EPIDEMIOLOGY OF RESPIRATORY PATHOGENS FROM THE INFLUENZA-LIKE ILLNESS AND PNEUMONIA SURVEILLANCE PROGRAMMES, SOUTH AFRICA, 2019

Jessica Yun[1,2], Jackie Kleynhans [2], Jocelyn Moyes[2], Jinal Bhiman[2], Amelia Buys[2], Florette Treurnicht[2], Orienka Hellferscee[2], Jo Mcanerney[2], Anne von Gottberg[2], Nicole Wolter[2], Fahima Moosa[2], Mignon du Plessis[2], Linda De Gouveia[2], Thulisa Mkhencele[2], Cheryl Cohen[2], Sibongile Walaza[2]

[1]Field Epidemiology Training Programme (FETP), NICD
[2]Centre for Respiratory Diseases and Meningitis, NICD

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 the Viral Watch programme at private practices) and the respiratory morbidity surveillance system. Nasopharyngeal samples collected from enrolled individuals meeting surveillance case definitions at sentinel sites were tested for influenza, respiratory syncytial virus (RSV) and *Bordetella pertussis* by real-time polymerase chain reaction. The 2019 influenza season in South Africa started earlier at the ILI sites (week 16 in the Viral Watch programme and at the public clinics), compared to the pneumonia surveillance sites which only reflected the start of the season in week 19. The 2019 influenza season was predominated by influenza A(H3N2) with co-circulation of influenza A(H1N1)pdm09 and very few cases of influenza B (influenza B/Victoria and B/Yamagata). The overall vaccine effectiveness (VE), adjusted for age and seasonality, was 52.8% (95% confidence interval (CI): 22.5% to 71.3%) against any influenza virus type and 53.2% (95% CI 22.5%-71.6%) against influenza A(H3N2). The RSV season, which preceded the influenza season, started in week 8 and ended in week 25. There was no apparent seasonality for *Bordetella pertussis* for which the number of cases decreased from month to month throughout the year among patients enrolled in the pneumonia surveillance programme. Among patients enrolled in the ILI surveillance programme, very few cases of *B. pertussis* were reported, with the highest number of *B. pertussis* cases (N=4) identified in May 2019. Among ILI cases, the most common pathogen identified in individuals aged <15 years was RSV (10.2%, 135/1321) followed by influenza

(8.7%, 115/1321) and *B. pertussis* (0.7%, 9/1321). Among individuals aged ≥15 years, influenza (9.0%, 38/423) was commonest followed by RSV (2.3%; 10/423), and no *B. pertussis* cases were detected. Among individuals enrolled as part of pneumonia surveillance aged <15 years, the commonest pathogen was RSV (24.7%, 778/3148) followed by influenza (4.7%, 147/3148) and *B. pertussis* (1.0%; 31/3148). Among individuals aged ≥15 years, influenza (6.2%, 88/1414) was commonest, followed by RSV (1.3%, 19/1414) and *B. pertussis* (0.3%, 4/1414). Overall, the in-hospital case fatality ratio among individuals enrolled as part of pneumonia surveillance was 2.8% (128/4534).

These surveillance programmes can be used to inform key stakeholders on influenza and *B. pertussis* vaccine effectiveness, identify vaccine failures, prompt prioritisation of vaccinations among certain groups who are at highest risk of the main respiratory pathogens (influenza and B. pertussis), and to inform the selection of vaccine strains for the southern hemisphere. This report also provides insight into the changing epidemiology of pertussis and provides data that could be used to assist stakeholders and policymakers in making informed decisions on implementing different prevention strategies (e.g. introducing pertussis vaccination for pregnant women) and new control strategies (e.g. RSV vaccine) when these become available. Ultimately, timely detection and characterisation of respiratory pathogens could mitigate respiratory illness-associated mortality, morbidity and the associated economic costs to South Africa.

Introduction

Respiratory infections such as influenza and respiratory syncytial virus (RSV) are part of the leading causes of medical consultations and are a major contributor to hospital admissions and mortality globally. In children, the elderly and those who have underlying chronic medical conditions, influenza may result in substantial direct healthcare costs.[1,2] The Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD) implements a set of syndromic respiratory illness surveillance programmes to monitor and describe the epidemiology of respiratory illness caused by selected pathogens in South Africa. Surveillance programmes include the pneumonia surveillance programme, the influenza-like illness (ILI) surveillance programme ((consisting of two programmes: systematic ILI surveillance at public health clinics and Viral Watch (VW), and ILI surveillance at private practitioners)) and the respiratory morbidity surveillance programme.

These programmes can be used to inform key stakeholders on influenza and *B. pertussis* vaccine effectiveness, identify vaccine failures, prompt prioritisation of vaccinations among certain groups who are at highest risk of the main respiratory pathogens (influenza and *B. pertussis*), and to inform the selection of vaccine strains for the southern hemisphere.[3,4] This information also provides insight into the changing epidemiology of pertussis and provides data that could be used to assist stakeholders and policymakers in making informed decisions on implementing different prevention strategies (e.g. introducing pertussis vaccination for pregnant women) and new control strategies (e.g. RSV vaccine) when these become available. Ultimately, timely detection and characterisation of respiratory pathogens could mitigate respiratory illness-associated mortality, morbidity and the associated economic costs to South Africa.

This annual report describes the epidemiology of respiratory illness in South Africa, using data from these surveillance programmes, for 2019.

Methods

A summary of each surveillance programme is included below. Respiratory specimens from ILI and pneumonia surveillance sites were tested for three pathogens: influenza virus, RSV and *Bordetella pertussis*. Viral Watch tested for influenza and RSV viruses.

Description of the surveillance programmes. The pneumonia surveillance programme was first introduced in 2009 and is an active, prospective hospital-based sentinel surveillance programme for severe respiratory illness (SRI).[4,5] The main aim of the surveillance programme is to describe the burden and epidemiology of SRI cases at sentinel surveillance sites and determine the relative contribution of influenza, RSV and *B. pertussis* to disease presentation in a high HIV prevalence setting.[6] Currently, the pneumonia surveillance programme was implemented at 8 sites (Klerksdorp Tshepong Hospital Complex, Rahima Moosa Mother and Child Hospital, Helen Joseph Hospital, Red Cross Hospital, Matikwana Hospital, Mapulaneng Hospital and Mitchell's Plain Hospital) in 5 provinces of South Africa namely Gauteng, KwaZulu-Natal, Mpumalanga, Western Cape and the North West Province (Table 1).[7] Hospitalised patients were prospectively enrolled by dedicated surveillance staff from Monday to Friday.

Patients were eligible to be enrolled in the pneumonia surveillance programme provided that the clinical case definition of SRI and/or suspected *B. pertussis* was met (Table 1). For analysis purposes, SRI was further subdivided into acute and chronic illness based on symptom duration. Patients with a symptom duration of ≤10 days were diagnosed with severe acute respiratory illness (SARI) and patients with a symptom duration of >10 days with severe chronic respiratory illness (SCRI). Clinical and epidemiological data were collected using standardised questionnaires.

The systematic ILI surveillance programme in public sector clinics was established in 2012 to describe the epidemiology of less severe outpatient ILI among adults and children at selected sentinel sites that are in the same catchment areas as the pneumonia surveillance programme sites. In 2019, the ILI surveillance programme was active at four sites (Eastridge Clinic, Edendale Gateway Clinic, Jouberton Clinic and Mitchell's Plain Clinic) in three provinces including KwaZulu-Natal Province, North West Province and Western Cape Province (Table 1). Dedicated staff prospectively enrolled patients who met the ILI and/or suspected pertussis case definitions from Monday to Friday. Clinical and epidemiological data were collected using standardised questionnaires. Nasopharyngeal samples were collected for testing (Table 2).

The Viral Watch programme (VW) is an active, prospective sentinel outpatient-based surveillance programme which was established in 1984.[8] The main objective of this programme is to describe the epidemiology of influenza and assess the effectiveness of the trivalent seasonal influenza vaccine in South Africa.[8] Participation in the programme is voluntary and clinicians are requested to send nasopharyngeal and/or oropharyngeal swabs from patients who meet the ILI case definition to the NICD. The programme is currently conducted at 91 sentinel sites in private practice across seven provinces of South Africa.

The respiratory morbidity surveillance system uses anonymised data from a private hospital network, in eight of South Africa's nine provinces, to track trends in the number of pneumonia and influenza hospitalisations.

Data from the VW 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.[9,10] For this report, patients presenting with ILI

to participating practitioners at the sentinel surveillance sites during the 2019 influenza season were used to calculate vaccine effectiveness (VE). Patients who tested influenza virus-positive were defined as cases, whereas those who tested negative were used as controls. Clinical, demographic and influenza vaccination data were collected from each patient at the time of specimen collection. Specimens that were collected during the influenza season from patients aged ≥6 months, and meeting the ILI case definition with available influenza vaccine history (self-reported), were included in the VE analysis. VE was measured by the proportionate reduction in cases among vaccinated persons and was calculated as 1-odds ratio (OR) for laboratory-confirmed influenza in vaccinated and unvaccinated patients. Multivariable logistic regression was used to adjust VE estimates by age, pre-existing underlying medical condition and seasonality.

Using data derived from the VW programme and pneumonia surveillance programme, influenza transmissibility and influenza season impact was established by applying the Moving Epidemic Method (MEM), a sequential analysis that calculated the intensity thresholds using the R Language statistical software. Graphs were produced using the MEM Web application, available from: http://CRAN.R-project.org/web/package=mem. The 2019 VW detection rate was plotted against thresholds set by data collected from VW between 2008 and 2018 (excluding the pandemic year: 2009). Similarly, the 2019 pneumonia surveillance detection rate was plotted against thresholds set by data collected from the pneumonia surveillance programme between 2010 and 2018.

For the RSV season, the 2019 RSV detection rate was plotted againts thresholds set by data collected from systematic ILI between 2010 and 2018. Similarly, the 2019 RSV pneumonia surveillance detection rate was plotted against thresholds set by data collected from the pneumonia surveillance programme between 2010 and 2018. Influenza and RSV thresholds of activity were defined as below seasonal threshold, low activity, moderate activity, high activity, and very high activity. The 40th, 90th and 97.5th percentiles were established using historical data to calculate activity thresholds using MEM. For influenza, thresholds from outpatient ILI (VW Programme) are used as an indicator of disease transmission in the community and thresholds from pneumonia surveillance are used as an indicator of impact of disease.

Sample and data collection for pneumonia and ILI surveillance. For pneumonia and ILI surveillance programmes, nasopharyngeal (NP) and oropharyngeal (OP) flocked swabs placed in universal transport medium were collected from patients of all ages for testing of influenza, RSV and *B. pertussis* (Table 2). In addition, nasopharyngeal swabs placed in Regan Lowe medium were collected for *B. pertussis* culture. Upper respiratory samples were stored at 4°C at the local site laboratory and were transported to the NICD on ice within 72 hours of collection. Epidemiological, clinical and laboratory-related data were collected by site surveillance officers.[11]

Detection of influenza, RSV and B. pertussis. Influenza A virus, influenza B virus and RSV were tested using a commercial multiplex real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) assay (Fast-Track Diagnostics, Luxembourg) at the NICD (Table 2). 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/). Influenza A and influenza B positive specimens were further subtyped using CDC rRT-PCR.[12] RSV specimens were subtyped into RSV (A), RSV (B) and RSV (AB). RSV (AB) indicates a coinfection where both RSV (A) and RSV (B) subgroups were identified. *Bordetella pertussis* was detected using a previously described method.[13] A specimen was considered positive for *B. pertussis* if IS481 and/or ptxS1 gene targets were detected with a Ct value <45 (Table 2).

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, 2019.

Case definition	Criteria	Surveillance site/programme
Influenza-like illness (ILI)	**Patients of all ages** Acute fever of ≥38°C and/or self-reported fever AND cough within the last 10 days	Viral Watch programme and public health clinics for systematic ILI surveillance: Jouberton Clinic, Edendale Gateway Clinic, Mitchell's Plain Community Clinic and Eastridge Clinic
Severe respiratory illness (SRI)	**2 days - <3 months** Any child hospitalised with a diagnosis of suspected sepsis or physician-diagnosed LRTI irrespective of signs and symptoms. **3 months - <5 years** Any child ≥3 months to <5 years hospitalised with physician-diagnosed LRTI including bronchiolitis, pneumonia, bronchitis and pleural effusion **≥5 years** Any person hospitalised with a respiratory infection with fever (≥38ºC) or history of fever AND cough	Pneumonia surveillance: 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.	Public health clinics for systematic ILI surveillance: Jouberton Clinic, Edendale Gateway Clinic, Mitchell's Plain Community Clinic and Eastridge Clinic Pneumonia surveillance: EDH, KTHC, Matikwana/Mapulaneng, RMMCH/HJH, RCH/MPH

EDH=Edendale Hospital (KwaZulu-Natal Province), KTHC=Klerksdorp-Tshepong Hospital Complex (North-West Province), RMMCH/HJH= Rahima Moosa Mother and Child Hospital/Helen Joseph Hospital (Gauteng Province), RCH/MPH=Red Cross War Memorial Children's Hospital/ Mitchell's Plain Hospital (Western Cape Province), 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 programmes, South Africa, 2019.

Pathogen	Programme (syndrome)	Specimens collected	Tests conducted
Influenza and RSV	Viral Watch (ILI) Systematic ILI Pneumonia surveillance (SRI)	Nasopharyngeal (NP) and oropharyngeal (OP) flocked swabs in universal transport medium (UTM)	Multiplex real-time reverse transcription polymerase chain reaction (rRT-PCR)
Bordetella pertussis	Systematic ILI Pneumonia surveillance (SRI)	NP and OP flocked swabs in UTM NP in Regan Lowe medium	Multiplex real-time PCR and Culture

ILI=influenza-like illness, SRI=severe respiratory illness

Data management and analysis. Data management was centralised at the NICD. Each enrolled patient's laboratory, clinical and demographic data from the above-mentioned surveillance programmes were recorded and stored on a Microsoft Access database with double data entry. Duplicate records and missing values, and the validity and integrity of the data were checked. Records with missing values were cross-checked against the original paper documents at CRDM. All analyses were conducted using Stata version 15 (StataCorp LP, College Station, TX, USA).

Results

In 2019, 6319 patients were enrolled in the 2 syndromic surveillance programmes conducted in the public sector (ILI and pneumonia surveillance). Of these, 6306 (99.8%) samples were tested for respiratory pathogens (Figure 1). For two patients with available influenza and RSV results, *B. pertussis* testing could not be conducted as NP/OP samples were not received in Regan Lowe medium. Of the samples that were tested, 27.7% (1744) were enrolled in the ILI programme and 72.3% (4562) were enrolled in the pneumonia surveillance programme (Figure 1). Individuals aged <15 years made up the majority of both ILI and SRI cases (75.7%, 1321/1744 and 69.0%, 3148/4562 respectively). Among SRI patients, the majority of individuals aged <15 years presented with an acute illness (SARI-symptom duration of ≤10 days) (95.9%, 3019/3148), while among individuals aged ≥15 years 53.4% (755/1414) presented with an acute illness. The overall HIV prevalence among patients with SRI was 20.3% (793/3898) and 6.3% (108/1703) among patients with ILI (Figure 2). The HIV prevalence varied by age group and case definition (Figure 2). HIV prevalence was highest in cases with severe chronic respiratory illness (SCRI) (59.4%, 368/620) followed by SARI and ILI cases respectively (13.0%, 425/3278 and 6.3%, 108/1703). HIV prevalence was highest in the 25-44 year age group for SCRI (35.6%, 221/620), SARI (6.4%, 210/3278) and ILI (3.2%, 54/1703) cases.

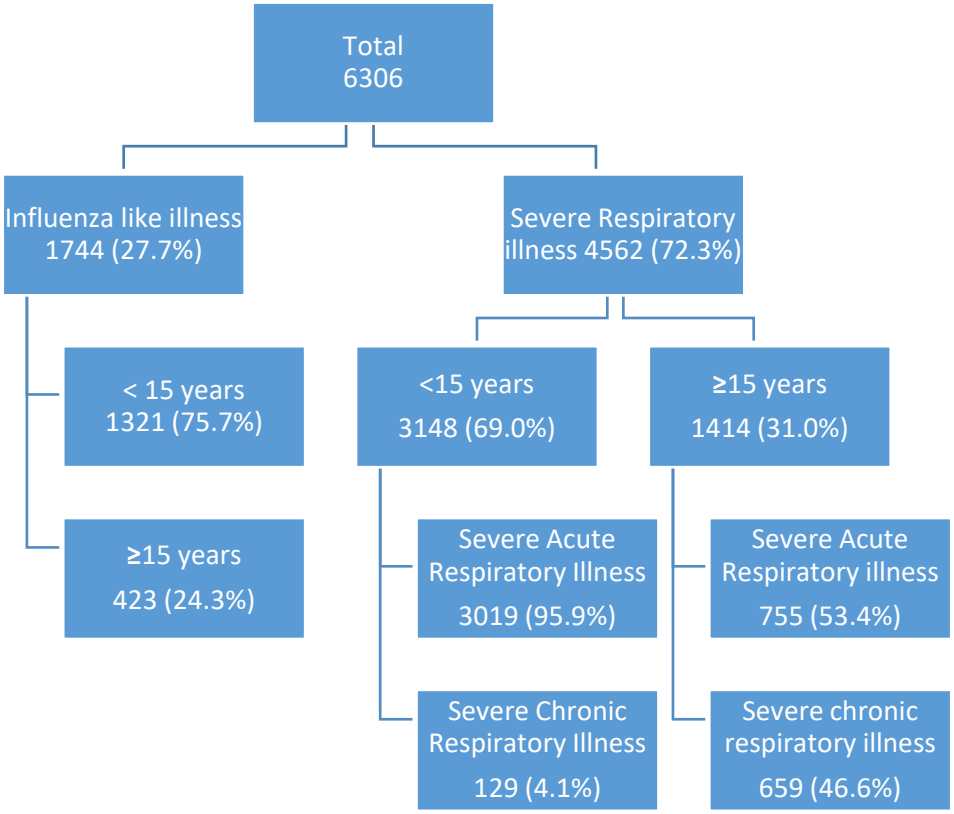

Figure 1. Individuals who had a nasopharyngeal and oropharyngeal sample collected and tested by case definition in the systematic influenza-like illness (ILI) and pneumonia surveillance programmes (SRI), South Africa, 2019.

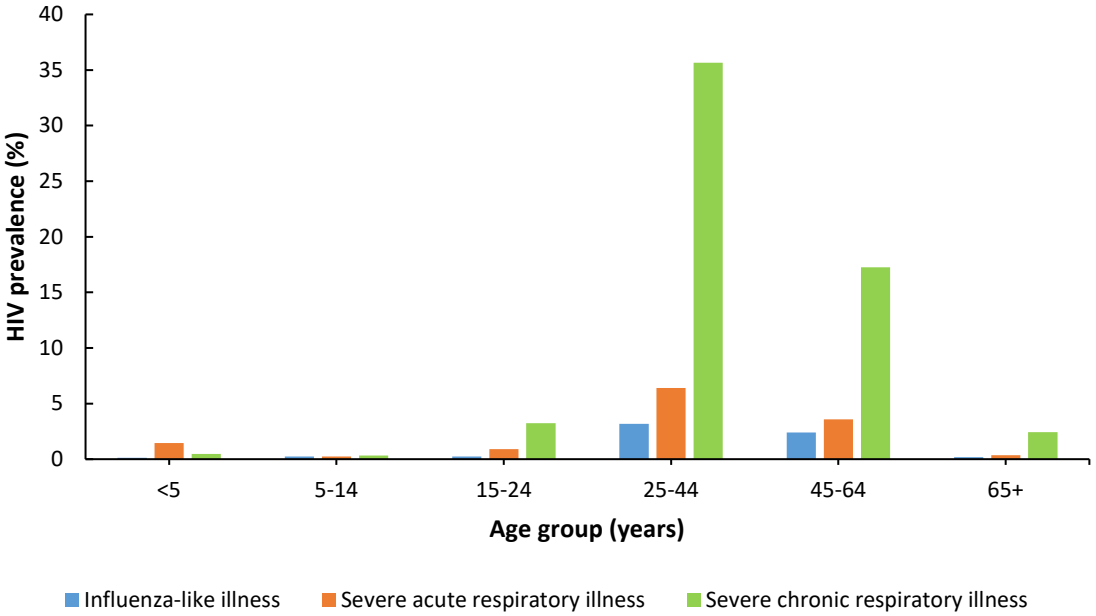

Figure 2. HIV prevalence by age group for individuals meeting case definitions of influenza-like illness and severe respiratory illness among patients enrolled in pneumonia surveillance and influenza-like illness surveillance, South Africa, 2019.

Influenza, RSV and B. pertussis among individuals aged <15 years enrolled into the ILI programme. Among ILI cases, the most common pathogen identified in individuals aged <15 years was RSV (10.2%, 135/1321) followed by influenza (8.7%, 115/1321) and *B. pertussis* (0.7%, 9/1321) (Table 3). Among those who tested positive for RSV, a majority of individuals (28.2%, 38/135) were in the 2-4 year age group. Comparatively, 40.0% (46/115) of individuals who tested positive for influenza were aged 5-14 years. Of the 9 pertussis cases, 33.3% (3/9) were in infants 0-2 months and 33.3% (3/9) were in children aged 5-14 years. There was a 93.9% (921/981) vaccine coverage for the 13-valent pneumococcal conjugate vaccine (PCV-13) and 94.2% (927/984) coverage for Diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, *haemophilius influenza*e type B and Hepatitis B combined (DTaP-IPV-HIB-HBV) vaccine (vaccine up to date for age). Vaccine coverage for DTaP-IPV-HIB-HBV was lower for those who tested positive for *B. pertussis* (83.3%, 5/6) as compared to those who tested negative for *B. pertussis* (94.3%, 921/977) (p=0.25), although this was not statistically significant.

Influenza, RSV and B. pertussis among individuals aged ≥15 years enrolled into the ILI programme. Of individuals aged ≥15 years who met the case definition for ILI, influenza (9.0%, 38/423) was the most commonly detected pathogen followed by RSV (2.4%; 10/423). No *B. pertussis* (0%, 0/423) cases were detected in the ILI surveillance programme among individuals aged ≥15 years (Table 4). The highest proportion of influenza cases were in the 25-44 year (42.1%, 16/38) age group. Of the RSV cases, 30% (3/10) were in the 24-44-years, 45-64- year (30.0%, 3/10) and ≥65 year (30.0%, 3/10) age groups respectively. Among those who were positive for influenza, 23.7% (9/38) were HIV infected. Among those aged ≥15 years in the ILI surveillance programme, 19.9% (84/423) had an underlying condition.

Table 3. Demographic and clinical characteristics of patients aged <15 years enrolled in the systematic influenza-like illness surveillance programmes, South Africa, 2019.

Characteristic	Overall	Influenza negative	Influenza positive	P-value	RSV negative	RSV positive	P-value	*B. pertussis* negative	*B. pertussis* positive	P-value
	n/N (%) N=1321****	n/N (%) N=1206	n/N (%) N=115		n/N (%) N=1186	n/N (%) N=135		n/N (%) N=1311	n/N (%) N=9	
Age group										
0-2 months	101/1321 (7.7)	96/1206 (8.0)	5/115 (4.4)	<0.001	88/1186 (7.4)	13/135 (9.6)	0.15	98/1311 (7.5)	3/9 (33.3)	0.04
3-5 months	127/1321 (9.6)	124/1206 (10.3)	3/115 (2.6)		112/1186 (9.4)	15/135 (11.1)		126/1311 (9.6)	1/9 (11.1)	
6-11 months	209/1321 (15.8)	204/1206 16.9)	5/115 (4.4)		188/1186 (15.9)	21/135 (15.6)		208/1311 (15.9)	1/9 (11.1)	
12-13 months	223/1321 (16.9)	205/1206 (17.0)	18/115 (15.7)		194/1186 (16.4)	29/135 (21.5)		222/1311 (16.9)	1/9 (11.1)	
2-4 years	359/1321 (27.2)	321/1206 (26.6)	38/115 (33.0)		321/1186 (27.0)	38/135 (28.2)		358/1311 (27.3)	0/9 (0.0)	
5-14 years	302/1321 (22.9)	256/1206 (21.2)	46/115 (40.0)		283/1186 (23.9)	19/135 (14.1)		299/1311 (22.8)	3/9 (33.3)	
Female sex	665/1321 (50.3)	601/1206 (49.8)	64/115 (55.7)	0.23	606/1186 (51.1)	59/135 (43.7)	0.10	659/1311 (50.3)	5/9 (55.6)	1.00
Race										
Black	643/1321 (48.7)	574/1206 (47.6)	69/115 (60.0)	0.001	576/1186 (48.6)	67/135 (49.6)	0.87	636/1311 (48.5)	6/9 (66.7)	0.34
Coloured	677/1321 (51.3)	632/1206 (52.4)	45/115 (39.1)		609/1186 (51.4)	68/135 (50.4)		674/1311 (51.4)	3/9 (33.3)	
Other	1/1321 (0.1)	0/1206 (0.0)	1/115 (0.9)		1/1186 (0.1)	0/135 (0.0)		1/1311 (0.1)	0/9 (0.0)	
Site										
Eastridge Clinic (WC)	906/1321 (68.6)	835/1206 (69.2)	71/115 (61.7)	<0.001	811/1186 (68.4)	95/135 (70.4)	0.43	901/1311 (68.7)	4/9 (44.4)	0.05
Edendale Gateway Clinic (KZN)	56/1321 (4.2)	39/1206 (3.2)	17/115 (14.8)		50/1186 (4.2)	6/135 (4.4)		54/1311 (4.1)	2/9 (22.2)	
Jouberton Clinic (NW)	356/1321 (27.0)	329/1206 (27.3)	27/115 (23.5)		323/1186 (27.2)	33/135 (24.4)		353/1311 (26.9)	3/9 (33.3)	
Mitchells Plain Clinic (WC)	3/1321 (0.2)	3/1206 (0.3)	0/115 (0.0)		2/1186 (0.2)	1/135 (0.7)		3/1311 (0.2)	0/9 (0.0)	
HIV-infected	6/1284 (0.5)	5/1169 (0.4)	1/115 (0.9)	0.43	6/1151 (0.5)	0/133 (0.0)	1.00	6/1275 (0.5)	0/8 (0.0)	1.00
HIV exposure (<1 year)										
HIV-unexposed uninfected	105/153 (68.6)	103/150 (68.7)	2/3 (66.7)	1.00	98/141 (69.5)	7/12 (58.3)	0.42	103/150 (68.7)	2/3 (66.7)	1.00
HIV-exposed uninfected	48/153 (31.4)	47/150 (31.3)	1/3 (33.3)		43/141 (30.5)	5/12 (41.7)		47/150 (31.3)	1/3 (33.3)	
HIV infected	0/153 (0.0)	0/150 (0.0)	0/3 (0.0)		0/141 (0.0)	0/12 (0.0)		0/150 (0.0)	0/3 (0.0)	
Malnutrition*	55/1018 (5.4)	50/949 (5.3)	5/69 (7.3)	0.48	52/901 (5.8)	3/117 (2.6)	0.19	55/1011 (5.4)	0/6 (0.0)	1.00

Premature**	95/1025 (9.3)	88/955 (9.2)	7/70 (10.0)	0.83	87/908 (9.6)	8/117 (6.8)	0.34	95/1018 (9.3)	0/6 (0.0)	1.00
Other underlying illness***	24/1321 (1.8)	23/ 1206 (1.9)	1/115 (0.9)	0.72	23/1186 (1.9)	1/135 (0.7)	0.50	24/1311 (1.8)	0/9 (0.0)	1.00
Up to date vaccination for age for PCV	921/981 (93.9)	860/916 (93.9)	61/65 (93.9)	1.00	816/867 (94.1)	105/114 (92.1)	0.40	915/974 (93.9)	5/6 (83.3)	0.32
Up to date DTaP-IPV-HIB-HBV vaccination for age	927/984 (94.2)	865/919 (94.1)	62/65 (95.4)	1.00	821/870 (94.4)	106/114 (93.0)	0.55	921/977 (94.3)	5/6 (83.3)	0.30

PCV=Pneumococcal conjugate vaccine, DTaP-IPV-HIB-HBV=Diptheria, tetanus, acellular pertussis, inactivated polio vaccine, *haemophilius influenza*e type B and Hepatitis B combined

WC=Western Cape Province, KZN=KwaZulu Natal Province, NW=North West Province

* Malnutrition as defined by <2 Z scores (-2 standard deviations) of the mean weight for age in months and gender. This also includes any children recorded as having Kwashiorkor or Marasmus

**Premature defined as early-term infants born before 37 completed weeks of gestation

***Underlying conditions included any of the following: Asthma, other chronic lung diseases, chronic heart disease (valvular heart disease, coronary heart disease, or heart failure excluding hypertension), stroke, seizures, anaemia, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy, autoimmune disease), diabetes, pregnancy, burns, obesity, asplenia, neurological disease (spinal cord injury, neuromuscular conditions)

****One patient with available influenza and RSV results was not tested for *B. pertussis* due to insufficient volume

Table 4. Demographic and clinical characteristics of patients aged ≥15 years enrolled into the systematic influenza-like illness surveillance programmes, South Africa, 2019.

Characteristic	Overall	Influenza negative	Influenza positive	P-value	RSV negative	RSV positive	P-value	*B. pertussis* negative	*B. pertussis* positive	P-value
	n/N (%) N=423	n/N (%) N=385	n/N (%) N=38		n/N (%) N=413	n/N (%) N=10		n/N (%) *N*=423	n/N (%) N=0	
Age group (years)										
15-24	83/423 (18.9)	66/385 (17.1)	14/38 (36.8)	0.01	79/413 (19.1)	1/10 (10.0)	0.27	80/423 (18.9)	0	-
25-44	160/423 (37.8)	144/385 (37.4)	16/38 (42.1)		157/413 (38.0)	3/10 (30.0)		160/423 (37.8)	0	
45-64	138/423 (32.6)	131/385 (34.0)	7/38 (18.4)		135/413 (32.7)	3/10 (30.0)		138/423 (32.6)	0	
≥65	45/423 (10.6)	44/385 (11.4)	1/38 (2.6)		42/413 (10.2)	3/10 (30.0)		45/423 (10.6)	0	
Female sex	272/423 (64.3)	248/385 (64.4)	24/38 (63.2)	0.88	266/413 (64.4)	6/10 (60.0)	0.77	272/423 (64.3)	0	-
Race										
Black	310/422 (73.5)	278/384 (72.4)	32/38 (84.2)	0.21	303/412 (73.5)	7/10 (70.0)	0.74	310/422 (73.5)	0	-
Coloured	112/422 (26.5)	106/384 (27.6)	6/38 (15.8)		109/412 (26.5)	3/10 (10.0)		112/422 (26.5)	0	
Other	0/422 (0.0)	0/385 (0.0)	0/38 (0.0)		0/412 (0.0)	0/10 (0.0)		0/422 (0.0)	0	
Site										
Eastridge Clinic (WC)	16/423 (3.8)	16/385 (4.2)	0/38 (0.0)	0.16	77/413 (18.6)	0/10 (0.0)	0.47	77/423 (18.2)	0	-
Edendale Gateway Clinic (KZN)	77/423 (18.2)	66/385 (17.1)	11/38 (29.0)		203/413 (49.2)	6/10 (60.0)		209/423 (49.4)	0	
Jouberton Clinic (NW)	210/423 (49.7)	190/385 (49.4)	20/38 (52.6)		15/413 (3.6)	0/10 (0.0)		15/423 (3.6)	0	
Mitchells Plain Clinic (WC)	120/423 (28.4)	113/385 (29.4)	7/38 (18.4)		118/413 (28.6)	4/10 (40.0)		122/423 (28.8)	0	
HIV-infected	102/419 (24.3)	93/381 (24.4)	9/38 (23.7)	0.92	102/409 (24.9)	0/10 (0.0)	0.13	102/419 (24.3)	0	-
Other underlying illness*	84/423 (19.9)	82/385 (21.3)	2/38 (5.3)	0.02	82/413 (19.9)	2/10 (20.0)	1.00	84/423 (19.9)	0	-

WC=Western Cape, KZN=KwaZulu Natal Province, NW=North West Province

*Underlying conditions included any of the following: Asthma, other chronic lung diseases, chronic heart disease (valvular heart disease, coronary heart disease, or heart failure excluding hypertension), stroke, seizures, anaemia, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy, autoimmune disease), diabetes, pregnancy, burns, obesity, asplenia, neurological disease (spinal cord injury, neuromuscular conditions).

Influenza, RSV and B. pertussis among individuals aged <15 years enrolled into the pneumonia surveillance programme. Of the 3148 individuals aged <15 years enrolled into the pneumonia surveillance programme, the most common pathogen was RSV (24.7%, 778/3148) followed by influenza (4.7%, 147/3148) and *B. pertussis* (1.0%; 31/3148) (Table 5). The majority of RSV and pertussis cases were infants aged 0-2 months (41.1%, 320/778 and 67.7%, 21/31 respectively). However, among the influenza cases, 29.9% (44/147) were aged 12-23 months. Overall, the majority presented with symptom duration of ≤10 days (96.0%, 2998/3123) and spent less than 5 days in hospital (76.0%, 2371/3120). Of the 146 influenza positive cases, 113 (77.4%) patients spent <5 days in hospital. In children aged <15 years enrolled in the pneumonia surveillance programme, the prevalence of malnutrition and prematurity was 16.7% (504/3021) and 18.4% (555/3021) respectively. Vaccine coverage was high with 90.7% (2170/2393) of enrolled individuals having PCV up to date whilst the vaccine coverage for DTaP-IPV-HIB-HBV was 76.2% (2187/2872). Vaccine coverage for DTaP-IPV-HIB-HBV in pertussis cases was significantly lower, with 39.3% (11/28) as compared to those who were tested negative for *B. pertussis* (76.5%, 2175/2843; p=<0.001). Among the RSV cases, 2.7% (21/776) were admitted to the Intensive Care Unit (ICU) as compared to 1.4% (2/145) of influenza cases. No pertussis cases were admitted to ICU. In-hospital mortality was at 0.5% (14/3135) for individuals aged <15 years enrolled in the surveillance programme. Influenza and RSV accounted for 0.7% (1/147) and 0.5% (4/777) in-hospital mortality. There were no in-hospital deaths reported among pertussis cases.

Influenza, RSV and B. pertussis among individuals aged ≥15 years enrolled in the pneumonia surveillance programme. Of the 1414 individuals aged ≥ 15 years meeting the SRI case definition, influenza (6.2%; 88/1414) was the most common pathogen identified, followed by RSV (1.3%, 19/1414) and *B. pertussis* (0.3%, 4/1414) (Table 6). The majority of those who tested positive for influenza (34.5%, 30/88) were aged 45-64 years and 42.1% (8/19) of those who tested positive for RSV were aged 25-44 years. Of the four pertussis cases, 2 were in the 15-24 year age group and 2 belonged to the 25-44 year age group. Of the 1295 individuals with available information on symptom duration, more than half had symptoms for ≤10 days (57.0%, 738/1295). Of the 1104 patients with available HIV status, two thirds were HIV infected (66.4%, 733/1104). The length of hospital stay was greater than in younger

individuals (<15 years), with 35.2% (493/1397) of those aged ≥15 years spending <5 days in hospital. The HIV prevalence for individuals who tested positive for influenza was 60.5% (52/86) and 68.4% (13/19) among those who tested positive for RSV. All pertussis cases were HIV infected (100.0%, 4/4). Overall, 0.9% (12/1408) of hospitalised patients <15 were admitted to ICU. Of the 87 positive influenza cases, 2.3% (2/87) were admitted to ICU. In-hospital mortality was lower in the <15 year age group (0.5%, 14/3135) as compared to those aged ≥15 years (8.2%, 114/1399). Among patients with influenza, 9.1% (8/88) died in hospital. There were no in-hospital deaths reported among RSV and pertussis cases.

Table 5. Demographic and clinical characteristics of patients aged <15 years enrolled in the pneumonia surveillance programme, South Africa, 2019.

Characteristic	Overall n/N (%) N=3148****	Influenza negative n/N (%) N=3001	Influenza positive n/N (%) N=147	P-value	RSV negative n/N (%) N=2370	RSV positive n/N (%) N=778	P-value	*B. pertussis* negative n/N (%) N=3116	*B. pertussis* positive n/N (%) N=31	P-value
Age group										
0-2 months	977/3148 (31.0)	966/3001 (32.2)	11/147 (7.5)	<0.001	657/2370 (27.7)	320/778 (41.1)	<0.001	956/3116 (30.7)	21/31 (67.7)	0.001
3-5 months	455/3148 (14.5)	432/3001 (14.4)	23/147 (15.7)		275/2370 (11.6)	180/778 (23.1)		453/3116 (14.5)	2/31 (6.5)	
6-11 months	558/3148 (17.7)	534/3001 (17.8)	24/147 (16.3)		420/2370 (17.7)	138/778 (17.7)		556/3116 (17.8)	2/31 (6.5)	
12-23 months	573/3148 (18.2)	529/3001 (17.6)	44/147 (29.9)		491/2370 (20.7)	82/778 (10.5)		569/3116 (18.3)	3/31 (9.7)	
2-4 years	455/3148 (14.5)	421/3001 (14.0)	34/147 (23.1)		401/2370 (16.9)	54/778 (6.9)		454/3116 (14.6)	1/31 (3.2)	
5-14 years	130/3148 (4.1)	119/3001 (4.0)	11/147 (7.5)		126/2370 (5.3)	4/778 (0.5)		128/3116 (4.1)	2/31 (6.5)	
Female sex	1357/3148 (43.1)	1291/3001 (43.0)	66/147 (44.9)	0.65	1003/2370 (42.3)	354/778 (45.5)	0.12	1343/3116 (43.1)	14/31 (45.2)	0.67
Race										
Black	2303/3147 (73.2)	2182/3000 (72.7)	121/147 (82.3)	0.02	1722/2370 (72.7)	581/777 (74.8)	0.11	2279/3115 (73.2)	23/31 (74.2)	0.78
Coloured	775/3147 (24.6)	752/3000 (25.1)	23/147 (15.7)		601/2370 (25.4)	174/777 (22.4)		768/3115 (24.7)	7/31 (22.6)	
Other	69/3147 (2.2)	66/3000 (2.2)	3/147 (2.0)		47/2370 (2.0)	22/777 (2.8)		68/3115 (2.2)	0/31 (0.0)	
Site										
Edendale Hospital (KZN)	432/3148 (13.7)	409/3001 (13.6)	23/147 (15.7)	0.001	309/2370 (13.0)	123/778 (15.8)	0.19	427/3116 (13.7)	5/31 (16.1)	0.90
KTHC (NW)	257/3148 (8.2)	234/3001 (7.8)	23/147 (15.7)		202/2370 (8.5)	55/778 (7.1)		256/3116 (8.2)	1/31 (3.2)	
Matikwana/ Mapulaneng (MP)	258/3148 (8.2)	240/3001 (8.0)	18/147 (12.2)		201/2370 (8.5)	57/778 (7.3)		255/3116 (8.2)	3/31 (9.7)	
RMMCH/HJH (GP)	661/3148 (21.0)	635/3001 (21.2)	26/147 (17.7)		492/2370 (20.8)	169/778 (21.7)		653/3116 (21.0)	8/31 (25.8)	
RCH/MPH (WC)	1540/3148 (48.9)	1483/3001 (49.4)	57/147 (38.8)		1166/2370 (49.2)	374/778 (48.1)		1525/3116 (48.9)	14/31 (45.2)	
Symptom duration (≤10 days)	2998/3123 (96.0)	2858/2979 (95.9)	140/144 (97.2)	0.66	2250/2348 (95.8)	748/775 (96.5)	0.40	2969/3091 (96.1)	28/31 (90.3)	0.13
HIV-infected	60/2794 (2.2)	58/2653 (2.2)	2/141 (1.4)	0.77	50/2030 (2.5)	10/764 (1.3)	0.06	60/2763 (2.2)	0/30 (0.0)	1.00
HIV exposure (<1 year)										
HIV-unexposed uninfected	1220/1641 (74.3)	1178/1589 (74.1)	42/52 (80.8)	0.59	761/1026 (74.2)	459/615 (74.6)	0.13	1203/1618 (74.4)	17/23 (73.9)	0.88
HIV-exposed uninfected	391/1641 (23.8)	381/1589 (24.0)	10/52 (19.2)		241/1026 (23.5)	150/615 (24.4)		385/1618 (23.8)	6/23 (26.1)	
HIV infected	30/1641 (1.8)	30/1589 (1.9)	0/52 (0.0)		24/1026 (2.3)	6/615 (1.0)		30/1618 (1.9)	0/23 (0.0)	
Malnutrition*	504/3021 (16.7)	478/2884 (16.6)	26/137 (19.0)	0.46	387/2249 (17.2)	117/772 (15.2)	0.19	496/2991 (16.6)	8/29 (27.6)	0.11

Premature**	555/3021 (18.4)	553/2884 (18.5)	22/137 (16.1)	0.47	410/2247 (18.3)	145/774 (18.7)	0.76	550/2991 (18.4)	5/29 (17.24)	0.87
Other underlying illness***	112/3148 (3.6)	108/3001 (3.6)	4/147 (2.7)	0.82	96/2370 (4.1)	16/778 (2.1)	0.01	111/3116 (3.6)	1/31 (3.2)	0.92
Up to date vaccination for age for PCV	2170/2393 (90.7)	2068/2278 (90.8)	102/115 (88.7)	0.45	1603/1757 (91.2)	567/636 (89.2)	0.12	2156/2375 (90.8)	13/17 (76.5)	1.00
Up to date DTaP-IPV-HIB-HBV vaccination for age	2187/2872 (76.2)	2082/2751 (75.7)	105/121 (86.8)	0.01	1615/2119 (76.2)	572/753 (76.0)	0.89	2175/2843 (76.5)	11/28 (39.3)	<0.001
Duration of hospitalisation <5 days	2371/3120 (76.0)	2258/2974 (75.9)	113/146 (77.4)	0.22	1821/2347 (77.6)	550/773 (71.2)	<0.001	2351/3088 (76.1)	19/31 (61.3)	0.16
ICU admission	55/3142 (1.8)	53/2995 (1.8)	2/145 (1.4)	0.71	34/2366 (1.4)	21/776 (2.7)	0.02	55/3110 (1.8)	0/31 (0.0)	0.46
In-hospital mortality	14/3135 (0.5)	13/2988 (0.4)	1/147 (0.7)	0.49	10/2358 (0.4)	4/777 (0.5)	0.76	14/3103 (0.5)	0/31 (0.0)	0.71

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

KZN=KwaZulu-Natal Province, NW=North West Province, MP=Mpumalanga Province, GP=Gauteng Province, WC=Western Cape Province

PCV=Pneumococcal conjugate vaccine, DTaP-IPV-HIB-HBV= Diphtheria, tetanus, acellular pertussis, inactivated polio vaccine, *haemophilius influenza*e type B and Hepatitis B combined

* Malnutrition as defined by <2 Z scores (-2 standard deviations) of the mean weight for age in months and gender. This also includes any children recorded as having Kwashiorkor or Marasmus

**Premature defined as early term infants born before 37 completed weeks of gestation

***Underlying conditions included any of the following: Asthma, other chronic lung diseases, chronic heart disease (valvular heart disease, coronary heart disease, or heart failure excluding hypertension), stroke, seizures, anaemia, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy, autoimmune disease), diabetes, pregnancy, burns, obesity, asplenia, neurological disease (spinal cord injury, neuromuscular conditions).

****One patient with available influenza and RSV results was not tested for *B. pertussis* due to insufficient volume

Table 6. Demographic and clinical characteristics of patients aged ≥15 years enrolled in the pneumonia surveillance programme, South Africa, 2019.

Characteristic	Overall n/N (%) N=1414	Influenza negative n/N (%) N=1326	Influenza positive n/N (%) N=88	P-value	RSV negative n/N (%) N=1395	RSV positive n/N (%) N=19	P-value	*B. pertussis* negative n/N (%) N=1410	*B. pertussis* positive n/N (%) N=4	P-value
Age group (years)										
15-24	105/1414 (7.4)	98/1326 (7.4)	7/88 (8.0)	<0.001	104/1395 (7.5)	1/19 (5.3)	0.95	103/1410 (7.3)	2/4 (50.0)	0.04
25-44	669/1414 (47.3)	641/1326 (48.3)	28/88 (31.8)		661/1395 (47.4)	8/19 (42.1)		667/1410 (47.3)	2/4 (50.0)	
45-64	462/1414 (32.7)	432/1326 (32.6)	30/88 (34.1)		455/1395 (32.6)	7/19 (36.8)		462/1410 (32.8)	0/4 (0.0)	
≥65	178/1414 (12.6)	155/1326 (11.7)	23/88 (26.1)		175/1395 (12.5)	3/19 (15.8)		178/1410 (12.6)	0/4 (0.0)	
Female sex	732/1414 (51.7)	679/1326 (51.2)	53/88 (60.2)	0.10	723/1395 (51.8)	9/19 (47.4)	0.70	730/1410 (51.8)	2/4 (50.0)	0.94
Race										
Black	1279/1413 (90.5)	1200/1325 (90.6)	79/88 (89.8)	0.85	1261/1394 (90.5)	18/19 (94.7)	0.76	1275/1409 (90.5)	4/4 (100.0)	0.81
Coloured	106/1413 (7.5)	99/1325 (7.5)	7/88 (8.0)		105/1394 (7.5)	1/19 (5.3)		106/1409 (7.5)	0/4 (0.0)	
Other	28/1413 (2.0)	26/1325 (2.0)	2/88 (2.3)		28/1394 (2.0)	0/19 (0.0)		28/1409 (2.0)	0/4 (0.0)	
Site										
Edendale Hospital (KZN)	264/1414 (18.7)	246/1326 (18.6)	18/88 (20.5)	0.38	257/1395 (18.4)	7/19 (36.8)	0.24	264/1410 (18.7)	0/4 (0.0)	0.75
KTHC (NW)	2/1414 (0.1)	2/1326 (0.2)	0/88 (0.0)		2/1395 (0.1)	0/19 (0.0)		2/1410 (0.1)	0/4 (0.0)	
Matikwana/ Mapulaneng (MP)	188/1414 (13.3)	172/1326 (13.0)	16/88 (18.2)		187/1395 (13.4)	1/19 (5.3)		187/1410 (13.3)	1/4 (25.0)	
RMMCH/HJH (GP)	426/1414 (30.1)	406/1326 (30.6)	20/88 (22.7)		420/1395 (30.1)	6/19 (31.6)		425/1410 (30.1)	1/4 (25.0)	
RCH/MPH (WC)	534/1414 (37.8)	500/1326 (37.7)	34/88 (38.6)		529/1395 (37.9)	5/19 (26.3)		532/1410 (37.7)	2/4 (50.0)	
Symptom duration (≤10 days)	738/1295 (57.0)	685/1211 (56.6)	53/84 (63.1)	0.24	726/1276 (56.9)	12/19 (63.2)	0.58	738/1292 (57.1)	0/3 (0.0)	0.08
HIV-infected	733/1104 (66.4)	681/1018 (66.9)	52/86 (60.5)	0.23	720/1085 (66.4)	13/19 (68.4)	0.85	729/1100 (66.3)	4/4 (100.0)	0.31
Other underlying illness*	226/1414 (16.0)	206/1326 (15.5)	20/88 (22.7)	0.08	224/1395 (16.1)	2/19 (10.5)	0.75	226/1410 (16.0)	0/4 (0.0)	0.38
Duration of hospitalisation <5 days	493/1397 (35.3)	457/1309 (34.9)	36/88 (40.9)	0.48	490/1378 (35.6)	3/19 (15.8)	0.03	493/1394 (35.4)	0/3 (0.0)	0.07
ICU admission	12/1408 (0.9)	10/1320 (0.8)	2/88 (2.3)	0.17	12/1389 (0.9)	0/19 (0.0)	0.68	12/1404 (0.9)	0/4 (0.0)	0.85
In-hospital mortality	114/1399 (8.2)	106/1311 (8.1)	8/88 (9.1)	0.74	114/1380 (8.3)	0/19 (0.0)	0.19	114/1396 (8.2)	0/3 (0.0)	0.61

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

KZN=KwaZulu-Natal Province, NW=North West Province, MP=Mpumalanga Province, GP=Gauteng Province, WC=Western Cape Province

PCV=Pneumococcal conjugate vaccine, HIB=*Haemophilus influenzae* type B

**Underlying conditions included any of the following: Asthma, other chronic lung diseases, chronic heart disease (valvular heart disease, coronary heart disease, or heart failure excluding hypertension), stroke, seizures, anaemia, liver disease (cirrhosis or liver failure), renal disease (nephrotic syndrome, chronic renal failure), immunocompromising conditions excluding HIV infection (organ transplant, immunosuppressive therapy, immunoglobulin deficiency, malignancy, autoimmune disease), diabetes, pregnancy, burns, obesity, asplenia, neurological disease (spinal cord injury, neuromuscular conditions).

The 2019 influenza season

Viral Watch Programme. In 2019, the influenza season started in week 16 (last week of April) when the detection rate in the Viral Watch Programme rose above the seasonal threshold as determined by the Moving Epidemic Method (MEM) (Figure 3). The season ended in week 28 (second week of July). For the 2019 influenza season, the transmissibility of influenza was moderate to high. In week 18, transmissibility crossed to the high level but dropped to moderate in week 19 (Figure 4). The VW Programme received 1378 specimens that were tested for influenza, of which 786 (57.0%) were positive. The season was dominated by influenza A(H3N2) (91.7%, 721/786), followed by A(H1N1)pdm09 (6.0%, 47/786), influenza B(Victoria) (0.3%, 2/786) and influenza B(Yamagata) (0.1%, 1/786). Fifteen influenza A samples (1.9%) were not subtyped due to a low viral load in the specimen.

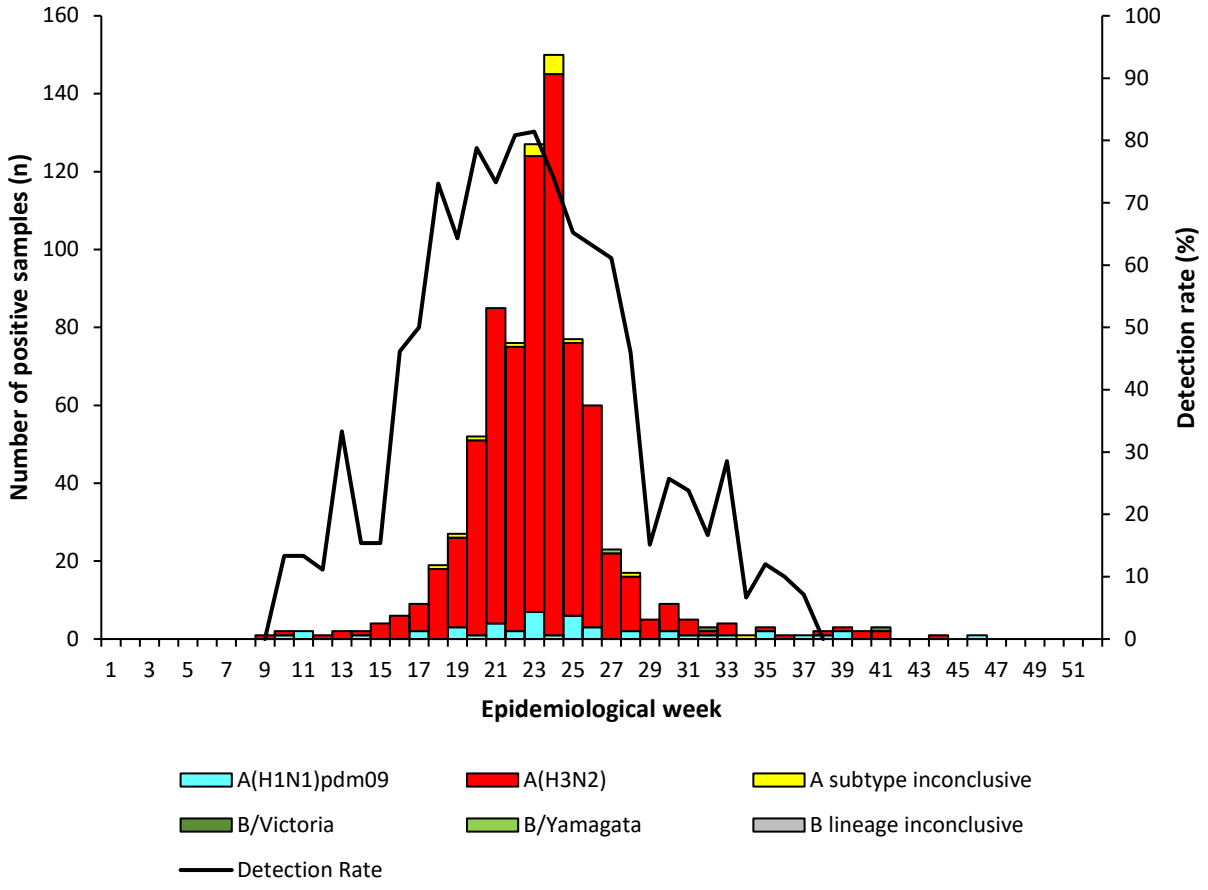

Figure 3. Number of positive samples and influenza detection rate by viral type, subtype and week for patients meeting the case definition for influenza-like illness (ILI), Viral Watch programme, South Africa, 2019.

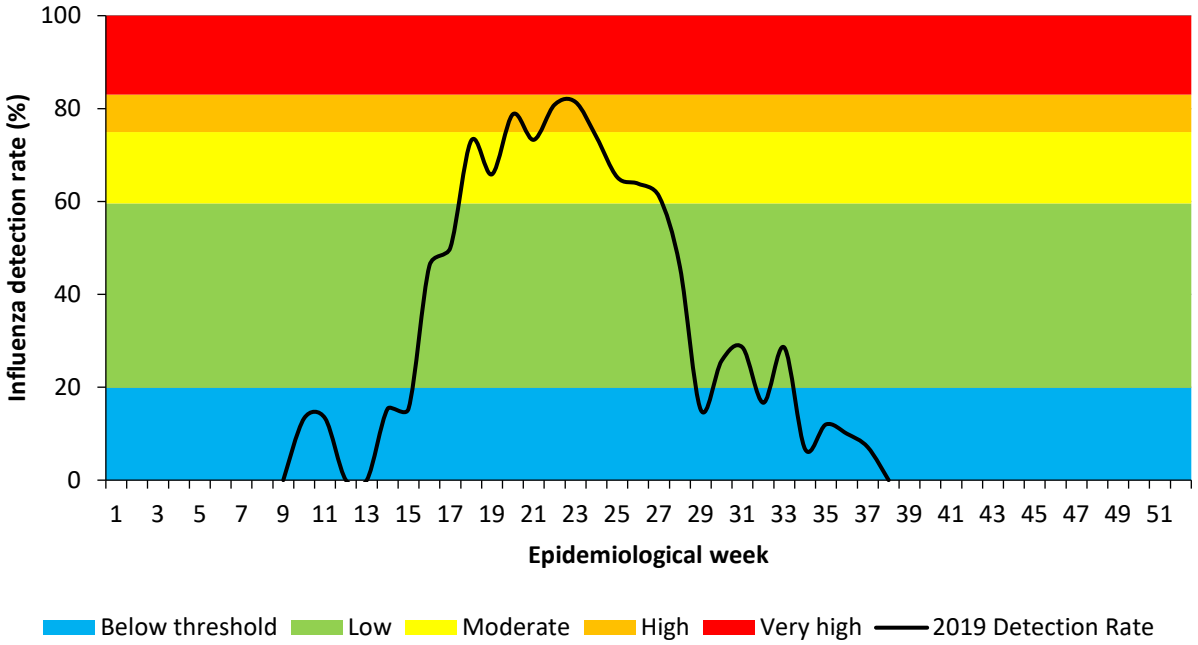

Figure 4. Viral Watch 2019 influenza transmissibility and thresholds based on 2008-2018 data (excluding the pandemic year: 2009), South Africa, 2019.

Influenza season systematic ILI programme. Of the 1744 specimens tested, 8.8% (153) were positive for influenza. Of the 153 influenza positive samples, 127 (83.0%), 23 (15.0%) were positive for influenza A(H3N2) and influenza A(H1N1)pdm09 respectively (Figure 5). Three influenza A samples (2.0%) were not subtyped due to a low viral load in the specimen. Influenza B was not detected in the systematic ILI programme. The detection rate rose to 16.1% in week 16 and remained above 10% until week 26. There was a small increase in the influenza detection rate in weeks 30 to 32.

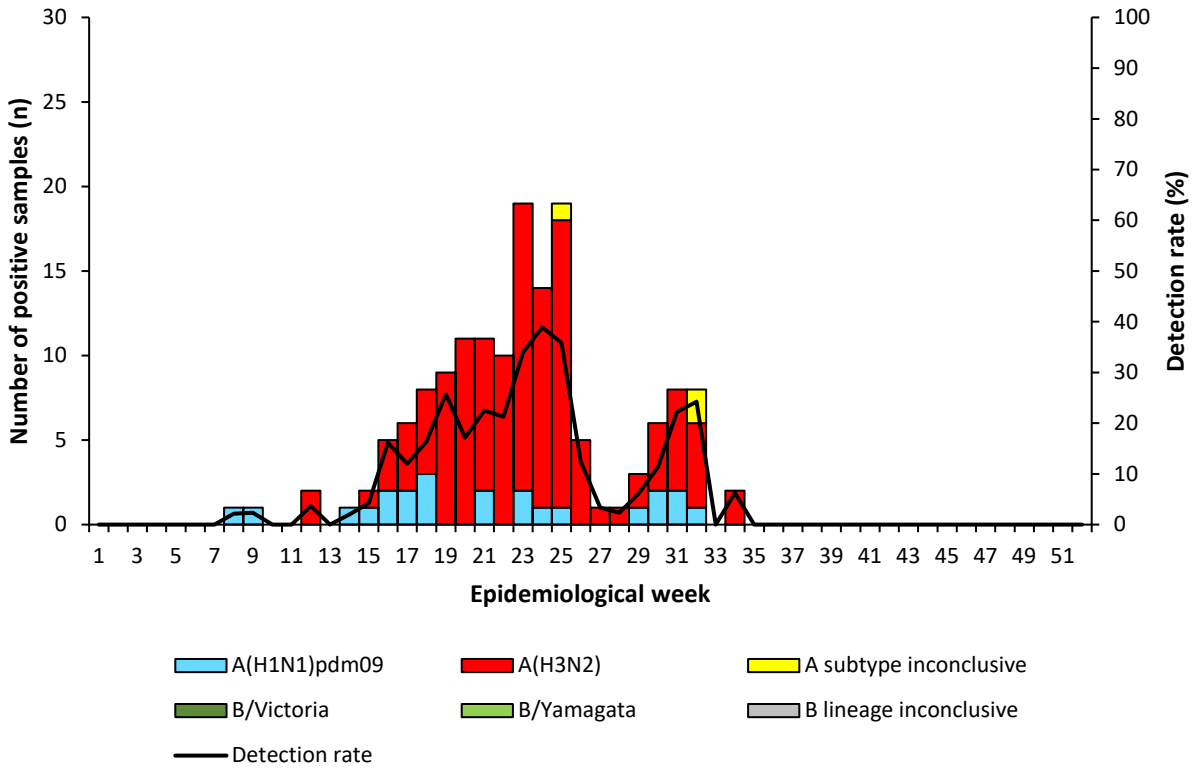

Figure 5. Influenza detection rate, by influenza type, subtype and week, in patients enrolled with influenza-like Illness (ILI) at public healthcare clinics, South Africa, 2019.

Pneumonia surveillance programme. The influenza season started in week 19, peaked in week 23 and ended in week 34 (Figure 6). The impact of the 2019 influenza season was moderate between weeks 22 and 25 (Figure 7). In the pneumonia surveillance programme, 5.1% (235/4562) of enrolled participants had influenza detected, most of which were influenza A (H3N2) (87.7%, 206/235). Influenza A(H1N1)pdm09 accounted for 7.2% (17/235) of cases. An equal number of influenza B(Victoria) and influenza B(Yamagata) (0.9%, 2/235 each) were detected. Eight influenza A (3.4%) were not subtyped due to low viral load. The peak detection rate for influenza was 26.3% (35/133) in week 23 (Figure 6).

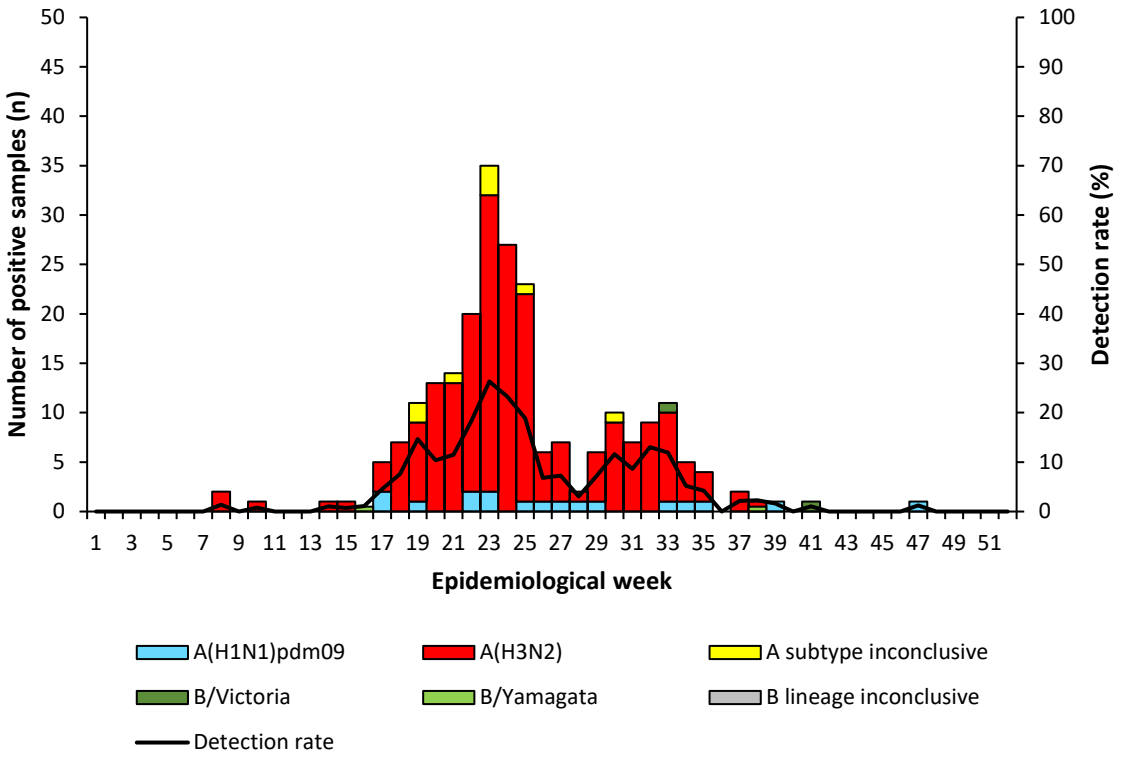

Figure 6. Numbers of samples positive for influenza and influenza detection rate, by type, subtype and week, in patients enrolled into the pneumonia surveillance programme in South Africa, 2019.

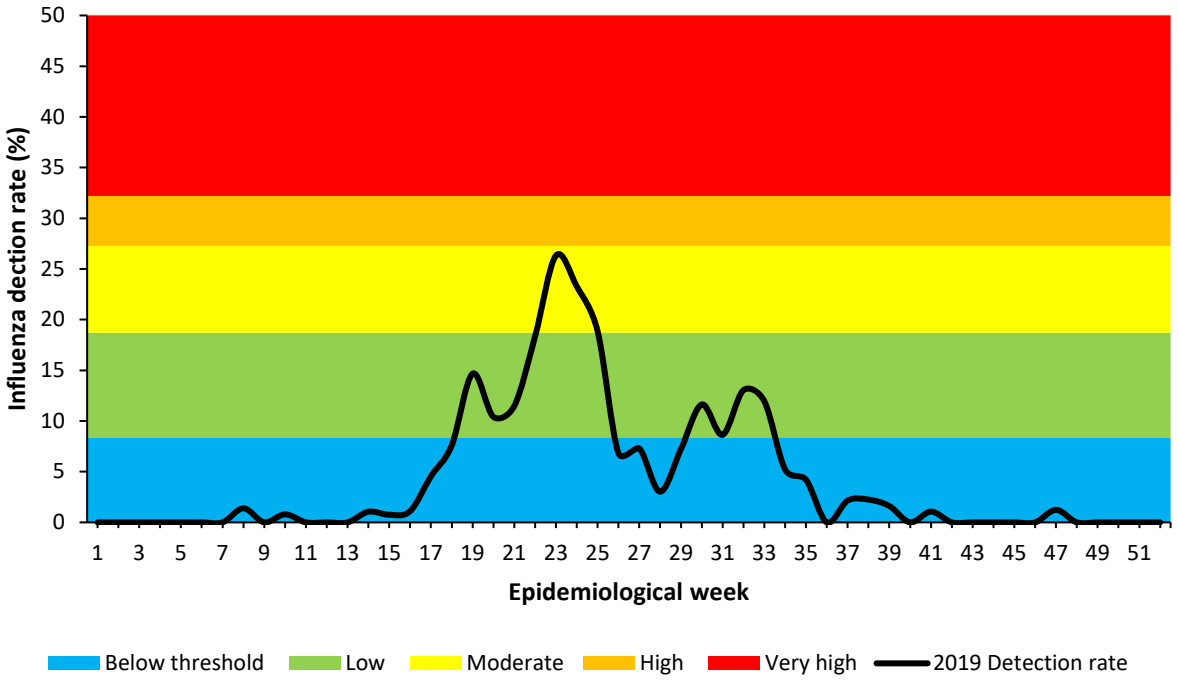

Figure 7. The impact of influenza based on the pneumonia surveillance programme influenza detection rate, South Africa, 2019. Thresholds are based on 2010 – 2018 data.

Respiratory syncytial virus

Systematic ILI programme. In the systematic ILI surveillance programme, RSV was first detected in week 4 and circulated throughout the year (Figure 8). The RSV detection in ILI rose above the seasonal threshold as determined by the MEM in week 12 (Figure 9). RSV demonstrated a defined seasonality which preceded the influenza season. The overall detection rate was 8.3% (145/1744). Of the 145 RSV positive samples, there were equal number of patients who tested positive for RSV(A) and RSV(B) (71 (49.0% each). Three patients (2.1%) were co-infected with RSV subgroup A and B (RSV(AB)).

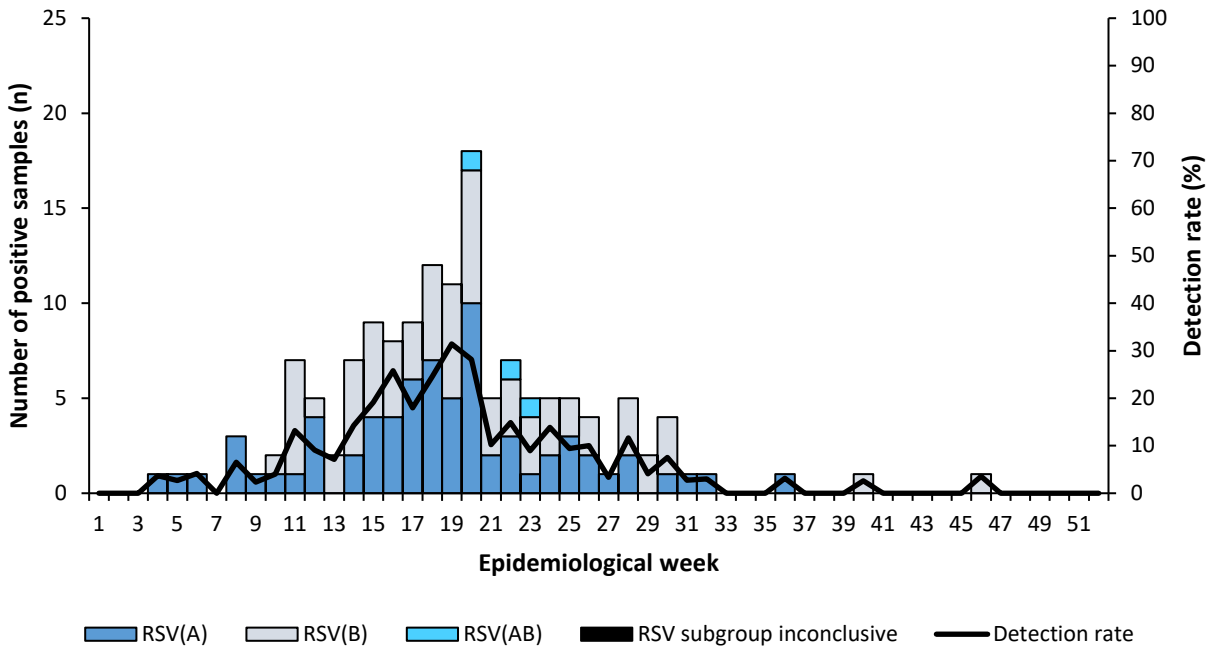

Figure 8. Number of positive samples and detection rate of respiratory syncytial virus (RSV) by subgroup and week in patients enrolled with influenza-like illness (ILI) at public healthcare clinics, South Africa, 2019.

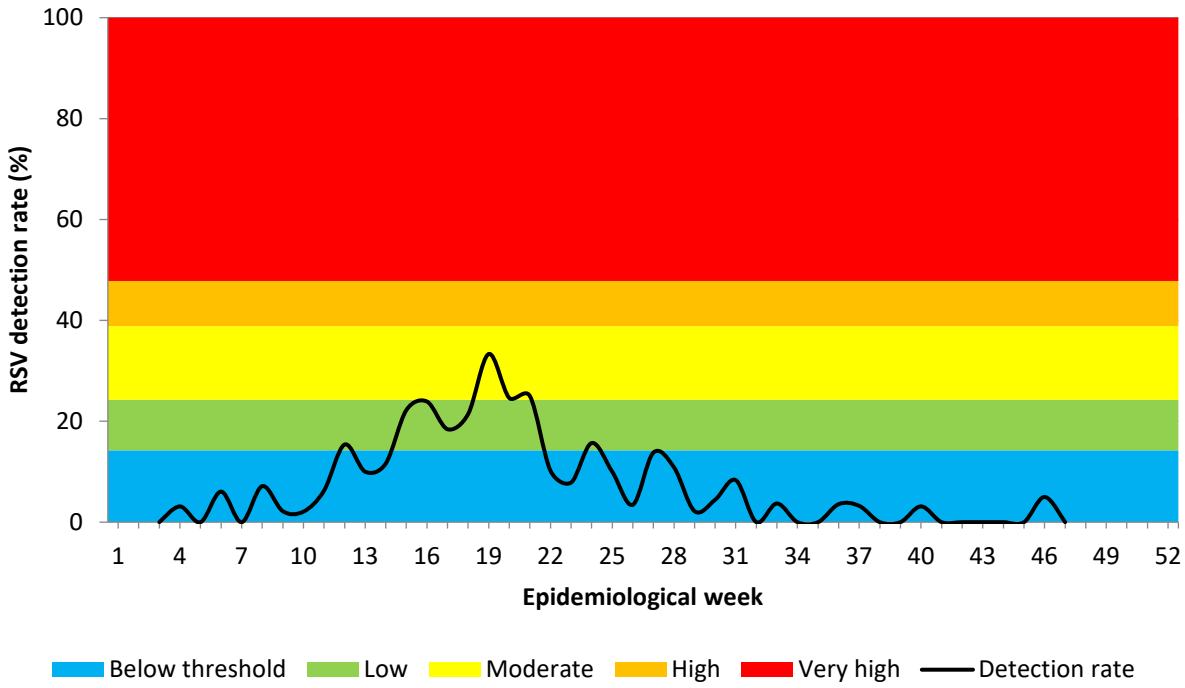

Figure 9. Influenza-like illness (ILI) programme 2019 respiratory syncytial virus (RSV) transmissibility and thresholds based on 2010-2018 data (excluding the pandemic year: 2009), South Africa, 2019.

Viral Watch Programme. Of the 1377 specimens received and tested, RSV was detected in the specimens of 30 (2%) patients.

Pneumonia surveillance programme. In 2019, the RSV season started in week 8 when the detection rate for RSV in the pneumonia surveillance rose above the seasonal threshold as determined by the MEM (Figure 11). The season ended in week 25. Similar to the ILI programme, RSV circulation in the pneumonia surveillance programme started in week 1 and circulated throughout the year. However, sporadic detections of RSV were observed later in the year (Figure 10). RSV demonstrated a defined seasonality which preceded the influenza season. Of the 4562 specimens tested, 17.5% (797) were positive for RSV. Of the 797 RSV positive samples, 435 (54.6%) and 349 (43.8%) were positive for RSV(A) and RSV(B). Seven patients (0.9%) were co-infected with RSV subgroup A and B (RSV(AB)). RSV subgroup for six samples was not determined due to low viral load.

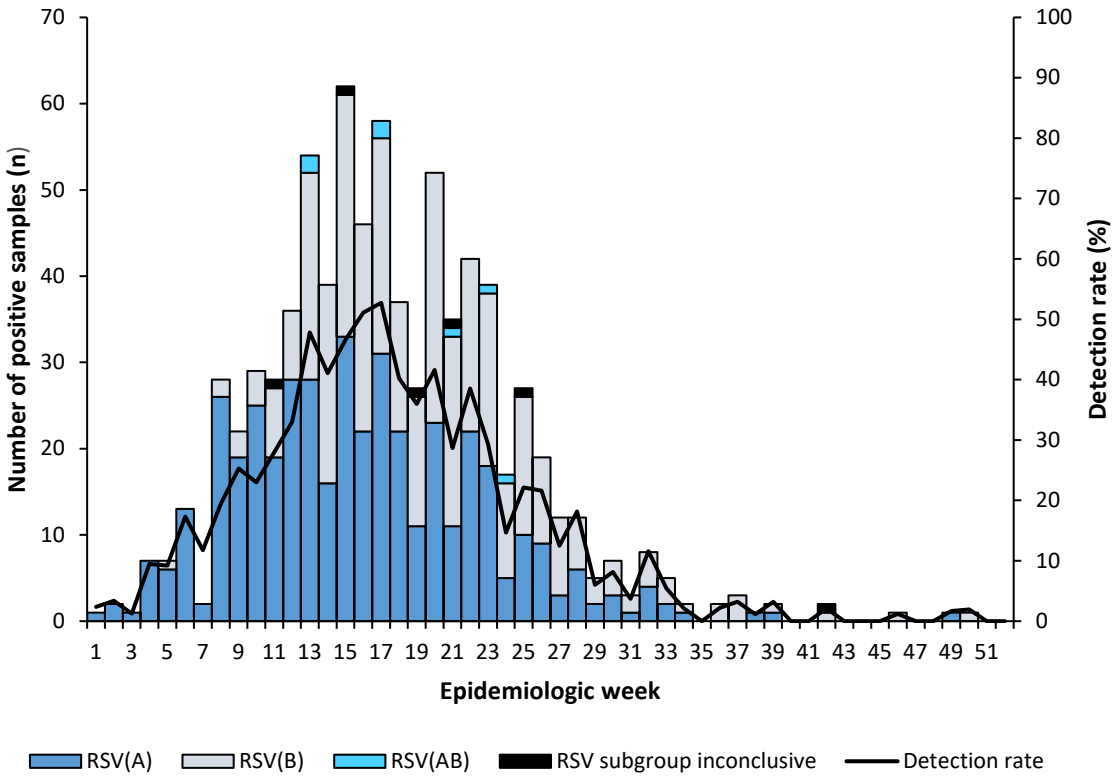

Figure 10. Numbers of positive samples collected and detection rates for respiratory syncytial virus (RSV) by subgroup and week in patients enrolled in the pneumonia surveillance programme, South Africa, 2019.

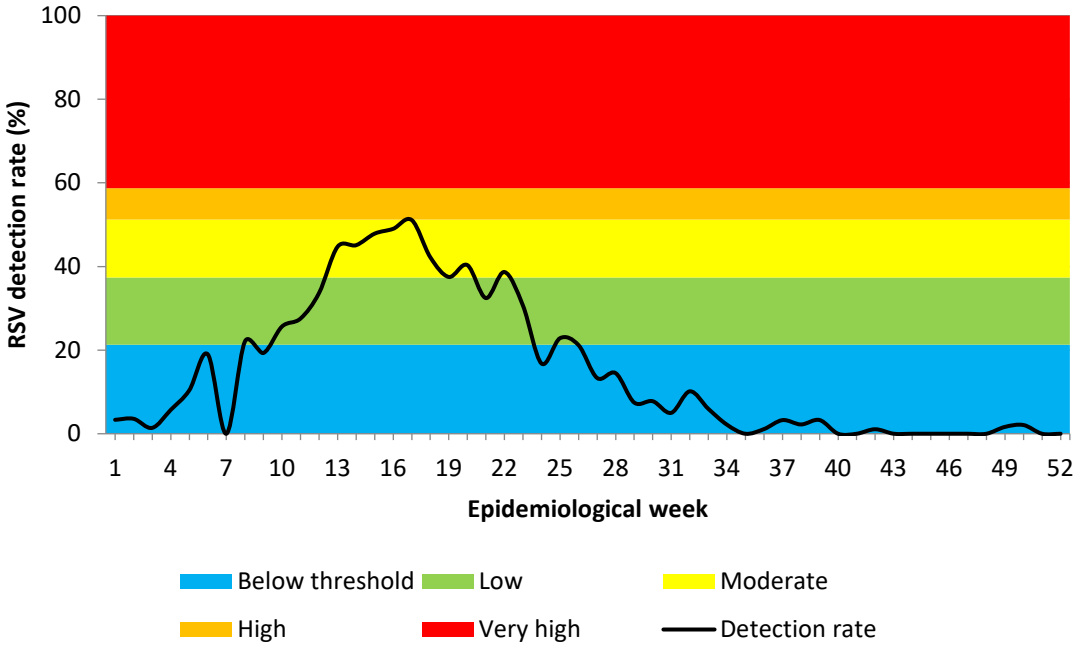

Figure 11. The impact of respiratory syncytial virus (RSV) based on the pneumonia surveillance programme influenza detection rate, South Africa, 2019. Thresholds are based on 2010 – 2018 data.

Bordetella pertussis

Systematic ILI programme. Of the 1748 patients enrolled with ILI and tested for *B. pertussis*, 9 (0.5%) tested positive. All pertussis positive cases met the ILI Surveillance case definition; however, 5 (55.6%, 5/9) did not meet the criteria for suspected pertussis. Pertussis cases were detected in the first half of the year (January-July) in the ILI surveillance programme with the highest detection rate at 1.9% (2/214) occurring in May (Figure 12). The majority of pertussis cases were detected at Eastridge Clinic (4/9) followed by Jouberton Clinic (2/9) and Edendale Gateway Clinic (3/9).

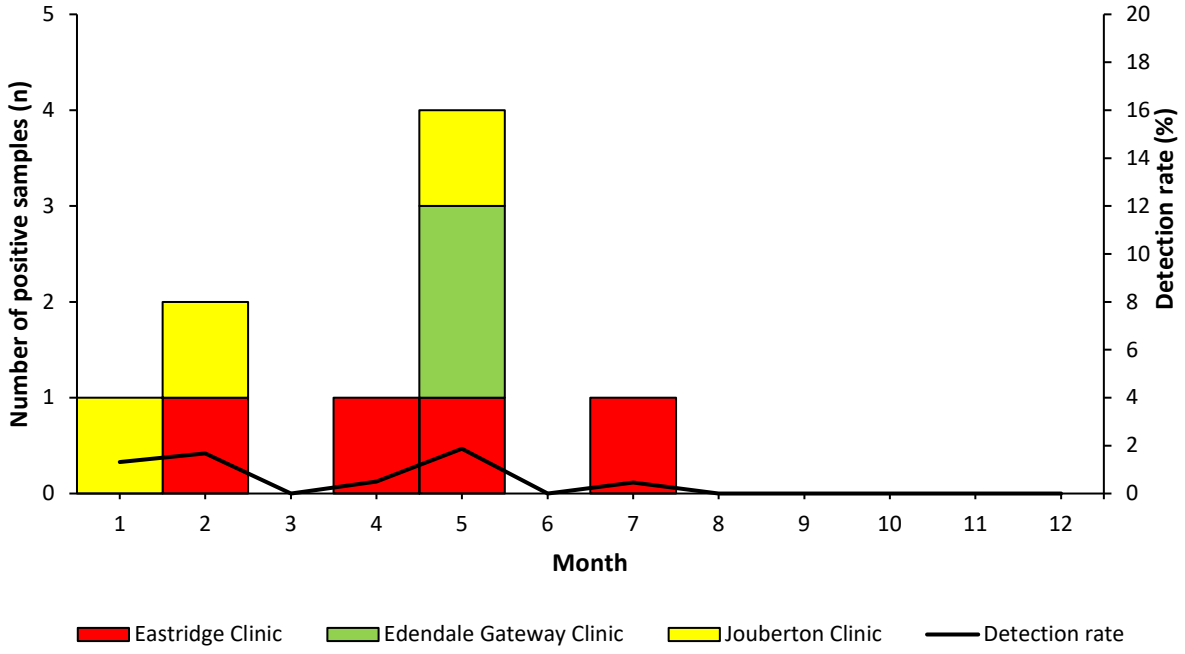

Figure 12. Numbers of positive samples and detection rate for *Bordetella pertussis* among patients enrolled in the influenza-like illness (ILI) programme, South Africa, 2019.

Pneumonia surveillance. Of the 4562 patients enrolled in pneumonia surveillance and tested for *B. pertussis*, 35 (0.8%) tested positive. All pertussis-positive cases met the pneumonia surveillance case definition; however, 18 (51.4%, 18/35) did not meet the criteria for suspected pertussis. There was no apparent seasonality for *B. pertussis*. However, there was a decrease in the numbers of cases testing positive for *B. pertussis* from January until November. The peak detection rate was in January at 3.6% (11/308). The majority of cases were identified at the RCH/MPH (40%, 14/35) (Figure 13). Overall, the detection of pertussis cases had decreased in comparison to the previous year (2018) which identified 98 pertussis cases with a detection rate of 2% (98/4630).[14]

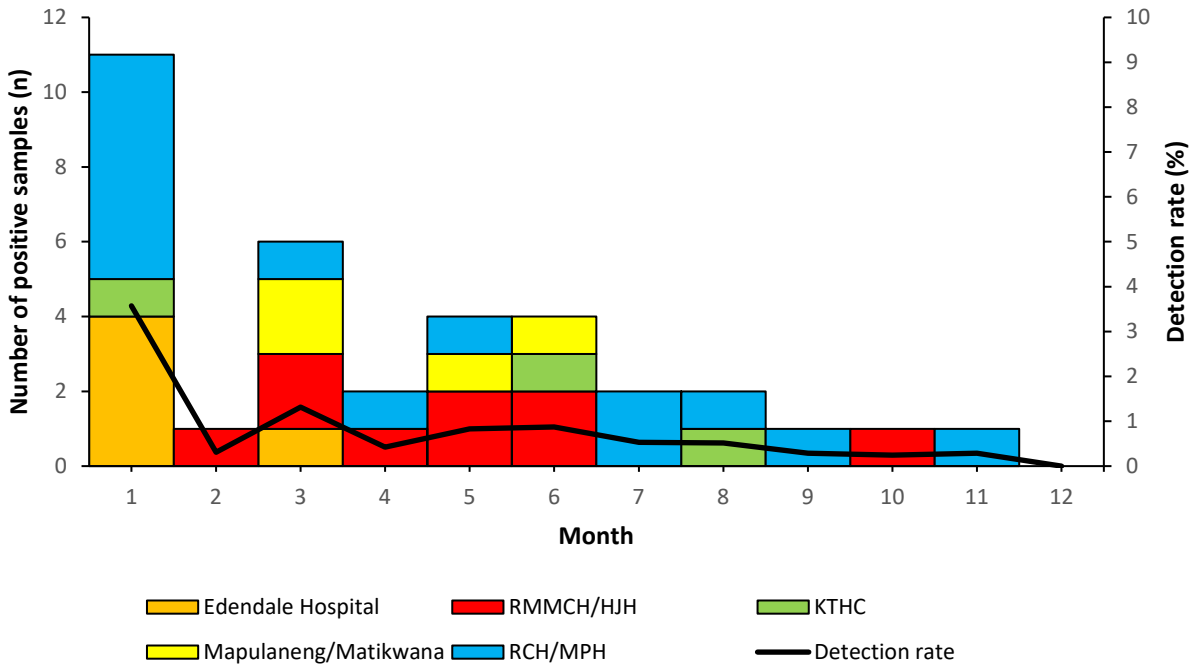

Figure 13. Detection rate and the number of samples positive for *Bordetella pertussis* by site and month, among patients enrolled in the pneumonia surveillance programme, South Africa, 2019.

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

Respiratory morbidity surveillance

During 2019 there were 1 130 733 consultations reported to the NICD through the respiratory morbidity data-mining surveillance system. Of these, 23 178 (2.1%) were due to pneumonia or influenza (P&I) (International Classification of Diseases 10 codes J10-18). There were 15 263 508 (65.9%) inpatients and 7 915 (34.1%) 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 detections reported to the viral watch and pneumonia surveillance programmes respectively (Figures 14 and 15). A second lower peak preceded the influenza season, corresponding to the circulation of respiratory syncytial virus.

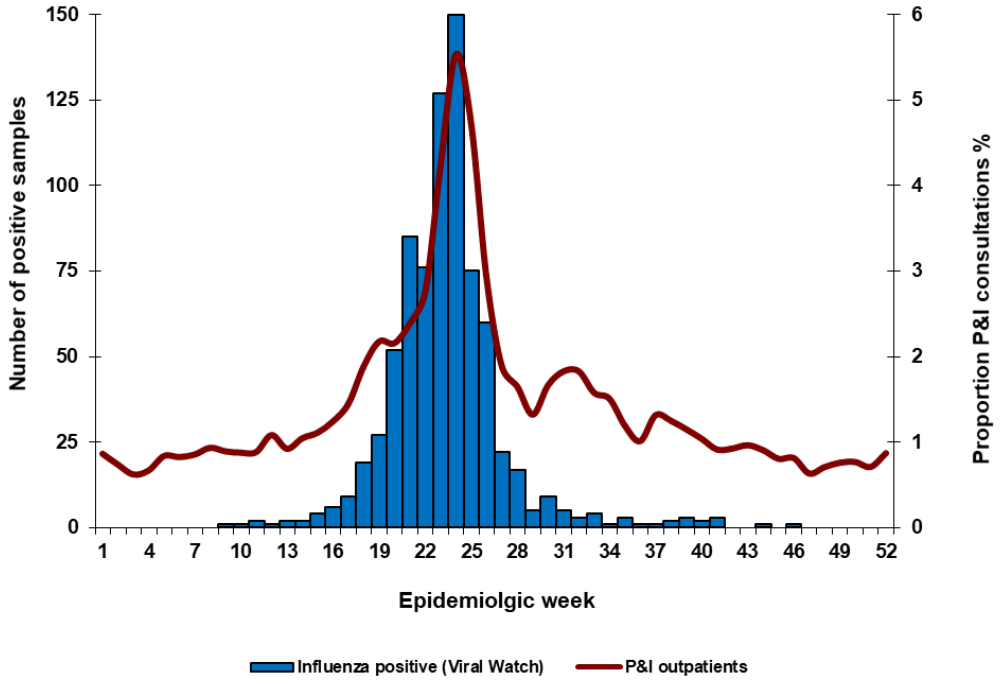

Figure 14. Numbers of private hospital outpatient consultations with a discharge diagnosis of pneumonia and influenza (P&I), and numbers of influenza-positive specimens (Viral Watch) by week, South Africa, 2019.

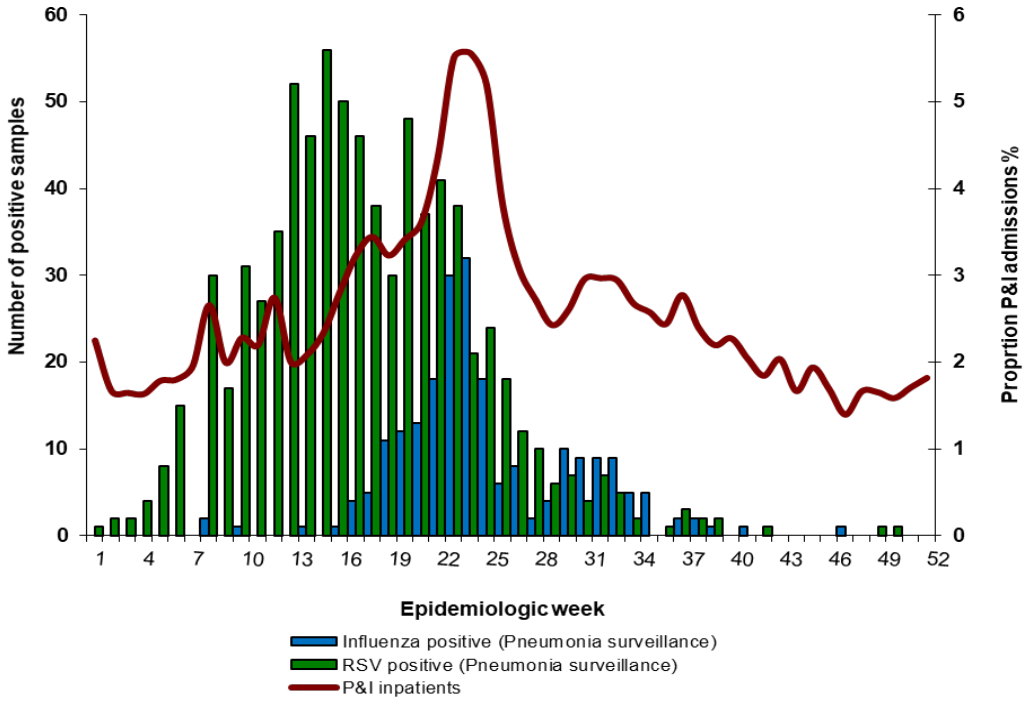

Figure 15. Numbers of private hospital admissions for pneumonia and influenza, as well as numbers of influenza-positive and respiratory syncytial virus (RSV) positive specimens by week, South Africa, 2019.

Vaccine effectiveness (VE), 2019 influenza season

Of the 1 378 individuals enrolled in VW and tested during the influenza season, 1 084 (78.7%) were eligible for the vaccine effectiveness (VE) analysis. The influenza detection rate was 67.2% (728/1084) amongst individuals included. The majority of influenza detections were A(H3N2) which accounted for 681/728 (95.3%) of the total number of subtypes. These were followed by influenza A(H1N1)pdm09 which accounted for 34 (4.7%) of detections and influenza B (Victoria) which accounted for 1 (0.1%) of detections. The remainder were influenza A that could not be subtyped (1.9%, 14/728) due to low viral load. The influenza vaccine coverage was 5.6% (41/728) in cases and 10.7% (38/356) in controls. Coverage in patients with underlying conditions was 7.4% (13/175) in cases and 12.6% (24/190) in controls and in those aged ≥65 years was 19.0% (8/42) in cases and 33.3% (6/18) in controls. The overall VE estimate, adjusted for age and seasonality, was 52.8% (95% CI: 22.5% to 71.3%) against any influenza virus type. Against influenza A(H3N2) it was 53.2% (95% CI 22.5% - 71.6%) in all patients, and 46.5% (95% CI -2.2% - 72.0%) in adults aged between 18 and 64 years (adjusted for seasonality only).

Discussion

The 2019 influenza season in South Africa was predominated by influenza A(H3N2) with co-circulation of influenza A(H1N1)pdm09. Influenza B/Victoria and B/Yamagata lineage viruses circulated at very low levels. In all the surveillance programmes, circulation in the initial period of the season was almost exclusively influenza A(H3N2) followed by influenza A(H1N1)pdm09. Unlike in previous years where a second smaller peak of influenza B was noted, there were very few cases of influenza B reported during the latter half of the year. The 2019 influenza season transmission was mostly moderate, with two weeks reaching high levels of activity. The impact was however mostly low with 3 weeks reaching moderate activity. The season started earlier at the ILI sites, in week 16 in the VW programme and at the public clinics, compared to the pneumonia sites which only reflected the start of the season in week 19. However, the start 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).[8] The influenza vaccine had a moderate effectiveness of 52.8% in South Africa in 2019. Additional information from this surveillance programme, including information on the risk groups for severe illness[15,16], annual estimates of influenza vaccine effectiveness[2,9,10], and details of

virus characterisation are presented in different reports and complement the information presented here.

The RSV season preceded the influenza season which was to be expected based on trends from previous years, and started in week 11 at the ILI sites and in week 6 at the pneumonia surveillance sites. There was no obvious seasonality identified for *B. pertussis* and the number of cases reported was lower compared to previous years. Among ILI and SRI cases aged <15 years, RSV was the commonest pathogen identified followed by influenza and *B. pertussis*. However, influenza was the commonest pathogen followed by RSV and *B. pertussis* among individuals aged ≥15 years in the ILI and pneumonia surveillance systems. In-hospital mortality for patients enrolled in the pneumonia surveillance programme was similar as compared to 2018 (2.8% vs 3%). Furthermore, it has been observed that there was a higher number of RSV cases admitted into ICU as compared to influenza and *B. pertussis* among those aged <15 years.

As is expected during the influenza season, there was a marked increase in cases of influenza in the community as well as people seeking care for influenza-like illness at health care facilities. This was similar to the RSV season. Unlike in 2018 where a number of *B. pertussis* outbreaks were reported, there was very little circulation of pertussis as detected at surveillance sites. By accurately describing and assessing the circulation of influenza, RSV and *B. pertussis*, a better understanding of the epidemiology of these pathogens can be obtained leading to timely disease prevention and management. This highlights the importance of surveillance for respiratory pathogens within South Africa.

Acknowledgements

Special thanks to all clinicians who participated in the Viral Watch programme in 2019. Contributors to the pneumonia surveillance and ILI surveillance are thanked for their inputs. These include: Amelia Buys, Maimuna Carrim, Cheryl Cohen, Mignon Du Plessis, Orienka Hellferscee, Jo McAnerney, Susan Meiring, Fahima Moosa, Liza Rossi, Karistha Ganesh, Kedibone Ndlangisa, Thabo Mohale, Malefu Moleleki, Sibusisiwe Zulu, Mpho Seleka, Jinal Bhiman, Florette Treurnicht, Ziyaad Valley-Omar, Anne von Gottberg, Sibongile Walaza and Nicole Wolter of the Centre for Respiratory Diseases and Meningitis, NICD; Halima Dawood, Sumayya Haffejee and Fathima Naby of Edendale Hospital; Erna du Plessis, Omphile Mekgoe and Ebrahim Variava of the Klerksdorp/Tshepong Hospital Complex;

Kathleen Kahn, Stephen Tollman and Rhian Twine of the MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt); Heather Zar of Red Cross Hospital and the University of Cape Town; Ashraf Coovadia, Jeremy Nel and Gary Reubenson of the Rahima Moosa Mother and Child and Helen Joseph Hospital, Wayne Ramkrishna of the South African National Department of Health - Communicable Diseases Directorate; Meredith McMorrow and Stefano Tempia of the United States Centers for Disease Control and Prevention (CDC), Kathrine Bishop, Zuliswa Kibi, Yekiwe Hlombe, Nombulelo Hoho; Vanessa Kok, Nondumiso Khoza, Nondyebo Madolo, Tshwanelo Mahloko, Wisdom Malinga, Seipati Matshogo, Phumelelo Mavundla, Kholiwe Mgidlana, Moeresi Mosepele, Bernard Motsetse, Myra Moremi, Elizabeth Motaung, Ndungiselo Muravha, Nothando Mthembu, Thandeka Ndlovu, Phindile Ngema, Wendy Ngubane, Patience Ngube, Nonceba Ngubo, Nosisa Simanga and Zanele Siwele of the Surveillance Officers & Research Assistants group; Hanif Carrim, Boitumelo Chuene, Boitumelo Letlape, Nthabiseng Mampa, Mvuyo Makhasi, Cleopatra Mdluli, Shadrack Makhubela, Robert Musetha, Shirley Mhlari, Dimakatso Maraka, Sanelisiwe Nkabinde of the data management team.

References

1. Iuliano AD, Roguski KM, Chang HH, Muscatello DJ, Palekar R, Tempia S, et al. Estimates of global seasonal influenza-associated respiratory mortality: a modelling study. *Lancet.* 2018;391(10127):1285–300.
2. Tempia S, Walaza S, Moyes J, Cohen AL, von Mollendorf C, Treurnicht FK, et al. Risk factors for influenza-associated severe acute respiratory illness hospitalization in South Africa, 2012-2015. *Open Forum Infect Dis*. 2017;4(1):1–10.
3. Ntshoe GM, McAnerney JM, Tempia S, Blumberg L, Moyes J, Buys A, et al. Influenza epidemiology and vaccine effectiveness among patients with influenza-like illness, viral watch sentinel sites, South Africa, 2005-2009. *PLoS One*. 2014;9(4):2005–9.
4. Cohen C, Moyes J, Tempia S, Groom M, Walaza S, Pretorius M, et al. Severe influenza-associated respiratory infection in high HIV prevalence setting, South Africa, 2009-2011. *Emerg Infect Dis*. 2013;19(11):1766–74.
5. Cohen C, Dreyer A, Frean J, Treurnicht F, Iyaloo S, Ismail N, et al. Respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, South Africa, 2014. *Natl Inst Commun Dis Bull*. 2014;13(1):10–30.
6. Walaza S, Buys A, Cohen C, Treurnicht F, Hellferscee O, Mcanerney J, et al. Epidemiology of

respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, 2017. *Natl Inst Commun Dis Bull.* 2017;16:36–60.

7. Walaza S, Cohen C, Treurnicht F, Ismail N, Dreyer A, Frean J, et al. Burden of respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, South Africa 2015. *Natl Inst Commun Dis Bull.* 2016;14(1):10-27.
8. McAnerney JM, Cohen C, Moyes J, Besselaar TG, Buys A, Schoub BD, et al. Twenty-five years of outpatient influenza surveillance in South Africa, 1984-2008. *J Infect Dis*. 2012;206(SUPPL.1):153–8.
9. Mcanerney JM, Treurnicht F, Walaza S, Cohen AL, Tempia S, Mtshali S, et al. Evaluation of influenza vaccine effectiveness and description of circulating strains in outpatient settings in South Africa, 2014. *Influenza Other Respi Viruses*. 2015;9(4):209–15.
10. McAnerney JM, Walaza S, Tempia S, Blumberg L, Treurnicht FK, Madhi SA, et al. Estimating vaccine effectiveness in preventing laboratory-confirmed influenza in outpatient settings in South Africa, 2015. *Influenza Other Respi Viruses.* 2017;11(2):177–81.
11. National Institute for Communicable Diseases. Study Protocol Sentinel Surveillance for Influenza-like (ILI) in South Africa: Enhanced Viral Watch. p. 1–18.
12. International Reagent Resource [Internet]. [cited 2019 Nov 28]. Available from: https://www.internationalreagentresource.org/
13. Tatti KM, Sparks KN, Boney KO, Tondella ML. Novel multitarget real-time PCR assay for rapid detection of Bordetella species in clinical specimens. *J Clin Microbiol.* 2011;49(12):4059–66.
14. Moyes J, Walaza S, Chikosha S, Buys A, Treurnicht A, Hellferscee O, et al. Epidemiology of respiratory pathogens from influenza-like illness and pneumonia surveillance programmes, South Africa, 2018. *Natl Inst Commun Dis Bull.* 2019;17(1):36–60.
15. Tempia S, Walaza S, Viboud C, Cohen AL, Madhi SA, Venter M, et al. Deaths Associated with Respiratory Syncytial and Influenza Viruses among Persons≥ 5 Years of Age in HIV-Prevalent Area, South Africa, 1998–2009. *Emerg Infect Dis.* 2015;21(4):600.
16. Tempia S, Walaza S, Viboud C, Cohen AL, Madhi SA, Venter M, et al. Mortality associated with seasonal and pandemic influenza and respiratory syncytial virus among children <5 years of age in a high HIV prevalence setting - South Africa, 1998-2009. *Clin Infect Dis*. 2014;58(9):1241–9.