

BURDEN OF RESPIRATORY PATHOGENS FROM INFLUENZA-LIKE ILLNESS AND PNEUMONIA SURVEILLANCE PROGRAMMES, SOUTH AFRICA, 2015

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Introduction and methods

The National Institute for Communicable Diseases (NICD) coordinates a number of syndromic respiratory illness surveillance programmes in order to describe the epidemiology of the respiratory pathogens in South Africa. These programmes include pneumonia surveillance, influenza-like illness (ILI) (systematic ILI at public health clinics and viral watch) and the respiratory morbidity surveillance system. This report describes the findings for these programmes for the year 2015.

The pneumonia surveillance and systematic ILI surveillance programmes have previously been described.¹ 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.

Pneumonia surveillance

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 acute or chronic respiratory illness are prospectively enrolled (Table 1). Dedicated staff screen and enrol patients from Monday to Friday. 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). Samples collected from all the pneumonia surveillance sites include nasopharyngeal aspirates in patients <5 years, combined oropharyngeal and nasopharyngeal swabs in patients ≥ 5 years, and blood. In addition, sputum (induced or expectorated) samples are collected from two enhanced sites, Edendale Hospital (EDH) and Klerksdorp-Tshepong Hospital Complex (KTHC) (Table 2).

Influenza like illness (ILI) surveillance

The systematic ILI surveillance programme was established in 2012 at two public health clinics serviced by the two enhanced sites (EDH and KTHC). Patients presenting at these sites meeting the ILI case definition (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, which started in 1984, was specifically designed to monitor influenza activity and has been fully described previously.² Participation in the programme is voluntary and is mainly composed of general practitioners who are requested to submit nasopharyngeal or oropharyngeal swabs from patients who meet the ILI case definition

(Table1). During 2015, 171 practitioners registered across South Africa submitted specimens throughout the year.

Respiratory morbidity surveillance

In order to describe the influence of the influenza season on the number of pneumonia and influenza hospitalizations, the NICD reviews anonymized data from a private hospital group. The number of hospitalizations for pneumonia and influenza during the influenza season are compared to those for the periods preceding and following the season. The start of the influenza season is defined as at least two consecutive weekly influenza detection rates of $\geq 10\%$, and the season is considered to have ended when the detection rate drops below 10% for two consecutive weeks.

In this report, findings from the pneumonia surveillance and systematic ILI surveillance are included for the following pathogens: influenza, respiratory syncytial virus (RSV), human metapneumovirus (hPMV), parainfluenza viruses 1, 2 and 3 (PIV1-3), *Streptococcus pneumoniae*, *Bordetella pertussis*, atypical bacterial causes of pneumonia (*Legionella species*, *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*), *Mycobacterium tuberculosis* and *Pneumocystis jirovecii* (PCP).

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, 2015.

Case definition	Criteria	Surveillance site/ programme
Influenza-like illness (ILI)	Patients of all ages Acute fever of $\geq 38^{\circ}\text{C}$ and/or self-reported fever within the last 10 days AND cough Absence of other diagnoses	Viral watch programme and public health clinics: Jouberton and Edendale Gateway clinics
Severe acute respiratory illness (SARI)/ Acute pneumonia Patient presenting ≤ 10 days of the onset of illness	2 days - <3 months Any child hospitalised with diagnosis of suspected sepsis or physician diagnosed lower respiratory tract infection (LRTI) irrespective of signs and symptoms.	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital
	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, Red Cross Hospital
	≥ 5 years Any person hospitalised with an acute respiratory infection with fever ($\geq 38^{\circ}\text{C}$) or history of fever AND cough.	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital
Severe chronic respiratory illness (SCRI)	Any child or adult meeting the above case definitions presenting with symptoms >10 days (all sites) or any patient from EDH or KTHC with a clinical diagnosis of suspected pulmonary tuberculosis (TB) AND not meeting any of the above criteria	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital
Severe Respiratory illness (SRI)	Anyone meeting either SARI or SCRI at EDH, KTHC	EDH, KTHC

EDH = Edendale Hospital, KTHC = Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH = RahimaMoosa Mother and Child Hospital/Helen Joseph Hospital

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, 2015.

Pathogen	Programme (syndrome)	Surveillance site	Specimen collected	Test conducted
Influenza and RSV	Viral watch (ILI)	All VW sites in 9 provinces	Nasopharyngeal (NP) and oropharyngeal (OP) flocced swabs	Multiplex real-time reverse transcription polymerase chain reaction (RT-PCR)
	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocced swabs >5 years. NPA ≤5years	Multiplex RT-PCR
	Pneumonia surveillance (SARI and SCRI)	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital	NP and OP flocced swabs > 5 years. NPA ≤5 years	Multiplex RT-PCR
Human metapneumovirus, parainfluenza 1, 2 and 3, adenovirus, enterovirus, rhinovirus	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocced swabs > 5 years. NPA≤5 years	Multiplex RT-PCR
	Pneumonia surveillance: (SARI and SCRI)	EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital	NP and OP flocced swabs > 5 years. NPA≤5 years	Multiplex RT-PCR
B. pertussis, M. pneumoniae, Legionella spp., C. pneumoniae	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocced swabs > 5 years. NPA≤5 years	Multiplex real-time PCR
	Pneumonia surveillance (SARI, SCRI)	Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital	NP and OP flocced swabs > 5 years. NPA≤5 years	Multiplex real-time PCR
	Pneumonia surveillance (SARI, SCRI)	EDH, KTHC	NP and OP flocced swabs > 5 years. NPA ≤5 years. Induced or expectorated sputum.	Multiplex real-time PCR
S. pneumoniae	Systematic ILI	Edendale Gateway Clinic and Jouberton Clinic	NP and OP flocced swabs > 5 years. NPA ≤5 years	lytA real-time PCR
	Pneumonia surveillance (SARI, SCRI)	Matikwana/Mapulaneng, RMMCH/HJH, Red Cross Hospital	NP and OP flocced swabs > 5 years. NPA ≤5 years, whole blood	lytA real-time PCR
	Pneumonia surveillance (SARI, SCRI)	EDH, KTHC	NP and OP flocced swabs > 5 years, NPA ≤5 years, induced or expectorated sputum, whole blood	lytA real-time PCR
Tuberculosis	Pneumonia surveillance (SARI, SCRI)	EDH, KTHC	Induced or expectorated sputum	GeneXpert and culture RT-PCR
Pneumocystis jirovecii	Pneumonia surveillance (SARI, SCRI)	EDH, KTHC,	Induced or expectorated sputum Oral washes, NP and OP flocced swabs > 5 years NPA ≤5 years,	Real-time PCR

ILI = influenza-like illness, SARI = severe acute respiratory illness, SCRI = severe chronic respiratory illness, EDH = Edendale Hospital, KTHC = Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH = RahimaMoosa Mother and Child Hospital/Helen Joseph Hospital.

Sample collection, transport and laboratory testing for the pneumonia and ILI surveillance

Procedures for sample collection and processing for the surveillance programmes have been described previously.^{1,3-5} Upper respiratory tract samples (NP/OP and NPA) were collected in universal transport medium. Whole blood specimens were collected in EDTA containing tubes. Oral washes and sputum were collected in universal containers. Following collection, 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 as well as for PCP and bacterial pathogens by PCR (Table 2).

Detection of viral pathogens

Respiratory specimens were tested by multiplex real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay for the following respiratory viruses: parainfluenza virus types 1, 2 and 3; human metapneumovirus, adenovirus; rhinovirus and enterovirus.⁶ A commercial multiplex real-time RT-PCR assay (Fast-Track Diagnostics, Sliema, Malta) was used for detection of influenza A, influenza B and respiratory syncytial viruses. Influenza A and B positive specimens were subtyped using US Centers for Diseases Control and Prevention (CDC) real-time reverse-transcription 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 (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).⁷ A positive result for pertussis was obtained when a specimen was positive for *IS481* and/or *ptxS1* genes.⁸ 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.⁹

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 MTBDR_{plus} v2 assay (Hain Life sciences, Germany).

Determination of PCP

Pneumocystis jirovecii was tested for one or more of the following specimens from each patient-oral wash, naso/oropharyngeal sample and sputum. 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*.¹⁰ 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

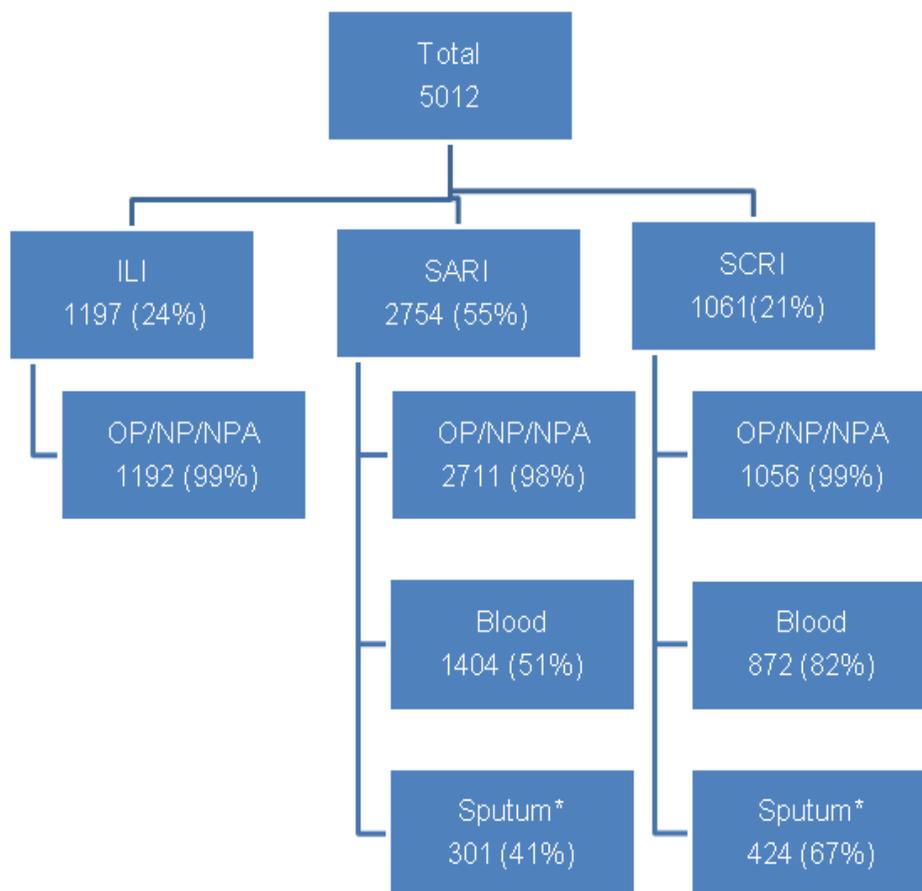
Data management was centralised at the NICD where laboratory, clinical and demographic data from enrolled patients were recorded on a Microsoft Access database.

Ethical considerations

The protocol was approved by the Research Ethics Committees of the University of the Witwatersrand, University of KwaZulu-Natal and University of Cape Town.

Results

Of the 5013 patients enrolled into the surveillance programmes in 2015, 5012 (99%) had complete data on case definition available; 1197 (24%), 2754 (55%) and 1061 (21%) met the case definition of ILI, SARI and SCRI respectively. Samples collected and tested for each of the case definitions is 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.



ILI = influenza-like illness, SARI = severe acute respiratory illness, SCRI = severe chronic respiratory illness, OP = oropharyngeal, NP = nasopharyngeal, NPA = nasopharyngeal aspirate
*Sputum collected from only two of the five sites.

Figure 1: Numbers of samples collected by case definition in the systematic influenza-like illness (ILI) and pneumonia surveillance programmes (SARI and SCRI), South Africa, 2015.

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, 2015.

Characteristic	Influenza-like Illness n/N (%) N=1192	Severe Acute Respiratory Illness n/N (%) N= 2711	Severe chronic Respiratory Illness n/N (%) N=1056
Age group years			
0-4	519/1182 (44)	1993/2699 (74)	128/1050(12)
5-14	130 /1182 (11)	102/2699 (4)	18/1050 (2)
15-24	137/1182 (12)	43/2699(2)	70/1050 (7)
25-44	294 /1182(25)	329/2699 (12)	426/1050 (41)
45-64	89 /1182 (8)	164/2699 (6)	311/1050 (30)
≥ 65	13/1182 (1)	68/2699 (3)	97/1050 (9)
Female gender	733/1192 (61)	1265 /2709(47)	518/1055 (49)
Site			
Edendale Gateway clinic	865/1192 (73)	N/A	N/A
Jouberton clinic	327/1192 (27)	N/A	N/A
EDH	N/A	264/2711 (10)	296/1056 (28)
KTHC	N/A	447/2711 (16)	336/1056 (35)
Matikwana/Mapulaneng hospitals	N/A	304/2711 (11)	40/1056 (4)
RMMCH/HJH	N/A	1036/2711 (38)	373/1056 (35)
Red Cross Hospital	N/A	660/2711(24)	11/1056 (1)
Underlying illness	50/1184 (4)	321/2693 (12)	149/1049 (14)
In-hospital case fatality ratio	N/A	73/2656 (3)	75/1014 (7)

EDH = Edendale Hospital, KTHC = Klerksdorp-Tshepong Hospital Complex, RMMCH/HJH = Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital

Pneumonia surveillance programme (SARI and SCRI) results

Viral pathogens

Of the 3815 patients enrolled in pneumonia surveillance, 3767 (99%) were tested for viral pathogens and 176 (5%) were positive for influenza. The influenza season started in week 20 and continued through week 25. It was predominated by influenza A(H1N1)pdm09 (80/176, 45%), followed by influenza A(H3N2) (50/176, 28%) and influenza B (45/176,26%). The peak detection rate was 23% in week 23 (Figure 2).

The overall detection rate for RSV was 13% (478/3767). The RSV season preceded the influenza season, it

started in week 9 and continued through week 29. The peak detection rate of 43% was in week 16. Parainfluenza viruses 1-3 were detected in 5% (168/3767) of samples and hMPV in 2% (89/3767) of samples. There was no clear seasonality for parainfluenza viruses and hMPV (Figure 3).

The majority of cases for the different respiratory viruses were in children <5 years (influenza112/175, 64%; RSV 445/475, 94%; PIV 1-3 145/166, 87% and hMPV 82/89, 92%). The case fatality ratio was similar across the cases positive for the respiratory viruses, and ranged between 1% and 3% (Table 4).

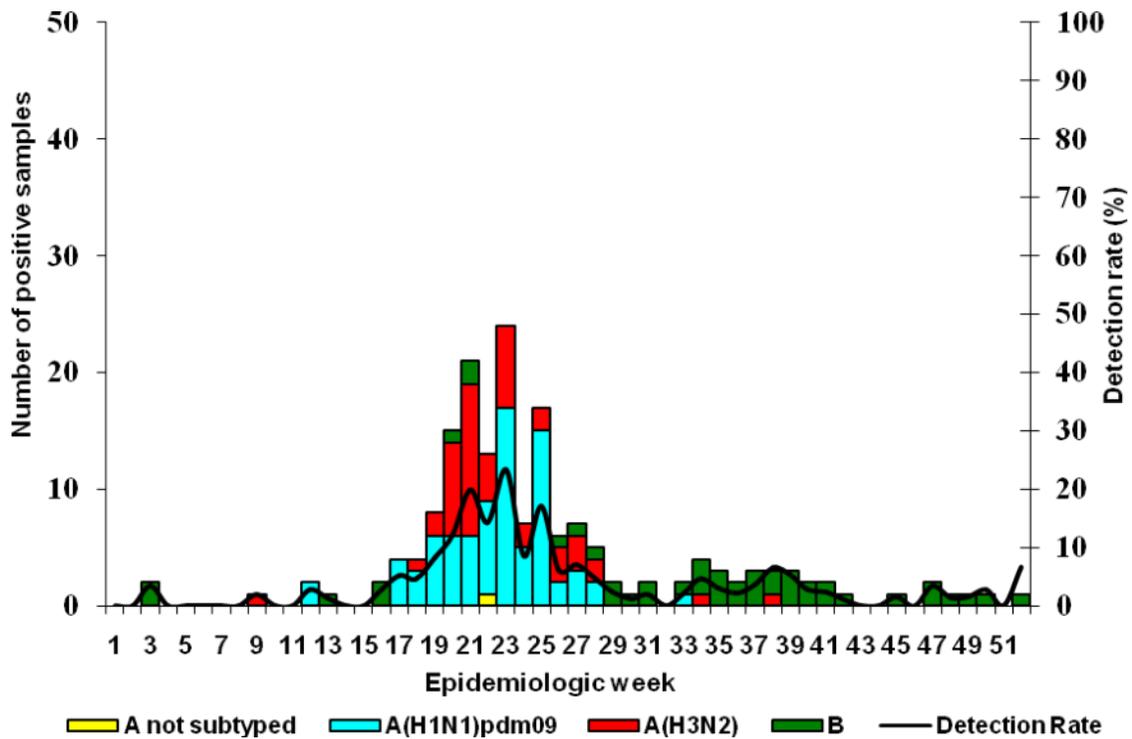


Figure 2: Numbers of samples positive for influenza and influenza detection rate, by subtype and week, in patients enrolled into the pneumonia surveillance programme and meeting the case definition of severe acute respiratory illness (SARI) or severe chronic respiratory illness (SCRI) in South Africa, 2015.

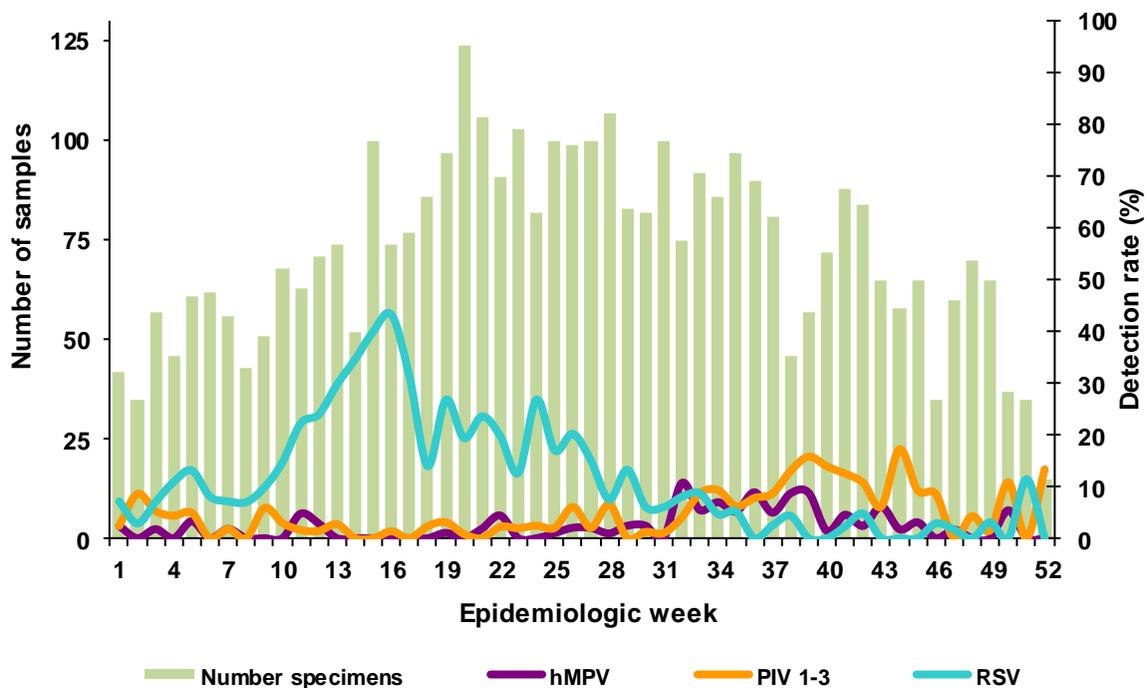


Figure 3: Numbers of samples collected and detection rates for respiratory syncytial virus (RSV), parainfluenza virus 1-3 (PIV1-3) and human metapneumovirus (hMPV), in patients meeting the case definition for severe acute respiratory illness (SARI) and severe chronic respiratory illness (SCRI), pneumonia surveillance, South Africa 2015.

Table 4: Detection rate and characteristics of patients meeting the case definition for severe respiratory illness (SARI) or severe chronic respiratory illness (SCRI) who tested positive for respiratory viruses (influenza, RSV, PIV1-3 or hMPV), pneumonia surveillance, South Africa, 2015.

	Influenza	RSV	PIV1-3	hMPV
Detection rate	176/3767 (5)	478/3767 (13)	168/3767(4)	5/3767 (2).
Age				
0-4	112/175 (64)	445/475 (94)	145/166 (87)	82/89 (92)
5-14	10//175 (6)	6/475 (1)	2/166 (1.2)	3/89(3)
15-24	2/175 (1)	1/475 (0.2)	2/166 (1.2)	0/89
25-44	27/175 (15)	10/475 (4)	13/166 (8)	3/89 (3)
45-64	17/175 (10)	9/475 (1)	2/166 (1.2)	1/89(1)
≥ 65	7/175 (4)	2/475 (0.4)	2/166 (1.2)	0/89
Female gender	81/176 (46)	216/478 (45)	83/167 (50)	50/89 (56)
Site				
EDH	31/176 (18)	63/478 (18)	20/68 (12)	8/89 (9)
KTHC	33/176 (19)	70/478 (15)	32/68 (19)	9/89 (10)
Matikwana/Mapulaneng	22/176 (12)	30/478 (6)	19/68 (11)	5/89(6)
RMMCH/HJH	63/176 (36)	164/478 (34)	49/68 (29)	21/89 (24)
Red Cross Hospital	27/176 (15)	151/478 (32)	48/68 (29)	46/89 (52)
In-hospital case fatality ration	6/174 (3)	5/468 (1)	4/167 (2)	2/89 (2)

RSV = respiratory syncytial virus, PIV = parainfluenza virus, hMPV = human metapneumovirus, RMMCH/HJH = Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital, KTHC = Klerksdorp Tshepong Hospital Complex, EDH = Edendale Hospital

Bacterial pathogens

Of the 3602 patients who had respiratory samples tested for bacterial pathogens 105/3602 (3%) were positive for *B. pertussis*, 12/3591 (0.6%) for *M. pneumoniae*, 5/3590 (0.1%) for *C. pneumoniae* and 3/3591 (0.1%) for *Legionella spp.* In the same group of patients, of the 2276 blood samples tested for *S. pneumoniae*, 295 (13%) were positive (Table 5). The

highest number of positive samples for the bacterial pathogens was in children <5 years, except for *Legionella spp.*, where all the cases were in the 25-44 year age group. The case fatality ratio was highest for patients testing positive for *B. pertussis* (7%, 7/101) (Table 5).The detection rate of *B. pertussis* and *S. pneumoniae* seemed to peak during the winter months (Figures 4 and 5).

Table 5: Detection rate among severe acute respiratory illness (SARI) and severe chronic respiratory illness (SCRI) cases tested, and characteristics of patients positive for *Bordetella pertussis*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella spp.* or *Streptococcus pneumoniae*, Pneumonia Surveillance Programme, South Africa 2015.

	B. pertussis* n/N (%)	M. pneumoniae* n/N (%)	C. pneumoniae* n/N (%)	Legionella spp.* n/N (%)	S. pneumoniae n/N (%)**
Detection rate	105/3602 (3)	21/3591 (0.6)	5/3590 (0.1)	3/3591 (0.1)	295/2276 (13)
Age					
0-4	76/104 (73)	13/21 (62)	5/5(100)	0/3	111/295 (38)
5-14	6/104 (6)	2/21 (10)	0/5	0/3	16/295 (5)
15-24	1/104 (1)	2/21 (10)	0/5	0/3	14/295 (5)
25-44	10/104 (10)	4/21(19)	0/5	3/3 (100)	89/295 (30)
45-64	9/104 (9)	0/21 (0)	0/5	0/3	50/295 (17)
≥ 65	2/104 (2)	0/21 (0)	0/5	0/3	15/295 (5)
Female gender	48/104 (46)	9/21 (43)	3/5 (60)	1/3 (33.3)	156/295 (47)
Site					
EDH [‡]	23/105 (23)	1/21 (5)	0/5	1/3 (33)	61/295 (21)
KTHC [‡]	26/105 (25)	3/ 21 (14)	3/5 (60)	2/3 (67)	89/295 (30)
Matikwana/Mapulaneng [#]	17/105 (16)	2/21 (10)	0/5	0/3	47/295 (16)
RMMCH/HJH [#]	32/105 (30)	8/21 (38)	1/5 (20)	0/3	72/295 (24)
Red Cross Hospital [#]	7/105 (7)	7/21 (33)	1/5 (20)	0/3	26/295 (9)
In-hospital case fatality ratio	7/101 (7)	1/19 (5)	0/5	0/3	9/290 (3)

*Nasopharyngeal ± sputum samples tested; **blood samples; ‡ Nasopharyngeal, sputum and blood samples collected; # Nasopharyngeal and blood samples collected.

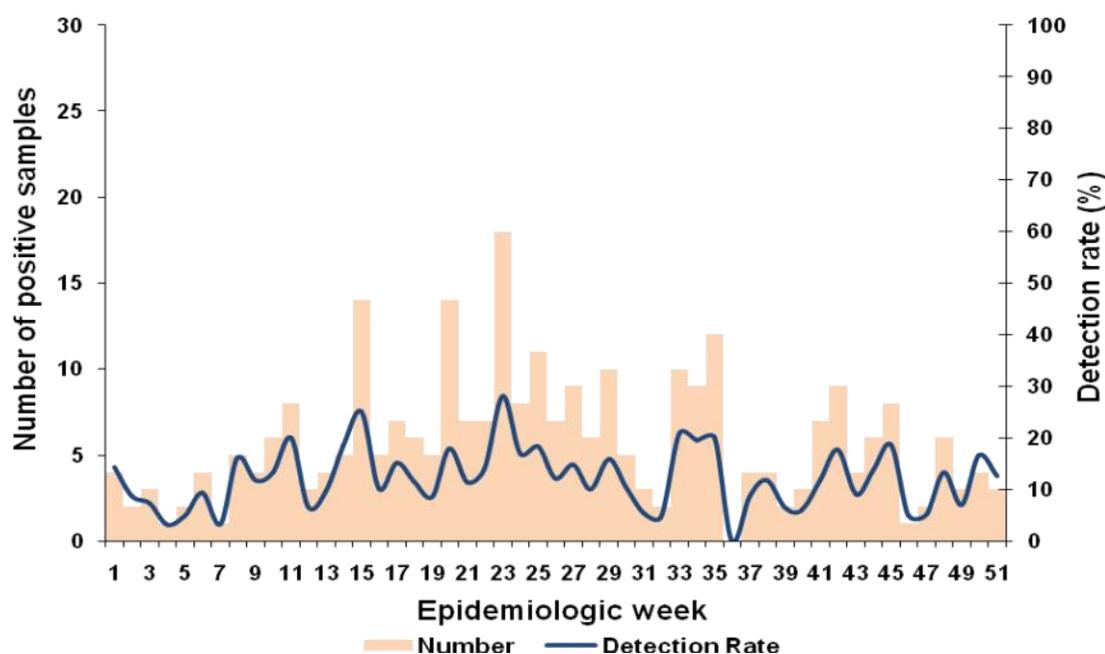


Figure 4: Numbers of positive samples and detection rate of *Streptococcus pneumoniae* from patients with severe acute respiratory illness (SARI) or severe chronic respiratory illness (SCRI) by week, Pneumonia Surveillance Programme, South Africa, 2015.

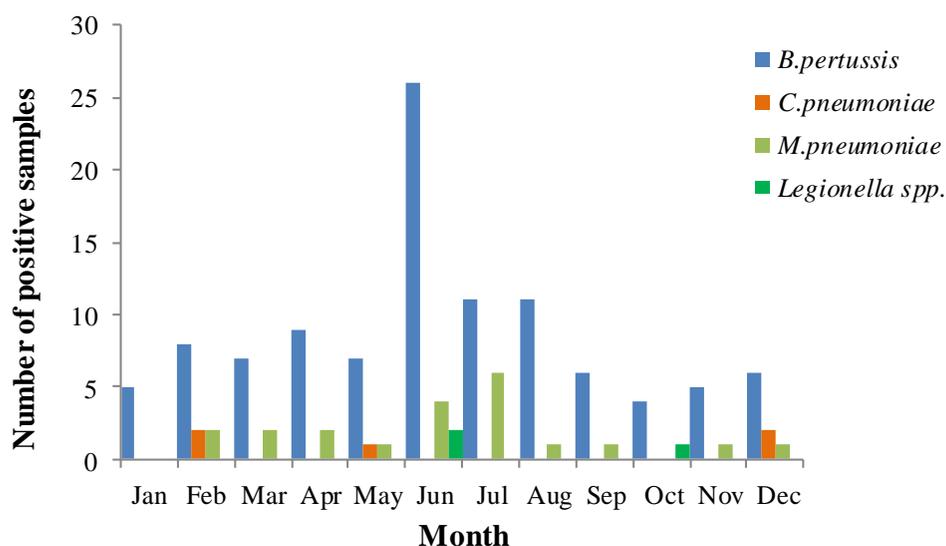


Figure 5: Numbers of positive samples of *Bordetella pertussis*, *Mycoplasma pneumoniae*, *Legionella spp.* and *Chlamydia pneumoniae* among patients with severe acute respiratory illness (SARI) or severe chronic respiratory illness (SCRI) by month, Pneumonia Surveillance Programme, South Africa, 2015.

Tuberculosis and *Pneumocystis jirovecii* pneumonia (PCP)

Of the 738 patients tested for *M. tuberculosis*, 82 (11%) were positive. Tuberculosis was detected throughout the year with no obvious seasonality (Figure 6). The majority of samples that tested positive for tuberculosis were collected at the KTHC site (57/82, 70%) and were in the 25 to 44 year age group (43/80, 54%) (Table 6).

Of the 258 (12%) samples that tested positive for PCP, 131 (51%) were from nasopharyngeal samples, 13 (5%) were from oral rinse samples and 114 (44.2%) from sputum. Similar to TB, there was no obvious seasonality (Figure 7). Most of the patients with positive samples were in the age group 25 to 44 years (87/198, 43.9%) and were female (113/201, 56.2%).

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

	Tuberculosis n/N(%)	<i>Pneumocystis jirovecii</i> n/N(%)
Detection rate	82/738 (11)	201/1282 (16)
Age group (years)		
0-4	2/80(2.5)	61/198 (31)
5-14	2/80 (1)	1/198 (1)
15-24	13/80 (16)	6/198 (3)
25-44	43/80 (54)	87/198 (44)
45-64	20/80 (25)	38/198 (19)
≥ 65	1/80 (1)	5/198 (2)
Female gender	41/82 (50)	113/201 (56)
Site		
EDH	25/82 (30)	84/201 (42)
KTHC	57/82 (70)	84/237 (35)
		117/201 (58)

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

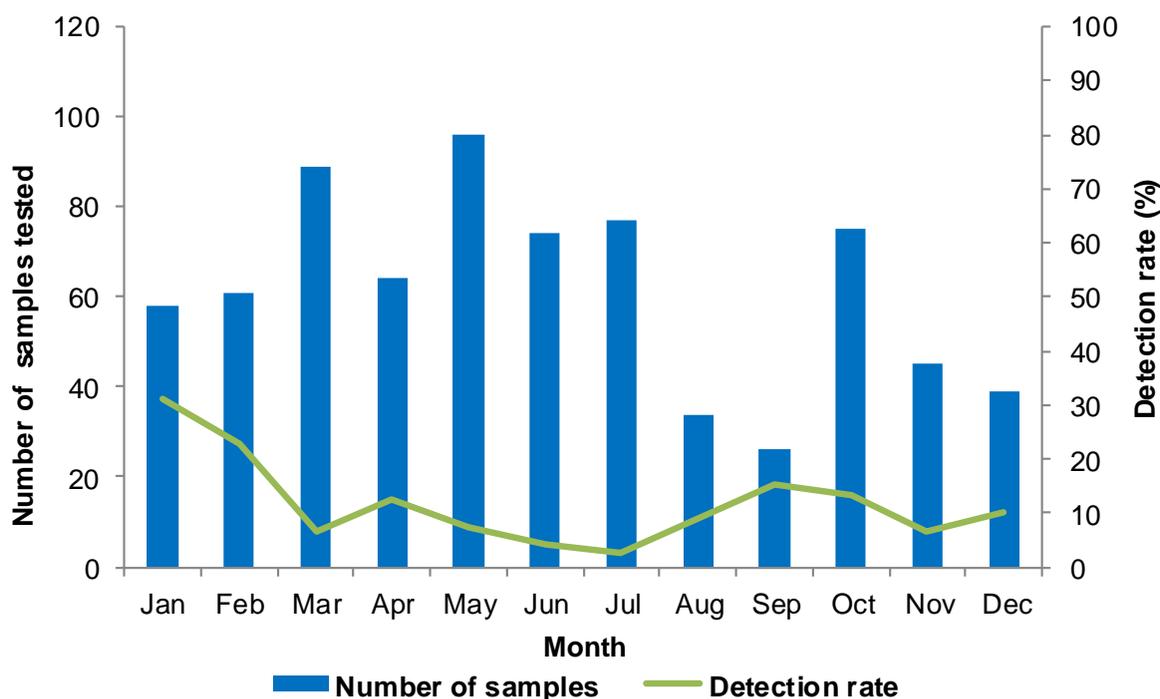


Figure 6: Numbers of samples tested for tuberculosis and detection rate among patients with severe acute respiratory illness (SARI) or severe chronic respiratory illness (SCRI) at Enhanced sites by month, Pneumonia Surveillance Programme, South Africa, 2015.

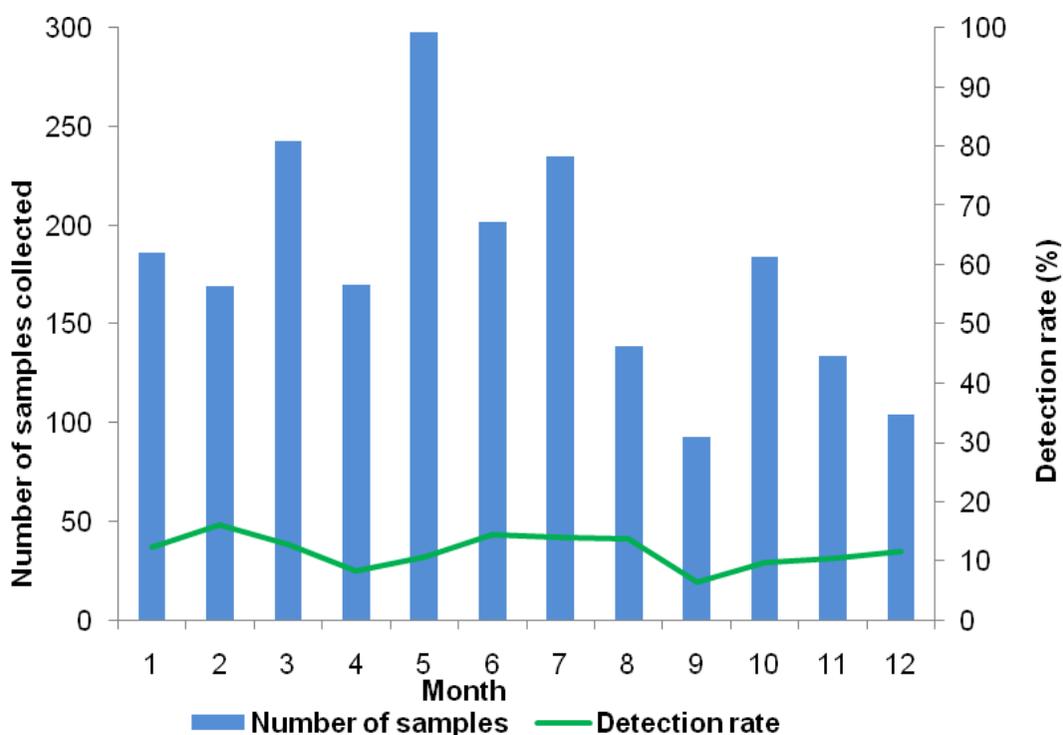


Figure 7: Numbers of samples tested for *Pneumocystis jirovecii* and detection rate for patients meeting the severe respiratory illness (SARI) or severe chronic respiratory illness (SCRI) case definition at the Enhanced sites, Pneumonia Surveillance Programme, South Africa, 2015.

Systematic ILI surveillance at primary health clinics

Respiratory viruses

During 2015, 1197 patients with ILI were enrolled at the two primary health clinics and 1192 (99%) samples were tested for respiratory pathogens. The overall detection rate of influenza was 11% (131). Of the 131 positive samples, 46 (35%), 44 (34%), 40 (31%) and 1 (<1%) were positive for influenza B, influenza A (H1N1)pdm09, influenza A(H3N2) and influenza A unsubtype respectively (Figure 8). There were no dual infections. Influenza positive samples were detected from week 9. The detection rate reached 10% in week 17 and was sustained above 10% until week 28 when it dropped to below 10%. It rose above 10% again in week 32 and 35 (Figure 8). Of the 1192 samples tested, 50 (4%) tested positive for parainfluenza 1-3, 81 (7%) for RSV, and 11 (1%) for human metapneumovirus. RSV demonstrated a defined seasonality which preceded the influenza season. The detection rate for RSV rose above 10% in

week 7 and was sustained at $\geq 10\%$ until week 17 (Figure 9).

Bacterial pathogens

Of the 1139 patients enrolled with ILI and tested for bacterial pathogens, 23/1136 (2%) tested positive for *B. pertussis*, 3/1139 (0.3%) for *M. pneumoniae* and 3/1139 (0.3%) for *C. pneumoniae* (Table 7). The highest number of positive samples for *B. pertussis* was in the 5-14 age group (6/23, 26%). The highest number of positive cases was in children <5 years (2/3, 67%) and in individuals <25 years for *M. pneumoniae* and *C. pneumoniae* respectively. There were no positive samples for *Legionella* spp. The number of cases positive for *B. pertussis* increased during the winter months (June to August). There was no clear seasonality for the other bacterial pathogens (Figure 10).

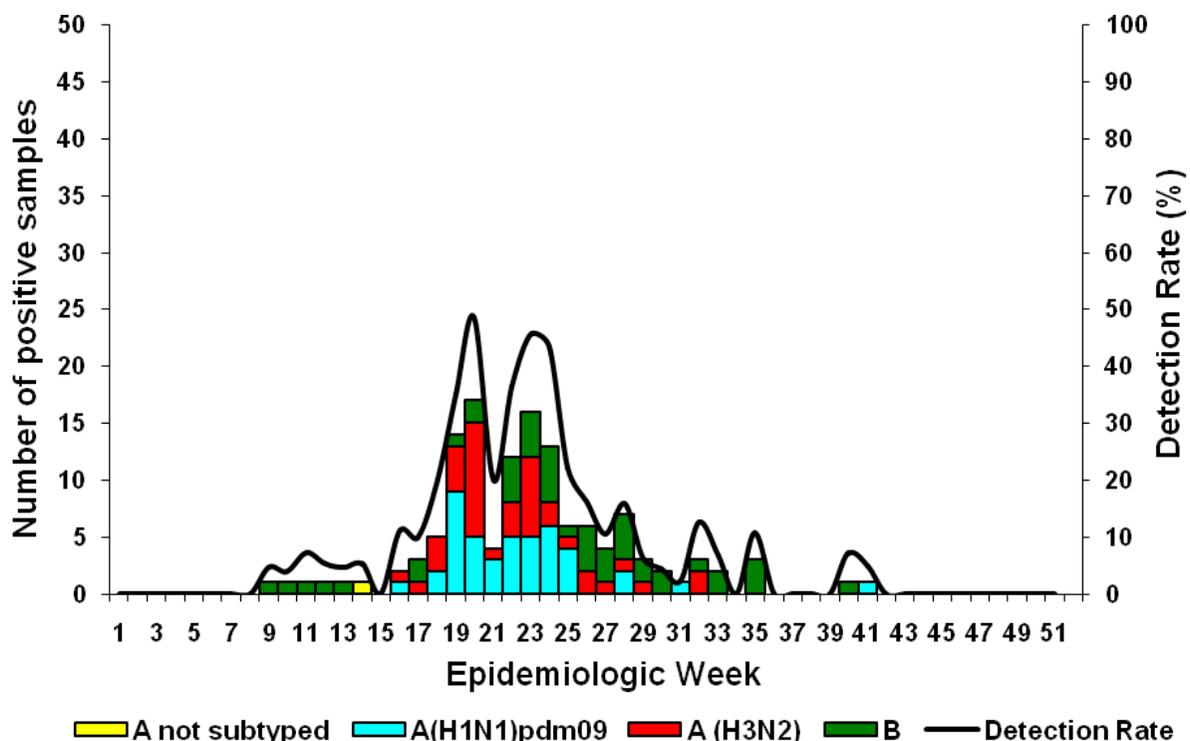


Figure 8: Influenza detection rate, by influenza subtype and week, in patients enrolled with influenza-like illness (ILI) at the two primary healthcare clinics, South Africa, 2015.

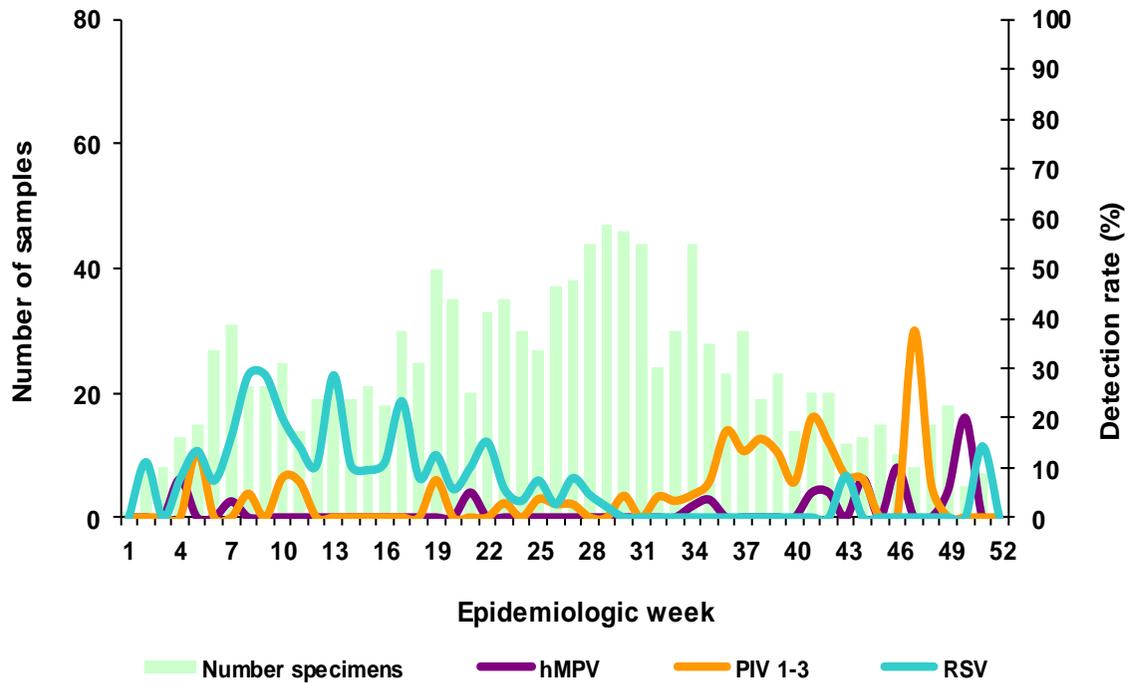


Figure 9: Detection rate of human metapneumovirus (hMPV), parainfluenza virus(PIV)1-3 and respiratory syncytial virus(RSV) by week in patients enrolled with influenza-like illness (ILI) at two primary health clinics, South Africa, 2015.

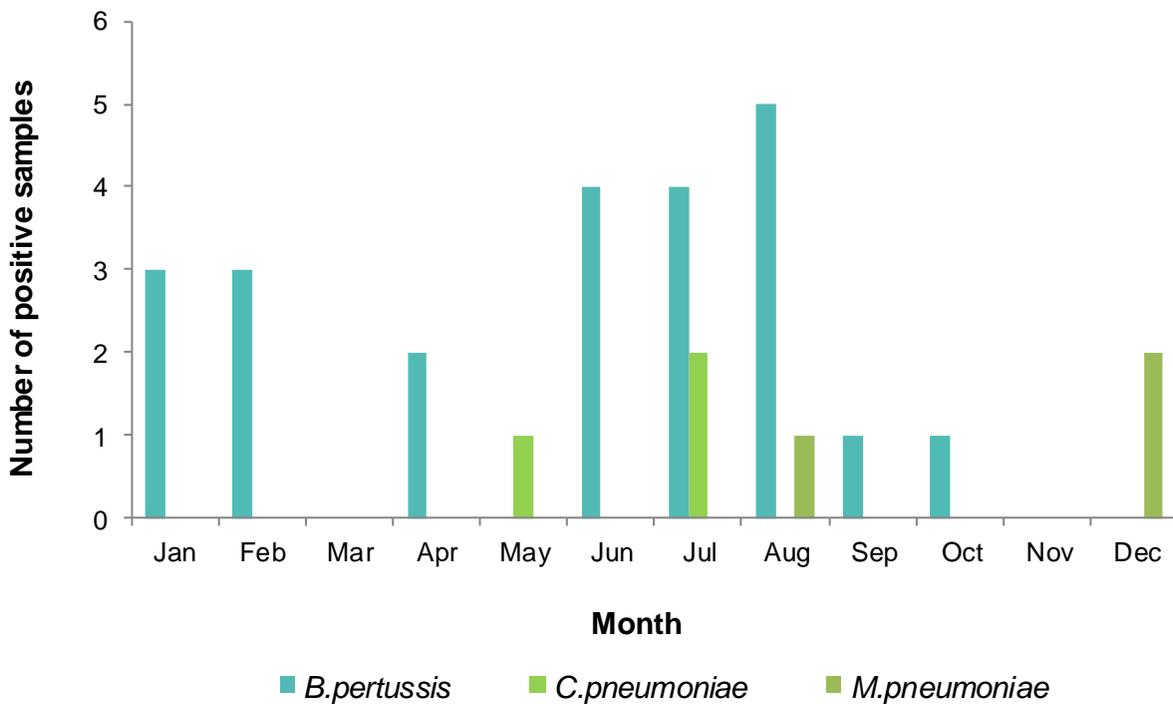


Figure 10: Numbers of positive samples for bacterial pathogens by month, in patients who met the influenza-like Illness (ILI) case definition at primary health clinics, South Africa, 2015.

Table 7: Detection rate and characteristics of patients with influenza-like illness (ILI) enrolled at public health clinics who tested positive for bacterial pathogens, South Africa, 2015.

	B. pertussis n/N(%)	M. pneumoniae n/N(%)	C. pneumoniae n/N(%)
Detection rate	23/1136 (2)	3/1139 (0.3)	3/1139(0.3)
Age group, years			
0-4	5/23(22)	2/3 (67)	1/3 (33.3)
5-14	6/23 (26)	0/3 (0)	1/3 (33.3)
15-24	4/23 (17)	0/7	1/3 (33.3)
25-44	4/23 (17)	1/3 (33)	0
45-64	4/23 (17)	0 /3	0
≥ 65	0/23 (0)	0/3 (0)	0
Female gender	16/23 (70)	2/3(67)	2/3(67)
Site			
Edendale Gateway clinic	17/23 (74)	2/3(67)	2/3(67)
Jouberton clinic	6/23 (26)	1/3(33)	1/7 (33)

Note: No samples tested positive for *Legionella spp.* in ILI patients

Additional surveillance activities

Viral watch (VW)

In 2015, 117 general practitioners across the 9 provinces participated in the VW programme. A total of 1136 samples was tested for influenza; of these 449 (40%) tested positive for influenza. The season was

dominated by influenza A(H1N1)pdm09 (256/449, 57%), followed by influenza A(H3N2) (191/515,42%); and influenza B (82/449 ,18%). The season started in week 16 (ending 19 April), peaked in week 23 (ending 7 June) and ended in week 37 (ending 13 September) (Figure 11).

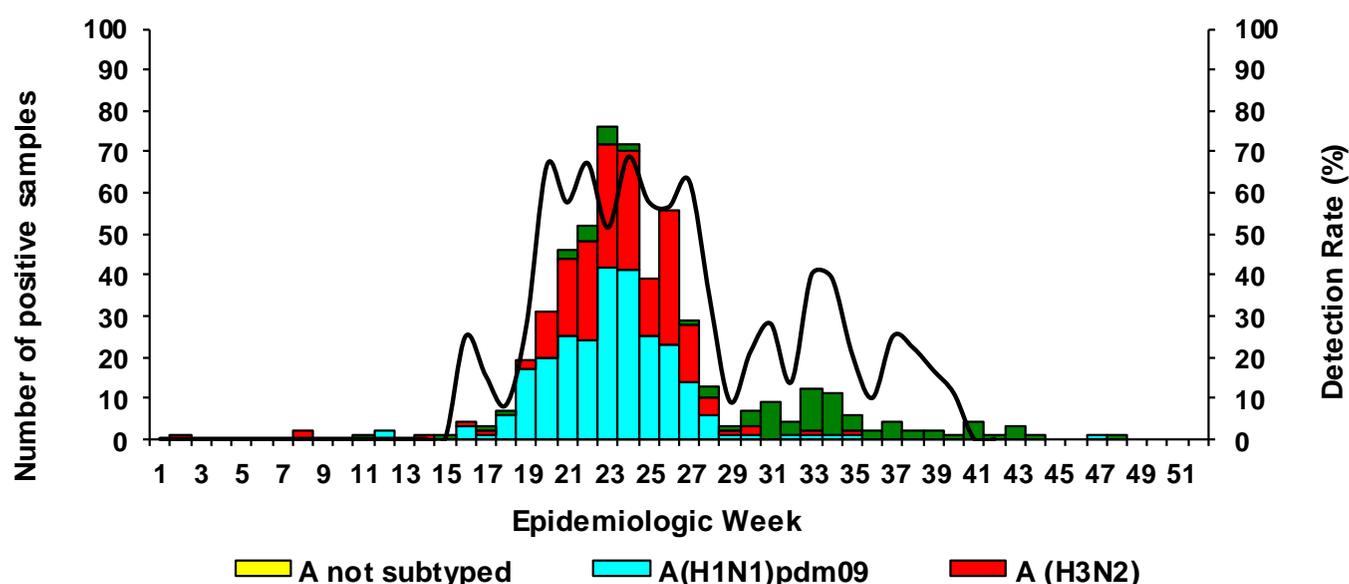


Figure 11: Numbers of samples and influenza detection rate by viral subtype and week for patients meeting the case definition of ILI, Viral Watch programme, South Africa, 2015.

Respiratory morbidity surveillance

During 2015 there were 1 169 554 consultations reported to the NICD through the respiratory morbidity data mining surveillance system. Of these, 28 655 (2%) were due to pneumonia or influenza (P&I) (International Classification of Diseases 10 codes J10-18). There were 21 401 (75%) inpatients and 7 254 (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 12 and 13). A second lower peak preceded the influenza season, corresponding to the circulation of respiratory syncytial virus (Figures 12 and 13, and cross reference Figure 3 - pneumonia surveillance viruses, and Figure 9 - ILI viruses).

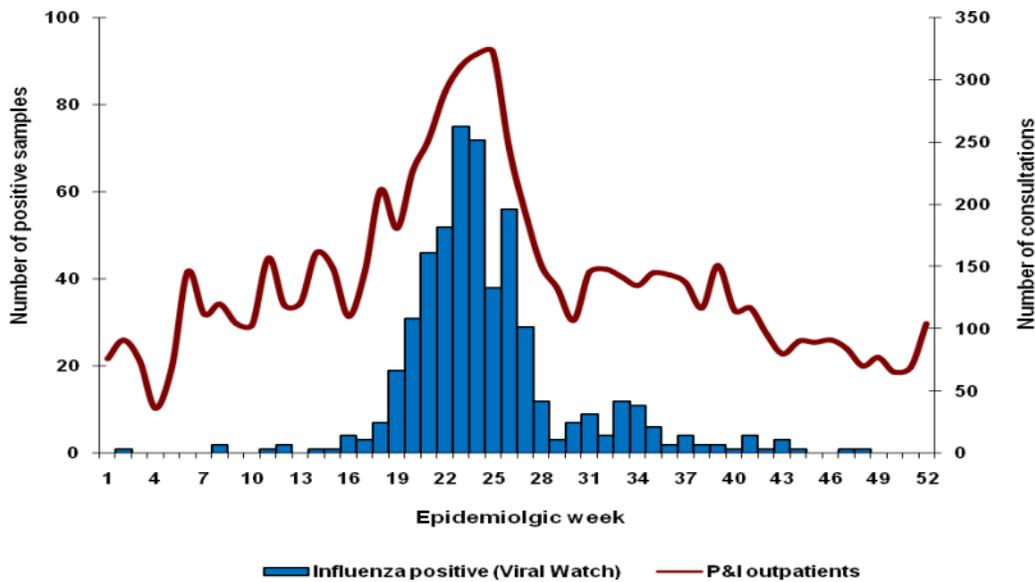


Figure 12: Numbers of private hospital outpatient consultations with a discharge diagnosis of pneumonia and influenza (P&I), and numbers of influenza positive viral isolates (Viral Watch) by week, South Africa, 2015.

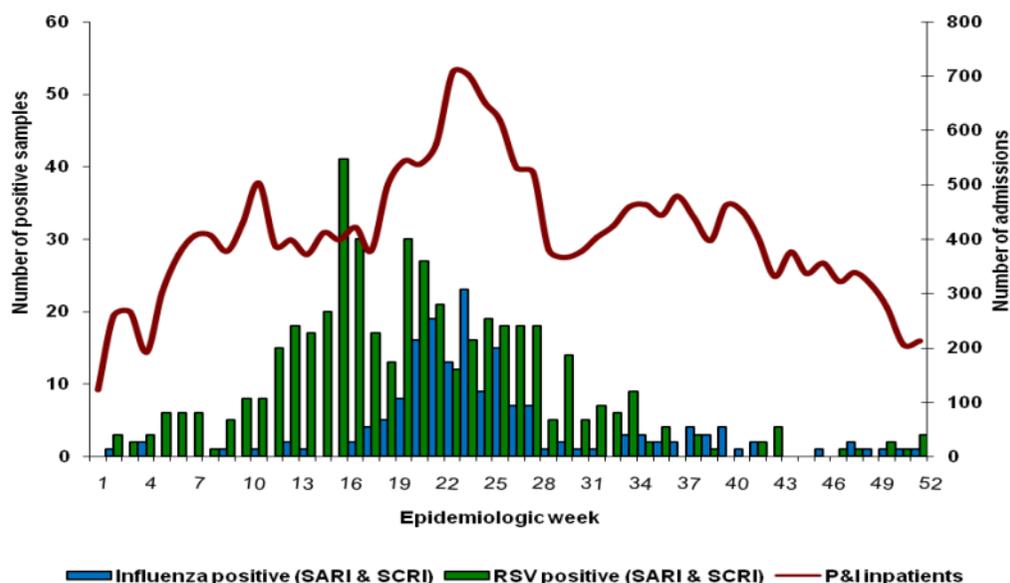


Figure 13: Numbers of private hospital admissions for pneumonia and influenza, as well as numbers of influenza positive viral isolates and respiratory syncytial virus (RSV) positive isolates (SARI and SCRI) by week, South Africa, 2015.

Discussion

The influenza season in South Africa in 2015 was predominately influenza A(H1N1)pdm09, followed by influenza A(H3N2) and influenza B. The season started in week 17 at the ILI sites but the detection rate in the pneumonia surveillance programme remained constantly above 10% from week 20. The 2015 influenza season started early compared to previous years in which the mean onset of the influenza season was week 22 (range 17-28), with an average duration of 13 weeks (range 7-25).² The RSV season preceded the influenza season, starting in week 7 at the ILI sites and in week 9 at the pneumonia surveillance sites. The 2015 RSV season started two weeks later than the 2014 season.¹ There was a suggestion of a winter peak for some of the bacterial pathogens including *B.pertussis* and *S.pneumoniae*. There was no defined seasonality for the other respiratory pathogens.

Among cases enrolled as part of pneumonia surveillance, the common pathogens detected were *S. pneumoniae* and RSV, followed by tuberculosis, PCP and influenza. All the other pathogens were detected in <5% of individuals tested. Pertussis, while relatively less common, was associated with a high case-fatality ratio of 7% (7/101). Among ILI cases the common pathogens detected were influenza followed by RSV and parainfluenza 1-3. The other respiratory pathogens were detected in $\leq 2\%$ of cases.

The Centre for Respiratory Diseases & Meningitis, NICD, is working towards comprehensive surveillance for the clinical syndromes of ILI and pneumonia. This is the second report to combine the viral pathogens with the additional testing for bacterial pathogens and some of the atypical causes of pneumonia in our setting. Work is being done on the interaction between these pathogens and the risk factors for severe disease which will assist clinicians and policy makers to improve health care and implement prevention strategies such as vaccines.

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