



GIHSN report of activity prior to the WHO Consultation on the Composition of Influenza Virus Vaccines for use in the 2026 Southern Hemisphere Influenza Season.

Report prepared the 8th of September 2025

1 - Description of the network

GIHSN is collecting clinical and virological information from hospitalized cases through a network of sites located in different regions of the world (Fig. 1). This combined clinical and virological surveillance allows the identification of viruses responsible for severe influenza. This severity is assessed by the oxygen requirement of cases registered by the sites. In this report, viruses detected and sequenced from cases requiring oxygen supplementation are identified in the phylogenetic trees provided, to determine if specific lineages or clades are associated with more frequent severe presentation.

For the 2025 surveillance in GIHSN, influenza activity was detected from 2025-02-19, with a co-circulation of A/H1N1 (n=273), A/H3N2 (n=218) and B viruses (n=319).

This report collates the sequencing data of hospitalized patients from 18 sites in 16 countries reporting 810 sequences available in the GISAID database on 2025/09/08: *Canada (36), Hong Kong (37), Kenya (15), Lebanon (27), Madagascar (37), Mexico (24), New Zealand (72), Pakistan (22), Peru (14), Romania (36), Russian Federation (268), Senegal (5), South Africa (95), Spain (41), Ukraine (54), United States (27)*. Samples were collected between 2025-02-19 and 2025-08-10. Additional sequences from Brazil are under analysis but could not be integrated in the report as deposited in the GISAID database after 2025/09/08.

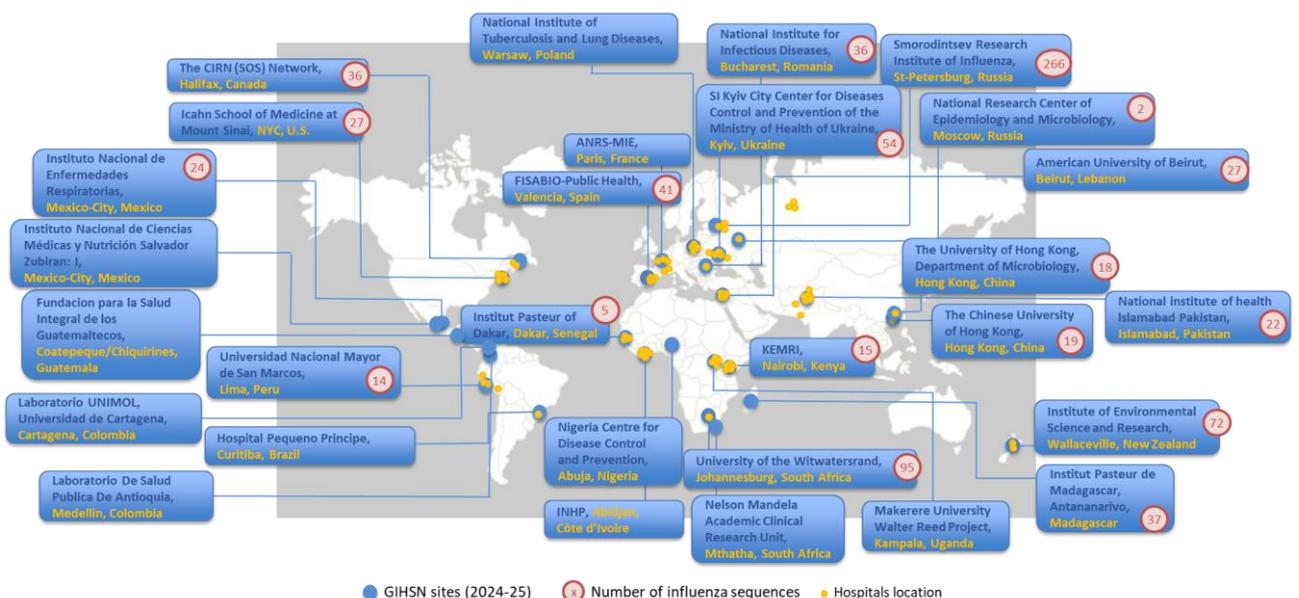


Fig. 1 Map showing the repartition of the participating countries, between February 2025 and August 2025, with the number of influenza sequences shared by sites.



2 - Description of the virus sequenced in the GIHSN

2.1 - Influenza A viruses

A(H1N1)pdm09 viruses

A(H1N1)pdm09 viruses were detected in all countries participating in the GIHSN network in 2025 except for Romania, with a total of 273 sequences reported.

Sequencing results indicated that 57.5% of these viruses (157/273) belonged to 6B.1A.5a.2a.1 clade represented by the reference strain A/Victoria/4897/2022, while 42.5% (116/273) belonged to 6B.1A.5a.2a clade (Fig. 2).

Among 5a.2a clade, all but one virus carried the HA1:T120A and K169Q substitutions that defines subclade **C.1.9**. In addition, 72 viruses (62% of the 5a.2a) belonged to **C.1.9.3** subclade characterized by HA1: S83P substitution.

Among 5a.2a.1 clade, most viruses (154/157, 98%) belonged to **D.3.1** subclade characterized by the HA1:T216A substitution also found in A/Victoria/4897/2022 reference strain, and additional HA1:T120A substitution.

Using a binomial logistic regression model, we observed a trend approaching significance ($p = 0.061$; OR = 1.87) toward a higher risk of requiring respiratory support among patients infected with the **D.3.1** subclade (57/117 patients with available oxygen data, 48.7%) compared to those infected with the C.1.9.3 subclade, which was the most prevalent A(H1N1) lineage in the 2024-2025 Northern Hemisphere season and taken as the reference (18/54 patients with available oxygen data, 33.3%). However, these findings should be interpreted with caution, as the analysis did not account for potential covariates such as age, geographic factors, and selection bias, which could represent important confounders.

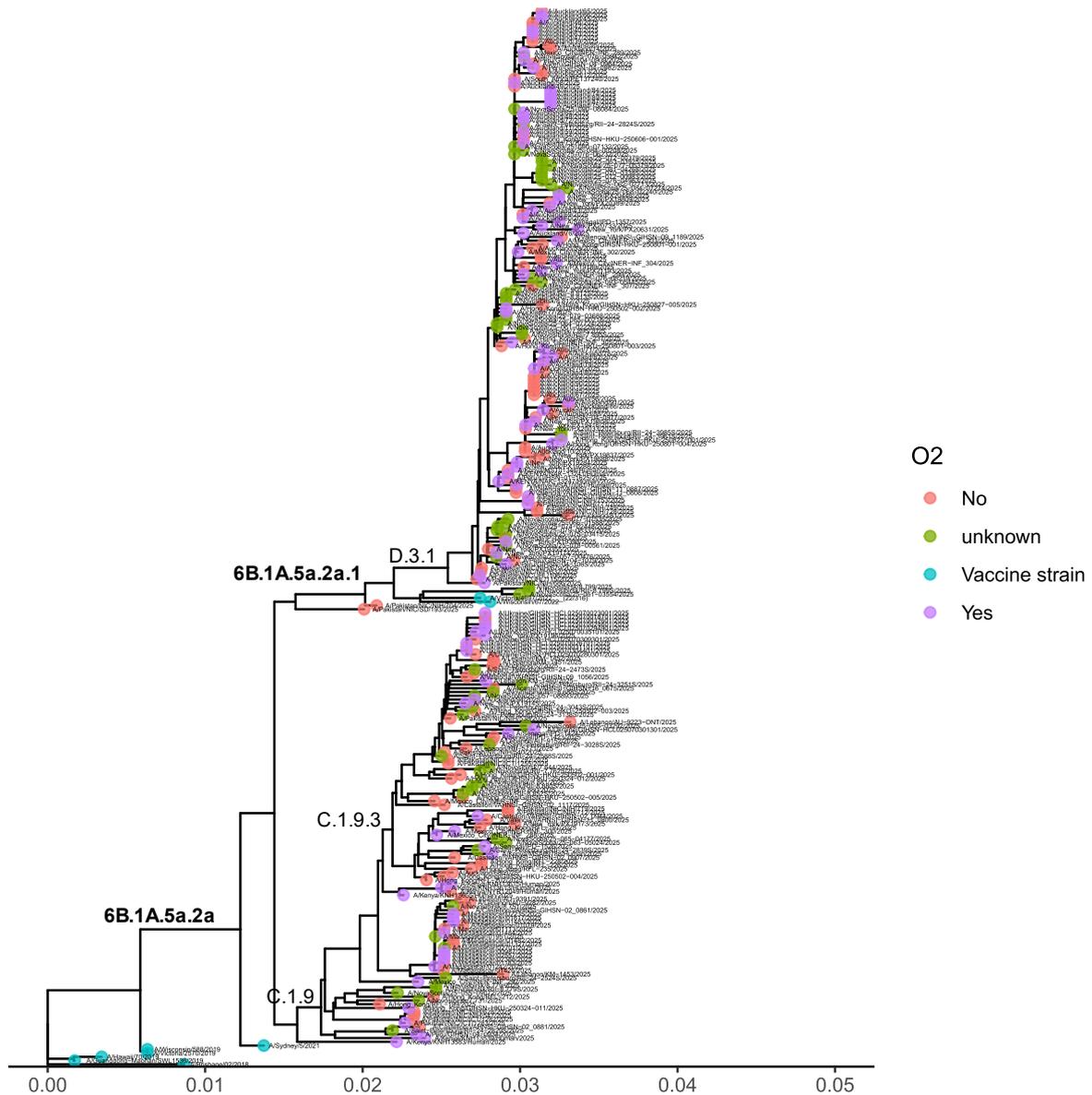


Fig 2: Phylogenetic tree of the A(H1N1pdm09) viruses analyzed between 2025-02-19 and 2025-08-10. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: purple; red:no) with vaccine reference strains displayed in cyan.

A(H3N2) viruses

A(H3N2) viruses were reported in most countries (n=13) participating in the GIHSN network during 2025, with 218 sequences reported.

All viruses belonged to 3C.2a1b.2a.2a.3a.1 clade, with 94% of viruses (204/218) falling into subclade J.2* characterized by the HA1:N122D and K276E substitutions and represented by SH 2025 vaccine strain A/Croatia/10136RV/2023 (Fig. 3).



Additional diversification on the J.2 branch occurred with a majority of viruses evolving into subclade **J.2.2** (130/204, 64%) defined by the HA1:S124N substitution. A minority of viruses evolved into subclade **J.2.1** (n=3) defined by HA1:F79L and P239S and into subclade **J.2.5** (n=2) characterized by HA1:N158K.

The remaining 6% of 2a.3a.1 viruses (14/218) fell into subclade **J.1.1** and were all detected in Madagascar except one sequence from Lebanon.

Using a binomial logistic regression model, we observed a trend approaching significance ($p = 0.069$; OR = 1.91) toward a higher risk of requiring respiratory support among patients infected with the **J.2.2** subclade (41/119 patients with available oxygen data, 34.5%) compared to those infected with the J.2 subclade, taken as the reference (14/65 patients with available oxygen data, 21.5%). However, these findings should be interpreted with caution, as the analysis did not account for potential covariates such as age, geographic factors, and selection bias, which could represent important confounders.

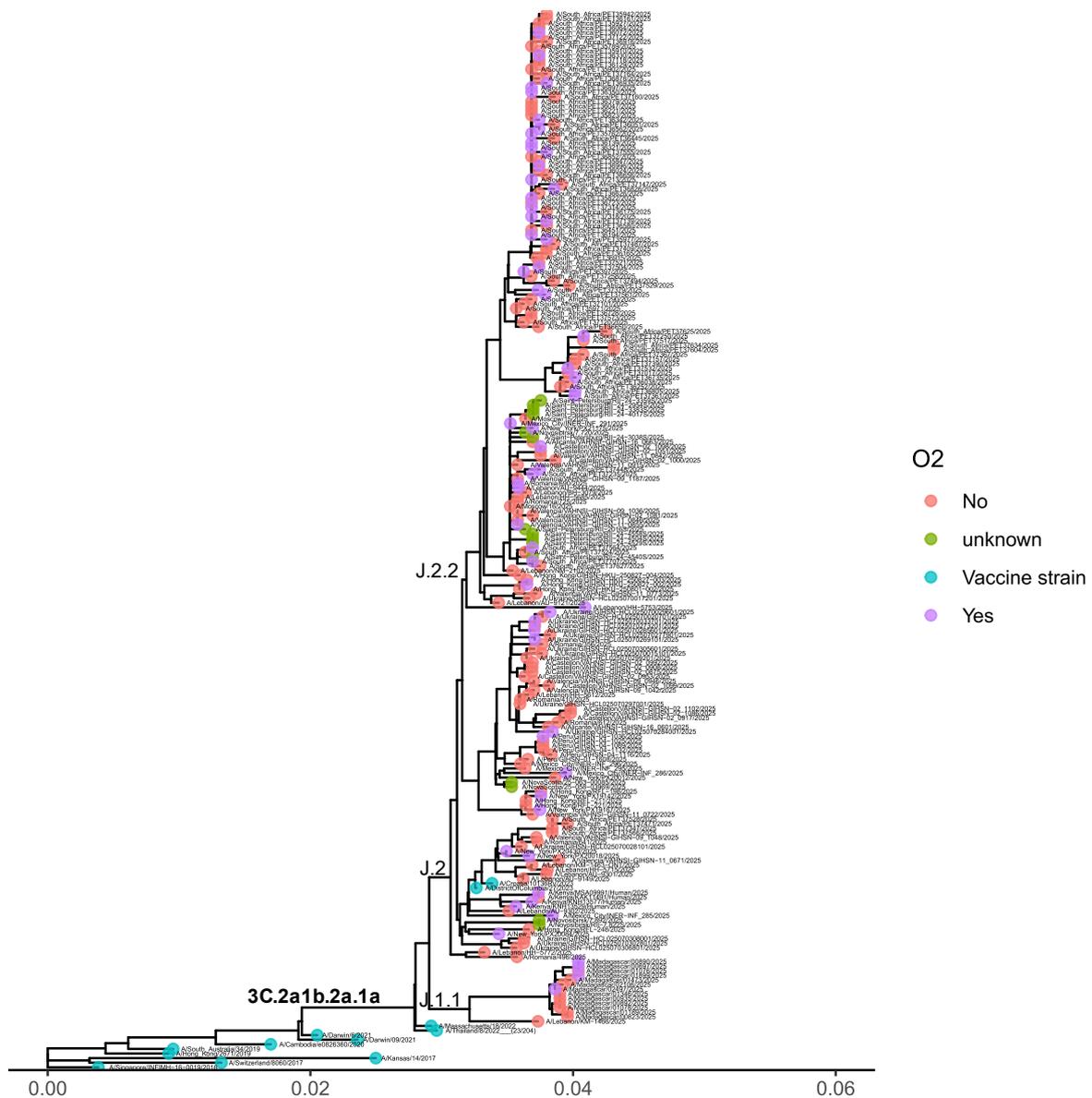


Fig 3: Phylogenetic tree of the A(H3N2) viruses analyzed between 2025-02-19 and 2025-08-10. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed



using *ggtree* in R. Tips (samples) colors correspond to Oxygen supplementation (yes: purple; red:no) with vaccine reference strains displayed in cyan.

2.2 - Influenza B viruses

B/Victoria Lineage

Influenza B/Victoria Lineage circulated in 9 countries from the GIHSN network, with 319 sequences reported.

All Influenza B viruses sequenced belonged to clade **V1A.3a.2** subclade C, with B/Austria/1359417/2021 as reference virus (Fig. 4).

All but one virus fell into C.5.* subclades characterized by HA1:D197E substitution compared with B/Austria/1359417/2021 reference strain, with a majority of the viruses (226/318, 71%) evolving into **C.5.6** subclade that further diversify into **C.5.6.1** subclade for 41 viruses, characterized by HA1:T37I. The majority of C.5.6.* viruses were detected in Russia (188/226, 83%).

Other C.5 viruses fell into **C.5.7** subclade (50/318, 16%) with HA1:E128G and **C.5.1** subclade (37/318, 12%).

No significant differences in the proportion of patients requiring respiratory support were observed between subclades of the B/Victoria lineage when analysed using a binomial logistic regression model.

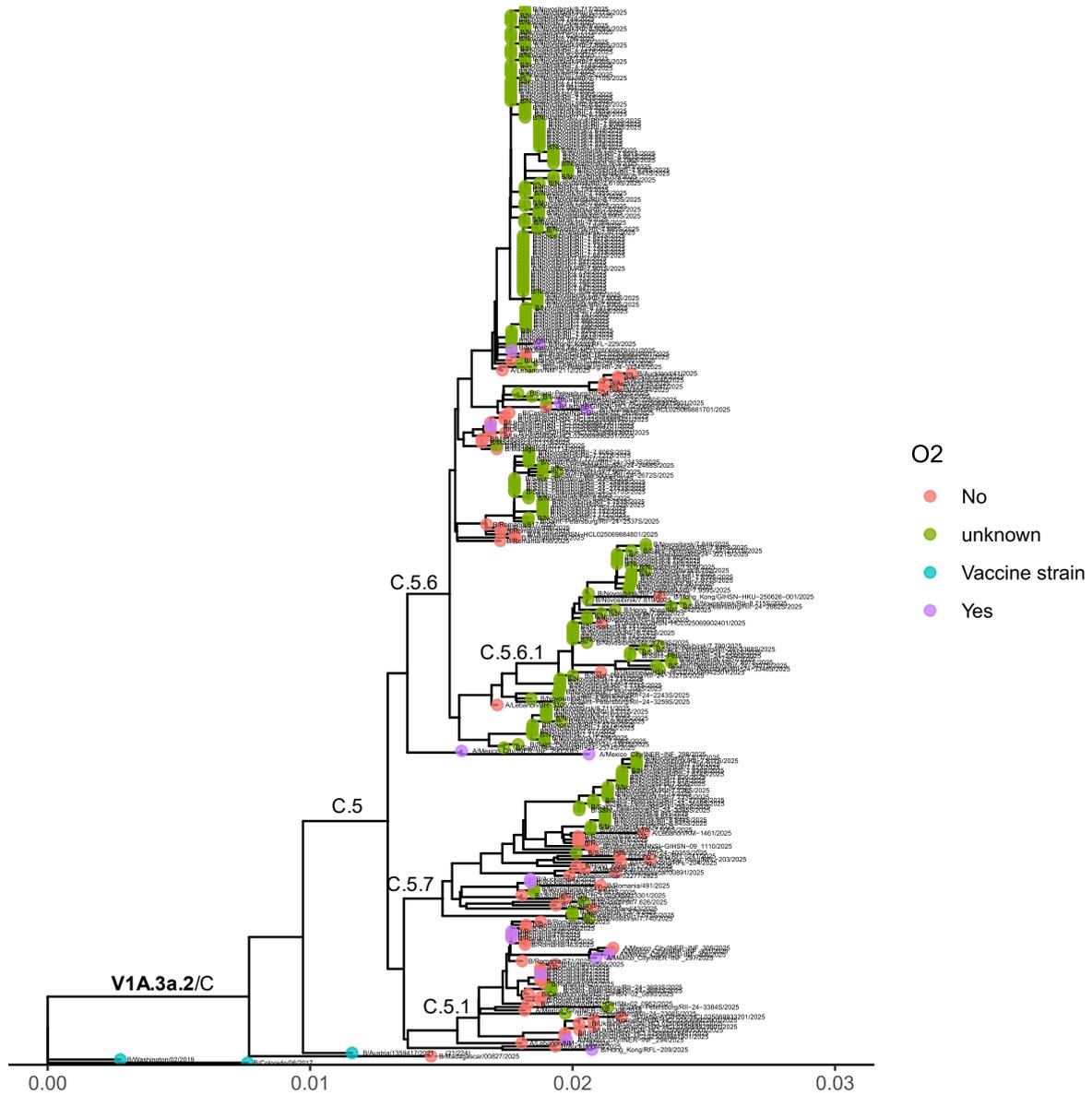


Fig 4: Phylogenetic tree of the B/Victoria viruses analyzed between 2025-02-19 and 2025-08-10. The phylogeny has been inferred using a Neighbor Joining approach (Seaview). Visualization was displayed using ggtree in R. Tips (samples) colors correspond to Oxygen supplementation (yes: purple; red:no) with vaccine reference strains displayed in cyan.

B/Yamagata viruses

No B/Yamagata/16/88 viruses have been detected.



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