RESPIRATORY PATHOGEN EPIDEMIOLOGY FROM THE SYSTEMATIC INFLUENZA-LIKE ILLNESS AND PNEUMONIA SURVEILLANCE PROGRAMMES, SOUTH AFRICA, 2020-2021

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Summary

Syndromic respiratory illness surveillance programmes coordinated by the National Institute for Communicable Diseases (NICD) include pneumonia surveillance and two influenza-like illness (ILI) programmes: systematic ILI surveillance at public health clinics (ILI-PHC surveillance programme) and the Viral Watch programme (ILI-Viral Watch) at private practices. Respiratory samples collected from enrolled individuals meeting case definitions at sentinel sites were tested for influenza, respiratory syncytial virus (RSV), *Bordetella pertussis* and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by real-time polymerase chain reaction.

Influenza was detected in all three programmes in 2020 (168/6 467, 2.6%) and 2021 (445/9 312, 4.8%). In 2020, influenza circulated mainly in the Western Cape Province prior to the start of the normal winter influenza season. In 2020, following the restrictions put in place for coronavirus disease identified in 2019 (COVID-19), influenza circulation decreased with no influenza season occurring (usually May to August). Influenza circulation was low at the start of 2021, but increased outside of the normal influenza season towards the end of 2021 (late spring, weeks 37 to 49). In the pneumonia surveillance programme in 2020, influenza A (H1N1)pdm09 (28/33, 84.8%) was most commonly detected followed by a few influenza B/Victoria (4/33, 12.1%) viruses. In 2021, the most common types and subtypes detected were influenza A (H1N1)pdm09 (108/217, 49.8%), influenza B/Victoria (57/217, 26.3%) and influenza A (H3N2) (35/217, 16.1%). Similar to influenza, no RSV season was observed in either year, although the virus was still detected in 2020 (643/6 467, 9.9%) and 2021 (522/9 312, 5.6%) in all three programmes. The most common RSV subgroup detected in the pneumonia surveillance programme in 2020 was RSV subgroup A (458/549, 83.4%), followed by RSV subgroup B (74/549,13.8%). In 2021, the most common RSV subgroups were RSV subgroup A (220/425, 51.8%) and RSV subgroup B (199/425, 46.8%). A total of 11 cases of *B. pertussis* was detected in 2020 (10/6 065, 0.2%) and 2021 (1/9 055, 0.01%) from ILI-PHC and pneumonia surveillance programmes.

SARS-CoV-2 testing commenced in March 2020 and was detected in all three programmes in 2020 (862/5 730, 15.0%) and 2021 (2 361/9 378, 25.2%). By the end of 2021, four periods of increased transmission had been observed, each driven by a different SARS-CoV-2 variant. The first was from week 21 to week 44 in 2020, peaking in week 30 and driven by the ancestral virus. The second and third periods of increased transmission were from week 52 of 2020 to week 10 in 2021, peaking in week 53 of 2020 (Beta variant), and week 24 to week 40 of 2021 peaking in week 29 (Delta variant),

respectively. The fourth period of increased transmission, driven by the Omicron BA.1 variant, started in week 46 and was ongoing at the end of 2021.

In the first two years of the COVID-19 pandemic, these surveillance programmes managed to monitor four pathogens (influenza, RSV, *B. pertussis* and SARS-CoV-2). With these surveillance programmes, we were able to report changes in transmission of respiratory pathogens and detect SARS-CoV-2 variants. This should be a sustainable platform to monitor for future changes in SARS-CoV-2 transmission and changes in epidemiology of other pathogens.

Introduction

Surveillance systems are used globally to monitor trends in diseases, detect seasonal changes and describe epidemiological characteristics of patients. Surveillance additionally assists in identifying groups at risk for severe disease, such as people with human immunodeficiency virus (HIV).[1] A well-functioning sentinel surveillance programme plays a crucial role in respiratory disease detection, control and monitoring.[2]

Respiratory diseases are a major contributor to hospitalization and death.[3] In South Africa, surveillance programmes such as the pneumonia surveillance programme and influenza-like illness (ILI-PHC surveillance programme and Viral Watch ILI-Viral Watch) programmes are managed by the National Institute for Communicable Diseases (NICD) and are used to monitor respiratory pathogens of public health importance.[4]

Data collected through these programmes are used to describe epidemiological characteristics of individuals infected with respiratory pathogens of public health importance, determine vaccine effectiveness, and to provide data and make recommendations to policymakers and stakeholders that inform monitoring and control measures. These data are summarized and distributed through regular reports and peer-reviewed publications.[4-7]

The aim of this report is to describe the epidemiology of key respiratory pathogens in South Africa using data from 2020-2021 to inform policies and practices concerning their ongoing control and management.

Methods

A summary of each surveillance programme is included below. Respiratory specimens from ILI-PHC surveillance programme and pneumonia surveillance sites were tested for four pathogens: influenza virus, respiratory syncytial virus (RSV), *Bordetella pertussis* and SARS-CoV-2. ILI-Viral Watch specimens were tested for influenza, respiratory syncytial virus (RSV), and SARS-CoV-2. Influenza, RSV and *B. pertussis* were tested in programmes from 1 January 2020 through 31 December 2021. Testing for SARS-CoV-2 was initiated in all three programmes in week 10 of 2020 (starting 2 March). Prior to March 2020, a combined nasopharyngeal (NP) and oropharyngeal swab was collected. From March 2020, only NP swabs were collected.

Description of surveillance programmes and study sites

The pneumonia surveillance programme in South Africa is a hospital-based, active, sentinel surveillance programme established in 2009. In 2020-2021 it included five provinces namely; Gauteng (GP), North West (NW), KwaZulu-Natal (KZN), Western Cape (WC) and Mpumalanga (MP), and nine hospitals (Rahima Moosa Mother and Child Hospital (GP), Helen Joseph Hospital (GP), Edendale Hospital (KZN), Mapulaneng Hospital (MP), Matikwana Hospital (MP), Klerksdorp-Tshepong Hospital Complex (NW), Red Cross Children's Hospital (WC), Mitchell's Plain Hospital (WC) and Tintswalo Hospital (MP) (added February 2021).

The ILI-PHC programme was established in 2012 and enrols outpatients with influenza-like illness at sentinel sites in four provinces (KZN, NW, MP and WC). The systematic ILI programme included individuals who were tested in public health clinics (ILI-PHC). The sites are Eastridge Clinic (WC), Mitchell's Plain Clinic (WC), Jouberton Clinic (NW), Agincourt Clinic (MP, added in November 2020) and Edendale Clinic (KZN).

The ILI-Viral Watch programme was established in 1984 and is a prospective sentinel outpatient-based surveillance programme operating through a general practitioner network.[8] This programme focuses on influenza, RSV and SARS-CoV-2, and aims to describe the epidemiology of these pathogens in outpatients and determine influenza vaccine effectiveness. This programme is active in eight provinces; Eastern Cape (EC), Free State (FS), Limpopo (LP), Northern Cape (NC), GP, NW and WC. General practitioners submit nasopharyngeal (NP) swabs from patients who meet the ILI case definition and suspected SARS-CoV-2 (outpatient) (Table 1) for laboratory testing.

Table 1. Case definitions by age group and surveillance site/programme for the clinical syndromes included in the influenza-like illness (ILI-PHC surveillance programme and ILI-Viral Watch) and pneumonia surveillance programmes, South Africa, 2020-2021.

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	ILI-Viral Watch and ILI-PHC surveillance programme
Severe respiratory illness (SRI)	**2 days to <3 months** Any child hospitalised with a diagnosis of suspected sepsis or physician-diagnosed LRTI irrespective of signs and symptoms. **3 months to <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 physician diagnosed-LRTI* or suspected COVID-19	Pneumonia surveillance
Suspected pertussis	Any patient presenting with cough illness of any duration and at least one of: paroxysms of cough, post-tussive vomiting, inspiratory whoop **OR** Infants <1 year with apnoea, with or without cyanosis	ILI-PHC surveillance programme Pneumonia surveillance ILI Viral Watch (on request only)
Suspected SARS-CoV-2 (outpatient)	Any person presenting with an acute (≤14 days) respiratory tract infection or other clinical illness compatible with COVID-19** and not meeting the ILI case definition	ILI-Viral Watch and ILI-PHC surveillance programme
Suspected SARS-CoV-2 (hospitalised)	Any person admitted with a physician-diagnosis of suspected COVID-19 and not meeting pneumonia surveillance case definition	Pneumonia surveillance

*LRTI =lower respiratory tract infection and includes suspected pulmonary TB, suspected pertussis

**Symptoms include ANY of the following respiratory symptoms: cough, sore throat, shortness of breath, anosmia (loss of sense of smell) or dysgeusia (alteration of the sense of taste), with or without other symptoms (which may include fever, weakness, myalgia or diarrhoea)

Sample and data collection

For the pneumonia and ILI-PHC surveillance programme, potentially eligible patients were approached for screening by a surveillance officer. For those meeting the case definitions and consented to inclusion, a paper-based or electronic case investigation form (CIF) was completed and uploaded to the NICD SQL (structured query language) database and an NP swab was collected for testing. In the ILI-Viral Watch programme, a short CIF form was completed by a physician and submitted to the NICD, which was then captured on an NICD Microsoft Access database. HIV status was determined based on testing undertaken as part of standard-of-care or medical record review. Samples were stored at 4°C before being transported on ice packs in cooler boxes to the NICD for testing within 72 hours of collection.

Laboratory testing for influenza, RSV, *B. pertussis* and SARS-CoV-2

Influenza A and B viruses, RSV and SARS-CoV-2 were tested at the NICD using a commercial multiplex RT-PCR assay (Allpex SARS-CoV-2/FluA/FluB/RSV PCR kit, Seegene Inc., Seoul, South Korea) A specimen was considered positive for SARS-CoV-2 when the PCR cycle threshold (C_t) was <40 for ≥1 of the gene targets S, N or RdRp. SARS-CoV-2 positive specimens were characterised on the Allplex™ SARS-CoV-2 Variants I and II PCR assays (Seegene Inc., Seoul, Korea) from March 2020 to June 2021, with some samples selected for sequencing. SARS-CoV-2 positive specimens were exclusively sequenced from July 2021 using the Illumina COVIDSeq protocol (Illumina, CA, USA). Influenza A and B positive specimens were subtyped using the US Centres for Disease Control and Prevention (CDC) RT-PCR protocol and reagents.[9] RSV A and B positive specimens were subgrouped using an in-house assay.[10]

Bordetella pertussis was tested using a previously described RT-PCR method.[11] A specimen was considered positive when the *IS481* and/or *ptxS1* gene targets are detected with a ct value of <45.

Data management and analysis

Data management was centralised at the NICD. All electronic data were saved on a Microsoft Access or SQL database. Data recorded for each enrolled patient included laboratory, clinical and demographic data. Data quality, including checks for missing data and duplicate entries, were managed by the CRDM data team.

Detection rates were calculated as the number of positive tests divided by the number of samples tested. A moving epidemic curve was generated using the Moving Epidemic Method (MEM), a sequential analysis using the R Language, available from: http://CRAN.R-project.org/web/package=mem, designed to calculate the duration, start and end of the annual influenza and RSV seasons. The detection rate for the year was plotted against the moving average for previous years (2009-2019) to determine the level of activity for the year using an algorithm.[12] MEM uses the historical 40th, 90th and 97.5th percentiles to calculate thresholds of activity, defined as:

- Epidemic threshold: Median of weekly values for all baseline years
- Low activity: Between epidemic threshold and 40th percentile
- Moderate activity: Between 40th and 90th percentiles
- High activity: Between 90th and 97.5th percentile
- Very high activity: 97.5th percentile and above

The season starts when the detection rate rises above the epidemic threshold and remains above the threshold for three consecutive weeks. The season ends when the detection rate falls below the epidemic threshold for three consecutive weeks. Data from 2020 and 2021 were plotted against the thresholds set by data collected from the ILI-PHC programme between 2013 and 2019 (pre-COVID-19 pandemic) and pneumonia surveillance between 2010 and 2019. All analyses were conducted using Stata (version 16, StataCorp LP, College Station, TX, USA).

Results

Patients enrolled and tested

In ILI-Viral Watch, 661 patients were enrolled from January 2020 through December 2021. These were tested for influenza, RSV, and *B. pertussis* (659/661, 99.7%), and for SARS-CoV-2 (532/661, 80.4%). From January 2020 through December 2021, 15 809 patients were enrolled in the two syndromic surveillance programmes conducted in the public sector (ILI- PHC and pneumonia surveillance). Of these, 15 355 (97.1%) samples were tested for respiratory pathogens (Figure 1). Of those individuals that were tested, 27.9% (4 283/15 355) were enrolled in the ILI-PHC surveillance programme, and 72.1% (11 072/15 355) were enrolled in the pneumonia surveillance programme. (Figure 1). In ILI-PHC surveillance programme, 4 279 specimens were tested for influenza, RSV and *B. pertussis* and, of these, 4 045 were also tested for SARS-CoV-2. Four specimens were exclusively tested for SARS-CoV-2.

In pneumonia surveillance, 97.9% (10 841/11 072) of specimens were tested for influenza, RSV and *B. pertussis*. From March 2020, 10 531 specimens were in addition tested for SARS-CoV-2 at the NICD. Of the 11 072 individuals enrolled, 231 (2.1%) were only tested for SARS-CoV-2 at the site laboratory with no additional specimen sent to the NICD. Individuals aged ≥15 years made up the majority of both ILI-PHC surveillance programme (2 946/4 283, 68.8%) and pneumonia surveillance cases (6 650/11 072, 60.1%). Among individuals aged <15 years in the ILI-PHC, the majority were aged ≤1 year old (532/752, 70.7%) (Table 2). Among individuals aged ≥15 years in the ILI-PHC, the majority were aged 25-44 years (1 601/2 946, 53.3%) (Table 3). Among individuals aged <15 years enrolled in the pneumonia surveillance programme in 2020 and 2021, most were in the ≤1year age group (3 473/4 422, 78.5%) (Table 4). Among individuals aged ≥15 years enrolled in the pneumonia surveillance programme, the majority of patients were aged 45-64 years (2 494/6 650, 37.5%) or 25-44 years (2 381/6 650, 35.8%) (Table 5).

The overall HIV prevalence was 26.0% (2 670/10 255) among patients in the pneumonia surveillance programme and 14.5% (598/4 131) among patients in the ILI-PHC surveillance programmes (Figure 2). The HIV prevalence varied by age group and surveillance programme case definition (Figure 2) with HIV prevalence being highest in the 25-44-year age group for individuals enrolled in ILI-PHC (378/1601, 23.6%) and pneumonia surveillance (1 356/2381, 57.0%) programmes.

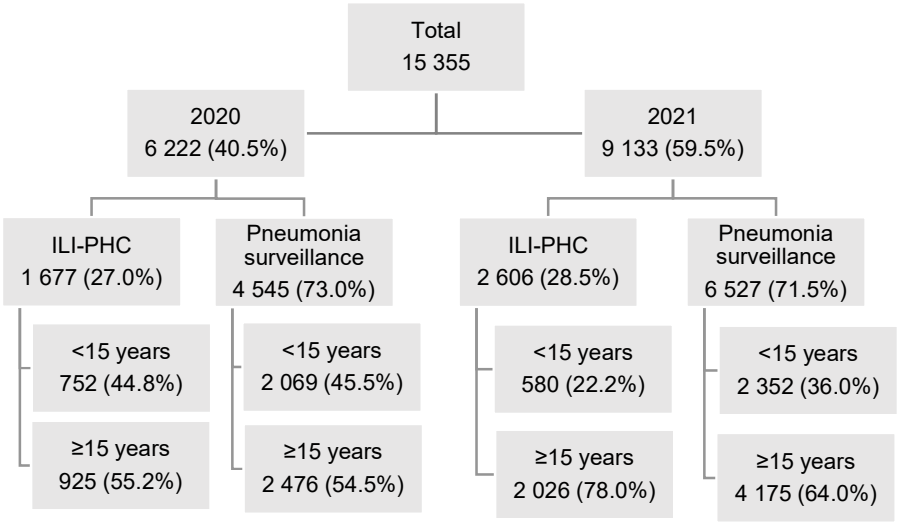

Figure 1. Numbers of samples tested for respiratory pathogens in the pneumonia surveillance and influenza-like illness in public health clinics (PHC) surveillance programme, South Africa, 2020-2021. Individuals <5 years in ILI-PHC n=904 and pneumonia surveillance n=4 131.

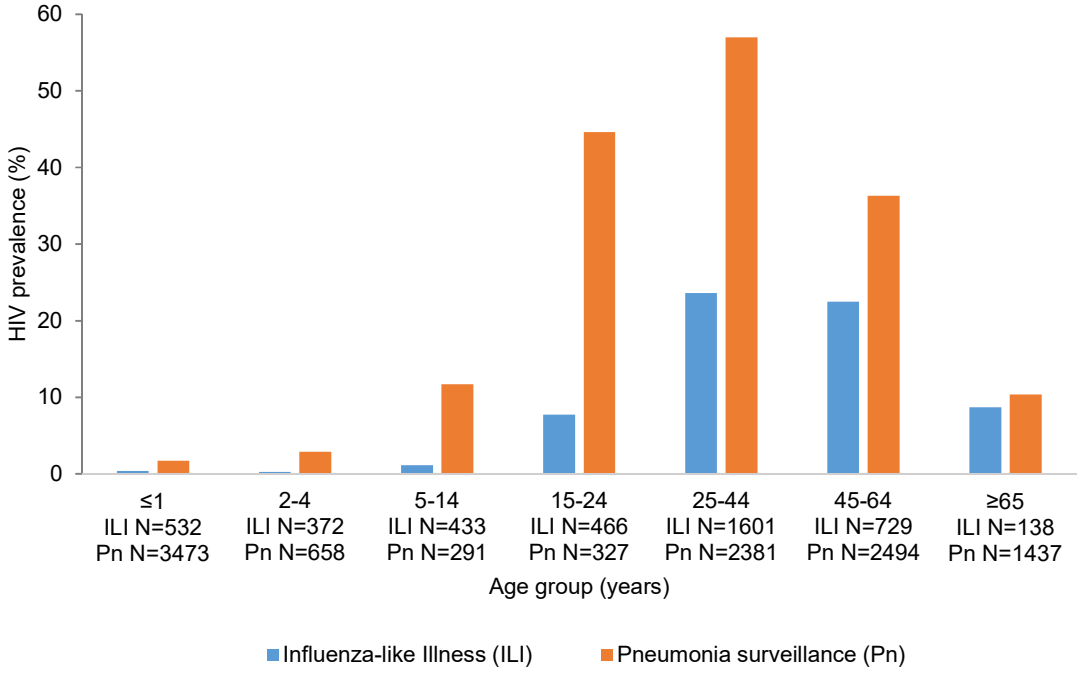

Figure 2. HIV prevalence by age group for individuals enrolled in the pneumonia surveillance and ILI-PHC surveillance programmes, South Africa, 2020-2021. The value below the age category depicts the total number enrolled in each surveillance programme per age group.

Respiratory pathogens

In 2020 and 2021 in the ILI-PHC surveillance programme, RSV was the most commonly detected pathogen in individuals <15 years old (128/1 337, 9.6%), followed by influenza (107/1 337, 8.0%), SARS-CoV-2 (76/1 337, 5.7%) and *B. pertussis* (2/1 337, 0.2%). In those patients <5 years old, RSV was most commonly detected, whereas SARS-CoV-2 was most commonly detected in individuals ≥5 -14 years old (41/76, 53.9%) (Table 2). In individuals aged ≥15 years old in the ILI-PHC surveillance programme, SARS-CoV-2 was the most commonly detected pathogen (720/2 946, 24.4%) followed by influenza (138/2 946, 4.7%) and RSV (53/2 946, 1.8%). *Bordetella pertussis* was not detected (Table 3).

Among individuals aged <15 years old enrolled in the pneumonia surveillance programme in 2020 and 2021, the most commonly detected pathogen was RSV (916/4 422, 20.7%), followed by SARS-CoV-2 (178/4 422, 4.0%), influenza (172/4 422, 3.9%) and *B. pertussis* (9/4 422, 0.2%) (Table 4). Overall, the in-hospital mortality was 1.0% (45/4 422) among patients <15 years old. Among individuals aged ≥15 years in the pneumonia surveillance programme, SARS-CoV-2 was the most commonly detected pathogen (2 149/6 650, 32.3%) followed by influenza (77/6 650, 1.2%) and RSV (58/6 650, 0.9%). *Bordetella pertussis* was not detected. Additionally, 25.8% (510/1 980) of individuals infected with

SARS-CoV-2 were people living with HIV. Of those infected with SARS-CoV-2, 17.1% (369/2 149) died. Overall, the in-hospital mortality was 13.0% (870/6 650) (Table 5).

Influenza

There was no influenza season declared in 2020 and 2021 in South Africa. In ILI-Viral Watch in 2020, influenza was detected in 83/402 (20.6%) patients. Out of the positive cases, 82/83 (98.8%) were before the national lockdown in March 2020. Of the total 83 cases, 79 (95.2%) were influenza A(H1N1)pdm09, three (3.6%) were influenza A(H3N2) and one (1.2%) influenza B/Victoria (Figure 3A). All cases detected were from the Western Cape (77/83, 92.8%) and Gauteng provinces (6/83, 7.2%). In 2021, 257 specimens were received from patients enrolled in ILI-Viral Watch in 6 provinces. Influenza was detected in 36 (14.0%) patients. Of these 36 cases, 17 (47.2%) were influenza A(H1N1)pdm09, seven (19.4%) were influenza A(H3N2), one (2.7%) was A subtype inconclusive and 11 (30.6%) influenza B/Victoria (Figure 3A). Most cases were detected from the Gauteng (183/257, 71.2%) followed by Western Cape (60/257, 23.3%), Eastern Cape (4/257, 1.6%), Free State (4/257, 1.6%), Mpumalanga (3/257 1.2%) and North West provinces (2/257, 0.8%). No specimens were received from Limpopo Province. An unseasonal increase in cases was detected towards the end of 2021.

In the ILI-PHC surveillance programme, of the 1 674 specimens tested in 2020, 52 (3.1%) were positive for influenza and detected before the national lockdown in March 2020. Of the 52 influenza positive specimens, 36 (69.2%) were identified as influenza A(H1N1)pdm09, one (1.9%) influenza A subtype inconclusive, 12 (23.1%) as influenza B/Victoria and three (5.8%) B lineage inconclusive due to low viral load (cycle threshold value (C_t) ≥35) for further characterization (Figure 3B). Of the 2 605 specimens tested in 2021, 193 (7.4%) were positive for influenza. Of the 193 influenza positive specimens, 100 (51.8%) were identified as influenza A(H1N1)pdm09, 28 (14.5%) were identified as influenza A(H3N2), five (2.6%) influenza A subtype inconclusive, 55 (28.5%) as influenza B/Victoria and five (2.6%) B lineage inconclusive due to too low viral load for further characterization (C_t≥35). (Figure 3B). Cases peaked in week 47 of 2021, with 23/62 (37.1%) influenza positive specimens. In 2020, the detection rate of influenza remained below the epidemic threshold, and transmissibility remained low during this period (Figure 3D). In contrast with 2020, the detection rate of influenza in 2021 remained below threshold until week 44 to week 48 where the detection rate was briefly in the low-moderate activity zone.

In the pneumonia surveillance programme in 2020, influenza was detected in 0.8% (33/4 391) of enrolled patients, and 28 (84.8%) were influenza A(H1N1)pdm09, one (0.3%) influenza A subtype inconclusive and four (12.1%) were influenza B/Victoria (Figure 6A). There was an increase in cases between weeks 6 through to week 15 with all specimens from the Western Cape Province, mostly influenza A(H1N1)pdm09 (24/33, 72.2%). All influenza cases were detected before the national lockdown in March 2020. In 2021, 3.4% (217/6 450) of enrolled patients had influenza detected, 108 (49.8%) were influenza A(H1N1)pdm09, 35 (16.1%) were influenza A(H3N2), 10 (4.6%) influenza A subtype inconclusive, 57 (26.3%) influenza B/Victoria, 6 (2.8%) B lineage inconclusive, 1 (0.5%) B lineage undetermined (Figure 3C). Moreover, the detection rate increased into the low activity zone for one week in week 12 in 2020 and again in week 38 to week 52 in 2021 (Figure 3E).

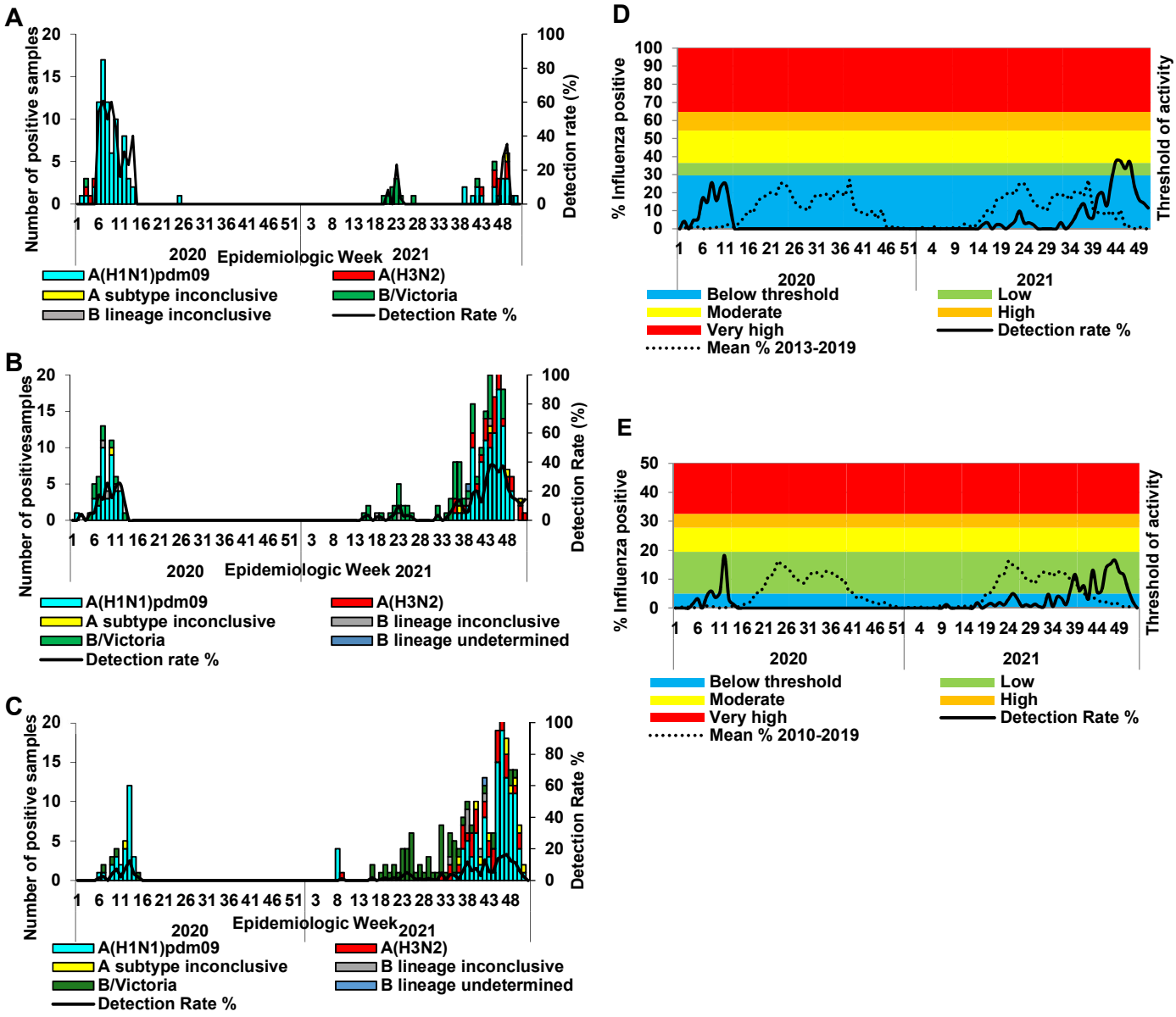

Figure 3. Number of influenza positive samples by influenza subtype and lineage and detection rate by week A) ILI-Viral Watch[1,7], B) ILI-PHC[2,7], C) pneumonia surveillance[3,7], and D) influenza percentage detections and epidemic threshold by epidemiological week for all age groups using the MEM[4] method, ILI-PHC[2,5] and E) pneumonia surveillance public hospitals[3,6], South Africa, 2020-2021.

[1]Specimens from patients with ILI-Viral Watch at 90 sentinel sites in 8 provinces

[2]Specimens from patients with ILI-PHC at 5 sentinel sites in 4 provinces

[3]Specimens from patients with influenza-like illnesses at 7 sentinel sites in 5 provinces

[4]MEM- Moving Epidemic Method

[5]Thresholds based on 2013-2019 data

[6]Thresholds based on 2010-2019 data

[7]Inconclusive: insufficient viral load in sample ($C_t \geq 35$) and unable to characterise further

Detection rate only reported for weeks with >10 specimens submitted

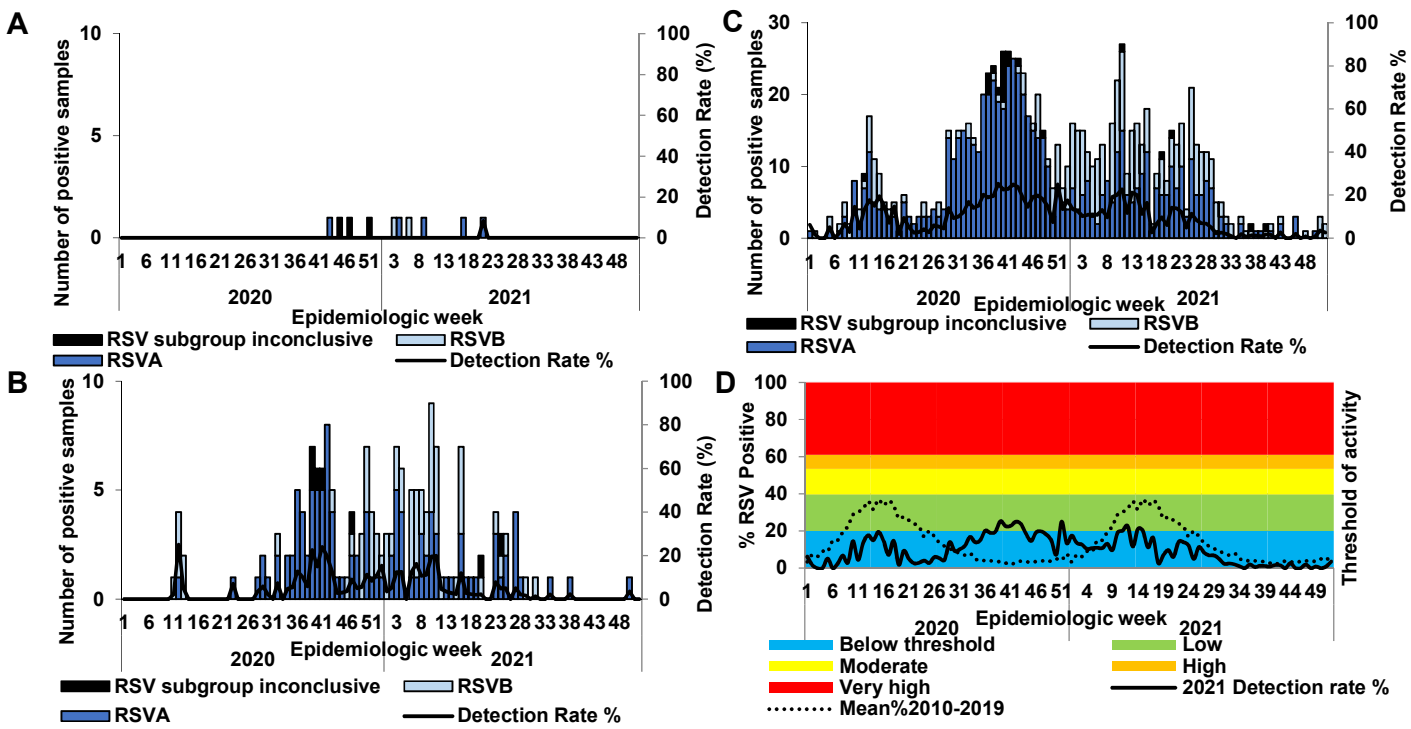

Figure 4. Number of RSV positive samples by subgroup and detection rate by week A) ILI-Viral Watch[1,6], B) ILI-PHC[2,6], C) pneumonia surveillance[3,6], and D) RSV detection rate and epidemic threshold by epidemiological week for all age groups using the MEM[4] method, pneumonia surveillance public hospitals[3,5], South Africa, 2020-2021.

[1]Specimens from patients with ILI-Viral Watch at 90 sentinel sites in 8 provinces

[2]Specimens from patients with ILI-PHC at 5 sentinel sites in 4 provinces

[3]Specimens from patients with influenza-like illnesses at 7 sentinel sites in 5 provinces

[4]MEM- Moving Epidemic Method

[5]Thresholds based on 2010-2019 data

[6]Inconclusive: insufficient viral load in sample ($C_t \geq 35$) and unable to characterise further

Detection rate only reported for weeks with >10 specimens submitted

As with influenza, no RSV season was declared during the 2020-2021 period. In the ILI-Viral Watch programme in 2020, RSV was detected in 1.0% (4/402) of specimens. Three of these patients were from Western Cape Province (3/4, 75.0%) and one was from Gauteng Province (1/4, 25.0%), (Figure 4A). In 2021, 257 specimens were received and tested. RSV was detected in six (2.3%) specimens. Of the six RSV positive patients, four (4/6, 66%) were from Gauteng Province and two (2/6, 33.3%) were from Western Cape Province.

In the ILI-PHC surveillance programme in 2020, RSV was detected in 5.4% (90/1 674) of patients tested (Figure 4B). Of the 90 RSV positive specimens, RSV subgroup A predominated (63/90, 70.0%), with sporadic detections of RSV subgroup B (22/90, 24.4%). There were 5/90 (5.6%) specimens that were inconclusive in subgroup due to too low viral load to allow further characterization. In 2021, RSV was detected in 3.4% (91/2 605) of patients tested (Figure 4B). Of these, 47/91 (51.6%) were characterised as RSV subgroup A, 41/91 (45.1%) were RSV subgroup B and 3/91 (3.3%) were inconclusive for subgroup due to low viral load.

RSV in the pneumonia surveillance programme circulated throughout 2020 and 2021 but had no defined season compared to previous years. Of the 4 391 specimens tested in 2020, 12.5% (549) were positive for RSV. RSV subgroup A (458/549, 83.4%) predominated (Figure 4C). Of the 6 450 specimens tested in 2021, 425 (6.5%) were positive for RSV. Of these positive specimens, 220/425 (51.8%) were characterised as RSV subgroup A, 199/425 (46.8%) were RSV subgroup B and 6/425 (1.4%) could not be subgrouped (RSV subgroup inconclusive). The RSV detection rate in pneumonia surveillance remained below the seasonal threshold for most of 2020-2021, except for brief durations in the low activity threshold between week 36 to week 43 in 2020 and week 11 and 14 in 2021 (Figure 4D).

Bordetella pertussis

Few *B. pertussis* cases were detected in the ILI-PHC surveillance programme and pneumonia surveillance programmes (2 and 9 cases, respectively) during 2020-2021. No *B. pertussis* cases were detected in the ILI-Viral Watch programme, as specimens were not routinely tested for this organism.

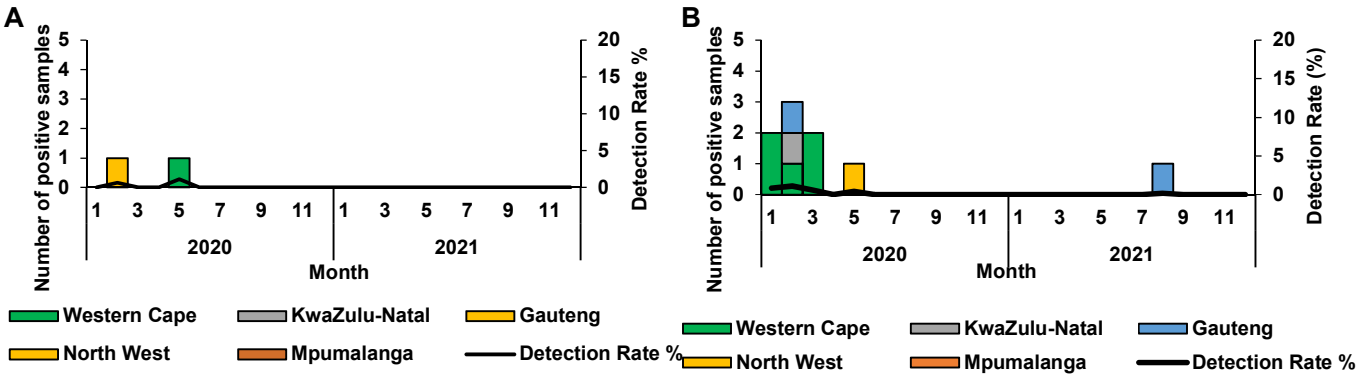

Figure 5. Number of B. pertussis positive samples and detection rate by province and month, A) ILI-PHC and B) pneumonia surveillance programme, South Africa, 2020-2021.

Among those who were enrolled in the ILI-PHC surveillance programme in 2020, 1 674 patients were tested for *B. pertussis*, two (0.1%) tested positive, one each from North West and Western Cape provinces. Both *B. pertussis* cases were detected in February and May and in individuals aged ≥5 years (Figure 5A). During 2021, 2 605 patients met the case definition, but none tested positive.

Among those who were enrolled in the pneumonia surveillance programme in 2020, 4 391 patients were tested for *B. pertussis*, of which eight (0.2%) tested positive. Of these, five (62.5%) were from Western Cape Province while North West, Gauteng and KwaZulu-Natal provinces had one case each (1/8, 12.5%) (Figure 5B). During 2021, 6 450 specimens were tested for *B. pertussis*, and one (0.02%) tested positive. This case was identified in Gauteng Province in a female aged ≤1 years old.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

The first case of SARS-CoV-2 from the three surveillance programmes was detected in week 14 (week starting, 30 March 2020) in the ILI-Viral Watch programme. During March 2020 through December 2021, 3 676 cases were identified from all three surveillance programmes.

In the ILI-Viral Watch programme, 276 specimens were submitted for testing for SARS-CoV-2, and 37/276 (13.4%) of specimens were positive (Figure 6A). SARS-CoV-2 was detected in 63/257 (24.5%) specimens tested (Figure 6A). Of the 63 SARS-CoV-2 positive individuals, the majority were from Gauteng Province (48/63, 76.2%) followed by Western Cape Province (15/63, 23.8%).

In the ILI-PHC surveillance programme from March through December 2020, SARS-CoV-2 was detected in 15.3% (221/1 442) of specimens tested (Figure 6B). The majority of cases were reported from the Western Cape (95/221, 43.0%) and the North West provinces (75/221, 33.9%). From week 48 (week starting 23 November 2020) the detection rate started to increase for the second period of increase in transmission and peaked at 64.3% (9/14) in week 53 (week starting 27 December 2020). In 2021, SARS-CoV-2 was detected in 22.1% (575/2 605) of patients tested (Figure 6B). The majority of cases were detected from the North West (306/576, 53.1%) and KwaZulu-Natal provinces (108/576, 18.8%). During 2020-2021, four periods of increase in transmission were observed with detection rates peaking at 48.8%, 64.3%, 59.6% and 75.0% in weeks 22 of 2020 to week 36 of 2020, weeks 48 of 2020 to week 8 of 2021, weeks 25 of 2021 to week 39 of 2021 and weeks 48 of 2021 to week 52 of 2021.

In the pneumonia surveillance programme from March through December 2020, SARS-CoV-2 was detected in 15.1% (604/4 013) of patients tested (Figure 6C). The first case among pneumonia cases was detected in week 17 (week starting 20 April 2020). The majority of cases were detected from KwaZulu-Natal (167/604, 27.6%), Gauteng (156/604, 25.8%) and North West (143/604, 23.7%) provinces (Figure 6C).

In 2021, 26.4% (1 723/6 521) of SARS-CoV-2 cases were detected in patients tested. The majority of cases were in Gauteng (434/1 724, 25.2%) and North West provinces (364/1 724, 21.1%) (Figure 6C). During 2020-2021, four periods of increased transmission were observed with detection rates peaking at 48.4%, 56.9%, 59.19% and 61.6% in week 22 in 2020 to week 40 of 2020, week 50 of 2020 to week 10 of 2021, week 24 of 2021 to week 38 of 2021 and week 47 of 2021 to week 52 of 2021, respectively.

In the ILI-PHC surveillance programme (Figure 6C) and pneumonia surveillance programme (Figure 6E), ancestral virus was detected in the first period of increase in transmission. The Beta variant was predominant in the second period of increase in transmission. The third period of increase in transmission was dominated by the Delta variant. Finally, the Omicron (21K/BA.1) variant was detected in the fourth period of increase in transmission.

Ten SARS-CoV-2 and influenza co-infections and 33 SARS-CoV-2 and RSV co-infections were detected during 2020-2021 in the ILI-PHC and pneumonia surveillance programmes.

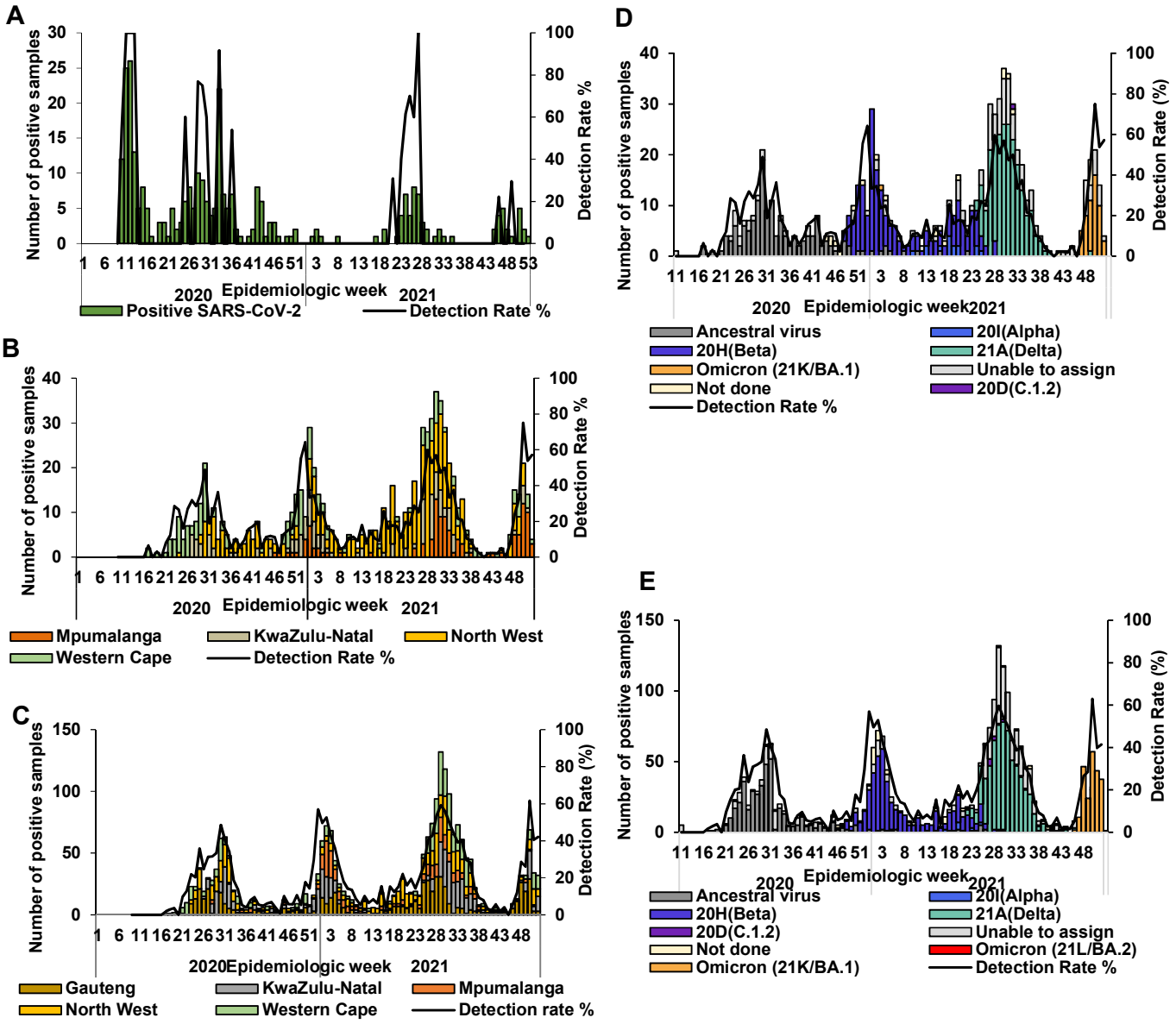

Figure 6. Numbers of SARS-CoV-2 positive samples by detection rate per week, A) ILI-Viral Watch[1], B) ILI-PHC[2], C) pneumonia surveillance programme[3], and by variant and detection rate per week D) ILI-PHC[2,4] and E) pneumonia surveillance programme[3,4], South Africa, 2020-2021.

[1]Specimens from patients with influenza-like illness at 90 sentinel sites in 8 provinces.

[2]Specimens from patients at 5 sentinel sites in 4 provinces who met suspected SARS-CoV-2 case definition and/or ILI-PHC surveillance programme case definition.

[3]Specimens from patients at 7 sentinel sites in 5 provinces who met suspected SARS-CoV-2 case definition and/or pneumonia surveillance case definition

[4]Unable to assign: no lineage assigned due to poor sequence quality **OR** low viral load ($C_t \geq 35$) **OR** variant PCR could not assign variant and no sequencing result

Detection rate only reported for weeks with >10 specimens submitted

Table 2. Demographic and clinical characteristics of patients aged <15 years enrolled in the ILI-PHC surveillance programme and testing positive for influenza, RSV, *Bordetella pertussis* and SARS-CoV-2, South Africa, 2020-2021.

	Enrolled n/N (%)	Influenza, n/N (%)	RSV, n/N (%)	*B. pertussis*, n/N (%)	SARS-CoV-2 n/N (%)
Characteristic					
Year					
2020	757/1,337 (57)	50/107 (47)	73/128 (57)	2/2 (100)	36/76 (47)
2021	580/1,337 (43)	57/107 (53)	55/128 (43)	0/2 (0)	40/76 (53)
Age group (years)					
≤1 years	532/1,337 (40)	27/107 (25)	74/128 (58)	0/2 (0)	24/76 (32)
2-4 years	372/1,337 (28)	40/107 (37)	40/128 (31)	0/2 (0)	11/76 (14)
5-14 years	433/1,337 (32)	40/107 (37)	14/128 (11)	2/2 (100)	41/76 (54)
Sex					
Male	704/1,337 (53)	48/107 (45)	69/128 (54)	0/2 (0)	36/76 (47)
Female	633/1,337 (47)	59/107 (55)	59/128 (46)	2/2 (100)	40/76 (53)
Province					
Mpumalanga	118/1,337 (9)	5/107 (5)	18/128 (14)	0/2 (0)	8/76 (11)
North West	104/1,337 (8)	7/107 (7)	5/128 (4)	1/2 (50)	5/76 (7)
KwaZulu-Natal	260/1,337 (19)	18/107 (17)	18/128 (14)	0/2 (0)	15/76 (20)
Western Cape	855/1,337 (64)	77/107 (72)	87/128 (68)	1/2 (50)	48/76 (63)
HIV-infected	8/1,287 (1)	2/105 (2)	0/122 (0)	0/2 (0)	1/75 (1)
Malnutrition*	50/899 (6)	5/66 (8)	6/115 (5)	0/0 (0)	0/35 (0)
Premature**	27/902 (3)	2/67 (3)	1/114 (1)	0/0 (0)	2/35 (6)
Underlying illness***	38/1,337 (3)	2/107 (2)	2/128 (2)	0/2 (0)	4/76 (5)

* Malnutrition 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 born before 37 completed weeks of gestation

***Underlying illness included any of: 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)

Total number of specimens tested for influenza, RSV and *B. pertussis* n=1 337, and SARS-CoV-2 n=1 184

Table 3. Demographic and clinical characteristics of patients aged ≥15 years enrolled in the ILI-PHC surveillance programme and testing positive for influenza, RSV, *Bordetella pertussis* and SARS-CoV-2, South Africa, 2020-2021.

	Enrolled n/N (%)	Influenza, n/N (%)	RSV, n/N (%)	*B. pertussis*, n/N (%)	SARS-CoV-2 n/N (%)
Characteristic					
Year					
2020	920/2,946 (31)	2/138 (1)	17/53 (32)	0/0 (0)	185/720 (26)
2021	2,026/2,946 (69)	136/138 (99)	36/53 (68)	0/0 (0)	535/720 (74)
Age group (years)					
15-24	466/2,946 (16)	14/138 (10)	8/53 (15)	0/0 (0)	102/720 (14)
25-44	1,601/2,946 (54)	96/138 (70)	30/53 (57)	0/0 (0)	388/720 (54)
45-64	729/2,946 (25)	26/138 (19)	11/53 (21)	0/0 (0)	193/720 (27)
>65	138/2,946 (5)	2/138 (1)	2/53 (4)	0/0 (0)	36/720 (5)
Unknown	12/2,946 (0)	0/138 (0)	2/53 (4)	0/0 (0)	1/720 (0)
Sex					
Male	1,275/2,946 (43)	69/138 (50)	24/53 (45)	0/0 (0)	277/720 (38)
Female	1,671/2,946 (57)	69/138 (50)	29/53 (55)	0/0 (0)	443/720 (62)
Province					
Mpumalanga	257/2,946 (9)	2/138 (1)	3/53 (6)	0/0 (0)	85/720 (12)
North West	1,359/2,946 (46)	64/138 (46)	26/53 (49)	0/0 (0)	375/720 (52)
KwaZulu-Natal	580/2,946 (20)	30/138 (22)	18/53 (34)	0/0 (0)	135/720 (19)
Western Cape	750/2,946 (25)	42/138 (30)	6/53 (11)	0/0 (0)	125/720 (17)
HIV-infected	590/2,844 (21)	30/137 (22)	16/49 (33)	0/0 (0)	143/700 (20)
Underlying illness*	346/2,946 (12)	18/138 (13)	6/53 (11)	0/0 (0)	71/720 (10)

*Underlying illness included any of: 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)

Total number of specimens tested for influenza, RSV and *B. pertussis* n=2 942, and SARS-CoV-2 n=2 861

Table 4. Demographic and clinical characteristics of patients aged <15 years enrolled in the pneumonia surveillance programme and testing positive for influenza, RSV, Bordetella pertussis and SARS-CoV-2, South Africa, 2020-2021.

	Enrolled n/N (%)	Influenza, n/N (%)	RSV, n/N (%)	*B. pertussis*, n/N (%)	SARS-CoV-2 n/N (%)
Characteristic					
Year					
2020	2,070/4,422 (47)	32/172 (19)	539/916 (59)	8/9 (89)	51/178 (29)
2021	2,352/4,422 (53)	140/172 (81)	377/916 (41)	1/9 (11)	127/178 (71)
Age group (years)					
≤1 years	3,473/4,422 (79)	112/172 (65)	847/916 (92)	8/9 (89)	148/178 (83)
2-4 years	658/4,422 (15)	43/172 (25)	62/916 (7)	1/9 (11)	16/178 (9)
5-14 years	291/4,422 (7)	17/172 (10)	7/916 (1)	0/9 (0)	14/178 (8)
Sex					
Male	2,562/4,422 (58)	104/172 (60)	475/916 (52)	4/9 (44)	102/178 (57)
Female	1,860/4,422 (42)	68/172 (40)	441/916 (48)	5/9 (56)	76/178 (43)
Province					
Mpumalanga	346/4,422 (8)	17/172 (10)	43/916 (5)	0/9 (0)	11/178 (6)
Gauteng	754/4,422 (17)	33/172 (19)	145/916 (16)	2/9 (22)	46/178 (26)
North West	333/4,422 (8)	12/172 (7)	58/916 (6)	1/9 (11)	15/178 (8)
KwaZulu-Natal	486/4,422 (11)	19/172 (11)	52/916 (6)	1/9 (11)	19/178 (11)
Western Cape	2,503/4,422 (57)	91/172 (53)	618/916 (67)	5/9 (56)	87/178 (49)
Symptom duration (≤ 10 days)	4,294/4,422 (97)	165/172 (96)	906/916 (99)	6/9 (67)	168/178 (94)
HIV-infected	113/4,041 (3)	2/149 (1)	6/846 (1)	0/9 (0)	7/161 (4)
Malnutrition*	719/4,077 (18)	33/152 (22)	118/905 (13)	1/9 (11)	38/161 (24)
Premature**	389/4,115 (9)	10/150 (7)	84/908 (9)	2/9 (22)	21/164 (13)
Underlying illness***	308/4,422 (7)	12/172 (7)	40/916 (4)	0/9 (0)	15/178 (8)
Hospital duration ≤5 days	4,058/4,422 (92)	160/172 (93)	863/916 (94)	7/9 (78)	147/178 (83)
ICU admission	77/4,412 (2)	2/172 (1)	17/914 (2)	1/9 (11)	4/177 (2)
In-hospital mortality	45/4,422 (1)	1/172 (1)	1/916 (0)	0/9 (0)	4/178 (2)

* Malnutrition 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 born before 37 completed weeks of gestation

***Underlying illness included any of: 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)

Total number of specimens tested for influenza, RSV and *B. pertussis* n=4 355, and SARS-CoV-2 n=4 115

Table 5. Demographic and clinical characteristics of patients aged ≥15 years enrolled in the pneumonia surveillance programme and testing positive for influenza, RSV, Bordetella pertussis and SARS-CoV-2, South Africa, 2020-2021.

	Enrolled n/N (%)	Influenza, n/N (%)	RSV, n/N (%)	*B. pertussis*, n/N (%)	SARS-CoV-2 n/N (%)
Characteristic					
Year					
2020	2,475/6,650 (37)	1/77 (1)	10/58 (17)	0/0 (0)	553/2,149 (26)
2021	4,175/6,650 (63)	76/77 (99)	48/58 (83)	0/0 (0)	1,596/2,149 (74)
Age group (years)					
15-24	327/6,650 (5)	3/77 (4)	5/58 (9)	0/0 (0)	71/2,149 (3)
25-44	2,381/6,650 (36)	30/77 (39)	24/58 (41)	0/0 (0)	579/2,149 (27)
45-64	2,494/6,650 (38)	34/77 (44)	20/58 (34)	0/0 (0)	939/2,149 (44)
>65	1,437/6,650 (22)	10/77 (13)	5/58 (9)	0/0 (0)	558/2,149 (26)
Unknown	11/6,650 (0)	0/77 (0)	4/58 (7)	0/0 (0)	2/2,149 (0)
Sex					
Male	2,986/6,650 (45)	29/77 (38)	26/58 (45)	0/0 (0)	812/2,149 (38)
Female	3,664/6,650 (55)	48/77 (62)	32/58 (55)	0/0 (0)	1,337/2,149 (62)
Province					
Mpumalanga	981/6,650 (15)	7/77 (9)	10/58 (17)	0/0 (0)	248/2,149 (12)
Gauteng	1,917/6,650 (29)	29/77 (38)	17/58 (29)	0/0 (0)	544/2,149 (25)
North West	1,294/6,650 (19)	16/77 (21)	10/58 (17)	0/0 (0)	492/2,149 (23)
KwaZulu-Natal	1,509/6,650 (23)	9/77 (12)	9/58 (16)	0/0 (0)	500/2,149 (23)
Western Cape	949/6,650 (14)	16/77 (21)	12/58 (21)	0/0 (0)	365/2,149 (17)
Symptom duration (≤ 10 days)	4,903/6,650 (74)	67/77 (87)	41/58 (71)	0/0 (0)	1,810/2,149 (84)
HIV-infected	2,557/6,214 (41)	41/73 (56)	28/52 (54)	0/0 (0)	510/1,980 (26)
Underlying illness*	2,230/6,650 (34)	18/77 (23)	13/58 (22)	0/0 (0)	865/2,149 (40)
Hospital duration ≤5 days	5,175/6,650 (78)	59/77 (77)	41/58 (71)	0/0 (0)	1,703/2,149 (79)
ICU admission	63/6,597 (1)	0/76 (0)	0/52 (0)	0/0 (0)	47/2,135 (2)
In-hospital mortality	870/6,650 (13)	8/77 (10)	6/58 (10)	0/0 (0)	369/2,149 (17)

*Underlying illness included any of: 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)

Total number of specimens tested for influenza, RSV and *B. pertussis* n=6 486, and SARS-CoV-2 n=6 416

Discussion

For the first time since the surveillance programmes were established, there was no influenza season observed during the South African winter period in 2020 and 2021. In all surveillance programmes influenza circulation, predominated by influenza A(H1N1)pdm09, was mostly limited to the Western Cape Province during the first few weeks of 2020 and was likely introduced by international travel. However, a sustained increase of A(H1N1)pdm09 in the late spring and early summer season was observed toward the end of 2021.

The absence of the influenza season in South Africa was similar to reports from other Southern Hemisphere countries.[13] COVID-19, the disease caused by SARS-CoV-2, with similar respiratory transmission to influenza, necessitated implementation of various levels of lockdown, physical and social distancing, promotion of good hand hygiene and compulsory wearing of masks. These measures likely contributed to the lack of transmission of influenza and other respiratory pathogens.[14] Compared to years prior to 2020 [15,16], the influenza cases in children remained the same throughout 2020 and 2021 in the ILI-PHC surveillance programme. However, the cases substantially increased in adults between 2020 and 2021. Due to low circulation of influenza in the country, it was not possible to assess influenza vaccine effectiveness for 2020 and 2021.

Similarly, there was no RSV season observed in 2020 and 2021, which usually precedes the influenza season in South Africa. This was also seen in other Southern Hemisphere countries.[17] Increased transmission of RSV was however noted from July to October in 2020 and March to May in 2021. The increase in RSV circulation from July 2020 could have been due to relaxation of COVID-19 restrictions and reopening of schools.[14]

There was very little *B. pertussis* detected (0.1% & 0.2% in 2020 and 2021, respectively) by the surveillance programmes compared to pre-pandemic years. The overall detection rate of pertussis decreased in comparison to the previous years (2018 and 2019: which identified 2.1% (98/4 630) and 0.8%, 33/4 383 cases respectively).[15,16] This is similar to what was observed in other countries such as England[18] and France.[19]

In 2020, the surveillance programmes were expanded to include surveillance for COVID-19. Although the pneumonia surveillance and ILI-PHC surveillance programmes in the public sector were sustained, the ILI-Viral Watch surveillance programme in the private sector was affected by the COVID-19 pandemic, with very few sites sending samples for testing compared to 2018 and 2019.[15,16] The lower number of submissions from this programme was likely due to a shift to tele-consultations by a number of general practitioners during 2020, or to doctors referring patients directly to laboratories instead of taking specimens themselves.

Using the surveillance programme data, the first period of increase in transmission of COVID-19 peaked in week 30 of 2020 and the second wave peaked in week 2 of 2021. The third period of increase in transmission peaked in week 28 of 2021 and the fourth period of increase in transmission peaked

in week 50 of 2021 which was similar to what was reported by the national surveillance of laboratory–confirmed cases of COVID-19[20] and DATCOV[21], these being national surveillance for COVID-19 hospitalisations. Compared to these, smaller numbers were reported through the syndromic surveillance programmes. The dominant variants detected in each period of increase in transmission corresponded to what was reported nationally by the Network for Genomic Surveillance in South Africa.[22] This is an indication that the pneumonia and systematic influenza-like illness programmes can be used to report on changes in transmission of respiratory pathogens, as well as to detect different variants of SARS-CoV-2, and should be considered a sustainable platform to monitor SARS-CoV-2.

Conclusion

In the first two years of the COVID-19 pandemic, these surveillance programmes managed to monitor four pathogens: influenza, RSV, *B. pertussis* and SARS-CoV-2. Changes in the transmission of respiratory pathogens and the detection of SARS-CoV-2 variants were reported through these surveillance programmes. It is envisioned that these programmes will be a sustainable platform to monitor increases in SARS-CoV-2 transmission and changes in epidemiology of other respiratory pathogens.

Recommendations

- The non-pharmaceutical interventions utilised during the COVID-19 pandemic (social distancing (staying home when ill), wearing of masks, hand washing/sanitising) can be utilised by persons experiencing respiratory symptoms, especially when mixing with individuals at risk of severed respiratory disease.
- Annual community awareness campaigns should be conducted by Department of Health and private sector partners including health insurance companies prior to the RSV (February - May) and influenza (May - August) seasons to highlight common symptoms, danger signs and when to seek clinical care, risk groups for severe disease, prevention strategies and to advocate for vaccination against influenza. Campaigns should include radio and poster campaigns as well as community health worker education sessions. Furthermore, clinics should be prepared in the RSV and influenza seasons for an increase in patients experiencing respiratory symptoms, assist patients with care and have basic medication ready to use. Additional information can be accessed in guidelines for influenza[23], COVID-19[24] and pertussis.[25]
- Syndromic respiratory surveillance should be sustained (and expanded, should resources be available), to allow ongoing systematic monitoring of trends disease, impact of interventions

and risk factors for severe illness for respiratory pathogens including SARS-CoV-2. Weekly and annual reports inform policy makers (such as Department of Health or WHO) of accurate trends in disease.

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