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Influenza surveillance in South Africa, weeks 1 to 52, 2024

Nicole Wolter[1,2], Amelia Buys[1], Sibongile Walaza[1,3], Jocelyn Moyes[1,3], Mvuyo Makhasi[1,3], Jackie Kleynhans[1], Jessica Yun[1], Mignon du Plessis[1,2], Fahima Moosa[1,2], Dikeledi Kekana[1], Anele Mnguni[1], Lorens Maake[1], Linda de Gouveia[1], Cheryl Cohen[1,3] and Anne von Gottberg[1,2]

[1] Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases (NICD), a division of the National Health Laboratory Service, Johannesburg, South Africa
[2] School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa
[3] School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Summary

This report summarises the findings from influenza surveillance in South Africa for weeks one through 52 of 2024. The report was compiled by the World Health Organization National Influenza Centre, based at the Centre for Respiratory Diseases and Meningitis within the National Institute for Communicable Diseases. Data were obtained from individuals meeting syndromic case definitions within three sentinel respiratory illness surveillance programmes: the Viral Watch influenza-like illness surveillance in outpatients at private general practitioners (n=1,540), the Influenza-like Illness (ILI) Surveillance Programme in outpatients at public health clinics (n=1,750) and the Pneumonia Surveillance Programme in hospitalised patients (n=4,400). Together, the three surveillance programmes contributed data from all nine provinces in South Africa. During 2024, influenza activity was observed from weeks one through 52, with an overall detection rate of 13% (997/7,690). An increased period of activity was observed in the normal winter influenza season. The influenza season started in week 17 (starting 22 April 2024), peaked in week 23 (starting on 3 June 2024), and ended in week 41 (starting 7 October 2024). The first peak of the season was dominated by influenza A(H1N1) pdm09, when influenza transmission and impact were at moderate and high levels in the ILI and Pneumonia Surveillance programmes, respectively. A second, smaller increase was observed, peaking in week 35 (starting 26 August 2024), that was dominated by B/Victoria. Although genetic characterisation showed that 2024 A(H1N1) pdm09 viruses belonged to clade 6B.1A.5a.2a (5a.2a), which differed from the clade of the 2024 Southern Hemisphere vaccine virus (5a.2a.1), antigenic characterisation using ferret antisera showed that the clade 5a.2a viruses were well inhibited by clade 5a.2a.1 (vaccine type) antisera. Ninety-six per cent (25/26) of A(H1N1) pdm09, 100% (2/2) of A(H3N2) and 100% (10/10) of B/Victoria viruses tested were phenotypically susceptible to zanamivir, oseltamivir, peramivir, and laninamivir. Mutational analysis of 398 sequenced viruses revealed one A(H1N1) pdm09 virus with a mutation known to be associated with antiviral resistance. Vaccine coverage in the Viral Watch surveillance programme was low (5.6%, 34/610). After adjusting for age and timing within the season, the vaccine effectiveness (VE) for any influenza in individuals of all ages was 72.7% (95% confidence interval (CI) 31.6%-89.2%). For A(H1N1) pdm09, the adjusted VE was 61.2% (95% CI -11.6%-86.6%), and for B/Victoria, the adjusted VE was 82.6% (95% CI:-31.6-97.7%). Due to the continuous evolution of influenza viruses, the World Health Organization uses these (and other) data sources to continuously monitor the epidemiology of influenza viruses circulating throughout the world and provides recommendations about strains to be included in the vaccine for the upcoming influenza season.

Introduction

South Africa is a Southern Hemisphere country with a temperate climate where influenza epidemics usually occur between April and October, with a peak during the winter months.[1,2] The following viruses were recommended for the trivalent and quadrivalent inactivated influenza vaccines (IIV) 2024 Southern Hemisphere influenza season: Egg-based tri/quadrivalent vaccines, including:

- An A/Victoria/4897/2022 (H1N1)pdm09-like virus (clade 6B.1A.5a.2a.1);
- An A/Thailand/8/2022 (H3N2)-like virus (clade 3C.2a1b.2a.2a.3a.1);
- A B/Austria/1359417/2021 (B/Victoria lineage)-like virus (clade V1A.3a.2); and
- A B/Phuket/3073/2013 (B/Yamagata lineage)-like virus (quadrivalent vaccine only).

These recommendations included a change to the A(H1N1)pdm09 and A(H3N2) components of egg-based and cell culture-based vaccine strains compared with the 2023 Southern Hemisphere trivalent and quadrivalent IIV. For the A(H1N1)pdm09 vaccine virus component, the A/Sydney/5/2021 (H1N1)pdm09-like virus was replaced with an A/Victoria/4897/2022 (H1N1)pdm09-like virus (egg-based IIV) and an A/Wisconsin/67/2022 (H1N1)pdm09-like virus (cell culture-based IIV). For the A(H3N2) component, A/Darwin/9/2021 (H3N2)-like virus was replaced with an A/Thailand/8/2022 (H3N2)-like virus (egg-based IIV) and an A/Massachusetts/18/2022 (H3N2)-like virus (cell culture-based IIV). In addition, the WHO advised that inclusion of the B/Yamagata lineage antigen in quadrivalent influenza vaccines is no longer warranted. In South Africa, the trivalent IIV was available in the private and public sectors (at designated clinics and hospitals), and the quadrivalent IIV was available in the private sector, generally from March or April.

South Africa has three influenza sentinel surveillance programmes that are co-ordinated by the Centre for Respiratory Diseases and Meningitis (CRDM) at the National Institute for Communicable Diseases (NICD), which houses the National Influenza Centre (NIC). These programmes include (i) Viral Watch influenza-like illness (VW) surveillance in outpatients at private general practitioners, (ii) systematic influenza-like illness (ILI) surveillance in outpatients at public health clinics, and (iii) national pneumonia surveillance in public health hospitals. Data from these surveillance programmes are shared weekly with the WHO Global Influenza Surveillance and Response System (GISRS), and reports are shared biannually in February and September in preparation for the influenza vaccine composition meetings.

Methods

For each of the sentinel surveillance programmes, individuals of all ages meeting the case definitions are approached for consent and enrolled in the programme. Details of the sites and case definitions for the respective surveillance programmes are summarised in Table 1.

Table 1. Description of influenza and respiratory surveillance programmes in South Africa, 2024.

Programme	Viral Watch	Influenza-like Illness (ILI)	Pneumonia Surveillance
Start year	1984	2012	2009
Provinces*	EC, FS, GP, LP, MP, NC, NW, WC	KZN, NW, WC, MP	EC, GP, KZN, MP, NW, WC**
Number of sites	98	5	13**
Type of site	General practitioners	Public primary health care clinics	Public hospitals
Case definition	An acute respiratory illness with a temperature (≥38°C) and cough, & onset ≤10 days.	• An acute respiratory illness with a temperature (≥38°C) and cough, & onset ≤10 days. • Suspected pertussis: Any person with an acute cough illness lasting ≥14 days (or cough illness of any duration for children <1 year), without a more likely diagnosis, AND one or more of the following signs or symptoms: paroxysms of coughing, inspiratory "whoop", post-tussive vomiting, or apnoea in children <1 year; OR any person in whom a clinician suspects pertussis.	• Patients aged 2 days to <3 months: Diagnosis of sepsis or suspected sepsis, or physician diagnosed LRTI AND symptoms of any duration. • Patients aged 3 months to <5 years: Physician diagnosed LRTI, symptoms of any duration. • Patients aged ≥5 years with fever (≥38) or history of fever AND cough AND symptoms of any duration. • Suspected pertussis: Any person with an acute cough illness lasting ≥14 days (or cough illness of any duration for children <1 year), without a more likely diagnosis, AND one or more of the following signs or symptoms: paroxysms of coughing, inspiratory "whoop", post-tussive vomiting, or apnoea in children <1 year; OR any person in whom a clinician suspects pertussis.
Specimens collected	Throat swabs and/or nasal/nasopharyngeal swabs	Mid-turbinate nasal swabs	Mid-turbinate nasal swabs

*EC: Eastern Cape; FS: Free State; GP: Gauteng Province; KZN: KwaZulu-Natal; LP: Limpopo Province; MP: Mpumalanga; NC: Northern Cape; NW: North West; WC: Western Cape.

**Enrolment ended on the 15th of March 2024 for the following sites: Tambo Memorial Hospital (GP), Tembisa Hospital (GP), and Tygerberg Hospital (WC); and on 31 May 2024 for Livingstone Hospital (EC).

Demographic and clinical information was collected through patient interview and medical record review. Respiratory specimens (combined oropharyngeal and nasopharyngeal/nasal swabs) were collected and tested by reverse transcription real-time PCR (rRT-PCR) using the Allplex™ SARS-CoV-2/influenza/RSV commercial kit (Seegene, Seoul, Korea), and influenza-positive specimens were subtyped using the US Centers for Disease Control and Prevention (CDC) subtyping method with reagents from the CDC International Reagent Resource (IRR).

Influenza transmission thresholds were calculated using the Moving Epidemic Method (MEM), a sequential analysis using the R language (http://CRAN.R-project.org/web/package=mem) designed to calculate the duration, start, and end of the annual influenza epidemic[3,4]. The MEM uses the 40th, 90th, and 97.5th percentiles established from available years of historical data to calculate thresholds of activity. Thresholds of activity for influenza are defined as follows: below threshold, low activity, moderate activity, high activity, and very high activity. Thresholds from the ILI Surveillance Programme at primary healthcare clinics (outpatients) are used as an indicator of disease transmission in the community, and thresholds from the Pneumonia Surveillance Programme (inpatients) are used as an indicator of morbidity and mortality and the impact of disease on healthcare provision.

The effectiveness of the trivalent/quadrivalent seasonal influenza vaccine to prevent influenza-associated medically attended acute respiratory illness was assessed using a test-negative, case-control study design. Patients meeting the case definition for influenza-like illness presenting to a private general practitioner were enrolled in the outpatient VW surveillance programme during the 2024 influenza season. Vaccine effectiveness (VE) estimates were adjusted for timing within the season and age.

Influenza rRT-PCR positive specimens with a Ct-value <30 were cultured Madin-Darby Canine Kidney (MDCK) cells. Influenza virus isolates were phenotypically subtyped using the haemagglutination inhibition (HAI) assay, with turkey red blood cells used as the indicator system. HAI assays were performed using reference reagents from the CDC IRR 2023-2024 WHO influenza reagent kit (including goat antisera). Influenza viruses circulating in 2024 in South Africa were genetically characterised by whole genome sequencing (WGS) using the Illumina platform and shared on the Global Initiative on Sharing All Influenza Data (GISAID). Sequences of viruses circulating in South Africa in 2024 (n=398) were obtained from GISAID on 22 January 2025. Phylogenetic analysis of the haemagglutinin (HA) genes was performed using MAFFT for alignment and IQ-TREE v 1.6.12 software for the construction of the tree. Groups and subgroups were identified by specific amino acid mutations relative to a designated reference strain on NextClade. Genotypic analysis for resistance mutation detection was conducted using CLC Genomics Workbench with the following reference sequences: A/California/07/2009 (CY121680) for A(H1N1)pdm09, A/Wisconsin/67/2005 (CY163680) for A(H3N2), and B/Brisbane/60/2008 (KX058884) for B/Victoria. The phenotypic effect of detected substitutions was predicted using Flusurver (https://flusurver.bii.a-star.edu.sg/).

Influenza virus cultures and original specimens were shared with the WHO Global Influenza Surveillance and Response System (GISRS) Collaborating Centres (WHO-CC) in Australia, the United Kingdom, and the United States of America for further antigenic and genetic characterisation. Antigenic characterisation by HAI testing using ferret antisera was conducted on South African viruses at WHO-CCs. Phenotypic susceptibility testing to zanamivir, oseltamivir, peramivir, and laninamivir was performed for South African samples at the WHO-CC in Australia (VIDRL).

Results

From 1 January (week 1) through 29 December 2024 (week 52), 7,690 individuals were enrolled with respiratory specimens collected and tested through the three surveillance programmes (Table 2). Influenza infections were identified in 997 individuals, resulting in an overall infection detection rate of 13.0% (997/7,690). Influenza detections occurred from week 1 through week 52. For influenza single infections where a subtype/lineage could be determined (96.8%, 965/997), infections were dominated by influenza A(H1N1)pdm09 (60.8%, 587/965), followed by B/Victoria (34.6%, 334/965). A(H3N2) accounted for only 4.6% (44/965) of single infections. Influenza B/Yamagata was not detected. Dual infections were detected in two individuals, with A(H1N1)pdm09 and B (lineage inconclusive) detected in one individual, and A(H1N1)pdm09 and B/Victoria detected in the other individual. Inconclusive results for subtyping occurred for 3.0% (30/997) of specimens. The latter samples had a primary identification reverse transcription real-time polymerase chain reaction (rRT-PCR) cycle threshold (Ct) value greater than 35 and therefore had insufficient viral load to determine the subtype/lineage.

The influenza season started in week 17 (week starting 22 April 2024) when the influenza detection rate (3-week moving average) breached the seasonal threshold among patients in the Pneumonia Surveillance Programme as determined by the MEM, and peaked in week 23 (starting on 3 June 2024) when the influenza transmission and impact were at moderate and high levels, respectively. A second increase in the detection rate was observed, peaking in week 35 (starting 26 August 2024), and was predominated by B/Victoria. The influenza season ended in week 41 (starting 7 October 2024).

Table 2. Number of influenza infections identified in all syndromic influenza surveillance programmes, South Africa, 1 January–29 December 2024.

Programme	Number of specimens tested	Number influenza positive (% of all specimens tested)	Influenza A				Influenza B			Dual infection#
			Total A	Subtype in-conclusive*	A(H1N1) pdm09	A(H3N2)	Total B	Lineage in-conclusive*	B/ Victoria	
			n (% of total influenza positives)							
Viral Watch	1 540	415 (27)	298 (72)	3 (1)	285 (69)	10 (2)	117 (28)	7 (2)	110 (27)	**0 (0)**
Influenza-like Illness Surveillance	1 750	285 (16)	152 (53)	2 (1)	127 (45)	23 (8)	133 (47)	7 (2)	126 (44)	**0 (0)**
Pneumonia Surveillance **	4 400	297 (7)	190 (64)	4 (1)	175 (59)	11 (4)	105 (35)	7 (2)	98 (33)	**2 (0)**
Total	**7 690**	**997 (13)**	**640 (64)**	**9 (1)**	**587 (59)**	**44 (4)**	**355 (36)**	**21 (2)**	**334 (34)**	**2 (0)**

*Inconclusive: insufficient viral load in the sample and unable to characterise further;

#Dual infections: A(H1N1)pdm09 and B (lineage inconclusive); and A(H1N1)pdm09 and B/Victoria **Enrolment ended on the 15th of March 2024 for the following sites: Tambo Memorial Hospital, Tembisa Hospital, and Tygerberg Hospital. Khayelitsha Hospital stopped enrolments on 30 April 2024, and Livingstone Hospital on 31 May 2024.

Viral Watch Surveillance Programme

Specimens from 1540 patients were received and tested from VW practitioners located in five of the nine provinces (Table 3), with the majority of specimens received from the Gauteng (69.2%, 1,066/1,540) and Western Cape (28.4%, 438/1,540) provinces. Influenza was detected in 415 (26.9%) patients. Among specimens that could be subtyped, 70.4% (285/405) were A(H1N1)pdm09 (Figure 1, Table 3). The highest 3-week moving average detection rate in the VW programme occurred in week 20 (55.9%) (Figure 1).

Table 3. Number of influenza infections by subtype/lineage and total number of specimens tested by province in the Viral Watch Surveillance Programme, South Africa, 1 January–29 December 2024.

Province	A(H1N1) pdm09	A (H3N2)	A subtype inconclusive*	B /Victoria	B lineage inconclusive*	Dual infection#	Total cases	Total specimens tested	Detection rate (%)
Eastern Cape	8	1	0	1	0	0	10	22	**45**
Free State	0	0	0	0	0	0	0	0	**0**
Gauteng	155	4	3	58	3	0	223	1066	**21**
Limpopo	0	0	0	0	0	0	0	0	**0**
Mpumalanga	6	0	0	0	0	0	6	12	**50**
North West	0	0	0	0	0	0	0	0	**0**
Northern Cape	0	0	0	0	0	0	0	2	**0**
Western Cape	116	5	0	51	4	0	176	438	**40**
Total	**285**	**10**	**3**	**110**	**7**	**0**	**415**	**1540**	**27**

*Inconclusive: insufficient viral load in the sample and unable to characterise further.

#No dual infections were detected.

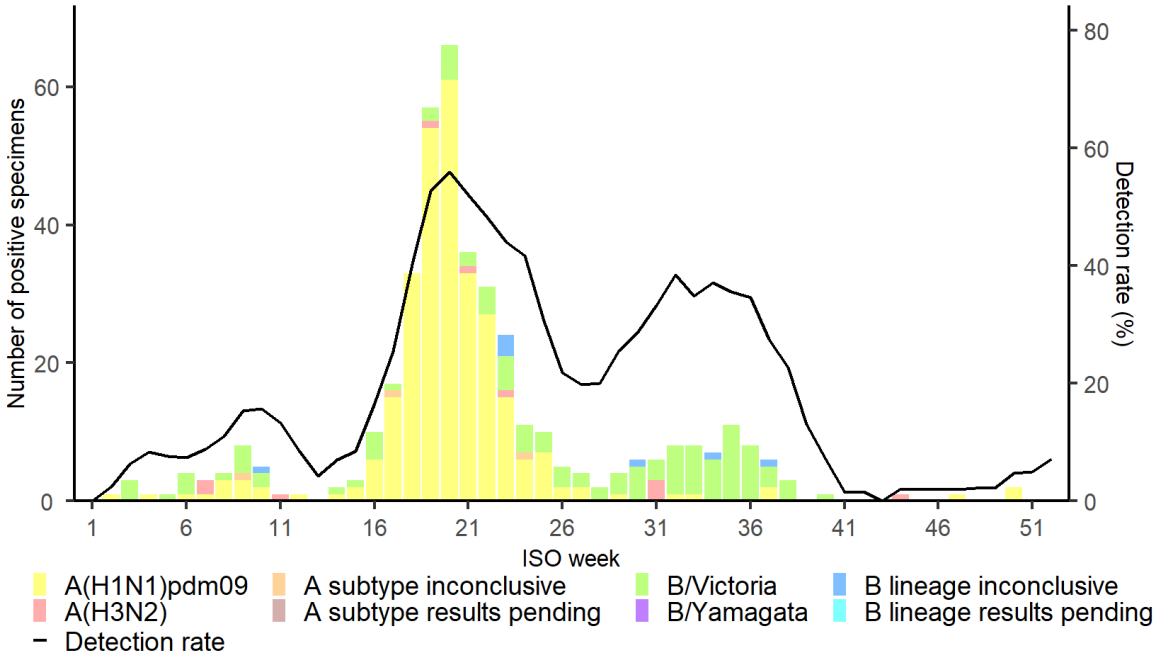

Figure 1. Number of influenza infections by influenza subtype/lineage and 3-week moving average detection rate by epidemiologic week—Viral Watch Surveillance Programme for influenza-like illness, South Africa, 1 January–29 December 2024.

Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics

Specimens from 1,750 patients with ILI were received from five primary health care clinics located in four provinces. In total, 285 (16.3%) individuals tested positive for influenza. Of influenza infections that could be subtyped, influenza A(H1N1)pdm09 accounted for 46.0% (127/276), and influenza B/Victoria accounted for 45.7% (126/276) of cases (Table 4, Figure 2). The 3-week moving average detection rate peaked in week 23 (50.6%).

Using the MEM for the ILI Surveillance Programme data, with a baseline determined from years pre- and post-COVID-19 pandemic (2016-2019 and 2022-2023), the estimated level of influenza disease transmission in the community was moderate, bordering on high-level activity (Figure 3).

Table 4. Number of influenza cases by subtype/lineage and total number of specimens collected by province for the Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 1 January–29 December 2024.

Province	A(H1N1) pdm09	A (H3N2)	A subtype inconclusive*	B /Victoria	B lineage inconclusive*	Dual infection#	Total cases	Total specimens tested	Detection rate (%)
Eastern Cape	8	1	0	1	0	0	10	22	**45**
Free State	0	0	0	0	0	0	0	0	**0**
Gauteng	155	4	3	58	3	0	223	1066	**21**
Limpopo	0	0	0	0	0	0	0	0	**0**
Mpumalanga	6	0	0	0	0	0	6	12	**50**
North West	0	0	0	0	0	0	0	0	**0**
Northern Cape	0	0	0	0	0	0	0	2	**0**
Western Cape	116	5	0	51	4	0	176	438	**40**
Total	**285**	**10**	**3**	**110**	**7**	**0**	**415**	**1540**	**27**

Surveillance sites included primary health care clinics in four provinces: KwaZulu-Natal (Edendale Clinic), Mpumalanga (Agincourt Clinic), North West (Jouberton Clinic), and Western Cape (Eastridge Clinic and Mitchell's Plain Clinic).

*Inconclusive: insufficient viral load in the sample and unable to characterise further (primary test PCR C_t value >35).

#No dual infections were detected.

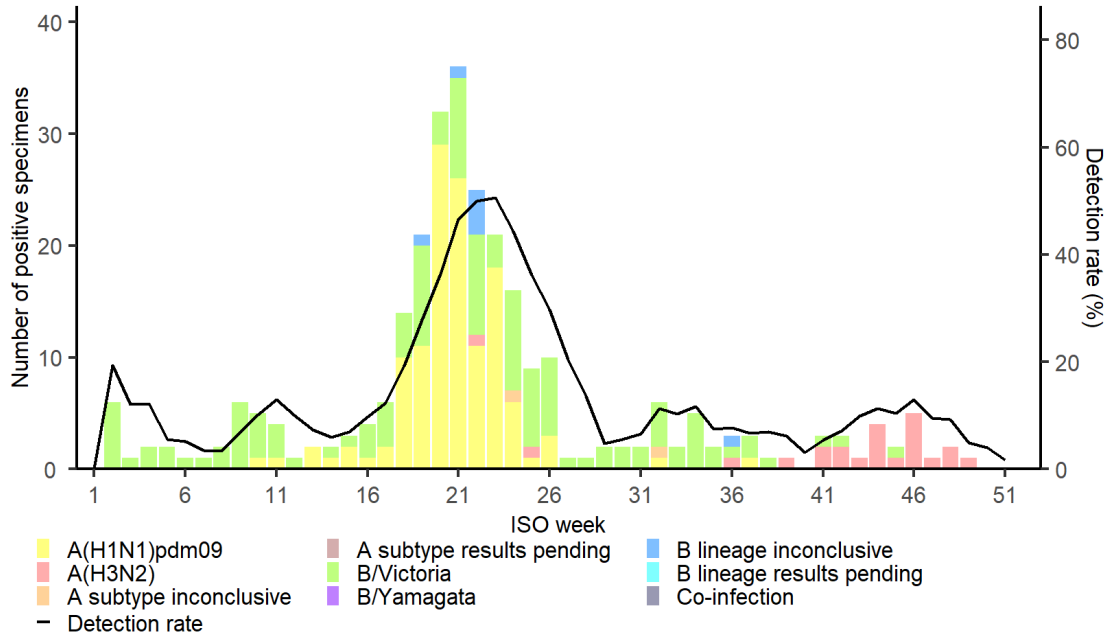

Figure 2. Number of influenza cases by subtype/lineage and 3-week moving average detection rate by epidemiologic week—Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 1 January–29 December 2024.

***Inconclusive: insufficient viral load in the sample and unable to characterise further. No dual infections were detected.

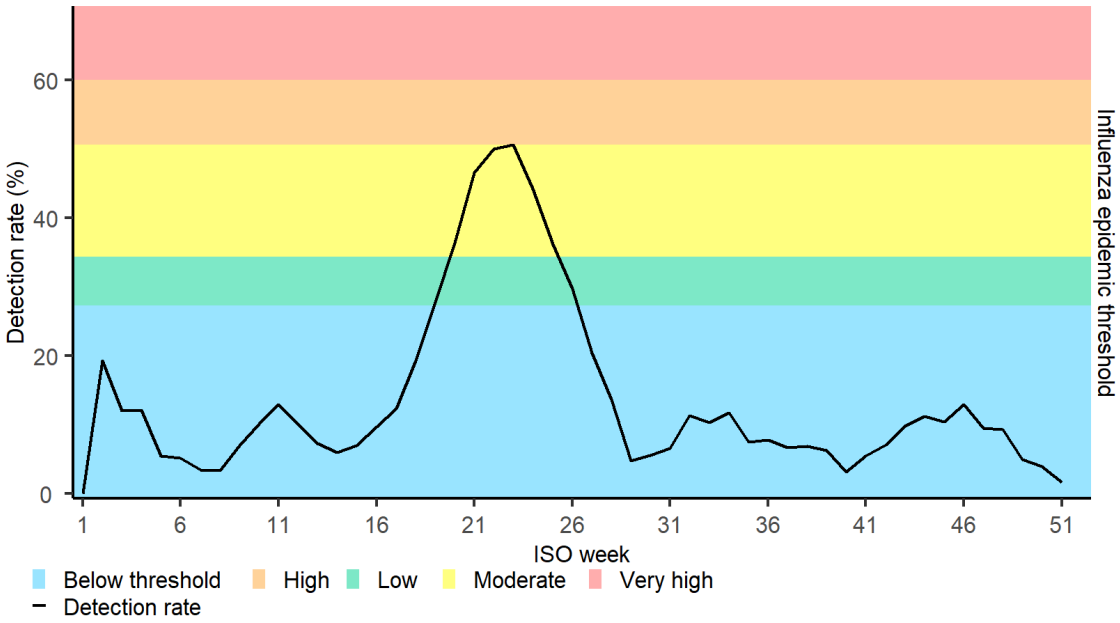

Figure 3. Influenza detection rate and epidemic thresholds*, Influenza-like Illness (ILI) Surveillance Programme at primary healthcare clinics, South Africa, 1 January–29 December 2024.

*Influenza transmission thresholds based on 2016–2019 and 2022–2023 data and calculated using the Moving Epidemic Method (MEM).

Pneumonia Surveillance Programme

Specimens from 4,400 patients hospitalised with severe respiratory illness were received from thirteen sentinel hospitals located in six provinces, and 297 (6.8%) influenza cases were detected. Of these, two individuals had a dual infection identified: A(H1N1)pdm09 and B (lineage inconclusive) (n=1); and A(H1N1)pdm09 and B/Victoria (n=1). Among single-infection influenza-positive specimens that could be further characterised, 61.6% (175/284) were influenza A(H1N1)pdm09 and 34.5% (98/284) were influenza B/Victoria (Table 5).

The 3-week moving average detection rate peaked in week 23 (starting 3 June 2024) (25.8%) (Figure 4). Data obtained through the Pneumonia Surveillance Programme among hospitalised patients pre- and post-COVID-19 pandemic (2016–2019 and 2022–2023) were used to set the MEM thresholds for the impact of influenza on healthcare provision. The impact of influenza in the 2024 season reached a high level (Figure 5).

Table 5. Number of influenza infections by subtype/lineage and total number of specimens collected by province for the Pneumonia Surveillance Programme, South Africa, 1 January–29 December 2024.

Province	A(H1N1) pdm09	A(H3N2)	A subtype inconclusive*	B/ Victoria	B lineage inconclusive*	Dual infection#	Total cases	Total specimens tested	Detection rate %
Eastern Cape	1	0	0	0	0	0	1	41	**2**
Gauteng	68	4	1	24	4	0	101	1198	**8**
KwaZulu-Natal	20	0	0	6	0	0	26	504	**5**
Mpumalanga	20	5	1	17	0	1	44	578	**8**
North West	38	0	1	23	1	0	63	527	**12**
Western Cape	28	2	1	28	2	1	62	1552	**4**
Total	**175**	**11**	**4**	**98**	**7**	**2**	**297**	**4400**	**7**

*Inconclusive: insufficient viral load in the sample and unable to characterise further. #Dual infections: A(H1N1)pdm09 and B (lineage inconclusive) (n=1); and A(H1N1)pdm09 and B/Victoria (n=1).

Surveillance sites included hospitals in six provinces: Gauteng (Helen Joseph Hospital, Rahima Moosa Hospital, Tembisa Hospital, Tambo Memorial Hospital), KwaZulu-Natal (Harry Gwala Memorial Hospital), Mpumalanga (Mapulaneng, Matikwana, and Tintswalo Hospitals), North West (Klerksdorp-Tshepong Hospital Complex), Eastern Cape (Livingstone Hospital), and Western Cape (Red Cross Children's Hospital, Tygerberg Hospital, and Mitchell's Plain Hospital). Enrolment ended on the 15th of March 2024 for the following sites: Tambo Memorial Hospital (GP), Tembisa Hospital (GP), and Tygerberg Hospital (WC). Khayelitsha Hospital (WC) stopped enrolments on 30 April 2024, and Livingstone Hospital (EC) on 31 May 2024.

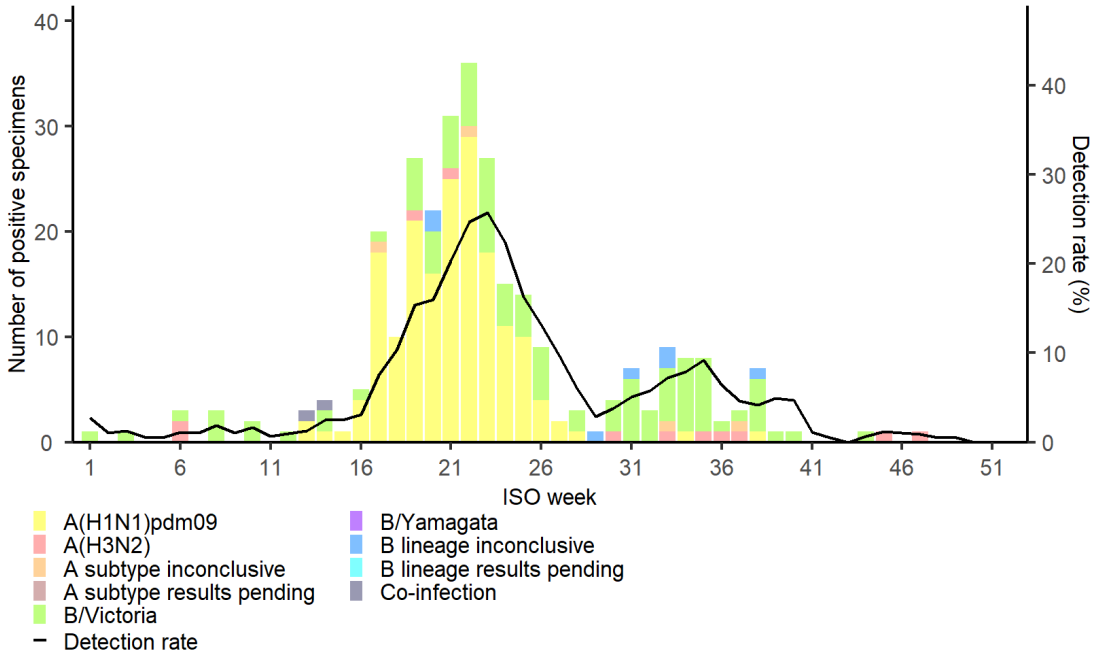

Figure 4. Number of influenza cases by subtype/lineage and 3-week moving average detection rate by epidemiologic week—Pneumonia Surveillance Programme, South Africa, 1 January–29 December 2024.

*****Inconclusive: insufficient viral load in the sample and unable to characterise further. Dual infections: A(H1N1)pdm09 and B (lineage inconclusive) (n=1); and A(H1N1)pdm09 and B/Victoria (n=1).

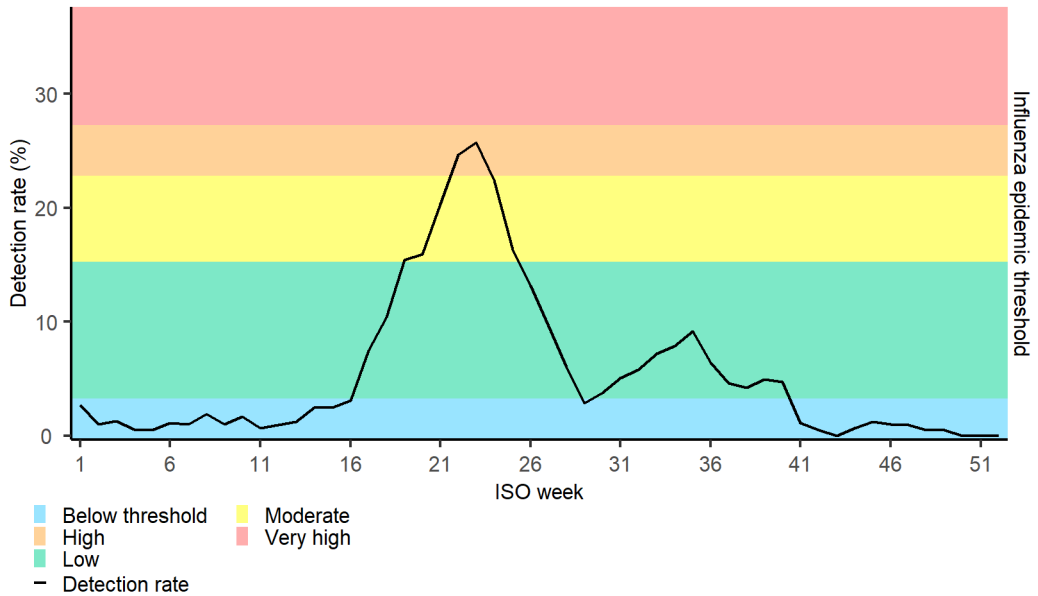

Figure 5. Influenza detection rate and epidemic thresholds*, Pneumonia Surveillance Programme, South Africa, 1 January–29 December 2024.

*Influenza morbidity and mortality thresholds based on 2016–2019 and 2022–2023 data and calculated using the Moving Epidemic Method (MEM).

Vaccine effectiveness

Of the 610 surveillance cases enrolled in the VW programme during the 2024 influenza season and included in the vaccine effectiveness (VE) analysis (individuals aged ≥6 months with known vaccination and influenza status), 283 (46.4%) were classified as cases (influenza test positive) and 327 (53.6%) as controls (influenza test negative). Vaccine coverage in the VW Programme was 5.6% (34/610) overall (Table 6): 2.1% (6/283) and 8.6% (28/327) among cases and controls, respectively. The adjusted VE, accounting for timing within the season and age, was 72.7% (95% confidence interval [CI]: 31.6% to 89.2%) for any influenza. For influenza A(H1N1)pdm09, the adjusted VE was 61.2% (95% CI: -11.6% to 86.6%), and for influenza B/Victoria, the adjusted VE was 82.6% (95% CI: -31.6% to 97.7%) (Table 6).

Table 6. Vaccine coverage and vaccine effectiveness (VE) by subtype and age group, Viral Watch Surveillance Programme, South Africa, 22 April–13 October 2024.

	Vaccine coverage			Adjusted VE % (95% confidence interval)*
	Cases n/N (%)	Controls n/N (%)	Total n/N (%)	
All specimens				
Any influenza	6/283 (2.1)	28/327 (8.6)	34/610 (5.6)	72.7 (31.6; 89.2)
A(H1N1)pdm09	5/202 (2.5)	28/327 (8.6)	33/529 (6.2)	61.2 (-11.6; 86.6)
B(Victoria)	1/71 (1.4)	28/327 (8.6)	29/398 (7.3)	82.6 (-31.6; 97.7)
Children aged <18 years				
Any influenza	0/81 (0.0)	4/82 (4.9)	4/163 (2.5)	81.2 (-283.7; 99.1)
A(H1N1)pdm09	0/52 (0.0)	4/82 (4.9)	4/134 (3.0)	38.1 (-1323.8; 97.3)
B(Victoria)	0/25 (0.0)	4/82 (4.9)	4/107 (3.7)	71.1 (-504.3; 98.6)
Adults aged 18–64 years				
Any influenza	6/186 (3.2)	22/221(10.0)	28/407 (6.9)	67.9 (17.5; 87.5)
A(H1N1)pdm09	5/135 (3.7)	22/221 (10.0)	27/356 (7.6)	58.1 (-22.6; 85.7)
B(Victoria)	1/45 (2.2)	22/221 (10.0)	23/266 (8.6)	78.8 (-63.3; 97.2)
Adults aged ≥65 years				
Any influenza	0/16 (0.0)	2/24 (8.3)	2/40 (5.0)	21.9 (-3818.0; 96.2)
A(H1N1)pdm09	0/15 (0.0)	2/24 (8.3)	2/39 (5.1)	-142.7 (-14554.7; 96.0)
B(Victoria)	0/1 (0.0)	2/24 (8.3)	2/25 (8.0)	-21.9 (-3818.0; 96.2)

*Adjusted for timing within season (early, mid, late) and age.

Influenza virus isolation

Influenza virus isolation was attempted on clinical specimens testing positive for influenza on rRT-PCR with a high viral load (C_t value ≤30). The overall isolation rate was 72.8% (147/202); 70.0% (77/110) for A(H1N1)pdm09, 60.0% (9/15) for A(H3N2), and 79.2% (61/77) for B/Victoria.

Influenza specimens shared with WHO Collaborating Centres

Influenza virus cultures and original specimens from 129 individuals were shared with the WHO Global Influenza Surveillance and Response System (GISRS) Collaborating Centres (WHO-CC) for antigenic and genetic characterisation. Among specimens shared, 50.4% (65/129) were A(H1N1)pdm09, 45.0% (58/129) were B/Victoria, and 4.7% (6/129) were A(H3N2).

Antigenic characterisation of influenza virus isolates

The HAI assays performed at the NIC in South Africa and results for subtype/lineage confirmation are summarised in Table 7. HAIs were performed for all isolates with haemagglutination (HA) titers (N=137). Subtype/lineage was confirmed phenotypically for 137 viruses, including 67 A(H1N1)pdm09, 9 A(H3N2), and 61 B/Victoria cultures. 1.5% (1/67) of A(H1N1)pdm09 viruses recognised A/Victoria/2570/2019 (clade 6B.1A.5a.2) antisera poorly, and 1.6% (1/58) of B/Victoria viruses recognised B/Michigan/01/2021 (clade V1A.3a.2) antisera poorly.

Table 7. Summary of haemagglutination inhibition (HAI) assay results, South Africa, 1 January–29 December 2024.

Programme	Number of cultures with HA titres	A(H1N1)pdm09	A(H3N2)	B/Victoria
		A/Victoria/2570/2019 (Clade 5a.2)	A/Delaware/01/2021 (Clade 2a.2a)	B/Michigan/01/2021 (Clade V1A.3a.2)
		Low reactors/ Total tested (%)	Low reactors/ Total tested (%)	Low reactors/ Total tested (%)
Viral Watch	36	0/19 (0)	0/5 (0)	0/12 (0)
Influenza-like illness	65	1/29 (3)	0/2 (0)	0/34 (0)
Pneumonia Surveillance	36	0/19 (0)	0/2 (0)	1/15 (7)
Total n/N (% per virus)	**137**	**1/67 (1)**	**0/9 (0)**	**1/61 (2)**

HAI testing using ferret antisera was conducted on South African viruses at WHO-CCs. Antigenic characterisation results from samples shared with the WHO-CC in Australia (VIDRL) showed that all tested (25/25) A(H1N1)pdm09 viruses were A/Victoria/4897/2022-like (clade 5a.2a.1), and all (10/10) B/Victoria viruses were B/Austria/1359417/2021-like (clade 3a.2). Among samples tested at the WHO-CC in the USA (US CDC), all (7/7) A(H1N1)pdm09 viruses were antigenically A/Wisconsin/67/2022-like (clade 5a.2a.1), and all (11/11) B/Victoria viruses were antigenically B/Austria/1359417/2021-like (clade 3a.2).

Neuraminidase inhibitor susceptibility

Phenotypic susceptibility testing showed that 96% (25/26) of A(H1N1)pdm09, 100% (2/2) of A(H3N2), and 100% (10/10) of B/Victoria viruses showed normal inhibition with all antivirals tested. One (3.8%, 1/26) A(H1N1)pdm09 virus showed highly reduced inhibition to oseltamivir and peramivir. The mutational analysis of the neuraminidase (NA) genes of sequenced 2024 South African viruses (A(H1N1)pdm09 n=221, A(H3N2) n=12, and B/Victoria n=165) revealed one virus with a mutation (H275Y) known to be associated with antiviral resistance (A/South Africa/R04202/2024).

Genetic characterisation of influenza viruses

Influenza viruses collected through respiratory illness surveillance programmes were sequenced by the NICD [A(H1N1)pdm09 n=163, A(H3N2) n=7, B/Victoria n=113], and by WHO-CCs in Australia, the United Kingdom, and the USA [A(H1N1)pdm09 n=58, A(H3N2) n=5, B/Victoria n=52].

Influenza A(H1N1)pdm09

Genetic analysis of the HA gene of South African influenza A(H1N1)pdm09 viruses indicated that almost all viruses collected in 2024 clustered within clade 6B.1A.5a.2a (5a.2a) (219/221, 99.1%), which circulated at low levels during the 2023 influenza season, while only two viruses belonged to clade 6B.1A.5a.2a.1 (5a.2a.1) (2/221, 0.9%), which dominated the 2022 A(H1N1)pdm09 influenza season (Figure 6). The 2024 clade 5a.2a viruses consisted of two main subclades: C.1.9 (characterised by the K169Q substitution with later viruses gaining the V321I substitution) (206/219, 94.1%) and C.1.8 (characterised by the V47I and I96T substitutions) (11/219, 5.0%). The 2024 Southern Hemisphere A(H1N1)pdm09 vaccine strain (A/Victoria/4897/2022) is a clade 5a.2a.1 virus, which differed from the clade of the majority of South African viruses in 2024 (Figure 6).

Influenza A(H3N2)

Twelve influenza A(H3N2) viruses circulating in South Africa in 2024 were sequenced, and all (12/12, 100%) belonged to clade 3C.2a1b.2a.3a.1 (2a.3a.1), and clustered together with the 2024 Southern Hemisphere vaccine strain (A/Thailand/8/2022) (Figure 7). The 2024 viruses were similar to A(H3N2) viruses that dominated the 2023 influenza season, with additional substitutions classified within two subclades: J.2 (11/12, 91.7%) with N122D and K276E substitutions and J.1 (1/12, 8.3%) with an I25V substitution.

Influenza B/Victoria

The majority (163/165, 98.8%) of influenza B/Victoria viruses circulating in South Africa in 2024 that were sequenced belonged to clade V1A.3a.2, similar to the B/Victoria viruses circulating in recent years (Figure 8). The 2024 viruses accumulated additional substitutions (E183K and D197E). The V1A.3a.2 clade consisted of three subclades: C.5 (7/163, 4.3%), C.5.6 (D129N substitution) (93/163, 57.1%), and C.5.7 (E128G substitution) (63/163, 38.7%). The 2024 Southern Hemisphere vaccine strain (B/Austria/1359417/2021) clustered within the same clade. The remainder of the 2024 B/Victoria viruses belonged to the V1A.3 clade (2/165, 1.2%).

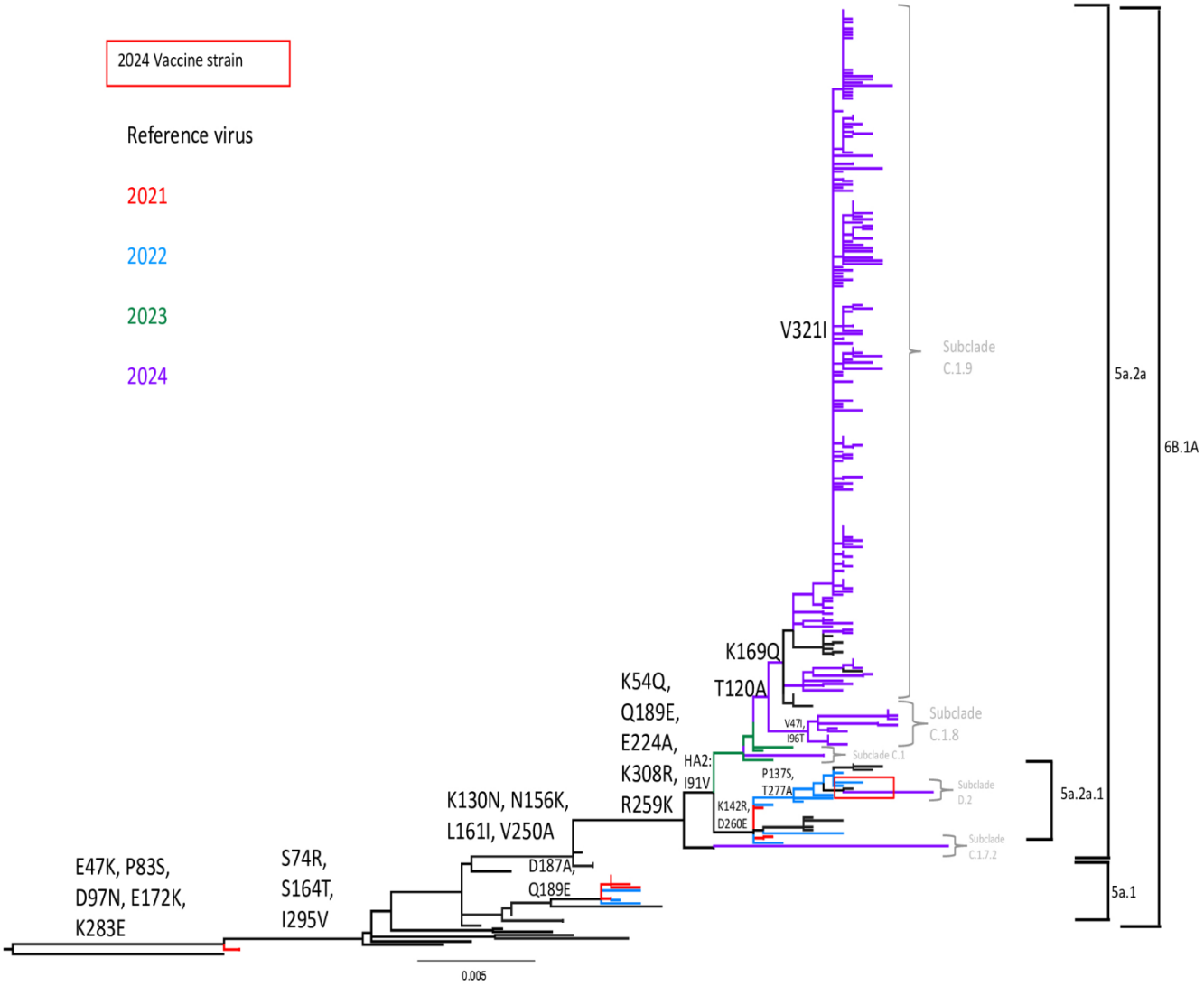

Figure 6. Maximum likelihood phylogenetic tree (best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H1N1)pdm09 viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box (A/Victoria/4897/2022), South African 2024 viruses in purple (n=221), 2023 viruses in green, 2022 viruses in blue, 2021 viruses in red, and reference strains in black. A/California/07/2009 was used as the root.

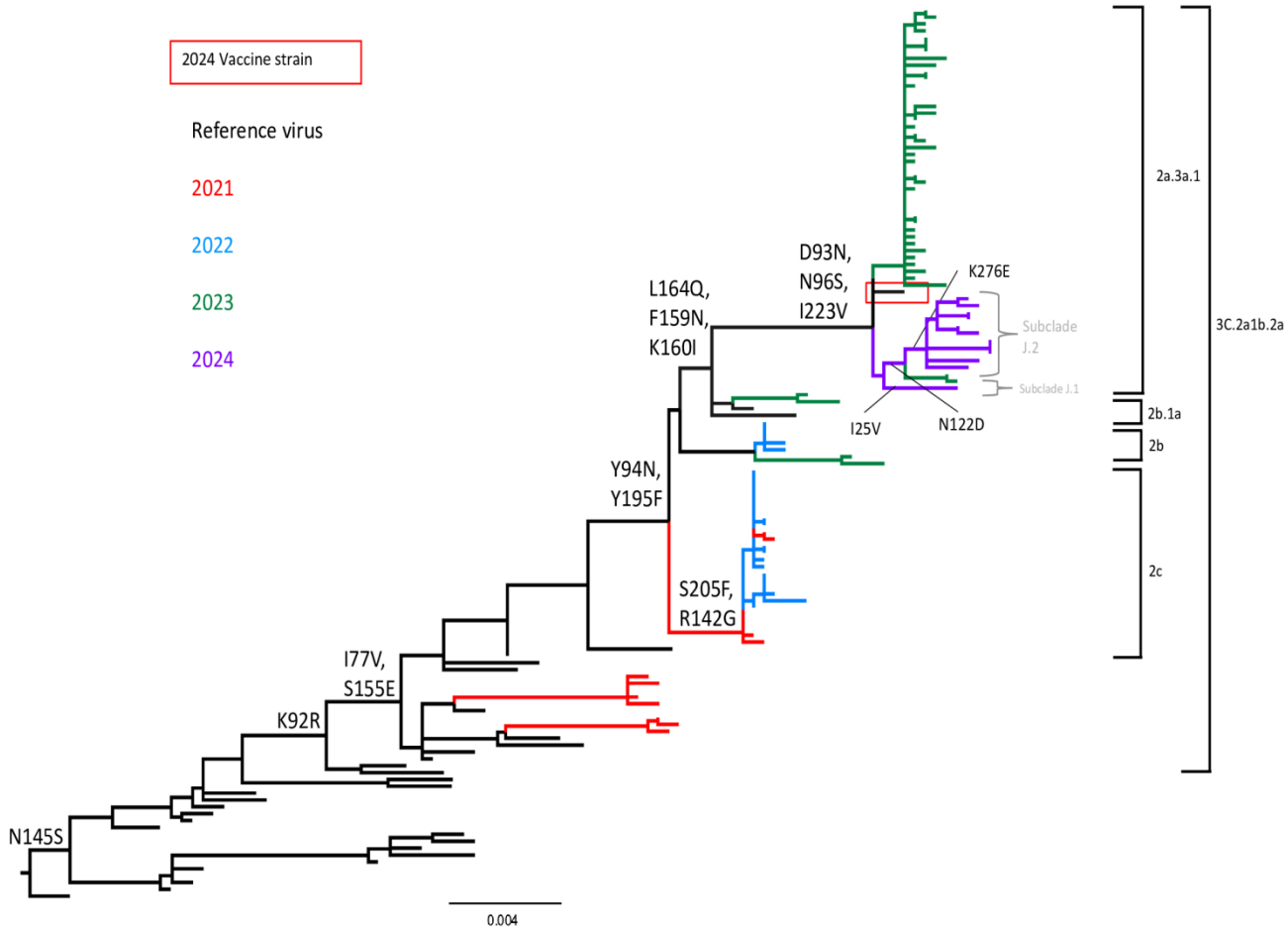

Figure 7. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H3N2) viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box, South African 2024 viruses in purple (n=12), 2023 viruses in green, 2022 viruses in blue, 2021 viruses in red, and reference strains in black. A/Wisconsin/67/2005 was used as the root.

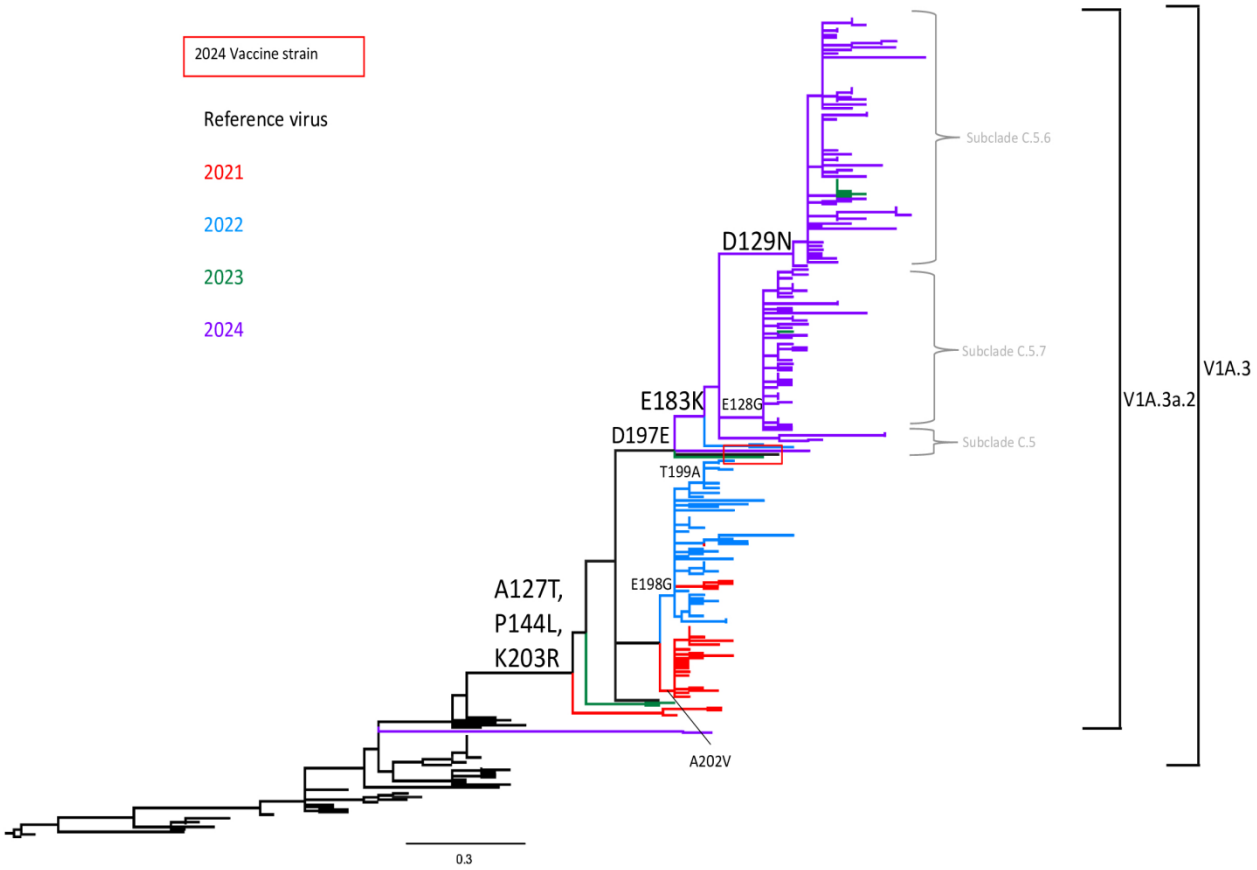

Figure 8. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza B/Victoria viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box, the South African 2024 virus in purple (n=165), the 2023 virus in green, the 2022 viruses in blue, the 2021 viruses in red, and reference strains in black. B/Brisbane/60/2008 was used as the root.

Discussion

During 2024, influenza activity was observed from weeks 1 through 52, with an increased period of activity in the normal winter influenza season. The influenza season started in week 17 (starting 22 April 2024), peaked in week 23 (starting 3 June 2024), and ended in week 41 (starting 7 October 2024). The first peak of the season was dominated by influenza A(H1N1)pdm09, when the influenza transmission and impact were at moderate and high levels, in the ILI and Pneumonia Surveillance programmes, respectively. A second lower peak was observed, peaking in week 35 (starting 26 August 2024), that was dominated by B/Victoria. In South Africa, from 2005–2019 and 2022–2023, the mean onset of the influenza season was week 17 (3rd week of April), ranging from weeks 16 to 25.

Almost all of the South African 2024 influenza A(H1N1)pdm09 viruses were clade 6B.1A.5a.2a (5a.2a), which differed from the 2024 Southern Hemisphere A(H1N1)pdm09 vaccine strain (A/Victoria/4897/2022, clade 5a.2a.1). However, antigenic analysis of South African viruses showed that they were well inhibited by subclade 5a.2a.1 vaccine-type ferret antisera. Phenotypic neuraminidase inhibitor susceptibility testing indicated that one A(H1N1)pdm09 virus showed highly reduced inhibition to oseltamivir and peramivir, and this was the only A(H1N1)pdm09 virus genotypically confirmed to contain the H275Y substitution in neuraminidase. This is the first neuraminidase inhibitor-resistant influenza virus detected through these surveillance programmes in South Africa, and this should be monitored closely moving forward. Influenza A(H3N2) viruses circulating in South Africa in 2024 belonged to clade 3C.2a1b.2a.3a.1 (2a.3a.1) together with the 2024 Southern Hemisphere vaccine strain (A/Thailand/8/2022). None of the A(H3N2) viruses were phenotypically or genotypically resistant to neuraminidase-inhibiting antivirals. The majority of sequenced B/Victoria viruses belonged to clade V1A.3a.2, clustering within the same clade as the 2024 Southern Hemisphere vaccine strain (B/Austria/1359417/2021). B/Victoria viruses were antigenically similar to the vaccine strain, and antiviral resistance was not detected.

Influenza VE is dependent on several factors, such as the age of vaccinees, the match between the strain included in the vaccine and the circulating virus, and a person's previous vaccination and infection history. When vaccine strains are antigenically well-matched to the circulating viruses, vaccine effectiveness would be expected to be 40% to 60%.[5] Similar to 2023, vaccine coverage in the Viral Watch surveillance programme in 2024 was low (2.7% and 5.6% in 2023 and 2024, respectively). After adjusting for age and timing within the season, the VE for any influenza in individuals of all ages was 72.7% in 2024, compared with 81% in 2023. VE estimates in South Africa in 2024 were higher than that reported in other Southern Hemisphere countries: the adjusted VE against influenza-associated severe acute respiratory illness hospitalisations during the 2024 influenza season in Argentina, Brazil, Chile, Paraguay, and Uruguay was 34.5% (36.5% against the predominating subtype A(H3N2) and 37.1% against A(H1N1)pdm09).[6] Interim VE estimates from 17 European countries in the 2024/2025 influenza season (dominated by A(H1N1)pdm09) indicated an all-age influenza A VE of 32-53% in primary care and 33–56% in hospital settings.[7]

Based on data obtained through global influenza surveillance, in September 2024, the WHO announced their recommendations for the composition of the 2025 Southern Hemisphere influenza vaccines.[8]

The WHO recommended that **trivalent** vaccines being used in the 2025 Southern Hemisphere influenza season contain the following:

Egg-based vaccines

- An A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- An A/Croatia/10136RV/2023 (H3N2)-like virus; and
- A B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Cell culture-, recombinant protein-, or nucleic acid-based vaccines

- An A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- An A/District of Columbia/27/2023 (H3N2)-like virus; and
- A B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

The recommendation for the B/Yamagata lineage component of quadrivalent influenza vaccines remains unchanged from previous recommendations:

- a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

While the majority of influenza infections cause mild illness, influenza may cause severe disease and death.[9] Groups at an increased risk of severe complications of influenza include pregnant women, persons living with HIV, those with chronic illnesses or conditions such as diabetes, lung disease, tuberculosis, heart disease, renal disease, and obesity, as well as the elderly (65 years and older) and children under the age of two years.[10] These groups should be encouraged to receive the influenza vaccine and seek medical help early.

Limitations

Influenza surveillance is conducted at sentinel sites and therefore may not be nationally representative. In addition, surveillance is dependent on patients presenting to one of the sentinel site healthcare facilities, which may be influenced by reduced access, financial constraints and healthcare-seeking behaviour.

Conclusion

The three long standing influenza surveillance systems in South Africa provide an important data source that enables the World Health Organization National Influenza Centre, based at the NICD, to contribute to monitoring the changing epidemiology of influenza viruses as well as to monitor viral evolution, to help guide decisions on the composition of influenza vaccine each year.

Recommendations

- Healthcare professionals should access the weekly updates on influenza activity in South Africa, available on the NICD website (https://www.nicd.ac.za/).
- Clinicians are encouraged to consider influenza as a differential diagnosis when managing patients presenting with respiratory illness.
- Groups at increased risk of severe complications of influenza infection should be encouraged to receive the influenza vaccine and seek medical help early. This includes pregnant women, persons living with HIV, those with chronic illnesses or conditions such as diabetes, lung disease, tuberculosis, heart disease, renal disease, and obesity, the elderly (65 years and older), and children under the age of two years.
- To prevent contracting or spreading influenza, it is recommended that patients:
    - Stay at home until symptoms have resolved (at least 24 hours after fever has resolved).
    - Avoid close contact with others, especially those at high risk for severe influenza.
    - Avoid close contact, such as kissing or sharing drinks.
    - Cover coughs and sneezes (cover mouth and nose with tissue or cough or sneeze into an elbow).
    - Wear a tight-fitting mask, especially in public places.
    - Wash hands with soap and water or disinfect with an alcohol-based hand rub regularly.
    - Limit the number of visitors.
    - Wipe down surfaces that are frequently touched or shared (doorknobs, remote controls) with a standard household disinfectant.

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Ethics

The ILI and Pneumonia Surveillance study protocols were approved by local Human Research Ethics Committees (HRECs), including the University of the Witwatersrand HREC (IM180832 and M140824), the University of KwaZulu-Natal Human Biomedical Research Ethics Committee (BF 080/12 and M496/14), and the University of Cape Town Faculty of Health Sciences HREC (573/2018 and 836/2014). Informed consent was obtained from parents or legal guardians. The Viral Watch protocol was approved by the University of Witwatersrand HREC (M150855).

Conflict of interest

CC has received grant support from Sanofi Pasteur, the US CDC, Wellcome Trust, the Task Force for Global Health, and the Gates Foundation. AvG has received grant support from the US CDC, ASLM/Africa CDC, and WHO Afro. NW reports receiving grants from Sanofi Pasteur, the US CDC, and the Gates Foundation. JM has received grant support from Sanofi Pasteur and PATH. Other authors declare no competing interests. SW has received grant support from the US CDC, the Task Force for Global Health, and the Gates Foundation.

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