INFLUENZA SURVEILLANCE IN SOUTH AFRICA:

WEEKS 1 - 32, 2022

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Summary

This report summarizes the results of influenza surveillance in South Africa for the period of week 1 through week 32, 2022, 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 2022, influenza activity was observed from week 1 through 32, with an increased period of activity in the normal winter influenza season. Influenza circulation was dominated by A(H1N1)pdm09, followed by A(H3N2) and B/Victoria. While some antigenic drift was observed, strains fell within the same phylogenetic clades as 2022 Southern Hemisphere vaccine strains. This report includes data from individuals meeting syndromic case definitions within three respiratory illness surveillance programmes: Viral Watch influenza-like illness (VW) surveillance in outpatients (n=732) at private general practitioners, influenza-like illness (ILI) surveillance in outpatients (n=1028) at public health clinics and pneumonia surveillance in hospitalized patients (n=4340). Together, the three surveillance programmes contributed data from all nine provinces in South Africa. Influenza activity was observed from weeks 1 through 32, with an overall detection rate for 2022 from 3 January through 14 August of 11% (648/6100). Using the Moving Epidemic Method (MEM), the levels of activity reached moderate and low levels in the ILI and pneumonia surveillance programmes, respectively. Influenza single infections were dominated by influenza A(H1N1)pdm09 (62%, 387/621), followed by A(H3N2) (30%, 186/621) and B/Victoria (8%,

48/621). Dual infections were detected in three individuals [A(H1N1)pdm09 and B lineage inconclusive, A(H1N1)pdm09 and A(H3N2), A(H1N1)pdm09 and B/Victoria]. Influenza B/Yamagata was not detected. Subtype/lineage could not be determined for 4% (24/648) of infections, due to low viral load. Despite a low vaccine coverage (12%, 61/521) in the Viral Watch programme, vaccine effectiveness for any influenza, influenza A(H1N1)pdm09 and influenza A(H3N2) adjusted for age and season was 65% (95%CI: 30%, 82%), 46% (95% CI: -20%, 76%) and 91% (95%CI: 31%, 99%), respectively. Vaccine effectiveness for influenza B/Victoria could not be determined due to small numbers. Cell culture-derived influenza virus isolates were obtained with an 85% (155/183) success rate. Haemagglutinin inhibition (HAI) assays performed at the NICD demonstrated that 46% (29/63) of tested A(H1N1)pdm09, 100% (22/22) of A(H3N2) and 100% (9/9) of B/Victoria viruses were recognized by antisera raised against current vaccine and vaccine-like strains. All samples tested for (12/12 A(H1N1) pdm09 and 3/3 A(H3N2)) were susceptible to zanamivir, oseltamivir, peramivir and laninamivir. No known resistance mutations were detected among the 91 sequenced viruses. Genetic analysis of the haemagglutinin gene of South African 2022 influenza viruses was available for 80 A(H1N1)pdm09, 9 A(H3N2) and 2 B/Victoria viruses. Influenza A(H1N1)pdm09 viruses clustered into two major genetic subgroups namely 6B.1A.5a.1 and 6B.1A.5a.2, with the majority (59/80, 74%) belonging to the 6B.1A.5a.2 clade together with the 2022 A(H1N1)pdm09 vaccine strain for the Southern Hemisphere (A/Victoria/2570/2019). All A(H3N2) strains clustered within the 3C.2a1b.2a.2 clade along with the current Southern Hemisphere A(H3N2) vaccine strain (A/Darwin/9/2021). Both B/Victoria viruses clustered in the V1A.3a.2 subclade together with the current Southern Hemisphere influenza vaccine strain (B/Austria/1359417/2021). Following easing of COVID-19 restrictions, South Africa experienced the first typical influenza season since the start of the pandemic. The influenza season was ongoing as of week 43 of 2022, with a biphasic pattern in which infections later in the season were dominated by B/Victoria and A(H3N2) viruses. Individuals, especially those in high risk categories, are encouraged to receive the annual influenza vaccine.

Introduction

Influenza epidemics in South Africa usually occurring between April and October, with a peak during the winter months.[1,2] The following strains were recommended for the trivalent and quadrivalent inactivated influenza vaccine (IIV) 2022 Southern Hemisphere influenza season:

Egg-based tri/quadri-valent vaccines including:

- an A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an A/Darwin/9/2021 (H3N2)-like virus;
- a B/Austria/1359417/2021 (B/Victoria lineage) like- virus; and
- a B/Phuket/3073/2013-like (B/Yamagata lineage) virus (quadrivalent vaccine only)

These recommendations included a change to the A(H3N2) and B/Victoria lineage component of egg-based vaccines strains compared with the 2021 Southern Hemisphere trivalent and quadrivalent IIV. For A(H3N2) vaccine virus component, A/Hong Kong/2671/2019-like virus was replaced with A/Darwin/9/2021-like virus and for B/Victoria lineage vaccine virus component, B/Washington/02/2019-like virus was replaced with a B/Austria/1359417/2021-like virus. In South Africa, the trivalent IIV was only available in the public sector (at designated clinics and hospitals), the quadrivalent IIV was available mostly in the private sector with limited doses in public sector, generally from March or April.

Methods

South Africa has three influenza surveillance programmes coordinated by the Centre for Respiratory Diseases and Meningitis (CRDM) at the National Institute for Communicable Diseases (NICD). 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 (Table 1).

Table 1. Characteristics of influenza and respiratory surveillance programmes in South Africa, 2022.

Programme	Viral Watch	Influenza-like illness surveillance	National syndromic surveillance for pneumonia
Start year	1984	2012	2009
Provinces*	EC, FS, GP, LP, MP, NC, NW, WC	KZN, NW, WC, MP	GP, KZN, MP, NW, WC, EC
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 fever (≥38°C), cough and symptom onset ≤10 days or **Suspected SARS-CoV-2:** Any person presenting with an acute (≤14 days) respiratory tract infection or other clinical illness compatible with COVID-19**	An acute respiratory illness with fever (≥38°C), cough and symptom onset ≤10 days or **Suspected SARS-CoV-2:** Any person presenting with an acute (≤14 days) respiratory tract infection or other clinical illness compatible with COVID-19**	Acute (symptom onset ≤10 days) or chronic (symptom onset >10 days) lower respiratory tract infection requiring hospitalisation or **Suspected SARS-CoV-2:** Any person admitted with a physician-diagnosis of suspected COVID-19 and not meeting SRI case definition
Specimens collected	Throat swabs and/or nasal/nasopharyngeal swabs	Combined oropharyngeal and nasopharyngeal swabs	Combined oropharyngeal and nasopharyngeal 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 ** Symptoms include ANY of the following respiratory symptoms: cough, sore throat, shortness of breath, anosmia (loss of sense of smell) or dysgeusia (alteration of the sense of taste), with or without other symptoms (which may include fever, weakness, myalgia, or diarrhoea)

Nasopharyngeal/nasal swabs were tested using the Allplex™ SARS-CoV-2/influenza/RSV commercial kit (Seegene, Seoul, Korea) and the US Centres for Disease Control and Prevention (CDC) subtyping method (with reagents sourced through the International Reagent Resource, IRR Portal).

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] 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 health care provision.

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 an outpatient influenza sentinel surveillance programme (Viral Watch) in South Africa during the 2022 influenza season were included in the analysis.

During 2022, influenza virus isolation was attempted on 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 isolations. Influenza virus cultures and original specimens were shared with the WHO Collaborating Centres for Influenza Surveillance and Research (WHO-CC) in Australia, United Kingdom and United States for antigenic and genetic characterization. Haemagglutination inhibition (HAI) assays were performed at the NIC in South Africa. Turkey red blood cells were used as indicator cells in the HA and HAI assays. All the HAI assays were completed using the IRR 2021-2022 WHO influenza reagent kit for identification of influenza isolates (CDC International Reagent Resource). HAIs were performed for all isolates with HAI titers.

Phenotypic susceptibility testing to zanamivir, oseltamivir, peramivir and laninamivir was performed for South African samples at the WHO Collaborating Centre in Australia (VIDRL). Genotypic analysis for resistance mutation detection was performed on CLC Genomics Workbench (Qiagen, Hilden, Germany) using the following GenBank references: 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/).

All influenza sequences analysed were obtained from GISAID on 25 August 2022. Viruses with incomplete sequence data for the haemagglutinin (HA) gene were excluded from the analysis. Genetic characterisation was carried out by phylogenetic analysis (using the Aliview alignment editor and IQTREE v1.6.12 software with ultrafast bootstraps) of the HA gene. Groups and sub-groups were identified by specific amino acid mutations relative to a designated reference strain on NextClade.

Results

From 3 January 2022 (week 1) through 14 August 2022 (week 32), 6179 individuals were enrolled and respiratory specimens from 6100 (99%) individuals were tested through the three surveillance programmes (Table 2). Influenza infections were identified in 648 individuals, resulting in an overall detection rate of 11% (648/6100). Influenza detections occurred from week 1 through 32. Influenza single infections were dominated by influenza A(H1N1)pdm09 (62%, 387/621), followed by A(H3N2) (30%, 186/621) and B/Victoria (8%, 48/621). Dual infections were detected in three individuals [A(H1N1)pdm09 and B lineage inconclusive, A(H1N1)pdm09 and A(H3N2), A(H1N1)pdm09 and B/Victoria]. Influenza B/Yamagata was not detected. Inconclusive results for subtyping occurred in 4% (24/648) of samples. The latter samples had a primary identification reverse transcription real-time polymerase chain reaction (rRT-PCR) cycle threshold (C_t) value greater than 35 and subsequent characterisation PCR was not performed to determine the subtype/lineage. The 2022 influenza season started in week 17 (week starting 25 April 2022) when the influenza detection rate among patients in the pneumonia surveillance programme breached the epidemic threshold as determined by the Moving Epidemic Method (MEM), and was continuing at the time of this report (week 32). The mean onset of influenza season in South Africa in 2005-2019 was week 17 (3rd week of April), ranging from week 16 to week 25.

Table 2. Numbers of influenza infections identified in all syndromic influenza surveillance programmes, South Africa, 3 January – 14 August 2022 (weeks 1-32).

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	B/ Yamagata	
			n (% of total influenza positives)								
Viral Watch	732	257 (35)	235 (91)	5 (2)	152 (59)	78 (30)	20 (8)	2 (1)	18 (7)	0	2 (1)
Influenza-like illness surveillance	1028	152 (15)	138 (91)	3 (2)	91 (60)	44 (29)	13 (9)	1 (1)	12 (8)	0	1 (1)
Pneumonia surveillance	4340	239 (6)	216 (90)	8 (3)	144 (60)	64 (27)	23 (10)	5 (2)	18 (8)	0	0
Total	**6100**	**648 (11)**	**589 (91)**	**16 (2)**	**387 (60)**	**186 (29)**	**56 (9)**	**8 (1)**	**48 (7)**	**0**	**3 (0)**

*Inconclusive: insufficient viral load in sample and unable to characterise further; #Dual infections: A(H1N1)pdm09 and B lineage inconclusive, A(H1N1)pdm09 and A(H3N2); A(H1N1)pdm09 and B/Victoria

Viral Watch programme

Specimens from 732 patients were received and tested from VW practitioners located in 7 of the 8 provinces participating in surveillance (Table 3), with the majority of specimens received from Gauteng (468/732, 64%) and Western Cape (178/732, 24%) provinces. Influenza was detected in 257 (35%) patients, of which 91% (235/257) were influenza A, 8% (20/257) were influenza B and 1% (2/257) were dual infections (Figure 1, Table 3). Among the influenza A infections for which a subtype could be determined, 66% (152/230) were A(H1N1)pdm09 and 34% (78/230) were A(H3N2). All influenza B infections for which a lineage was determined were B/Victoria (18/18). The two dual infections detected were (i) A(H1N1)pdm09 and B lineage inconclusive and (ii) A(H1N1)pdm09 and A(H3N2).

Table 3. Numbers of influenza infections by subtype/lineage, and total number of specimens tested by province in the Viral Watch surveillance programme, South Africa, 3 January – 14 August 2022 (Weeks 1-32).

Province	A(H1N1) pdm09	A (H3N2)	A subtype inconclusive*	B /Victoria	B /Yamagata	B lineage inconclusive*	Dual infection#	Total cases	Total specimens tested	Detection rate (%)
Eastern Cape	20	6	0	4	0	2	0	32	45	**71**
Free State	7	0	0	0	0	0	0	7	8	**88**
Gauteng	80	24	4	8	0	0	2	118	468	**25**
Limpopo	2	2	1	1	0	0	0	6	8	**75**
Mpumalanga	7	0	0	1	0	0	0	8	19	**42**
Northern Cape	0	0	0	0	0	0	0	0	0	**-**
North West	3	0	0	0	0	0	0	3	6	**50**
Western Cape	33	46	0	4	0	0	0	83	178	**47**
Total	**152**	**78**	**5**	**18**	**0**	**2**	**2**	**257**	**732**	**35**

*Inconclusive: insufficient viral load in sample and unable to characterise further; # A(H1N1)pdm09 and B lineage inconclusive, A(H1N1)pdm09 and A(H3N2)

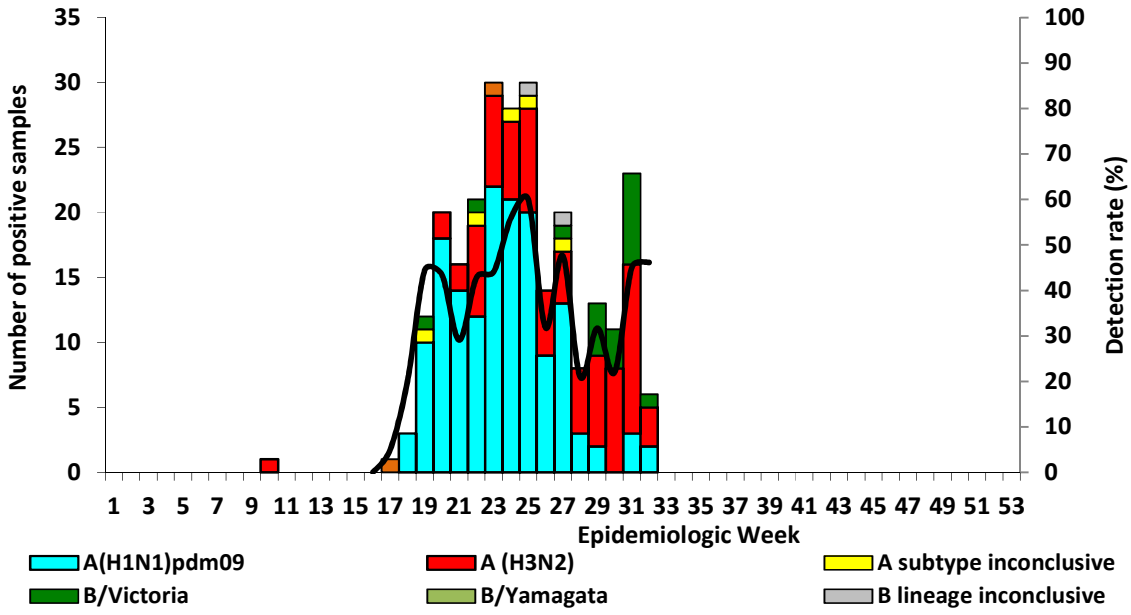

Figure 1. Number of influenza infections by influenza subtype/lineage and detection rate by epidemiologic week - Viral Watch programme for influenza-like illness surveillance, South Africa, Weeks 1 to 32, 2022 (n=257). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infections: A(H1N1)pdm09 and B lineage inconclusive, A(H1N1)pdm09 and A(H3N2).

Influenza-like illness (ILI) surveillance programme at primary health care clinics

Specimens from 1028 patients with ILI were received from five primary health care clinics located in four provinces. In total, 152 (15%) individuals tested positive for influenza. Among the single infections that could be further characterised, influenza A(H1N1)pdm09 accounted for 62% (91/147), A(H3N2) for 30% (44/147) and influenza B/Victoria for 8% (12/147) of cases. One individual had a dual infection [A(H1N1)pdm09 and B/Victoria]. Influenza B/Yamagata was not detected in 2022 (Table 4, Figure 2). The influenza detection rate increased from week 13, peaking in week 23 (48%, 25/52), and subsequently decreased (Figure 2). Individuals aged ≥5 years accounted for 76% (116/152) of influenza infections.

Table 4. Number of influenza cases by subtype/lineage, and total number of specimens collected by province for the influenza-like illness surveillance programme at primary healthcare clinics, South Africa, Weeks 1-32, 2022 (n=152).

Province	A(H1N1) pdm09	A (H3N2)	A subtype inconclusive*	B/ Victoria	B/ Yamagata	B lineage inconclusive*	Dual infection#	Total cases	Total specimens	Detection rate
KwaZulu-Natal	22	26	0	1	0	0	0	49	295	**17**
Mpumalanga	20	0	0	10	0	1	0	31	167	**19**
North West	24	0	1	0	0	0	0	25	217	**12**
Western Cape	25	18	2	1	0	0	1	47	349	**13**
Total	**91**	**44**	**3**	**12**	**0**	**1**	**1**	**152**	**1028**	**15**

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: A(H1N1)pdm09 and B/Victoria.

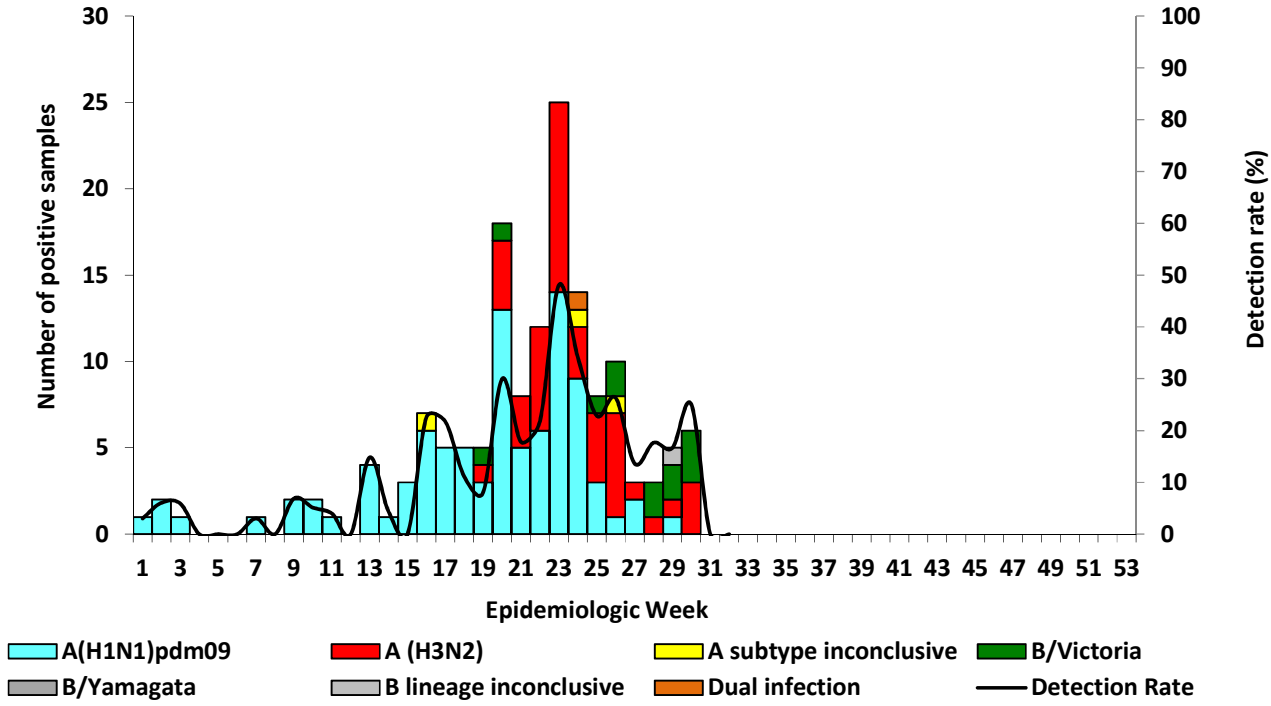

Figure 2. Number of influenza cases by subtype/lineage and detection rate by epidemiologic week - Influenza-like illness (ILI) surveillance programme at primary health care clinics, South Africa, Weeks 1 to 32, 2022 (n=152). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infection: A(H1N1)pdm09 and B/Victoria

Using the MEM, with a baseline determined from previous years (2012-2019), the estimated level of influenza disease transmission in the community reached a level of moderate activity in week 23 of 2022 in the ILI surveillance programme at public healthcare clinics (Figure 3).

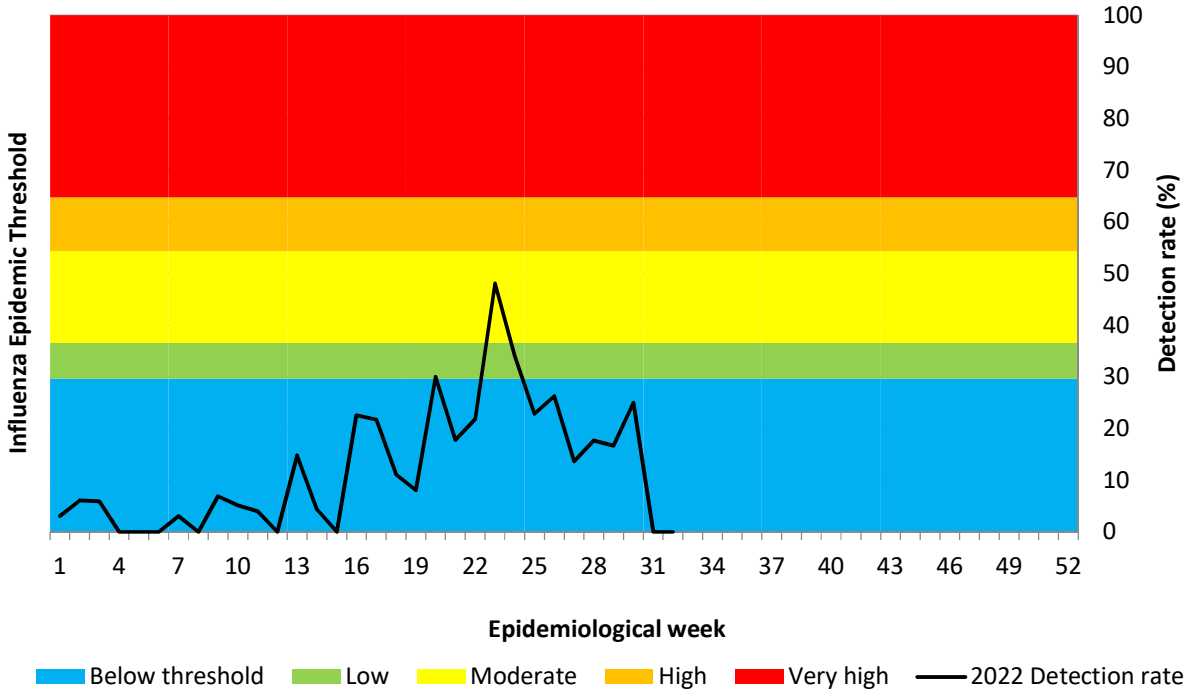

Figure 3. Influenza detection rate and epidemic thresholds*, influenza-like illness surveillance at primary health care clinics, South Africa, 3 January – 14 August 2022 (Weeks 1-32).
*Influenza transmission thresholds based on 2012-2019 data and calculated using the Moving Epidemic Method (MEM)

Pneumonia surveillance programme

Specimens from 4340 patients hospitalised with severe respiratory illness were received from the thirteen sentinel hospitals located in six provinces, and 239 (6%) influenza cases were detected. Among influenza-positive samples which could be further characterised, 64% (144/226) were A(H1N1)pdm09, 28% (64/226) were A(H3N2) and 8% (18/226) were B/Victoria (Table 5). Influenza B/Yamagata infection was not detected in the pneumonia surveillance programme in weeks 1 through 32 of 2022. The influenza detection rate increased from week 16, with a peak detection rate of 16% (30/188) in week 25, and subsequently decreased (Figure 4). Individuals aged ≥5 years accounted for 56% (134/239) of influenza cases. The impact of the 2022 influenza disease was estimated to be low from week 17 through week 27, and was below the threshold outside of this time period (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, 3 January – 14 August 2022 (Weeks 1-32).

Province	A(H1N1) pdm09	A(H3N2)	A subtype inconclusive*	B/ Victoria	B/ Yamagata	B lineage inconclusive*	Total cases	Total specimens tested	Detection rate %
Eastern Cape	8	1	1	6	0	2	18	212	**8**
Gauteng	37	13	1	3	0	3	57	1110	**5**
KwaZulu-Natal	26	12	1	1	0	0	40	630	**6**
Mpumalanga	29	4	1	6	0	0	40	592	**7**
North West	27	1	0	0	0	0	28	368	**8**
Western Cape	17	33	4	2	0	0	56	1428	**4**
Total	**144**	**64**	**8**	**18**	**0**	**5**	**239**	**4340**	**6**

Surveillance sites included hospitals in six provinces: Gauteng (Helen Joseph Hospital, Rahima Moosa Hospital, Tembisa Hospital), KwaZulu-Natal (Edendale Hospital), Mpumalanga (Mapulaneng, Matikwana and Tintswalo Hospitals), North West (Klerksdorp-Tshepong Hospital Complex) and Western Cape (Red Cross Children's Hospital, Tygerberg Hospital and Mitchell's Plain Hospital). *Inconclusive: insufficient viral load in sample and unable to characterise further

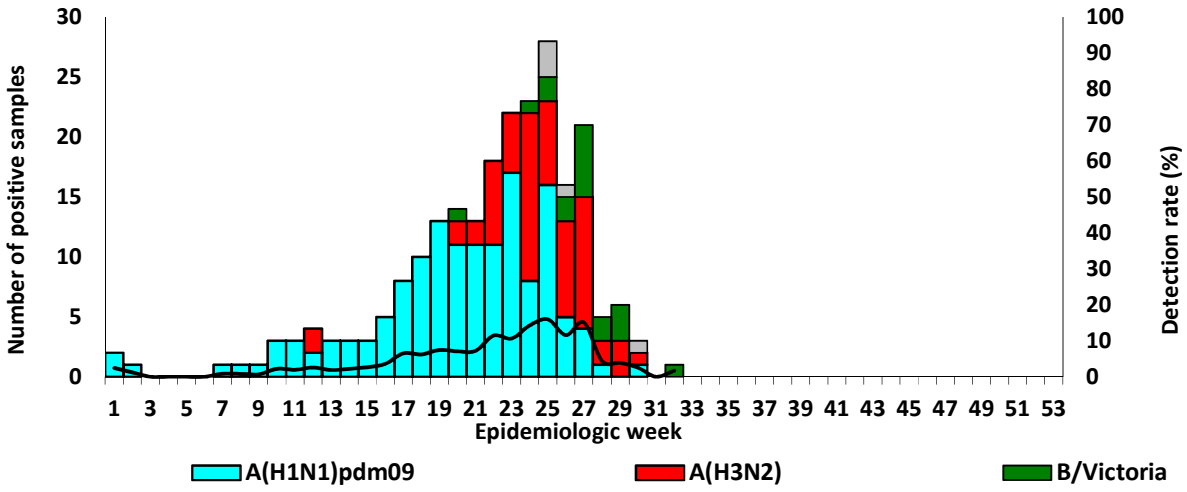

Figure 4. Number of influenza cases by subtypes/lineages and detection rate by epidemiologic week – National pneumonia surveillance, South Africa, 3 January – 14 August 2022 (Weeks 1-32). Inconclusive: insufficient viral load in sample and unable to characterise further.

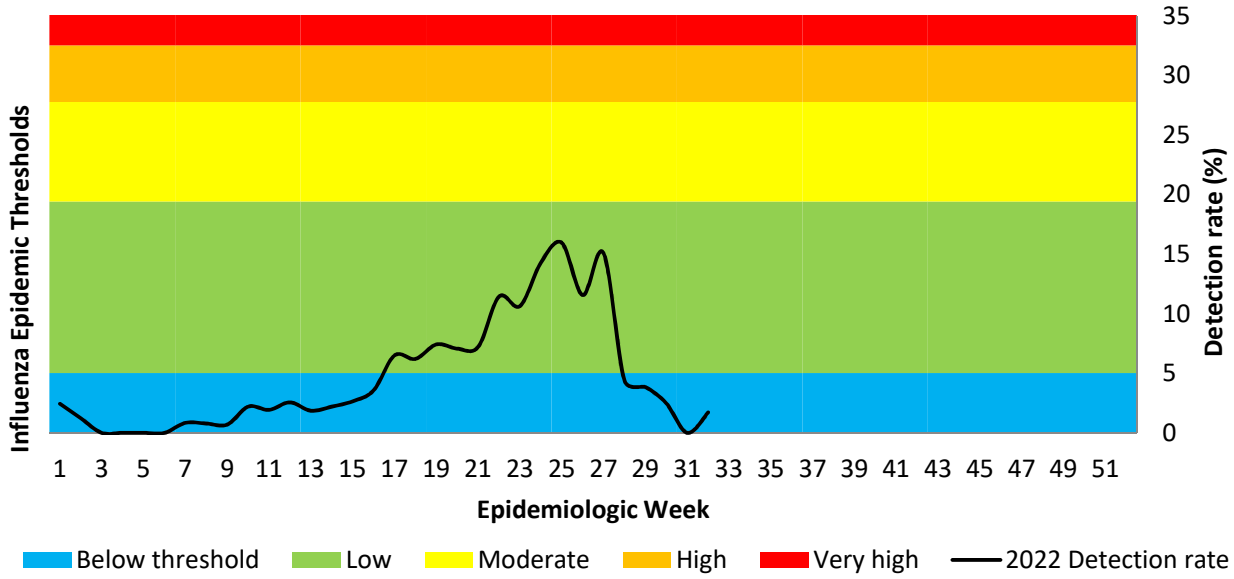

Figure 5. Influenza detection rate and epidemic thresholds*, National pneumonia surveillance programme, South Africa, 3 January – 14 August 2022 (Weeks 1-32).
*Influenza transmission thresholds based on 2010-2019 data and calculated using the Moving Epidemic Method (MEM)

Vaccine effectiveness

Of the 521 surveillance cases enrolled in the VW programme during the season and included in vaccine effectiveness (VE) analysis (aged >6 months with known vaccination status), 207 (40%) were classified as cases (influenza test positive) and 314 (60%) as controls (influenza test negative). Vaccine coverage was 12% (61/521) overall in the VW programme (Table 6): 6% (12/207) and 16% (49/314) among cases and controls respectively. Coverage was highest in the ≥65 years age group (53%) and lowest among cases aged <18 years (8.8%).

The overall (any influenza) VE estimate, adjusted for age and seasonality was 65% (95% confidence interval (CI): 30%, 82%) (Table 7). Influenza A(H1N1)pdm09 VE estimate, adjusted for age and seasonality was 46% (95% CI: -20%, 76%). The influenza A(H3N2) estimate, adjusted for age and seasonality was 91% (95% CI: 31%, 99%). VE was not able to be determined for B/Victoria due to small numbers.

Table 6. Vaccine coverage and vaccine effectiveness (VE) by age group and timing within season, 2022.

	Vaccine coverage			Unadjusted VE
	Cases n/N (%)	Controls n/N (%)	Total n/N (%)	% (95% confidence interval)
All	12/207 (6)	49/314 (16)	61/521 (12)	66.7 (35.7, 82.8)
<18 years	4/72 (6)	10/86 (12)	14/158 (9)	55.3 (-49.1, 86.6)
18-64 years	7/128 (6)	28/201 (14)	47/329 (10)	62.3 (15.5, 84.8)
≥65 years	1/7 (1)	11/27 (41)	18/34 (53)	75.8 (-130.4, 97.5)
Early-season (week 16-21)	3/47 (6)	9/96 (9)	12/143 (8)	34.1 (-155.8, 83.2)
Mid-season (week 22-27)	7/113 (6)	20/117 (17)	27/230 (12)	68.0 (20.9, 87.0)
Late-season (week 28-31)	2/47 (4)	20/101 (20)	22/148 (15)	82.0 (19.4, 96.0)

Table 7. Vaccine coverage and vaccine effectiveness (VE) by influenza subtype, adjusted by age and seasonality, 2022.

	Vaccine coverage			Adjusted VE
	Cases n/N (%)	Controls n/N (%)	Total n/N(%)	% (95% confidence interval)
Any influenza	12/207 (5.8)	49/314 (15.6)	61/521 (11.7)	64.5 (29.9-82.0)
Influenza A(H1N1)pdm09	9/122 (7.4)	49/314 (15.6)	58/436 (13.3)	45.8 (-20,75.5)
Influenza A (H3N2)	1/58 (1.7)	49/331 (14.8)	50/389 (12.8)	90.8 (31.4,98.8)

Influenza virus isolation

During 2022, influenza virus isolation was attempted on 183 clinical specimens with an overall isolation rate of 85% (155/183) (Table 8). The isolation success rate was highest for A(H1N1)pdm09 viruses (89%). In total, 93 A(H1N1)pdm09, 44 A(H3N2) and 18 B/Victoria and viruses were isolated. Influenza virus isolation in embryonated hens' eggs remains challenging and was not attempted.

Table 8. Summary of influenza virus isolations in Madin-Darby Canine Kidney (MDCK) cell cultures, South Africa, 3 January – 14 August 2022 (Weeks 1-32).

Programme	Specimens cultured	Successful cultures	Number of cultures/ attempted (%)		
			A(H1N1)pdm09	A(H3N2)	B/Victoria
Viral Watch	34	23	16/20 (80)	5/7 (71)	2/7 (29)
Influenza-like illness surveillance	59	53	26/29 (90)	20/23 (87)	7/7 (100)
Pneumonia surveillance	90	79	51/56 (91)	19/21 (90)	9/13 (69)
Total	**183**	**155**	**93/105 (89)**	**44/51 (86)**	**18/27 (67)**

Influenza specimens shared with WHO Collaborating Centres

Among virus cultures and original specimens from 132 individuals shared with WHO Collaborating Centres, 65% (86/132) were A(H1N1) pdm09, 24% (32/132) were A(H3N2) and 11% (14/132) were B/Victoria (Table 9).

Table 9. Summary of influenza virus specimens collected in South Africa and shared with WHO-Collaborating Centers for Influenza Surveillance and Research, 3 January – 14 August 2022 (Weeks 1-32).

WHO-CC	A(H1N1)pdm09	A(H3N2)	B/Victoria	Total
Australia	40	17	5	62
United Kingdom	37	2	1	40
United States	9	13	8	30
Total	**86**	**32**	**14**	**132**

Antigenic characterisation of influenza virus isolates

Results for antigenic characterisation of influenza A(H1N1)pdm09, A(H3N2) and B/Victoria are summarised in Table 10. HAIs were performed for all isolates with HAI titers (n=94). A total of 94 virus cultures were characterised antigenically, including 63 A(H1N1)pdm09, 22 A(H3N2) and 9 B/Victoria cultures. 46% (29/63) of A(H1N1)pdm09 viruses had A/Indiana/02/2020-like reactivity and 100% (22/22) of A(H3N2) had A/Tasmania/503/2020-like activity. For the B/Victoria viruses, 100% (9/9) were classified as B/Washington/02/2019-like reactors.

Table 10. Summary of haemagglutination inhibition (HAI) assay results, South Africa, 3 January – 14 August 2022 (Weeks 1-32).

Programme	Number of cultures with HAI titres	A(H1N1)pdm09		A(H3N2)		B/Victoria	
		A/Indiana/02/2020		A/Tasmania/503/2020		B/Washington/02/2019	
		Normal reactors	Low reactors	Normal reactors	Low reactors	Normal reactors	Low reactors
Viral Watch	11	0	9	1	0	1	0
Influenza-like illness	34	10	8	11	0	5	0
Pneumonia surveillance	49	19	17	10	0	3	0
Total n/N (% per virus)	94	29/63 (46)	34/63 (54)	22/22 (100)	0/22 (0)	9/9 (100)	0/9 (0)

HAI assay results from samples shared with the WHO Collaborating Centre in Australia (VIDRL) showed that for A(H1N1) pdm09, 17/30 (57%) were A/Victoria/2570/2019-like and 13/30 (43%) were A/Victoria/2570/2019 low reactors; for A(H3N2), 3/3 (100%) were A/Darwin/6/2021 low reactors; and for B/Victoria, 1/1 (100%) were B/Austria/1359417/2021-like.

Neuraminidase inhibitor susceptibility

For phenotypic susceptibility testing to zanamivir, oseltamivir, peramivir and laninamivir, all samples (12/12 A(H1N1) pdm09 and 3/3 A(H3N2)) showed normal inhibition with all antivirals tested. The mutational analysis on NA segments from sequenced viruses [A(H1N1)pdm09 (n=80), A(H3N2) (n=9), B/Victoria (n=2)], showed that known typical drug-resistance substitutions were not detected.

Genetic characterisation of influenza viruses

The 2022 viruses (n=91) included for genetic characterisation were sequenced at the WHO-CCs for Influenza Surveillance and Research in Australia and the United Kingdom [A(H1N1)pdm09 (n=53), A(H3N2) (n=4) and B/Victoria (n=2)]. Additional sequences deposited by the Vaccine and Infectious Disease Analytics-University of the Witwatersrand (WITS-VIDA) [A(H1N1)pdm09 (n=17) and A(H3N2) (n=5)] and 10 viruses sequenced by the NICD [A(H1N1)pdm09 (n=10)], were also included. Sequences of 2021 viruses were from WHO-CCs (n=157), WITS-VIDA (n=4) and NICD (n=5).

Influenza A(H1N1)pdm09

Genetic analysis of the HA gene of South African influenza A(H1N1)pdm09 viruses indicated that all 50 viruses collected in 2021 and 80 collected in 2022 belong to clade 6B (Figure 6). Strains further clustered into two major genetic subgroups namely 6B.1A.5a.1 (containing Q189E, R113K, D187A

amino acid mutations) and 6B.1A.5a.2 (containing Q189E, K142R, K45Q, T277A, P137S amino acid mutations). The majority of the of the 2021 viruses (44/50, 88%) belonged to the 6B.1A.5a.1 clade. In contrast, the majority of the of the 2022 viruses (59/80, 74%) belonged to the 6B.1A.5a.2 clade together with the 2022 A(H1N1)pdm09 vaccine strain for the Southern Hemisphere (A/Victoria/2570/2019) while only 21 (26%) clustered within the 6B.1A.5a.1 clade (Figure 6).

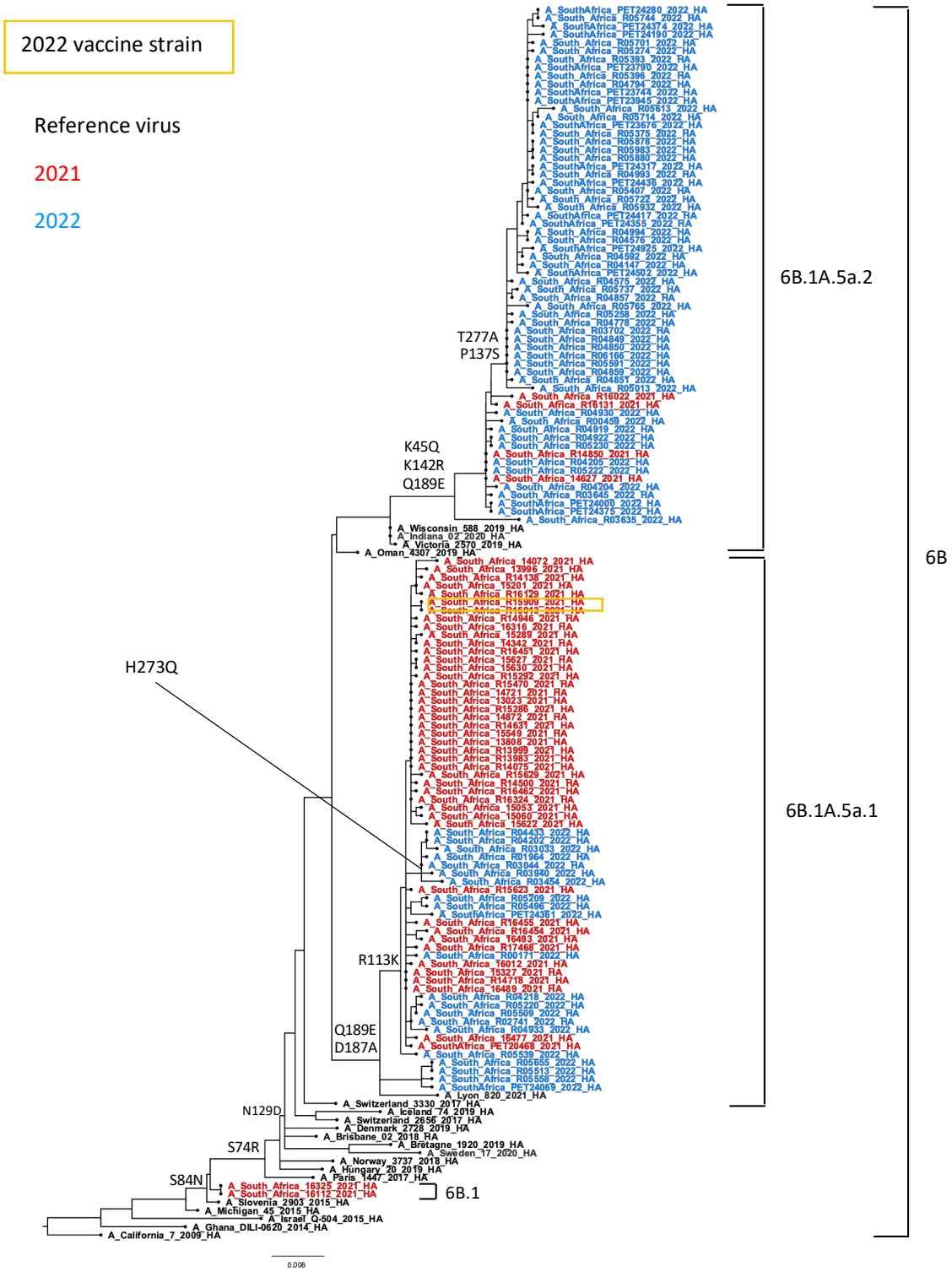

Figure 6. Maximum likelihood phylogenetic tree (ML tree, TPM2u+F+G4 (Best model), No. of Bootstrap replications n=2000, constructed with IQTREE) of the haemagglutinin gene of influenza A(H1N1)pdm09 viruses. The 2022 Southern Hemisphere vaccine strain is indicated by the green block, South African 2021 viruses in red (n=50) and South African 2022 viruses in blue (n=80), and reference strains in black. A/California/07/2009 (H1N1) was used as the root.

Influenza A(H3N2)

Genetic analysis of the HA gene of 2021 and 2022 South African influenza A(H3N2) viruses (n=31) indicated that they belonged to the 3C.2a clade (Figure 7). The 2021 strains (n=22) belonged to three different genetic subgroups with each subgroup characterised by different amino acid substitutions in the HA [3C.2a1b.1b (K310R), 3C.2a1b.1a (T131N, R261Q) and 3C.2a1b.2a.2 (S205F)]. All 2022 (n=9) strains clustered within the 3C.2a1b.2a.2 clade along with the current Southern Hemisphere A(H3N2) vaccine strain (A/Darwin/9/2021).

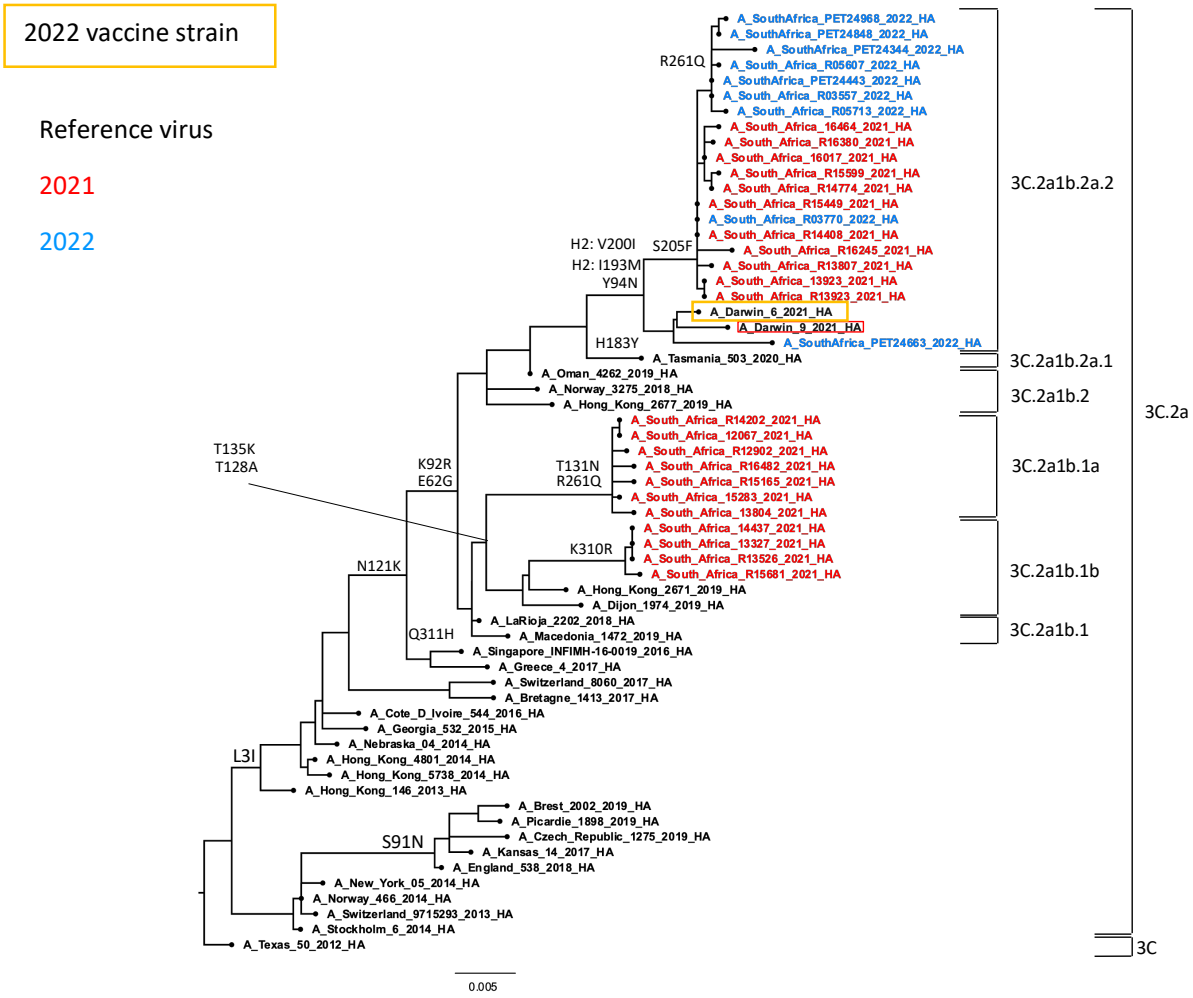

Figure 7. Maximum likelihood phylogenetic tree (ML tree, TPM2u+F+G4 (Best model), No. of Bootstrap replications n=2000, constructed with IQTREE) of the haemagglutinin gene of influenza A(H3N2) viruses. The 2022 Southern Hemisphere vaccine strain is indicated in a green box. South African 2021 viruses are in red (n=22), South African 2022 viruses are in blue (n=9) and reference strains are in black. A/Texas/50/2012 (H3N2) was used as the root.

Influenza B

Genetic analysis of 96 influenza B/Victoria viruses from 2021 and 2022 showed that all belonged to clade V1A (Figure 8). The V1A.3a.2 subclade (K203R, P144L, N126S, T221A, T182A, A202V) consisted of all the 2021 viruses (n=94) and two of the 2022 viruses (with an additional E198G substitution). The current Southern Hemisphere influenza vaccine strain (B/Austria/1359417/2021) also clustered within the same subclade.

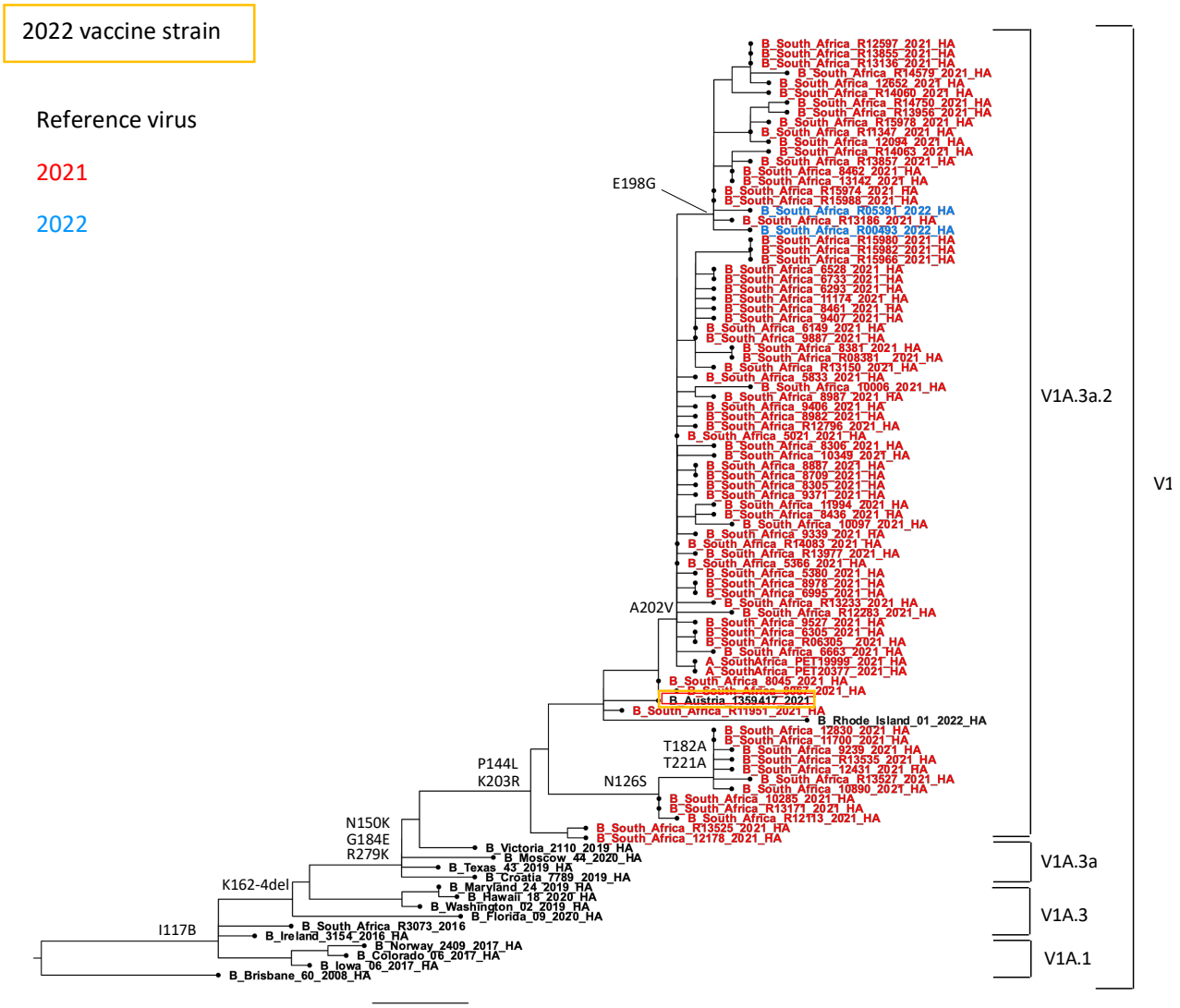

Figure 8. Maximum likelihood phylogenetic tree (ML tree, TPM2u+F+G4 (Best model), No. of Bootstrap replications n=2000, constructed with IQTREE) of the haemagglutinin gene of influenza B/Victoria viruses. The 2022 Southern Hemisphere vaccine strain is indicated in a green box, South African 2021 viruses are in red (n=94) and South African 2022 viruses are in blue (n=2), reference strains are in black. B/Brisbane/60/2008 was used as the root.

Discussion

As of the end of week 32 2022, influenza activity had been observed from week 1 through 32, with an increased period of activity in the normal winter influenza season, and was ongoing at the time of this report. Levels of activity reached moderate and low levels in the ILI and pneumonia surveillance programmes, respectively. However, as the baseline for MEM is established using data from prior to the COVID-19 pandemic, and that COVID-19 now contributes to the enrolled number of ILI and pneumonia surveillance cases, this may result in an underestimation of the detection rate and resulting thresholds, and the determination of the influenza season may therefore be biased.

Influenza circulation was dominated by A(H1N1)pdm09, followed by A(H3N2) and B/Victoria. Influenza B/Yamagata was not detected. Haemagglutinin inhibition assays demonstrated that 46% of tested A(H1N1)pdm09, 100% of A(H3N2) and 100% of B/Victoria viruses were recognised by antisera raised against current vaccine and vaccine-like strains. All samples tested were susceptible to zanamivir, oseltamivir, peramivir and laninamivir, and no known resistance mutations were detected. While some antigenic drift was observed, strains fell within the same phylogenetic clades as 2022 Southern Hemisphere vaccine strains.

Despite a low vaccine coverage (12%) in the Viral Watch programme, vaccine effectiveness for any influenza, influenza A(H1N1)pdm09 and influenza A(H3N2) adjusted for age and season was 65% (95% CI: 30%, 82%), 46% (95% CI: -20%, 76%) and 91% (95% CI: 31%, 99%), respectively. Vaccine effectiveness for influenza B/Victoria could not be determined due to small numbers at the time of this report. Vaccine effectiveness calculations will be updated when the 2022 influenza season has ended.

Following easing of COVID-19 restrictions, South Africa experienced the first typical influenza season since the start of the pandemic. The influenza season was ongoing as of week 43 of 2022, with a biphasic pattern in which infections later in the season were dominated by B/Victoria and A(H3N2) viruses.[5]

Recommendations

- Individuals are encouraged to receive the annual flu vaccine. Ideally the flu vaccine should be taken early (March/April each year) before the flu season so that it has sufficient time to protect a person. However, it is never too late to vaccinate as long as the flu virus is circulating.
- Groups recommended to receive influenza vaccination include:

- Healthcare workers
- Persons aged ≥ 65 years
- Persons with underlying chronic health conditions
- HIV–infected adults
- Pregnant women at any stage of pregnancy including up to 6 weeks postpartum
- Residents of old-age homes, chronic care and rehabilitation institutions
- Persons aged 6 months to ≤18 years on long-term aspirin therapy
- Any persons wishing to minimise the risk of influenza acquisition

- People who are sick with flu-like symptoms can prevent spread by:
  - Covering their mouth when coughing with a tissue or cough into the elbow
  - Wearing a mask
  - Washing their hands frequently with soap and water or cleaning hands using an alcohol-based sanitiser
  - Staying at home and trying to keep a distance from others

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ILI Clinic-based surveillance
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Eastridge Clinic and Mitchell's Plain Clinic, Western Cape Province
Jouberton Clinic, North West Province
Edendale Gateway Clinic, KwaZulu-Natal Province

Pneumonia surveillance
Edendale Hospital, KwaZulu-Natal Province
Helen Joseph and Rahima Moosa Mother and Child Hospitals and Tembisa Hospital, Gauteng Province
Klerksdorp and Tshepong Hospital Complex, North West Province
Tintswalo Hospital, Mapulaneng and Matikwana Hospitals, Mpumalanga Province
The Red Cross Childrens' War Memorial Hospital, Mitchell's Plain Hospital and Tygerberg Hospital Western Cape Province

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