional facilities and hospitals. Food prepared or consumed in households accounted for 27.2% (89/327) of the outbreaks, and outbreaks in the community (foodstuffs shared amongst neighbours and affected more than one household) accounted for 10.7% (35/327) of those reported.

Table 1. Number of FBD outbreaks reported to ORU/NICD, South Africa, 2013-2017

Year	No. of FBD outbreaks reported	No. of persons involved (N)	No. of cases visiting healthcare facilities	No. of cases admitted	No. of deaths (n)	Death rate (n/N)
2013	57	1725	1007	75	6	0.3%
2014	57	3296	2591	73	19	0.6%
2015	55	1723	1461	132	4	0.2%
2016	85	2096	1651	139	12	0.6%
2017	73	2315	1970	75	8	0.3%
Total	327	11155	8680	494	49	0.4%

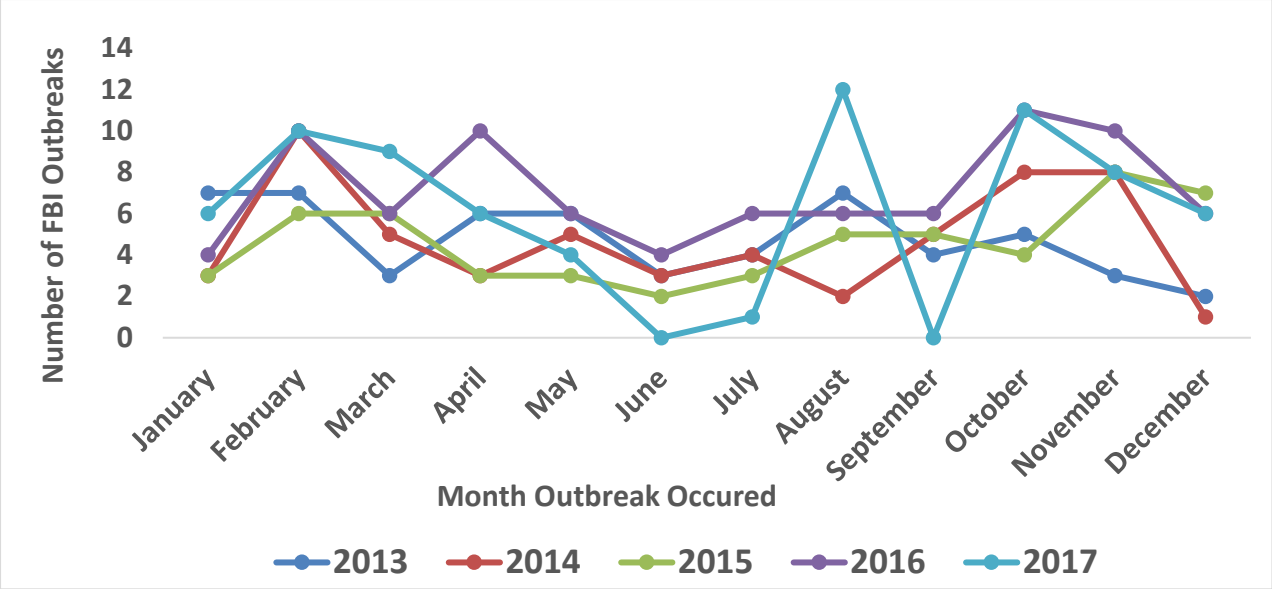

Figure 1. Number of food borne disease outbreak occurrences/reported per month over 5-years, 2013-2017.

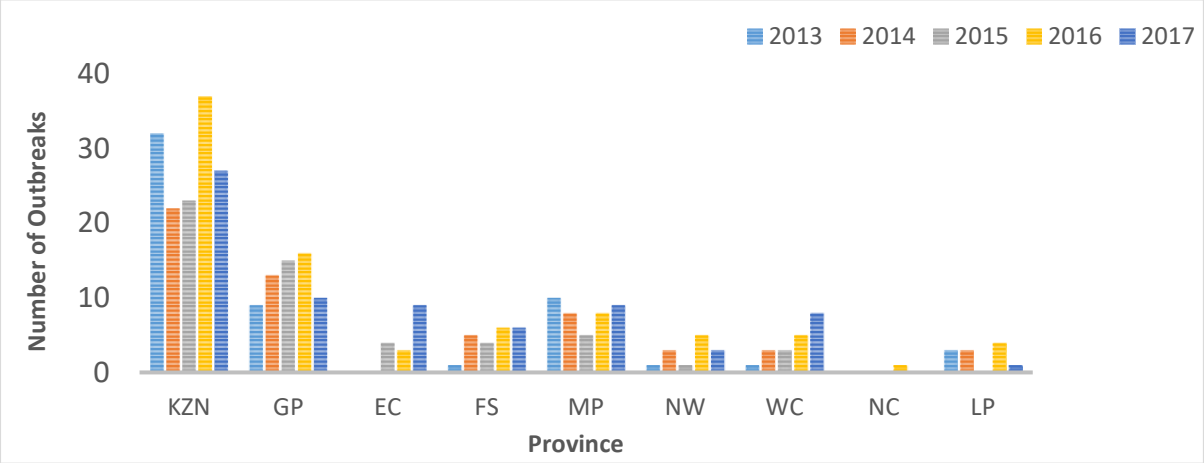

Figure 2. Number of food borne disease outbreaks reported to the Outbreak Response Unit, NICD, per Province over 5-years, 2013-2017. (KZN: KwaZulu-Natal; GP: Gauteng; EC: Eastern Cape; FS: Free State; MP: Mpumalanga; NW: North West; WC: Western Cape; NC: Northern Cape; LP: Limpopo).

Laboratory investigation. Stool and environmental specimens were collected in 239/327 (73.1%) of reported outbreaks. Stool samples were collected in 147/239 (61.5%); food samples in 132/239 (55.2%) and water samples in 33/239 (13.8%) of the outbreaks reported.

Enteric pathogens isolated in stool samples included *Salmonella* species (29/147, 19.7%), *Clostridium perfringens* (12/147, 8.2%), *Bacillus cereus* (7/147, 4.8%), *Shigella* species (6/147, 4.1%) and *Listeria monocytogenes* (2/147, 1.4%). Pathogens isolated from food samples were *Salmonella* species (15/132, 11.4%), *Escherichia coli (E. coli) species* (14/132, 10.6), *Bacillus cereus* (13/132, 9.8%), *Clostridium perfringens* (4/132, 3.0%), and *Listeria monocytogenes* (4/132, 3.0%). Water contamination indicators found in water samples were high count of *E*. coli and total coliforms (3/33, 9.1%).

Discussion and conclusions

Although FBD outbreaks are classified as a notifiable medical condition in South Africa, they are likely underreported. A total of 327 FBD outbreaks was reported over a 5-year period. FBD outbreaks were more commonly reported during warmer months, and three provinces reported 74% of all outbreaks (KwaZulu-Natal, 43%; Gauteng, 19%; and Mpumalanga, 12%). The province reporting the least number of FBD outbreak reports over the 5-year period was Northern Cape Province (0.3%).

There is inconsistency in FBD outbreak investigation and report writing at local/district levels, and the lack of epidemiological data hinders more detailed description of the outbreaks. For example, the actual date of the outbreak is not always recorded; the place/location where the outbreak occurred is omitted in some reports; the age and gender of affected individuals were usually not recorded, and the total number and proportion of cases that developed disease following consumption of the implicated food is not always recorded in the reports. Most of the outbreaks occurred in institutions, followed by the home/household setting and then the community. In some instances, community and household outbreaks occurred following consumption of meat from an animal deceased or slaughtered following an unknown illness.

This review shows that appropriate food exposure history, clinical and environmental specimens are not always collected. Stool specimens were collected in 61.5%, food samples in 55.2% and water samples in 13.8%. Lack of proper food exposure history data for cases and non-cases limited the investigation to establish the possible vehicle of infection. Lack of specimen collection and appropriate testing makes it difficult to identify the cause and source of FBD outbreaks. As a result, the source and cause for most of the reported outbreaks were not identified. This failure to obtain food exposure history in cases and non-case, and failure to obtain clinical and food samples for appropriate laboratory investigations is a major gap in FBD outbreak investigations. S*almonella* species was the most commonly isolated bacterial pathogen in both stools (19.7%) and food (11.4%) samples. Other bacterial enteric pathogens isolated were *Clostridium perfringens, Bacillus cereus, Shigella* species, *Listeria monocytogenes,* and *Escherichia coli.* According to WHO FERG report, diarrhoeal diseases due to non-typhoidal *Salmonella*, foodborne cholera and *E*. coli were responsible for 70% of FBI burden in 2010.[1]

In conclusion, there is great variability in how FBD outbreaks are reported and investigated throughout the country. Timeous and appropriate clinical and food/environmental sample collection and testing hinders the definitive identification of the outbreak source. FBDs are mostly preventable and the number of illnesses and deaths due to diseases caused by consumption of contaminated food are a public health concern. Government authorities should make food safety a public health priority and implement measures to prevent and promptly investigate FBDs in communities.[6] Personal hygiene and safe food practices (including proper storage and preparation of food) is important to prevent food contamination and FBD outbreaks. Food safety education for consumers has been shown to affect change in behaviour.[6]

Limitations of the review include the use of secondary data abstracted from district outbreak investigation reports. This review suggests that there are major gaps in FBD outbreak investigations, poor data collection during outbreak investigations, and great variability in quality of report writing at

local/district municipality levels. Laboratory investigations were limited to bacterial pathogens as viruses and parasites are not routinely tested and appropriate tests for such pathogens were generally not requested. This review is based on the number of FBDs reported to ORU/NICD, and is not representative of the actual burden of FBD in the country.

We recommend strengthening and training of ORT to improve FBD outbreak investigations, including specimen and epidemiological data collection and report writing. Health promotion on food safety should be carried out regularly in the communities and institutions to prevent FBD outbreaks.

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LEPROSY CASE INVESTIGATION - LIMPOPO PROVINCE, SOUTH AFRICA, JANUARY 2017

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Executive Summary

Leprosy still occurs in South Africa despite the country having attained the World Health Organization (WHO) elimination target of one case of leprosy per 10,000 population. Due to the long incubation period of the disease, affected persons can still show symptoms many years after initial infection. Leprosy elimination in South Africa was accomplished in 2005 through a partnership between the government, the National Department of Health, and a non-governmental organization, the Leprosy Mission Southern Africa (TLMSA). Early diagnosis and complete treatment with multi-drug therapy (MDT) remain the key strategies for reducing the disease burden. Two cases of leprosy were identified from a tertiary hospital in November 2016. Both reside in the Vhembe district of Limpopo Province and are outpatients receiving MDT monthly. They will need long-term follow-up to ensure treatment compliance.

Background

Leprosy is a communicable bacterial disease caused by *Mycobacterium leprae. M. leprae* spreads between humans by nasal droplets following long-term close contact with an infected host, usually within a household setting.[1] Leprosy has a long incubation period ranging from 9 months to 20 years or longer.[2] Symptoms of leprosy include skin lesions, muscle weakness, and loss of sensation in the hands, arms, feet and legs.[2] Although infectious, persons receiving multi-drug therapy (MDT) and those having completed treatment cannot transmit the disease.[3]

The distribution of leprosy is restricted to a few countries.[1] In 2015, a total of 210,758 new cases of leprosy was detected globally with the majority (95%) notified in 14 countries[1]: Bangladesh, Brazil, Democratic Republic of Congo, Ethiopia, India, Indonesia, Madagascar, Myanmar, Nepal, Nigeria, the Philippines, Sri Lanka, Mozambique and the United Republic of Tanzania. Within countries, leprosy is found to be spatially unevenly distributed in areas with low socio-economic status.[4,5]

Leprosy is treated with a combination of antibiotics (MDT),[1] that includes rifampicin, clofazimine and dapsone.[3] The introduction of MDT to leprosy programmes in the mid-1980s resulted in a significant reduction in the prevalence of the disease, from 5.4 million cases to a few hundred thousand currently.[1] MDT is provided free of charge by the World Health Organization (WHO) in collaboration with the manufacturers Novatis/Sandoz.[3]

The WHO classifies leprosy disability into grades, according to the disability of the eyes, hands and feet. For the hands and feet, grade 0 means that there is no sensory loss nor visible deformity, grade 1 means that there is loss of sensation but no visible damage or disability, and grade 2 includes those patients with visible damage or disability.[1] For the eyes, grade 0 means no problem due to leprosy i.e. no evidence of visual loss, grade 1 means problems due to leprosy present, but vision not severely affected as a result, and grade 2 means severe visual impairment, including lagophthalmos, iridocyclitis and corneal opacities.[1]

Leprosy was declared a notifiable medical condition in South Africa in 1921.[3] Cases of leprosy are rarely seen in South Africa,[3] with only 170 cases registered nationally between 2007 and 2016. Leprosy elimination in South Africa was accomplished through a partnership between the government, the National Department of Health, and a non-governmental organization, the Leprosy Mission Southern Africa (TLMSA).[3] TLMSA provides technical assistance by training primary health care (PHC) workers, and conducts leprosy clinics at district and provincial hospitals where patients are seen after referral from PHC clinics.[3]

On December 8, 2016, the Limpopo Department of Health was notified of two confirmed leprosy patients in a tertiary hospital. Confirmation was done by Wade-Fite acid fast stain on skin punch biopsy. Following these reports, a provincial team comprising the Division of Public Health Surveillance and Response of the National Institute for Communicable Diseases (NICD), Limpopo Department of Health, and a resident from the South African Field Epidemiology Training Programme (SAFETP), conducted an investigation. The aim of this investigation was to identify the source of infection for each patient and their close contacts, and to assess these contacts for any signs of leprosy.

Methods

The tertiary institution that reported the two confirmed cases was visited in order to review the medical records and to collect clinical data. Patients were interviewed using a standardized case investigation form, to collect data on symptoms, travel, contact history and other exposures at their respective residences. A case of leprosy was defined as any person who presented to a tertiary hospital in Limpopo Province in November 2016 having one or more of the following: reddish skin lesion(s) with definitive loss of sensation on hands and feet, and a positive skin-smear for acid-fast bacilli. A contact was defined as any person living in the same household as a known leprosy patient. Contacts were assessed for any signs and symptoms of leprosy.

Results

Both patients were seen at a tertiary hospital leprosy clinic on 30 November 2016 after being referred from their respective district hospitals. Patient 1 was a newly-diagnosed 50-year-old, HIV-positive male with grade 1 disability (loss of sensation in both hands and feet with no visible deformity or damage). The patient worked in Tanzania, Mauritius and Namibia until 2007. He started to develop lumps on his face and a hoarse voice in 2013. In 2013, the patient consulted the local primary health care facility and was treated for sunburn, until this tertiary hospital consultation. A skin biopsy was done, and found to be positive for *M. leprae*. He was immediately started on MDT. The patient lives with 6 family members (three adults and three children).

Patient 2 was a 29-year-old female with grade 0 disability (no loss of sensation, no visible deformity or damage). She lived in Mozambique for 17 years before returning to South Africa in 2011, when she began experiencing unexplained sores on her body. She was diagnosed with leprosy in 2011 and began treatment, but defaulted due to lack of transport to the hospital. The patient was re-initiated on treatment in November 2016. In her previous residential address, she lived with seven family members (two adults and five children). In her current residential address, she lives with 11 family members (four adults and seven children).

There were no epidemiological links between the two cases. A total of 24 contacts was reported, 18 of whom were available for examination, and none showed signs of leprosy. Both patients were educated on treatment adherence and follow-up. Contacts were advised to report to hospital if experiencing skin lesions coupled with sensory loss, discolored patches of skin and/ or loss of eyebrows. The respective district hospital was encouraged to arrange for a directly observed treatment (DOT) supporter to assist with patient 2 in reminding and observing her treatment intake as she had defaulted before.

Discussion

Complacency after achieving the goal of leprosy elimination at country level may result in its return as a re-emerging disease. Maintaining public health care (PHC) workers' knowledge and awareness of leprosy is strongly encouraged as a patient's first contact with a health worker is typically at the PHC level.[3]

Contacts of leprosy patients are known to have an increased risk of contracting leprosy themselves given that leprosy is spread from person to person mainly through nasal discharges. The extent of the risk is dependent on the closeness of contact; household contacts (those living in the same house and sharing the same facilities) appear to have the highest risk. Age has also been found to be a potential risk factor for contacts to develop leprosy. Several studies found that among household contacts, the risk of developing leprosy was substantially higher in children less than 14 years of age than in adults.[4] Of the examined contacts in this investigation, none showed signs and symptoms of leprosy at the time. However, due to the disease's long incubation period, continued examination of contacts is encouraged as leprosy control includes early detection of new cases.[1]

Conclusion and recommendations

The reported patients are unrelated and both had lived in leprosy-endemic countries outside of South Africa for extended periods. Owing to the long incubation period of leprosy and low prevalence in South Africa, it is concluded that they likely acquired their infections outside South Africa. The very low prevalence of the disease in South Africa, including Limpopo Province, suggests that health workers may not be knowledgeable about or suspect leprosy as a differential diagnosis. It is therefore recommended that:

- Training of health workers in leprosy-specific skills should be offered so as to improve early diagnosis and treatment in South Africa
- An appropriate index of suspicion in patients that have a history of prolonged stays in leprosy-endemic countries should be maintained

Acknowledgements

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ACUTE FLACCID PARALYSIS SURVEILLANCE FOR POLIO, SOUTH AFRICA, AND OTHER AFRICAN COUNTRIES, 2017

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Executive summary

Acute flaccid paralysis cases caused by polioviruses are at the lowest levels in history. Routine vaccination programs essential for the elimination of polio have succeeded in reducing the circulation of the viruses. The non-polio acute flaccid paralysis detection rate in South Africa in 2017 was 2.3 cases/100 000 under 15 years of age, lower than the 2016 level of 3.0. The detection rate reaches the WHO target of 2.0/100 000 but not the heightened 2015 country target of 4.0/100 000. There were three provinces and 21 districts that did not reach 2.0 cases/100 000, and 3 districts did not report any cases for 2017. Surveillance performance will need to be strengthened in these districts to ensure detection of any poliovirus that may be transmitted in these populations. A case of acute flaccid paralysis caused by a vaccine-derived poliovirus was detected in an immunocompromised child in December 2017, with a rapid, coordinated event response through the surveillance network.

Introduction

Since the beginning of the Global Polio Eradication Initiative in 1988, the numbers of cases of acute flaccid paralysis (AFP) caused by polio have dropped from approximately 350 000 cases to 21 cases in 2017, the lowest number ever recorded. The drop in cases is due to routine vaccination, supplementary immunization activities, and the efforts of the AFP surveillance network. Currently, only Afghanistan and Pakistan harbour wild poliovirus type 1. Nigeria has not encountered a case of wild poliovirus type 1 since August 2016. Wild poliovirus type 3 has not been detected since 2012, and wild poliovirus type 2 was declared eradicated in 2015.

Polioviruses occur as various strains. Wild type viruses are the natural virus strains that can cause AFP. Vaccine strains (Sabin viruses) were developed in the 1950s and 1960s and are live, attenuated strains used in the oral polio vaccine (OPV). Sabin viruses are commonly detected as coincidental findings in stool samples in countries using OPV. Related to the vaccine strains are vaccine derived polio viruses (VDPVs). These are viruses that can transmit to susceptible individuals in a population due to insufficient vaccination coverage. The prolonged transmission from person to person allows time for

accumulation of mutations in the genome and the virus may rarely revert from the protective vaccine strain to a neurovirulent form.

South Africa has one national laboratory, based at the National Institute for Communicable Diseases, for the detection of polio in patient samples. This laboratory also supports AFP surveillance in neighbouring countries (Angola, Botswana, Lesotho, Mozambique, Namibia and Swaziland). The NICD is also the regional reference laboratory for the World Health Organization polio laboratory network in the African Region, performing genetic characterisation for polioviruses received from other national laboratories in this region. South Africa has been free of wild poliovirus since 1989, and there were no wild viruses detected in the entire African region in 2017. A VDPV type 2 was detected in Mozambique at the end of 2016, and supplemental immunisation activities were conducted in 2017 to prevent the circulation of the virus. There is an outbreak of VDPV type 2 in the Democratic Republic of Congo that began in mid-2017 and is currently ongoing. Somalia has also had a VDPV type 2 outbreak that began late 2017 and two more cases have been detected in January 2018. Outside the African region, there has been one major outbreak of VDPV type 2 in Syria. Seventy-four cases of circulating VDPVs were detected in 2017, with the last being identified in September (www.polioeradication.org). In this report we summarise results of AFP surveillance for South Africa from 1 January 2017 to 31 December 2017.

Surveillance methods

Field surveillance

All cases of AFP from any health facility are notified to the National Department of Health, together with samples for investigation. Case investigation requires that two stool samples, collected within 14 days of onset of paralysis, 24-48 hours apart, be sent on ice to NICD for each case, and should arrive within 3 days of collection. Samples are accompanied by a case investigation form detailing the paralysis, vaccination status and the collection details of the stool samples from the patient. Field surveillance occurs through active case finding, with targets for the under 15-year age group monitored by the WHO to assess surveillance adequacy. The South African operational AFP target detection rate is 4/100 000 children under the age of 15 years (doubled from the 2015 target of 2/100 000), while the international target is 2/100 000. The National Polio Expert Committee (NPEC) performs case classification of all investigated AFP cases quarterly (Table 1).

Laboratory methods

Presence of poliovirus in a stool sample is identified by virus isolation and real-time PCR. Faecal material is inoculated into cell culture, and microscopic inspection of the cells for cytopathic effect may indicate a poliovirus is present. Samples with suspected polioviruses are characterised by intratypic differentiation polymerase chain reaction (PCR), which confirms the presence of poliovirus. Any identified poliovirus that is possibly wild type or vaccine derived is then sequenced to genetically classify the virus (vaccine, wild type or VDPV). All South African polioviruses are sequenced. If a possible epidemiological link is suspected through field investigations, then phylogenetic analysis can indicate transmission patterns and transmission links via the number of mutations detected.

Table 1. Classification system used by the National Polio Expert Committee in South Africa.

Status	Classification	Code	Reason
Final	Confirmed (wild type)	A1	Wild type poliovirus found in stool sample of case or one of the contacts.
	Confirmed (vaccine-associated)	B1	Vaccine-type poliovirus found in stool sample of case, which has residual paralysis at 60-day follow-up; and is confirmed clinically.
	Compatible	C1	AFP case lost to follow-up at 60 days.
		C2	Death related to the illness within 60 days.
		C3	Residual paralysis for which other no medical reason is evident.
	Discarded	D1	No residual paralysis and no wild polio found in stool samples.
		D2	Confirmed alternative diagnosis
		D3	Non-polio enterovirus isolated.
		D4	No virological investigation and a clinical picture incompatible with polio.
		D5	Two adequate negative stool specimens with 14 days of onset of paralysis
	Denotified	E1	Not an AFP case
Pending	Inadequate Information	F1	PEC is unable to make a decision due to the lack of information. The investigating team is given 30 days from the committee meeting to find further details. The final decision is taken at the next PEC meeting.
	60-day follow-up not yet done	F2	Final decision is referred to the next PEC meeting for final decision.

Results

South Africa

Sample results: 916 faecal samples were received from 470 South African cases of AFP with date of onset of paralysis between 1 January 2017 and 31 December 2017. No wild type strains were detected. Sabin (vaccine) poliovirus types 1 and 3 were detected in one case. Detection of Sabin virus from stool is usually a coincidental finding in countries using OPV; and no case was classified by the NPEC as vaccine acquired paralytic poliomyelitis (VAPP).

A VDPV type 3, with a date of onset of paralysis on the 29th December 2017, was detected in a three-month-old child in December 2017. The detection of the AFP case and virus in the sample prompted a series of events: case investigation, contact and community sampling, vaccine coverage review, and enhanced active surveillance. The child was diagnosed with a severe B-cell deficiency (agammaglobulinaemia), which prevented clearance of the poliovirus after infection. No other viruses had been detected through the contact and community sampling. The local vaccine coverage review showed that 234/488 (48%) households surveyed had at least one child under the age of five. Two hundred and ninety-two children under the age of five were surveyed and 76% (223) had Road to Health cards available. The polio vaccination schedule for South Africa comprises bivalent OPV at birth and 6 weeks, and IPV at 6, 10, 14 and 18 weeks. All age-appropriate vaccines had been administered to 77.1% (172) of the children. At least one of the Extended Program for Immunisation (EPI)-prescribed

vaccine doses were missing from 22.9% (51) of the children. Of the children that were partially immunised, 74.5% (38) missed an eligible poliovirus-containing vaccination. Active surveillance in hospitals found nine additional cases that were referred to the NPEC (Table 1).

Surveillance indicators

The AFP detection rate for South Africa was 2.3 cases of AFP per 100 000 individuals under the age of 15 years, lower than the 2016 rate of 3/100 000. While this rate was below the country target of 4.0/100 000, it exceeded the World Health Organization target of 2.0/100 000. This indicator measures the sensitivity of the surveillance program and is calculated on a district, provincial and country level (Table 2). Mpumalanga and Limpopo provinces reached the target of 4.0/100 000; Free State, Gauteng, Kwa-Zulu Natal and Northern Cape provinces reached the WHO target, but not the country target; and Eastern Cape, North West and Western Cape provinces had detection rates below 2.0/100 000.

The adequacy of the stool samples depends on the temperature at which the sample was transported, and whether two stool samples were collected 24-48 hours apart within 14 days of onset of paralysis. The samples were transported on ice with 98% of all samples received at the correct temperature, but only 49% were received within three days or had two samples collected correctly. The global target is that at least 80% of the stool samples should reach the laboratory within 72 hours of stool collection. Improvements in transport logistics are needed to ensure that the samples reach the laboratory within the stipulated timeframe, and continued health care worker awareness is needed to ensure the correct samples are collected.

The African Regional Certification Committee (ARCC) expressed concern over South Africa's poliovirus-free status in October 2017, and requested a resubmission of surveillance and routine immunisation adequacy evidence from the country.

Laboratory indicators

The laboratory results were obtained within a turnaround time of 14 days for 99% of the samples.

Table 2. Field surveillance adequacy for Acute Flaccid Paralysis (AFP) by district, South Africa, January – December 2017 (case-based data, courtesy National Department of Health).

Province	District	Population <15 years old	Non-polio AFP cases < 15 years old	Non-polio AFP detection rate (<15 years old)	AFP cases with two adequate stools 24-48 hrs apart within 14 days	AFP Stool Adequacy (%)
Eastern Cape	A Nzo DM	301,446	2	1.0	1	50
	Amathole DM	267,323	5	1.9	3	33
	Buffalo City MM	229,739	5	2.2	1	20
	C Hani DM	283,118	7	2.5	5	71
	Joe Gqabi DM	120,522	3	2.5	1	33
	N Mandela Bay MM	337,125	6	1.8	5	71
	O Tambo DM	498,162	11	2.2	2	15
	Sarah Baartman DM	130,543	3	2.3	2	67
		2,167,978	**42**	**1.9**	**20**	**41**
Free State	Fezile Dabi DM	136,262	3	2.2	0	0
	Lejweleputswa DM	129,656	1	0.8	0	0
	Mangaung MM	236,059	7	3.0	4	57
	T Mofutsanyane DM	190,239	5	2.6	2	40
	Xhariep DM	29,530	0	0.0	0	0
		721,746	**16**	**2.2**	**6**	**38**
Gauteng	Ekurhuleni MM	726,492	18	2.5	9	50
	Johannesburg MM	1,163,100	34	2.9	26	68
	Sedibeng DM	210,082	6	2.9	3	38
	Tshwane MM	759,383	11	1.4	8	62
	West Rand DM	189,276	7	3.7	3	100
		3,048,333	**76**	**2.5**	**49**	**61**
KwaZulu-Natal	Amajuba DM	175,862	5	2.8	5	83
	eThekwini MM	958,805	12	1.3	6	46
	Harry Gwala DM	180,130	1	0.6	1	100
	iLembe DM	196,668	1	0.5	2	67
	King Cetshwayo DM	355,683	9	2.5	5	45
	Ugu DM	265,863	14	5.3	8	47
	uMgungundlovu DM	324,076	11	3.4	10	77
	Umkhanyakude DM	243,379	2	0.8	2	50
	Umzinyathi DM	185,555	3	1.6	2	50
	Uthukela DM	239,827	9	3.8	6	67
	Zululand DM	301,111	3	1.0	3	100
		3,426,959	**70**	**2.0**	**50**	**60**
Limpopo	Capricorn DM	421,479	16	3.8	11	65
	Mopani DM	330,076	13	3.9	15	88
	Sekhukhune DM	347,165	19	5.5	16	73
	Vhembe DM	445,864	25	5.6	20	71

	Waterberg DM	243,505	6	2.5	7	78
		1,788,089	**79**	**4.4**	**69**	**74**
Mpumalanga	Ehlanzeni DM	620,240	18	2.9	22	81
	G Sibande DM	295,999	18	6.1	14	70
	Nkangala DM	363,702	21	5.8	23	92
		1,279,941	**57**	**4.5**	**59**	**82**
North West	Bojanala Platinum DM	508,819	2	0.4	1	50
	Dr K Kaunda DM	199,222	5	2.5	4	80
	Ngaka Modiri Molema DM	217,806	3	1.4	3	75
	Ruth Segomotsi Mompati	157,229	3	1.9	2	50
		1,083,076	**13**	**1.2**	**10**	**67**
Northern Cape	Frances Baard DM	110,675	4	3.6	3	75
	J T Gaetsewe DM	77,734	3	3.9	2	67
	Namakwa DM	28,314	2	7.1	1	50
	Pixley ka Seme DM	55,291	4	7.2	3	75
	ZF Mgcawu DM	68,757	0	0.0	0	0
		340,771	**13**	**3.8**	**9**	**69**
Western Cape	Cape Town MM	1,027,552	17	1.7	13	65
	Cape Winelands DM	221,142	6	2.7	5	53
	Central Karoo DM	18,557	0	0.0	0	0
	Eden DM	149,163	2	1.3	1	50
	Overberg DM	70,777	1	1.4	1	100
	West Coast DM	106,514	2	1.9	1	50
		1,593,705	**28**	**1.8**	**21**	**68**
South Africa		**15,450,598**	**394**	**2.6**	**293**	**65**

Legend Colour	**Non-polio AFP detection Rate**	**Stool Adequacy**
	Silent district (No reported AFP cases)	Silent district (No reported AFP cases)
	<1.0/100 000	<60%
	1.0-2.0/100 000	60-80%
	>= 2.0/100 000	>=80%

DM=district municipality, MM=metropolitan municipality

Neighbouring Countries Supported by NICD

The neighbouring countries supported by the NICD sent 1797 samples to the Polio Reference Laboratory. Thirteen samples yielded Sabin strains of polio. Two of those samples were Sabin-like poliovirus type 2, likely due to the monovalent oral polio vaccine that was used to halt VDPV type 2 circulation in Mozambique early in the year. All samples were received in good condition and 97% of

the results were returned within 14 days of receipt. The non-polio isolation rate was 18% for these samples. This implies that the sensitivity of the testing is adequate to pick up polioviruses.

The broader African region

For 2017, 87 samples were sent to the NICD for molecular analysis from both cases and contacts of cases. There was one case of VDPV type 1, four cases and one contact of VDPV type 2 that were detected in the samples sent to the NICD. All were from the Democratic Republic of Congo. The VDPV type 1 was classified as ambiguous as there were no other detections of related viruses. The VDPV type 2 viruses were circulating VDPVs, and comprised the initial detection of the outbreak that is currently ongoing in the Democratic Republic of Congo. There were 9 cases and 17 contacts from various countries that had Sabin-like poliovirus type 2 samples, most likely from mop-up campaigns using monovalent OPV type 2 to restrict VDPV type 2 circulation in countries where VDPV type 2 had been detected. Current information is available at the website for the Global Polio Eradication Initiative: www.polioeradication.org/

Environmental Surveillance for the African Region

The polio laboratory provides a reference service to the WHO by routinely testing environmental samples from eight sites in Angola, four sites in Mozambique, and four sites in South Sudan, for polioviruses. In addition, the laboratory completed parallel testing of environmental samples with the Uganda and Ivory Coast National Polio Laboratories. From 01 January 2017 to 31 December 2017, 80 samples were tested from Angola with 61 non-polio enteroviruses (76.3%) and one Sabin-like poliovirus type 3 detected. Forty-seven samples were tested from Mozambique with non-polio enteroviruses isolated from 22 samples (46.8%). Fifty-four samples were received from South Sudan with 23 non-polio enteroviruses (42.6%), one Sabin-like poliovirus type 1, and 5 Sabin-like poliovirus type 3 detected.

Conclusion

The AFP surveillance network is crucial in ensuring that the eradication of polioviruses is successful. The African Regional Certification Committee expressed concern over the poliovirus-free status due to the surveillance adequacy indicators not reaching the international targets. The 3 provinces and 21 districts not reaching the international AFP detection rate target of 2.0 cases per 100 000 individuals under the age of 5 years old (Table 1), and three silent districts, were a concern, along with stool adequacy being sup-optimal. Despite these issues, the detection of the VDPV in South Africa shows that the surveillance is able to detect and respond to a poliovirus event.

Acknowledgments

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INCREASED IMPORTATION OF DENGUE CASES INTO SOUTH AFRICA: A RISK FOR ESTABLISHMENT OF LOCAL ENDEMICITY?

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Executive summary

The global incidence of dengue has increased in recent decades. Currently, more than one-third of the world's population live in a region where dengue is endemic. Although this virus is not currently in circulation in South Africa, 176 confirmed imported cases were recorded during the period 2000 to 2016, with incidence increasing over this period. Sources of infection were Southeast Asia (38%), parts of Africa (29%), India and South-central Asia (20%), Latin America, Central America and the Caribbean (10%), and Oceania (3%). Dengue is primarily transmitted by the mosquito *Aedes aegypti*. In South Africa, populations of this species occur along the Indian Ocean coast and in portions of Limpopo, Mpumalanga and Gauteng provinces. In general, suitable environmental, climatic, vector and population vulnerability factors that could enable urban arboviral transmission are present in some parts of the country. There is therefore an urgent need to address the potential risks of dengue introduction into those parts of South Africa where it could become endemic. This can be done by establishing strategic, long-term vector surveillance programmes, by improving the country's capacity for rapid recognition and response to arbovirus outbreaks and by testing local populations, migrants and returning travellers for arbovirus infection. In this vein, a research programme to assess the current prevalence and future risk of dengue and other arbovirus endemicity in northern KwaZulu-Natal Province has recently been initiated.

Arboviruses – a global public health burden and threat

Arthropod-borne viruses (arboviruses) are important causes of human disease worldwide. Many arboviruses are endemic to Africa, and a number of them are capable of causing a haemorrhagic syndrome. Arboviruses belong to taxonomically distinct families, thus timely recognition of a specific causative agent may constitute a challenging task for laboratory and public health systems globally, but particularly in countries with poor diagnostic capacity.

In recent decades, many arboviruses have increased in importance as human pathogens. For example, in 1999 West Nile virus underwent a dramatic geographic expansion into the Americas where it caused the largest epidemic of arboviral encephalitis ever reported in this part of the world.[1] Japanese encephalitis virus, the most frequent arboviral cause of encephalitis worldwide, has spread

throughout most of Asia and as far south as Australia from its putative origin in Indonesia and Malaysia.[2]

The incidence of dengue has grown dramatically around the world in recent decades, and the World Health Organization (WHO) currently estimates that 96 million dengue cases occur in 100 countries.[3] In 2015 dengue was rated as the fastest spreading vector-borne viral disease, with global epidemic potential. Dengue is a major cause of morbidity and mortality and a leading cause of hospitalization of children in many countries in tropical and subtropical regions. The cost of dengue-related illness is considerable, ranging from loss of wages and decreased productivity to costs associated with healthcare and treatment. The cost of dengue in the Western Hemisphere alone is estimated at $ 2.1 billion annually.[4]

The recent rapid expansion of the geographic range of Zika virus is also of concern, imposing a significant burden on affected public health systems and families. Until very recently, this jungle virus was unknown outside confined regions of Africa and Asia and was generally considered to be of low public health importance globally. About ten years ago, Zika virus started to spread through the Pacific Ocean islands. In 2015, Zika virus emerged in the New World, first in Brazil and then spreading throughout Latin and Central America, the Caribbean, and into Florida, Texas, and other parts of the United States. Its spread revealed high virulence and pathogenicity, affecting thousands of infants through infection-associated microcephaly and significantly increasing numbers of Guillain-Barré syndrome.[5]

These examples exemplify a high propensity of arboviruses to become epidemic in previously unaffected areas after being introduced unintentionally via infected travellers or infected mosquito vectors. This is especially true in regions that are highly receptive and vulnerable because of the presence of an immunologically naïve population, the presence of competent vectors, suitable ecological conditions for rapid vector population growth, lack of surveillance programs and poor health systems.

Dengue virus distribution and ecology

More than one-third of the world's population currently live in a region where dengue is endemic, culminating in an estimated 390 million infections per year of which 96 million develop disease.[3] This includes sub-tropical and tropical regions in Africa (excluding South Africa), Southeast Asia, the Indian subcontinent, the Pacific Islands, Australia, South and Central America and the Caribbean.[3] In non-endemic areas, dengue is a common cause of fever in returned travellers from endemic regions, and is second only to malaria as a cause of tropical fever in affected persons.[6]

Evidence to date suggests that many arboviruses of high public health importance (including dengue, chikungunya, yellow fever & Zika) have the potential to be transmitted globally by the container-breeding mosquito, *Aedes aegypti*. This species has expanded its range from its ancestral home in the forests of sub-Saharan Africa and has become a domesticated and competent arbovirus vector that is highly abundant in urban environments in the tropics and subtropics.[7] This adaptive geographical expansion - an unwelcome companion to globalization - comes from its ability to breed in natural and artificial water-filled receptacles, and from the desiccation-resistant property of its eggs.[8] *Aedes*

albopictus is also a potential vector whose recent rapid geographical spread must be considered in arboviral risk assessment.[9]

The dengue viruses were originally confined to tropical forests in the Indochinese Region, South East Asia and in Africa in non-human primate-mosquito sylvatic cycles.[10] However, these viruses have since adapted to the domesticated vector, *Ae. aegypti*, and a peri-urban cycle of human-mosquito-human transmission.[7] In highly urbanized environments in the subtropics and tropics, water is commonly stored in open containers due to lack of access to piped water. Such storage containers provide ideal breeding conditions for these mosquitoes.[11] It thus follows that expanding human populations in the tropics may inadvertently lead to increased abundances of *Ae. aegypti* populations. Temperature increases as a result of climate change may also lead to increased mosquito abundance and an extended mosquito season beyond the summer months in certain regions.[7] Currently, outbreaks of dengue occur primarily in areas between 35º N and 35° S. These latitudes roughly correspond to a 10ºC mid-winter isotherm to which *Ae. aegypti* mosquitoes are confined.[12] Populations of the secondary vector, *Ae. albopictus,* consist of two sub-species which were formed by divergent adaptation to environmental stimuli but are nevertheless fully capable of interbreeding. One sub-species is adapted to tropical/subtropical/Mediterranean climates while the other is adapted to survive in colder latitude regions including Japan and North America.[9]

Dengue disease

Infection with one of the four existing dengue viruses may result in an asymptomatic infection, a self-limiting febrile illness or severe disease. Symptoms of dengue fever, usually lasting 5-7 days, include sudden onset of high fever, severe headaches, skin rash and myalgia and arthralgia.[13] Infection with a specific virus results in lifelong protection against re-infection with the same virus and also produces a moderate degree of cross-protective immunity against the other three virus types. However, this cross-immunity is short-lived and has no or only partial neutralising capacity. Thus, the antibodies against the infecting virus do not always block infection of the other virus types. This results in antibody-mediated uptake into cells that the dengue virus does not normally infect, such as macrophages. This phenomenon, referred to as Antibody-Dependent Enhancement (ADE) of a viral infection, results in higher levels of virus replication and a more severe form of disease such as dengue haemorrhagic fever or dengue shock syndrome.[14] This is especially the case in areas where different viruses are endemic. Up to 90% of severe dengue cases are the result of a secondary heterotypic infection, with the remainder resulting from primary infections of infants under one year old.[15] The risk of infection with different viruses is higher in areas of hyper-endemicity and amongst travellers who visit areas where different viruses are circulating. Therefore, it is important to differentiate between primary and secondary dengue infection in order to evaluate the risk of disease severity. Because of ADE, dengue and other flavivirus vaccination is problematic. Not only do antibodies to one dengue virus promote ADE of other dengue virus types, but recent studies indicate that antibodies to dengue virus can enhance the severity of Zika virus infection.[16]

Risk of dengue introduction and establishment of endemicity

Dengue virus can be introduced to non-endemic areas either through movement of infected humans or by the introduction of infected mosquitoes. The probability of importation of dengue virus via viraemic travellers into a local competent vector population is likely higher than by introduction of infected mosquitoes.[17]

Vector competence of local mosquito populations

Several species of mosquito that are potentially capable of spreading dengue virus are present in South Africa, including *Ae. aegypti.*[18] No recent data are available on vector competence of local mosquito populations for dengue virus. The only study conducted 24 years ago showed that local *Ae. aegypti* could potentially support dengue (dengue 1 and 2 viruses) and yellow fever transmission, with the Durban population being the most efficient.[19]

There is no current evidence for the presence of *Ae. albopictus* in South Africa. Nonetheless, this species occurs in other African urban areas and has previously been imported from Japan into South Africa via trade in used tyres.[20-21]

Historical autochthonous transmission of dengue in South Africa

There have been at least three likely events of autochthonous transmission of dengue in South Africa, following importation through infected human travellers. These caused outbreaks in KwaZulu-Natal in 1897, 1901 and in the summer of 1926/1927, when 50,000 cases and 60 deaths were reported. Despite the large 1926/27 outbreak, the virus did not become endemic in South Africa.[22]

Imported cases of dengue in South Africa, 2000-2016

From 2000 to 2016, returned travellers that were managed by South African health care facilities for pyrexias of unknown origin were referred for dengue diagnostic testing at the National Institute for Communicable Diseases (NICD). Of 176 dengue cases that were laboratory confirmed during this period (Figure 1), approximately 30% were male. Females formed the bulk of cases in the younger age groups (<30 years old). The mean age was 39 years old. The median age was 41 years ranging from 4 to 78 years old.

The travel duration, drawn from 113 travelers, was short-term (<30 days) for 69%, long-term for 21% and 10% were permanently resident in a dengue-endemic location, and were visiting South Africa. The median time to onset of illness after return from travel was 2 days, with a range of 3 days before and 17 days after returning (data from 24 travelers). The median consultation date at a health care facility in South Africa was approximately one week after return (data from 39 travellers).

At least 28% of the cases experienced acute illness at the time of sample collection and testing; 20% were not acute at sample collection but may have been viraemic between the time they re-entered South Africa and the date they sought medical care. IgM antibodies against dengue virus were detected in 143 of the 176 cases.

Dengue symptoms and signs were reported for 107 cases i.e. fever in 67%, thrombocytopaenia in 36%, rash in 31%, headache in 25%, myalgia in 24%, arthralgia in 15% and diarrhoea/vomiting/nausea in 20%. Thrombocytopenia and rash were significantly associated with travellers presenting with evidence of dengue infection ($p<0.0001$) (2000-2015: 36% versus 8% and 36% versus 9%).

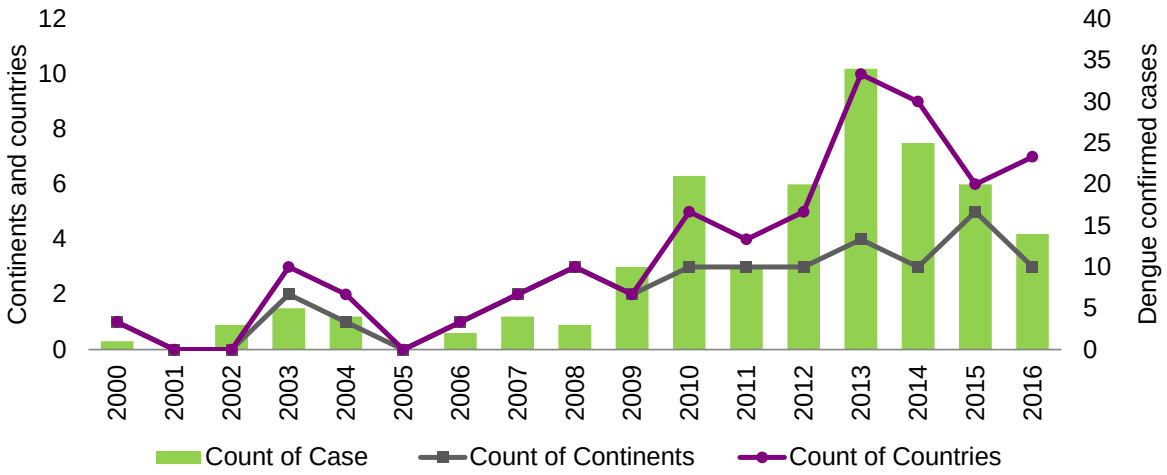

Figure 1: Imported dengue case incidence in South Africa as confirmed by the National Institute for Communicable Diseases (NICD) during the period 2000-2016 (n=176). The number of countries and continents from which these cases were imported is given by year.

Between 2000 and 2016, 119 confirmed dengue cases in South Africa occurred in travellers with known travel history. Their sources of infection were Southeast Asia (38%), parts of Africa (29%), India and South-central Asia (20%), Latin America, Central America and the Caribbean (10%) and Oceania (3%) (Figure 2). Countries from which the largest numbers of cases originated were Thailand (31), Angola (18), India (18) and Brazil (7).

Travellers with evidence of dengue infections were almost three times more likely ((2000-2015 odds ratio: 2.8 (95%CI: 1.6-4.9)) to have visited Southeast Asia than other regions. Travellers to Angola in 2013 had twice the risk ((relative risk: 2.1 (95%CI: 1.6-2.6)) of contracting dengue infection compared to those travelling to other endemic regions of the world. These data compare well with other findings showing that, between 1997 and 2006, dengue was imported most commonly from South-east Asia (51%), followed by South-central Asia (17%), Latin America (15%), the Caribbean (9%), parts of Africa (5%) and Oceania (2%).[23]

Dengue cases imported into South Africa from the Americas did not occur before 2010, appearing in 2011, 2013 and 2015. From 2000 to 2009, most dengue cases were imported from India (n=5), and cases have continued to originate from there to date. An increase in the number of cases in travellers from South-east Asia occurred between 2012 and 2015. Dengue-infected travellers from parts of Africa were regularly detected, peaking in 2013 and 2014. This coincides with an outbreak of dengue virus 1 in 2013 in Angola (12 March–July 2013). During this outbreak 1,214 suspected dengue cases were reported of which 811 (67%) were confirmed by laboratory testing, nearly all (98%) of whom resided in Luanda. Seventeen South African travelers returning from Angola were dengue-positive during the period of the outbreak.

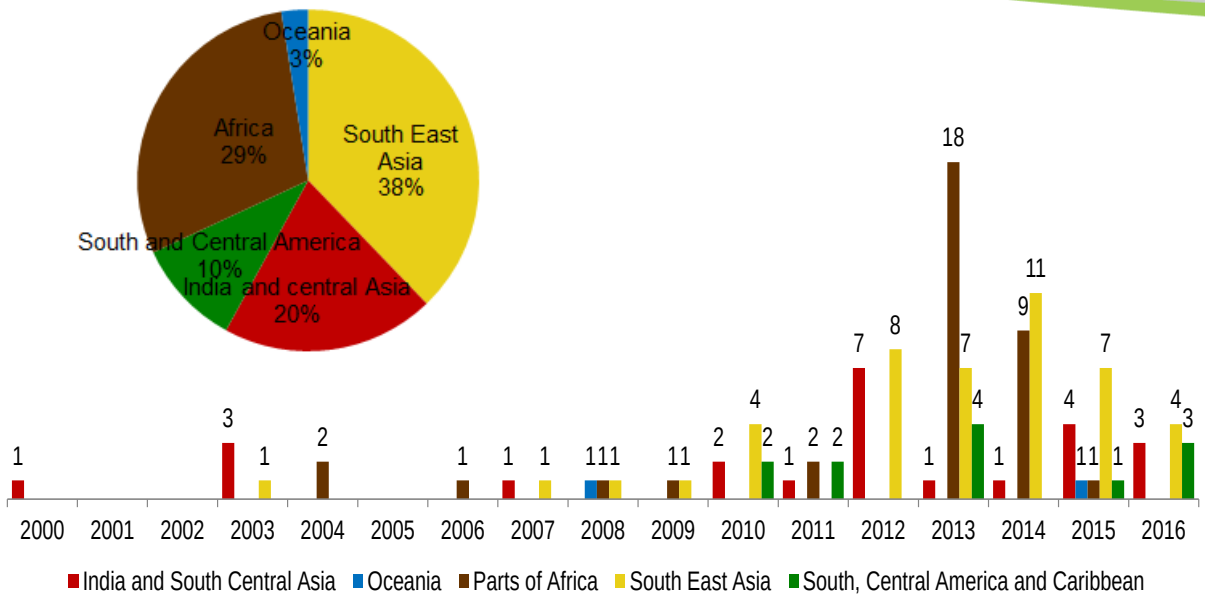

Figure 2: Dengue incidence in returning travellers to South Africa and the origin of their infections, 2000-2016.

Geographical distribution of *Aedes aegypti* in South Africa

The range of *Ae. aegypti* is concentrated along the Indian Ocean coast[18], and the eastern portions of Limpopo and Mpumalanga provinces. There are also populations of this species in Gauteng Province and in southern Limpopo (Bela-Bela).[24] Almost half of the dengue cases imported into South Africa were identified in Gauteng (48%), followed by the Western Cape (28%) and KwaZulu-Natal (19%) provinces (n=80).

Challenges and capacity building priorities

Of all emerging infectious diseases in the last decade, 29% were arthropod-borne.[25] Vector-borne diseases account for more than 17% of all infectious diseases, causing more than 1 billion cases and over 1 million deaths annually. The considerable public health and economic impacts of arboviruses are expected to continue in the 21st century, given limited domestic and international capabilities for rapid detection, identification, forecasting and controlling of epidemics. This situation is further complicated by lack of affordable and safe vaccines and chemotherapeutics.

Geographic expansion and severe outbreaks of arboviral infections with high health and socio-economic impacts are challenging public health and animal health systems in Africa, and pose biosafety and biosecurity threats. There are also insufficient surveillance and research programmes on vector-borne diseases, limited regional capacity to develop and produce diagnostic reagents, and inadequate biocontainment infrastructures for working with arboviruses. Moreover, regional external quality assurance programmes for African endemic arbovirus pathogens do not exist.

There are intricate linkages between travel, transportation of goods, migration, urbanization and health challenges. In Africa, urbanization, urban growth and increasing urban agriculture are restructuring the environment of cities, often providing suitable conditions for mosquito breeding and spread of arbovirus diseases. Poor urban conditions and limited or no access to basic services, including health services and medication, compounded by social and economic vulnerability, result in health inequities. Despite pressing needs, urban health and urban health equity have not yet emerged

as major research and policy priorities, and South Africa, like many other African countries, lags behind in addressing these issues.

There is an urgent need to address potential risks of exotic arboviruses (dengue, yellow fever, Zika) being introduced and becoming endemic in South Africa, as well as for establishing strategic, long-term vector surveillance programmes and improving the country's capacity for rapid recognition and response to arbovirus outbreaks. To address gaps in capacities in the field of arboviral diagnostics, ecology and epidemiology, promotion and implementation of One Health policies and practices are needed, as are capacity strengthening to enable rapid response to the emergence of epidemic-prone arbovirus infections, and expansion of human resource capacity with highly skilled scientific and technical staff. Further studies are required in order to elucidate which poverty indicators are most relevant to dengue and other arbovirus transmission, and in which socio-environmental contexts such transmission occurs. These studies would benefit from using standardised measures for poverty indicators amongst others and need a greater understanding of *Ae. aegypti* ecology.

Conclusions

In recent years, there has been an increase in the introduction of dengue cases from endemic countries into South Africa. Considering that suitable environmental, climatic, vector and population vulnerability factors could enable urban arboviral transmission in some parts of the country, there is a significant risk of introduction of endemic transmission of dengue and other exotic viruses.

The northern coastal plain of KwaZulu-Natal (KZN) Province was the focus of extensive arbovirus studies in the 1950s, 1960s and 1970s. Several arboviruses new to science were isolated from humans, mosquitoes and livestock in this region. The coastal plain as far south as Lake St Lucia is classified as tropical based on the 18°C mid-winter isotherm which suggests that arboviruses, including dengue, that are present in East Africa may well occur in South Africa as well. Dengue is endemic in neighbouring Mozambique and *Mozambique-South Africa* border crossings, formal and informal, are common. Therefore, northeast KZN may serve as a gateway for the importation of exotic arboviruses from Mozambique into South Africa. This necessitates adequate surveillance to evaluate the potential risk of introduction on an ongoing basis, not only by monitoring local populations, migrants, transportation of goods and returning travellers but also by monitoring vector distribution, vector competence and behavioural changes. Currently the surveillance for dengue and other arboviruses in South Africa is heavily biased towards patients that can afford private healthcare when returning home from endemic areas. It is almost certain that the available data hugely underrepresents the true burden of arbovirus infections in South Africa. To date, no recent baseline data are available from local urban or rural populations in areas at risk for arboviral infections.

Most air-travellers to South Africa arrive at Johannesburg or Cape Town where the risk of triggering autochthonous transmission is negligible due to the low abundance of competent mosquito vectors. However, ground migration of people and transportation of goods from neighbouring regions poses risks via the introduction of viraemic people and infected mosquitoes into arbovirus-permissive areas. Persons experiencing mild symptoms of arboviral infection are unlikely to seek medical care, thus introductions of dengue and other exotic arboviruses could go unnoticed until an endemic transmission cycle is established. Arbovirus diseases are probably more common than are thus far documented in South Africa, but early recognition and diagnosis remain a challenge for healthcare

professionals, particularly in the public sector. Febrile patients may be misdiagnosed as being ill with malaria or common infections such as influenza due to their similar clinical presentation. In many cases, arbovirus cases are not diagnosed at all because clinical manifestations are not always apparent and the infections are usually self-limiting, and/or access for testing is difficult. Hence, data produced by current limited passive surveillance systems do not provide accurate information on the prevalence and risk status of dengue and other arbovirus infections.

In order to better assess the current prevalence and future risk of dengue and other arbovirus endemicity in South Africa, the Centre for Emerging Zoonotic and Parasitic Diseases, NICD, in collaboration with the Provincial Departments of Health, the US Global Disease Detection Programme, CDC, and the local Poliomyelitis Research Foundation have established an arbovirus research and surveillance programme in the northern coastal plain of KZN province. This programme aims to: 1. determine the presence, seasonal abundance and vector competence of local mosquito populations, 2. establish baseline data for current prevalence and burden of arbovirus infections, 3. develop risk maps for arbovirus transmission and endemicity, 4. contribute to strengthening basic public health systems for recognition and response to arboviral infections, and 5. improve diagnostic and arboviral diseases predictive tools.

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MALARIA VECTOR SURVEILLANCE REPORT, SOUTH AFRICA, JANUARY – DECEMBER, 2017

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Executive summary

Malaria in South Africa is seasonal and primarily occurs in the Limpopo, Mpumalanga and KwaZulu-Natal provinces. The control of malaria vector mosquito species is based on indoor spraying of residual insecticides (IRS) and limited larval source management. Malaria incidence in 2017 was unusually high and was characterised by a substantial increase in sporadic, locally acquired cases. Unusually high rainfall and delayed IRS activities in some municipalities may have facilitated this higher rate of transmission. Vector surveillance in collaboration with the National Institute for Communicable Diseases (NICD) during 2017 revealed the presence of three malaria vector species - *Anopheles arabiensis*, *An. merus* and *An. vaneedeni* – which have previously been shown to contribute to ongoing residual malaria transmission in South Africa. Several closely related non-vector *Anopheles* species were also collected. Most of the specimens analysed were collected from Mpumalanga (46.8%) and KwaZulu-Natal (32.2%) provinces with smaller proportions collected from Limpopo Province (10.2%) and the Kruger National Park (10.8%). The surveillance information by province and municipality shows that IRS-based vector control needs to be maintained at a high rate of coverage, that IRS activities should ideally be completed before the onset of each malaria season and that winter larviciding based on the WHO's 'few, fixed and findable' approach may enhance the effect of IRS in high incidence areas.

Introduction

South Africa's malaria affected areas include the low altitude border regions of Limpopo, Mpumalanga and KwaZulu-Natal Provinces. These regions typically experience active malaria transmission, especially during the peak malaria season that spans the summer months of November to April. However, 2017 proved to be an extraordinary year with incidence peaking in May and October. In general, malaria incidence increased approximately three-fold (+/- 31000 cases) in 2017 over that

recorded in 2016 (9478 cases), with Limpopo and Mpumalanga provinces most affected, especially the Vhembe, Mopani (Limpopo) and Ehlanzeni (Mpumalanga) districts.[1]

Each of South Africa's malaria endemic provinces have developed well-coordinated malaria control operations including routine vector control which is primarily based on the application of indoor residual insecticide spraying (IRS) and, to a lesser extent, larval source management.[2] Although IRS has proven efficacy spanning many decades, residual malaria transmission continues and is likely caused by outdoor feeding and resting *Anopheles* vector mosquitoes that are unaffected by indoor applications of insecticide.[3,4] In addition, populations of the major malaria vector species, *Anopheles funestus* and *An. arabiensis*, have developed resistance to insecticides, especially in northern KwaZulu-Natal.[5] However, the pyrethroid resistance phenotype in *An. arabiensis* in this region is currently of low intensity and is unlikely to be operationally significant at this stage, unlike the pyrethroid-carbamate resistance profile in *An. funestus* which is of high intensity, is highly significant epidemiologically and was at least partly causative of the malaria epidemic experienced in South Africa during the period 1996 to 2000.[6]

Residual malaria transmission, substantially increased incidence and burgeoning insecticide resistance in malaria vector populations within South Africa's borders necessitate ongoing and enhanced vector surveillance. This is especially pertinent in terms of South Africa's malaria elimination agenda.[7] Currently, surveillance is routinely conducted by the entomology teams of Limpopo, Mpumalanga and KwaZulu-Natal provinces with support from partner institutions including the National Institute for Communicable Diseases (NICD), the Wits Research Institute for Malaria (WRIM), University of the Witwatersrand, the Institute for Sustainable Malaria Control, University of Pretoria and the South Africa Medical Research Council. This report summarises malaria vector surveillance in South Africa in 2017 based on specimens referred to the Vector Control Reference Laboratory (VCRL) of the Centre for Emerging Zoonotic and Parasitic Diseases (CEZPD), NICD.

Methods

During the period January to December 2017, *Anopheles* mosquitoes were collected by the provincial entomology teams and partner institution personnel. Adult specimens were obtained by rearing larvae from routine larval collections and adults were also periodically collected using trapping techniques including exit window traps, clay pots, modified buckets, human landing catches (HLC) and CO^2 baited net traps. One or more of these collection techniques were deployed at sentinel sites in Limpopo, Mpumalanga and KwaZulu-Natal provinces (Figure 1). Adult mosquitoes were preserved on silica and sent to the NICD for species identification. Identification of all mosquito specimens was based on the use of morphological keys and PCR. All results were subject to rigorous quality assurance according to the ISO/IEC 17025:2005 accreditation system before being entered into the database.

Results & Discussion

A total of 1 898 *Anopheles* mosquitoes was collected from sentinel sites during the period under review (Figure 1). Of these, 889 (46.8%) were collected from Mpumalanga, 611 (32.2%) from KwaZulu-Natal, 193 (10.2%) from Limpopo and 205 (10.8%) from the Kruger National Park. The vast majority were members of the *An. gambiae* species complex (1 551; 81.7%) and the remaining 18.3% (347) were members of the *An. funestus* species group. Subsequent PCR analysis revealed that the *An. gambiae* complex included *An. arabiensis*, *An. merus* and *An. quadriannulatus*. The *An. funestus* group

were identified as *An. rivulorum*, *An. vaneedeni*, *An. parensis*, *An. rivulorum*-like and *An. leesoni*. A summary of the species collected by relative proportion by province and species group is given in Figure 2.

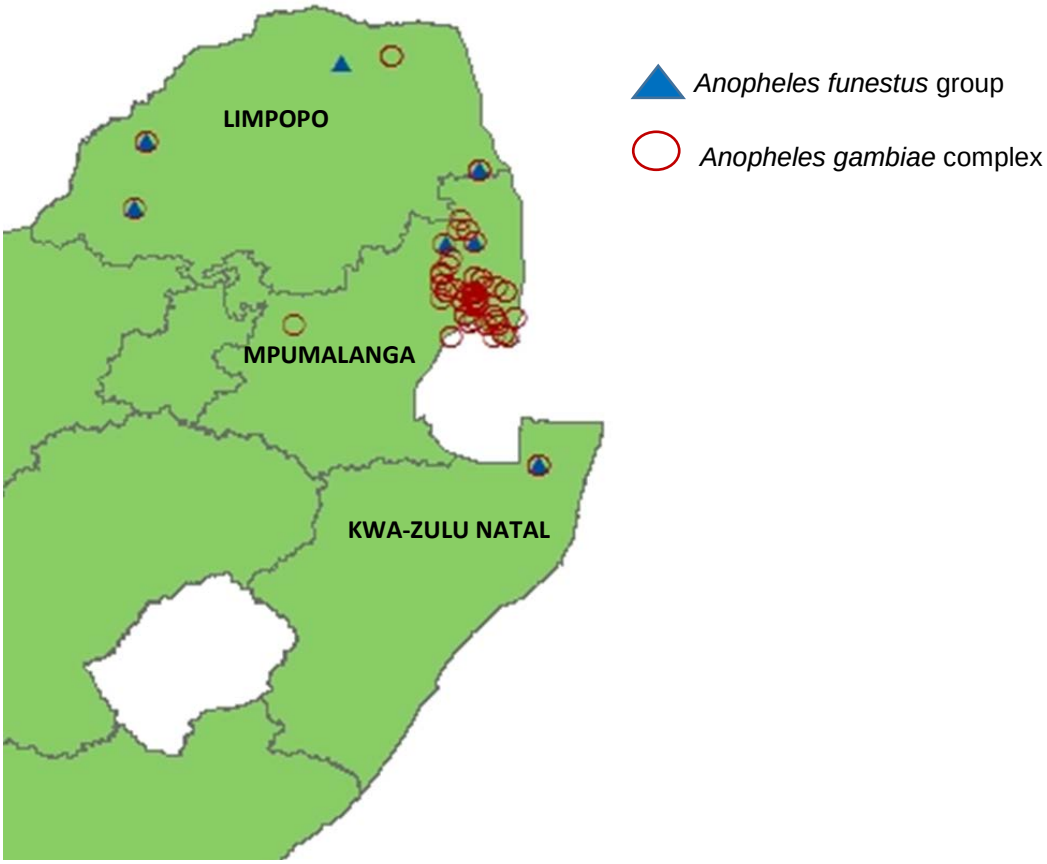

Figure 1: Malaria vector surveillance sentinel sites disaggregated by *Anopheles* species group/complex, Limpopo, Mpumalanga and KwaZulu-Natal provinces, South Africa, January to December 2017.

Anopheles arabiensis was predominant in Mpumalanga and KwaZulu-Natal provinces (Figure 2 A,C) and was collected in smaller numbers in Limpopo Province and the Kruger National Park (KNP). It is a major malaria vector in South Africa[4] with variable feeding and resting behaviours. Outdoor feeding and resting components of *An. arabiensis* populations are at least partially responsible for ongoing residual malaria transmission.

Anopheles merus was collected in the greatest relative proportion in Mpumalanga followed by KwaZulu-Natal provinces with only one specimen collected in the KNP (Figure 2 A,C,G). This species has previously been detected in Limpopo province. *Anopheles merus* is a minor or secondary malaria vector in South Africa[2] and has also been implicated in transmission in southern Mozambique. Interestingly, this species is traditionally described as a salt-water coastal breeder but the larval collections from which most of these specimens accrued were found in fresh-water breeding sites. Recent data from Mpumalanga Province suggest that this species is increasing its inland range and abundance by adapting to breeding in fresh-water habitats.

Anopheles quadriannulatus is a non-vector member of the *An. gambiae* complex that is common in the southern African region including South Africa. This species predominated in Limpopo Province and the KNP, was detected in smaller numbers in Mpumalanga Province and in low numbers in KwaZulu-Natal Province (Figure 2A,C,E,G).

Anopheles vaneedeni was collected in all three endemic provinces in varying abundance. This species tends to rest outdoors and will readily feed on humans. It has recently been implicated as a secondary malaria vector in Mpumalanga and KwaZulu-Natal provinces[3] (Figure 2 B,D,F).

No *An. funestus sensu stricto* were collected during the review period. In the absence of vector control, this species is the predominant malaria vector in the southern African region where it is especially prevalent in neighbouring Mozambique and Zimbabwe. Although the eastern Lowveld regions of South Africa form part of the natural range of this species, its absence is likely attributable to intensive IRS programmes in KwaZulu-Natal, Mpumalanga and Limpopo provinces. However, the possibility of transmission by this species in the border regions of Limpopo cannot be ruled out owing to a paucity of data from that region. Other members of the *An. funestus* group were detected in Limpopo, Mpumalanga, and KwaZulu-Natal provinces and in the KNP in comparatively low numbers (Figure 2 B,D,F,H). *Anopheles leesoni*, *An. rivulorum*-like and *An. parensis* are generally considered to be non-vector species while *An. rivulorum* has been implicated as a minor malaria vector in East Africa. The possibility of one or more of these species playing a role in residual malaria transmission in South Africa cannot be ruled out.

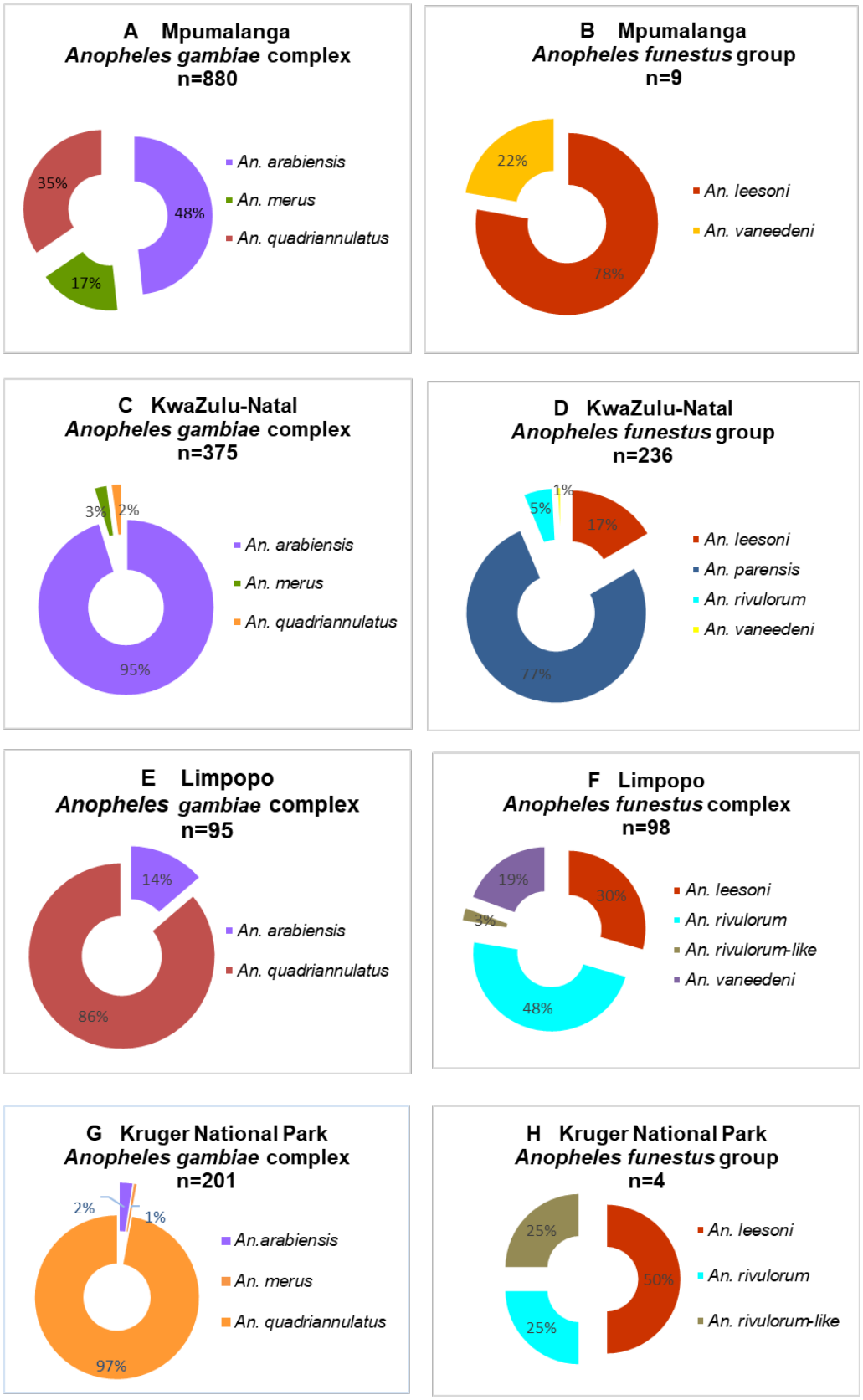

Figure 2: Relative proportions of member species of the *Anopheles gambiae* complex and *An. funestus* group by province/locality, South Africa. These proportions are based on *Anopheles* specimens collected during the period January to December 2017.

The sporadic nature of entomological surveillance activities in 2017 coupled with the sporadic occurrence of local cases negates the possibility of establishing direct correlations between the *Anopheles* samples described here and the unusually high incidence of locally acquired malaria in South Africa's endemic areas in 2017. Nevertheless, one or more confirmed or suspected vector species were detected in all of the high-incidence / high-risk municipalities of Mpumalanga and Limpopo provinces, and in the lower risk municipalities of Jozini in northern KwaZulu-Natal Province and Waterberg in western Limpopo Province (Table 1).

Table 1: Occurrence of confirmed or suspected *Anopheles* malaria vector species by province and municipality, South Africa, January to December 2017.

Province	Municipality/District	Vector species
Mpumalanga	Bushbuckridge	*An. arabiensis, An. merus, An. vaneedeni*
	Mbombela & Nkomazi	*An. arabiensis, An. merus*
Limpopo	Vhembe	*An. arabiensis, An. rivulorum*
	Mopani	*An. rivulorum*
	Waterberg	*An. arabiensis, An. vaneedeni*
KwaZulu-Natal	Jozini	*An. arabiensis, An. merus, An. rivulorum, An. vaneedeni*

Conclusion & recommendations

Several anophelines, including malaria vector species, occur in the north-eastern Lowveld regions of South Africa. Despite coordinated provincial IRS programmes that generally achieve high spray coverage rates (80% or more of targeted structures in endemic areas), populations of these species persist and at least three of them - *An. arabiensis*, *An. merus* and *An. vaneedeni* – have previously been implicated in ongoing residual transmission (tentative in the case of *An. merus*). The reasons for this are multiple and certainly include outdoor-biting and outdoor-resting components of these species. In addition, unusually high rainfall and delayed IRS activities in some municipalities may have facilitated a higher rate of transmission, notwithstanding a range of other sociological variables that are beyond the scope of this report.

Based on this information it is recommended that:

- IRS based vector control be maintained at a high rate of coverage in endemic districts
- IRS activities should ideally be completed before the onset of each malaria season
- Winter larviciding based on the WHO's 'few, fixed and findable'[8] approach be implemented to enhance the effect of IRS in high incidence areas

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EPIDEMIOLOGY OF RESPIRATORY PATHOGENS FROM INFLUENZA-LIKE ILLNESS AND PNEUMONIA SURVEILLANCE PROGRAMMES, SOUTH AFRICA, 2017

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Executive summary

Syndromic respiratory illness surveillance programmes coordinated by the National Institute for Communicable Diseases include pneumonia surveillance, influenza-like illness (ILI) (2 programmes- systematic ILI at public health clinics and viral watch) and the respiratory morbidity surveillance system. South Africa's 2017 influenza season started in week 21 and was predominated initially by influenza A(H3N2) with circulation of influenza B towards the end of the season, and co-circulation of influenza A(H1N1)pdm09 at low levels. The influenza vaccine had low adjusted effectiveness (28%, 95% CI: -11.5% to 54.5%) against any influenza virus type in South Africa during 2017.

The respiratory syncytial virus (RSV) season preceded the influenza season, starting in week 7. There was no obvious seasonality identified for *Bordetella pertussis* and *Streptococcus pneumoniae*. However, an increase in pertussis cases was noted among patients enrolled in pneumonia surveillance at Western Cape sites from July with a further increase in positive cases from October to December.

Among individuals enrolled as part of pneumonia surveillance, aged <5 years, the most common pathogen identified was RSV (24%) followed by influenza (6%) and *B. pertussis* (3%), compared to influenza (6%), RSV (2%) and *B. pertussis* (0.8%) in individuals aged ≥5 years. *Streptococcus pneumoniae* using lytA PCR of blood was detected in 7% of cases from three of the six pneumonia surveillance sites that conducted testing. Among ILI cases the commonest pathogen identified among individuals aged <5 years was influenza (10%) and RSV (10%) followed by *B. pertussis* (0.7%)%), compared to influenza (17%), RSV (2%) and *B. pertussis* (0.6%) in individuals aged ≥5 years. The overall case fatality ratio among individuals enrolled for pneumonia surveillance was 3% (131/4178).

Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) coordinates the following syndromic respiratory illness programmes: pneumonia surveillance, influenza-like illness (ILI) (2 programmes - systematic ILI at public health clinics and Viral Watch) and the respiratory morbidity surveillance system. This report describes the findings from these programmes for the year 2017 for the following core respiratory pathogens:

influenza virus, respiratory syncytial virus (RSV) and *Bordetella pertussis*. In addition, surveillance for *Streptococcus pneumoniae* was conducted at 3 pneumonia surveillance sites.

Methods

A brief summary of each surveillance programme is included below. Respiratory specimens from all sites were tested for three core pathogens: influenza virus, RSV and *B. pertussis*. As part of enhanced surveillance at three selected sites, blood specimens were tested for *S. pneumoniae*.

Description of the surveillance programmes

The primary objectives of the pneumonia and systematic ILI surveillance programmes are to describe the burden and aetiology of inpatient severe respiratory illness and outpatient ILI, respectively, in HIV-infected and HIV-uninfected individuals of all ages at selected sentinel sites in South Africa. In addition, specific objectives include describing the timing and severity of the influenza and RSV seasons, characterising circulating influenza virus strains to guide decisions around Southern Hemisphere influenza vaccine composition, annual estimates of influenza vaccine effectiveness and detecting outbreaks caused by the pathogens included as part of surveillance.

Pneumonia surveillance is an active, prospective hospital-based surveillance programme for severe respiratory illness. Patients admitted at the surveillance sites and meeting the standardized clinical case definition of severe respiratory illness (SRI) are prospectively enrolled (Table 1). Dedicated staff screen and enrol patients from Monday to Friday each week. Clinical and epidemiological data are collected using standardized questionnaires. Information on in-hospital management and outcome are collected. Samples collected and tested vary by site and case definition (Table 2). Combined nasopharyngeal and oropharyngeal swabs (NPS and OPS) are collected at all sites which conduct core surveillance. At the three enhanced sites, nasopharyngeal aspirates are collected instead of combined NPS and OPS from children <1 year. Additional samples collected at enhanced sites include blood and sputum (induced or expectorated) samples (Table 2).

The systematic ILI surveillance programme was established in 2012. It is currently active at public health clinics serviced by Edendale Hospital (EDH) and Klerksdorp Tshepong Hospital Complex (KTHC) as well as Agincourt clinic, which covers a community serviced by Mapulaneng and Matikwana Hospitals in Mpumalanga Province. Patients presenting at these sites meeting the ILI and suspected pertussis case definitions (Table 1) are enrolled prospectively. Clinical and epidemiological data are collected using standardized questionnaires and nasopharyngeal samples are collected for testing (Table 2). Dedicated staff screen and enrol patients for systematic ILI surveillance from Monday to Friday.

The Viral Watch sentinel surveillance programme, was started in 1984, to monitor influenza activity. The programme is mainly composed of general practitioners who voluntarily submit NPS or OPS from patients who meet the ILI and suspected pertussis case definitions. (Table1). Data from this programme have been used since 2005 to estimate the effectiveness of trivalent seasonal influenza vaccine (TIV) against influenza-associated medically-attended acute respiratory illness using a test-negative case-control study design.[1,2] For this report, patients with ILI presenting to the sentinel surveillance sites during the 2017 influenza season were used to calculate vaccine effectiveness (VE).

During 2017, 97 practitioners, registered across South Africa, submitted specimens throughout the year.

The respiratory morbidity surveillance system tracks trends in the number of pneumonia and influenza hospitalizations, using anonymized data from a private hospital group.

Table 1. Case definitions by age group and surveillance site/programme for the clinical syndromes included in the influenza-like illness (ILI) and pneumonia surveillance programmes, South Africa, 2017.

Case definition	Criteria	Surveillance site/programme
Influenza-like illness (ILI)	**Patients of all ages** Acute fever of ≥38°C and/or self-reported fever within the last 10 days AND cough Absence of other diagnoses	Viral watch programme and public health clinics for systematic ILI surveillance: Jouberton, Edendale Gateway and Agincourt clinics
Severe respiratory illness (SRI)	**2 days - <3 months** Any child hospitalised with diagnosis of suspected sepsis or physician diagnosed LRTI irrespective of signs and symptoms.	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, RCH/MPH
	3 months - <5 years Any child ≥3 months to <5 years hospitalised with physician-diagnosed LRTI including bronchiolitis, pneumonia, bronchitis and pleural effusion	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, RCH/MPH
	≥5 years Any person hospitalised with a respiratory infection with fever (≥38ºC) or history of fever AND cough	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, RCH/MPH
Suspected pertussis	Any patient presenting with cough illness of any duration and at least one of the following: paroxysms of cough, post tussive vomiting, inspiratory whoop **OR** Infants <1 year with apnoea, with or without cyanosis.	Viral watch programme and public health clinics for systematic ILI surveillance: Jouberton, Edendale Gateway and Agincourt clinics

EDH=Edendale Hospital, KTHC=Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, RCH/MPH=Red Cross War Memorial Children's Hospital/ Mitchell's Plain Hospital, LRTI=Lower respiratory tract infection

Table 2. Pathogens tested for by clinical syndrome/programme, surveillance site, type of specimen collected and tests conducted, influenza-like illness (ILI) and pneumonia surveillance, South Africa, 2017.

Pathogen	Programme (syndrome)	Surveillance site	Specimens collected	Tests conducted
Influenza and RSV	Viral watch (ILI)	All Viral Watch sites in 8 provinces	Nasopharyngeal (NP) and oropharyngeal (OP) flocked swabs in universal transport medium (UTM)	Multiplex real-time reverse transcription polymerase chain reaction (PCR)
	Systematic ILI	Edendale Gateway Clinic, Jouberton Clinic and Agincourt Clinic	NP and OP flocked swabs ≥1years and NPA <1years in UTM	
	Pneumonia surveillance (SRI)	RMMCH/HJH, RCH/MPH	NP and OP flocked swabs (all age groups) in UTM	
		EDH, KTHC and Matikwana/ Mapulaneng	NP and OP flocked swabs ≥ 1 years. NPA in UTM <1 years	
Bordetella pertussis	Viral watch (ILI)	All Viral Watch sites in 8 provinces	NP and OP flocked swabs in UTM	Multiplex real time PCR
			NP in Regan Lowe medium	Culture
	Systematic ILI	Edendale Gateway Clinic, Jouberton Clinic and Agincourt Clinic	NP and OP flocked swabs in UTM	Multiplex real time PCR
			NP in Regan Lowe medium	Culture
	Pneumonia surveillance (SRI)	RMMCH/HJH, RCH/MPH	NP and OP flocked swabs in UTM	Multiplex real time PCR
				Culture
		EDH, KTHC and Matikwana/ Mapulaneng	NP and OP flocked swabs ≥ 1 years, NPA in UTM <1 years in UTM	Multiplex real time PCR
			Sputum (induced/expectorated)	
			NPS in Regan Lowe medium	Culture
			Sputum (induced/expectorated)	
Streptococcus pneumoniae	Pneumonia surveillance (SRI)	EDH, KTHC and Matikwana/ Mapulaneng	Whole blood KTHC and Matikwana/Mapulaneng (All ages), Edendale (<1 year)	*lytA* real-time PCR

ILI=influenza-like illness, SRI=severe respiratory illness, EDH=Edendale Hospital, KTHC=Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, RCH/MPH=Red Cross War Memorial Children's Hospital/Mitchell's Plain. NPA=nasopharyngeal aspirate, NPS=nasopharyngeal swab

Sample collection and laboratory testing for pneumonia and ILI surveillance

Upper respiratory tract samples (NP/OP and NPA) were collected and placed into universal transport medium. Whole blood specimens were collected in EDTA-containing tubes and sputum was collected in universal containers. Upper

respiratory samples and blood were stored at 4°C at the local site laboratory, and were transported to NICD on ice within 72 hours of collection. Sputum samples were stored separately at -20°C at the local site laboratory before being transported to NICD on dry ice on weekly basis.

Detection of RSV and influenza

A commercial multiplex real-time reverse transcriptase PCR assay (Fast-Track Diagnostics, Luxembourg) was used for detection of influenza A virus, influenza B virus and RSV. Influenza A and B positive specimens were subtyped using US Centers for Diseases Control and Prevention (CDC) real-time RT PCR protocol and reagents (https://www.influenzareagentresource.org/).

Detection of B. pertussis and S. pneumoniae

Induced/expectorated sputum and nasopharyngeal samples were tested for *B. pertussis.* DNA was extracted from the clinical specimens and tested for bacterial pathogens by real-time-PCR. A specimen was considered positive for pertussis if it tested positive for *IS481* and/or *ptxS*1 genes with a Ct<45. A positive case of *B. pertussis* is defined as having either or both specimens testing positive by real-time PCR. Blood specimens were tested using quantitative real-time PCR for the presence of pneumococcal DNA (*lyt*A gene). For *lytA* testing, specimens with a *lytA* Ct-value <40 are considered positive.

Data management and analysis

Data management is centralised at the NICD where laboratory, clinical and demographic data from enrolled patients are recorded on a Microsoft Access database with double data entry. The start of the influenza and RSV seasons is defined as at least two consecutive weekly detection rates of ≥10% of influenza and RSV respectively and the season is considered to have ended when the detection rate of influenza or RSV drops below 10% for two consecutive weeks. Data included in this report are preliminary and may change as data cleaning is finalised.

Results: Pneumonia and systematic ILI surveillance

In 2017, a total of 6340 patients was enrolled into the systematic ILI and pneumonia surveillance programmes, 1996 (31%) and 4344 (69%) met the case definition of ILI and SRI respectively. Of the SRI cases, the majority (75%, 3248) presented with symptoms for ≤10 days. Numbers of samples collected and tested for each of the case definitions are shown in Figure 1. The type and number of samples collected and tested varied depending on type of surveillance and availability of suitable samples for testing. The demographic characteristics of patients enrolled in the surveillance programmes are described in Table 3. The HIV prevalence varied by age group and case definition met. Overall HIV prevalence was highest in cases with severe chronic respiratory illness (SCRI) (545/1011, 54%) and lowest in cases with severe acute respiratory illness (SARI) (523/3126,17%). HIV prevalence was highest in the 25-44-year age group across all case definitions (ILI 274/1352, 20%; SARI 523/3126, 17%; SCRI 545/1011, 54%) (Figure 2). There was a high prevalence of underlying illnesses in children aged ≤5 years, 829/2706 (31%) and 13% (102/784) among SRI and ILI cases respectively. The most prevalent underlying illness in this age group was prematurity 517/828 (62%) among SRI and malnutrition (56/100) among ILI cases.

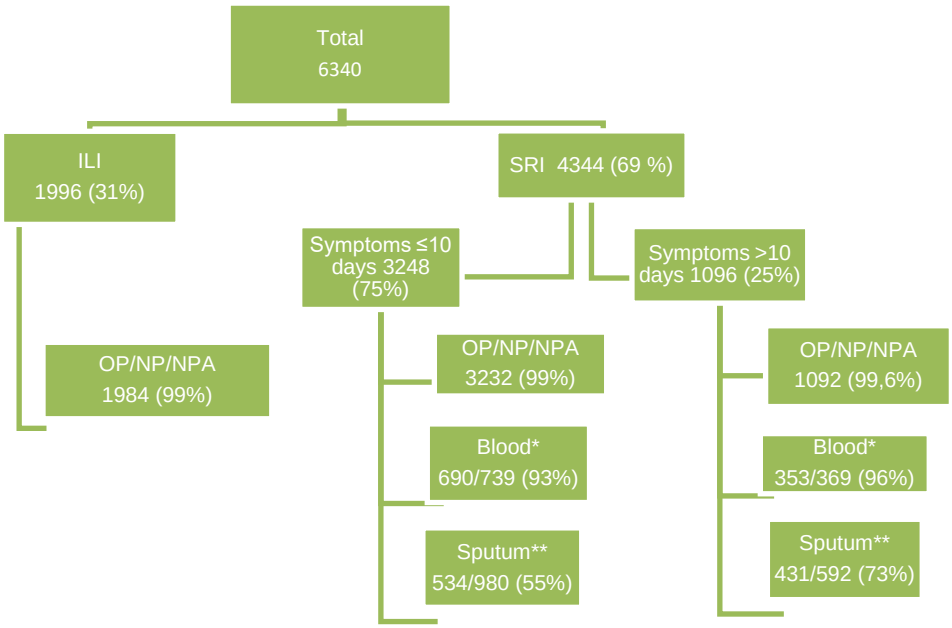

Figure 1. Numbers of samples collected by case definition in the systematic influenza-like illness (ILI) and pneumonia surveillance programmes (SRI), South Africa, 2017.

ILI=influenza-like illness, SRI=severe respiratory illness, OP=oropharyngeal, NP=nasopharyngeal, NPA=nasopharyngeal aspirate. *Blood collected from three of the six sites, Edendale only collecting from <1 years. Denominators represent total enrolled and eligible. **Sputum collected from three of the six sites. Denominators represent total enrolled and eligible.

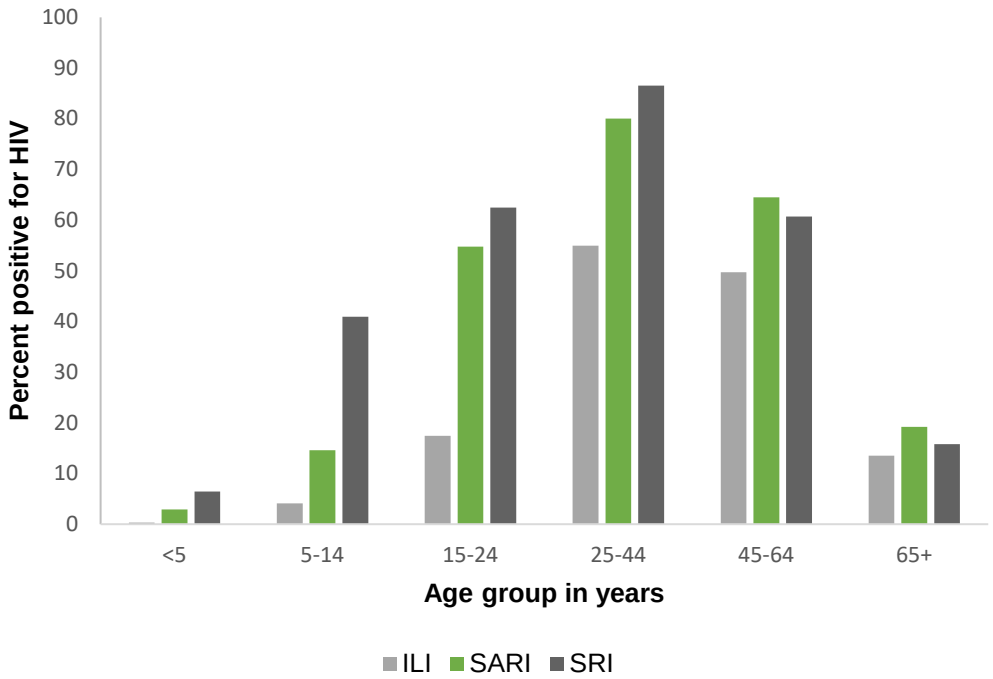

Figure 2. HIV prevalence by age group for individuals meeting case definitions of influenza-like illness (ILI=274/1352), severe acute respiratory illness (SARI=523/3126) and severe chronic respiratory illness (SCRI=545/1011), among patients enrolled in pneumonia surveillance and influenza-like illness surveillance, 2017.

Table 3. Demographic and clinical characteristics of patients enrolled into the systematic influenza-like illness and pneumonia surveillance programmes, South Africa, 2017.

Characteristic	Influenza-like illness n/N (%) N=1974	Severe acute respiratory illness n/N N=3248	Severe chronic respiratory illness n/N (%) N= 1096
Age group			
0-4	815/1974 (41)	2469/3241 (76)	285/1081 (26)
5-14	244 /1974 (12)	103/3241 (3)	27/1081 (3)
15-24	142/1974 (7)	39/3241 (1)	44/1081 (4)
25-44	397/1974 (20)	361/3241 (11)	410/1081 (38)
45-64	267/1974 (14)	196/3241 (6)	230/1081 (21)
≥ 65	109/1974 (6)	86/3241 (3)	85/1081 (8)
Female gender	1106/1922 (56)	1486/3238 (46)	494/1025 (48)
Site			
Edendale Gateway clinic	914/1996 (45)	N/A	N/A
Jouberton clinic	539/1996 (27)	N/A	N/A
Agincourt Clinic	543/1996 (27)	N/A	N/A
EDH	N/A	402/3248 (12)	245/1096 (22)
KTHC	N/A	389/3248 (12)	235/1096 (22)
Matikwana/Mapulaneng	N/A	189/3248 (6)	112/1096 (10)
RMMCH/HJH	N/A	780/3248 (74)	277/1096 (25)
RCH/MPH	N/A	1488/3248 (46)	277/1096 (21)
Underlying illness*	221/1921 (12)	893/3238 (28)	190/1025 (19)
HIV-infected	274/1352 (20)	523/3126 (17)	545/1011 (54)
Influenza positive	278/1984 (14)	140/3232 (4)	61/1092 (6)
RSV positive	108/1984 (5)	631/3232 (20)	57/1092 (5)
B. pertussis positive	11/1755 (0.6)	66/3137 (2)	20/1069 (2)
S. pneumococcus	N/A	62/693 (9)	19/359 (5)
In-hospital case fatality ratio	N/A	58/3157 (2)	73/1021 (7)

EDH=Edendale Hospital, KTHC=Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, RCH/MPH=Red Cross Hospital/Mitchell's Plain Hospital*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy.

Pneumonia surveillance programme (SRI) results–influenza and RSV

Influenza

Of the 4344 SRI cases tested for influenza, 201 (5%) were positive for influenza (Table 3). The influenza detection rate was 4% (140/3232) and 6% (61/1092) among cases with duration of symptoms ≤10 days and >10 days respectively (p=0.089), and among individuals aged <5 years (100/2739, 4%) and those aged ≥5 years (99/1573, 6%)(p<0.001). Using multivariable analysis, and compared to influenza negative cases, influenza positive cases were more likely to be older than 3 months and to report underlying illnesses. They were less likely to be enrolled from Edendale and Klerksdorp Tshepong Hospital Complex sites (AOR 0.5 95%CI 0.3-0.9) as compared to Agincourt. Mortality among influenza-positive cases was less than 1% (1/196) (Table 4).

The influenza season started in week 24, peaked in week 27 and continued through week 39. It was predominated by influenza A(H3N2) (114/201, 57%) with co-circulation of influenza B (63/201, 31%) and A(H1N1)pdm09 (23/201,11%). Influenza B predominated in the last weeks of the season (Figure 3).

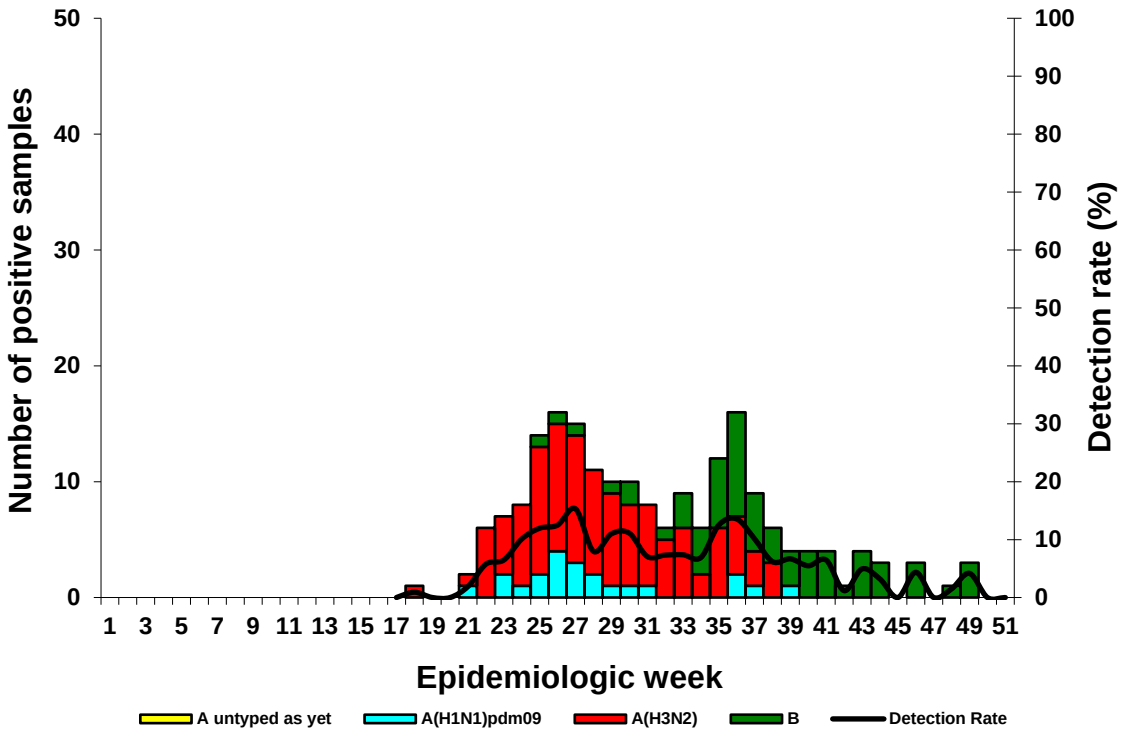

Figure 3. Numbers of samples positive for influenza and influenza detection rate, by type, subtype and week, in patients enrolled into the pneumonia surveillance programme and meeting the case definition of severe respiratory illness (SRI) in South Africa, 2017.

Table 4. Demographic and clinical characteristics associated with influenza among patients meeting the case definition for severe respiratory illness (SRI), pneumonia surveillance, South Africa, 2017

Characteristic	Influenza negative n/N (%) N=4123	Influenza positive n/N N=201	Odds ratio 95% CI- value	P-value	Adjusted odds ratio (95% CI)	p-value
Age group						
<3months	953/4117 (23)	10/200 (5)	Reference		1	1
3 months-<1 year	913/4117 (22)	42/200 (21)	4.4 (2.1- 8.8)	<0.001	**4.4 (2.2-8.8)**	**<0.001**
1-4	777/4117 (19)	49/200 (25)	6 (3.0-8.8)	<0.001	**6 (3-12)**	**<0.001**
5-24	220/4117 (5)	15/200 (8)	7 (2.9-14.6)	<0.001	**6.9 (3.0-15.6)**	**<0.001**
25-44	723/4117 (18)	35/200 (18)	5 (2.3-9.4)	<0.001	**4.8 (2.3-9.9)**	**<0.001**
45+	531/4117 (13)	49/200 (25)	9 (4.4-17.5)	<0.001	**8.9 (4.3-18.0)**	**<0.001**
Female gender	1871/4046 (46)	105/198 (53)	1.3 (1.0-.74)	0.062		
Site						
Mapulaneng/Matikwana	278/4123 (6)	23/201 (11)	Reference		1	
Edendale Hospital	609/4123 (16)	32/201 (16)	0.6 (0.4-1.1)	0.108	**0.5 (0.3-0.9)**	**0.019**
KTHC	589/4123 (15)	31/201 (15)	0.6 (0.4-1.1)	0.112	**0.5 (0.3-0.9)**	**0.028**
RMMCH/HJH	1005/4123 (24)	50/201 (25)	0.6 (0.4-1.0	0.051	0.6 (0.4-1.1)	0.078
RCH/MPH	1642/4123 (40)	65/201 (32)	**0.5 (0.3-0.8)**	**0.003**	0.6 (0.4-1.0)	0.068
Symptoms ≤10 days	3092/4123 (21)	140/201 (70)	0.8 (0.6-1.0)	0.090		
Underlying illness*	1014/4046 (25)	67/198 (34)	**1.5 (1.1-2.1)**	**0.006**	**1.7 (1.2-2.3)**	**0.002**
HIV-infected	1017/3930 (26)	50/197 (25)	0.9 (0.7-1.4)	0.876		
In-hospital mortality	130/3966 (3)	1/196 (0.5)	0.2 (0.02-.1)	0.061		

RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, KTHC=Klerksdorp Tshepong Hospital Complex, EDH=Edendale Hospital, RCH/MPH =Red Cross Hospital/Mitchell's Plain Hospital

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), prematurity, malnutrition, seizures, immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy

Respiratory Syncytial virus

Overall, RSV was detected in 16% (688/4324) of individuals hospitalised with SRI, 20% (631/3232) and 5% (57/1092) among cases presenting with symptoms for ≤10 days and>10 days respectively. The RSV detection rate was 24% (659/2739) among individuals aged <5 years and 2% (29/1573) among those aged ≥5 years (p<0.001). Using multivariable analysis, and compared to RSV negative cases, RSV positive cases were more likely to be younger than 1 year [<3 months (AOR 2,7, 95%CI: 2.1—3.5) and 3-11 months old (AOR 2.8, 95% CI:2.1- 3.6)] compared to 1-4 years, and were less likely to be in age groups older than the 1-4 age group, [AOR 0.2 ,95%CI:0.1-0.6; AOR 0.3, 95%CI: 0.1-0.6, AOR 0.3, 95%CI: 0.1-0.6 in 5-24, 24-44 and ≥ 45 years respectively]. They were more likely to present with symptom duration ≤10 days (AOR 1.6, 95%CI:1.2-2.2). They were less likely to be enrolled from Edendale (AOR 0.6 95% CI:0.3-0.9) vs Agincourt sites and to be HIV-infected (AOR 0.5, 95% CI: 0.3-0.8).

RSV circulated throughout the year. The RSV season preceded the influenza season, starting in week 7 and continuing through week 32 when the detection rate fell below 10%. The peak detection rate of 48% was in week 16 (Figure 4). The case fatality ratio among RSV-positive individuals was 1% (6/667) (Table 5).

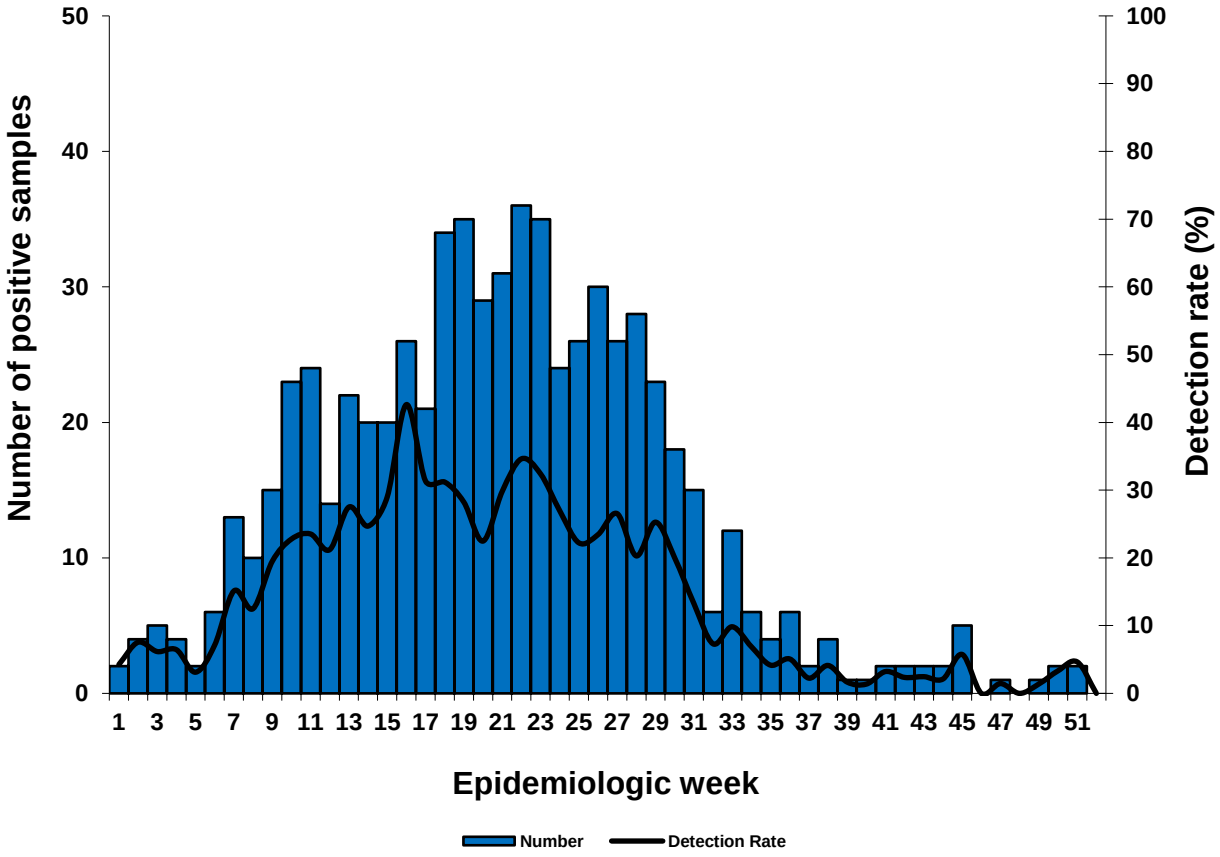

Figure 4. Numbers of samples collected and detection rates for respiratory syncytial virus (RSV), in patients meeting the case definition for severe respiratory illness (SRI), pneumonia surveillance, South Africa, 2017.

Table 5. Comparison of characteristics of respiratory syncytial virus (RSV) positive and negative patients meeting the case definition for severe respiratory illness (SRI), pneumonia surveillance, South Africa, 2017.

Characteristic	RSV negative n/N (%) N=3636	RSV positive n/N N=688	Odds ratio 95% CI-	P-value	Adjusted Odds ratio 95%CI	p value
Age group						
<3months	683/3629 (19)	280/688 (41)	3 (2.3-3.7)	<0.001	**2.7 (2.1-3.5)**	**<0.001**
3 months-<1 year	678/3629 (19)	277/688 (40)	2.9 (2.2 -3.7)	<0.00	**2.8 (2.1-3.6)**	**<0.001**
1-4	724/3629 (20)	102/688 (15)	Reference	1	1	
5-24	229/3629 (6)	6/688 (1)	0.2 (0.1-0.4)	<0.001	**0.2 (0.1-0.6**	**0.001**
25-44	745/3629 (21)	13/688 (2)	0.1 (0.1-0.2)	<0.001	**0.3 (0.1-0.6)**	**0.001**
45+	570/3629 (16)	10/688 (1)	0.1 (0.1-0.2)	<0.001	**0.3 (0.1-0.5)**	**<0.001**
Female gender	1658/3560 (47)	318/684 (46)	1.0 (0.8-1.2)	0.969		
Site						
Mapulaneng/Matikwana	267/3636 (7)	34/688 (4)	Reference		1	
Edendale Hospital	598/3636 (16)	43/688 (6)	0.6 (0.4-0.9)	0.018	**0.6 (0.3-0.9)**	**0.035**
KTHC	575/3636 (16)	45/688 (6)	0.6 (0.4-0.9)	0.042	1.1 (0.7-2.0)	0.647
RMMCH/HJH	926/3636 (25)	129/688 (19)	1.1 (0.7-1.6)	0.661	0.9 (0.6-1.5)	0.787
RCH/MPH	1270/3636 (35)	437/688 (64)	2.7 (1.8-3.9)	<0.001	1.3 (1.0-2.0)	0.156
Symptoms ≤10 days	2601/3636 (72)	631/688 (91)	4.4 (3.3-5.8)	<0.001	**1.6 (1.2-2.2)**	**0.004**
Underlying illness	909/3560 (26)	172/684 (25)	1.0 (0.8-1.2)	0.831		
HIV-infected	1044/3463 (30)	23/644 (3)	0.1 (0.05-0.1)	<0.001	**0.5 (0.3-0.8)**	**0.06**
In-hospital mortality	125/3495 (4)	6/667 (1)	0.2 (0.2-0.6)	<0.001		

RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, KTHC=Klerksdorp Tshepong Hospital Complex, EDH=Edendale Hospital, RCH/MPH =Red Cross Hospital/Mitchell's Plain Hospital

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), prematurity, malnutrition, seizures, immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy

Pneumonia surveillance programme (SRI) results– *Bordetella pertussis and Streptococcus pneumoniae*

Bordetella pertussis

Of the 4344 patients enrolled in pneumonia surveillance, 4206 (97%) were tested for *B. pertussis*. Overall, *B. pertussis* was detected in 86/4206 (2%) of patients, 66/3137 (2%) and 20/1069 (2%) among cases presenting with symptoms for ≤10 days and >10 days respectively. The *B. pertussis* detection rate was (74/2650, 3%) among individuals aged <5 years and (12/1545, <1%) among those aged ≥5 years (p<0.001). The majority of *B. pertussis* positive cases were in children <3 months (56%,48/86). Using multivariable analysis, and compared to *B. pertussis* negative patients, *B. pertussis* positive cases were more likely to be aged <3 months old (AOR 3.3, 95%CI 1.8-6.2) compared to 1-4 years, enrolled at Mpumalanga (AOR 3.5, 95%C:1.2-10.2**)** and Western Cape sites (AOR 3.3,95%CI: 1.6-6.9) compared to Gauteng sites, and to have underlying illnesses (AOR1.7 95%CI:1.1-2.7). The case fatality ratio was 1% (1/84) (Table 6). There was no apparent seasonality for *B. pertussis*. However, there was an increase in numbers of cases testing positive for *B. pertussis* from July, with a further increase in numbers of positive cases, especially from Western Cape sites in the last 3 months of the year (Figure 5). A summary of the increase in pertussis cases is available at: http://www.nicd.ac.za/index.php/increase-in-pertussis-whooping-cough-in-children-in-western-cape-province/ (Figure 5).

Table 6. Comparison of the characteristics of patients testing positive for *Bordetella pertussis* to patients who tested negative for *B. pertussis* among individuals meeting the case definition for severe respiratory illness (SRI), pneumonia surveillance, South Africa, 2017.

Characteristic	B. pertussis negative n/N (%) N=4120	B. pertussis positive n/N N=86	Odds ratio 95% CI-value	P-value	Adjusted odds ratio (95% CI)	p-value
Age group						
<3months	875/4114 (21)	48/86 (56)	3.3 (1.8-6.2)	<0.001	**3.3 (1.8-6.2)**	**<0.001**
3 months-<1 year	917/4114 (22)	13/86 (15)	0.9 (0.4-1.9)	0.704	0.8 (0.4-1.7)	0.576
1-4	789/4114 (19)	13/86 (15)	Reference		1	
5-24	223/4114 (5)	3/86 (3)	Reference	0.8 (0.4-2.9)	1.1 (0.3-3.9)	0.880
25-44	738/4114 (18)	7/86 (8)	0.6 (0.2-1.4)	0.242	0.9 (0.3-3.5)	0.825
45+	572/4114 (14)	2/86 (2)	0.3 (0.04-0.9)	0.042	0.3 (0.1-1.6)	0.168
Female gender	2155/4052 (47)	45/84 (46)	01.0 (0.6-1.5)	0.944		
Site						
Mapulaneng/Matikwana	281/4120 (7)	7/86 (8)	2.8 (1.0-7.6)	0.042	**3.5 (1.2-10.2)**	**0.020**
Edendale Hospital	624/4120 (15)	9/86 (10)	1.6 (0.6-4.1)	0.304	2.1 (0.8-5.4	0.124
KTHC	608/4120 (15)	3/86 (4)	0.6 (0.2-2.1)	0.381	0.9 (0.2-3.5)	0.911
RMMCH/HJH	1016/4120 (25)	9/86 (10)	Reference	1	1	
RCH/MPH	1591/4120 (39)	58/86 (67)	4.1 (2.0-8.3)	<0.001	**3.3 (1.6-6.9)**	**0.001**
Symptom duration ≤10 days	1049/4120 (26)	66/86 (77)	0.9 (0.5-1.5)	0.642		
Underlying illness*	1031/4052 (25)	31/84 (37)	1.7 (1.1-2.7)	0.019	**1.7 (1.1-2.7)**	**0.023**
HIV-infected	1041/3945 (26)	12/83 (15)	0.5 (0.3-0.9)	0.017		
In-hospital mortality	130/3977(3)	1/84 (1)	0.4 (0.1-2.6)	0.307		

RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, KTHC=Klerksdorp Tshepong Hospital Complex, EDH=Edendale Hospital, RCH/MPH =Red Cross Hospital/Mitchell's Plain Hospital

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy

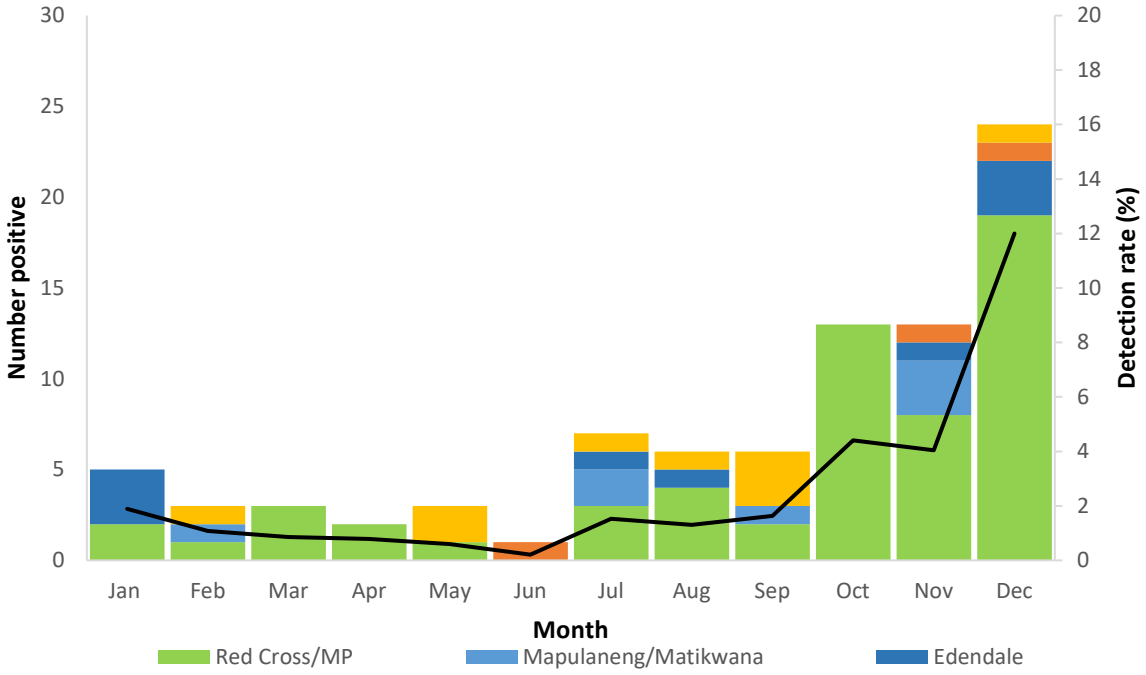

Figure 5. Detection rate and numbers of samples positive for *Bordetella pertussis by site*, among patients with severe respiratory illness (SRI) by month, Pneumonia Surveillance Programme, South Africa, 2017. MP – Mitchells Plein

Streptococcus pneumoniae

Of the 1052 blood samples tested for *S. pneumoniae,* 81 (7%) were positive. The *S. pneumoniae* detection rate was (40/455, 9%) among individuals aged <5 years and 7% (40/592) among those aged ≥5 years (p=0.219). The highest number of *S. pneumoniae* positive cases were enrolled from Klerksdorp Tshepong Hospital Complex. Compared to *S. pneumoniae* negative cases, *S. pneumoniae* positive cases were more likely to present with symptom duration ≤10 days (AOR 1.8, 95%CI:1.1-3.2). The case fatality ratio for *S. pneumoniae* was 4% (3/78) (Table 7). There was no apparent seasonality for *S. pneumoni*ae (Figure 6).

Table 7. Comparison of characteristics of patients testing positive for S*treptococcus pneumoniae* to patients who tested negative for *S. pneumoniae* enrolled as part of SRI, Pneumonia Surveillance Programme, South Africa 2017.

Characteristic	*S. pneumoniae* negative n/N (%)N=971	*S. pneumoniae* positive n/N (%) N=81	Odds ratio 95% CI-value	p-value	Adjusted odds ratio	p- value
Age group						
<3months	110/968 (11)	9/80 (11)	Reference		1	
3 months-<1 year	196/968 (20)	21/80 (10)	1.3 (0.6-3.0)	0.517	1.4 (0.6-3.1)	0.462
1-4	110/968 (11)	10/80 (13)	1.1 (0.4-2.8)	0.826	1.2 (0.2-3.0)	0.748
5-24	76/968 (8)	7/80 (9)	1.1 (0.4-3.1)	0.822	1.4 (0.5-3.9)	0.549
25-44	272/968 (28)	17/80 (21)	0.8 (0.3-1.7)	0.529	1.0 (0.4-3.2)	0.946
45+	204/968 (21)	45/80 (6)	0.9 (0.4-2.2)	0.922	1.2 (0.5-3.0)	0.642
Female gender	447/950 (47)	42/79 (53)	1.3 (0.8-2.0)	0.297		
Site						
Mapulaneng/Matikwana	265/971 (27)	23/81 (28)	Reference			
Edendale Hospital	158/971 (16)	12/81 (15)	0.9 (0.4-1.8)	0.718		
KTHC	548/971 (56)	46/81 (57)	1.0 (0.6-1.6)	0.900		
Symptom duration ≤10 days	631/971 (65)	62/81 (77)	**1.8 (1.0-3.0)**	**0.037**	**1.8 (1.1-3.2)**	**0.046**
Underlying illness*	173/950 (18)	17/79 (22)	1.2 (0.7-2.1)	0.467		
HIV-infected	423/949 (45)	35/77(45)	1.0 (0.6-1.7)	0.881		
In-hospital mortality	45/935 (5)	3/78 (4)	0.8 (0.2-2.6)	0.700		

RMMCH/HJH=Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, KTHC=Klerksdorp Tshepong Hospital Complex, EDH=Edendale Hospital, RCH/MPH =Red Cross Hospital/Mitchell's Plain Hospital

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy

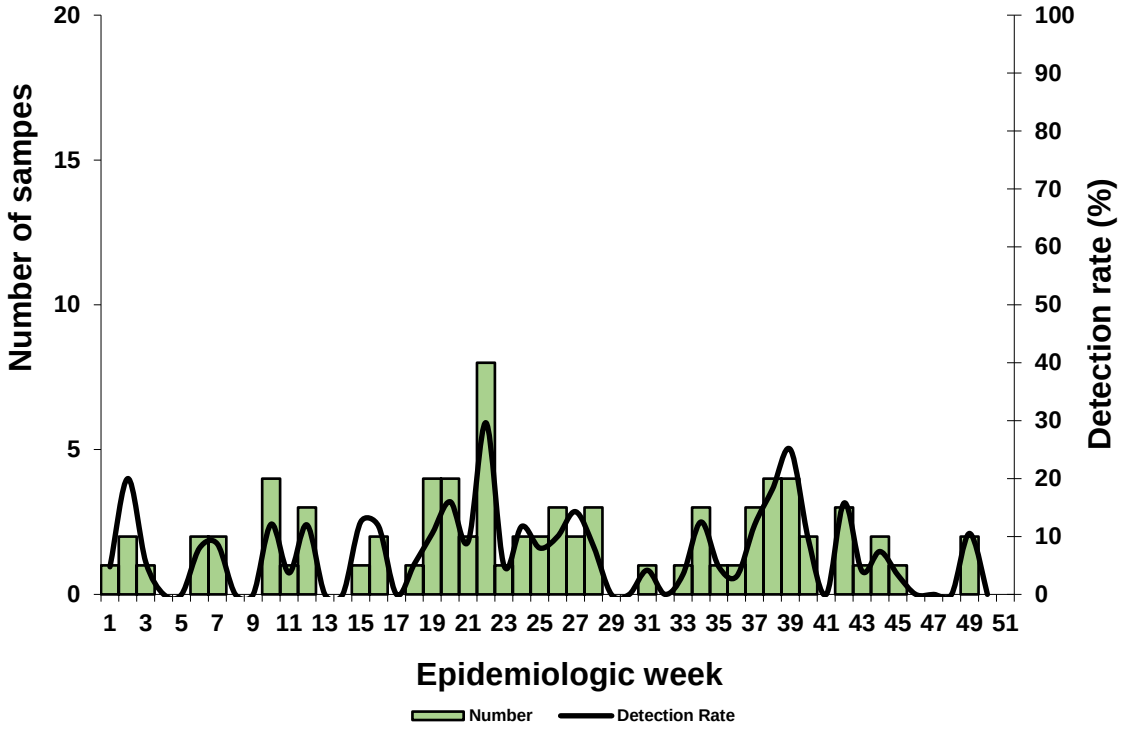

Figure 6. Numbers of positive samples and detection rate of *Streptococcus pneumoniae* from patients enrolled at enhanced sites with severe respiratory illness (SRI) by week, Pneumonia Surveillance Programme, South Africa, 2017.

Results: Systematic ILI surveillance at primary health clinics

Influenza

During 2017, 1996 patients with ILI were enrolled at the three primary health clinics and 1984 (99%) samples were tested for influenza. The overall influenza detection rate was 14% (278/1984). Of the 278 influenza positive samples, 174 (63%), 103 (37%) and1 (<1 %) were positive for influenza A(H3N2), influenza B and influenza A(H1N1)pdm09 respectively (Figure 7). The influenza detection rate was 10% (82/808) among individuals aged <5 years and 17% (195/1175) among those aged ≥5 years (p<0.001). The influenza detection rate rose above 10% in week 23 and remained above 10% until week 43 (Figure 7).

Compared to influenza negative patients, influenza positive patients were more likely to be between ages 5 and 24 years as compared to <3 months (AOR 4.5, 95% CI:1.5-16.1), and to present with symptom duration ≤10 days (AOR 1.8, 95% CI 1.1-3.1) (Table 8).

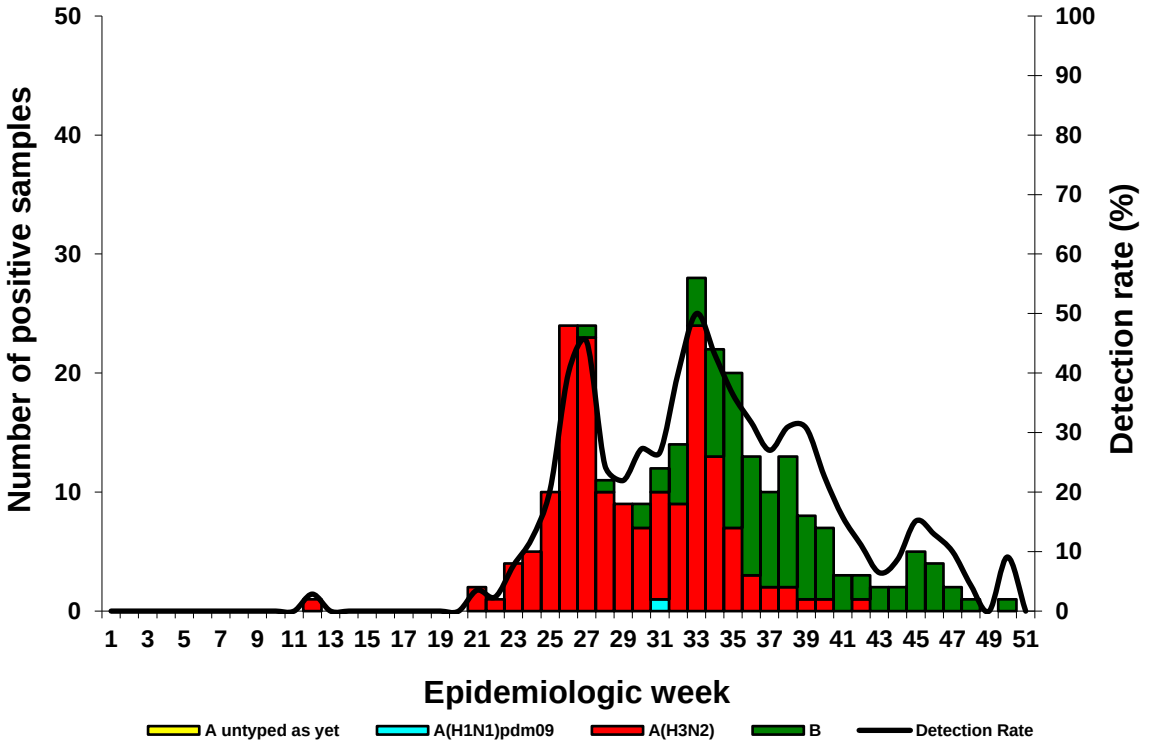

Figure 7. Influenza detection rate, by influenza type, subtype and week, in patients enrolled with influenza-like Illness (ILI) at the two primary healthcare clinics, South Africa, 2017.

Table 8. Characteristics of patients with influenza-like illness (ILI) enrolled at public health clinics testing positive for influenza compared to those who tested negative, South Africa, 2017.

Characteristic	Influenza negative (%) N=1706	Influenza positive n/N N=278	Odds ratio (95% CI)	P-value	Adjusted Odds ratio (95% CI)	p value
Age group						
<3months	54/1706 (3)	5/278 (2)	Reference			1
3 months - <1 year	248/1706 (14)	16/278 (6)	0.7 (0.2-2.0)	0.449	0.9 (0.3-3.5)	0.968
1-4	424/1706 (25)	62/278 (22)	1.6 (0.6-4.1)	0.348	2.2 (0.7-7.3)	0.199
5-24	309/1706 (18)	99/278 (36)	**3.5 (1.3-8.9)**	**0.010**	**4.5 (1.5-16.1)**	**0.009**
25-44	346/1706 (20)	51/278 (18)	1.6 (0.6-4.2)	0.334	2.3 (0.7-7.8)	0.170
45+	325/1706 (19)	45/278 (16)	1.5 (0.6-3.9)	0.415	2.2 (0.7-7.5)	0.200
Female gender	956/1644 (58)	145/266 (54)	0.6 (0.7-1.1)	0.265		
Site						
Jouberton	468/1706 (27)	63/278 (23)	Reference			
Edendale Gateway	766/1706 (45)	145/278 (52)	**1.4 (1.02-1.9)**	**0.035**		
Agincourt Clinic	472/1706 (28)	70/278 (25)	1.1 (0.8-1.9)	0.602		
Symptoms ≤10days	1427/1615 (88)	244/261 (93)	1.9 (1.1-3.2)	0.015	**1.8 (1.1-3.1)**	**0.028**
Underlying illness*	191/1643 (12)	29/266 (11)	0.9 (0.6-1.4)	0.732		
HIV-infected	237/1150 (21)	37/196 (19)	0.9 (0.6-1.3)	0.578		

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, ,seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy

Respiratory syncytial virus

Of the 1984 patients with ILI, 108 (5%) tested positive for RSV. Respiratory syncytial virus demonstrated a defined seasonality which preceded the influenza season. The RSV detection rate was 10% (82/808) among individuals aged <5 years and 2% (26/1175) among those aged ≥5 years (p<0.001). The detection rate rose above 10% in week 7 and was sustained at ≥10% until week 14 (Figure 9). The detection rate peaked at 32% in week 11. The majority of cases positive for RSV were in children <5 years (73/108, 68%). On univariate analysis, RSV positive cases compared to RSV negative cases were more likely to be younger than 5 years and were less likely to present at Edendale as compared to Jouberton clinic, and to be HIV positive. However, these were not significant on multivariable analysis (Table 9).

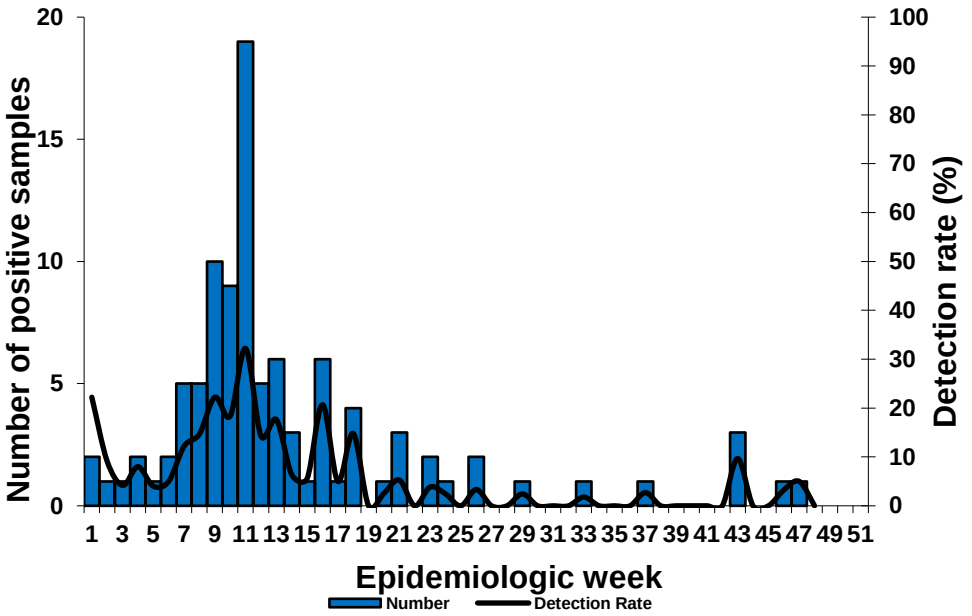

Figure 8. Detection rate of respiratory syncytial virus (RSV) by week in patients enrolled with influenza-like illness (ILI) at three primary health clinics, South Africa, 2017.

Table 9. Comparison of characteristics of patients with influenza-like illness (ILI) enrolled at public health clinics testing positive for RSV to patients testing negative for RSV, South Africa, 2017.

Characteristic	Respiratory syncytial virus negative (%) N=1854	Respiratory syncytial virus positive n/N N=108	Odds ratio 95% CI-value	P-value
Age group				
<3months	53/1876 (3)	6/108 (6)	7.6 (2.4-24.4)	0.001
3 months-<1 year	237/1876 (13)	27/108 (25)	7.6 (3.1-18.8)	<0.001
1-4	437/1876 (23)	49/108 (45)	7.5 (3.2-17.7)	<0.001
5-24	402/1876 (21)	6/108 (6)	Reference	1
25-44	386/1876 (21)	11/108 (10)	1.9 (0.7 -5.2)	0.207
45+	361/1876 (19)	9/108 (5)	1.7 (0.6-4.7)	0.335
Female gender	1038/1085 (57)	42/63 (60)	1.1 (0.7-1.7)	0.615
Site				
Jouberton	498/1876 (27)	33/108 (31)	Reference	
Edendale Gateway	876/1876 (47)	35/108 (32)	0.6 (0.4-0.9)	0.042
Agincourt Clinic	502/1876 (27)	40/108(37)	1.2 (0.7-1.9)	0.449
Symptoms ≤10 days	1580/1773 (89)	91/103 (88)	0.9 (0.5-1.7)	0.809
Underlying illness	1201/1804 (11)	15/105 (14)	1.3 (0.7-2.3)	0.363
HIV-infected	268/1283 (21)	6/63 (10)	0.4 (0.2-0.9)	0.034

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, ,seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy.

Bordetella pertussis

Of the 1621 patients enrolled with ILI and tested for *B. pertussis*, 5 (0.3%) tested positive (Table 10 and Figure 9). The *B. pertussis* detection rate was <1% (5/721) among individuals aged <5 years and <1% (6/1033) among those aged ≥5 years (p=0.769). The highest number of positive samples for *B. pertussis* was in children aged <5 years (5/11, 45%) and was from Agincourt clinic (4/5, 80%). Compared to pertussis negative patients, patients with pertussis were less likely to present with symptom duration of ≤10 days (AOR 0.5 95%CI:0.3-0.8) and to be enrolled from Edendale as compared to Agincourt (AOR 0.4, 95%CI 0.2-0.8).

Table 10. Comparison of characteristics of *B. pertussis*-positive and negative patients meeting the case definition for influenza like illness (ILI) surveillance, South Africa, 2017

Characteristic	B. pertussis negative n/N (%) N=1744	B. pertussis positive n/N N=11	Odds ratio 95% CI-value	p-value	Adjusted odds ratio	p-value
Age group						
<3months	57/1744 (3)	1/11 (9)	Reference		1	
3 months - <1 year	236 /1744 (14)	1/11 (9)	0.2 (0.02-2.4)	0.224	0.2 (0.5-1.2)	0.076
1-4	424/1744 (24)	3/11 (27)	0.3 (0.05-2.2)	0.243	0.6 (0.2-2.2)	0.460
5-24	354/1744 (20)	3/11 (27)	0.4 (0.1-2.6)	0.325	1.1 (0.3-3.6)	0.929
25-44	367/1744 (21)	0/11 (0)	0.1 (0.002-1.3)	0.072	0.6 (0.2-2.2)	0.444
45+	306/1744 (18)	3/11 (27)	0.4 (0.1-3.0)	0.402	0.4 (0.1-1.7)	0.241
Gender						
Female gender	961/1679 (57)	3/10 (30)	0.3 (0.1-1.2)	0.100		
Site						
Jouberton	520/1744 (30)	5/11 (45)	Reference			1
Edendale Gateway	894/1744 (51)	0/11 (0)	**0.1 (0.01-0.9)**	**0.047**	**0.5 (0.3-0.8)**	**0.003**
Agincourt Clinic	330/1744 (19)	6/11(55)	1.9 (0.6-5.8)	0.287		
Symptom duration ≤10 days	1503/1650	5/9 (56)	0.1(0.03-0.5)	0.002	**0.4 (0.2-0.8)**	**0.016**
Underlying illness	182/1678 (11)	0/10 (0)	0.4 (0.02-6.7)	0.517		
HIV-infected	267/1321 (20)	2/5 (40)	2.6 (0.4-15.8)	0.291		

*Underlying conditions included any of the following: Asthma, other chronic lung disease, chronic heart disease (valvular heart disease, coronary artery disease, or heart failure excluding hypertension), prematurity, malnutrition, ,seizures, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy), neurological disease (cerebrovascular accident, spinal cord injury, seizures, neuromuscular conditions) or pregnancy.

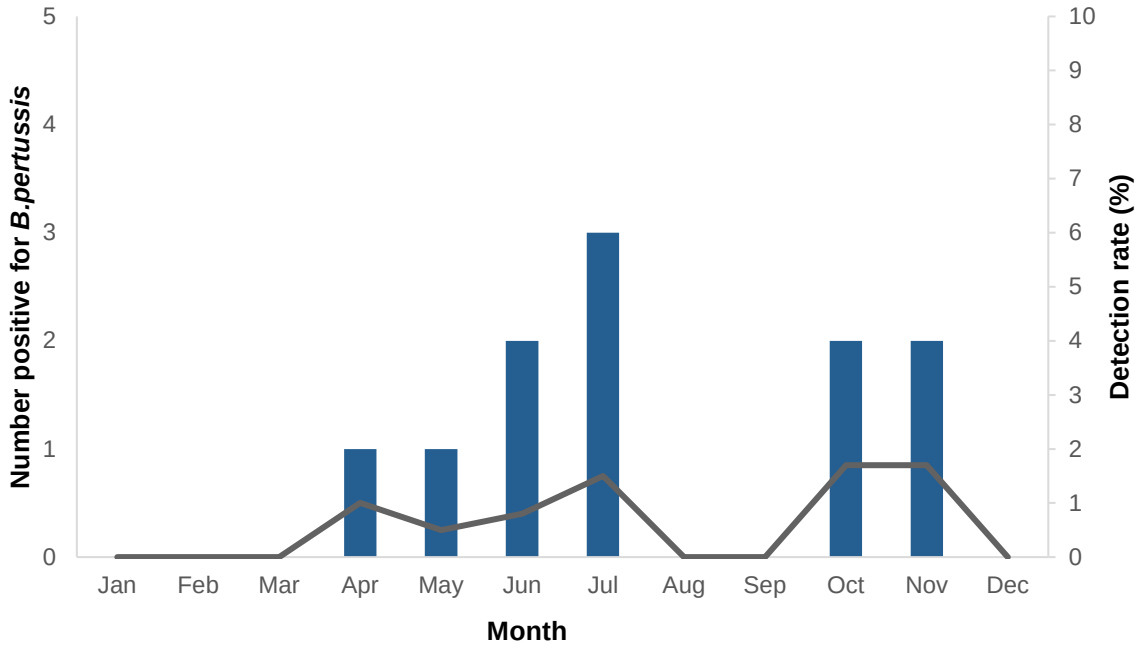

Figure 9. Numbers of positive samples for *Bordetella pertussis* among patients enrolled with influenza-like illness (ILI) at three primary health clinics, South Africa, 2017.

Viral watch (VW)

In 2017, 97 general practitioners across eight of South Africa's nine provinces (KwaZulu-Natal excluded) participated in the VW programme. A total of 1318 samples was tested for influenza; of these 682 (52%) tested positive. The season was dominated by influenza A(H3N2) (488/682, 72%), followed by influenza B (150/682, 22%) and influenza A(H1N1)pdm09 (41/682, 6%). Dual influenza positive A(H1N1)pdm09 and A(H3N2) was detected in two patients and dual influenza A(H3N2) and influenza B in one patient. The season started in week 21, peaked in week 32 and ended in week 42 (Figure 10). Of the 1318 samples tested for RSV, 22 (2%) were positive.

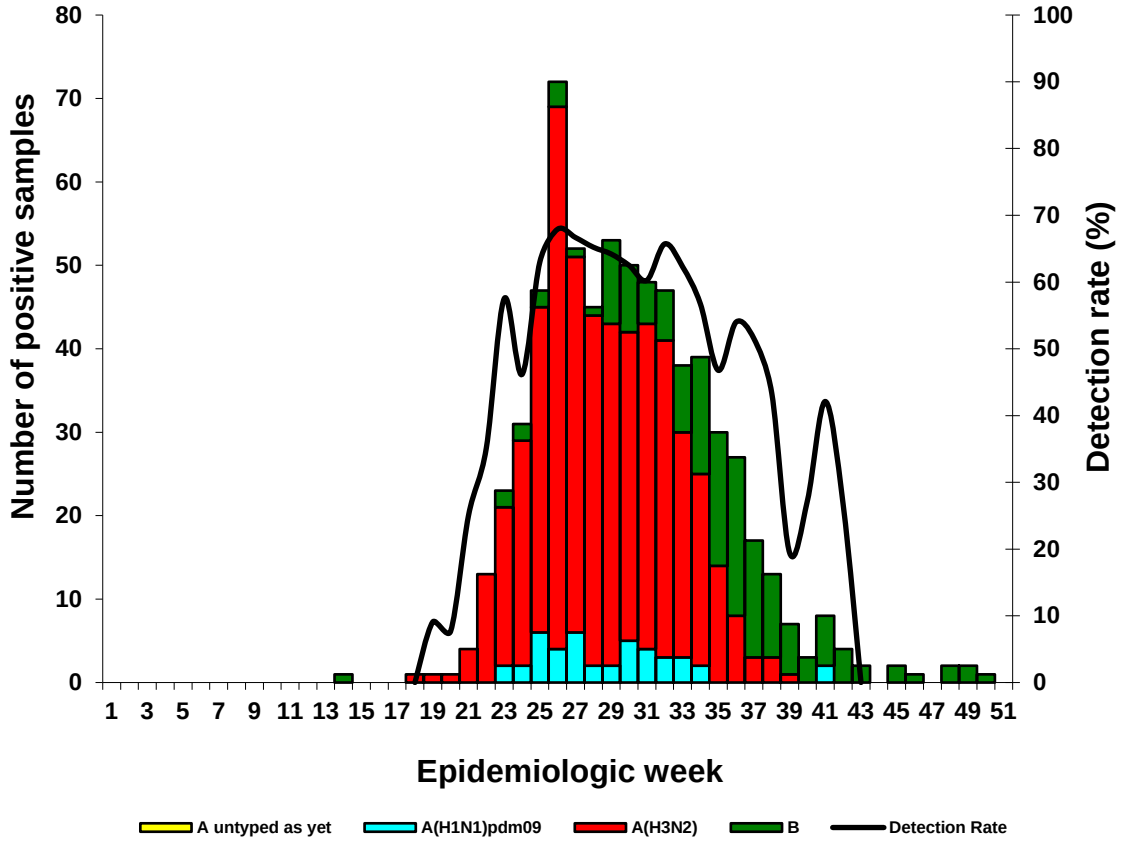

Figure 10. Numbers of samples and influenza detection rate by viral type, subtype and week for patients meeting the case definition of ILI, Viral Watch programme, South Africa, 2017.

Respiratory morbidity surveillance

During 2017 there were 1 175 888 consultations reported to the NICD through the respiratory morbidity data mining surveillance system. Of these, 29 134 (2%) were due to pneumonia or influenza (P&I) (International Classification of Diseases 10 codes J10-18). There were 21 563 (74%) inpatients and 7 571 (26%) outpatients with P&I discharge data.

An increase in P&I consultations and admissions was observed during the period with a higher number of seasonal influenza virus isolations reported to the viral watch and pneumonia surveillance programmes respectively (Figures 11 & 12). A second lower peak preceded the influenza season, corresponding to the circulation of respiratory syncytial virus.

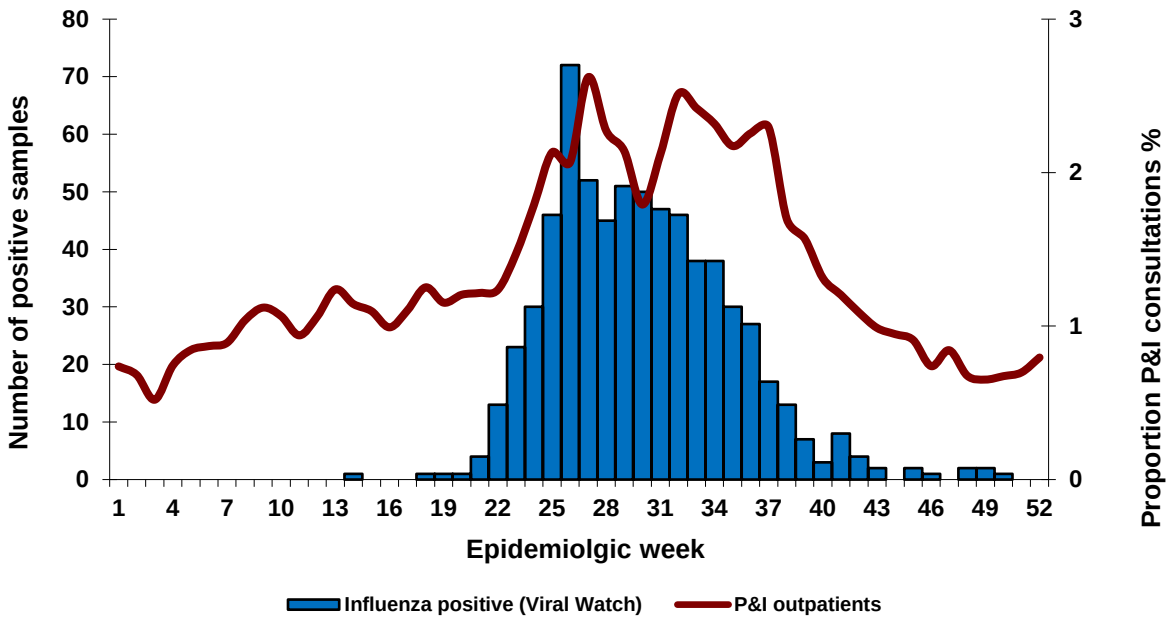

Figure 11. Numbers of private hospital outpatient consultations with a discharge diagnosis of pneumonia and influenza (P&I), and numbers of influenza positive viral isolates (Viral Watch) by week, South Africa, 2017.

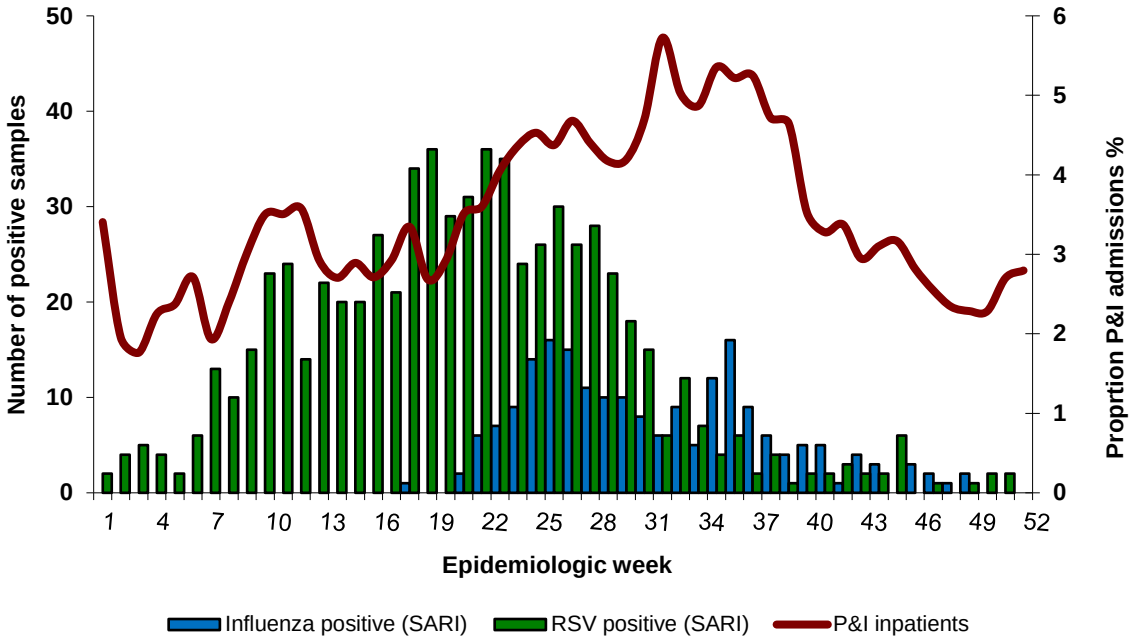

Figure 12. Numbers of private hospital admissions for pneumonia and influenza, as well as numbers of influenza positive viral isolates and respiratory syncytial virus (RSV) positive isolates SRI by week, South Africa, 2017.

Vaccine effectiveness (VE), 2017 influenza season

Of the 1177 individuals enrolled in Viral Watch and tested during the influenza season, 1136 (97%) were eligible for the VE analysis. The influenza detection rate was 57% (653/1136) amongst individuals included. The majority of influenza detections were influenza A(H3N2) which accounted for 481/653 (74%) of the total influenza subtypes, followed by influenza B which accounted for 139 (21%) of detections with the remainder being influenza A(H1N1)pdm09. Overall, the influenza vaccine coverage was 8% (88/1136), 6% (43/635) in cases and 9% (45/483) in controls. Coverage in patients with underlying conditions was 11% (6/53) in cases and 16% (8/50) in controls, and in those aged ≥65 years was 15% (8/88) in cases and 23% (8/34) in controls. The overall VE estimate, adjusted for age, underlying conditions and seasonality, was 28% (95% CI: -11.5% to 54.5%) against any influenza virus type, -31.2% (95% CI -297.2% to 56.6%) against influenza A(H1N1)pdm09, 33.8% (95% CI:-10.5.% to 60.4%) against influenza A(H3N2) and 19.8 (95%CI -71.0% to 62.4%) against any lineage of influenza B.

Discussion

The influenza season in South Africa in 2017 was predominated by influenza A(H3N2) with co-circulation of influenza B and influenza A(H1N1)pdm09. In all the surveillance programmes, circulation in the initial period of the season was almost exclusively A(H3N2) with influenza B predominating during the last weeks of the season. The season started earlier at the ILI sites, week 21 in the Viral Watch programme and week 22 at the public clinics, compared to the pneumonia sites which only reflected the start of the season in week 24. The 2017 season started two weeks later than the 2016 season. However, it was within the average onset period compared to previous years in which the mean onset was week 22 (range 17-28), with an average duration of 13 weeks (range 7-25). The influenza vaccine had low effectiveness in South Africa in 2017. The low vaccine coverage affected statistical estimates of the significance of VE among sub-groups such as individuals >65 years of age and individuals with underlying illness. Additional information from this surveillance programme, including information on the risk groups for severe illness[3-5], annual estimates of influenza vaccine effectiveness[1,2] and details of virus characterisation are presented in different reports and complement the information presented here.

The RSV season preceded the influenza season, starting at the same time as in 2016, in week 7 at the ILI sites and in week 8 at the pneumonia surveillance sites. There was no obvious seasonality identified for *S. pneumoniae* and *B. pertussis*. The surveillance programme identified an increase in pertussis cases from the sentinel sites in the Western Cape, which was predominantly in children <3 months. A summary of the increase in pertussis cases is available at: http://www.nicd.ac.za/index.php/increase-in-pertussis-whooping-cough-in-children-in-western-cape-province/. In response to this increase an alert was circulated to clinicians in the Western Cape Province to keep a high index of suspicion for pertussis and to initiate early treatment and public health action.

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