Influenza Surveillance in South Africa: 2024

Week 1 to 33 of 2024

This report was compiled by Dr Nicole Wolter on behalf of the WHO National Influenza Centre housed at the Centre for Respiratory Diseases and Meningitis of the National Institute for Communicable Diseases, South Africa.

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
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Table of Contents

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Summary

This report summarises the results of influenza surveillance in South Africa for the period of weeks 1 through 33 of 2024 and was compiled by the World Health Organization (WHO) National Influenza Centre (NIC) housed at the Centre for Respiratory Diseases and Meningitis (CRDM) of the National Institute for Communicable Diseases (NICD).

During 2024, influenza activity was observed from weeks 1 through 33, with an increased period of activity in the normal winter influenza season. The season started in week 17 (week starting 22 April 2024) and peaked in week 23 (week starting 3 June 2024), when influenza transmission and impact reached moderate and high levels, respectively. Thereafter the detection rate declined until week 29 (week starting 15 July 2024) when an increase in influenza B was detected. Influenza circulation this season to date has been dominated by influenza A(H1N1)pdm09. Although genetic characterization showed that 2024 A(H1N1)pdm09 viruses belonged to subclade 6B.1A.5a.2a (5a.2a), which differed to the subclade of the 2024 Southern Hemisphere vaccine virus (5a.2a.1), antigenic characterisation showed that the subclade 5a.2a viruses were well inhibited by subclade 5a.2a.1 (vaccine type) antisera.

Epidemiology

This report includes data from individuals meeting syndromic case definitions within three sentinel respiratory illness surveillance programmes: Viral Watch influenza-like illness (VW) surveillance in outpatients at private general practitioners (n=1182), Influenza-like Illness (ILI) surveillance in outpatients at public health clinics (n=1244) and Pneumonia Surveillance in hospitalised patients (n=3164). Together, the three surveillance programmes contributed data from all nine provinces in South Africa.

Influenza activity was observed from weeks 1 through 33, with an overall detection rate from 1 January through 18 August 2024 of 15.9% (887/5590). Using the Moving Epidemic Method (MEM) the levels of activity reached moderate and high levels in the ILI and Pneumonia Surveillance programmes, respectively. Influenza single infections where a subtype/lineage could be determined were dominated by A(H1N1)pdm09 (67.4%, 580/860) followed by B/Victoria (30.6%, 263/860). Low numbers of influenza A(H3N2) (1.9%, 17/860) were detected. Influenza B/Yamagata was not detected.

Vaccine coverage in the VW programme was low (5.5%, 28/505). After adjusting for age and timing within the season, the vaccine effectiveness (VE) for any influenza in individuals of all ages was 74.7% (95% confidence interval (CI) 30.9%-90.7%), and for A(H1N1)pdm09 was 69.6% (95% CI 5.3%-90.2%).

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A(H1N1)pdm09 viruses

Almost all of the South African 2024 influenza A(H1N1)pdm09 viruses were subclade 6B.1A.5a.2a (5a.2a) (203/205, 99.0%), with two additional substitutions, T120A and K169Q, compared to the 2023 viruses. The 2024 Southern Hemisphere A(H1N1)pdm09 vaccine strain (A/Victoria/4897/2022) is a subclade 5a.2a.1 virus, which differed to the subclade of the viruses circulating in South Africa in 2024. However, antigenic analysis of South African viruses showed that all (32/32, 100%) were well inhibited by subclade 5a.2a.1 vaccine-type antisera (A/Victoria/4897/2022 and A/Wisconsin/67/2022). Phenotypic neuraminidase inhibitor susceptibility testing indicated that one (1/26, 3.8%) A(H1N1)pdm09 virus showed highly reduced inhibition to oseltamivir and paramivir, this virus was genotypically confirmed to contain the H275Y substitution in neuraminidase.

A(H3N2) viruses

Six influenza A(H3N2) viruses circulating in South Africa in 2024 were sequenced, and all (6/6, 100%) 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 found to be phenotypically (n=2) or genotypically (n=6) resistant to neuraminidase inhibiting antivirals.

B/Victoria viruses

Sequenced B/Victoria viruses (n=73) belonged to subclade V1A.3a.2, clustering within the same subclade as the 2024 Southern Hemisphere vaccine strain (B/Austria/1359417/2021). B/Victoria viruses were also antigenically like the vaccine strain (10/10, 100%), and antiviral resistance was not detected phenotypically (10/10, 100%) or genotypically (73/73, 100%).

1. Epidemiology of the 2024 influenza season

South Africa is a Southern Hemisphere country with a temperate climate and with influenza epidemics usually occurring between April and October, with a peak during the winter months[1,2].

1.1 Recommended influenza vaccine formulation for 2024

The following viruses were recommended for the trivalent and quadrivalent inactivated influenza vaccine (IIV) 2024 Southern Hemisphere influenza season:

Egg-based tri/quadri-valent 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 vaccines strains compared with the 2023 Southern Hemisphere trivalent and quadrivalent IIV. For A(H1N1)pdm09 vaccine virus component, 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 World Health Organization (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.

1.2 Description of the surveillance systems

South Africa has three influenza sentinel surveillance programmes, which are coordinated by the CRDM at the NICD, which houses the 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 primary health care clinics, and (iii) inpatient Pneumonia Surveillance in public health hospitals (**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	• 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
Specimens collected	Throat swabs and/or nasal/nasopharyngeal swabs	Mid-turbinate nasal swabs	Mid-turbinate nasal swabs

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*EC: Eastern Cape; FS: Free State; GP: Gauteng; KZN: KwaZulu-Natal; LP: Limpopo; 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).

From 1 January (week 1) through 18 August 2024 (week 33), 5590 individuals were enrolled with respiratory specimens collected and tested through the three surveillance programmes (**Table 2**), using the Allplex™ SARS-CoV-2/influenza/RSV commercial kit (Seegene, Seoul, Korea) and the US Centers for Disease Control and Prevention (CDC) subtyping method (with reagents sourced through the International Reagent Resource, IRR Portal).

Influenza infections were identified in 887 individuals, resulting in an overall infection detection rate of 15.9% (887/5590). Influenza detections occurred from week 1 through week 33. For influenza single infections where a subtype/lineage could be determined (97.0%, 860/887), infections were dominated by influenza A(H1N1)pdm09 (67.4%, 580/860) followed by B/Victoria (30.6%, 263/860). A(H3N2) accounted for only 1.9% (17/860) of single infections. Influenza B/Yamagata was not detected. A dual infection was 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 2.8% (25/887) 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 subsequent characterisation PCR was not performed 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 Moving Epidemic Method (MEM), and peaked in week 23 (week starting on 3 June 2024) when the influenza transmission and impact were at moderate and high levels, respectively. Since then the detection rate declined until week 29 (week starting 15 July 2024) when an increase in influenza B was detected, mostly in the Viral Watch programme. The mean onset of influenza season in South Africa in 2005-2019 and 2022-2023 was week 17 (3rd week of April), ranging from week 16 to week 25.

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Table 2. Number of influenza infections identified in all syndromic influenza surveillance programmes, South Africa, 1 January – 18 August 2024 (Weeks 1-33)

Programme	Number of specimens tested	Number influenza positive (% of all specimens tested)	Influenza A				Influenza B			Dual infection#
			Total A	Subtype inconclusive*	A(H1N1) pdm09	A(H3N2)	Total B	Lineage inconclusive*	B/ Victoria	
			n (% of total influenza positives)							
Viral Watch	1182	372 (31)	291 (78)	3 (1)	279 (75)	9 (2)	81 (22)	5 (1)	76 (20)	**0 (0)**
Influenza-like Illness Surveillance	1244	248 (20)	130 (52)	2 (1)	126 (51)	2 (1)	118 (48)	6 (2)	112 (45)	**0 (0)**
Pneumonia Surveillance **	3164	267 (8)	183 (69)	2 (1)	175 (66)	6 (2)	82 (31)	7 (3)	75 (28)	**2 (1)**
Total	**5590**	**887 (16)**	**604 (68)**	**7 (1)**	**580 (65)**	**17 (2)**	**281 (32)**	**18 (2)**	**263 (30)**	**2 (0)**

*Inconclusive: insufficient viral load in 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; and on 31 May 2024 for Livingstone Hospital.

1.3 Viral Watch Surveillance Programme

Specimens from 1182 patients were received and tested from VW practitioners located in 8 of the 9 provinces (**Table 3**), with the majority of specimens received from Gauteng (66.1%, 781/1182) and the Western Cape (31.6%, 373/1182) provinces. Influenza was detected in 372 (31.4%) patients, of which 75.0% (279/372) were A(H1N1)pdm09 (**Figure 1, Table 3**). The highest 3-week moving average detection rate in the VW programme occurred in week 20 (56.1%) (**Figure 1**).

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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 – 18 August 2024 (Weeks 1-33)

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	0	0	0	9	16	**56**
Free State	0	0	0	0	0	0	0	0	**0**
Gauteng	155	4	3	30	1	0	193	781	**25**
Limpopo	0	0	0	0	0	0	0	0	**0**
Mpumalanga	6	0	0	0	0	0	6	10	**60**
North West	0	0	0	0	0	0	0	0	**0**
Northern Cape	0	0	0	0	0	0	0	2	**0**
Western Cape	110	4	0	46	4	0	164	373	**44**
Total	**279**	**9**	**3**	**76**	**5**	**0**	**372**	**1182**	**31**

*Inconclusive: insufficient viral load in sample and unable to characterise further; #Dual infection: Not detected

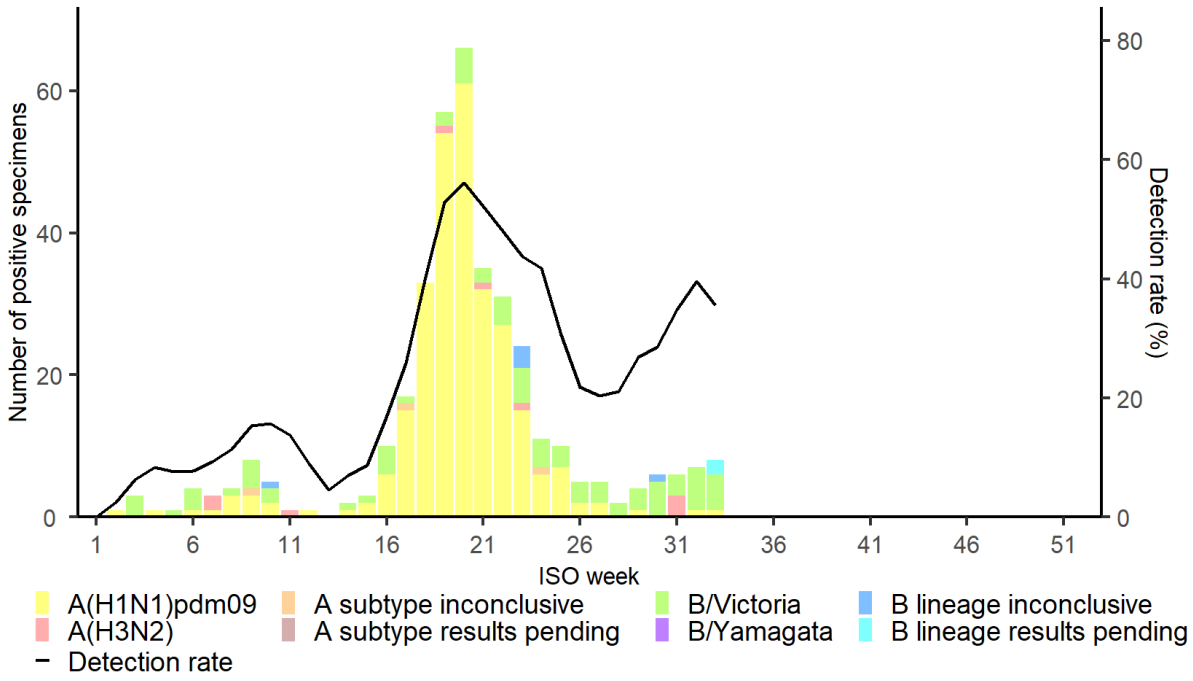

Figure 1. Number of influenza infections by influenza subtype/lineage and 3-week moving average detection rate by epidemiologic week - Viral Watch Surveillance Programme for influenza-like illness, South Africa, 1 January – 18 August 2024 (Weeks 1-33)

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

Specimens from 1244 patients with ILI were received from five primary health care clinics located in four provinces. In total, 248 (19.9%) individuals tested positive for influenza. Of influenza infections which could be subtyped, influenza A(H1N1)pdm09 accounted for 52.5% (126/240) and influenza B/Victoria accounted for 46.7% (112/240) of cases (**Table 4, Figure 2**). The 3-week moving average detection rate peaked in week 23 (50.6%).

Influenza transmission thresholds are 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]. 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 ILI surveillance at primary healthcare clinics (outpatients) are used as an indicator of disease transmission in the community and thresholds from Pneumonia Surveillance (inpatients) are used as an indicator of impact of disease on healthcare provision.

Using the MEM for the ILI Surveillance Programme data, with a baseline determined from years pre and post the COVID-19 pandemic (2012-2019 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 – 18 August 2024 (Weeks 1-33)

Province	A(H1N1) pdm09	A (H3N2)	A subtype inconclusive *	B/ Victoria	B lineage inconclusive *	Dual infection#	Total cases	Total specimens tested	Detection rate %
KwaZulu-Natal	47	0	0	20	0	0	67	349	**19**
Mpumalanga	17	2	1	32	1	0	53	186	**28**
North West	41	0	1	45	5	0	92	431	**21**
Western Cape	21	0	0	15	0	0	36	278	**13**
Total	**126**	**2**	**2**	**112**	**6**	**0**	**248**	**1244**	**20**

Surveillance sites included primary health care clinics in 4 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 sample and unable to characterise further (primary test PCR C_t value >35). #Dual infection: Not detected

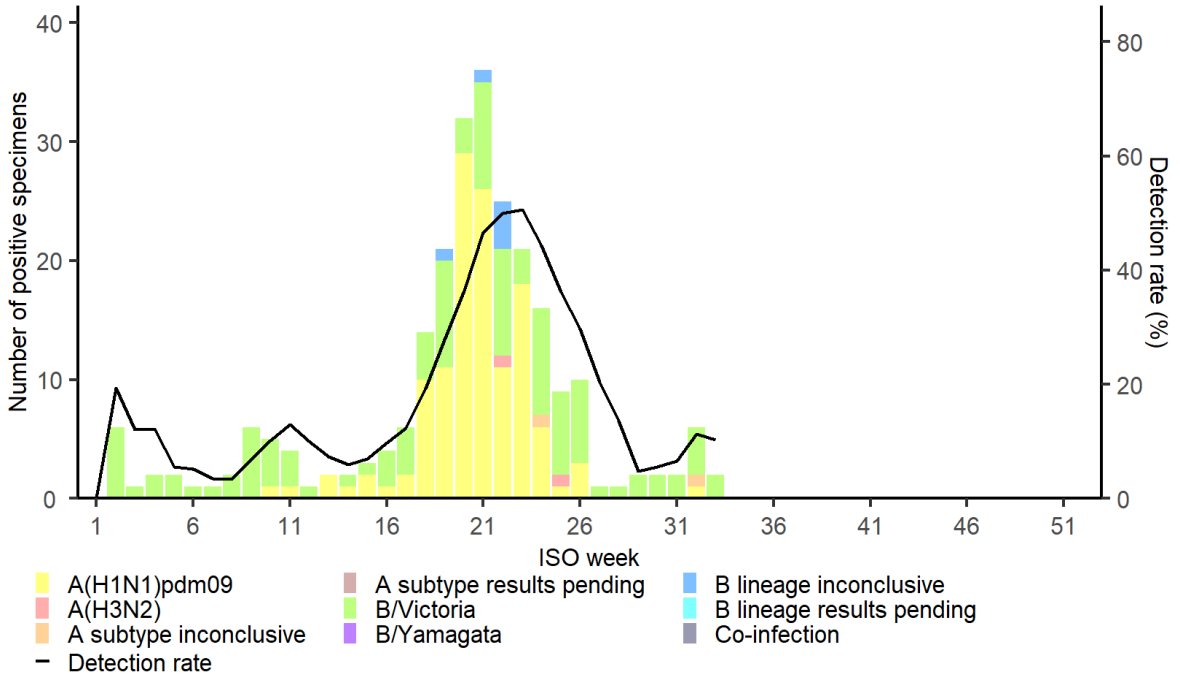

Figure 2. Number of influenza cases by subtype/lineage and 3-week moving average detection rate by epidemiologic week - Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 1 January – 18 August 2024 (Weeks 1-33). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infection: Not detected

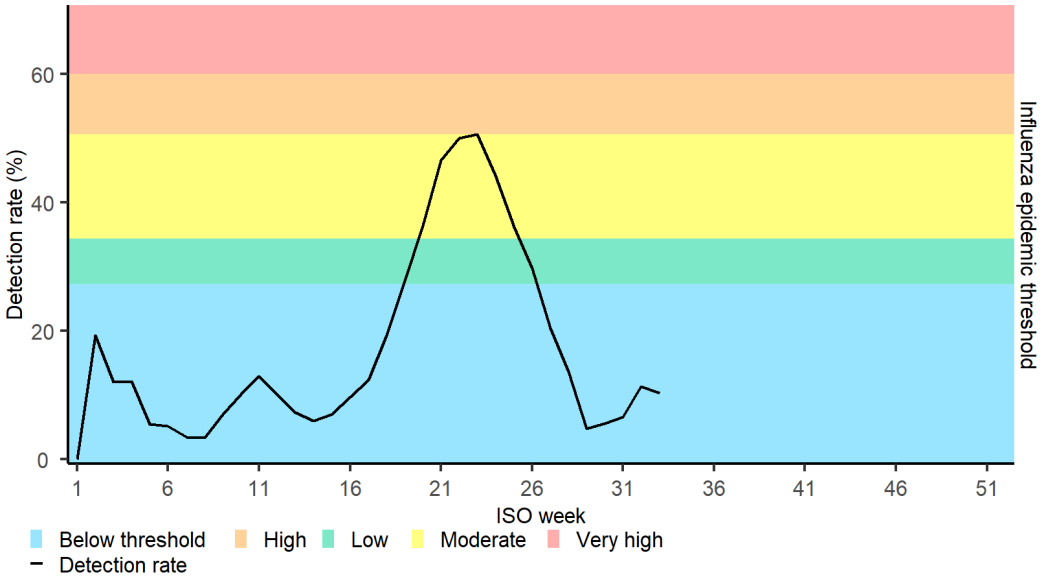

Figure 3. Influenza detection rate and epidemic thresholds*, Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 1 January – 18 August 2024 (Weeks 1-33). *Influenza transmission thresholds based on 2012-2019 and 2022-2023 data and calculated using the Moving Epidemic Method (MEM)

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1.5 Pneumonia Surveillance Programme

Specimens from 3164 patients hospitalised with severe respiratory illness were received from the thirteen sentinel hospitals located in six provinces, and 267 (8.4%) 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, 68.4% (175/256) were influenza A(H1N1)pdm09 and a further 29.3% (75/256) were influenza B/Victoria (**Table 5**).

The 3-week moving average detection rate peaked in week 22 (27%) (**Figure 4**). Data obtained through the Pneumonia Surveillance Programme among hospitalised patients pre and post the COVID-19 pandemic (2016-2019 and 2022-2023) were used to set MEM thresholds for 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 – 18 August 2024 (Weeks 1-33)

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	3	0	15	3	0	89	848	**10**
KwaZulu-Natal	20	0	0	4	0	0	24	326	**7**
Mpumalanga	20	2	0	15	1	1	39	412	**9**
North West	38	0	1	18	1	0	58	380	**15**
Western Cape	28	1	1	23	2	1	56	1157	**5**
Total	**175**	**6**	**2**	**75**	**7**	**2**	**267**	**3164**	**8**

Surveillance sites included hospitals in six provinces: Gauteng (Helen Joseph Hospital, Rahima Moosa Hospital, Tembisa Hospital, Tambo Memorial Hospital), KwaZulu-Natal (Edendale 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); and on 31 May 2024 for Livingstone Hospital (EC). *Inconclusive: insufficient viral load in sample and unable to characterise further. #Dual infection: A(H1N1)pdm09 and B (lineage inconclusive) (n=1); and A(H1N1)pdm09 and B/Victoria (n=1).

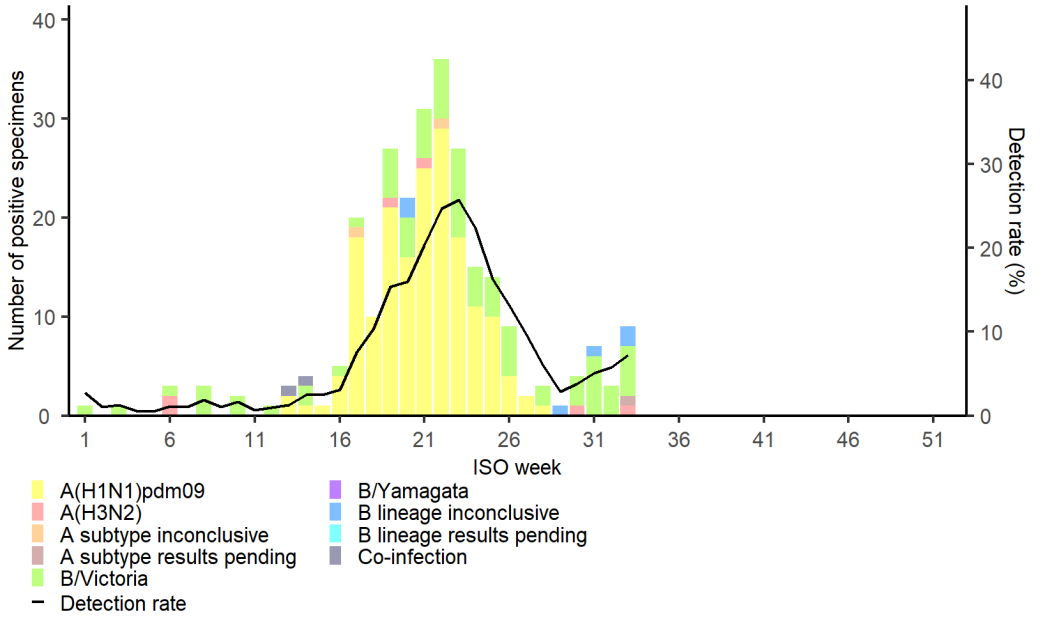

Figure 4. Number of influenza cases by subtype/lineage and 3-week moving average detection rate by epidemiologic week – Pneumonia Surveillance Programme, South Africa, 1 January – 18 August 2024 (Weeks 1-33). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infection: A(H1N1)pdm09 and B (lineage inconclusive) (n=1); and A(H1N1)pdm09 and B/Victoria (n=1).

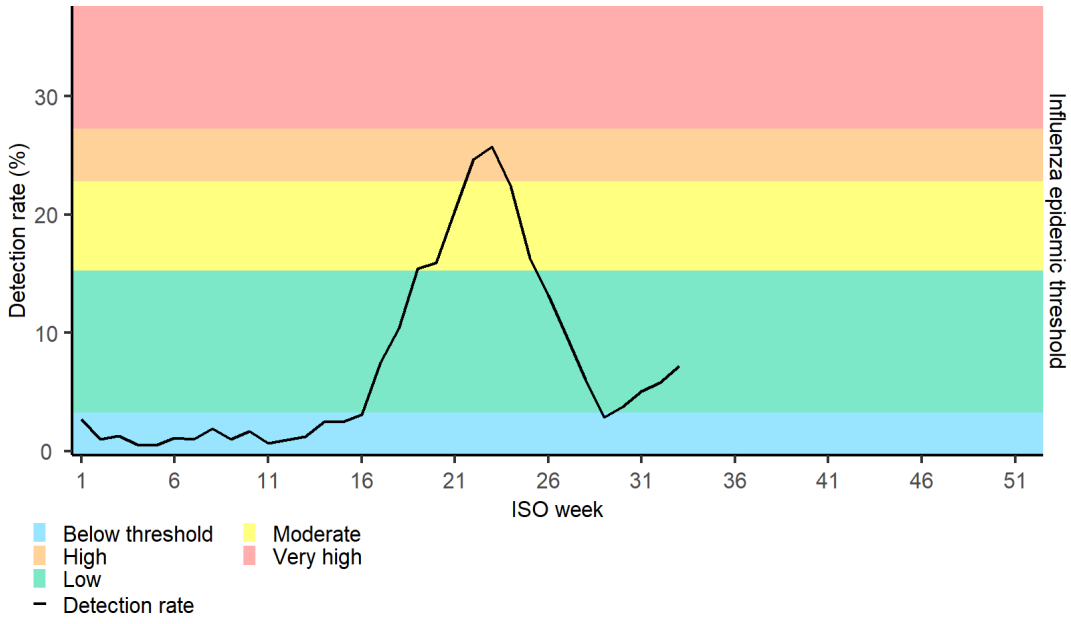

Figure 5. Influenza detection rate and epidemic thresholds*, Pneumonia Surveillance Programme, South Africa, 1 January – 18 August 2024 (Weeks 1-33). *Influenza transmission thresholds based on 2016-2019 and 2022-2023 data and calculated using the Moving Epidemic Method (MEM).

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1.6 Vaccine effectiveness

The effectiveness of the trivalent/quadrivalent seasonal influenza vaccine (TIV/QIV) 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 programme during the 2024 influenza season.

Of the 505 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), 251 (49.7%) were classified as cases (influenza test positive) and 254 (50.3%) as controls (influenza test negative). Vaccine coverage was 5.5% (28/505) overall in the VW programme (**Table 6**): 2.0% (5/251) and 9.1% (23/254) among cases and controls respectively. Adjusted VE (adjusting for timing within season and age) for any influenza was 74.7% (95% confidence interval (95% CI) 30.9%-90.7%) and for influenza A(H1N1)pdm09 was 69.6% (95% CI 5.3%-90.2%) (**Table 6**).

Table 6: Vaccine coverage and vaccine effectiveness (VE) by subtype and age group, Viral Watch Surveillance Programme, South Africa, 22 April-18 August 2024

	Vaccine coverage			Adjusted VE % (95% confidence interval)*
	Cases n/N (%)	Controls n/N (%)	Total n/N (%)	
All specimens				
Any influenza	5/251 (2.0)	23/254 (9.1)	28/505 (5.5)	74.7 (30.9; 90.7)
A(H1N1)pdm09	4/197 (2.0)	23/254 (9.1)	27/451 (6.0)	69.6 (5.3; 90.2)
Children aged <18 years				
Any influenza	0/71 (0.0)	4/62 (6.5)	4/133 (3.0)	84.0 (-223.3; 99.2)
A(H1N1)pdm09	0/51 (0.0)	4/62 (6.5)	4/113 (3.5)	71.1 (-504.3; 98.6)
Adults aged 18 – 64 years				
Any influenza	5/164 (3.0)	18/171(10.5)	23/335 (6.9)	69.4 (14.0; 89.1)
A(H1N1)pdm09	4/131 (3.1)	18/171 (10.5)	22/302 (7.3)	63.9 (-16.5; 88.8)
Adults aged ≥65 years				
Any influenza	0/16 (0.0)	1/21 (4.8)	1/37 (2.7)	40.0 (-1998.1; 98.3)
A(H1N1)pdm09	0/15 (0.0)	1/21 (4.8)	1/36 (2.8)	40.0 (-1998.1; 98.3)

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

2. Influenza virus isolation

During weeks 1 through 33 of 2024, influenza virus isolation was attempted on clinical specimens (n=183) testing positive for influenza on rRT-PCR with a high viral load (C_t value ≤30). Madin-Darby Canine Kidney (MDCK) cells were used for virus isolations with an overall isolation rate of 73.2% (134/183) (**Table 7**).

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Table 7: Summary of influenza virus isolations in Madin-Darby Canine Kidney (MDCK) cell cultures, South Africa, 1 January – 18 August 2024 (Weeks 1-33)

Programme	Specimens cultured	Successful cultures	Number of cultures/ attempted (%)		
			A(H1N1)pdm09	A(H3N2)	B/Victoria
Viral Watch	55	33	20/38 (53)	2/3 (67)	11/14 (79)
Influenza-like illness surveillance	73	62	29/31 (94)	0/0 (0)	33/42 (79)
Pneumonia Surveillance	55	39	23/36 (64)	2/2 (100)	14/17 (82)
Total	**183**	**134**	**72/105 (69)**	**4/5 (80)**	**58/73 (79)**

3. Influenza specimens shared with WHO Collaborating Centres

Influenza virus cultures and original specimens from 99 individuals were shared in three shipments in July 2023 with the WHO GISRS Collaborating Centres (WHO-CC) in Australia, United Kingdom and United States for antigenic and genetic characterisation (**Table 8**). Among specimens shared, 65.7% (65/99) were A(H1N1)pdm09, 31.3% (31/99) were B/Victoria and 3.0% (3/99) were A(H3N2).

Table 8: Summary of influenza virus specimens collected in South Africa and shared with WHO-CCs, 1 January – 18 August 2024 (Weeks 1-33)

WHO-CC	A(H1N1)pdm09	A(H3N2)	B/Victoria	Total
Australia	27	2	10	39
United Kingdom	23	1	11	35
United States	15	0	10	25
Total	**65**	**3**	**31**	**99**

4. Antigenic characterisation of influenza virus isolates

The haemagglutination inhibition (HAI) assays performed at the NIC in South Africa, and results for antigenic characterisation are summarised in **Table 9**. Turkey red blood cells were used as indicator cells in the HA and HAI assays. All the HAI assays were completed using the IRR 2023-2024 WHO influenza reagent kit for identification of influenza isolates (CDC International Reagent Resource). HAIs were performed for all isolates with haemagglutination (HA) titers (n=126).

A total of 126 viruses were characterised antigenically, including 64 A(H1N1)pdm09, 4 A(H3N2), and 58 B/Victoria cultures (**Table 9**). 2% (1/64) of A(H1N1)pdm09 viruses recognised A/Victoria/2570/2019 (clade 6B.1A.5a.2) antisera poorly, and 2% (1/58) of B/Victoria viruses recognised B/Michigan/01/2021 (clade V1A.3a.2) antisera poorly.

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Table 9: Summary of haemagglutination inhibition (HAI) assay results, South Africa, 1 January – 18 August 2024 (Weeks 1-33)

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	30	0/17 (0)	0/2 (0)	0/11 (0)
Influenza-like illness	62	1/29 (3)	0/0 (0)	0/33 (0)
Pneumonia Surveillance	34	0/18 (0)	0/2 (0)	1/14 (7)
Total n/N (% per virus)	**126**	**1/64 (2)**	**0/4 (0)**	**1/58 (2%)**

HAI assay 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). In addition, all (7/7) A(H1N1)pdm09 viruses tested at the WHO-CC in the USA (US CDC) were A/Wisconsin/67/2022-like (clade 5a.2a.1).

5. Neuraminidase inhibitor susceptibility

Phenotypic susceptibility testing to zanamivir, oseltamivir, peramivir and laninamivir was performed for South African samples at the WHO-CC in Australia (VIDRL). 96% (25/26) A(H1N1)pdm09, 100% (2/2) A(H3N2) and 100% (10/10) 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.

Genotypic analysis for resistance mutation detection was conducted using Nextclade 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/). The mutational analysis of the neuraminidase (NA) genes of sequenced 2024 South African viruses (A(H1N1)pdm09 n=205, A(H3N2) n=6 and B/Victoria n=73), revealed only one virus with a mutation (H275Y) known to be associated with antiviral resistance.

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6. Genetic characterisation of influenza viruses

Influenza viruses circulating in 2024 in South Africa were genetically characterised by whole genome sequencing (WGS) and shared on GISAID. Sequences of viruses circulating in South Africa in 2024 (n=284) were obtained from GISAID on the 26 August 2024. These included viruses collected through respiratory illness surveillance programmes and sequenced by the NICD [A(H1N1)pdm09 n=147, A(H3N2) n=4, B/Victoria n=48], and by WHO-CCs in Australia, the United Kingdom and the USA [A(H1N1)pdm09 n=58, A(H3N2) n=2, B/Victoria n=25]. Phylogenetic analysis of the haemagglutinin (HA) genes was performed using the MAFFT for alignment and IQ-TREE v 1.6.12 software for the construction of the tree. Groups and sub-groups were identified by specific amino acid mutations relative to a designated reference strain on NextClade.

6.1 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 subclade 6B.1A.5a.2a (5a.2a) (203/205, 99.0%), and only two viruses were subclade 6B.1A.5a.2a.1 (5a.2a.1) (2/205, 1.0%) (**Figure 6**). Clade 5a.2a viruses circulated at low levels during the 2023 influenza season. The clade 5a.2a viruses had two additional substitutions, T120A and K169Q, compared to the viruses circulating in 2023, but no changes in glycosylation sites were observed. The 2024 Southern Hemisphere A(H1N1)pdm09 vaccine strain (A/Victoria/4897/2022) is a clade 5a.2a.1 virus, which differed to the clade of the South African viruses in 2024 (**Figure 6**).

6.2 Influenza A(H3N2)

Six influenza A(H3N2) viruses circulating in South Africa in 2024 were sequenced, and all (6/6, 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 the A(H3N2) viruses that circulated in the 2023 influenza season, with two additional substitutions N122D and K276E.

6.3 Influenza B/Victoria

Seventy-three influenza B/Victoria viruses circulating in South Africa in 2024 were sequenced and all (73/73, 100%) belonged to subclade V1A.3a.2 (characterised by A127T, P144L, K203R substitutions), similar to the B/Victoria viruses circulating in recent years (**Figure 8**). The 2024 viruses accumulated several additional substitutions (E128G, D129N, E183K and D197E). The 2024 Southern Hemisphere vaccine strain (B/Austria/1359417/2021) clustered within the same clade.

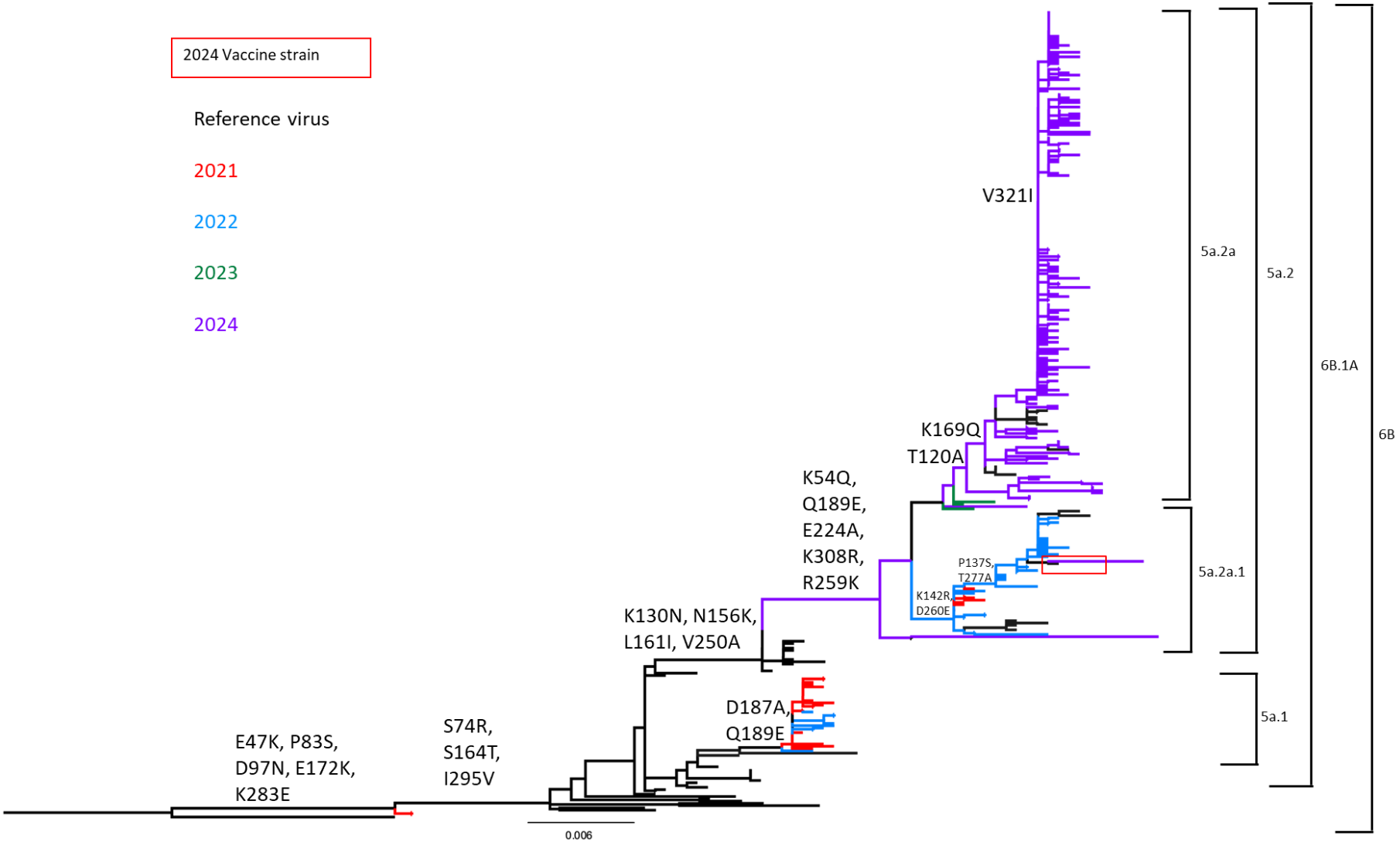

Figure 6. Maximum likelihood phylogenetic tree (best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H1N1)pdm09 viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box (A/Victoria/4897/2022), South African 2024 virus in purple (n=205), 2023 viruses in green, 2022 viruses in blue, 2021 viruses in red and reference strains in black. A/California/07/2009 was used as the root.

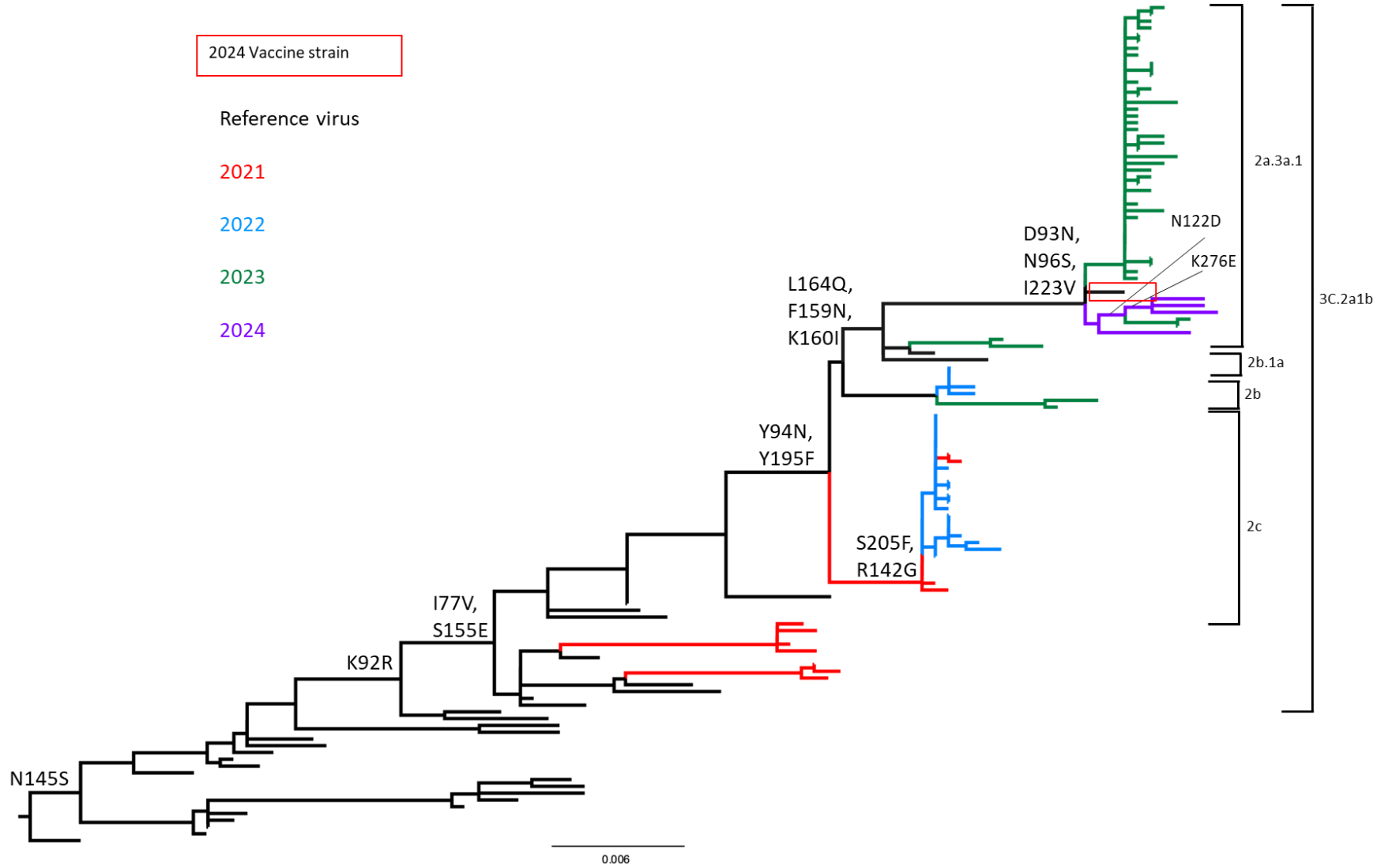

Figure 7. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H3N2) viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box, South African 2024 viruses in purple (n=6), 2023 viruses in green, 2022 viruses in blue, 2021 viruses in red and reference strains in black. A/Wisconsin/67/2005 was used as the root.

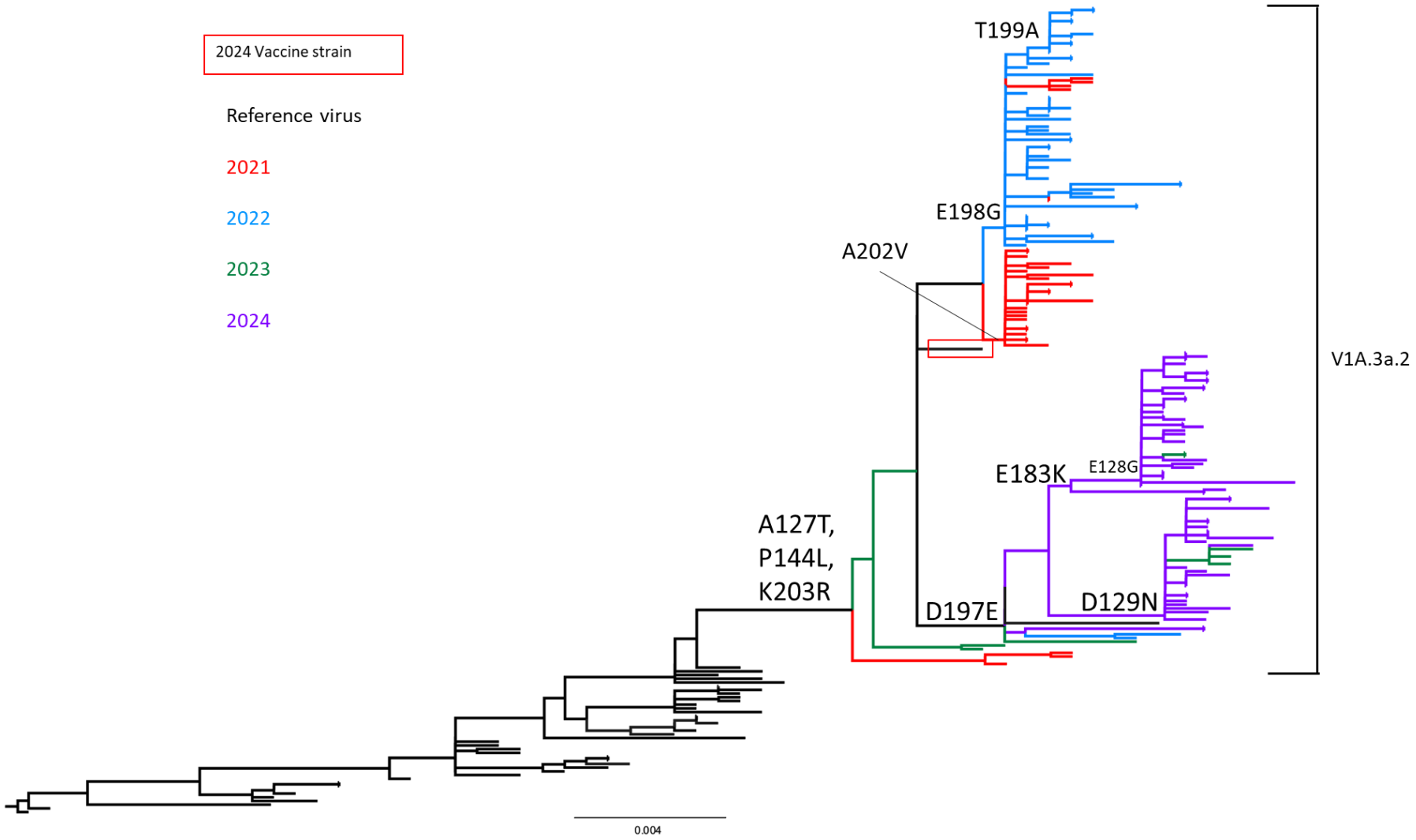

Figure 8. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza B/Victoria viruses. The 2024 Southern Hemisphere vaccine strain is indicated in a red box, South African 2024 virus in purple (n=73), 2023 virus in green, 2022 viruses in blue, 2021 viruses in red and reference strains in black. B/Brisbane/60/2008 was used as the root.

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8. Acknowledgements

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