

Influenza Surveillance in South Africa: 2025

Week 1 to 34 of 2025

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Table of Contents

Summary.....	3
1. Epidemiology of the 2025 influenza season.....	4
2. Influenza virus isolation.....	14
3. Influenza specimens shared with WHO Collaborating Centres.....	14
4. Antigenic characterisation of influenza virus isolates	14
5. Neuraminidase inhibitor susceptibility.....	15
6. Genetic characterisation of influenza viruses	16
7. References.....	21
8. Acknowledgements	21



Influenza Surveillance in South Africa: 2025

Summary

This report summarises the findings from influenza surveillance in South Africa for the period of weeks 1 through 34 of 2025 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 2025, influenza activity was observed from weeks 2 through 34, with an increased period of activity in the normal winter influenza season although the season began earlier than in previous years. The influenza season started in week 13 (week starting 24 March 2025), peaked in week 20 (week starting 12 May 2025) and ended in week 30 (week starting 21 July 2025). The influenza season was dominated by subtype A(H3N2), with only few detections of A(H1N1)pdm09 and B/Victoria viruses. The circulating A(H3N2) viruses belonged to clade 3C.2a1b.2a.3a.1 (2a.3a.1), together with the 2025 southern hemisphere vaccine strain (A/Croatia/10136RV/2023); and were predominantly subclade J.2.2. Antigenic characterisation using ferret antisera showed that the majority of 2025 A(H3N2) viruses were well inhibited by clade 2a.3a.1 (vaccine type) antisera, with <10% showing low reaction.

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=1194), Influenza-like Illness (ILI) Surveillance Programme in outpatients at public health clinics (n=1123) and the Pneumonia Surveillance Programme in hospitalised patients (n=2839). Together, the three surveillance programmes contributed data from all nine provinces in South Africa.

Influenza activity was observed from weeks 2 through 34, with an overall detection rate from 30 December 2024 through 24 August 2025 of 10.4% (538/5156). Using the Moving Epidemic Method (MEM) the levels of activity did not surpass the low level in both the ILI and Pneumonia Surveillance programmes. Influenza infections where a subtype/lineage could be determined were dominated by A(H3N2) (96.8%, 508/525). A(H1N1)pdm09 (2.7%, 14/525) and B/Victoria (0.6%, 3/525) only accounted for a small proportion of cases.

Vaccine coverage in the VW programme was low (3.4%, 26/768). After adjusting for age and timing within the season, the vaccine effectiveness (VE) for any influenza in individuals of all ages was 51.3% (95% confidence interval (CI) -31.3%; 86.0%). For A(H3N2), the adjusted VE was 49.3% (95% CI -36.9%; 85.5%).

Characterisation of A(H3N2) viruses

All sequenced A(H3N2) viruses (n=321) clustered within clade 3C.2a1b.2a.3a.1 (2a.3a.1), together with the 2025 southern hemisphere vaccine strain (A/Croatia/10136RV/2023). The majority were assigned to subclade J.2.2 (86.6%, 278/321). Antigenic characterisation using ferret antisera showed that 92.6% (25/27) of A(H3N2) viruses were A/Croatia/10136RV/2023-like (clade 2a.3a.1, subclade J.2) and 93.8% (15/16) of A(H3N2) viruses were antigenically A/Massachusetts/18/2022-like (clade 2a.3a.1, subclade J.2.2).



1. Epidemiology of the 2025 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 2025

The following viruses were recommended for the egg-based trivalent and quadrivalent inactivated influenza vaccines (IIV) for the 2025 southern hemisphere influenza season³:

- an A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- an A/Croatia/10136RV/2023 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- a B/Phuket/3073/2013-like (B/Yamagata lineage) virus

These recommendations included a change to the A(H3N2) component of egg-based vaccine strains compared with the 2024 southern hemisphere trivalent and quadrivalent IIV. For the A(H3N2) vaccine component, the A/Thailand/8/2022-like virus (clade 2a.3a.1, subclade J) was replaced with an A/Croatia/10136RV/2023-like virus (clade 2a.3a.1, subclade J.2). The WHO-recommended trivalent IIV was available in the public sector (at designated clinics and hospitals). The trivalent and quadrivalent IIV were additionally available in the private sector, generally from March or April. As influenza B/Yamagata has not circulated for a number of years, the WHO influenza vaccine composition advisory committee maintains that the inclusion of a B/Yamagata lineage antigen in quadrivalent influenza vaccines is no longer warranted, and every effort should be made to exclude this component as soon as possible.

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 surveillance (VW) 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 illness surveillance programmes in South Africa, 2025

Programme	Viral Watch (VW)	Influenza-like Illness (ILI)	Pneumonia Surveillance
Start year	1984	2012	2009
Provinces*	EC, FS, GP, KZN, LP, MP, NC, NW, WC	KZN, NW, WC, MP	GP, KZN, MP, NW, WC
Number of sites	71	5	10
Type of site	General practitioners	Public primary health care clinics	Public hospitals
Case definition	An acute respiratory illness with a temperature ($\geq 38^{\circ}\text{C}$) or history of fever and cough, & onset ≤ 10 days	<ul style="list-style-type: none"> An acute respiratory illness with a temperature ($\geq 38^{\circ}\text{C}$) or history of fever 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, or inspiratory "whoop", or post-tussive vomiting or apnoea in children < 1 year; OR any person in whom a clinician suspects pertussis 	<ul style="list-style-type: none"> 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, or inspiratory "whoop", or post-tussive vomiting or apnoea in children < 1 year; OR any person in whom a clinician suspects pertussis
Specimens collected	Throat and/or nasal/nasopharyngeal swabs	Mid-turbinate nasal swabs	Mid-turbinate nasal swabs

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

Influenza epidemic thresholds were calculated 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 epidemic^{4,5}. We used the "original method" included in the package to determine the start of the season. MEM uses the 40th, 90th and 97.5th percentiles established from available years of historical data to calculate thresholds of activity. Thresholds of activity were defined as follows: below seasonal threshold, low activity, moderate activity, high activity, and very high activity.



Thresholds from outpatient influenza-like illness (ILI in primary health care clinics or private general practitioners) are used as an indicator of disease transmission in the community and thresholds from pneumonia surveillance are used as an indicator of influenza-associated morbidity and mortality. For influenza, the start and end of the season is defined as once the three-week moving average of the detection rate remains above or below the seasonal threshold (in any of the three programmes) for two consecutive weeks, respectively.

From 30 December 2024 (week 1) through 24 August 2025 (week 34), 5156 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 538 individuals, resulting in an overall infection detection rate of 10.4% (538/5156). Influenza detections occurred from week 2 through week 34. For influenza single infections where a subtype/lineage could be determined (97.6%, 525/538), infections were dominated by influenza A(H3N2) (96.8%, 508/525). A(H1N1)pdm09 (2.7%, 14/525) and B/Victoria (0.6%, 3/525) only accounted for a small proportion of cases. Influenza B/Yamagata was not detected. Dual infections were also not detected. Inconclusive results for subtyping occurred for 2.4% (13/538) of specimens. The latter samples had a primary identification real-time reverse transcription 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 13 (week starting 24 March 2025), peaked in week 20 (week starting 12 May 2025) and ended in week 30 (week starting 21 July 2025). The season began earlier than in the previous years, and throughout the season, the detection rate remained within the low threshold. The mean onset of influenza season in South Africa in 2005-2019 and 2022-2024 was week 17 (3rd week of April), ranging from week 16 to week 25.



Table 2. Number of influenza infections identified in all syndromic influenza surveillance programmes, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

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	1194	259 (22)	257 (99)	7 (3)	9 (3)	241 (93)	2 (1)	0 (0)	2 (1)	0 (0)
Influenza-like Illness Surveillance	1123	117 (10)	117 (100)	1 (1)	1 (1)	115 (98)	0 (0)	0 (0)	0 (0)	0 (0)
Pneumonia Surveillance	2839	162 (6)	161 (99)	5 (3)	4 (2)	152 (64)	1 (1)	0 (0)	1 (1)	0 (0)
Total	5156	538 (10)	535 (99)	13 (2)	14 (3)	508 (94)	3 (1)	0 (0)	3 (1)	0 (0)

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

1.3 Viral Watch (VW) Surveillance Programme

Specimens from 1194 patients were received and tested from VW practitioners located in 6 of the 9 provinces (Table 3), with the majority of specimens received from Gauteng (71.8%, 857/1194) and the Western Cape (22.7%, 271/1194) provinces. Influenza was detected in 259 (21.7%) patients. Among specimens which could be subtyped, 95.6% (241/252) were A(H3N2) (Figure 1, Table 3). The highest detection rate in the VW programme occurred in week 23 (Figure 1). Using the MEM for the VW programme data, with a baseline determined from 2022-2024 detection rates, the estimated level of influenza transmission in the community was low (Figure 2).



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, 30 December 2024 – 24 August 2025 (Weeks 1-34)

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	0	9	0	0	0	0	9	16	56
Free State	0	0	0	0	0	0	0	1	0
Gauteng	2	131	3	1	0	0	137	857	16
KwaZulu-Natal	0	4	0	0	0	0	4	15	27
Limpopo	0	0	0	0	0	0	0	0	ND
Mpumalanga	0	4	1	0	0	0	5	34	15
North West	0	0	0	0	0	0	0	0	ND
Northern Cape	0	0	0	0	0	0	0	0	ND
Western Cape	7	93	3	1	0	0	104	271	38
Total	9	241	7	2	0	0	259	1194	22

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

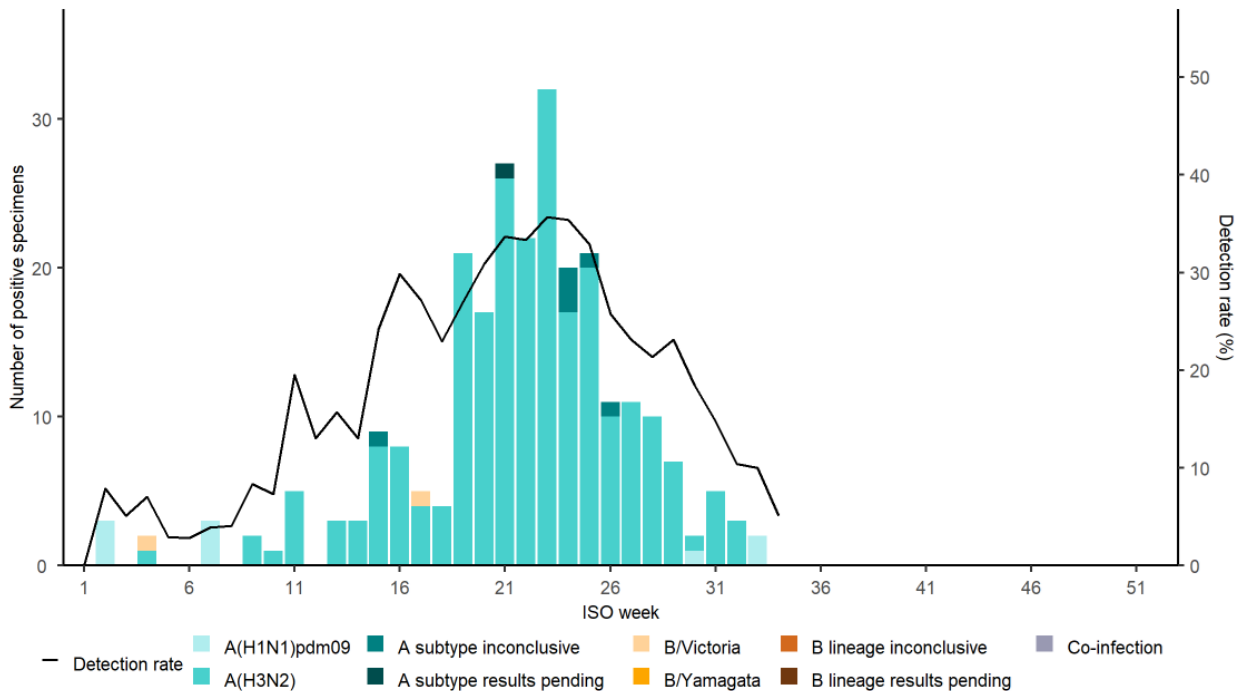


Figure 1. Number of influenza infections by influenza subtype/lineage and detection rate by week - Viral Watch Surveillance Programme for influenza-like illness, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

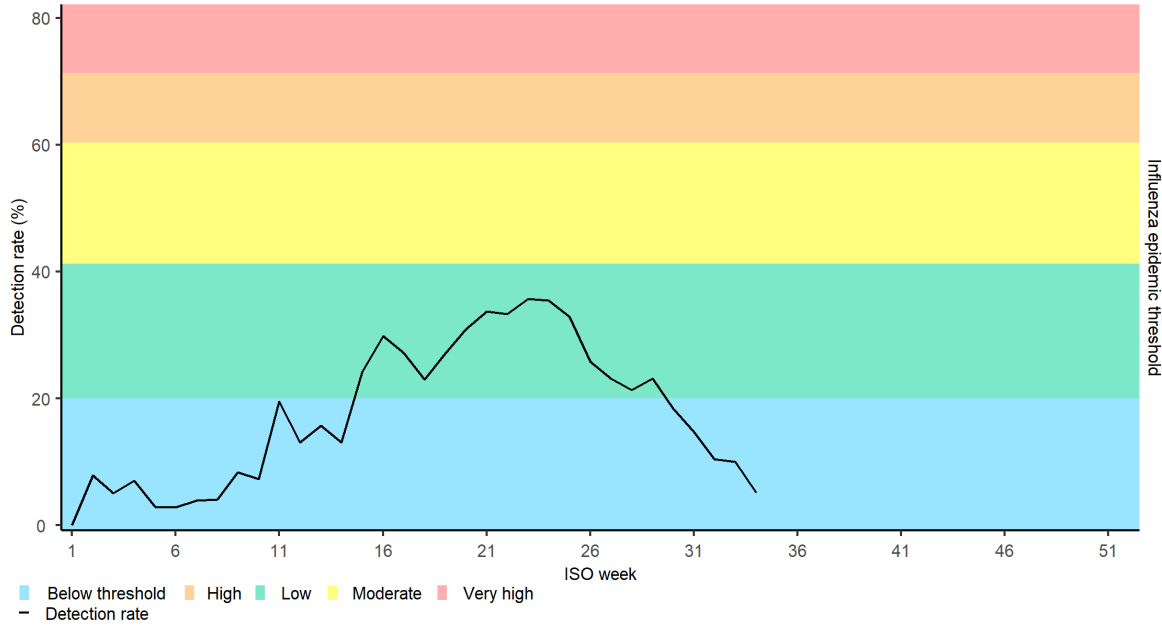


Figure 2. Influenza detection rate and epidemic thresholds*, Viral Watch Surveillance Programme for influenza-like illness, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

*Influenza transmission thresholds based on 2022-2024 data and calculated using the Moving Epidemic Method (MEM)

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

Specimens from 1123 patients with ILI were received from five primary health care clinics located in four provinces. In total, 117 (10.4%) individuals tested positive for influenza. Of influenza infections that could be subtyped, A(H3N2) accounted for 99.1% (115/116) of cases (Table 4, Figure 3). The detection rate peaked in week 25. Using the MEM for the ILI Surveillance Programme data, with a baseline determined from 2022-2024 detection rates, the estimated level of influenza transmission in the community was low (Figure 4).

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, 30 December 2024 – 24 August 2025 (Weeks 1-34)

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	0	27	0	0	0	0	27	385	7
Mpumalanga	0	2	0	0	0	0	2	41	5
North West	0	17	0	0	0	0	17	232	7
Western Cape	1	69	1	0	0	0	71	465	15
Total	1	115	1	0	0	0	117	1123	10

Surveillance sites included primary health care clinics in 4 provinces: KwaZulu-Natal (Edendale Gateway 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

Influenza Surveillance in South Africa: 2025

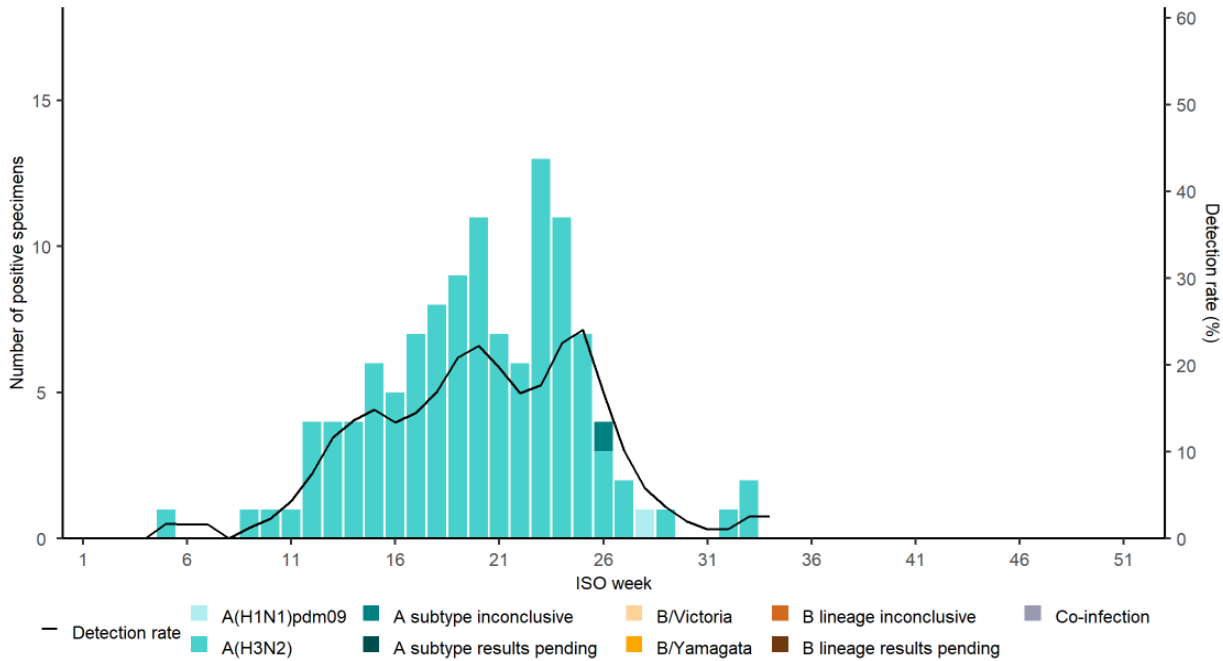


Figure 3. Number of influenza cases by subtype/lineage and detection rate by week - Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34) *Inconclusive: insufficient viral load in sample and unable to characterise further.

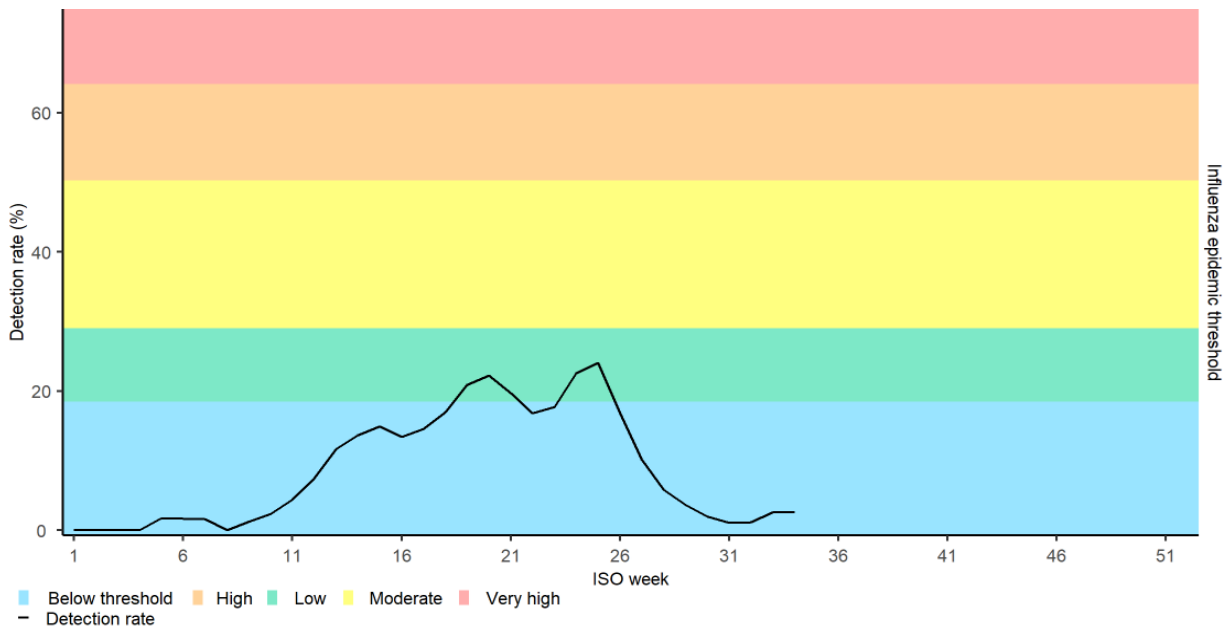


Figure 4. Influenza detection rate and epidemic thresholds*, Influenza-like Illness (ILI) Surveillance Programme at primary health care clinics, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

*influenza transmission thresholds based on 2022-2024 data and calculated using the Moving Epidemic Method (MEM)



1.5 Pneumonia Surveillance Programme

Specimens from 2839 patients hospitalised with severe respiratory illness were received from ten sentinel hospitals located in five provinces, and 162 (5.7%) influenza cases were detected. Among influenza-positive specimens that could be further characterised, 61.6% (175/284) were A(H3N2) (**Table 5**). The detection rate peaked in week 20 (**Figure 5**).

Data obtained through the Pneumonia Surveillance Programme among hospitalised patients in 2022-2024 were used to set MEM thresholds for the impact of influenza on morbidity and mortality. The impact of influenza in the 2025 season reached a low level (**Figure 6**).

Table 5. Number of influenza infections by subtype/lineage, and total number of specimens collected by province for the Pneumonia Surveillance Programme, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

Province	A(H1N1) pdm09	A(H3N2)	A subtype inconclusive*	B/Victoria	B lineage inconclusive*	Dual infection#	Total cases	Total specimens tested	Detection rate %
Gauteng	0	32	0	0	0	0	32	503	6
KwaZulu-Natal	1	25	2	0	0	0	28	425	7
Mpumalanga	0	12	1	0	0	0	13	322	4
North West	1	27	0	0	0	0	28	415	7
Western Cape	2	56	2	1	0	0	61	1174	5
Total	4	152	5	1	0	0	162	2839	6

Surveillance sites included hospitals in five provinces: Gauteng (Helen Joseph Hospital, Rahima Moosa Hospital), KwaZulu-Natal (Harry Gwala Memorial Hospital), Mpumalanga (Mapulaneng, Matikwana and Tintswalo Hospitals), North West (Klerksdorp-Tshepong Hospital Complex) and Western Cape (Red Cross Children’s Hospital and Mitchell’s Plain Hospital).

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

Influenza Surveillance in South Africa: 2025

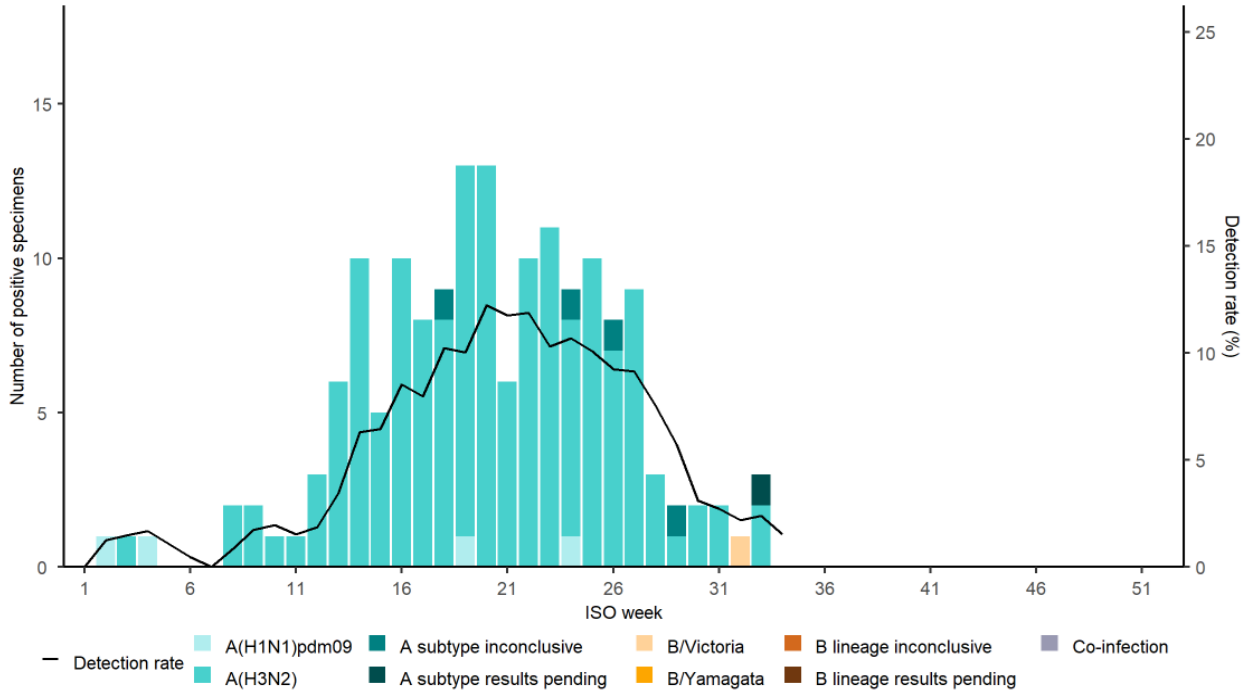


Figure 5. Number of influenza cases by subtype/lineage and detection rate by week – Pneumonia Surveillance Programme, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

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

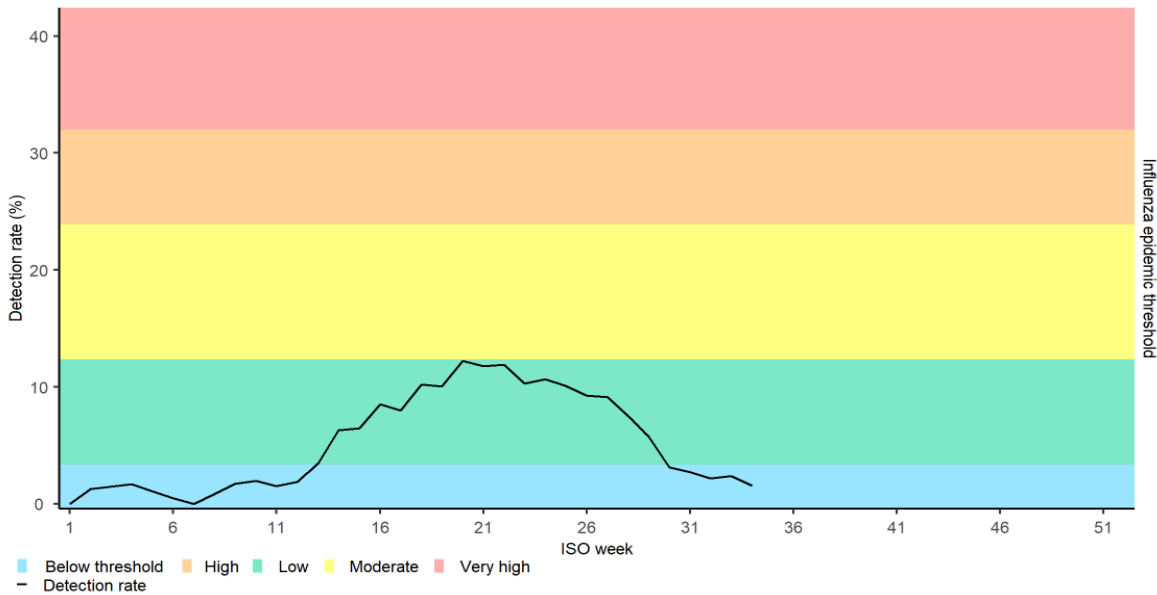


Figure 6. Influenza detection rate and epidemic thresholds*, Pneumonia Surveillance Programme, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

*Influenza transmission thresholds based on 2022-2024 data and calculated using the Moving Epidemic Method (MEM).



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 2025 influenza season.

Of the 768 surveillance cases enrolled in the VW programme during the 2025 influenza season and included in the vaccine effectiveness (VE) analysis (individuals aged ≥ 6 months with known vaccination and influenza status), 216 (28.1%) were classified as cases (influenza test positive) and 552 (71.9%) as controls (influenza test negative). Vaccine coverage was 3.4% (26/768) overall in the VW programme (**Table 6**): 1.9% (4/216) and 4.0% (22/552) among cases and controls respectively. The adjusted VE, accounting for timing within the season and age, was 51.3% (95% confidence interval [CI]: -31.3% to 86.0%) for any influenza. For influenza A(H3N2), the adjusted VE was 49.3% (95% CI: -36.9% to 85.5%) (**Table 6**).

Table 6: Vaccine coverage and vaccine effectiveness (VE) by subtype and age group, Viral Watch Surveillance Programme, South Africa, 24 March – 27 July 2025

	Vaccine coverage			Adjusted VE % (95% confidence interval)*
	Cases n/N (%)	Controls n/N (%)	Total n/N (%)	
All ages				
Any influenza	4/216 (1.9)	22/552 (4.0)	26/768 (3.4)	51.3 (-31.3; 86.0)
A(H1N1)pdm09	0/1 (0)	26/761 (3.4)	26/762 (3.4)	-499.7 (-9611.7; 95.8)
A(H3N2)	4/208 (1.9)	22/554 (4.0)	26/762 (3.4)	49.3 (-36.9; 85.5)
B/Victoria	0/1 (0)	26/767 (3.4)	26/768 (3.4)	-817.2 (-27805; 94.3)
Children aged <18 years				
Any influenza	1/62 (1.6)	2/102 (2.0)	3/164 (1.8)	9 (-899.7; 95.9)
A(H3N2)	1/59 (1.7)	2/102 (2.0)	3/161 (1.9)	3.9 (-960.3; 95.7)
Adults aged 18 – 64 years				
Any influenza	3/146 (2.1)	18/384 (4.7)	21/530 (4.0)	55.8 (-35.1; 89.8)
A(H3N2)	3/141 (2.1)	18/386 (4.7)	21/527 (4.0)	53.9 (-40.8; 89.4)
Adults aged ≥ 65 years				
Any influenza	0/8 (0)	2/66 (3.0)	2/74 (2.7)	Not determined
A(H3N2)	0/0 (0)	2/74 (2.7)	2/74 (2.7)	Not determined

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

2. Influenza virus isolation

During weeks 1 through 34 of 2025, influenza virus isolation was attempted for 147 (147/538, 27.3%) clinical specimens 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 isolation with an overall isolation rate of 77.6% (114/147) (**Table 7**).

Table 7: Summary of influenza virus isolations in Madin-Darby Canine Kidney (MDCK) cell cultures, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

Programme	Specimens cultured	Successful cultures	Number of cultures/ attempted (%)		
			A(H1N1)pdm09	A(H3N2)	B/Victoria
Viral Watch	62	47	2/2 (100)	45/58 (78)	0/2 (0)
Influenza-like illness surveillance	37	34	1/1 (100)	33/36 (92)	0/0
Pneumonia Surveillance	48	33	1/1 (100)	32/47 (68)	0/0
Total	147	114	4/4 (100)	110/141 (78)	0/2 (0)

3. Influenza specimens shared with WHO Collaborating Centres

Influenza virus cultures and original specimens from 90 individuals, representative of different age groups and geographic locations, were shared in three shipments between June and August 2025 with the WHO Global Influenza Surveillance and Response System (GISRS) Collaborating Centres (WHO-CC) in Australia and the United States of America for antigenic and genetic characterisation (**Table 8**). Among specimens shared, 95.6% (86/90) were A(H3N2), 3.3% (3/90) were A(H1N1)pdm09 and 1.0% (1/90) were B/Victoria.

Table 8: Summary of influenza virus specimens collected in South Africa and shared with WHO-CCs, 30 December 2024 – 24 August 2025 (Weeks 1-34)

WHO-CC	A(H1N1)pdm09	A(H3N2)	B/Victoria	Total
Australia	1	59	0	60
United States of America	2	27	1	30
Total	3	86	1	90

4. Antigenic characterisation of influenza virus isolates

The haemagglutination inhibition (HAI) assays performed at the NIC in South Africa, and results for subtype/lineage confirmation 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) titres of ≥ 4 (N=75).



Subtype/lineage was confirmed phenotypically for 75 viruses, including 4 A(H1N1)pdm09, 69 A(H3N2), and 2 B/Victoria cultures (**Table 9**). 7.2% (5/69) of A(H3N2) viruses recognised A/Delaware/01/2021 (Clade 2a.2a, subclade G.1) antisera poorly.

Table 9: Summary of haemagglutination inhibition (HAI) assay results, South Africa, 30 December 2024 – 24 August 2025 (Weeks 1-34)

Programme	Number of cultures with HA titres	A(H1N1)pdm09	A(H3N2)	B/Victoria
		A/Victoria/2570/2019 (Clade 5a.2, subclade C)	A/Delaware/01/2021 (Clade 2a.2a, subclade G.1)	B/Michigan/01/2021 (Clade V1A.3a.2, subclade C)
		Low reactors/ Total tested (%)	Low reactors/ Total tested (%)	Low reactors/ Total tested (%)
Viral Watch	33	0/2 (0)	2/29 (7)	0/2 (0)
Influenza-like illness	21	0/1 (0)	1/20 (5)	0/0
Pneumonia Surveillance	21	0/1 (0)	2/20 (10)	0/0
Total n/N (% per virus)	75	0/4 (0)	5/69 (7)	0/2 (0)

HAI testing using ferret antisera was conducted on South African viruses at WHO-CCs. Antigenic characterisation results that were available from samples shared with the WHO-CC in Australia (VIDRL) showed that all tested (2/2) A(H1N1)pdm09 viruses were A/Victoria/4897/2022-like (clade 5a.2a.1, subclade D), 92.6% (25/27) of A(H3N2) viruses were A/Croatia/10136RV/2023-like (clade 2a.3a.1, subclade J.2) and all (1/1) B/Victoria viruses were B/Austria/1359417/2021-like (clade V1A.3a.2, subclade C). Among samples tested at the WHO-CC in the USA (US CDC) for which results were available, all (1/1) A(H1N1)pdm09 viruses were antigenically A/Wisconsin/67/2022-like (clade 5a.2a, subclade C.1.9.3), and 93.8% (15/16) of A(H3N2) viruses were antigenically A/Massachusetts/18/2022-like (clade 2a.3a.1, subclade J.2.2).

5. Neuraminidase inhibitor susceptibility

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 were predicted using Flusurver (<https://flusurver.bii.a-star.edu.sg/>). The mutational analysis of the neuraminidase (NA) gene of 2025 South African viruses with available sequences (A(H1N1)pdm09 n=2, A(H3N2) n=319 and B/Victoria n=1) revealed five (1.6%, 5/319) A(H3N2) viruses that contained substitutions associated with reduced inhibition. A/South_Africa/NICD-R03783/2025 carried the K249E substitution and two viruses (A/South_Africa/NICD-R05224/2025 and A/South_Africa/NICD-R03766/2025) carried the S329R substitution; both substitutions have been associated with reduced inhibition by oseltamivir. Finally, S331R/G was detected in



two viruses (A/South_Africa/NICD-R03832/2025 and A/South_Africa/4762/2025), a substitution linked to reduced inhibition by both oseltamivir and zanamivir.

Two A(H3N2) viruses with substitutions associated with reduced susceptibility (A/South_Africa/NICD-R03783/2025 and A/South_Africa/NICD-R05224/2025) A(H3N2) were tested phenotypically at the NICD using the neuraminidase inhibition (NAI) assay against three antivirals (oseltamivir, zanamivir and peramivir); both viruses showed normal inhibition.

6. Genetic characterisation of influenza viruses

Influenza viruses circulating in 2025 in South Africa were genetically characterised by whole genome sequencing (WGS) and shared on Global Initiative on Sharing All Influenza Data (GISAID). Sequences of viruses circulating in South Africa in 2025 (n=354) were obtained from GISAID on the 25 August 2025. These included viruses collected through respiratory illness surveillance programmes and sequenced by the NICD [A(H3N2) n=320 and A(H1N1)pdm09 n=1], and by WHO-CCs in Australia and the USA [A(H3N2) n=31, A(H1N1)pdm09 n=1 and B/Victoria n=1]. In the case where the same virus was sequenced at both a WHO-CC and the NICD, only one sequence with the highest quality data was retained; therefore, 324 viruses were analysed [A(H3N2) n=321, A(H1N1)pdm09 n=2 and B/Victoria n=1]. 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. Clades and subclades were identified by specific amino acid mutations relative to a designated reference strain on NextClade.

6.1 Influenza A(H1N1)pdm09

Two A(H1N1)pdm09 viruses detected in South Africa in 2025 were sequenced: one belonged to clade 6B.1A.5a.2a (5a.2a), which dominated the 2024 influenza season, and one belonged to clade 6B.1A.5a.2a.1 (5a.2a.1), which circulated at low levels in 2024 (**Figure 7**). The 2024 clade 5a.2a viruses consisted of two main subclades: C.1.9 and C.1.8, with the 2025 virus in this clade clustering within the C.1.9.3 subclade (D129N, H273Y, E283D). The 2025 5a.2a.1 clade virus belonged to the D.3.1 subclade (R113K). The 2025 southern hemisphere A(H1N1)pdm09 vaccine strain (A/Victoria/4897/2022) is a clade 5a.2a.1 (subclade D) virus (**Figure 6**).

6.2 Influenza A(H3N2)

Genetic analysis of the HA gene from South African A(H3N2) viruses collected in 2025 showed that all viruses (n=321) clustered within clade 3C.2a1b.2a.3a.1 (2a.3a.1), together with the 2025 southern hemisphere vaccine strain (A/Croatia/10136RV/2023) (**Figure 8**). The majority were assigned to subclade J.2.2 (86.6%, 278/321) and shared the T65K and N145S substitutions; the remainder were classified as subclades J.2 (12.1%, 39/321), J.2.4 (0.6%, 2/321), J.2.3 (0.3%, 1/321) and J.2.1 (0.3%, 1/321). All 2025 viruses carried the N122D substitution, removing the N122 glycosylation site. Within the J.2 subclade, 71.8% (28/39) of viruses had the T135A/K substitution, which removes the N133 glycosylation site. In addition to the loss of the glycosylation site above (N122), J.2.2 subclade viruses additionally lost the N63 site via T65K, and J.2.4 viruses lost the N133 site via



T135K. The 2025 southern hemisphere vaccine strain (A/Croatia/10136RV/2023) is a clade 2a.3a.1 (subclade J.2) virus.

6.3 Influenza B/Victoria

Only one B/Victoria virus from 2025 was sequenced, and the virus clustered within clade V1A.3a.2, characterised by A127T, P144L, and K203R substitutions, consistent with viruses circulating in recent years (**Figure 9**). The virus was assigned to subclade C.5.7 (E128G). The 2025 southern hemisphere vaccine strain (B/Austria/1359417/2021) also belongs to clade V1A.3a.2 (subclade C).

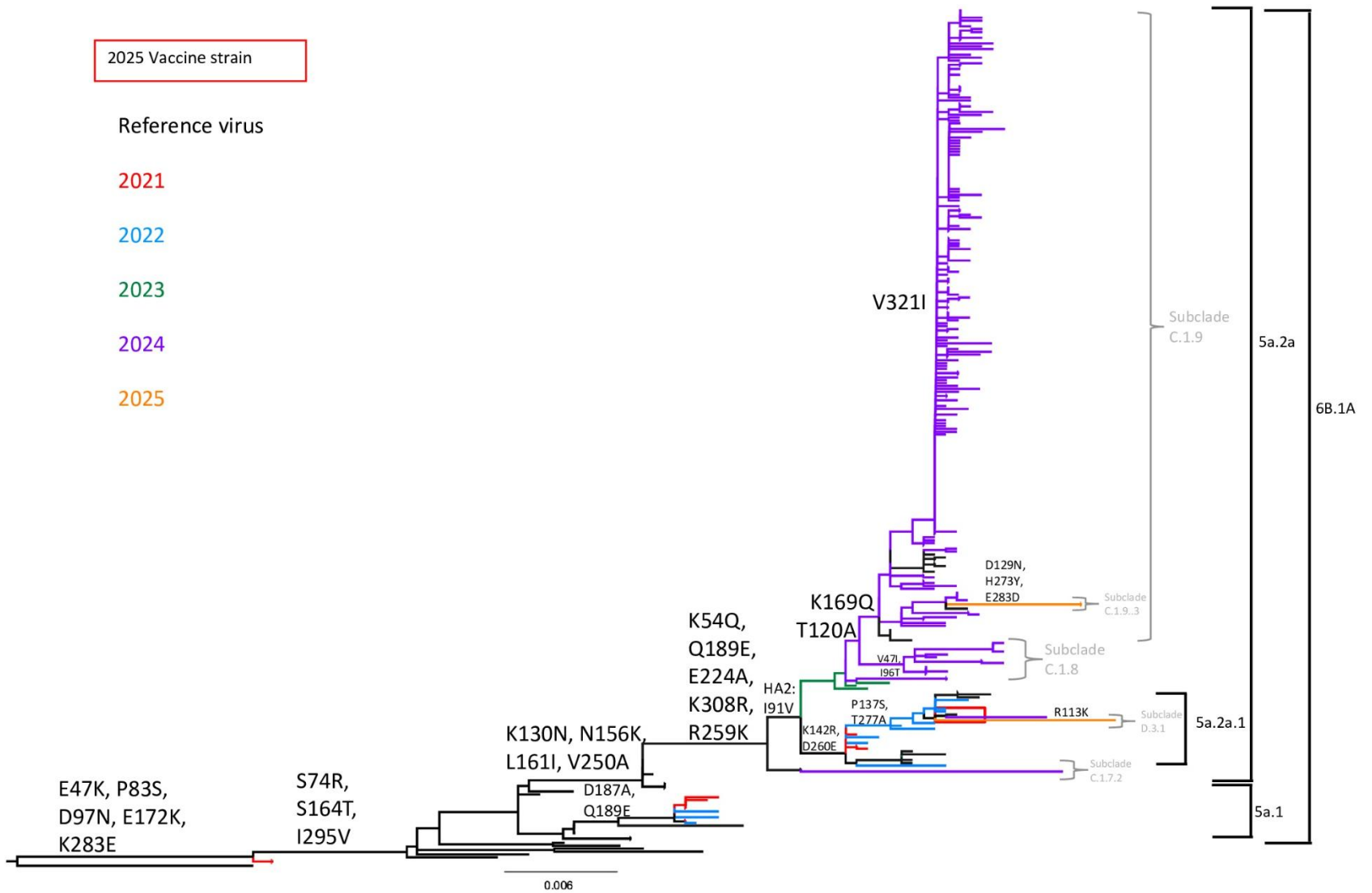


Figure 7. Maximum likelihood phylogenetic tree (best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H1N1)pdm09 viruses. The 2025 southern hemisphere vaccine strain is indicated in a red box (A/Victoria/4897/2022) and South African 2025 viruses in orange (n=2). The tree additionally includes all South African A(H1N1)pdm09 viruses with sequences available from 2021-2024 and representative global reference strains. A/California/07/2009 was used as the root.

Influenza Surveillance in South Africa: 2025

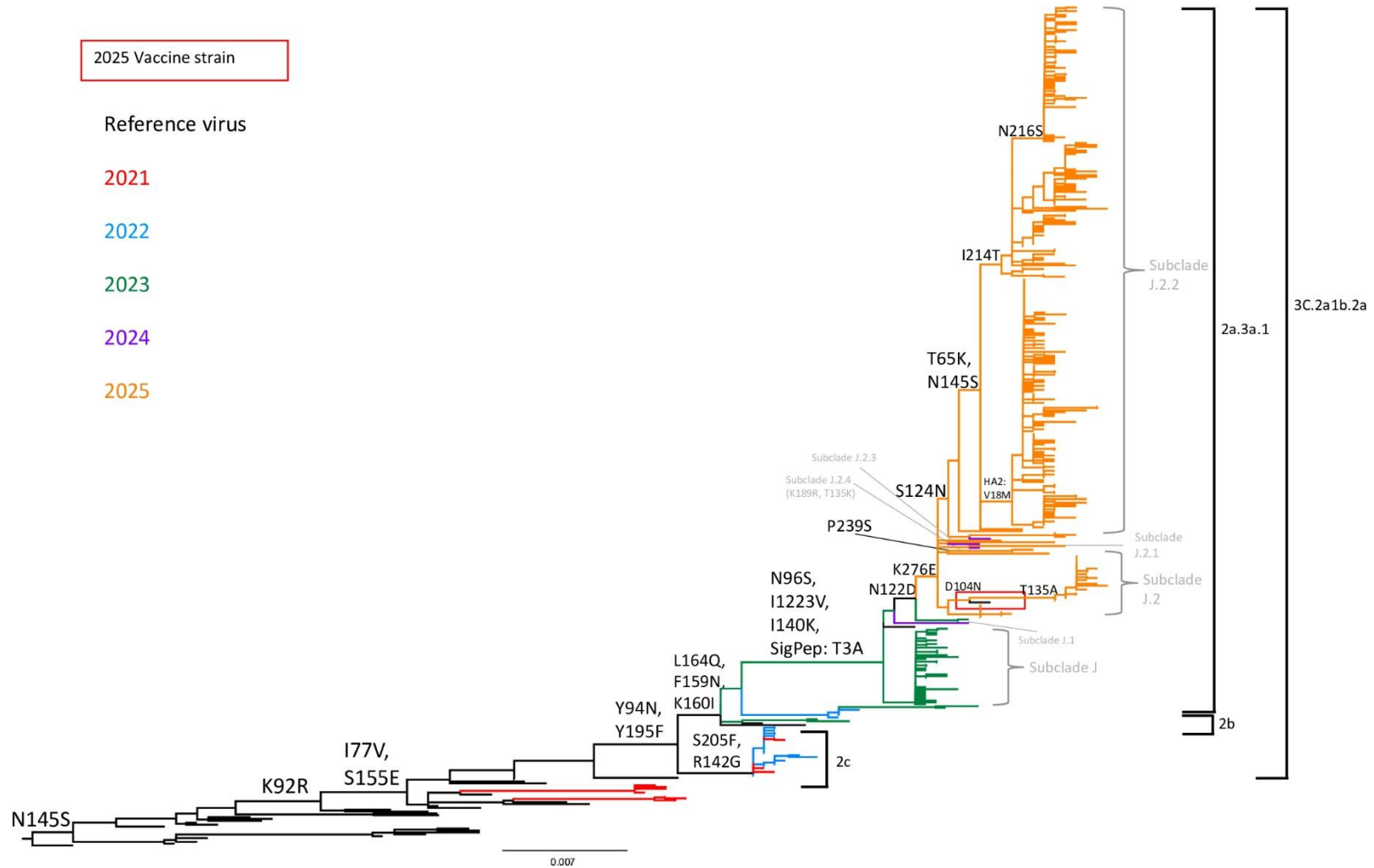


Figure 8. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza A(H3N2) viruses. The 2025 southern hemisphere vaccine strain (A/Croatia/10136RV/2023) is indicated in a red box and South African 2025 viruses in orange (n=321). The tree additionally includes all South African A(H3N2) viruses with sequences available from 2021-2024 and representative global reference strains. A/Texas/50/2012 was used as the root.

Influenza Surveillance in South Africa: 2025

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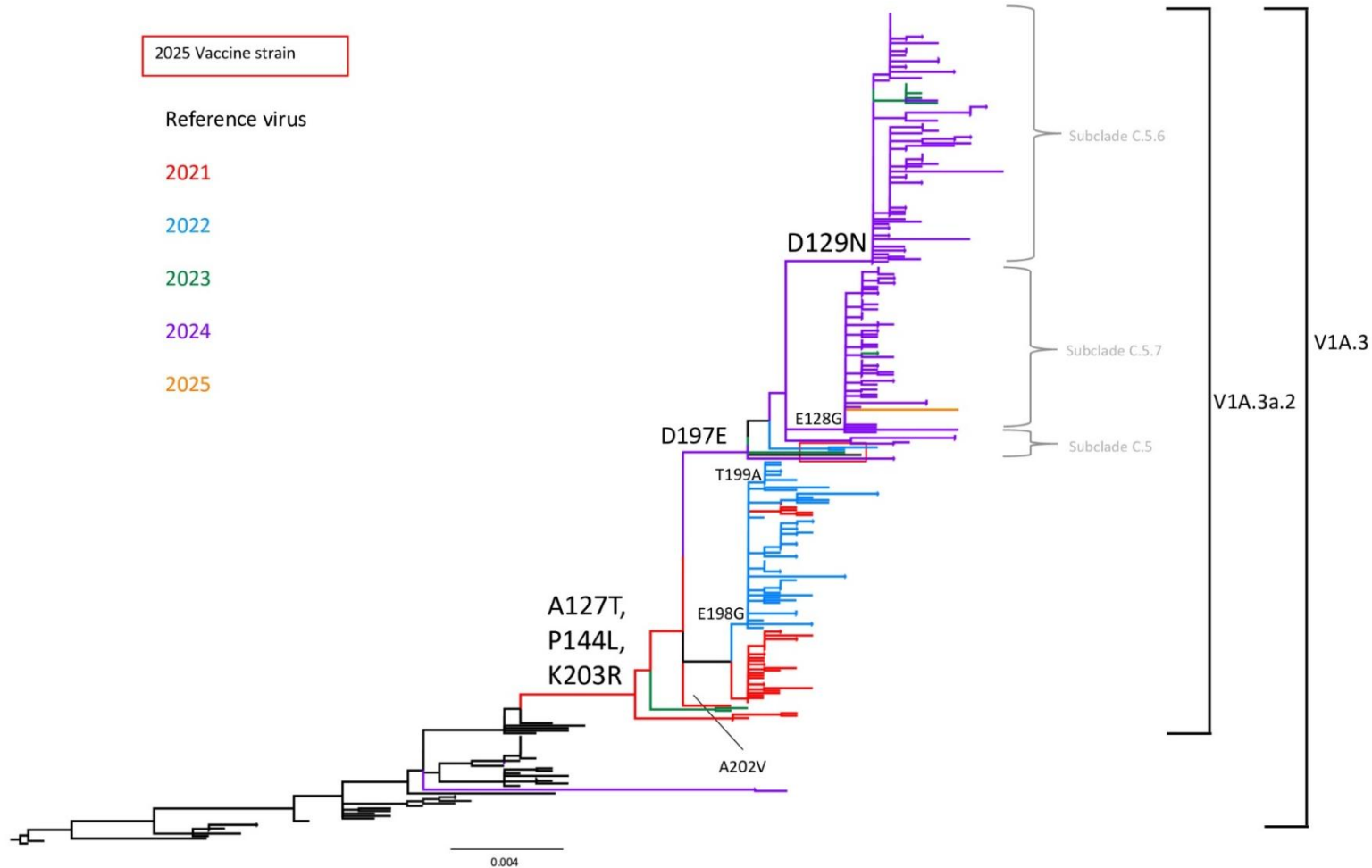


Figure 9. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin (HA) gene of influenza B/Victoria viruses. The 2025 southern hemisphere vaccine strain (B/Austria/1359417/2021) is indicated in a red box and South African 2025 virus in orange (n=1). The tree additionally includes all South African B/Victoria viruses with sequences available from 2021-2024 and representative global reference strains. B/Brisbane/60/2008 was used as the root.

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8. Acknowledgements

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ILI Surveillance Programme

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Jouberton Clinic, North West Province
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Pneumonia Surveillance Programme

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