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Acute flaccid paralysis surveillance is the mainstay of the global polio eradication initiative, which aims to eradicate polio by 2018. All suspected acute flaccid paralysis cases require laboratory investigation of stool samples for poliovirus. For January to December 2016, the South African national acute flaccid paralysis rate was 3 per 100 000 children under 15 years of age. This rate is above the previous target from 2014 of 2/100 000 but not yet at the 2015-2016 heightened target of 4/100 000. Surveillance adequacy amongst various districts was heterogeneous, with 2 silent districts and 5...

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Epidemiology of respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, South Africa, 2016

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 2016 influenza season started in week 19 and reflected mixed circulation of influenza subtypes with initial circulation of influenza B, followed by influenza A(H3N2) and influenza A(H1N1)pdm09 as the season progressed. The 2016 influenza season started two weeks later than the 2015 season, but was within...

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Microbiologically confirmed tuberculosis in South Africa, 2004-2015

South Africa has the highest incidence of TB in the world. A total of 3 327 876 mPTB cases occurred in South Africa between 2004 and 2015. Four provinces (KwaZulu-Natal, Eastern Cape, Gauteng and Western Cape) accounted for 74.2% of the absolute mPTB burden in South Africa during 2015. mPTB incidence rates are on the decline with reductions of -4.1%, -6.0% and -4.8% year-on-year for 2013, 2014 and 2015 respectively, which is half of that required by the WHO End TB Strategy. Females between the ages of 25-44 have shown the sharpest decline in incidence rates...

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FOREWORD

South Africa has the highest incidence of tuberculosis (TB) in the world. KwaZulu-Natal, Eastern Cape, Gauteng and Western Cape provinces account for the vast majority of South Africa's TB cases. Fortunately, microbiologically confirmed pulmonary tuberculosis (mPTB) incidence rates are now declining. This issue details trends in mPTB incidence in South Africa for the period 2004 to 2015. Also in this issue is the 2016 respiratory diseases surveillance report for South Africa, which shows that the influenza vaccine had low effectiveness last year.

South Africa's 2016/17 malaria season is now drawing to a close. The malaria vector surveillance report for 2016 reveals the presence of three vector species - *Anopheles arabiensis, An. merus* and *An. vaneedeni* – which contribute to ongoing residual malaria transmission in South Africa. Distribution details of each of these and other species are given in this issue, which also contains the 2016 acute flaccid paralysis surveillance report for polio in South Africa and other African countries. Acute flaccid paralysis surveillance is the mainstay of the global polio eradication initiative, and this report shows that surveillance needs to be strengthened in certain districts within South Africa.

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

Basil Brooke,
Editor

Acute flaccid paralysis surveillance for polio, South Africa and other African countries, 2016

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Executive summary

Acute flaccid paralysis surveillance is the mainstay of the global polio eradication initiative, which aims to eradicate polio by 2018. All suspected acute flaccid paralysis cases require laboratory investigation of stool samples for poliovirus. For January – December 2016, the South African national acute flaccid paralysis rate was 3 per 100 000 children under 15 years of age. This rate is above the previous target from 2014 of 2/100 000 but not yet at the 2015-2016 heightened target of 4/100 000. Surveillance adequacy amongst various districts was heterogeneous, with 2 silent districts and 5 districts with case detection rates at less than 1/100 000. Surveillance should be strengthened in these areas and vigilance maintained for any imported case.

Introduction

The National Institute for Communicable Diseases (NICD) serves as the national polio reference laboratory for acute flaccid paralysis (AFP) surveillance for South Africa and neighbouring countries including Botswana, Lesotho, Swaziland, Mozambique and Namibia, as well as Angola. In addition, the NICD is a regional reference laboratory for the World Health Organization polio laboratory network within the African region, performing molecular characterisation of suspected polio isolates from other national laboratories including, but not limited to, Central African Republic, Ethiopia, Zimbabwe, Ghana, Kenya, Madagascar, Democratic Republic of Congo, Senegal, Uganda and Zambia.

In 2016, there were historic changes in the global polio eradication initiative. Following the declaration of eradication of wild poliovirus type 2 in September 2015, April 2016 saw a globally coordinated withdrawal of Sabin poliovirus type 2 worldwide, termed the 'switch' from trivalent to bivalent oral polio vaccine. Since the switch, the NICD has upgraded its facilities to incorporate a biosafety level 3 laboratory equipped to deal with poliovirus type 2 material in a high containment environment.

Background to polio epidemiology

The polio eradication initiative dates to May 1988 when the 41st World Health Assembly adopted a resolution to globally eradicate polio. Polio would be the second human disease eradicated, the only other being smallpox, eradicated in 1979. The number of polio-endemic countries has reduced from more than 125 in 1988 to only three currently - Nigeria, Pakistan and Afghanistan - with a greater than 99% reduction in the number of global polio cases. In 2012, global eradication of polio was declared a programmatic emergency for public health, and in May 2014 further declared a Public Health Emergency of International Concern. The new target for global certification of polio eradication has been set for 2018.

Currently, only wild poliovirus type 1 continues to circulate. For wild poliovirus type 3, the last detection event occurred in Nigeria in 2012. For wild poliovirus type 2, the last identification was in India in 1999. For South Africa, the last wild type polio case occurred in 1989.

Surveillance methods

Field surveillance

Surveillance is conducted through national notification of all cases of acute flaccid paralysis from any health facility to the National Department of Health, together with appropriate sample collection. Adequate case investigation requires that two stool samples be sent to NICD for each case, collected within 14 days of onset of paralysis, 24-48 hours apart, and must arrive at the laboratory on ice within 3 days of collection. 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 (doubled from the 2015 target of 2/100 000). Case classification of all inadequately investigated AFP cases is performed quarterly by the National Polio Expert Committee (Table 1).

Laboratory methods

Virus isolation is performed by inoculation of faecal material into cell culture, followed by microscopic detection of cytopathic effect caused by enteroviruses. Samples with suspected polioviruses are characterised by PCR, termed 'intratypic differentiation'. Any identified poliovirus is then sequenced to further classify the virus (vaccine, wild-type or vaccine derived poliovirus (VDPV)). Phylogenetic analysis can indicate transmission patterns and transmission links via the number of mutations detected through sequence analysis.

Results

South Africa

Sample results: 1035 faecal samples from 526 South African cases of acute flaccid paralysis were processed. No wild type or VDPV strains were detected. Sabin (vaccine) polioviruses were isolated from seven cases. Detection of Sabin virus from stool is usually a coincidental finding in oral polio vaccine (OPV)-using countries and no case was classified by the National Polio Expert Committee NPEC as vaccine associated paralytic poliomyelitis (VAPP).

Surveillance adequacy: The 2016 national non-polio AFP detection rate in children less than 15 years of age was 3/100 000. In comparison, the national non-polio AFP rate for 2015 was 3.2/100 000 and for 2014 was 2.5/100 000, according to annual polio update reports. Of South Africa's nine provinces, only Mpumalanga met the new surveillance target with a rate of 7.1/100 000. Of 52 districts, 13 districts obtained the target detection rate, with two silent districts. This data reflects that most districts are not reaching the new target. For the full list, see Table 1.

Laboratory surveillance indicators showed that 99% of samples reported within fourteen days of receipt (target of 80%). The non-polio enterovirus isolation rate was 14% (target 10%) showing adequate laboratory systems for enterovirus detection. More than 45% of samples were received beyond 3 days of collection, showing difficulties with logistics concerning sample transport to the laboratory.

Table 1. Classification system used by the National Polio Expert Committee, 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.

Table 2. Field surveillance adequacy for acute flaccid paralysis by district, South Africa, January – December 2016 (case-based data, courtesy National Department of Health).

Districts	Population non-polio AFP under 15 years of age	Non-polio AFP cases (under 15 years)	Non-polio AFP detection rate (under 15 years)	AFP cases with two adequate stools 24-48 hours apart within 14 days	Stools adequate rate (%)
A Nzo DM	301 726	6	2	5	83
Amathole DM	269 612	10	3.7	9	90
Buffalo City MM	229 061	5	2.2	4	80
C Hani DM	283 478	4	1.4	4	100
Joe Gqabi DM	120 678	1	0.8	1	100
N Mandela Bay MM	336 721	7	2.1	7	100
O Tambo DM	498 847	12	2.4	9	75
Sarah Baartman DM	130 338	4	3.1	3	75
Fezile Dabi DM	136 576	4	2.9	4	100
Lejweleputswa DM	136 603	4	2.9	3	75
Mangaung MM	234 916	3	1.3	3	100
T Mofutsanyane DM	195 614	8	4.1	7	88
Xhariep DM	31 173	1	3.2	0	0
Ekurhuleni MM	730 979	23	3.1	17	74
Johannesburg MM	1 151 935	37	3.2	29	78
Sedibeng DM	212 617	10	4.7	9	90
Tshwane MM	750 173	15	2	11	73
West Rand DM	191 354	9	4.7	8	89
Amajuba DM	174 586	7	4	7	100
eThekwini MM	963 624	13	1.3	11	85
iLembe DM	178 497	9	5	9	100
Harry Gwala DM	196 118	8	4.1	5	63
Ugu DM	264 219	8	3	6	75
uMgungundlovu DM	321 593	19	5.9	15	79
Umkhanyakude DM	243 945	2	0.8	1	50
Umzinyathi DM	186 532	5	2.7	2	40
Uthukela DM	240 302	8	3.3	8	100
King Cetshwayo DM	354 331	9	2.5	7	78
Zululand DM	301 261	6	2	6	100
Capricorn DM	421 539	9	2.1	6	67
Gr Sekhukhune DM	332 426	14	4.2	14	100
Mopani DM	347 674	14	4	13	93

Districts	Population non-polio AFP under 15 years of age	Non-polio AFP cases (under 15 years)	Non-polio AFP detection Rate (under 15 years)	AFP cases with two adequate stools 24-48 hours apart within 14 days	Stools adequate rate (%)
Vhembe DM	444 113	4	0.9	2	50
Waterberg DM	240 023	2	0.8	2	100
Ehlanzeni DM	620 876	49	7.9	48	98
G Sibande DM	300 467	16	5.3	16	100
Nkangala DM	364 056	25	6.9	23	92
Bojanala Platinum DM	502 223	6	1.2	5	83
Dr K Kaunda DM	199 551	4	2	3	75
Ngaka Modiri Molema DM	221 145	6	2.7	6	100
Ruth Segomotsi Mompati DM	158 450	9	5.7	7	78
Frances Baard DM	111 725	3	2.7	3	100
J T Gaetsewe DM	77 548	5	6.4	5	100
Namakwa DM	29 157	0	0	0	0
Pixley ka Seme DM	55 773	2	3.6	1	50
ZF Mgcawu DM	69 041	2	2.9	2	100
Cape Town MM	1 026 629	22	2.1	14	64
Cape Winelands DM	219 535	5	2.3	5	100
Central Karoo DM	18 761	0	0	0	0
Eden DM	149 587	5	3.3	4	80
Overberg DM	70 384	2	2.8	2	100
West Coast DM	106 238	1	0.9	1	100
South Africa	**15454330**	**462**	**3.0**	**394**	**85**

Colours shown per 'traffic light system' – green represents detection rate above 4/100 000; yellow represents 2-4/100 000; red represents <2/100 000; blue represents silent districts. Stool adequacy defined as two stools sent on ice, within 14 days of onset of paralysis, 24-48 hours apart. There were 2 silent districts and 5 districts with rates less than 1/100 000. DM = district municipality, MM = metropolitan municipality

African region

In 2016, 129 samples were referred to NICD. Not all samples were derived from AFP cases – some were from contacts of cases. Prior to the switch in April 2016, two samples from Madagascar were identified as VDPV type 1; six samples from Guinea as VDPV type 2 and two samples from the Democratic Republic of Congo as VDPV type 2. The Madagascar samples were related to the 2015 VDPV type 1 outbreak in the country. Appropriate responses were conducted in the relevant areas by the World Health Organization. Following the switch there were two Sabin polio type 2 viruses detected, one from Cameroon and the other from Guinea. There was one VDPV type 2 confirmed from Mozambique, prompting a vaccination campaign using monovalent OPV2 vaccine. Further information is available from the website of the Global Polio Eradication initiative, updated weekly at http://www.polioeradication.org/

Environmental surveillance activities for the African region
Environmental samples were received from four sites in Angola for enterovirus isolation. Non-polio enteroviruses were commonly isolated, with a non-polio enterovirus isolation rate of 90%, indicating robust laboratory systems for enterovirus detection. Sabin poliovirus type 3 was isolated from three samples, indicating that appropriate sites are being sampled.

In addition, isolates detected through environmental sampling from Madagascar, Burkina Faso, Cameroon and Senegal were referred to the NICD for sequencing. Two environmental isolates were confirmed as VDPV type 2, one from Niger and one from Senegal, both dating prior to the switch.

Discussion and conclusions

Heightened surveillance and rapid responses are required to any poliovirus event as global eradication nears. As global incidence decreases, the significance of an imported case in any country escalates. Continuous in-service training and communication is required to support surveillance staff nationally and to address surveillance gaps. Acute flaccid surveillance can serve as a model of a functioning surveillance system and lessons learnt can be applied to other notifiable medical conditions.

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Epidemiology of respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, South Africa, 2016

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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 2016 influenza season started in week 19 and reflected mixed circulation of influenza subtypes with initial circulation of influenza B, followed by influenza A(H3N2) and influenza A(H1N1) pdm09 as the season progressed. The 2016 influenza season started two weeks later than the 2015 season, but was within the average onset period compared to previous years. The influenza vaccine had low effectiveness in South Africa during 2016. The respiratory syncytial virus (RSV) season preceded the influenza season, starting in week 7. There was no obvious seasonality identified for the bacterial pathogens. Among cases enrolled as part of pneumonia surveillance, the common pathogens detected were RSV followed by *Pneumocystis jirovecii*, *Mycobacterium tuberculosis*, *Streptococcus pneumoniae* and influenza. Among ILI cases the common pathogens detected were influenza followed by RSV.

Introduction

The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) coordinates a number of syndromic respiratory illness surveillance programmes. They include 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 2016 for the following pathogens: influenza virus, respiratory syncytial virus (RSV), *Streptococcus pneumoniae*, *Bordetella pertussis*, atypical bacterial causes of pneumonia (*Legionella* species, *Chlamydophila pneumoniae* and *Mycoplasma pneumoniae*), *Mycobacterium tuberculosis* and *Pneumocystis jirovecii* (PCP).

Methods

A brief summary of each surveillance programme is included below. In order to reduce costs, changes in sample collection and testing for the different respiratory pathogens were implemented during the course of 2016. Thus, specimens from all sites were tested for three core pathogens: influenza virus, RSV and *B. pertussis*. As part of enhanced surveillance at selected sites, specimens were additionally tested for *S. pneumoniae*, bacterial causes of atypical pneumonia, *M. tuberculosis* and *P. jirovecii*.

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 included 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 and annual estimates of influenza vaccine effectiveness.

Pneumonia surveillance is an active, prospective hospital-based surveillance programme for severe respiratory illness. Patients admitted at the surveillance sites meeting the standardized clinical case definition of severe respiratory illness (SRI) were prospectively enrolled (Table1). Dedicated staff screened and enrolled patients from Monday to Friday each week. Clinical and epidemiological data were collected using standardized questionnaires. Information on in-hospital management and outcome were collected. Samples collected and tested varied by site and case definition (Table 2). In 2016, nasopharyngeal aspirates (NPA) in children <5 years were replaced by combined nasopharyngeal and oropharyngeal swabs (NPS and OPS) at the sites which conduct surveillance for core pathogens. Sites which conducted enhanced surveillance continued to collect nasopharyngeal aspirates in children <5 years until July 2016, at which point these were replaced by combined NPS and OPS in children aged ≥1 year. Additional samples collected at enhanced sites included blood and sputum (induced or expectorated) samples (Table 2).

The systematic ILI surveillance programme was established in 2012 at two public health clinics serviced by the two enhanced sites (Edendale Hospital (EDH) and Klerksdorp Tshepong Hospital Complex (KTHC)). Patients presenting at these sites meeting the ILI and suspected pertussis case definitions (Table1) were enrolled prospectively. Clinical and epidemiological data were collected using standardized questionnaires and nasopharyngeal samples were collected for testing (Table 2). Dedicated staff screened and enrolled patients for systematic ILI surveillance from Monday to Friday.

The Viral Watch sentinel surveillance programme, which started in 1984, was specifically designed to monitor influenza activity. Participation in the programme is voluntary and is mainly composed of general practitioners, who were requested to submit nasopharyngeal or oropharyngeal swabs from patients who met 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 2016 influenza season were used to calculate vaccine effectiveness (VE). During 2016, 97 practitioners registered across South Africa submitted specimens throughout the year.

The respiratory morbidity surveillance tracks trends in the number of pneumonia and influenza hospitalizations, using anonymised 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, 2016.

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 and Edendale Gateway 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 (all sites) or any patient from EDH or KTHC with a clinical diagnosis of suspected pulmonary tuberculosis AND not meeting any of the above criteria	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 and Edendale Gateway 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, 2016.

Pathogen	Programme (syndrome)	Surveillance site	Specimen collected	Test conducted
Influenza, RSV and *B. pertussis*	Viral Watch (ILI)	All Viral Watch sites in 8 provinces	Nasopharyngeal (NP) and oropharyngeal (OP) flocked swabs	Multiplex real-time reverse transcription polymerase chain reaction (RT-PCR)
	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocked swabs ≥5 years EDH and KTHC. *NPA <5 years	RT-PCR
	Pneumonia surveillance (SRI)	Matikwana/ Mapulaneng RMMCH/ HJH, RCH/MPH EDH & KTHC	NP and OP flocked swabs (all age groups)	
			NP and OP flocked swabs ≥5 years. *NPA <5 years	Multiplex real-time PCR
M. pneumoniae, Legionella spp.,	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocked swabs ≥5 years. *NPA <5 years	Multiplex real-time PCR
C. pneumoniae	Pneumonia surveillance (SRI)	**Matikwana/ Mapulaneng RMMCH/ HJH, RCH/MPH	NP and OP flocked swabs (all age groups) **NPA <1 year	
		EDH, KTHC	NP and OP flocked swabs >5 years. *NPA ≤5 years. Induced or expectorated sputum.	
****S. pneumoniae*	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocked swabs ≥5 years. **NPA <5 years	Multiplex real-time PCR
	Pneumonia surveillance (SRI)	Matikwana/ Mapulaneng, RMMCH/ HJH, RCH/MPH	NP and OP flocked swabs (all age groups),	*lyt*A real-time PCR
		EDH, KTHC	NP and OP flocked swabs ≥5 years, **NPA <5 years, induced or expectorated sputum, whole blood	
Tuberculosis	Pneumonia surveillance (SRI)	EDH, KTHC	Induced or expectorated sputum	GeneXpert and culture+ line probe assay real-time PCR
Pneumocystis jirovecii	Pneumonia surveillance (SRI)	EDH, KTHC	Induced or expectorated sputum, NP and OP flocked swabs ≥5 years **NPA <5 years	Real-time PCR

*NPA in <5 years until June 2016, changed to NPA <1 years in September 2016 and NPS for ≥1 year** NPA/NPS tested for *S. pneumoniae* until June 2016. 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 VW=Viral Watch

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 a weekly basis. One sputum sample was tested at the surveillance site laboratory for *M. tuberculosis* using GeneXpert, and a second sputum sample was tested at the NICD for *M. tuberculosis* by culture and line probe assay (MTBDRplus) as well as for PCP and bacterial pathogens by PCR (Table 2).

Detection of viral pathogens
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 bacterial pathogens other than tuberculosis
Induced/expectorated sputum and nasopharyngeal samples were tested for *M. pneumoniae, C. pneumoniae, Legionella* spp. and *B. pertussis*. DNA was extracted from the clinical specimens and tested for bacterial pathogens by real-time-PCR. A specimen was considered positive for *M. pneumoniae* if the MP181 target was detected (cycle threshold (Ct) <45), *C. pneumoniae* if the CP-*Arg* target was detected (Ct<45) and *Legionella* spp. if the Pan-Leg target was detected (Ct<45) a positive result for pertussis was obtained when a specimen was positive for IS481 and/or ptxS1 genes with a Ct<45. A positive case for any of the above bacterial pathogens was defined as having either or both specimens test positive by real-time PCR. Blood specimens were tested using quantitative real-time PCR for the presence of pneumococcal DNA (*lytA* gene). For *lytA* testing, specimens with a *lytA* Ct-value <40 were considered positive.

Detection of tuberculosis
Microbiological investigation for tuberculosis at site was performed by smear microscopy, culture and/or XpertMTB/Rif. At NICD, smear microscopy of sputum samples was performed using fluorescent auramine-O staining for acid-fast bacilli (AFB). Culture was performed using liquid media with the Bactec MGIT 960 (Becton Dickinson, USA) system. Positive cultures were identified as *M. tuberculosis* complex using Ziehl-Neelsen staining and MPT64 antigen testing (Becton Dickinson, USA). Genotypic resistance to isoniazid and rifampicin in tuberculosis-positive patients was tested using the Genotype MTBDRplus v2 assay (Hain Life Sciences, Germany).

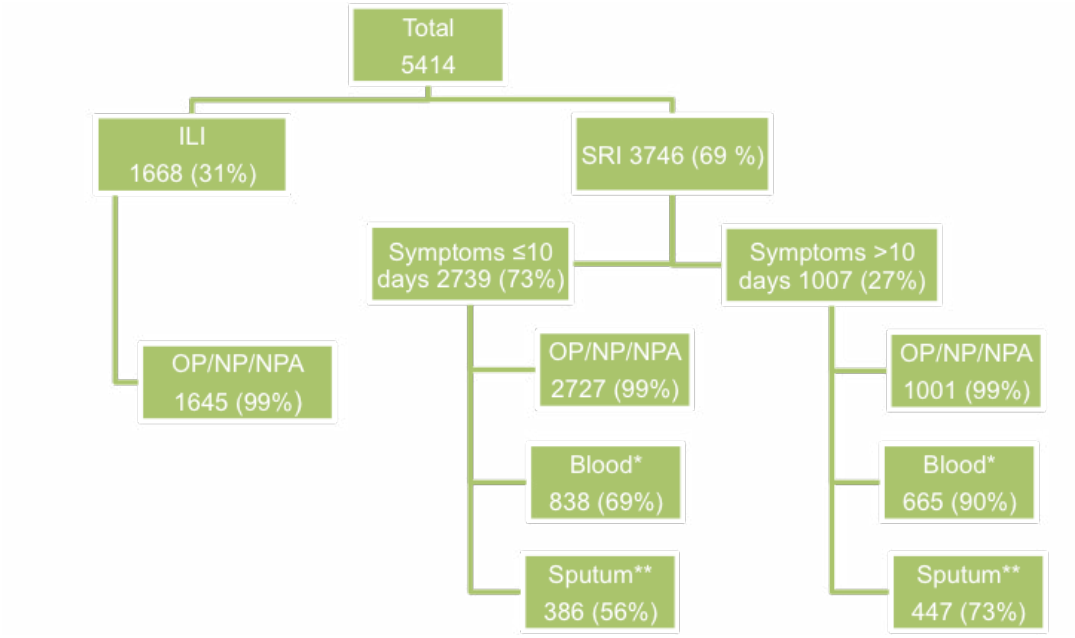
Detection of P. jirovecii
Pneumocystis jirovecii was tested for in one or more of the following specimens from each patient: naso/oropharyngeal sample and induced/expectorated sputum samples. DNA was extracted from the clinical specimens using an automated DNA extraction system. Fungal load was determined using a quantitative real-time PCR targeting the region coding for the mitochondrial large subunit rRNA for *P. jirovecii*. All specimens with copy numbers >0 copies/µl were included as positive. These include both cases of infection and colonisation with *P. jirovecii.*

Data management and analysis
Data management was centralised at the NICD where laboratory, clinical and demographic data from enrolled patients were recorded on a Microsoft Access database with double data entry. The start of the influenza season is defined as at least two consecutive weekly influenza detection rates of ≥10%, and the season is considered to have ended when the detection rate drops below 10% for two consecutive weeks.

Results: Pneumonia and systematic ILI surveillance

Of the 5418 patients enrolled into the surveillance programmes in 2016, 5414 (98%) had complete data on case definition available; 1668 (31%) and 3746 (69%) met the case definition of ILI and SRI respectively. Of the SRI cases, 73% (2739) presented with symptoms for ≤10 days. Samples collected and tested for each of the case definitions are outlined in Figure 1. The type and number of samples collected and tested varied depending on the case definition and suitable samples available for testing. The demographic characteristics of patients enrolled in the surveillance programmes are described in Table 3.

Figure 1. Numbers of samples collected by case definition in the systematic influenza-like illness (ILI) and pneumonia surveillance programmes (SRI), South Africa, 2016.



ILI= influenza-like illness, SRI=severe respiratory illness, OP= oropharyngeal, NP= nasopharyngeal, NPA= nasopharyngeal aspirate. *Blood collected from three of the six sites. **Sputum collected from only two of the six sites

Table 3. Demographic and clinical characteristics of patients with an upper respiratory sample available for testing and enrolled into the systematic influenza-like illness and pneumonia surveillance programmes, South Africa, 2016.

Characteristic	Influenza-like illness n/N (%) N=1668	Severe respiratory illness n/N (%) N=3746
Age group		
0-4	639/1645 (39)	2276/3732 (61)
5-14	198/1645 (12)	93/3732 (2)
15-24	168/1645 (10)	84/3732 (2)
25-44	420/1645 (26)	718/3732 (19)
45-64	152/1645 (9)	400/3732 (11)
≥ 65	68/1645 (4)	161/3732 (4)
Female gender	984/1644 (60)	1770/3716 (48)
Site		
Edendale Gateway Clinic	1209/1668 (72)	N/A
Jouberton Clinic	459/1668 (28)	N/A
EDH	N/A	692/3746 (18)
KTHC	N/A	608/3746 (16)
Matikwana/Mapulaneng hospitals	N/A	341/3746 (9)
RMMCH/HJH	N/A	851/3746 (23)
RCH/MPH	N/A	1254/3746 (25)
Symptoms ≤ 10 days	N/A	2739/3746 (73)
Symptoms >10 days	N/A	1007/3746 (27)
Underlying illness	72/1643 (4)	522/3721 (14)
Influenza positive	216/1645 (13)	229/3728 (7)
RSV positive	100/1645 (6)	629/3728 (17)
B. pertussis positive	5/1621 (0.3)	37/3604 (1)
In-hospital case fatality ratio	N/A	119/3338 (4)

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

Pneumonia surveillance programme (SRI) results–influenza and RSV

Of the 3746 patients enrolled in pneumonia surveillance, 3732 (99%) were tested for influenza and RSV. Of these 229 (6%) and 629 (17%) were positive for influenza and RSV respectively (Table 3).

The influenza detection rate was 7% (183/2727) and 5% (46/1001) among cases with duration of symptoms ≤10 days and >10 days respectively (p=0.02).The influenza season started in week 24 and continued through week 39. It was predominated by influenza B (106/229, 46%) followed by influenza A(H1N1)pdm09 (78/229, 34%) and influenza A(H3N2) (46/229, 20%). The peak detection rate was 22% in week 35 (Figure 2).

The RSV detection rate was 22% (589/2727) and 4% (40/1001) among cases presenting with symptoms for ≤ 10 days and >10 days respectively. The RSV season preceded the influenza season, starting in week 8 and continuing through week 29 when the detection rate fell below 10%. The peak detection rate of 53% was in week 18 (Figure 3). The case fatality ratio was 6% (11/197) and <1 % (4/572) among cases positive for influenza and RSV respectively (Table 4).

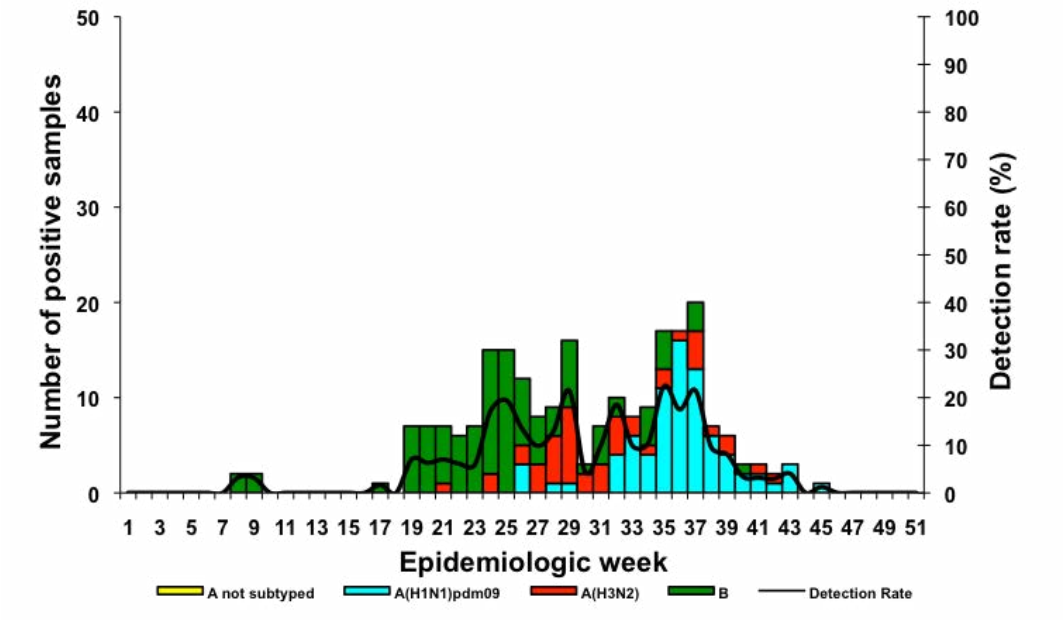


Figure 2. Numbers of samples positive for influenza and influenza detection rate, by type, subtype and week, in patients enrolled into the pneumonia surveillance programme and meeting the case definition of severe respiratory illness (SRI) in South Africa, 2016.

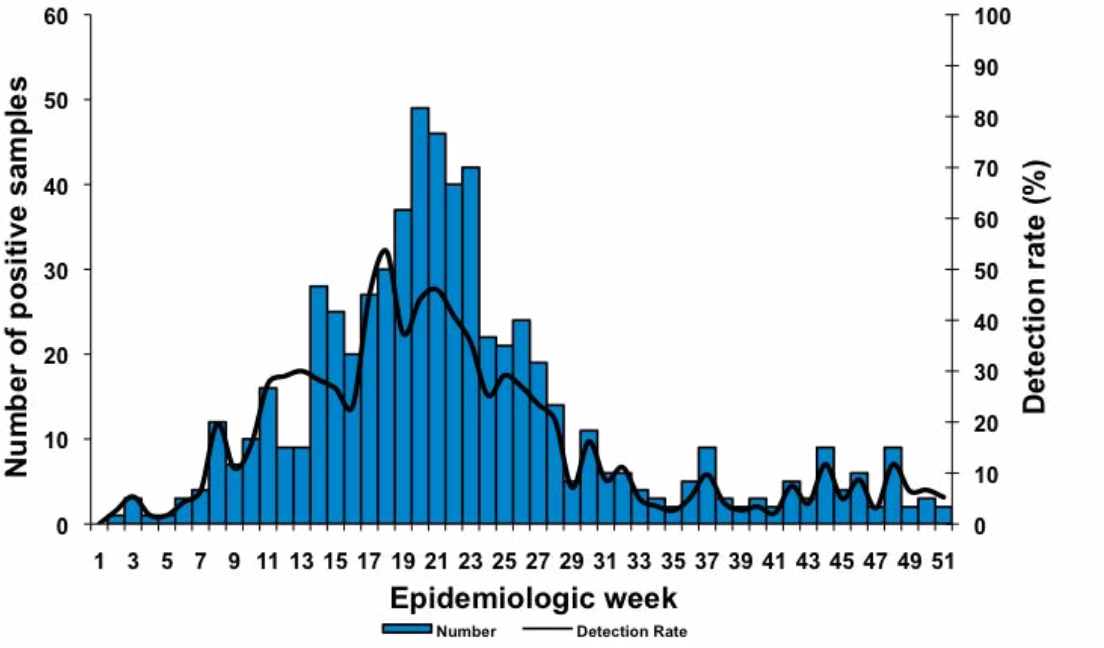


Figure 3. Numbers of samples collected and detection rates for respiratory syncytial virus (RSV), in patients meeting the case definition for severe respiratory illness (SRI), pneumonia surveillance, South Africa, 2016.

Table 4. Characteristics of patients meeting the case definition for severe respiratory illness (SRI) who tested positive for influenza and RSV, pneumonia surveillance, South Africa, 2016.

Characteristic	Influenza	RSV
Age group		
0-4	142/228 (62)	607/629 (94)
5-14	8//228 (4)	1/629 (1)
15-24	3/228 (1)	12/629 (0.2)
25-44	41/228 (18)	4/629 (2)
45-64	20/228 (9)	5/629 (1)
≥ 65	14/228 (6)	2/629 (1)
Female gender	124/227 (45)	287/623 (46)
Site		
EDH	28/229 (12)	98/629 (16)
KTHC	48/229 (21)	35/629 (6)
Matikwana/Mapulaneng	39/229 (17)	35/629 (6)
RMMCH/HJH	44/229 (19)	138/629 (22)
RCH/MPH	27/229 (31)	323/629(51)
Duration of symptoms		
≤10 days	183/229 (80)	589/629 (96)
>10 days	46/229 (20)	40/629 (4)
In-hospital case fatality ratio	11/197 (6)	4/572 (1)

RSV=respiratory syncytial virus, 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

Bacterial pathogens

Of the 3746 patients enrolled in pneumonia surveillance, 3607 (96%) were tested for *B. pertussis*. *B. pertussis* was detected in 37/3607 (1%) patients (Table 3); 27/2628 (1%) and 10/976 (1%) among cases presenting with symptoms for ≤10 days and >10 days respectively. Of the patients who had respiratory samples tested for other bacterial pathogens, 5/2707 (0.7%) were positive for *M. pneumoniae*, 5/2705 (0.2%) for *C. pneumoniae* and 6/2706 (0.2%) for *Legionella* spp. Of the 1503 blood samples tested for *S. pneumoniae*, 141 (9%) were positive (Table 5). The highest number of positive samples for the bacterial pathogens was in children <5 years, except for *C. pneumoniae*, which had a higher number of positive cases in the 15-24 year age group. The case fatality ratio was highest for patients testing positive for *S. pneumoniae* 14/124 (11%) (Table 5).There was no apparent seasonality for bacterial pathogens (Figures 4 and 5).

Table 5. Characteristics of patients testing positive for *Bordetella pertussis, Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella spp*. or *Streptococcus pneumoniae*, Pneumonia Surveillance Programme, South Africa 2016.

Characteristic	B. pertussis* n/N (%)	M. pneumoniae* n/N (%)	C. pneumoniae* n/N (%)	Legionella spp.* n/N (%)	S. pneumoniae n/N (%)**
Age					
0-4	26/36 (72)	11/19 (58)	2/5(40)	4/6 (67)	63/139 (45)
5-14	2/36 (6)	1/19 (5)	3/5 (60)	0/6 (0)	5/139 (4)
15-24	1/36 (3)	0/19 (0)	0/5 (0)	0/6 (0)	2/139 (1)
25-44	3/36 (8)	5/19(26)	0/5 (0)	2/6(33)	48/139 (35)
45-64	3/36 (8)	2/19 (11)	0/5 (0)	0/6 (0)	20/139 (14)
≥ 65	1/36 (3)	0/19 (0)	0/5 (0)	0/6 (0)	1/139 (0.7)
Female gender	16/36 (44)	9/19 (47)	1/5 (20)	4/6 (67)	69/139 (50)
Site					
EDH‡	6/37 (16)	8/19 (42)	2/5 (40)	2/6 (33.3)	49/141 (35)
KTHC‡	8/37 (22)	11/19 (58)	1/5 (20)	2/6 (33.3)	65/141 (46)
Matikwana/ Mapulaneng#	3/37 (8)	0/19 (0)	2/5 (40)	0/3 (0)	27/141 (19)
RMMCH/HJH$	8/37 (22)	0/19 (0)	0/5 (0)	1/6 (17)	N/A
RCH/MPH$	12/37 (32)	0/19 (0)	0/5 (0)	1/6 (17)	N/A
Duration of symptoms					
≤10 days	27/37 (73)	14/19 (74)	4/5 (80)	4/6 (67)	93/141 (66)
>10 days	10/37 (27)	5/19 (26)	1/5 (20)	2/6 (33)	48/141 (34)
In-hospital case fatality ratio	1/32 (3)	1/16 (6)	0/4 (0)	0/5 (0)	14/124 (11)

*Nasopharyngeal ± sputum samples tested; **blood samples; ‡ nasopharyngeal, sputum and blood samples collected; # nasopharyngeal and blood samples collected, $nasopharyngeal samples collected. RCH/MPH= Red Cross Hospital/Mitchell's Plain Hospital; EDH = Edendale Hospital; RMMCH/HJH = Rahima Moosa Mother and Child Hospital

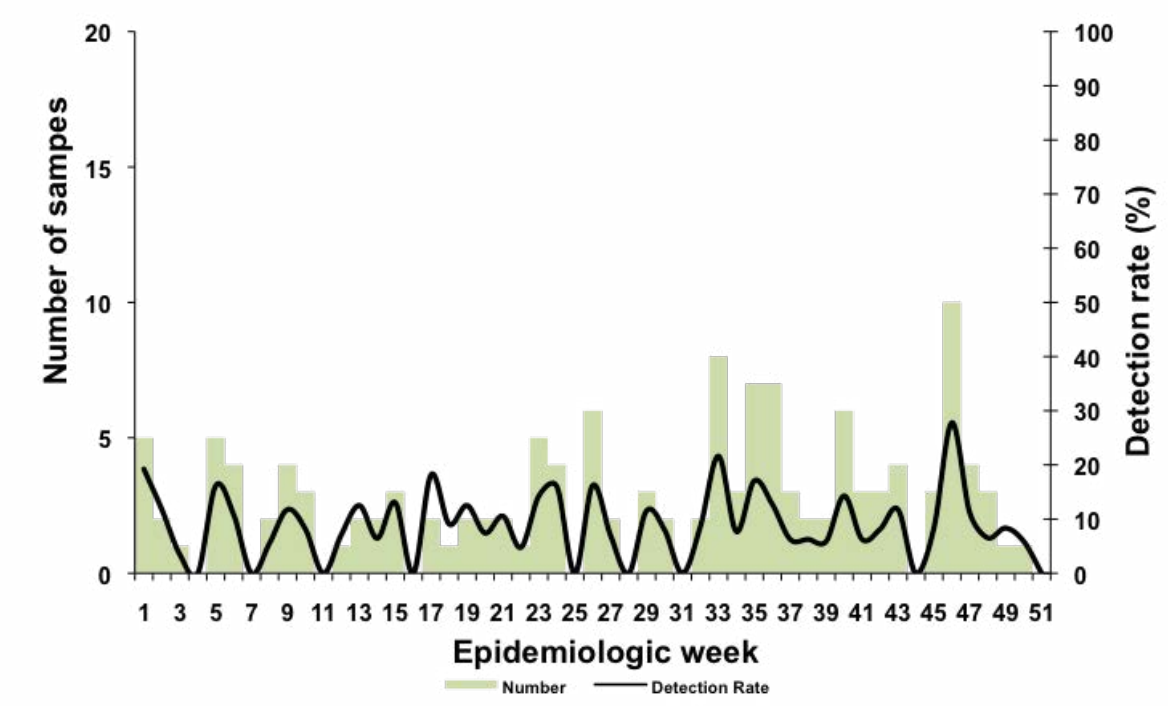


Figure 4. Number of positive samples and detection rate of *Streptococcus pneumoniae* from patients enrolled at enhanced sites with severe respiratory illness (SRI) by week, Pneumonia Surveillance Programme, South Africa, 2016.

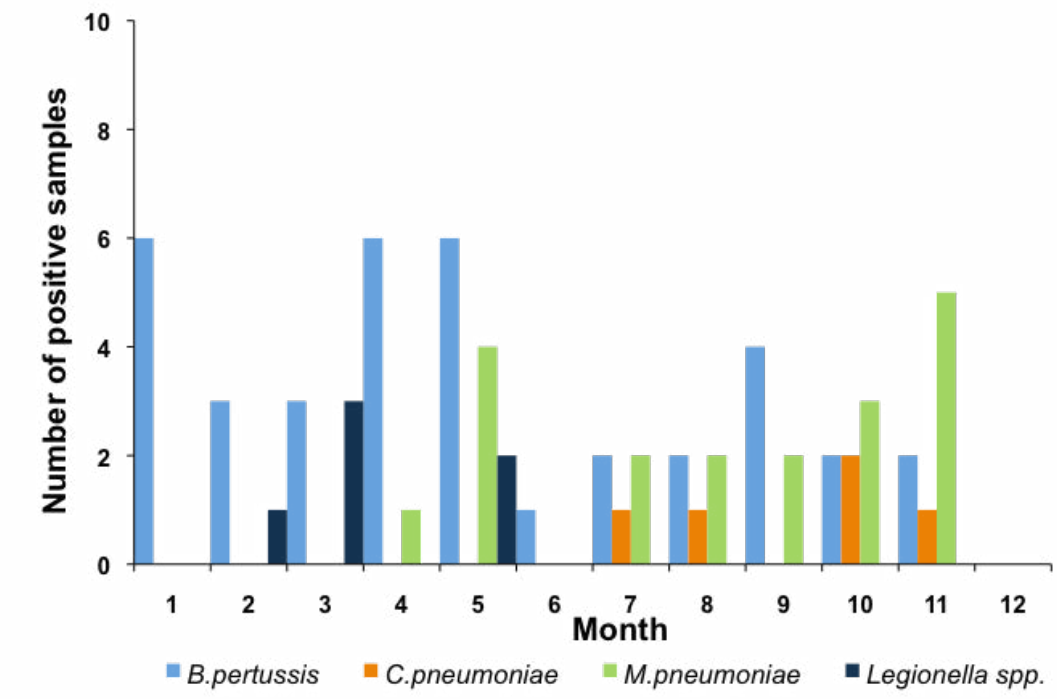


Figure 5. Numbers of positive samples of *Bordetella pertussis, Mycoplasma pneumoniae*, *Legionella* spp. and *Chlamydia pneumoniae* among patients with severe respiratory illness (SRI) by month, Pneumonia Surveillance Programme, South Africa, 2016.

Tuberculosis and PCP

Of the 863 patients tested for *M. tuberculosis*, 118 (14%) were positive. Tuberculosis was detected throughout the year with no obvious seasonality (Figure 6). The majority of samples which tested positive for tuberculosis were collected at the KTHC site (65/118, 55%) and were in the 25 to 44 year age group (77/116, 66%) (Table 6). Among patients with tuberculosis with outcome information available the case fatality ratio was 7% (7/104).

Of the 265 (14%) samples that tested positive for *P. jirovecii* in 2016, 126 (48%) were from nasopharyngeal samples and 139 (52%) from induced sputum. The proportion of nasopharyngeal samples which tested positive for *P. jirovecii* by PCR was 11% (126/1129) versus 17% in induced sputum samples (139/837). The majority of patients with positive samples (n=218) were in the age groups 25 to 44 years (80/218, 37%) and <5 years (77/218, 35%). More than half of patients were male (54%, 118/217). The case fatality ratio for patients positive for *P. jirovecii* was 7% (16/218).

Table 6. Characteristics of patients fitting the case definition of severe respiratory illness (SRI) enrolled into pneumonia surveillance and testing positive for tuberculosis and *Pneumocystis jirovecii*.

Characteristic	Tuberculosis n/N(%)	Pneumocystis jirovecii n/N(%)
Age group (years)		
0-4	4/116 (3)	77/218 (35)
5-14	0/116 (0)	5/218 (2)
15-24	5/116 (4)	8/218 (4)
25-44	77/116 (66)	80/218 (37)
45-64	26/116 (22)	34/218 (16)
≥ 65	4/116 (3)	14/218 (6)
Female gender	55/118 (47)	99/217 (46)
Site		
EDH	53/118 (45)	123/218 (56)
KTHC	65/118 (55)	95/218 (44)
Duration of symptoms		
≤10 days	21/118 (18)	112/214 (52)
>10 days	97/118 (82)	102/214 (48)
In-hospital case fatality ratio	7/104 (7)	16/218 (7)

EDH = Edendale Hospital, KTHC = Klerksdorp-Tshepong hospital complex

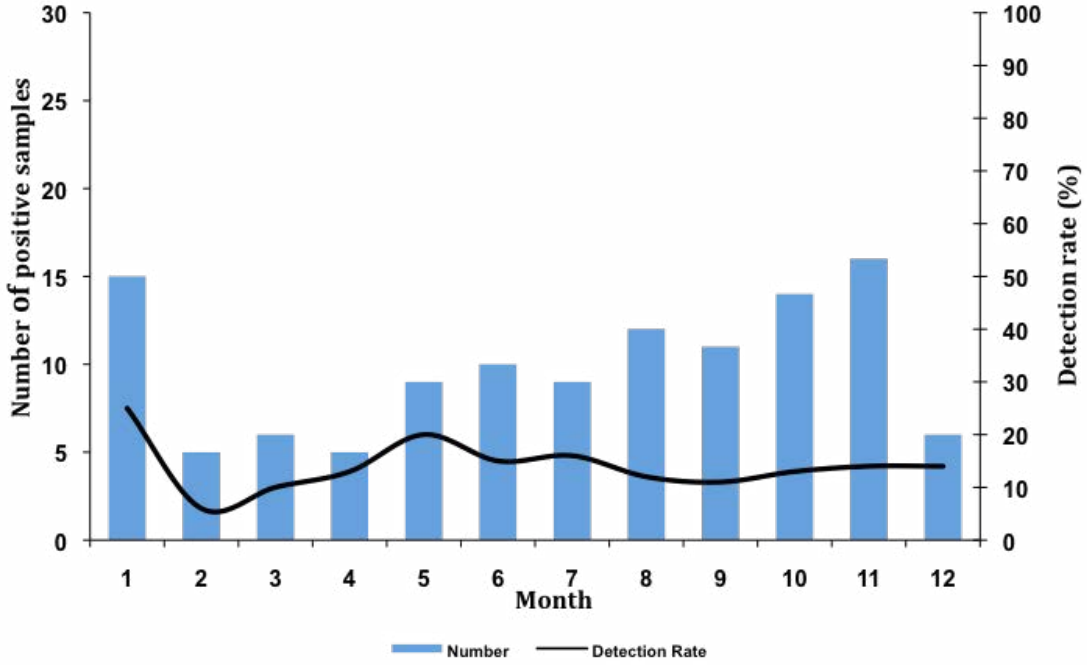


Figure 6. Numbers of samples positive for tuberculosis and detection rate among patients with severe respiratory illness (SRIat enhanced sites by month, Pneumonia Surveillance Programme, South Africa, 2016.

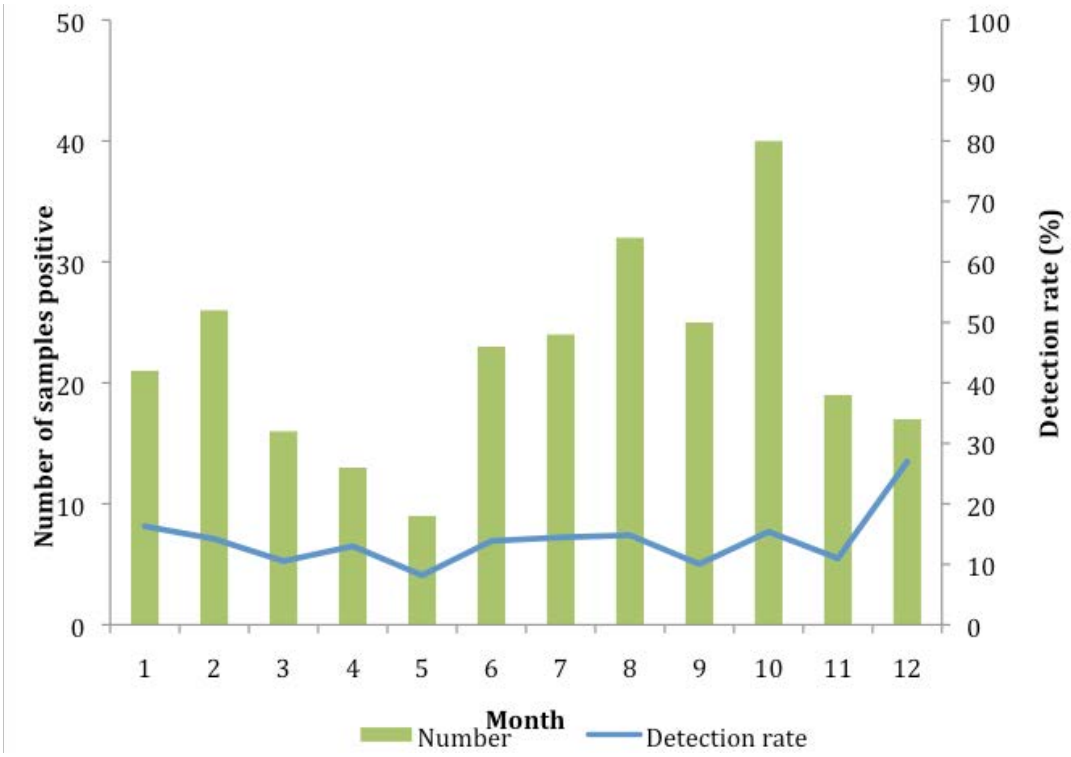


Figure 7. Numbers of samples positive for *Pneumocystis jirovecii* and detection rate for patients meeting the severe respiratory illness (SRI) case definition at the enhanced sites, Pneumonia Surveillance Programme, South Africa, 2016.

Results: Systematic ILI surveillance at primary health clinics

Respiratory viruses

During 2016, 1668 patients with ILI were enrolled at the two primary health clinics and 1645 (99%) samples were tested for respiratory pathogens. The overall detection rate of influenza was 13% (216/1645). Of the 216 influenza positive samples, 106 (49%), 56 (26%) and 54 (25%) were positive for influenza B, influenza A(H1N1)pdm09 and influenza A(H3N2) respectively (Figure 8). The detection of influenza rate rose above 10% in week 19 and was sustained above 10% until week 39 (Figure 8). RSV demonstrated a defined seasonality which preceded the influenza season. The overall detection rate of RSV was 6% (100/1645), the detection rose above 10% in week 7 and was sustained at ≥10% until week 17 (Figure 9). The majority of cases positive for influenza and RSV were in children < 5 years, 79/214 (37%) and 67/100 (67%) respectively.

Bacterial pathogens

Of the 1621 patients enrolled with ILI and tested for *B. pertussis*, 5/1621 (0.3%) tested positive. A total of 762 were tested for bacteria that cause atypical pneumonia, of which 2/762 (0.3%) tested positive for *C. pneumoniae* (Table 7). The highest number of positive samples for *B. pertussis* was in children < 5 years (2/5, 40%) and was from Edendale (4/5, 80%). There were no positive samples for *Legionella* spp. *and M. pneumoniae*.

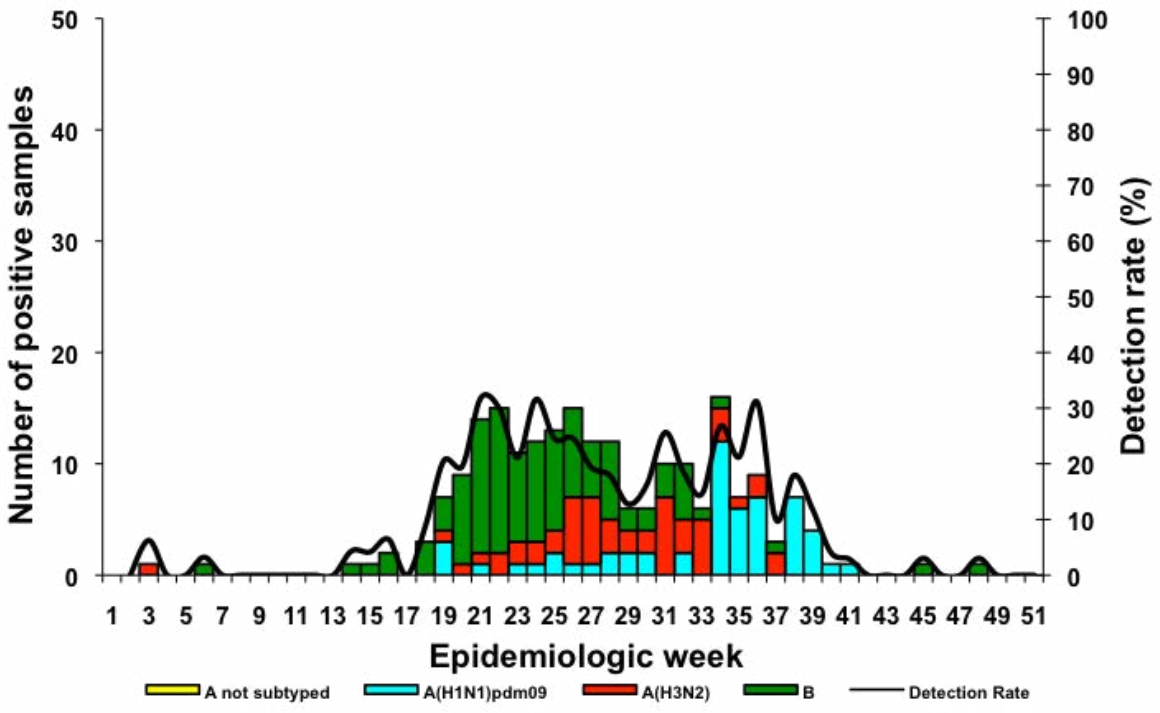


Figure 8. Influenza detection rate, by influenza type, subtype and week, in patients enrolled with influenza-like illness (ILI) at the two primary healthcare clinics, South Africa, 2016.

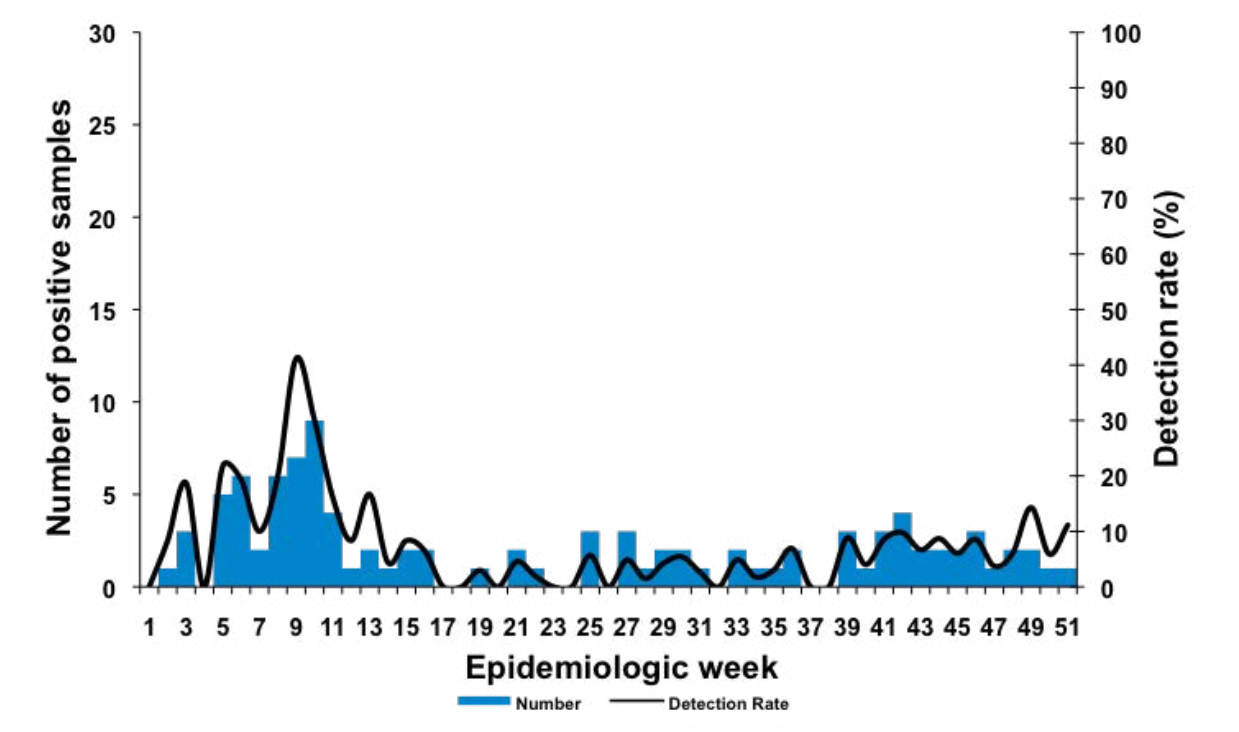


Figure 9. Detection rate of respiratory syncytial virus (RSV) by week in patients enrolled with influenza-like illness (ILI) at two primary health clinics, South Africa, 2016.

Table 7. Characteristics of patients with influenza-like illness (ILI) enrolled at public health clinics testing positive for viral and bacterial pathogens, South Africa, 2016.

Characteristic	Influenza n/N (%)	RSV n/N (%)	B. pertussis n/N (%)	C. pneumoniae** n/N (%)
Age				
0-4	79/214 (37)	67/100 (67)	2/5 (40)	2/2 (100)
5-14	54/214 (25)	8/100 (8)	1/5 (20)	0/2 (0)
15-24	22/214 (10)	1/100 (1)	0/5 (0)	0/2(0)
25-44	44/214 (21)	17/100 (17)	1/5 (20)	0/2 (0)
45-64	11/214 (5)	5/100 (5)	1/5 (20)	0/2 (0)
≥ 65	4/214 (2)	2/100 (2)	0/5 (0)	0/2 (0)
Female gender	120/212 (57)	59/98 (60)	5/5 (100)	2/2 (100)
Site				
Edendale Gateway Clinic	179/216 (83)	80/100 (80)	4/5 (80)	2/2 (100)
Jouberton Clinic	37/216 (17)	20/100 (20)	1/5 (20)	0/2 (0)

Note: No samples tested positive for *Legionella* spp. and *M. pneumoniae* in ILI patients
** testing up to June 2016

Viral Watch (VW)
In 2016, 97 general practitioners across 8 of South Africa's 9 provinces (KwaZulu-Natal excluded) participated in the VW programme. A total of 1144 samples was tested for influenza; of these 543 (47%) tested positive. The season was dominated by influenza B (216/543, 40%), followed by influenza A(H3N2) (209/543,38%) and influenza A(H1N1)pdm09 (118/543, 22%). The season started in week 19 (starting 9 May), peaked in week 35 (week starting 29 August) and ended in week 40 (starting 3 October) (Figure 10). Specimens from 52 patients with suspected pertussis were tested for *B. pertussis*, three (5.8%) of which were positive.

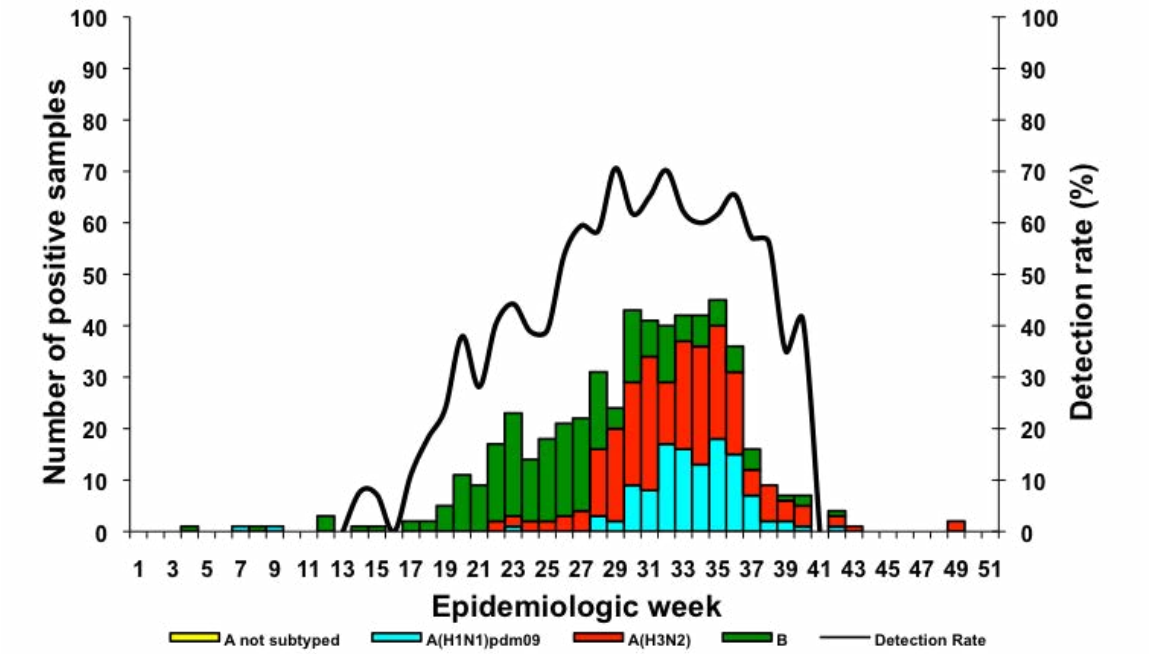


Figure 10. Numbers of samples and influenza detection rate by viral type, subtype and week for patients meeting the case definition of ILI, Viral Watch programme, South Africa, 2016.

Respiratory morbidity surveillance

During 2016 there were 1 181 269 consultations reported to the NICD through the respiratory morbidity data mining surveillance system. Of these, 28 283 (2%) were due to pneumonia or influenza (P&I) (International Classification of Diseases 10 codes J10-18). There were 21 285 (75%) inpatients and 6 998 (25%) 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 Viral Watch and pneumonia surveillance programmes respectively (Figures 11 and 12). A second lower peak preceded the influenza season, corresponding to the circulation of respiratory syncytial virus (Figures 11 and 12, and cross-reference Figure 3 - pneumonia surveillance viruses, and Figure 9 - ILI viruses).

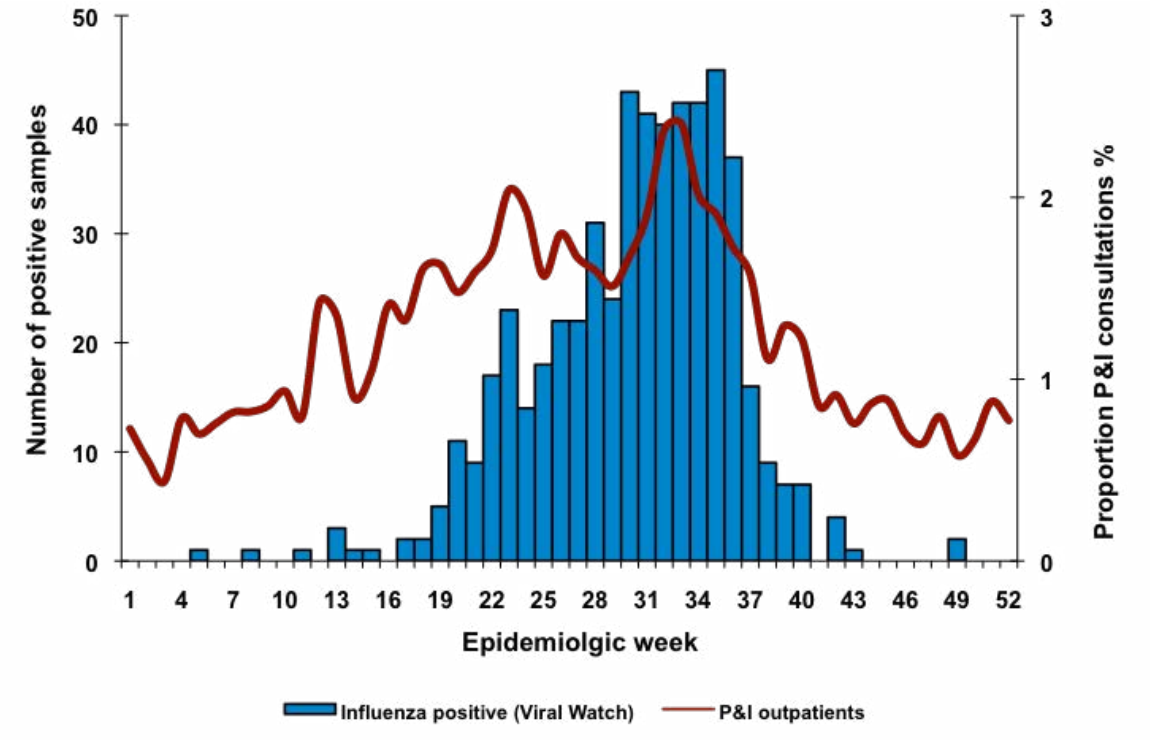


Figure 11. Numbers of private hospital outpatient consultations with a discharge diagnosis of pneumonia and influenza (P&I), and numbers of influenza positive viral isolates (Viral Watch) by week, South Africa, 2016.

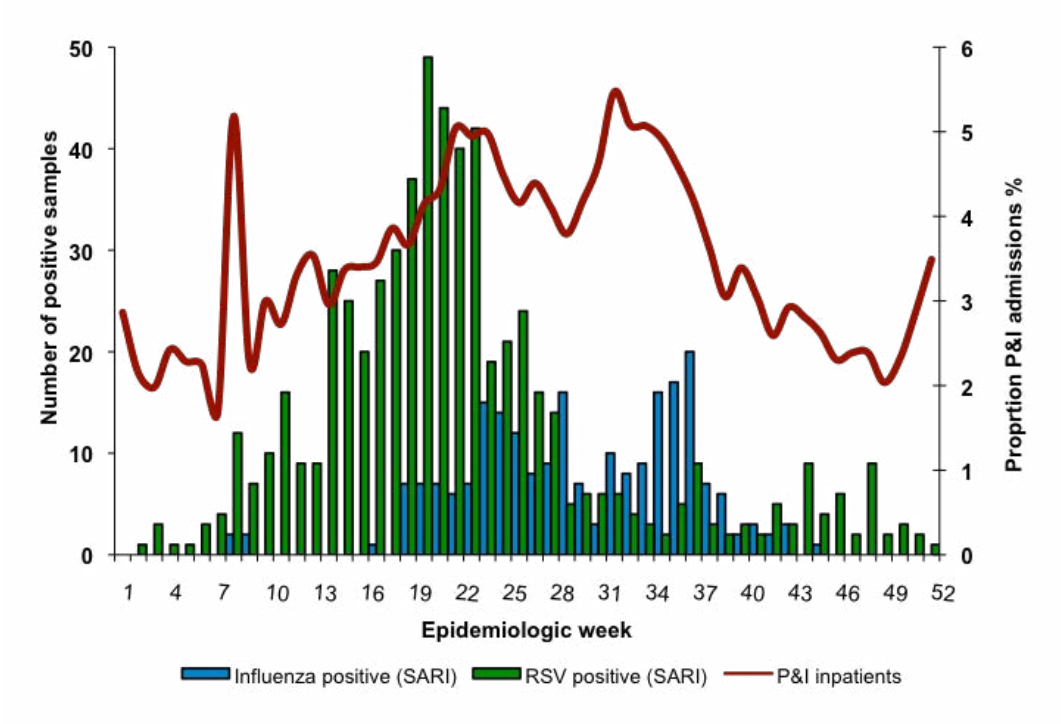


Figure 12. Numbers of private hospital admissions for pneumonia and influenza, as well as numbers of influenza-positive viral isolates and respiratory syncytial virus (RSV)-positive isolates SRI by week, South Africa, 2016.

Vaccine effectiveness (VE), 2016 influenza season

Of the 988 individuals enrolled in viral watch and tested during the influenza season, 956 (97%) were eligible for the VE analysis. Influenza detection rate was 56% (522/956) amongst individuals included. The majority of influenza detections were influenza A(H3N2) which accounted for 207/522 (40%) of the total influenza subtypes, followed by influenza B which accounted for 202 (39%) of detections with the remainder being influenza A(H1N1)pdm09. Overall, the influenza vaccine coverage was 4.0% (21/522) in cases and 4.8% (21/434) in controls. Coverage in patients with underlying conditions was 7.1% (7/63) in cases and 4.8% (3/62) in controls and in those aged ≥45 years was 12.1% (12/99) in cases and 6.4% (7/109) in controls. The overall VE estimate, adjusted for age, underlying conditions and seasonality, was 18.1% (95% CI: -54.89% to 56.7%) against any influenza virus type, 54.2% (95% CI -65.3% to 87.3%) against influenza A(H1N1)pdm09, 0.4% (95% CI: -124.0% to 55.7%) against influenza A(H3N2) and 11.5 (95%CI -119.6% to 64.3%) against any lineage of influenza B.

Discussion

The influenza season in South Africa in 2016 reflected mixed circulation of influenza subtypes with initial circulation of influenza B, followed by influenza A(H3N2) and influenza A(H1N1)pdm09 as the season progressed. The season started in week 19 at the ILI sites, with a lag in onset at pneumonia sites which only reflected the start of the season in week 24 when the detection rate for hospitalised patients reached 17%. Although the 2016 influenza season started two weeks later than the 2015 season, 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 2016. The low vaccine coverage affected statistical estimates of the significance of VE among sub-groups such as individuals >65 years of age. The RSV season preceded the influenza season, starting at the same time as in 2015, in week 7 at the ILI sites and in week 8 at the pneumonia surveillance sites. There was no obvious seasonality identified for the bacterial pathogens.

Among cases enrolled as part of pneumonia surveillance, the common pathogens detected were RSV followed by *P. jirovecii, M. tuberculosis, S. pneumoniae* and influenza. All the other pathogens were detected in <5% of individuals tested. Among ILI cases the common pathogens detected were influenza followed by RSV. From 2017 the programme will no longer test *M. tuberculosis* and *P. jirovecii* as part of surveillance.

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. Together these data will assist clinicians and policy makers to improve health care and implement prevention strategies such as vaccines.

Acknowledgements

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Microbiologically confirmed tuberculosis in South Africa, 2004-2015

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Executive Summary

South Africa has the highest incidence of TB in the world. A total of 3 327 876 mPTB cases occurred in South Africa between 2004 and 2015. Four provinces (KwaZulu-Natal, Eastern Cape, Gauteng and Western Cape) accounted for 74.2% of the absolute mPTB burden in South Africa during 2015. mPTB incidence rates are on the decline with reductions of -4.1%, -6.0% and -4.8% year-on-year for 2013, 2014 and 2015 respectively, which is half of that required by the WHO End TB Strategy. Females between the ages of 25-44 have shown the sharpest decline in incidence rates (-33.6%) between 2008 and 2015, reflective of efforts in the HIV programme targeting this age group. Change in incidence rates among males has been minimal for the age group 25-44 years over the same period (-13.4%) and shows the highest incidence (2.5 times the national average), requiring initiatives aimed at this population. Among South Africa's provinces, KwaZulu-Natal has shown the sharpest decline in mPTB incidence rates and achieved a reduction of 37.1% over a four-year period (2011-2015). Antiretroviral therapy expansion, which has probably led to important early successes, has tapered off in several provinces (Gauteng, North West and Western Cape) and other aspects of TB control need to be targeted (pre-treatment loss to follow up, contact tracing etc.).

Introduction

Despite instituting interventions to control tuberculosis (TB) in South Africa over many years, it is still the leading cause of death due to an infectious bacterial agent[1]. The World Health Organization (WHO) estimated 454 000 new TB cases in South Africa in 2015[2] – the fifth highest globally. After adjustments for population size, South Africa has the highest incidence of TB among the 22 high-TB burdened countries in the world. It also has the largest number of HIV-associated TB cases. In 2015, 294 603 cases were registered on treatment[1] – presenting a very different picture from the estimated 450 000 cases by WHO. These variances could be due to poor health access or health seeking behaviour, incomplete records in registry data, loss to follow up of diagnosed cases or death prior to accessing treatment.[3-5]

A recent review[3] demonstrated the powerful utility of laboratory data in providing a robust surveillance system for tracking incidence, albeit only for microbiologically confirmed cases in South Africa. Most importantly, transformation of the laboratory data allowed for trend analysis at multiple levels of the healthcare system. These findings were made possible by South Africa's unique position, compared to many other developing and developed countries globally, in having a single integrated laboratory network that covers all public health sector facilities.

Since the publication of the review,[3] the algorithms used have been further refined to improve the accuracy of the system as attested by the updated incidence rates now reported for the preceding years. Three additional aspects were considered important for developing this report: 1. inclusion of more recent annual data, given that the Xpert MTB/Rif rollout only began in 2011 and the previous findings were reported up to and including 2012; 2. analysis performed at a much lower geographical unit to be meaningful in guiding future interventions; 3. presentation of data in a format that is easy to access, and easy to understand and interpret.

Methods

Data were sourced from the National Health Laboratory Service's (NHLS) Corporate Data Warehouse (CDW). The CDW collates information from the laboratory information management systems (LIMS) used by the NHLS. Specimens collected from people presenting at public health facilities with signs and symptoms of TB are sent to the NHLS' network of laboratories for testing and these results were the primary data included. Probabilistic matching of demographic data was performed to achieve patient-level analysis.

For each patient identified by the record linking process, TB-confirmed status was determined based on a positive TB result using an Xpert MTB/Rif test, culture, line probe assay or smear. A 12-month window period for each patient was calculated based on the date of the first confirmatory test with a positive result, and used to distinguish new episodes from existing episodes. This approach was based on the understanding that treatment for drug-susceptible TB spans six months, and that smear conversion for drug-susceptible TB is usually achieved within three months and allows for some delay between diagnosis and entry into treatment. If a case that was confirmed to have drug-susceptible TB was found to develop drug resistance later, the 12-month episode window was extended to 24 months to allow for the extension of treatment.

Geographic data in the form of shape files and boundaries with associated population data by gender and five-year age group were obtained from the Municipal Demarcation Board and Statistics SA respectively. Data from annual population estimates aggregated to sub-districts were linked to the laboratory-confirmed TB data at sub-district level. This enabled calculation of sub-district, district, provincial and national TB incidence rates as well as age/sex standardized incidence rates. Ninety-five percent confidence intervals were calculated for these incidence rates. Incidence trend graphs with fitted trend lines and confidence intervals were plotted for each administrative level. Population pyramids were used to show the age/sex distribution of TB cases nationally and provincially. All statistical analysis was undertaken using Stata v14.0 (Statacorp, College Station, TX, USA). All maps were developed using the Esri Maps for Microstrategy plugin (Esri, Redlands, CA).

Results

Over the 12-year period, a total of 3 327 876 incident microbiologically confirmed cases of pulmonary TB (mPTB) were diagnosed in South Africa (Table 1). This total excludes KwaZulu-Natal (KZN) Province for the period 2004-2010, for which data were unavailable as a laboratory information system covering the whole province was only introduced post-2010. Excluding KZN, incident mPTB peaked at 272 702 cases nationally in 2008, and was recorded at 214 543 cases during 2015. In 2015, KZN accounted for an additional 66 512 mPTB cases giving a total of 281 055 incident mPTB cases. The highest burden of mPTB incident cases in 2015 occurred in four provinces ranked by order: KwaZulu-Natal (66 512), Eastern Cape (59 205), Gauteng (44 822), and Western Cape (37 967) (Figure 1; Table 2). Together they account for 74.2% of the total burden in 2015. The overall trend in TB has been declining both in numbers of mPTB incident cases and in rates (Table 1) since 2008. Incidence peaked in 2008 at 689 (95% CI: 687-692) per 100 000 population, and declined to 520 (95% CI: 519-522) per 100 000 population in 2015. The annual change in incidence rates have been -4.1%, -6.0% and -4.8% respectively, for the last three years (2013, 2014, 2015).

Incidence trends by province have shown similar consistent declines in recent years, although variation in incidence rates did occur (Figure 2, Table 2). In 2015, Limpopo Province recorded the lowest incidence rate (251 per 100 000 population; 95% CI: 246-255) that is more than three-fold lower than that of the Eastern Cape (865 per 100 000 population; 95% CI:858-872), which recorded the highest incidence rate that year. However, all provincial incidence rates were still above 250 per 100 000 population in 2015, the threshold level above which WHO has previously declared to be a health emergency. Northern and Western Cape provinces recorded their highest incidence rates in 2004/5 and also showed sharp declines up to 2010; the former showing increases in the subsequent period coinciding with the implementation of the GXP, while for Western Cape Province the recent trend has stabilized. Although the KwaZulu-Natal data only date from 2011, modeled data previously published indicate that it too is one of the provinces with the highest incidence rates, and the downward trend only began in 2011. This province has shown the largest year-on-year declines since 2011 (988; 95% CI: 982-995) and in 2015 (621; 95%CI: 616-626) was down to the 4th highest in terms of incidence rates – a 37.1% reduction in mPTB incidence rate over the 4-year period.

The most affected age groups with mPTB were those in the economically active 25-44 year age group with an overall male dominance in 2015 (Figure 3). The absolute number of cases was however higher among females in the younger age groups and are reflective of the pattern seen with HIV-infected persons. The encouraging finding of a declining mPTB incidence rate is primarily driven by large declines in incidence rates in females (25-44 year age group) with a 33.6% decline in incidence rates between 2008 (1059 per 100 000 population; 95% CI: 1050-1067) and 2015 (703 per 100 000 population; 95% CI: 698-708) nationally.

In contrast, the changes in incidence rates among males in the most affected 25-44 year age groups remained relatively small for the same period (13.4%) starting at 1272 (95% CI:1262-1281) and declining to 1101 (95% CI:1094-1108) per 100 000 population respectively. These numbers are four times higher than the WHO threshold of 250 per 100 000 for a health emergency. The age/

gender specific incidence rates show a marked difference between the 25-44 year age group (703; 95% CI: 698-708) for males and the 45-64 year age group (439; 95% CI: 433-446) for females in the most recent year. Another interesting finding is the small but consistent upward trend in incidence over time in the >65y age group – especially among females.

Discussion

South Africa is on the World Health Organization (WHO) list of priority countries with regard to the categories of tuberculosis (TB), drug-resistant tuberculosis (DR-TB) and HIV-associated TB.[2] Important positive changes have occurred globally with signs of declining TB incidence, which has led to the launch of the END TB strategy by WHO. This strategy aims at reducing incidence and mortality with ambitious targets set for 2035. The current study builds on previously published data for South Africa, is updated to 2015, and confirms the trend in year-on-year reductions in mPTB incidence rates since 2012 (-4.1%, -6% and -4.8% nationally for the years 2013-2015). Although this is approximately half of what is required by the WHO END TB strategy (10%), it is higher than the global average of 2%.[6]

The national decline in mPTB incidence is the sum total of the efforts of South Africa's nine provinces. KwaZulu-Natal Province, which carries the highest absolute burden in the country, has shown the greatest success in the recent past with annual reductions of mPTB incidence rates in line with the END TB targets i.e. -13.4%, -9.7% and -8.5% for 2013-2015. Similar trends were also observed in Limpopo (much lower burden) and Free State (-2.5% in 2013, -4.8% in 2015 and approaching target in 2015 at -9.2%) provinces.

Gauteng, North West and Western Cape provinces showed excellent reductions in the early years but these trends have recently slowed. Western Cape Province showed an annual change of -0.8%, -1.3% and +1.8% for the period 2013-2015. The impact of the ART program on reducing mPTB incidence has been shown to be an important contributor in these provinces. However, this alone will not be enough even though these provinces initiated ART programs much earlier than the other provinces.
The newly revised national TB Plan updated for the period 2017-2021 has targeted five strategic interventions along the cascades of care; starting with finding undiagnosed cases and ending with the final objective of successful patient outcomes. In addition, two cross-cutting themes, namely quality improvement and data utilization, are envisioned. These sets of interventions will hopefully address the stagnation observed in some provinces. It is also encouraging to see that the National Department of Health's new TB plan will use a data-driven targeted approach and it is envisioned that this report will provide a solid foundation for monitoring progress of the END TB targets.

Northern Cape Province is an area where health systems and access are key elements impacting on success or failure. This province has demonstrated a concerning increase in mPTB incidence rates, and although it carries a relatively low mPTB burden nationally (3.4%), by incidence it is one of the highest, requiring further investigation.

A striking clue to the success and failure of the achieved reduction in incidence was observed by disaggregating data by gender. Most of the declines observed across the provinces and reflected nationally have been driven by successes achieved among females aged between 25-44 years. This group showed a 33.6% reduction between 2008 and 2015 nationally. This links closely with the large emphasis of the HIV program and greater health-seeking behaviour of this population. In stark contrast, the reduction among males in the same age category nationally was only 13.4% for the same period and, in addition, this is the age group with the highest mPTB incidence. Specific strategies aimed at this population are urgently required if the country is to reach the END TB targets, including targeted public messaging, increased access through men's health and wellness centres or days, and male role models.

South Africa's burden of mPTB is not homogenous and becomes more apparent at each successive tier in the health system. The highest burden is carried by just four provinces, yet upon closer inspection it is clear that selected areas, particularly the urban metropolitans, have the largest concentration. Efforts can thus be focused on specific geographic areas with achievable results.
Unlike HIV, TB is curable and the majority of infected individuals have achieved cure – a statistic often underappreciated.
This study cannot explain the reasons for the changes observed nor the relative burden of disease. These questions will need to be interrogated and research studies undertaken where appropriate. What this report has achieved is an important analysis of trend over a 10-year period. The reporting of mPTB data does however have its limitations – especially the lack of clinically diagnosed cases, which account for up to 30% of the case burden. This may well explain the difference in incidence observed in 2015 (510 per 100 000 population) compared with the substantially higher WHO estimate (834 per 100 000 population) for South Africa.

The current report provides valuable insights up to and including 2015 that should be closely integrated into TB control planning for the next five years. Annual updates will be provided to more closely monitor the situation of this priority disease in South Africa. Trend analysis of drug-resistant TB and extrapulmonary TB will be addressed in future reports.
Lastly, the National Institute for Communicable Diseases (NICD) proudly announces the release of an online dashboard upon

which this report is based and which will provide regular updates which cannot easily be achieved in a report format. The dashboard is accessible from the NICD website: www.nicd.ac.za.

Acknowledgements

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Table 1. Pulmonary tuberculosis (mPTB) incident case burden and rates by year, South Africa, 2004-2015.

Year	n	Incidence/100 000 population (95% CI)	Annual change in cases (n)	Annual change in incidence (%)
2004	214166	572 (569-574)	-	-
2005	260855	687 (685-690)	46689	20.1
2006	269197	700 (697-702)	8342	1.9
2007	260406	668 (665-670)	-8791	-4.6
2008	272702	689 (687-692)	12296	3.1
2009	252467	629 (627-632)	-20235	-8.7
2010	251951	619 (616-621)	-516	-1.6
2011*	343960	667 (665-669)	-$	-$
2012*	317439	606 (604-609)	-26521	-9.1
2013*	309088	581 (579-584)	-8351	-4.1
2014*	294590	546 (544-548)	-14498	-6.0
2015*	281055	520 (519-522)	-13535	-4.8

*includes data for Kwa-Zulu Natal Province

$ Annual change restarted with addition of Kwa-Zulu Natal Province data

Table 2. Pulmonary tuberculosis (mPTB) incident case burden and rates (per 100 000 population) by province, South Africa, 2004-2015.

Year	Eastern Cape		Free State		Gauteng		KwaZulu-Natal	
	n	Incidence	n	Incidence	n	Incidence	n	Incidence
		(95% CI)		(95% CI)		(95% CI)		(95% CI)
2004	42879	724(717-731)	16767	677(666-687)	49398	446(442-450)	-	-
2005	49511	825(818-832)	19160	763(752-774)	68352	609(604-614)	-	-
2006	51828	852(845-859)	18360	721(711-732)	69189	608(604-613)	-	-
2007	54455	883(876-890)	18594	721(710-731)	59155	513(509-517)	-	-
2008	64336	1029(1021-1037)	18870	721(711-731)	61327	524(520-528)	-	-
2009	62421	984(976-992)	17979	677(667-687)	58122	490(486-494)	-	-
2010	68440	1063(1055-1071)	16751	622(612-631)	57364	476(473-480)	-	-
2011	65236	998(991-1006)	16489	603(594-612)	54722	448(444-452)	101058	988(982-995)
2012	63018	950(942-957)	16552	596(587-605)	46490	375(371-378)	90075	868(862-873)
2013	65281	969(961-976)	16369	581(572-590)	47376	376(373-379)	79290	752(747-757)
2014	60518	884(877-891)	15833	553(544-562)	46467	363(360-366)	72743	679(674-684)
2015	59205	865(858-872)	14387	502(494-511)	44822	350(347-353)	66512	621(616-626)

Table 2. Pulmonary tuberculosis (mPTB) incident case burden and rates (per 100 000 population) by province, South Africa, 2004-2015 continues...

Limpopo		Mpumalanga		North West		Northern Cape		Western Cape	
n	Incidence	n	Incidence	n	Incidence	n	Incidence	n	Incidence
	(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)
10184	209(205-213)	15906	436(429-443)	15854	500(493-508)	11669	1128(1108-1149)	51509	980(972-989)
13280	269(264-273)	18691	506(499-513)	24584	766(756-775)	12812	1223(1201-1244)	54465	1023(1014-1031)
15825	316(311-321)	20018	535(527-542)	27100	833(823-843)	11582	1090(1071-1110)	55295	1024(1016-1033)
18383	362(357-367)	22384	590(582-597)	23370	708(699-718)	10564	981(962-1000)	53501	978(969-986)
21034	408(403-414)	25558	664(656-672)	23355	698(689-707)	10615	972(953-991)	47607	858(850-866)
21698	415(410-421)	23485	601(594-609)	22191	654(645-663)	8487	766(750-782)	38084	676(670-683)
20775	392(386-397)	22294	562(555-570)	21675	629(621-638)	7129	634(619-649)	37523	657(650-664)
19765	367(362-372)	20447	508(501-515)	19205	549(542-557)	8796	771(755-787)	38242	660(653-666)
18706	342(337-347)	20192	494(488-501)	17014	479(472-487)	8502	734(718-750)	36890	627(620-633)
17071	308(303-312)	19413	468(461-475)	17545	487(480-494)	9550	812(796-828)	37193	622(616-628)
15921	282(278-287)	18439	438(431-444)	17790	486(479-493)	9607	804(788-820)	37272	614(607-620)
14124	251(246-255)	17271	410(404-416)	17085	467(460-474)	9682	810(794-826)	37967	625(619-631)

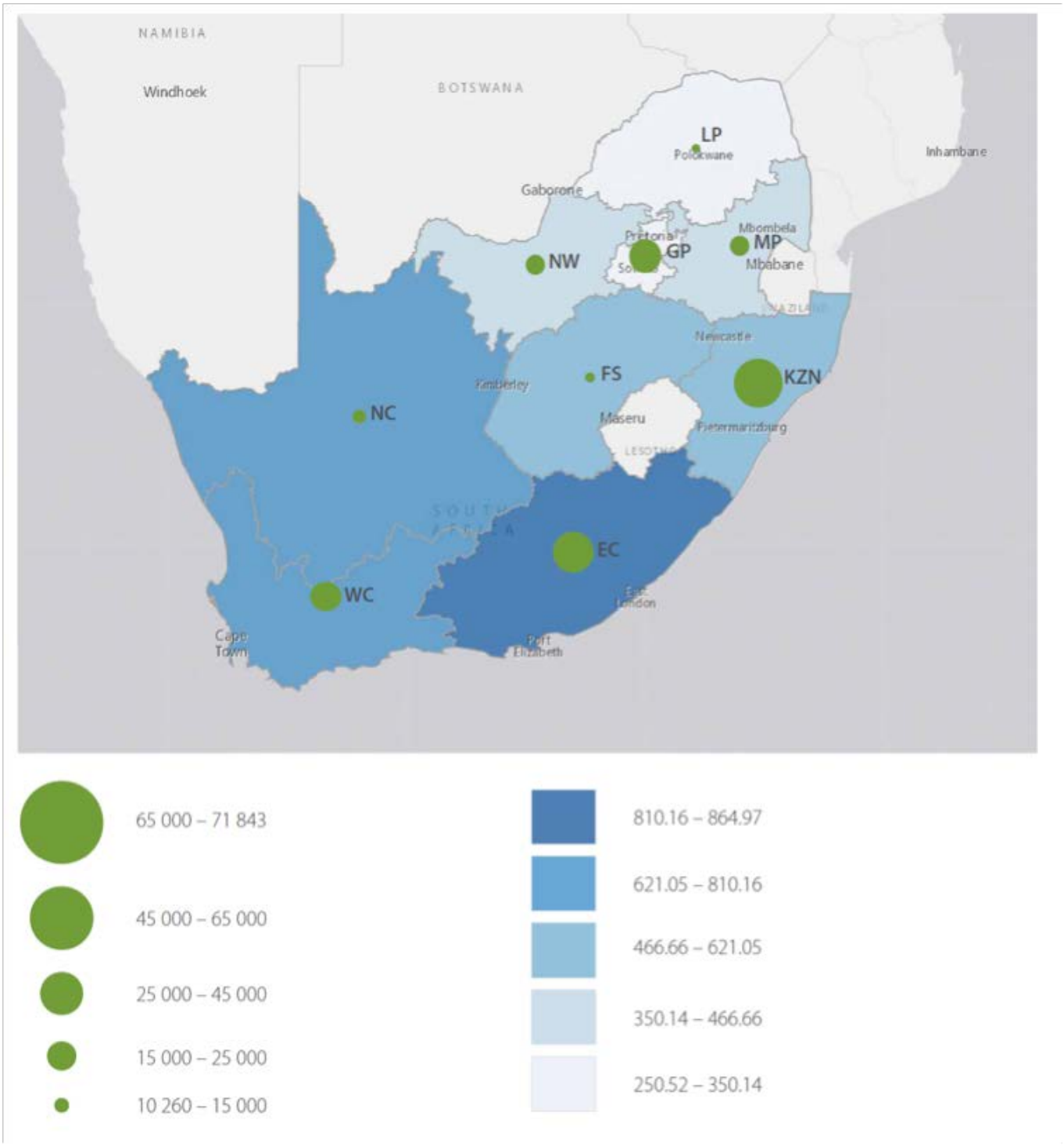

Figure 1. Spatial distribution of the pulmonary tuberculosis (mPTB) incident case burden (circles) and rates (shading), South Africa, 2015.

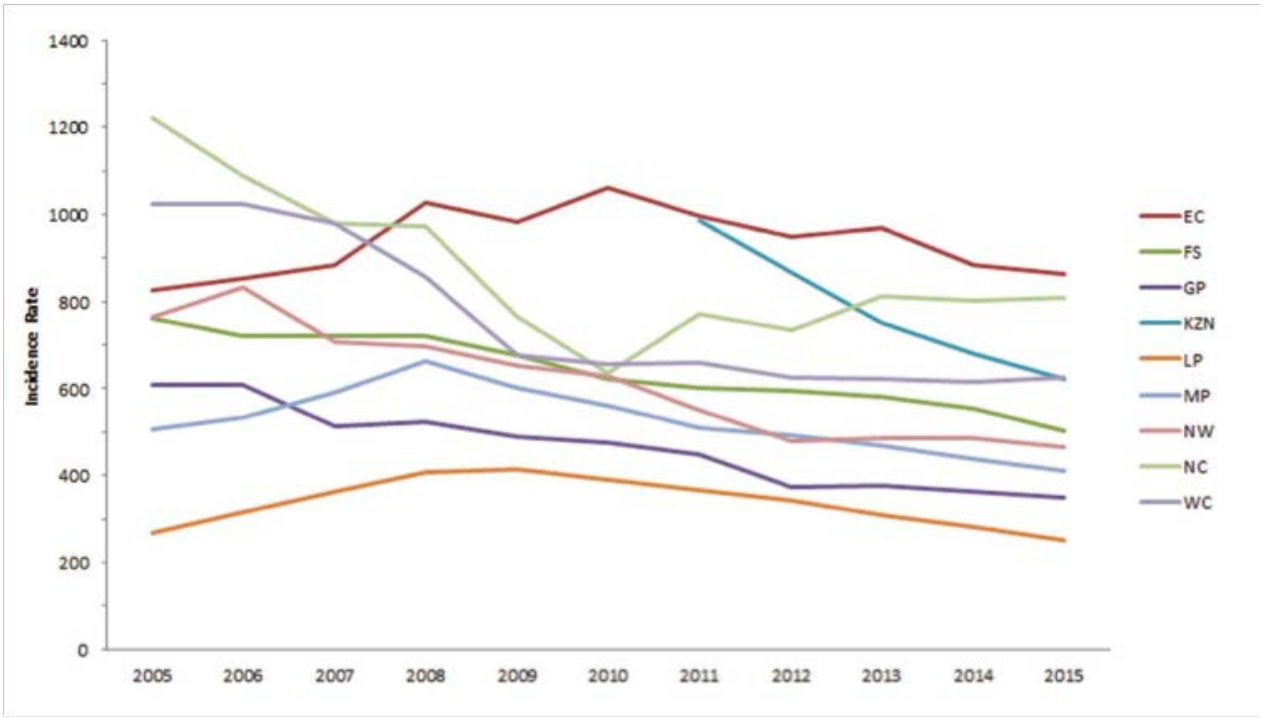

Figure 2. Trends in pulmonary tuberculosis (mPTB) incidence rates (per 100 000 population) by province, South Africa, 2004-2015.

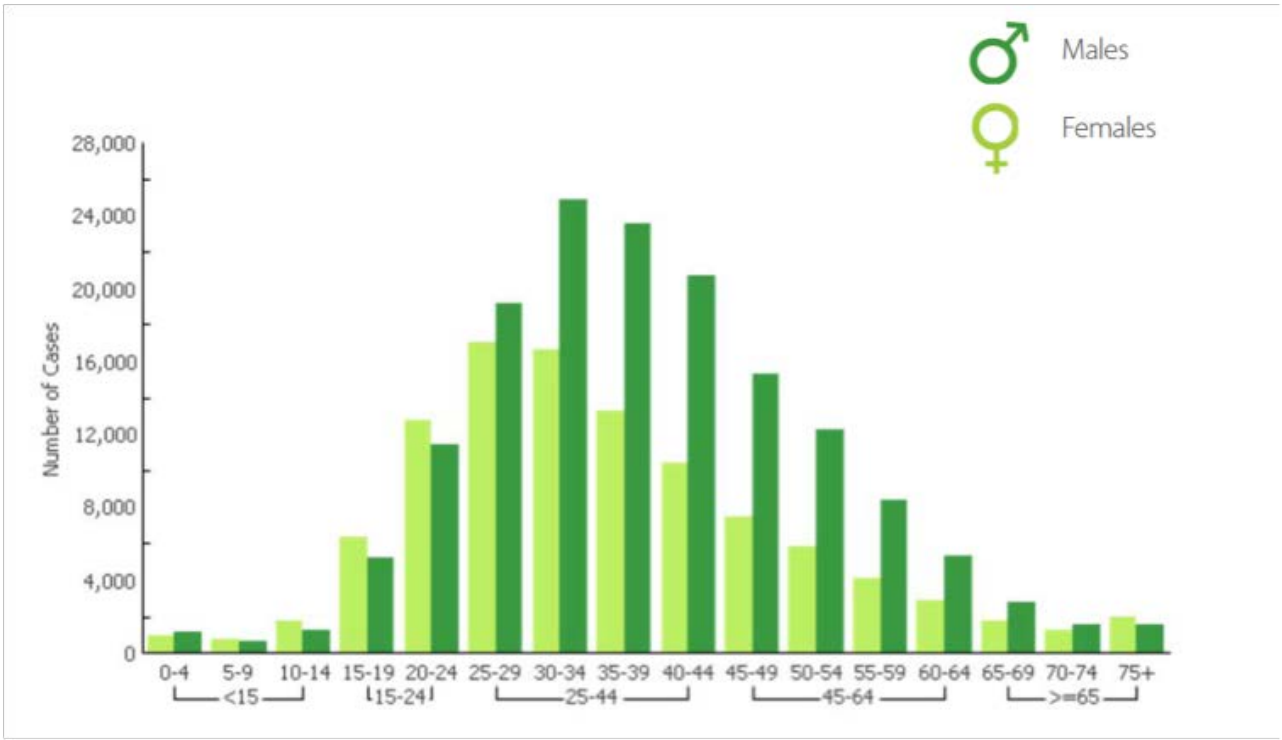

Figure 3. Age and gender population pyramid of pulmonary tuberculosis (mPTB) incident cases, South Africa, 2015.

Malaria vector surveillance report, South Africa, January – December 2016

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Executive Summary

Malaria in South Africa 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 and limited larval source management. Vector surveillance in collaboration with the NICD during 2016 revealed the presence of three malaria vector species - *Anopheles arabiensis*, *An. merus* and *An. vaneedeni* – which 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 KwaZulu-Natal (53%) and Mpumalanga (39%) provinces with only small proportions collected from Limpopo Province (7%) and the Kruger National Park (1%). This information shows that an intensification of vector control activities to include methods designed to target outdoor feeding vector populations is necessary to achieve malaria elimination in South Africa. The continued absence of the major malaria vector *An. funestus(s.s)* within South Africa's borders is indicative of the continued high-level effectiveness of the provincial insecticide-based vector control programmes.

Introduction

South Africa's malaria affected areas include the low-altitude border regions of Limpopo, Mpumalanga and KwaZulu-Natal provinces. These regions experience active malaria transmission, especially during the peak malaria season which spans the summer months (November to April). Each of these 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.[1]

Although IRS has proven efficacy spanning many decades, low-level residual malaria transmission continues and is likely caused by outdoor feeding and resting *Anopheles* vector mosquitoes that are unaffected by indoor applications of insecticide.[2] In addition, populations of the major malaria vector species, *Anopheles funestus* and *An. arabiensis*, have developed resistance to insecticides, especially in northern KwaZulu-Natal.[3] The pyrethroid-carbamate resistance profile in *An. funestus* is highly significant epidemiologically and was at least partly causative of the malaria epidemic experienced in South Africa during the period 1996 to 2000.[4]

Residual malaria transmission and burgeoning insecticide resistance in malaria vector populations within South Africa's borders necessitate ongoing vector surveillance. This is especially pertinent in terms of South Africa's malaria elimination agenda,[5] which includes the following key objectives:

- To strengthen passive and active surveillance and monitoring and evaluation systems so that 100% of districts report promptly and routinely on key malaria indicators by 2015

- To ensure that all levels of the malaria programme have sufficient capacity to coordinate and implement malaria interventions by 2016
- To ensure 100% of the population has adequate knowledge, attitudes and practices on malaria by 2018 through appropriate IEC, social mobilization and advocacy
- To effectively prevent malaria infections and eliminate all parasite reservoirs in South Africa by 2018

Malaria vector surveillance forms an integral part of these objectives. Surveillance is routinely conducted by the entomology teams of Limpopo, Mpumalanga and KwaZulu-Natal with operational field and laboratory support from the Vector Control Reference Laboratory (VCRL) of the Centre for Emerging, Zoonotic and Parasitic Diseases (CEZPD), NICD, and Wits Research Institute for Malaria (WRIM). This report summarises malaria vector surveillance in South Africa in 2016 based on specimens referred to the VCRL.

Methods

During the period January to December 2016, *Anopheles* mosquitoes were collected by the provincial entomology teams and VCRL 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 identification to species. Identification of all mosquito specimens was based on the use of morphological keys and PCR.

Results & Discussion

A total of 1 521 *Anopheles* mosquitoes was collected from sentinel sites during the period under review (Figure 1). Of these, 815 (53%) were collected from KwaZulu-Natal, 592 (39%) from Mpumalanga, 105 (7%) from Limpopo and 9 (<1%) from the Kruger National Park. The vast majority were members of the *An. gambiae* species complex (1 348; 89%) and the remaining 11% (173) 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.

Anopheles arabiensis was collected in comparatively large numbers in Mpumalanga and KwaZulu-Natal (Figure 2 C,E) but did not appear in the Limpopo collections although this species has previously been detected there. It is a major malaria vector in South Africa[2] 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 Limpopo followed by Mpumalanga with only a small number collected in KwaZulu-Natal (Figure 2 A,C,E). This species 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 suggest that this species is increasing its inland range 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 was detected in Mpumalanga in a comparatively large relative proportion and in small relative proportions in Limpopo and KwaZulu-Natal (Figure 2A,C,E).

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

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 can be attributed to intensive IRS programmes in KwaZulu-Natal, Mpumalanga and Limpopo provinces. Other members of the *An. funestus* group were detected in Limpopo, Mpumalanga, and KwaZulu-Natal in comparatively low numbers (Figure 2 D,F). *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.

The occurrence of *An. merus* and *An. quadriannulatus* in the northern Kruger National Park (Figure 2B) has previously been documented.[6] These species tend to occur in sympatry, especially at the Malahlapanga site. During the review period *An. quadriannulatus* predominated at Malahlapanga but previous surveys have shown a predominance of *An. arabiensis* there.[6] *Anopheles rivulorum*-like was also found in the Kruger National Park in low numbers.

Conclusion

Several anophelines, including malaria vector species, occur in the north-eastern Lowveld regions of South Africa despite well-coordinated IRS programmes that generally achieve high spray coverage rates (80% or more of targeted structures in endemic areas). At least three of these species (*An. arabiensis*, *An. merus* and *An. vaneedeni*) are responsible for ongoing residual transmission within South Africa's borders. This information shows that an intensification of vector control activities to include methods designed to target outdoor-feeding vector populations is necessary to achieve malaria elimination. The continued absence of *An. funestus sensu stricto* within South Africa's borders is indicative of the continued high-level effectiveness of the provincial IRS-based vector control programmes.

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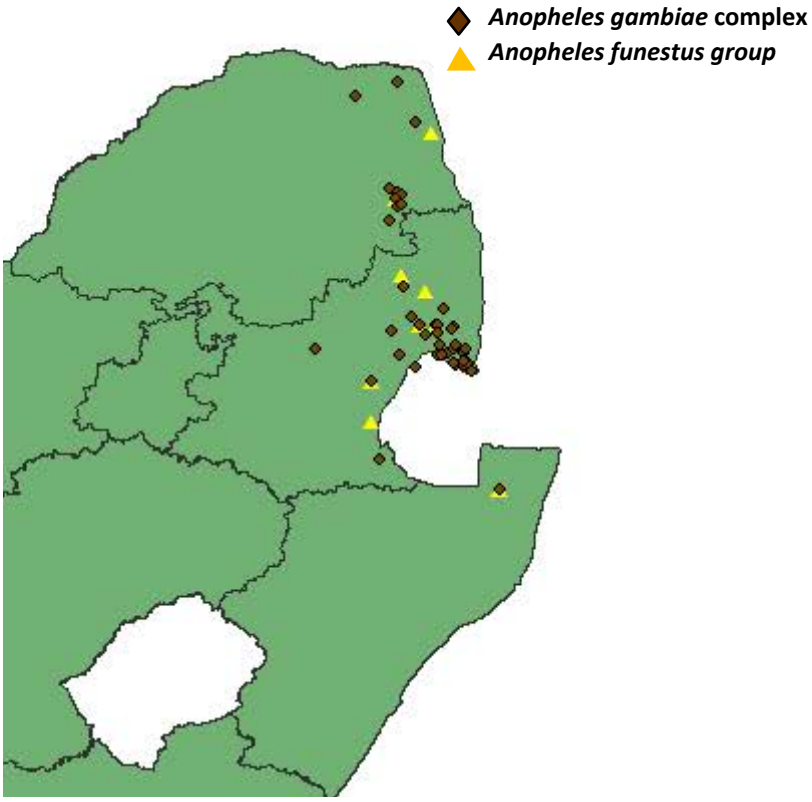
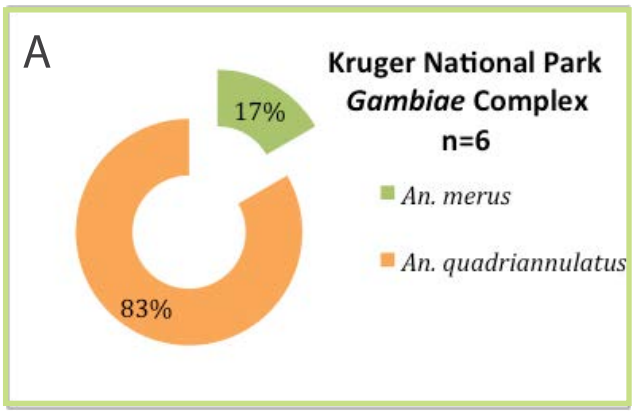
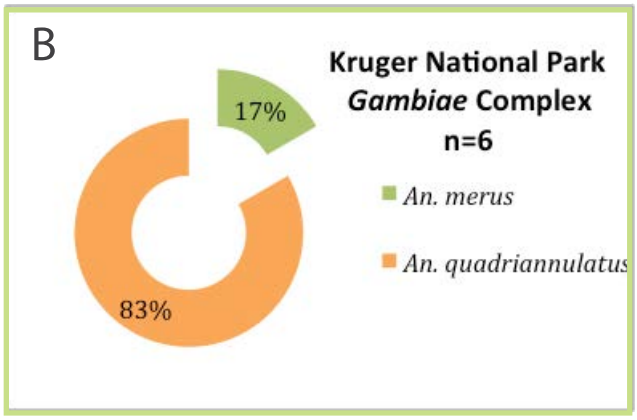
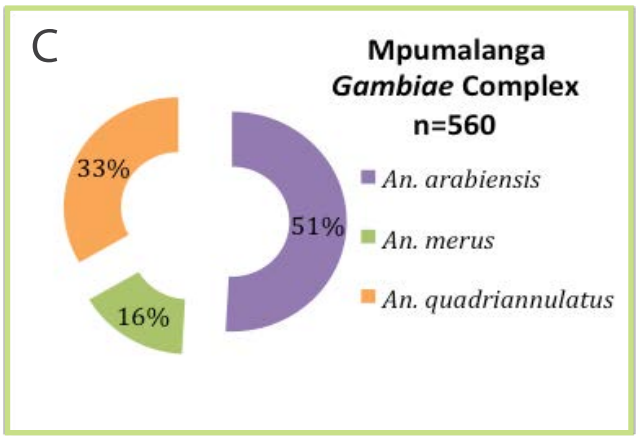
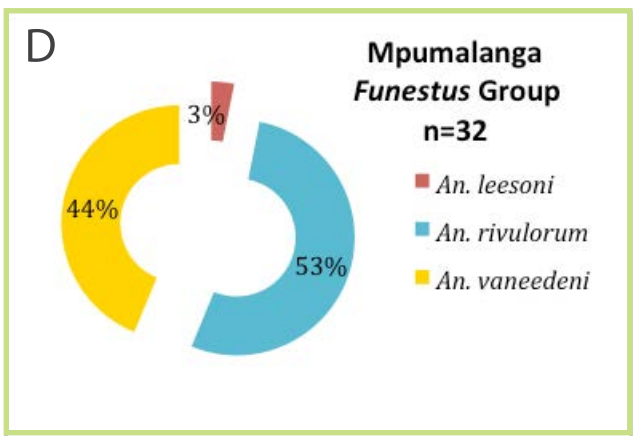


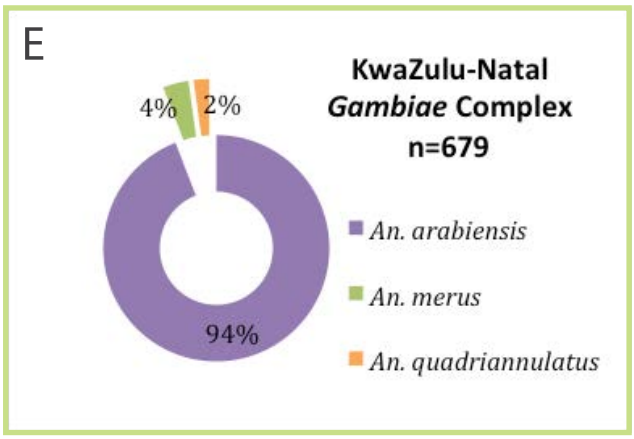
Figure 1. Malaria vector surveillance sentinel sites disaggregated by *Anopheles* species group/complex, Limpopo, Mpumalanga and KwaZulu-Natal provinces, South Africa, January to December 2016.











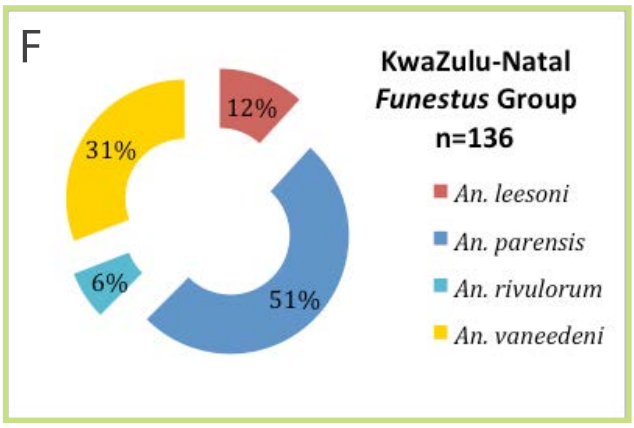


Figure 2. Relative proportions of member species of the *Anopheles gambiae* species complex and *An. funestus* species group by province/locality, South Africa. These proportions are based on *Anopheles* specimens collected during the period January to December 2016.

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