

Influenza Surveillance in South Africa, Week 1 to 34, 2023

Nicole Wolter^{1,2}, Amelia Buys¹, Sibongile Walaza^{1,3}, Jocelyn Moyes^{1,3}, Mvuyo Makhasi^{1,3}, Jackie Kleynhans¹, Mignon du Plessis^{1,2}, Fahima Moosa^{1,2}, Anele Mnguni¹, Dikeledi Kekana¹, Lorens Maake¹, Linda de Gouveia¹, Cheryl Cohen^{1,3} and Anne von Gottberg^{1,2}

¹Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases (NICD) of the National Health Laboratory Service, Johannesburg, South Africa

²School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

³School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Summary

Influenza activity was observed from weeks 1 through 34, with an overall detection rate of 12% (942/7880) from 1 January 2023 through 26 August 2023. Using the Moving Epidemic Method (MEM), the levels of activity reached low, high, and moderate levels in the Viral Watch (VW), influenza-like illness (ILI), and pneumonia surveillance programmes, respectively. Influenza single infections were dominated by A(H3N2) (98%, 895/915). As of week 34, low numbers of A(H1N1)pdm09 (1%, 8/915) and B/Victoria (1%, 12/915) were detected. Haemagglutination inhibition (HAI) assays demonstrated that 6% (5/81) of A(H3N2) viruses and 0% (0/3) of B/Victoria viruses showed poor recognition of antisera raised against current vaccine-like strains. All viruses tested [A(H3N2) n=9] were phenotypically susceptible to zanamivir, oseltamivir, peramivir, and laninamivir. No mutations associated with antiviral resistance were detected among sequenced viruses [A(H1N1)pdm09 n=1, A(H3N2) n=421, and B/Victoria n=1]. Phylogenetic analysis of the haemagglutinin (HA) gene of 2023 influenza viruses showed that all A(H3N2) viruses belonged to the 3C.2a1b clade and the 3C.2a1b.2a.2 (2a.2) subclade. There was diversification within the 2a.2 subclade, with the majority of the 2023 viruses clustering within the 2a.3a.1 subgroup. The 2023 Southern Hemisphere A(H3N2) vaccine strain (A/Darwin/9/2021) belongs to the 2a.2a subgroup. Vaccine coverage was low (3%, 14/516) in the Viral Watch programme. After adjusting for age and timing within the season, the vaccine effectiveness (VE) for any influenza in individuals of all ages was 81% [95% confidence interval (CI) 29%-95%], and for A(H3N2), it was 76% [95% CI 10%-94%].









Introduction

Because of South Africa's locality and temperate climate, in-country influenza epidemics usually occur between April and October, peaking during the winter months. 1.2 The following strains were recommended for the trivalent and quadrivalent inactivated influenza vaccine (IIV) for the 2023 Southern Hemisphere influenza season:

- A/Sydney/5/2021 (H1N1)pdm09-like virus;
- A/Darwin/9/2021 (H3N2)-like virus;
- B/Austria/1359417/2021 (B/Victoria lineage) like- virus; and
- B/Phuket/3073/2013-like (B/Yamagata lineage) virus (quadrivalent vaccine only).

These recommendations included a change to the A(H1N1)pdm09 component of egg-based and cell culture-based vaccine strains compared with the 2022 Southern Hemisphere trivalent and quadrivalent IIV vaccine strains. For A(H1N1)pdm09 vaccine virus component, A/Victoria/2570/2019 (H1N1)pdm09-like virus was replaced with an A/Sydney/5/2021 (H1N1)pdm09-like virus. In South Africa, the trivalent IIV was only available in the public sector (at designated clinics and hospitals) and the quadrivalent IIV was available mostly in the private sector, generally from March or April.

South Africa has three influenza sentinel surveillance programmes, which are co-ordinated by the Centre for Respiratory Diseases and Meningitis (CRDM) at the National Institute for Communicable Diseases (NICD). These programmes include: (i) Viral Watch (VW) influenza-like illness surveillance in outpatients at private general practitioners (Eastern Cape, Free State, Gauteng, Limpopo, Mpumalanga, Northern Cape, North West, and Western Cape provinces), (ii) systematic influenza-like illness (ILI) surveillance in outpatients at public health clinics (KwaZulu-Natal, North West, Western Cape, and Mpumalanga provinces), and (iii) national pneumonia surveillance in public health hospitals (Eastern Cape, Gauteng, KwaZulu-Natal, Mpumalanga, North West, and Western Cape provinces). Data from these surveillance programmes are shared weekly with the World Health Organization (WHO) Global Influenza Surveillance and Response System (GISRS), and reports are shared bi-annually in February and September in preparation for the influenza vaccine composition meetings.



Methods

Individuals of all ages meeting the following case definitions are approached for consent and enrolled in the respective surveillance programmes:

- Influenza-like illness (VW and ILI): Acute respiratory illness with fever (≥38°C), cough, and symptom onset ≤10 days, or any person presenting with an acute (≤14 days) respiratory tract infection or other clinical illness compatible with COVID-19.
- Severe respiratory illness (SRI, pneumonia surveillance): Acute (symptom onset ≤10 days) or chronic (symptom onset >10 days) lower respiratory tract infection requiring hospitalisation or any person admitted with a physician-diagnosis of suspected COVID-19 and not meeting SRI case definition.

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

Influenza transmission thresholds were calculated using the Moving Epidemic Method (MEM), a sequential analysis using the R language (http://CRAN.R-project.org/web/package=mem) designed to calculate the duration, start, and end of the annual influenza epidemic^{3,4}. 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 Viral Watch surveillance at general practitioners (outpatients) and 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. However, as the baseline for MEM is established using data from prior to the COVID-19 pandemic, and with COVID-19 now contributing to the enrolled number of ILI and pneumonia surveillance cases, this may result in an underestimation of the detection rate. This underestimation may result in bias in thresholds and therefore the determination of the influenza season.

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 Viral Watch surveillance programme during the 2023 influenza season. Vaccine effectiveness (VE) estimates were adjusted for timing within the season and age.

Influenza virus isolates were antigenically characterised using the haemagglutination inhibition (HAI) assay, with turkey red blood cells used as an indicator system. HAI assays were performed using reference reagents from the CDC IRR 2022-2023 WHO influenza reagent kit.

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/).

Influenza viruses circulating in 2023 in South Africa were genetically characterised with whole genome sequencing using the Illumina platform and shared on GISAID. Phylogenetic analysis of the HA gene was performed using the Aliview alignment editor and IQ-TREE v 1.6.12 software. Groups and sub-groups were identified by specific amino acid mutations relative to a designated reference strain on NextClade.



Results

From 1 January 2023 (week 1) through 26 August 2023 (week 34), 7880 individuals were enrolled with respiratory specimens collected and tested through the three surveillance programmes (Table 1). Influenza infections were identified in 942 individuals, resulting in an overall infection detection rate of 12% (942/7880). Influenza detections occurred from week 1 through week 34. For influenza single infections where a subtype/lineage could be determined (97%, 915/942), infections were dominated by influenza A(H3N2) (98%, 895/915).

Influenza A(H1N1)pdm09 and B/Victoria accounted for only 1% (8/915) and 1% (12/915) of single infections, respectively. Influenza B/Yamagata was not detected. A dual infection was detected in one individual, with A(H3N2) and B (lineage inconclusive) detected. Inconclusive results for subtyping occurred for 3% (26/942) of samples. 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 by PCR was not performed to determine the subtype/lineage.

The season started in week 17 (week starting 24 April 2023) 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), peaked in week 22 (week starting on 4 June 2023) and ended in week 27 (week starting 3 July 2023). The mean onset of the influenza season in South Africa in 2005-2019 was week 17 (3rd week of April), ranging from week 16 to week 25.

Table 1. Number of influenza infections identified in all syndromic influenza surveillance programmes, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

Programme	Number of specimens tested	Number of influenza positive (% of all specimens tested)		Influenza A				Influenza B			
			Total A	Subtype in- conclusive*	A(H1N1) pdm09	A(H3N2)	Total B	Lineage in- conclusive*	B/ Victoria	B/ Yamagata	

n (% of total influenza positives)

Programme	1181	379 (32)	366 (97)	9 (2)	8 (2)	349 (92)	13 (3)	3 (1)	10 (3)	0 (0)	0 (0)
Influenza- like illness surveillance	1240	217 (18)	217 (100)	3 (1)	0 (0)	214 (99)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pneumonia surveillance	5459	346 (6)	343 (99)	11 (3)	0 (0)	332 (96)	2 (1)	0 (0)	2 (1)	0 (0)	1 (0)
Total	7880	942 (12)	926 (98)	23 (2)	8 (1)	895 (95)	15 (2)	3 (0)	12 (1)	0 (0)	1 (0)

*Inconclusive: insufficient viral load in sample and unable to characterise further; #Dual infections: A(H3N2) and B (lineage inconclusive) [n=1]



Viral Watch programme

Specimens from 1181 patients were received and tested from VW practitioners located in 7 of the 9 provinces (Table 2), with the majority of specimens received from Gauteng (57%, 679/1181) and the Western Cape (34%, 403/1181) provinces. Influenza was detected in 379 (32%) patients, of which 92% (349/379) were A(H3N2) (Figure 1, Table 2). The highest 3-week moving average detection rate in the VW programme occurred in week 24 (45%) (Figure 1). Using the MEM, with a baseline determined from previous years prior to the COVID-19 pandemic (2015-2019), the estimated level of influenza disease transmission in the VW programme reached a level of low activity (Figure 2).

Table 2. 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 – 26 August 2023 (Weeks 1-34).

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	0	17	0	0	0	0	0	17	37	46
Free State	0	2	0	0	0	0	0	2	2	100
Gauteng	3	125	4	1	0	1	0	134	679	20
Limpopo	0	2	0	0	0	0	0	2	6	33
Mpumalanga	1	19	2	0	0	0	0	22	51	43
North West	0	3	0	0	0	0	0	3	3	100
Western Cape	4	181	3	9	0	2	0	199	403	49
Total	8	349	9	10	0	3	0	379	1181	32

 $[*]Inconclusive: insufficient viral load in sample and unable to characterise further; \\ *Dual infection: Not detected$

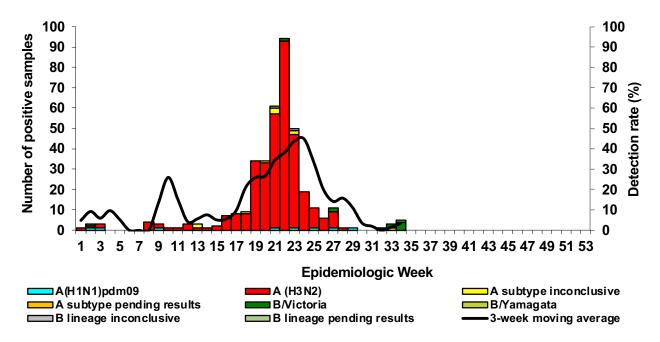


Figure 1. Number of influenza infections by influenza subtype/lineage and 3-week moving average detection rate by epidemiologic week - Viral Watch programme for influenza-like illness surveillance, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

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



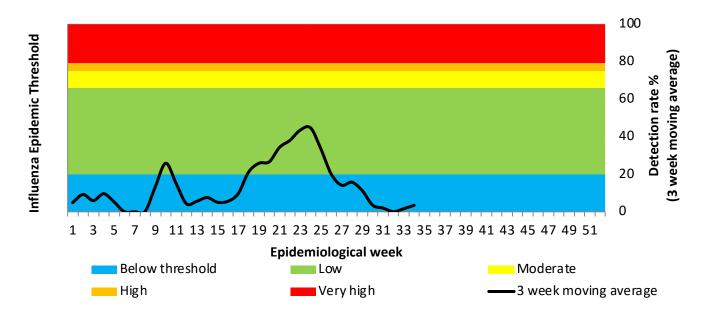


Figure 2. Influenza detection rate and epidemic thresholds*, Viral Watch programme for influenza-like illness surveillance, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

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

Specimens from 1240 patients with ILI were received from five primary health care clinics located in four provinces. In total, 217 (18%) individuals tested positive for influenza. Among infections that could be further characterised, A(H3N2) accounted for 100% (214/214) of cases (Table 3, Figure 3). The 3-week moving average detection rate peaked in week 22 (59%). Using the MEM, with a baseline determined from previous years prior to the COVID-19 pandemic (2012-2019), the estimated level of influenza disease transmission in the community reached a level of high activity in the ILI surveillance programme at public healthcare clinics (Figure 4).

Table 3. Number of influenza cases by subtype/lineage, and total number of specimens collected by province for the influenza-like illness surveillance programme at primary health care clinics, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

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 (%)
KwaZulu-Natal	0	53	2	0	0	0	0	55	406	14
Mpumalanga	0	41	0	0	0	0	0	41	206	20
North West	0	76	0	0	0	0	0	76	279	27
Western Cape	0	44	1	0	0	0	0	45	349	13
Total	0	214	3	0	0	0	0	217	1240	18

Surveillance sites included primary healthcare clinics in four provinces: KwaZulu-Natal (Edendale Clinic), Mpumalanga (Agincourt Clinic), North West (Jouberton Clinic) and Western Cape (Eastridge Clinic and Mitchell's Plain Clinic). *Inconclusive: insufficient viral load in sample and unable to characterise further (primary test PCR Ct value >35). *Dual infection: Not detected

^{*}Influenza transmission thresholds based on 2015-2019 data and calculated using the Moving Epidemic Method (MEM)



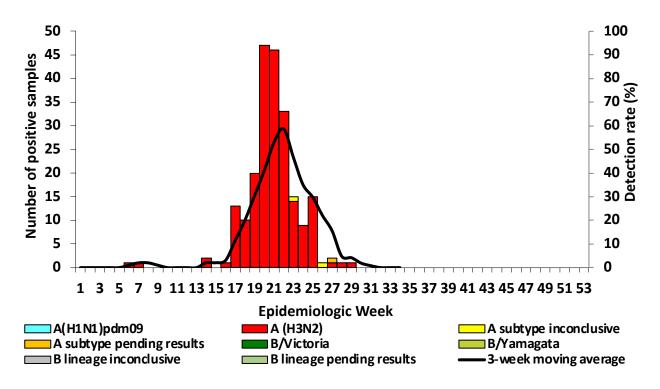


Figure 3. Number of influenza cases by subtype/lineage and 3-week moving average detection rate by epidemiologic week - Influenza-like illness (ILI) surveillance programme at primary health care clinics, South Africa, 1 January – 26 August 2023 (Weeks 1-34). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infection: Not detected.

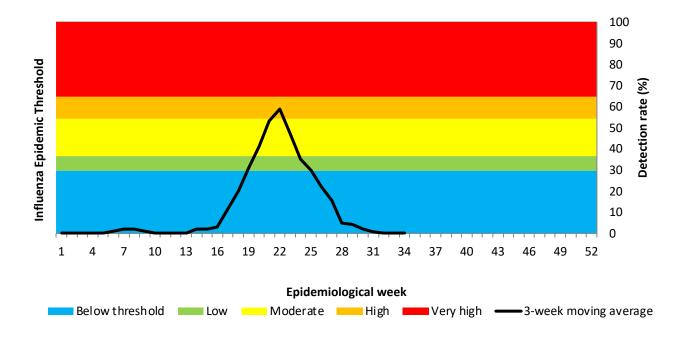


Figure 4. Influenza detection rate and epidemic thresholds*, influenza-like illness surveillance at primary health care clinics, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

^{*}Influenza transmission thresholds based on 2012-2019 data and calculated using the Moving Epidemic Method (MEM)



Pneumonia surveillance programme

Specimens from 5459 patients hospitalised with severe respiratory illness were received from the thirteen sentinel hospitals located in six provinces, and 346 (6%) influenza cases were detected. Of these, one individual had a dual infection with both A(H3N2) and B (lineage inconclusive) detected. Among single infection influenza-positive samples that could be further characterised, 99% (332/334) were A(H3N2) (Table 4). The 3-week moving average detection rate peaked in week 22 (27%) (Figure 5). Data obtained through pneumonia surveillance in hospitalised patients prior to the COVID-19 pandemic (2010-2019) was used to set MEM thresholds for impact of influenza on healthcare provision. The impact of influenza disease in the 2023 season reached the moderate level (Figure 6).

Table 4. Number of influenza infections by subtype/lineage, and total number of specimens collected by province for the pneumonia surveillance programme, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

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	0	21	1	0	0	0	0	22	490	4
Gauteng	0	123	4	0	0	0	0	127	1838	7
KwaZulu-Natal	0	29	1	1	0	0	0	31	520	6
Mpumalanga	0	33	2	0	0	0	0	35	580	6
North West	0	47	1	0	0	0	0	48	419	11
Western Cape	0	79	2	1	0	0	1	83	1612	5
Total	0	332	11	2	0	0	1	346	5459	6

Surveillance sites included hospitals in six provinces: Gauteng (Helen Joseph Hospital, Rahima Moosa Hospital, Tembisa Hospital), KwaZulu-Natal (Edendale Hospital), Mpumalanga (Mapulaneng Hospital, Matikwana Hospital, and Tintswalo Hospital), 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. *Dual infection: A(H3N2) and B lineage inconclusive

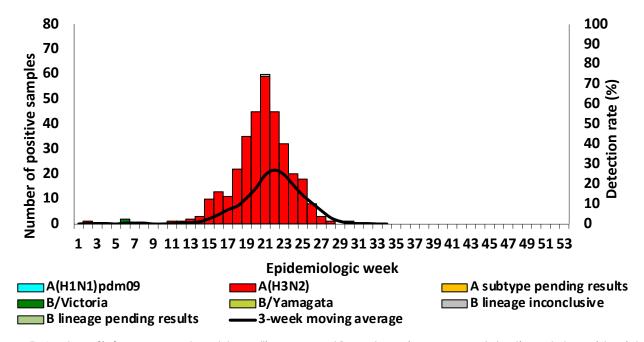


Figure 5. Number of influenza cases by subtypes/lineages and 3-week moving average detection rate by epidemiologic week – National pneumonia surveillance, South Africa, 1 January – 26 August 2023 (Weeks 1-34). Inconclusive: insufficient viral load in sample and unable to characterise further. Dual infection: A(H3N2) and B lineage inconclusive



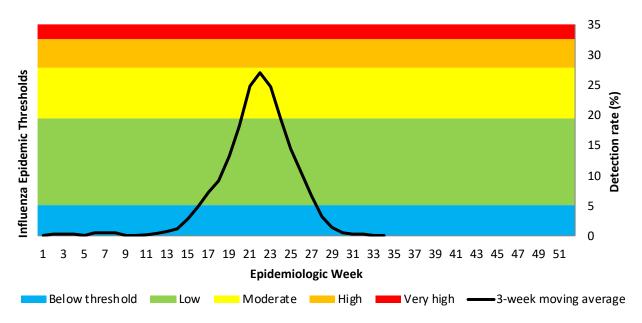


Figure 6. Influenza detection rate and epidemic thresholds*, National pneumonia surveillance programme, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

Vaccine effectiveness

Of the 516 surveillance cases enrolled in the VW programme during the 2023 influenza season and included in the VE analysis (individuals aged ≥6 months with known vaccination and influenza status), 276 (54%) were classified as cases (influenza test positive) and 240 (47%) as controls (influenza test negative). Vaccine coverage was 3% (14/516) overall in the VW programme (Table 5): 1% (3/276) and 5% (11/240) among cases and controls, respectively. Adjusted VE (adjusting for timing within season and age) for any influenza was 81% (95% confidence interval (95% CI) 29%-95%) and for influenza A(H3N2), it was 76% (95% CI 10%-94%) (Table 5).

Table 5. Vaccine coverage and vaccine effectiveness (VE) by subtype and age group, Viral Watch surveillance programme, South Africa, 24 April – 13 August 2023.

Vaccine coverage								
	Cases n/N (%)	Controls n/N (%)	Total n/N (%)	Adjusted VE % (95% confidence interval)*				
All specimens								
Any influenza	3/276 (1.1)	11/240 (4.6)	14/516 (2.7)	81.4 (28.6; 95.1)				
A(H3N2)	3/256 (1.2)	11/260 (4.2)	14/516 (2.7)	76.1 (9.5; 93.7)				
Children aged <18 years								
Any influenza	1/88 (1.1)	4/60 (6.6)	5/148 (3.4)	79.8 (-117.3; 98.1)				
A(H3N2)	1/81 (1.2)	4/67 (0.6)	5/148 (3.4)	72.1 (-193.1; 97.3)				
Adults aged 18 – 64 years								
Any influenza	2/175 (1.1)	5/159 (3.1)	7/334 (2.1)	78.9 (-12.5; 96.1)				
A(H3N2)	2/164 (12.2)	5/170 (2.9)	7/334 (2.1)	74.1 (-37.8; 95.1)				
Adults aged ≥65 years								
Any influenza	0/13 (0.0)	2/21 (9.5)	2/34 (5.9)	Not determined				
A(H3N2)	0/11 (0.0)	2/23 (8.7)	2/34 (5.9)	Not determined				

^{*}Adjusted for timing within season and age

^{*}Influenza transmission thresholds based on 2010-2019 data and calculated using the Moving Epidemic Method (MEM).



Antigenic characterisation of influenza virus isolates

A total of 84 virus cultures were characterised antigenically, including 81 A(H3N2) and 3 B/Victoria cultures (Table 6). 6% (5/81) of A(H3N2) viruses reacted poorly to A/Delaware/01/2021 antisera, and 0/3 of B/Victoria reacted poorly to B/Michigan/01/2021 antisera.

Table 6. Summary of haemagglutination inhibition (HAI) assay results, South Africa, 1 January – 26 August 2023 (Weeks 1-34).

		A(H1N1)pdm09	A(H3N2)	B/Victoria	
Programmo	Number of cultures with	A/Victoria/2570/2019	A/Delaware/01/2021	B/Michigan/01/2021	
Programme	HA titres	Low reactors/ Total tested (%)	Low reactors/ Total tested (%)	Low reactors/ Total tested (%)	
Viral Watch	26	0/0 (0)	3/23 (13)	3/23 (13)	
Influenza-like illness	14	0/0 (0)	1/14 (7)	1/14 (7)	
Pneumonia surveillance	44	0/0 (0)	1/44 (2)	1/44 (2)	
Total n/N (% per virus)	84	0/0 (0)	5/81 (6)	5/81 (6)	

Neuraminidase inhibitor susceptibility

All samples tested phenotypically [9/9 A(H3N2)] showed normal inhibition to zanamivir, oseltamivir, peramivir, and laninamivir. The mutational analysis of neuraminidase (NA) segments of sequenced 2023 South African viruses [A(H1N1)pdm09 n=1, A(H3N2) n=385, and B/Victoria n=1] showed no mutations associated with antiviral resistance.

Genetic characterisation of influenza viruses

Sequences were obtained from GISAID on the 4th of September 2023, and after incomplete sequences were excluded (n=2), 387 complete sequences were analysed. These included viruses obtained through syndromic surveillance and sequenced at the NICD [A(H3N2) n=337, A(H1N1)pdm09 n=1], and WHO Collaborating Centres (CC) for Influenza Surveillance and Research in Australia, the United Kingdom, and the US CDC [A(H3N2) n=48, B/Victoria n=1].

One 2023 A(H1N1)pdm09 virus from South Africa was sequenced and belonged to the 6B.1a.5a clade together with the 2021 and 2022 viruses (Figure 7). The 2023 virus clustered within the 6B.1A.5a.2a (5a.2a) clade together with the 2023 Southern Hemisphere vaccine strain (A/Sydney/5/2021). Genetic analysis of the HA gene of 2023 South African influenza A(H3N2) viruses (n=385) indicated that all A(H3N2) viruses belonged to the 3C.2a1b clade and the 3C.2a1b.2a.2 (2a.2) subclade (Figure 8). There was diversification within the 2a.2 subclade with 2022 viruses clustered in the 2a.2b and 2a.2c genetic subgroups, while the majority of the 2023 viruses clustered within the 2a.3a.1 subgroup, characterised by D93N (HA1), N96S (HA1), 1223V (HA1) and N49S (HA2) substitutions. Viruses in this subgroup gained a new glycosylation site due to the N96S mutation. A reversion in position 122 to the wildtype D amino acid (compared to A/Wisconsin/67/2005 as the reference) in a group of viruses within 2a.3a.1 resulted in a loss of a glycosylation site at this position. The 2023 Southern Hemisphere A(H3N2) vaccine strain (A/Darwin/9/2021) belongs to the 2a.2a subgroup, within the same 2a.2 subclade. One 2023 B/Victoria virus from South Africa was sequenced, and it belonged to subclade V1A.3a.2 (characterised by A127T, P144L, K203R) together with the 2021 and 2022 viruses (Figure 9). However, the 2023 virus had accumulated several unique substitutions (E128K, A154E and S208P). The 2023 Southern Hemisphere vaccine strain (B/Austria/1359417/2021) clustered within the same subclade.



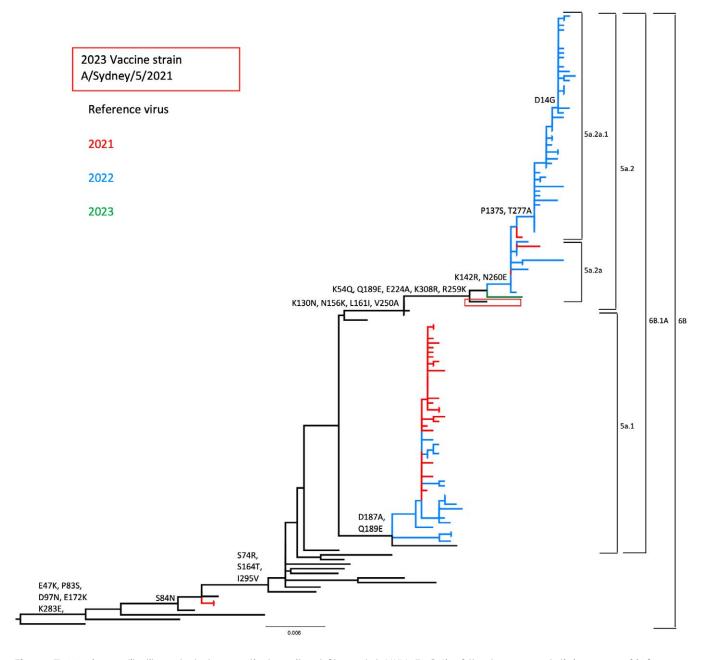


Figure 7. Maximum likelihood phylogenetic tree (best-fit model: HKY+F+G4) of the haemagglutinin gene of influenza A(H1N1)pdm09 viruses. The 2023 Southern Hemisphere vaccine strain is indicated in a red box, South African 2023 virus in green (n=1), South African 2022 viruses in blue, South African 2021 viruses in red, and reference strains in black. A/California/07/2009 was used as the root.



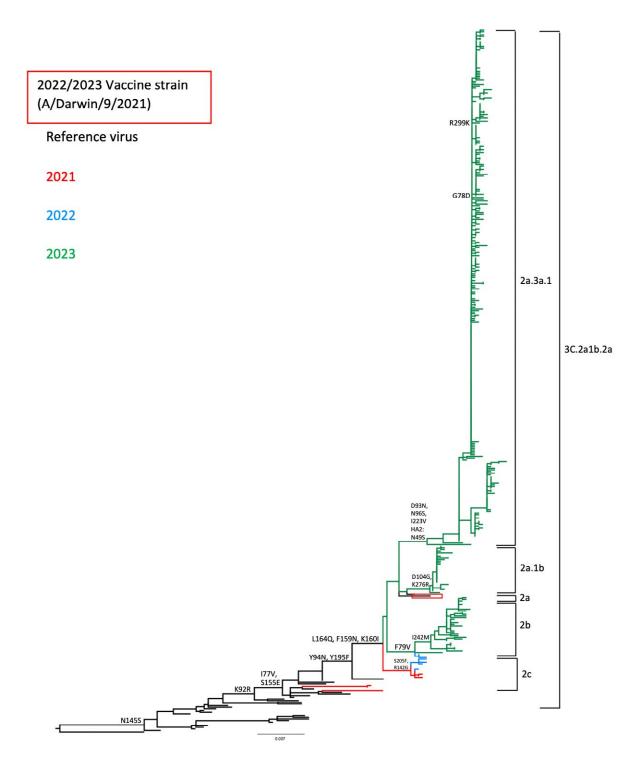


Figure 8. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin gene of influenza A(H3N2) viruses. The 2023 Southern Hemisphere vaccine strain is indicated in a red box, South African 2023 viruses in green (n=385), South African 2022 viruses in blue, South African 2021 viruses in red, and reference strains in black. A/Wisconsin/67/2005 was used as the root.



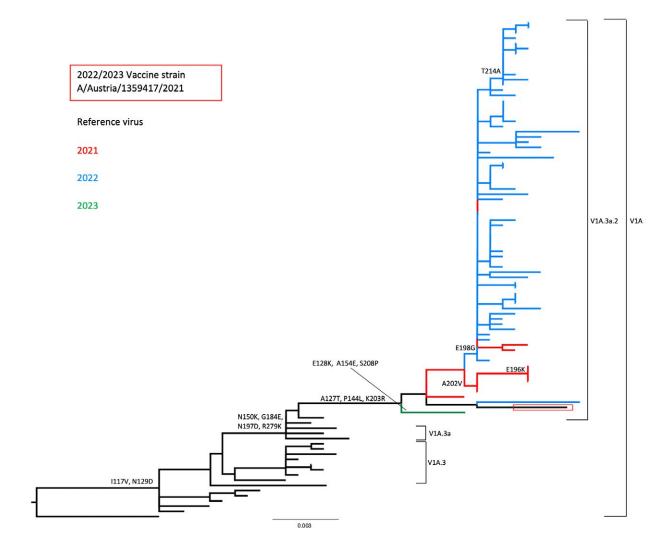


Figure 9. Maximum likelihood phylogenetic tree (Best-fit model: HKY+F+G4) of the haemagglutinin gene of influenza B/Victoria viruses. The 2023 Southern Hemisphere vaccine strain is indicated in a red box, South African 2023 virus in green (n=1), South African 2022 viruses in blue, South African 2021 viruses in red, and reference strains in black. B/ Brisbane/60/2008 was used as the root.



Discussion and conclusions

During 2023, influenza activity was observed from weeks 1 through 34, with an increased period of activity in the normal winter influenza season. The season started in week 17 (week starting 24 April 2023), peaked in week 22 (week starting on 4 June 2023), and ended in week 27 (week starting 3 July 2023), within the mean circulation. Influenza circulation was dominated by the A(H3N2) subtype. Antigenic characterisation showed that A(H3N2) viruses circulating in 2023 were antigenically similar to the 2023 Southern Hemisphere vaccine strain. However, genotypic characterisation showed that the majority of A(H3N2) viruses clustered in a different genetic sub-group (2a.3a.1) to that of the vaccine strain (2a.2a).

Because of the changing nature of influenza viruses, the WHO continuously monitors the epidemiology of influenza viruses circulating throughout the world. Each year, recommendations about strains to be included in the vaccine for the upcoming influenza season are made. WHO recently announced their recommendations for the composition of the 2024 Southern Hemisphere influenza vaccines5, including a change to the A(H3N2) component of the vaccine, as listed below. In addition, the WHO stated that inclusion of a B/Yamagata lineage antigen in quadrivalent influenza vaccines is no longer warranted.

Egg-based vaccines:

- A/Victoria/4897/2022 (H1N1)pdm09-like virus;
- A/Thailand/8/2022 (H3N2)-like virus;
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- B/Phuket/3073/2013 (B/Yamagata lineage)-like virus (quadrivalent IIV vaccine).

Cell culture- or recombinant-based vaccines:

- A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- A/Massachusetts/18/2022 (H3N2)-like virus;
- B/Austria/1359417/2021 (B/Victoria lineage)-like virus; and
- B/Phuket/3073/2013 (B/Yamagata lineage)-like virus (quadrivalent IIV vaccine only)

While the majority of influenza infections cause mild illness, influenza may cause severe disease and death.² Groups at an increased risk of severe complications of influenza include pregnant women, persons living with HIV, those with chronic illnesses or conditions such as diabetes, lung disease, tuberculosis, heart disease, renal disease, and obesity, the elderly (65 years and older), and children under the age of two years.⁶ These groups should be encouraged to receive the influenza vaccine and seek medical help early.



Recommendations

To prevent contracting or spreading influenza, it is recommended that patients should:

- Stay at home until symptoms have resolved (at least 24 hours after fever has defervesced);
- Avoid close contact with others, especially those at high risk for severe influenza;
- Avoid close contact, such as kissing or sharing drinks;
- Cover coughs and sneezes (cover mouth and nose with tissue or cough or sneeze into an elbow);
- Wear a tight fitting mask, especially in public places;
- Wash hands with soap and water or disinfect with an alcohol-based hand rub regularly;
- Limit the number of visitors;
- Wipe down surfaces that are frequently touched or shared (doorknobs, remote controls) with a standard household disinfectant.

Clinicians are encouraged to consider influenza as a differential diagnosis when managing patients presenting with respiratory illness.

Weekly updates on influenza activity in South Africa are available on the NICD website.⁷

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Conflicts of interest

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References

- 1. Cohen, Adam L et al. Epidemiology of influenza virus types and subtypes in South Africa, 2009-2012. Emerging Infectious Diseases vol. 20,7 (2014): 1162-9
- 2. Tempia, Stefano et al. Risk Factors for Influenza-Associated Severe Acute Respiratory Illness Hospitalization in South Africa, 2012-2015. Open Forum Infectious Diseases vol. 4,1 ofw262. 10 Feb. 2017.
- 3. Vega T, Lozano JE, Meerhoff T, et al. Influenza surveillance in Europe: establishing epidemic thresholds by the moving epidemic method". *Influenza Other Respi Viruses*. 2013;7(4):546-558.
- 4. World Health Organisation. Pandemic Influenza Severity Assessment (PISA): a WHO guide to assess the severity of influenza in seasonal epidemics & pandemics [Internet]. 2017. Available from: Pandemic influenza severity assessment (PISA): a WHO guide to assess the severity of influenza in seasonal epidemics and pandemics
- 5. World Health Organization. Recommended composition of influenza virus vaccines for use in the 2024 southern hemisphere influenza season. Available at: https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2024-southern-hemisphere-influenza-season. Accessed 18 October 2023.
- 6. National Institute for Communicable Diseases. *Influenza NICD recommendations for the diagnosis, management, prevention and public health response, April 2023*. Available at: https://www.nicd.ac.za/wp-content/uploads/2023/05/Influenza-guidelines_-25April-2023-final.pdf. Accessed 18 October 2023.
- 7. National Institute for Communicable Diseases. Weekly respiratory pathogens report. Available at: https://www.nicd.ac.za/diseases-a-z-index/disease-index-covid-19/surveillance-reports/weekly-respiratory-pathogens-surveillance-report-week/. Accessed 18 October 2023.