Influenza virus characterization

Summary report, Europe, September 2024

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Acknowledgements

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Summary of the latest WHO Influenza Vaccine Composition meetings

Genetic and antigenic characterization data generated at the Worldwide Influenza Centre for viruses with collection dates from 1 February 2024 until 31 August 2024 informed the WHO influenza vaccine composition meeting (VCM) in September 2024 when recommendations were made for the Southern hemisphere (SH) 2025 influenza season. At the September 2024 VCM it was recommended to change the A(H3N2) vaccine components for the 2025 SH season. Previously, at the February 2024 VCM, which focused on data from viruses collected from 1 September 2023 until 31 January 2024, it was also recommended to change the A(H3N2) vaccine components for the 2024–2025 NH season

It is recommended that vaccines for use in the 2025 SH influenza season contain the following:

Trivalent: Egg-based Vaccines

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

Trivalent: Cell- or recombinant-based Vaccines

- an A/Wisconsin/67/2022 (H1N1)pdm09-like virus;
- an A/District of Columbia/27/2023 (H3N2)-like virus; and
- a B/Austria/1359417/2021 (B/Victoria lineage)-like virus.

Quadrivalent (egg- or cell culture- or recombinant-based vaccines): Above 3 components; and a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus.

Influenza B/Yamagata-lineage

No B/Yamagata-lineage viruses with collection dates after March 2020 have been detected or sequences released in GISAID as of 31 August 2024.

The absence of confirmed detection of naturally occurring B/Yamagata lineage viruses is indicative of very low risk of infection by B/Yamagata lineage viruses. Therefore, it is the opinion of the WHO influenza vaccine composition advisory committee that 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. A continued effort by all NICs of GISRS is required to identify B/Yamagata-lineage viruses for detailed characterization to determine if there are any in circulation.

Influenza by type/subtype

Worldwide

Geographical and time-dependent distribution of influenza viruses with collection dates from 1 September 2023 through to 31 August 2024 as deposited in GISAID (data accessed on 23/09/2024), coloured by Type/subtype. Geographic markers scaled to detection proportions. Full length HA. Map provided by WHO GIS Centre for Health, DNA/DDI. Timeline obtained with Microreact

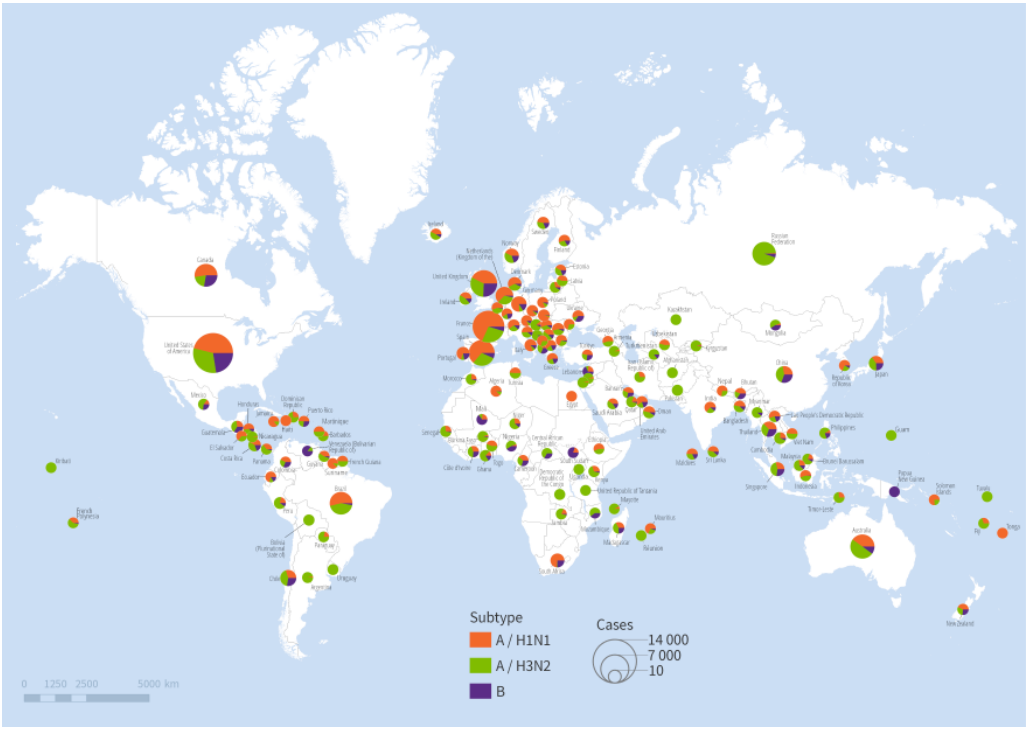


Figure 1: Global distribution of influenza virus subtypes

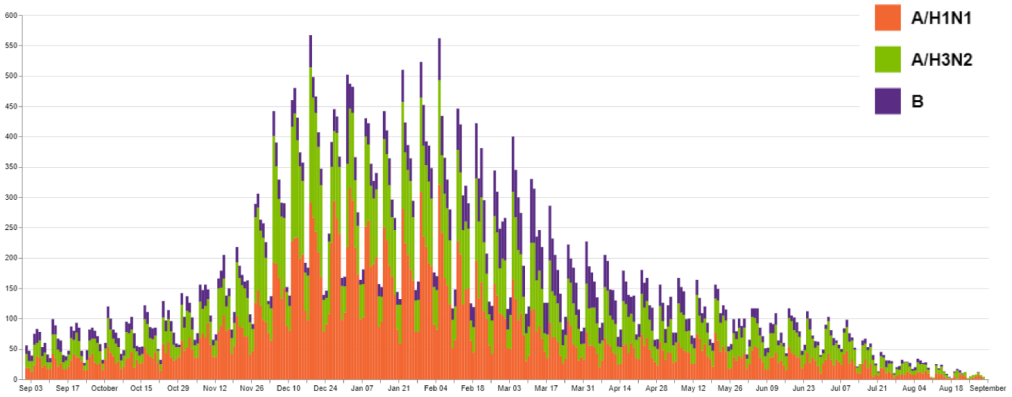


Figure 2: Timeline of circulation of influenza virus subtypes

Globally, influenza detections reached a peak in December 2023, have decreased since the report in January 2024 and continue to be low since the last report in May 2024 and throughout the Northern hemisphere summer. The relative proportions of A/H1N1, A/H3N2 and B/Victoria varied by geographic region. Subtype A/H1N1 predominated in Europe, South-East Asia and North America, the Caribbean region, Brazil, South

Africa, Algeria, Egypt, Republic of Korea and United Arab Emirates. Subtype A/H3N2 predominated in Central and South America, eastern Europe, Africa and Western Pacific region. Some countries showed some predominance of B/Victoria such as Venezuela, Lebanon, Mali, South Sudan and Papua New Guinea, as indicated by the different colours in the pie charts by country.

European region

Geographical distribution in the European region of influenza viruses with collection dates from 1 September 2023 through to 31 August 2024 as deposited in GISAID (data accessed on 23/09/2024), coloured by Type/subtype. Geographic markers scaled to detection proportions. Full length HA.Map provided by WHO GIS Centre for Health, DNA/DDI.Timeline obtained with Microreact

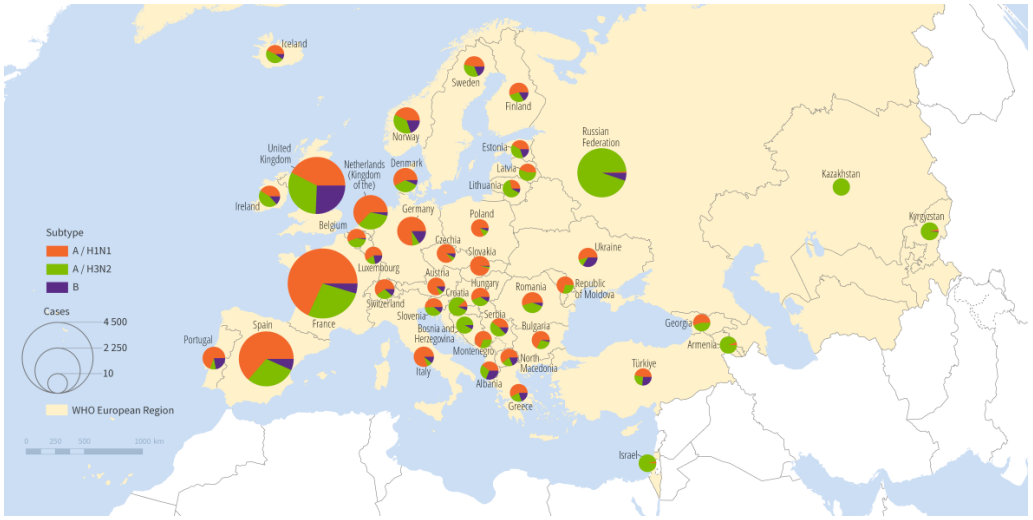


Figure 3: European region - Distribution of influenza virus subtypes

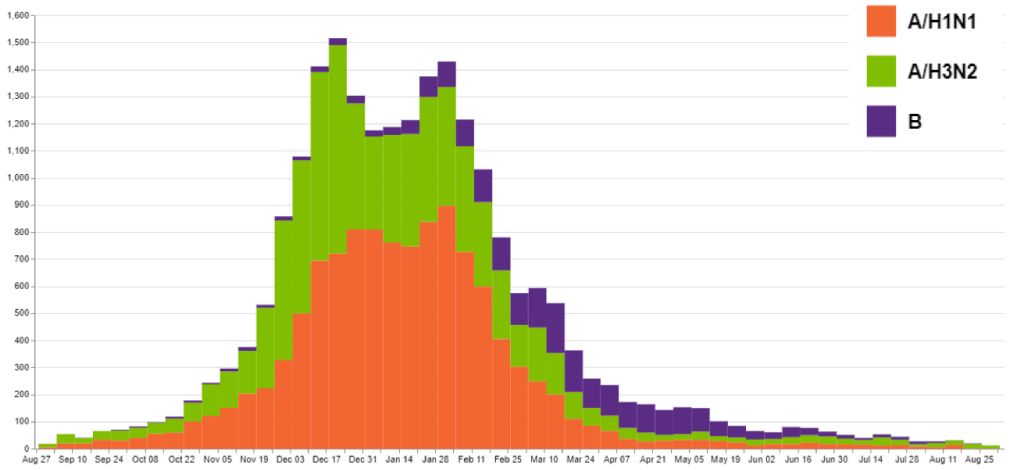


Figure 4: European region - Timeline of circulation of influenza virus subtypes

In the European region, influenza detections have continued to be low since the last report in May 2024 and throughout the summer.

The majority of countries which reported detections showed some co-circulation of A/H1N1 and A/H3N2 with predominance of A/H1N1 viruses and sporadic detections of influenza B/Victoria, as indicated by the different colours in the pie charts.

Summary of influenza detections in the WHO European Region, week 35/2023 to 35/2024

Table 1 shows influenza virus detections in the WHO European Region reported to The European Surveillance System (TESSy) database from 1 September 2023 to 31 August 2024 (weeks 35/2023 to 35/2024) compared with the same period in the previous season. For type-percentage calculations, the denominator is total detections; for subtype and lineage, it is the total influenza A subtyped and total influenza B lineage determined, respectively. As not all countries have a true non-sentinel testing denominator, no percentage calculations for total tested are shown (Data taken from Flu News Europe reports and from ERVISS (European Respiratory Virus Surveillance Summary)).

Table 1. Sentinel and non-sentinel influenza detections. Comparison of current season 2023-24 with last season 2022-23

	Cumulative number of detections for weeks 35/2023 to 35/2024				Cumulative number of detections for weeks 35/2022 to 35/2023			
Virus type/subtype/lineage	Sentinel sources	Non-sentinel sources	Totals	%	Sentinel sources	Non-sentinel sources	Totals	%
Influenza A	13404	163608	177012	94	10573	124815	135388	69
A(H1N1)pdm09	8936	25329	34265	73	3135	19832	22967	61
A(H3N2)	2468	10365	12833	27	4312	10441	14753	39
A not subtyped	2000	127914	129914	NA	3126	94542	97668	NA
Influenza B	1453	9377	10830	6	6527	55334	61861	31
Victoria lineage	801	1659	2460	100	1682	3233	4915	100
Yamagata lineage	0	0	0	NA	0	0	0	NA
Lineage not ascribed	652	7718	8370	NA	4845	52101	56946	NA
Total detections	14857	172985	187842	NA	17100	180149	197249	NA
Total tested	107646	2037899	2145545	NA	93459	1847629	1941088	NA

Compared with the same period (weeks 35/2022 to 35/2023), for both sentinel and non-sentinel surveillance the number of specimens tested is higher, whereas the number of influenza detections has decreased. During the current season, the proportion of influenza A of unknown subtype among sentinel cases has maintained consistently around 15% of the total influenza A detected, compared with 30% in last season; for non-sentinel cases, not-subtyped influenza A detections accounted for 78% of the total influenza A detected in 2023–24, compared with 76% for 2022–23.

Relative frequencies of type A vs B influenza viruses continue to show predominance of influenza A with a proportion of 94% compared with 69% in 2022–2023. Currently, in Europe there are sporadic detections of influenza B (6%), and predominance was circumscribed to a few countries. Relative frequencies of influenza A subtypes have also shifted, with A/H1N1 viruses increasing from 61% to 73% frequency and a higher proportion of circulating A/H1N1 viruses (73% A/H1N1 vs 27% A/H3N2) compared to last season (61% A/H1N1 vs 39% A/H3N2).The relative frequencies of A/H1N1 vs A/H3N2 have maintained since the last report in May 2024.

Sentinel surveillance system dynamics, week 35/2023 to 22/2024

Figure adapted from ERVISS

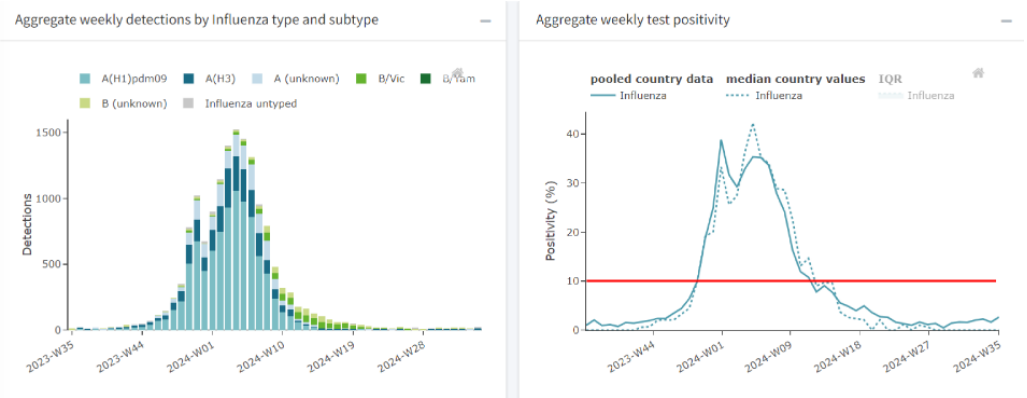


Figure 5: Aggregate sentinel weekly detections

During the period from week 35/2023 to week 35/2024, influenza activity remained at low levels through the reporting period until week 46 when it started to increase, crossing the epidemic threshold of 10% in week 50. This marks a late start of the influenza season when compared with the previous season where the epidemic threshold of 10% had been crossed by week 45.Influenza activity peaked briefly in week 1 and then again in week 5, then started to decrease until it fell below the 10% threshold in week 11. Since the last report in week 22, influenza activity remained low in the European region.

Across sentinel surveillance, influenza A/H3N2 and A/H1N1 viruses cocirculated with predominance of A/H1N1 during most of this period, with overall frequencies of 79% for A/H1N1 and 21% for A/H3N2. From week 8 onwards the proportion of influenza B increased slightly, to become predominant from week 13 up to week 21. After week 21 up to week 35, overall influenza detections have been low.

Genetic diversity by Type/Lineage and group

Number of viruses classified by genetic clades (subclades), obtained with full HA sequences as deposited in GISAID and classified using Nextclade. Collection dates 01/09/2023 to 31/08/2024.

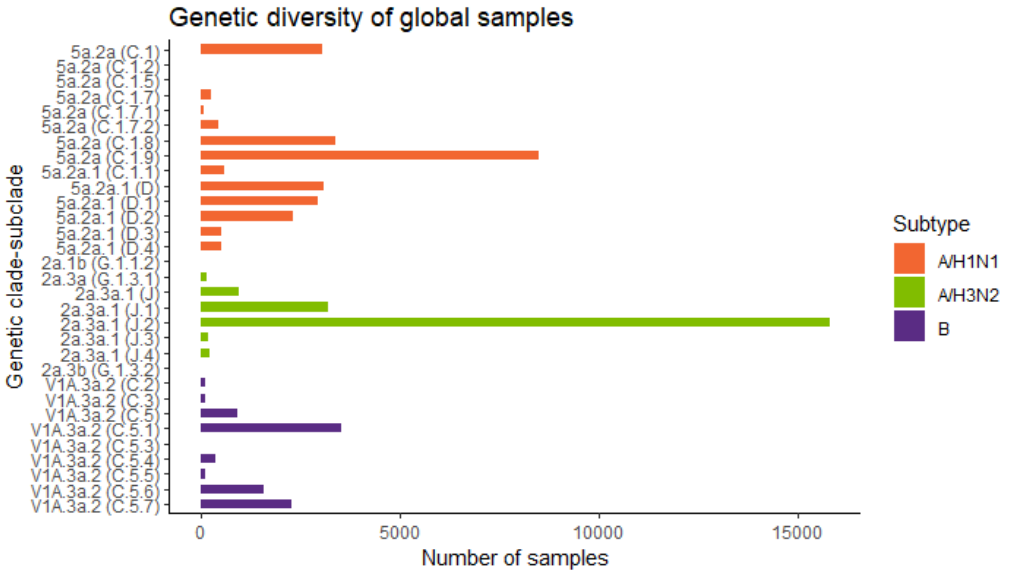


Figure 6: Global proportion of genetic subclades

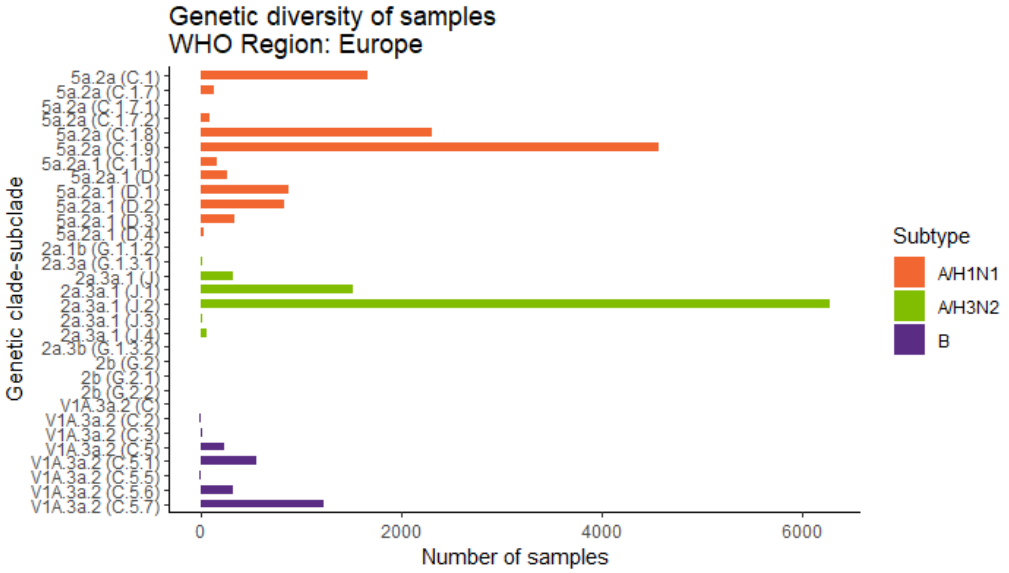


Figure 7: European region - Proportion of genetic subclades

Influenza A/H1N1

Genetic analyses: A/H1N1

6B.1A.**5a.2a** and 6B.1A.**5a.2a.1** clade viruses both continued to circulate with changing relative proportions throughout this period. Since September 2023, predominance of clade 5a.2a subclade C.1 and clade 5a.2a.1 subclade D1 was observed, which shifted during the NH winter season towards increased predominance of clade 5a.2a subclades C.1.9 and C.1.8 with minor circulation of clade 5a.2a.1 subclade D. These relative proportions continued to be observed during the NH summer season up to end of August 2024.

Globally, there is predominance of clade 5a.2a except in the Americas where there is a slight predominance of clade 5a.2a.1. In Europe, viruses from clade 5a.2a were detected with much higher frequency than clade 5a.2a.1.

Within the 5a.2a viruses, characterised by substitutions K54Q, A186T, E224A, R259K and K308R, several subclades were observed: subclade C.1 defined by substitution I418V which split into two further subclades: C.1.8, characterised by V47I with I96T in most sequences, and C.1.9, with substitution K169Q; the majority (>80%) of H1pdm viruses sequenced globally belong to subclade C.1.9, with viruses from C.1.8 as a minority subclade mostly observed in Europe. Minor subclades C.1.7 with substitution I533V and C.1.7.2 with T120A and K142R predominated only in Indonesia and were detected in low proportions in a few other countries.

Within the 5a.2a.1 viruses, characterised by substitutions P137S, K142R, D260E, T277A, E356D and N451H, there are two main groups of viruses: major subclade D (former C.1.1.1) with T216A represented by A/Victoria/4897/2022, which has split into four subclades: D.1 with R45K, D.2 with R113K and V427I, D.3 with T120A and I372V and D.4 with T120A. Of these, only subclade D circulates in significant proportions, albeit predominating only in the Americas. Subclade C.1.1 is a minor clade within 5a.2a.1 viruses with no additional substitutions represented by A/Wisconsin/67/2022, which has been detected in significant proportions only in Iceland.

Phylogenetic tree in Figure 11 with coloured tips for viruses dated from February to August 2024 (older viruses in grey) shows that, across the topology of the tree, the most recent viruses detected in Europe belong to subclade C.1.9, with some viruses also clustering within 5a.2a.1 subclade D.

Global and European geographical distribution of influenza A/H1N1 genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using Nextclade.Geographic markers scaled to detection proportions. Map provided by WHO GIS Centre for Health, DNA/DDI

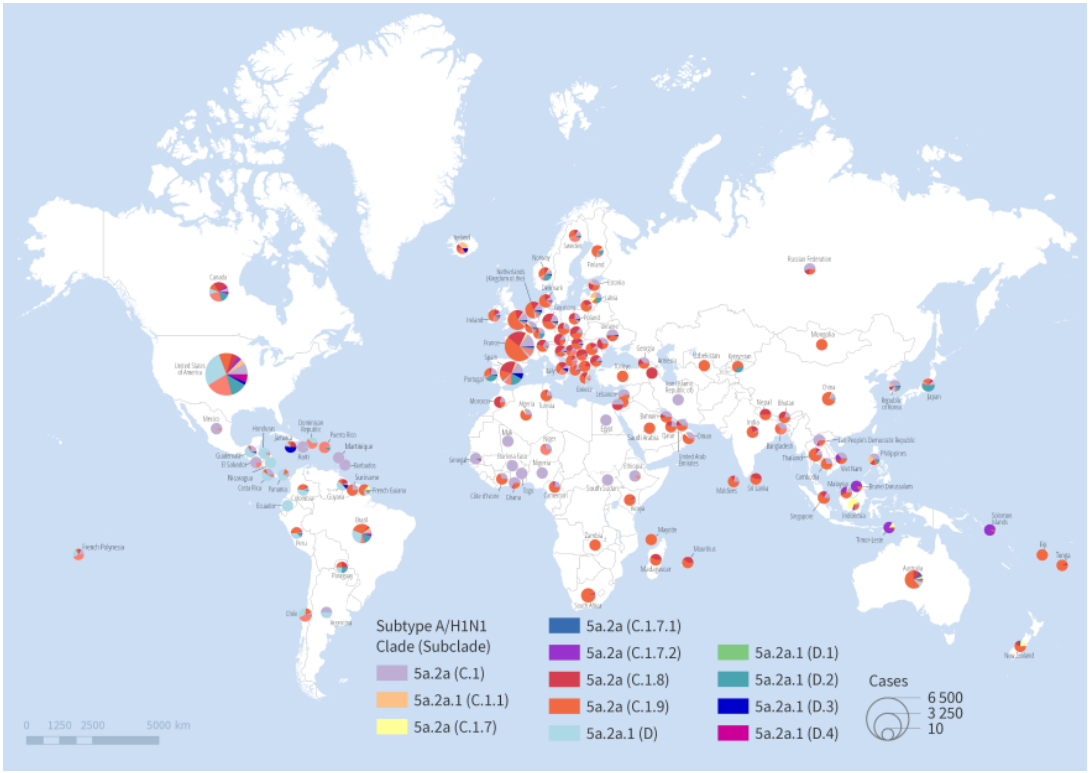


Figure 8: Global geographical distribution of influenza A/H1N1 genetic clades (subclades)

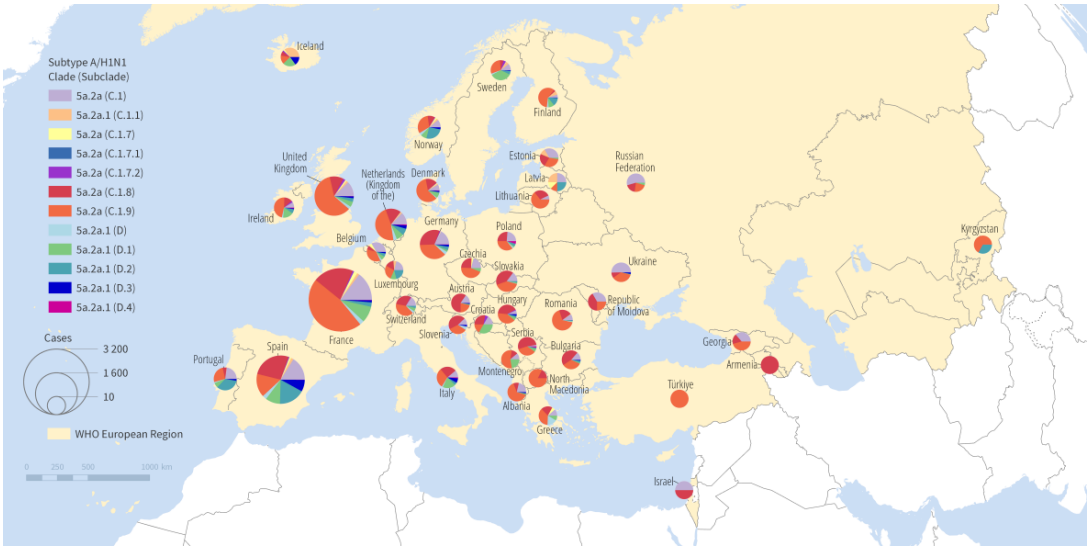


Figure 9: European region - Geographical distribution of influenza A/H1N1 genetic clades (subclades)

Global time-dependent variation in frequencies of genetic clades (subclades) of A/H1N1 viruses, collection dates 01/09/2023 to 31/08/2024.

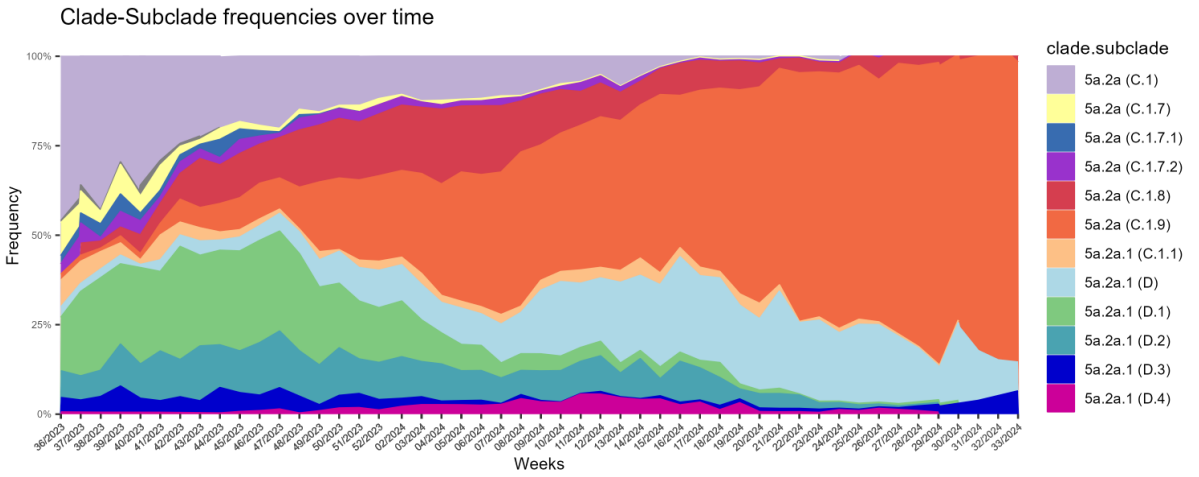


Figure 10: Global time-dependent variation in frequencies of A/H1N1 genetic clades (subclades)

Maximum likelihood Phylogenetic trees: A/H1N1

Maximum likelihood (ML) phylogenetic trees inferred using Iqtree2 from HA sequence data obtained from GISAID. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction; all reference viruses and tree nodes with more than one sequence were annotated. References and CVVs are marked as Cell or Egg.

Phylogenetic tree in Figure 11 was built with all European GISRS A/H1N1 sequences uploaded to GISAID with collection dates from September 2023 to August 2024 (n~9000) with coloured tips for viruses dated from February to August 2024 (older viruses in grey).

Phylogenetic tree in Figure 12 was initially built with all European GISRS A/H1N1 sequences uploaded to GISAID with collection dates from February to August 2024, downsampled using Treemer to retain a representative tree topology of 200 sequences.

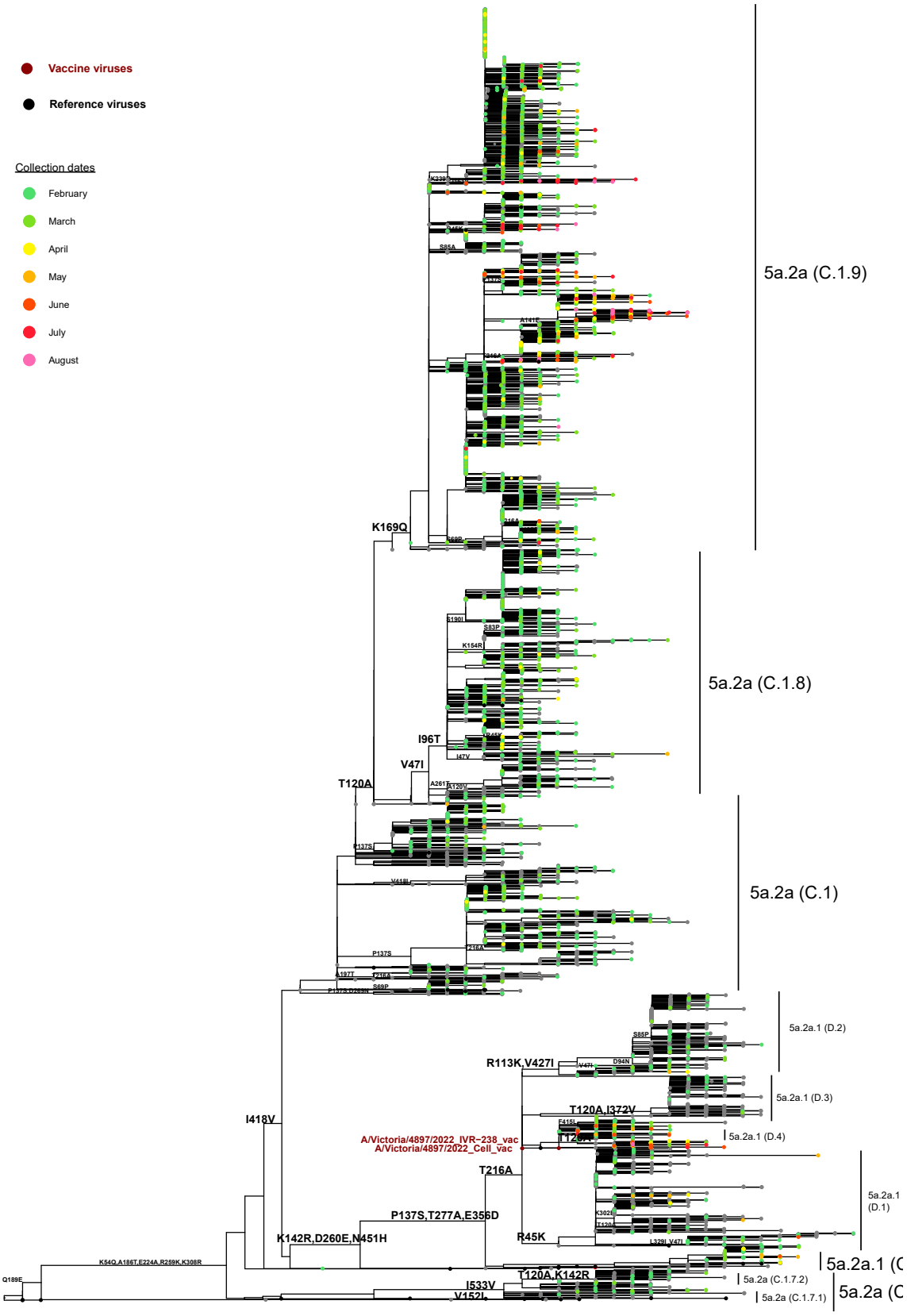


Figure 11: ML phylogenetic tree, all European GISRS A/H1N1 sequences from September 2023 to August 2024

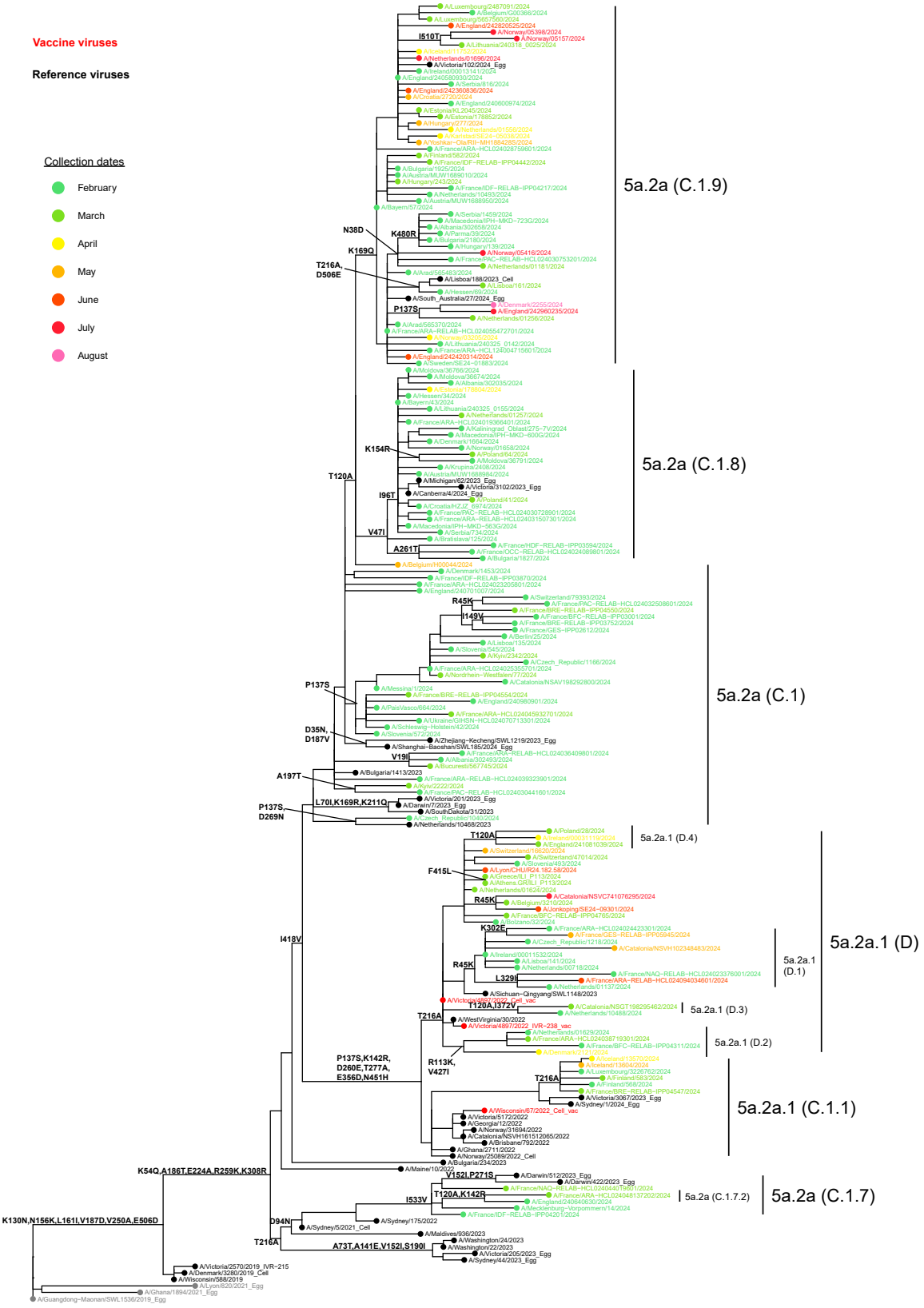


Figure 12: ML phylogenetic tree, 200 representative European GISRS A/H1N1 sequences from February to August 2024

Summary of the antigenic properties of A/H1N1 viruses circulating in the reporting period

Table 2 and Figure 13 show that NH 2023-24, 2024-25 and SH 2024 strains, cell-based A/Wisconsin/67/2022 and egg-based A/Victoria/4897/2022, generally recognised both 5a.2a and 5a.2a.1 clade viruses well. Some four-fold drops were observed with the cell- based A/Wisconsin/67/2022 strain that were not seen with the egg-based A/Victoria/4897/2022.

For an overall picture of the genetic and antigenic relationships across viruses collected during the previous season, see the Annex.

Heatmapped phylogenetic trees represent the combined genetic and antigenic analyses (HI) where the correlation between genetic groups, signature amino acids and their antigenic profile can be observed.

Figure 13: ML phylogenetic tree with combined heatmap representing antigenic reactivities by HI

Table 2. A/H1N1 fold-reduction table

		<4-fold difference		4-fold difference		>4-fold difference		
Reference Virus	Clade	Number	Percentage	Number	Percentage	Number	Percentage	Total
IVR-215 (A/Victoria/2570/2019) Egg	5a.2 (C)	38	100.0	0	0.0	0	0.0	38
A/Sydney/5/2021 Cell	5a.2a (C.1)	358	95.5	17	4.5	0	0.0	375
A/Sydney/5/2021 Egg	5a.2a (C.1)	38	100.0	0	0.0	0	0.0	38
A/Lisboa/188/2023 Cell	5a.2a.1 (C.1)	340	95.2	16	4.5	1	0.3	357
A/Wisconsin/67/2022 Cell	5a.2a.1 (C.1.1)	303	80.8	67	17.8	5	1.3	375
A/Victoria/4897/2022 Cell	5a.2a.1 (D)	329	87.7	42	11.2	4	1.0	375
IVR-238 (A/Victoria/4897/2022) Egg	5a.2a.1 (D)	365	97.3	9	2.4	1	0.3	375

Table 3. A/H1N1 HI reagents and references

Virus	Genetic group	Virus passage	Ferret ID
A/Sydney/5/2021	5a.2a (C.1)	MDCK3/MDCK4	F46/22
A/Victoria/4897/2022	5a.2a.1 (D)	SIAT2/MDCK3	F05/23
IVR-238 (A/Victoria/4897/2022)	5a.2a.1 (D)	E3/D6/E1	F07/23
A/Wisconsin/67/2022	5a.2a.1 (C.1.1)	MDCK2	F17/23
A/Lisboa/188/2023	5a.2a.1 (C.1)	SIAT1/MDCK2	F09/24

Influenza A/H3N2

Genetic analyses: A/H3N2

Please note that within clade 2a.3a.1, former subclade H and derivatives (H.1 to H.4) have been renamed as J (J.1 to J.4).

Clade 3C.2a1b.2a.2 (renamed as **2**) predominated since February 2023 in all geographic regions where A/H3N2 circulated.

Since September 2023, the majority of circulating A/H3N2 viruses belong to clade 2a.3a.1, with subclades J, J.1 and J.2 cocirculating in similar proportions, which shifted during the NH winter season towards an increased predominance of subclade J.2. This predominance continued to be observed during the NH summer season up to end of August 2024.

During this reporting period, the great majority of H3 viruses detected belong to clade 2a.3a.1, which share substitution E50K with clade 2a.3a and present additional substitutions I140K and I223V (subclade J, vaccine reference A/Thailand/8/2022). Subclade J split into 4 further subclades: of these, subclade J.2 (reference A/Sydney/878/2023) characterised by N122D (-CHO) and K276E became the dominant subclade, predominating in the majority of continents with >90% frequency. Subclade J.1 (reference A/Sydney/856/2023) characterised by I25V, V347M with additional I418V (in some viruses) was detected in minor frequencies (<10%) in Europe, South-East Asia, Africa and Oceania. Minor subclade J.4 characterised by Q173R, K276E and some viruses with K189R predominated in West Africa earlier during the season.

Clade 2a.3a (subclade G.1.3.1, reference A/Finland/402/2023) with substitutions K276E and V347M was detected in West Africa earlier during the season.

Phylogenetic tree in Figure 17 with coloured tips for viruses dated from February to August 2024 (older viruses in grey) shows that, across the topology of the tree, the most recent viruses detected in Europe belong to subclade J.2. Convergent evolution was observed with several sequences in separate clades characterised by substitutions such as S124N, S145N and fewer viruses with substitutions N158K and K189R.

Global and European geographical distribution of influenza A/H3N2 genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using Nextclade.Geographic markers scaled to detection proportions. Map provided by WHO GIS Centre for Health, DNA/DDI

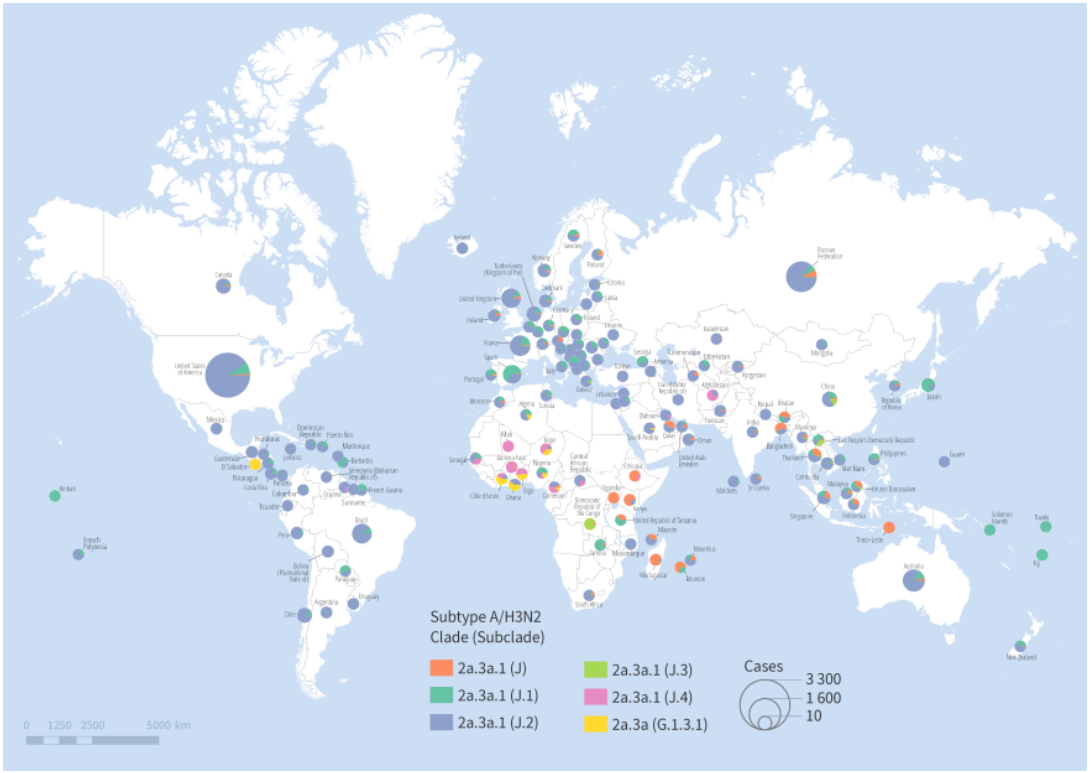


Figure 14: Global geographical distribution of influenza A/H3N2 genetic clades (subclades)

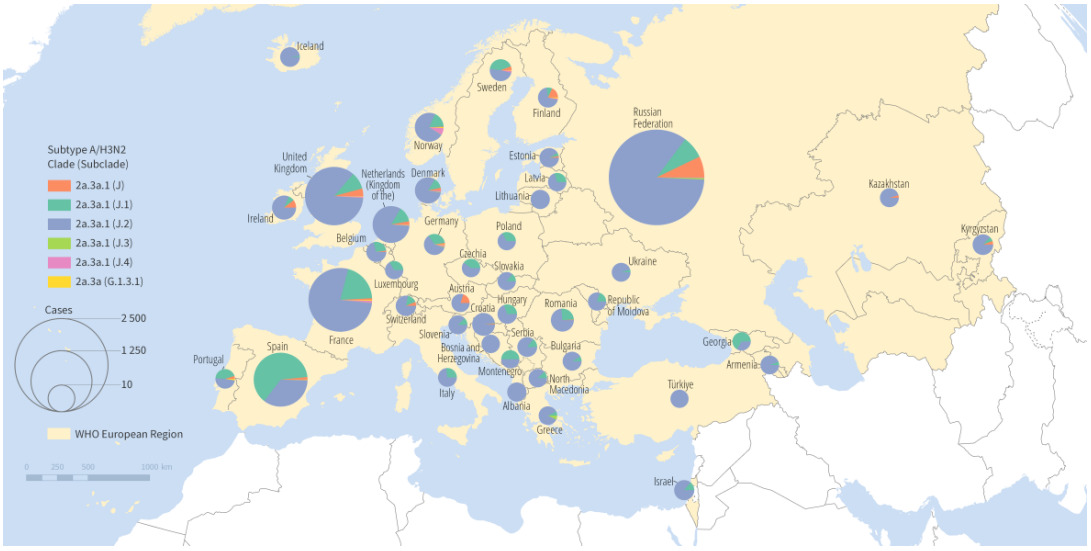


Figure 15: European region - Geographical distribution of influenza A/H3N2 genetic clades (subclades)

Global time-dependent variation in frequencies of genetic clades-subclades of A/H3N2 viruses collected since 1 September 2023 to 31 August 2024.

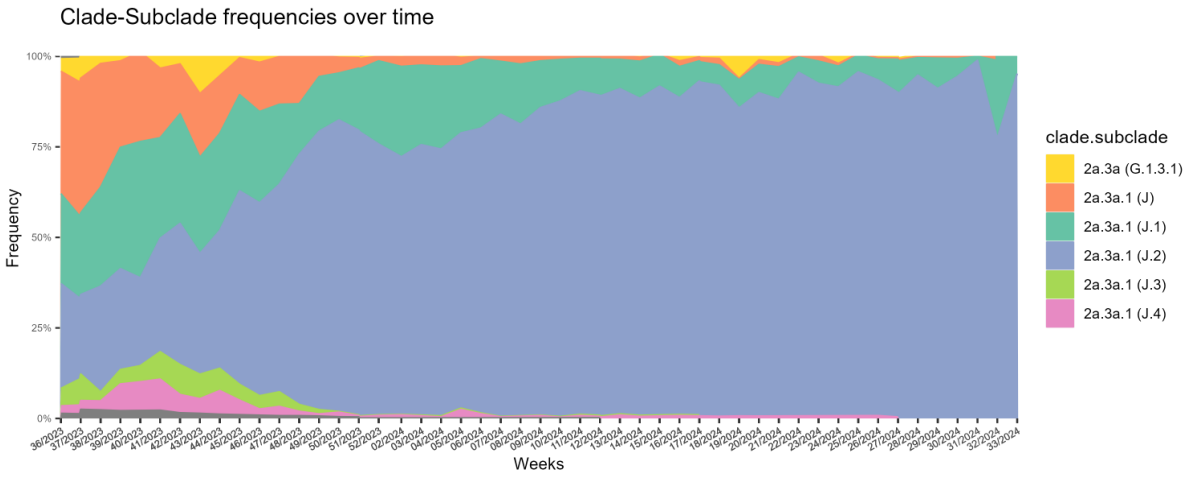


Figure 16: Global time-dependent variation in frequencies of A/H3N2 genetic clades (subclades)

Maximum likelihood phylogenetic tree: A/H3N2

Maximum likelihood phylogenetic trees inferred using Iqtree2 from HA sequence data obtained from GISAID. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction; all reference viruses and tree nodes with more than one sequence were annotated. References and CVVs are marked as Cell or Egg.

Phylogenetic tree in Figure 17 was built with all European GISRS A/H3N2 sequences uploaded to GISAID with collection dates from September 2023 to August 2024 (n~6700) with coloured tips for viruses dated from February to August 2024 (older viruses in grey).

Phylogenetic tree in Figure 18 was initially built with all European GISRS A/H3N2 sequences uploaded to GISAID with collection dates from February to August 2024, downsampled using Treemer to retain a representative tree topology of 200 sequences.

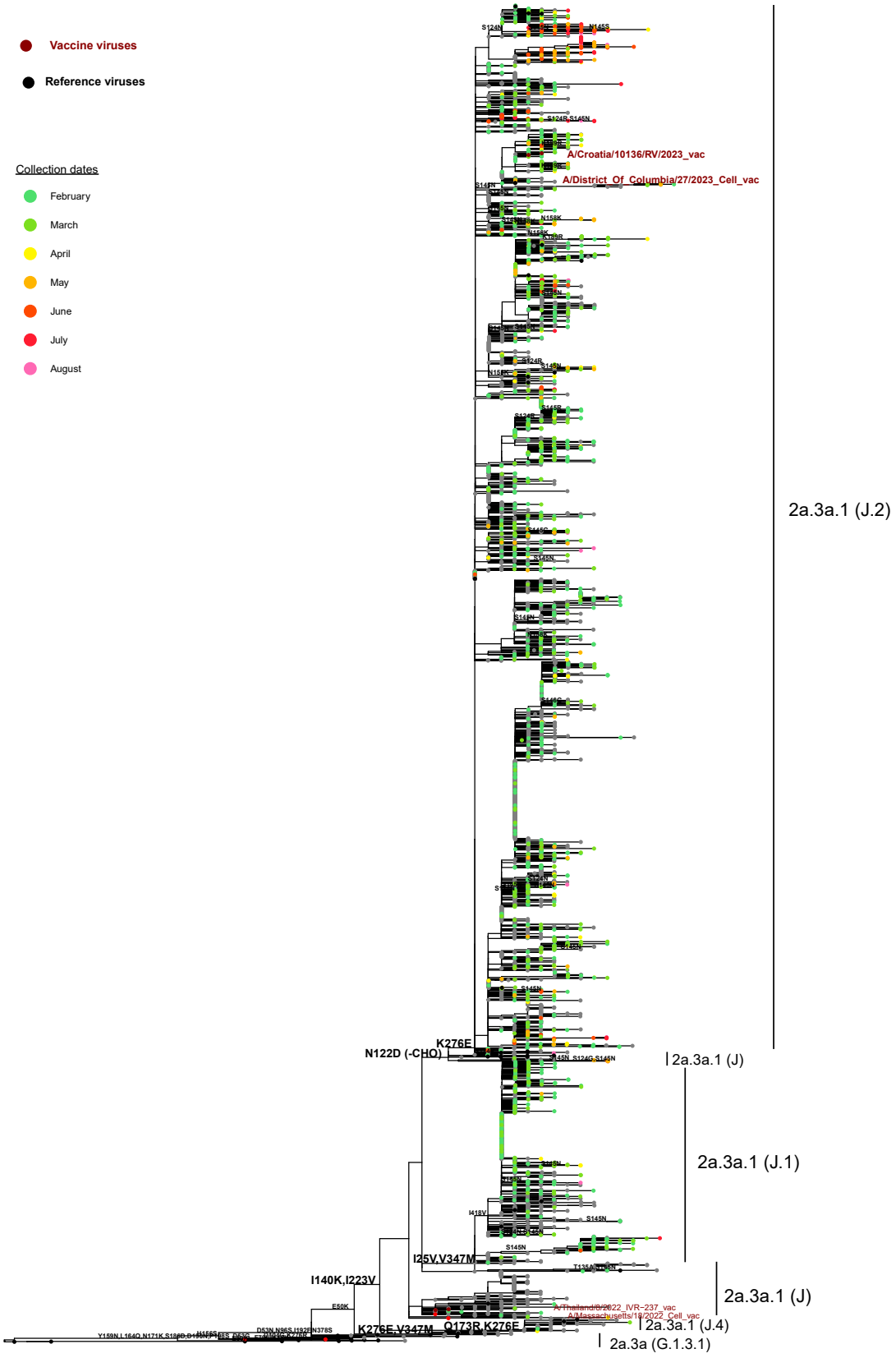


Figure 17: ML phylogenetic tree, all European GISRS A/H3N2 sequences from September 2023 to August 2024

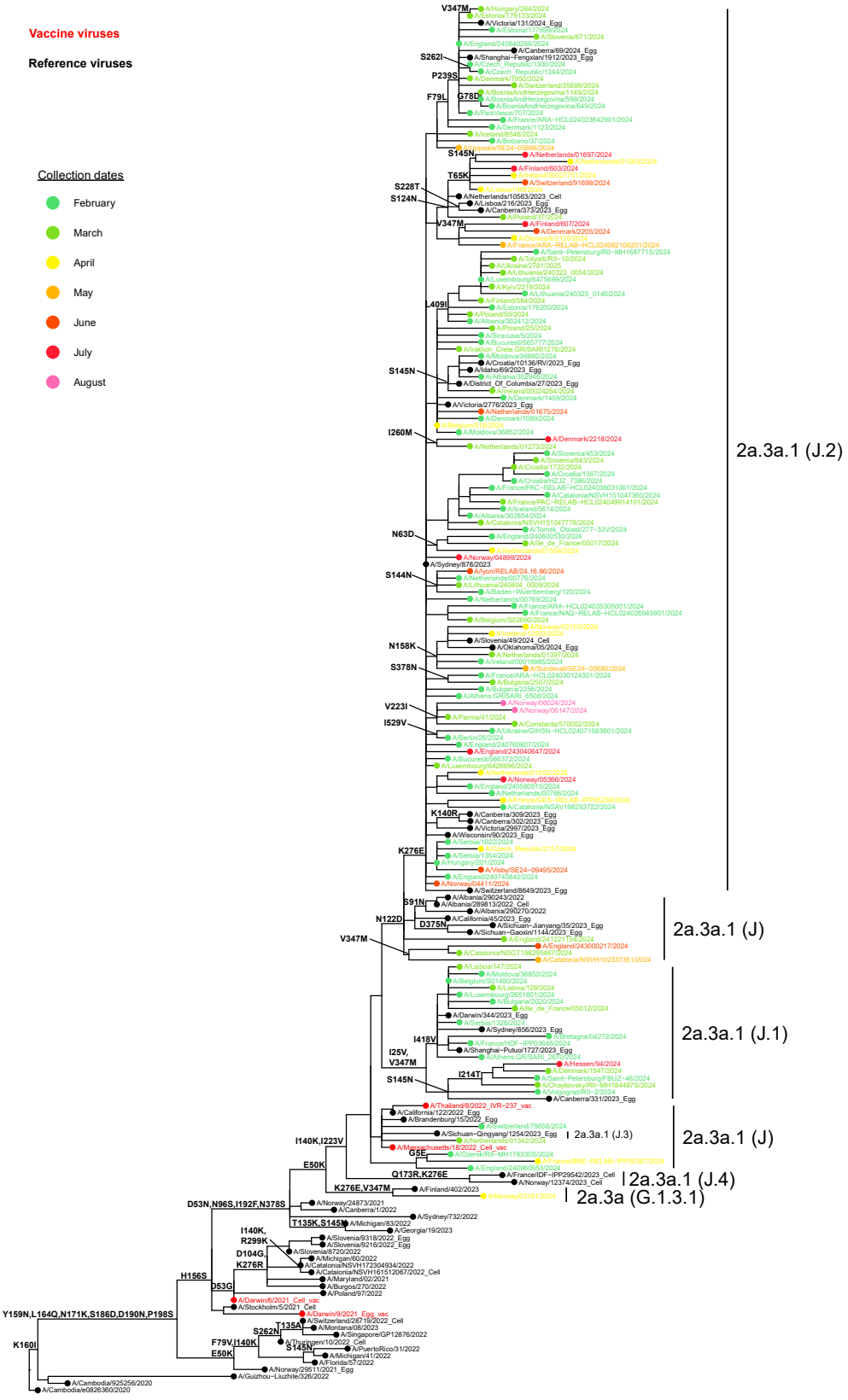


Figure 18: ML phylogenetic tree, 200 representative European GISRS A/H3N2 sequences from February to August 2024

Summary of the antigenic properties of A/H3N2 viruses circulating in the reporting period

Table 4 and Figure 19 show that the SH 2024 and NH 2024-25 vaccine strains, egg-based A/Thailand/08/2022 (2a.3a.1 (J)) and cell-based A/Massachusetts/18/2022 (2a.3a.1 (J)), demonstrate reduced recognition against a significant number of samples in the J.2 and J.4 subclades. MN titres show that the SH 2024 and NH 2024-25 vaccine strain, egg-based A/Thailand/08/2022 (2a.3a.1 (J)) shows reduced reactivity to the vast majority of viruses tested. The cell-based SH 2024 and NH 2024-25 vaccine strain, A/Massachusetts/18/2022 (2a.3a.1 (J)) recognised most viruses tested within 2-fold, but showed significant drop in titre to some J.2 and all J.4 viruses tested to date.

For an overall picture of the genetic and antigenic relationships across viruses collected during the previous season, see the Annex.

Heatmapped phylogenetic trees represent the combined genetic and antigenic analyses (HI) where the correlation between genetic groups, signature amino acids and their antigenic profile (including microneutralisation (MN) for A/H3N2) can be observed.

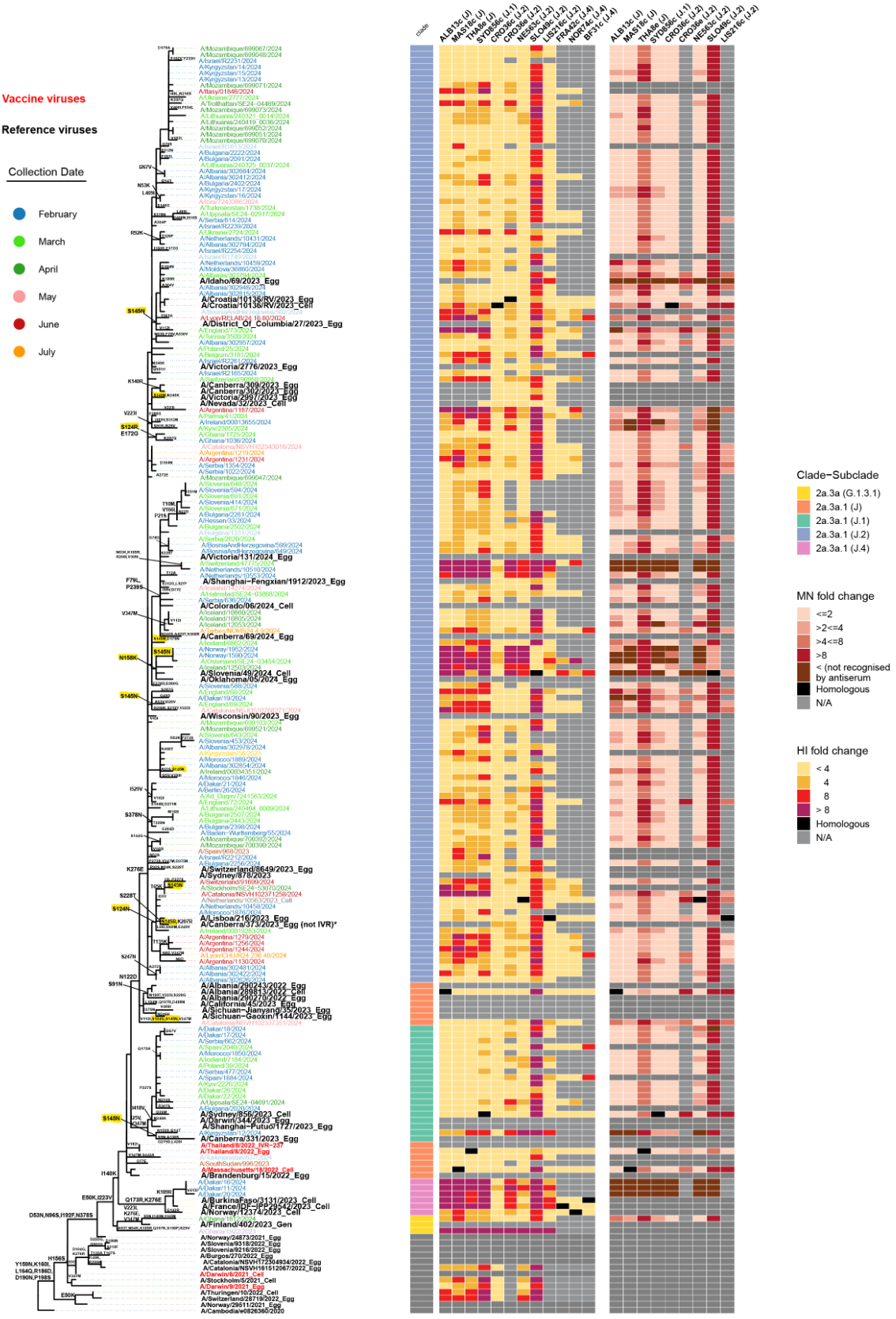


Figure 19: ML phylogenetic tree with combined heatmap representing antigenic reactivities by HI and MN

Table 4. A/H3N2 fold-reduction table

		<4-fold difference		4-fold difference		>4-fold difference		
Reference Virus	Clade	Number	Percentage	Number	Percentage	Number	Percentage	Total
A/Thuringen/10/2022 Cell	2b	10	30.3	22	66.7	1	3.0	33
A/Switzerland/28719/2022 Cell	2b	3	9.1	21	63.6	9	27.3	33
A/Stockholm/5/2021 Cell	2a	8	24.3	12	36.4	13	39.4	33
A/Darwin/9/2021 Egg	2a	24	72.7	9	27.3	0	0.0	33
A/Catalonia/NSVH161512067/2022 Cell	2a.1b	3	9.1	22	66.7	8	24.2	33
A/Albania/289813/2022 Cell	2a.3a.1 (J)	236	56.6	114	27.3	67	16.1	417
A/Massachusetts/18/2022 Cell	2a.3a.1 (J)	110	26.4	148	35.5	159	38.1	417
A/Thailand/08/2022 Egg	2a.3a.1 (J)	182	43.6	131	31.4	104	24.9	417
A/Sydney/856/2023 Cell	2a.3a.1 (J.1)	140	33.6	118	28.3	159	38.1	417
A/Croatia/10136/RV/2023 Cell	2a.3a.1 (J.2)	402	96.4	15	3.6	0	0.0	417
A/Croatia/10136/RV/2023 Egg	2a.3a.1 (J.2)	159	41.4	160	41.7	65	16.9	384
A/Netherlands/10563/2023 Cell	2a.3a.1 (J.2)	353	84.7	48	11.5	16	3.8	417
A/Lisboa/216/2023 Egg	2a.3a.1 (J.2)	303	78.9	70	18.2	11	2.9	384
A/Slovenia/49/2024 Cell	2a.3a.1 (J.2)	7	1.8	17	4.4	360	93.8	384
A/Vasteras/SE23-14213/2023 Cell	2a.3a.1 (J.2)	4	100.0	0	0.0	0	0.0	4
A/Switzerland/8649/2023 Egg	2a.3a.1 (J.2)	3	100.0	0	0.0	0	0.0	3
A/France/IDF-IPP29542/2023 Cell	2a.3a.1 (J.4)	234	99.2	1	0.4	1	0.4	236
A/Norway/12374/2023 Cell	2a.3a.1 (J.4)	186	78.8	43	18.2	7	3.0	236
A/BurkinaFaso/3131/2023 Cell	2a.3a.1 (J.4)	62	49.6	5	4.0	58	46.4	125

Table 5. A/H3N2: HI/MN reagents and references

Virus	Genetic group	Virus passage	Ferret ID
A/Albania/289813/2022	2a.3a.1 (J)	MDCK1	F21/23
A/Massachusetts/18/2022	2a.3a.1 (J)	SIAT3/SIAT1	F36/23
A/Thailand/08/2022	2a.3a.1 (J)	E3/E1	F34/23
A/Sydney/856/2023	2a.3a.1 (J.1)	SIAT1/SIAT2	F01/24
A/Croatia/10136/RV/2023	2a.3a.1 (J.2)	SIAT3	F06/24
A/Croatia/10136/RV/2023	2a.3a.1 (J.2)	E3 (Am1Al2)	F16/24
A/Netherlands/10563/2023	2a.3a.1 (J.2)	MDCK-MIX2/SIAT2	F08/24
A/Slovenia/49/2024	2a.3a.1 (J.2)	MDCKx/SIAT2	F11/24
A/Lisboa/216/2023	2a.3a.1 (J.2)	E3 (Am1Al2)	F15/24
A/Norway/12374/2023	2a.3a.1 (J.4)	SIAT4	F21/24
A/France/IDF-IPP29542/2023	2a.3a.1 (J.4)[K189R]	MDCK1/SIAT2	F22/24
A/BurkinaFaso/3131/2023	2a.3a.1 (J.4)[K189R]	SIAT3	F32/24

Influenza B

Genetic analyses: B/Victoria

Clade V1A.3a.2 viruses characterised by substitutions A127T, P144L, N150K, G184E, N197D (-CHO), K203R and R279K (B/Austria/1359417/2021, subclade C) predominated since February 2023 in geographic regions where B/Victoria-lineage viruses were detected.

Since September 2023, the majority of circulating B/Victoria viruses belong to clade V1A.3a.2, subclade C.5 which has further split into several subclades. Of these, subclades C.5.1, C.5.4, C.5.6, C.5.7 and basal C.5 represented the majority of cocirculating variants. The proportion shifted during the NH winter season towards an increased predominance of subclades C.5.1 and C.5.7 by the end of the NH winter (weeks 10-12). This predominance continued to be observed during the NH summer season up to end of August 2024.

During this reporting period, only a minority of B/Victoria viruses were detected and characterised in Europe.

Within V1A.3a.2, subclade C.5 with D197E represents the majority of influenza B viruses characterised during the current influenza season. The most frequent subclades observed within C.5 are: C.5.1 with E183K represented by B/Catalonia/2279261NS/2023, as the dominant subclade predominating in the Americas, Portugal, Ukraine, New Zealand and detected in several other countries in minor proportions; C.5.6 (B/Norway/08717/2023) with D129N predominating in South East Asia, Middle East, South Africa and some European countries; C.5.7 with E183K and E128G predominating in China, Japan, Australia, Russian Federation, Mongolia and some countries in Europe. Minor subclades such as C.5.4 (B/Slovenia/924/2023) with V117I, E128K, A154T and K326R were detected in Chile and the US, and C.5.5 (B/Paraguay/2102/2023) with R80G, E184K were detected in North America in very low proportions.

Outside of C.5 viruses, other subclades such as C.2 (T182A, D197E, B/Netherlands/10335/2023) and C.3 (E128K, A154E, S208P, B/Norway/5216/2023) were detected in low frequency in West Africa and Madagascar earlier during the season.

Phylogenetic tree in Figure 23 with coloured tips for viruses dated from February to August 2024 (older viruses in grey) shows that the majority of B/Victoria viruses from Europe were detected from February onwards. The most recent viruses detected in Europe are dispersed across the topology of the tree, clustering within the three main predominating subclades C.5.7, C.5.6 and C.5.1.

No Clade V1A.3 viruses were detected since 1 February 2023.

No B/Yamagata lineage viruses have been detected since March 2020.

Global and European geographical distribution and time-dependent frequencies of influenza B/Victoria genetic clades (subclades) viruses, obtained with full HA sequences as deposited in GISAID and classified using Nextclade.Geographic markers scaled to detection proportions. Map provided by WHO GIS Centre for Health, DNA/DDI

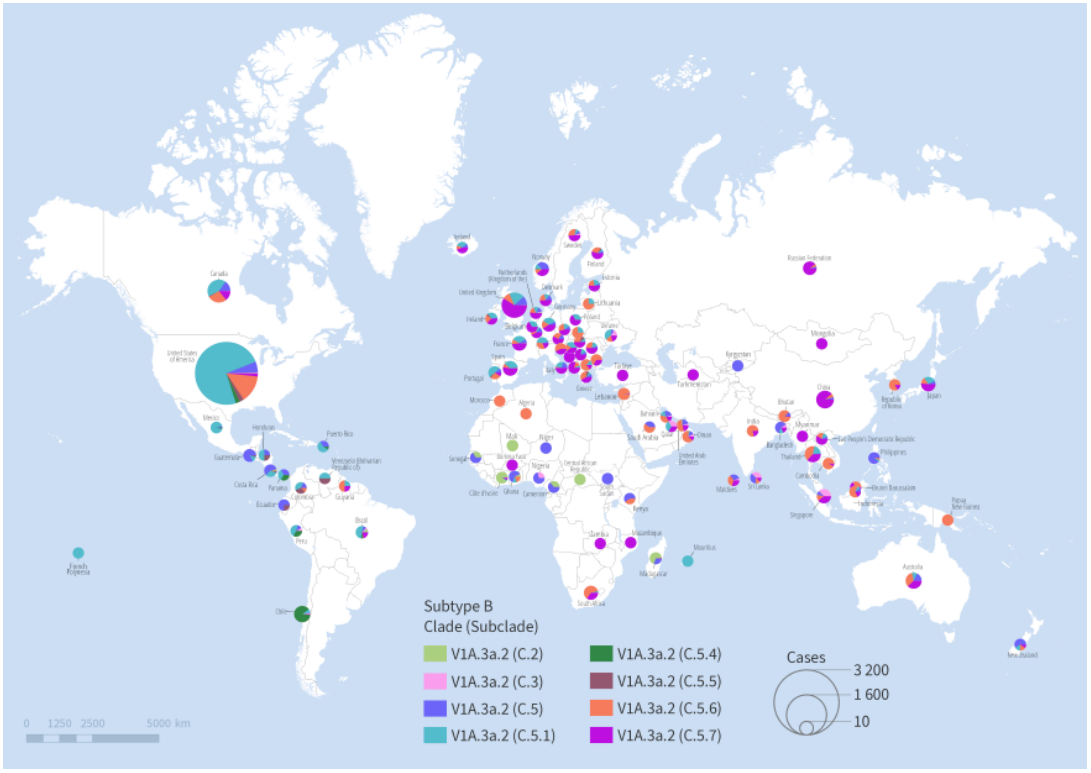


Figure 20: Global geographical distribution of influenza B/Victoria genetic clades (subclades)

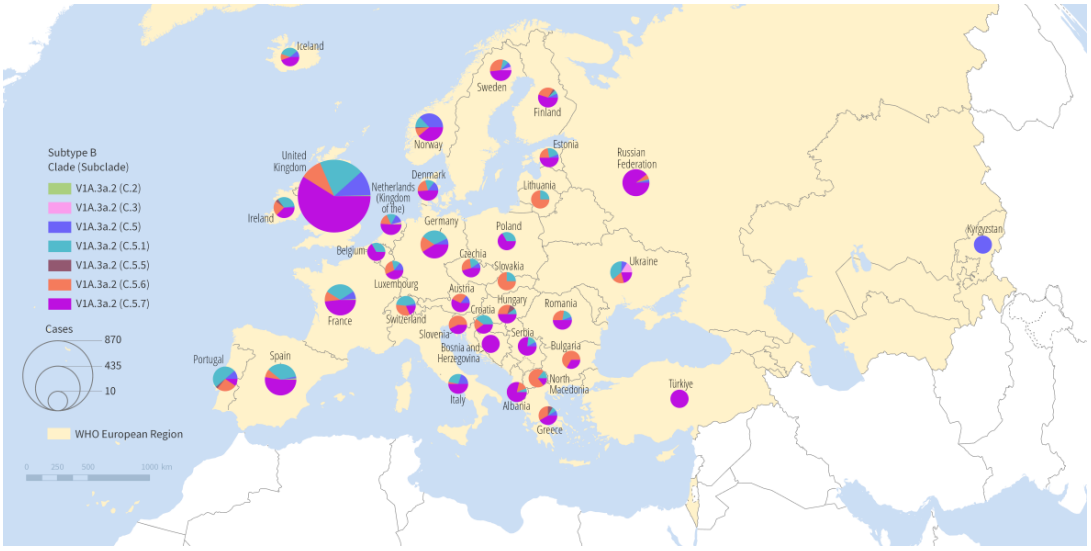


Figure 21: European region - Geographical distribution of influenza B/Victoria genetic clades (subclades)

Global time-dependent variation in frequencies of genetic clades-subclades of B/Victoria viruses collected since 1 September 2023.

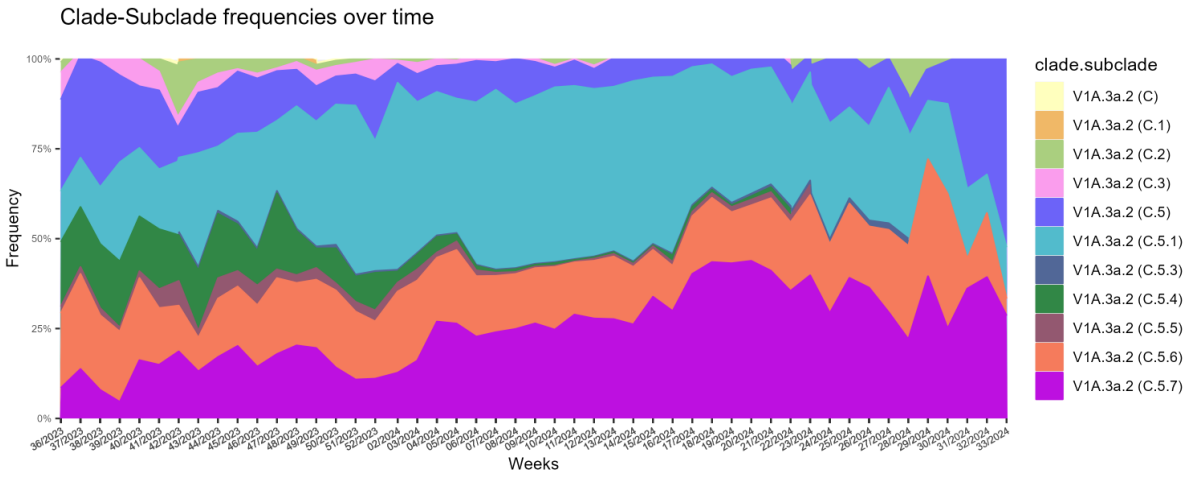


Figure 22: Global time-dependent variation in frequencies of B/Victoria genetic clades (subclades)

Maximum likelihood phylogenetic tree: B/Victoria

Maximum likelihood phylogenetic trees inferred using Iqtree2 from HA sequence data obtained from GISAID. Annotation of amino acids substitutions was performed with Treetime ancestral reconstruction; all reference viruses and tree nodes with more than one sequence were annotated. References and CVVs are marked as Cell or Egg.

Phylogenetic tree in Figure 23 was built with all European GISRS B/Victoria sequences uploaded to GISAID with collection dates from September 2023 to August 2024 (n~2000) with coloured tips for viruses dated from February to August 2024 (older viruses in grey).

Phylogenetic tree in Figure 24 was initially built with all European GISRS B/Victoria sequences uploaded to GISAID with collection dates from February to August 2024, downsampled using Treemer to retain a representative tree topology of 200 sequences.

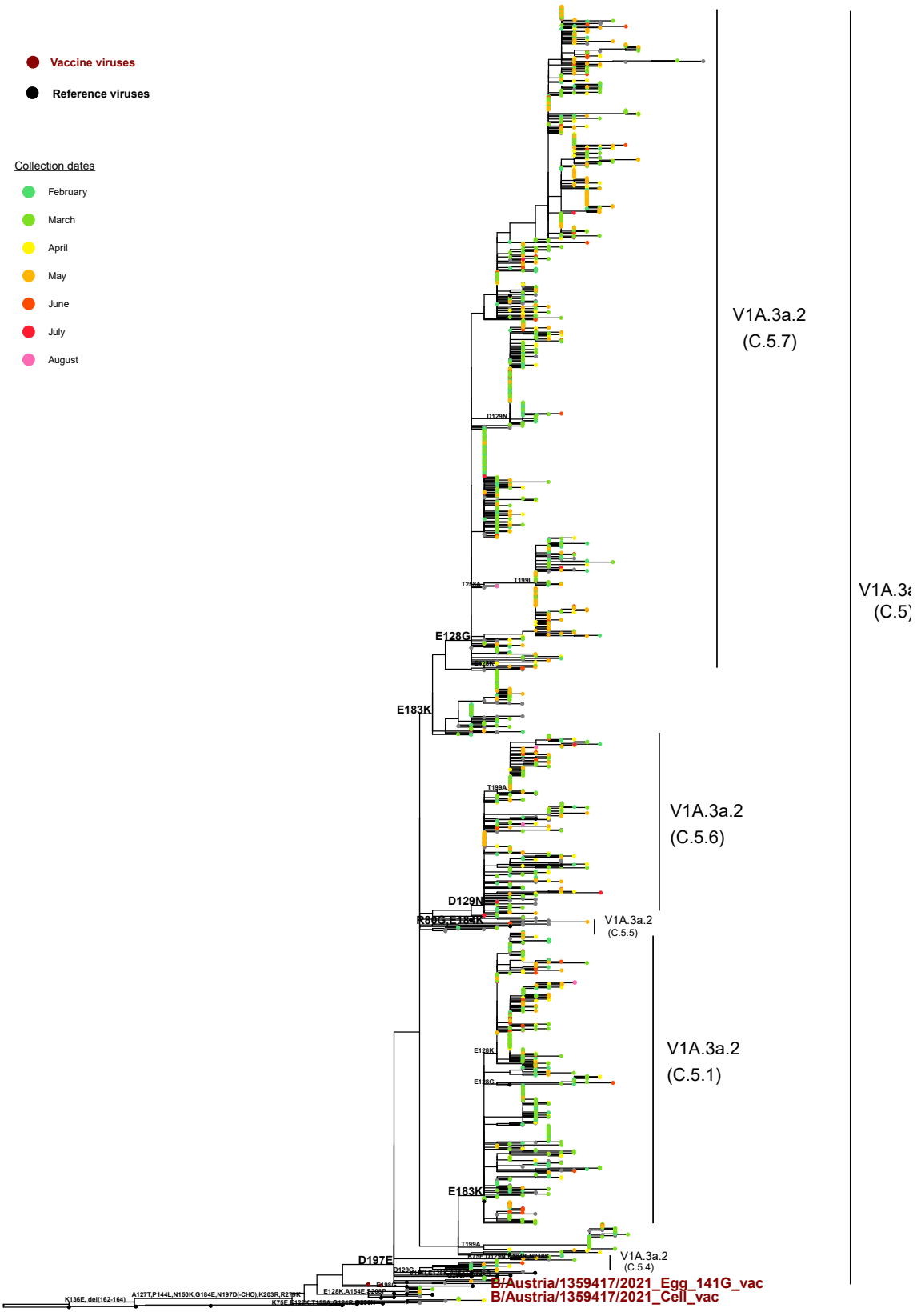


Figure 23: ML phylogenetic tree, all European GISRS B/Victoria sequences from September 2023 to August 2024

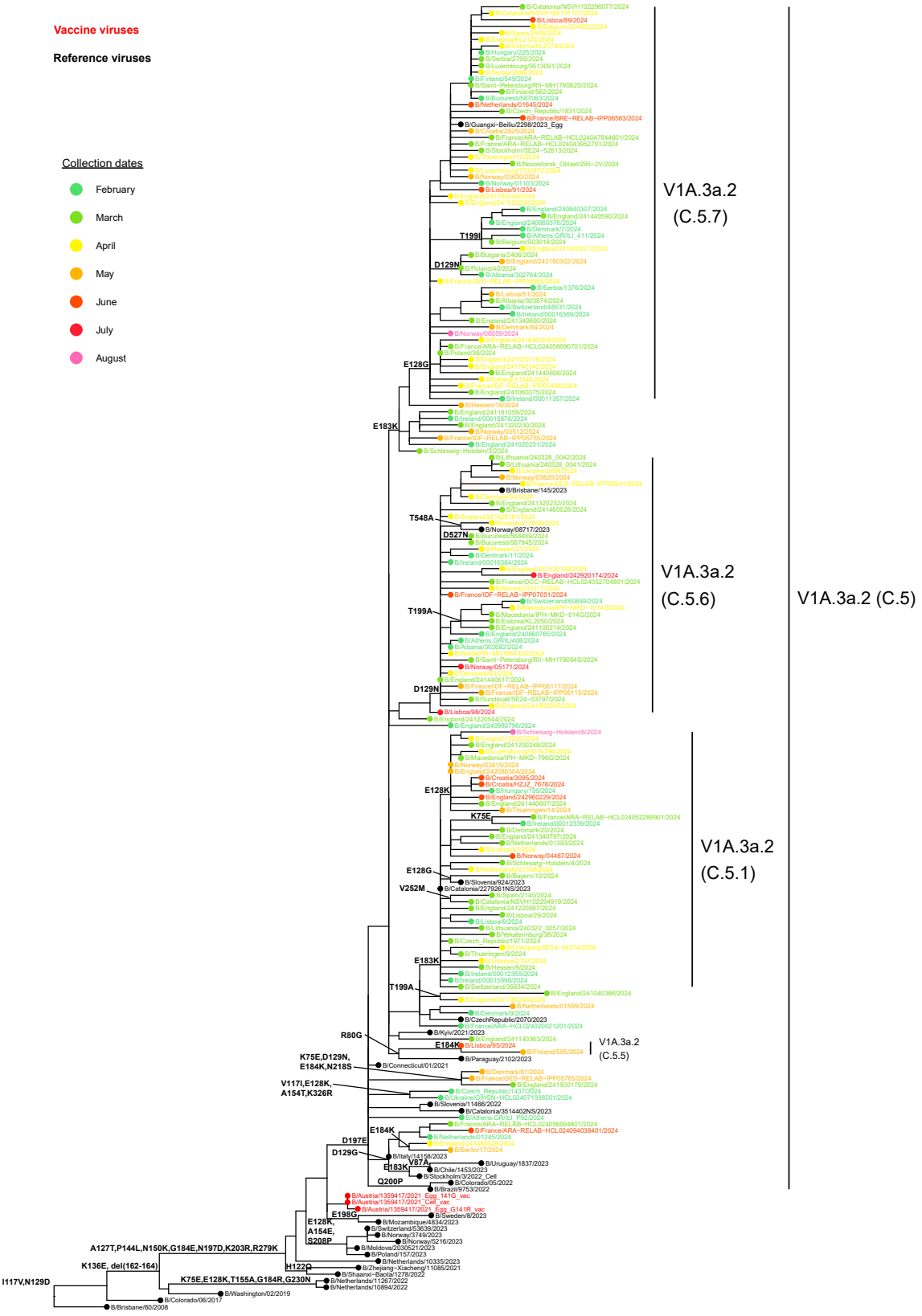


Figure 24: ML phylogenetic tree, 200 representative European GISRS B/Victoria sequences from February to August 2024

Summary of the antigenic properties of B/Victoria lineage viruses circulating in the reporting period

Table 6 and Figure 25 show that all V1A.3a.2 viruses tested were well-recognised by antisera raised against B/Austria/1359417/2021 and -like viruses.

For an overall picture of the genetic and antigenic relationships across viruses collected during the previous season, see the Annex.

Heatmapped phylogenetic trees represent the combined genetic and antigenic analyses (HI) where the correlation between genetic groups, signature amino acids and their antigenic profile can be observed.

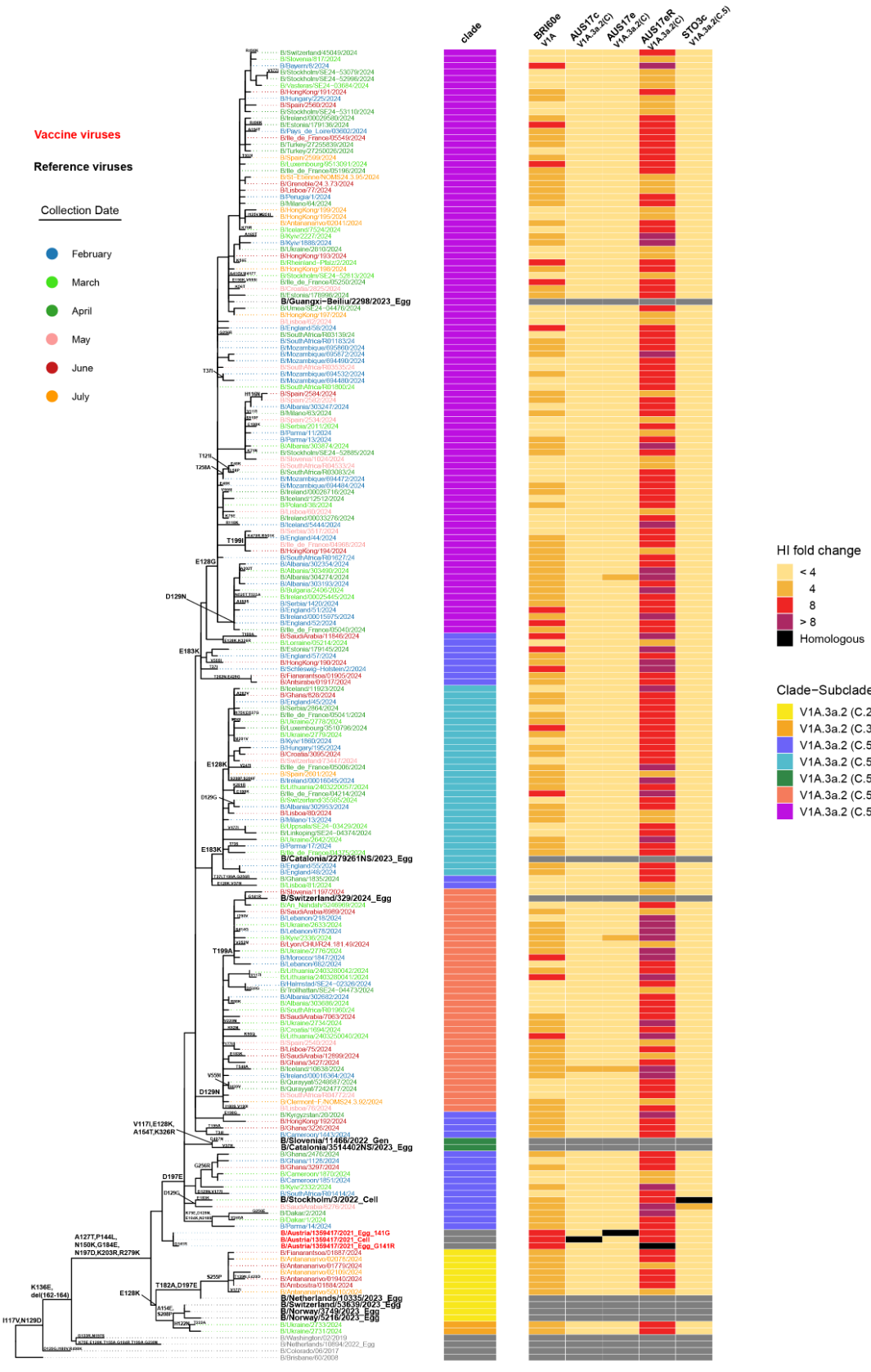


Figure 25: ML phylogenetic tree with combined heatmap representing antigenic reactivities by HI

Table 6. B/Victoria fold-reduction table

		<4-fold difference		4-fold difference		>4-fold difference		
Reference Virus	Clade	Number	Percentage	Number	Percentage	Number	Percentage	Total
B/Austria/1359417/2021 Cell	V1A.3a.2 (C)	266	98.9	3	1.1	0	0	269
B/Austria/1359417/2021 Egg G141	V1A.3a.2 (C)	263	97.8	5	1.8	1	0.4	269
B/Austria/1359417/2021 Egg G141R	V1A.3a.2 (C)	1	0.4	58	21.5	210	78.1	269
B/Stockholm/3/2022 Cell	V1A.3a.2 (C.5)	267	99.3	2	0.7	0	0	269

Table 7.B/Victoria: HI reagents and references

Virus	Genetic group	Virus passage	Ferret ID
B/Brisbane/60/2008	V1A	E4/E3	sheep pool
B/Austria/1359417/2021	V1A.3a.2 (C)	SIAT1/MDCK4	NIB F01/21
B/Austria/1359417/2021 G141	V1A.3a.2 (C)	E3/E4	F40/21
B/Austria/1359417/2021 G141R	V1A.3a.2 (C)	E3/E5	F44/21
B/Stockholm/3/2022	V1A.3a.2 (C.5)	SIAT1/MDCK3	F28/22

Antiviral susceptibility testing

At the WIC, influenza viruses detected within the WHO European Region since 1 September 2023 to 31 August 2024 (weeks 35/2023 to 35/2024) were assessed for phenotypic and/or genotypic susceptibility to antivirals. Of these, 291 A/H1N1, 298 A/H3N2 and 144 B/Victoria viruses were phenotypically assessed against oseltamivir and zanamivir. Most viruses showed Normal Inhibition (NI) by both NAIs except for nine A/H1N1 showing HRI with substitutions H275Y alone or with S247N, three A/H1N1 showing borderline RI with substitutions I223V and/or S247N and one virus showing HRI to zanamivir with substitution Q136K.

Phenotypic testing for susceptibility to baloxavir marboxil was performed for 237 A/H1N1, 225 A/H3N2 viruses and 87 B/Victoria viruses, with all of them showing Normal Inhibition.

Genotypic assessment of 1035 A/H1N1, 674 A/H3N2 and 271 B/Victoria neuraminidase (NA) gene sequences found some viruses with markers associated with reduced susceptibility to NAI, in addition to those described above: two A/H1N1 viruses with substitution H275Y, 38 A/H1N1 with S247N (phenotypic test showing NI for those tested), four A/H1N1 viruses with I223V, three A/H1N1 with I223V+S247N (double mutants), one A/H3N2 virus with substitution E119V/E (NI) and one B/Victoria virus with substitution R150K (virus isolation and phenotypic tests in process).

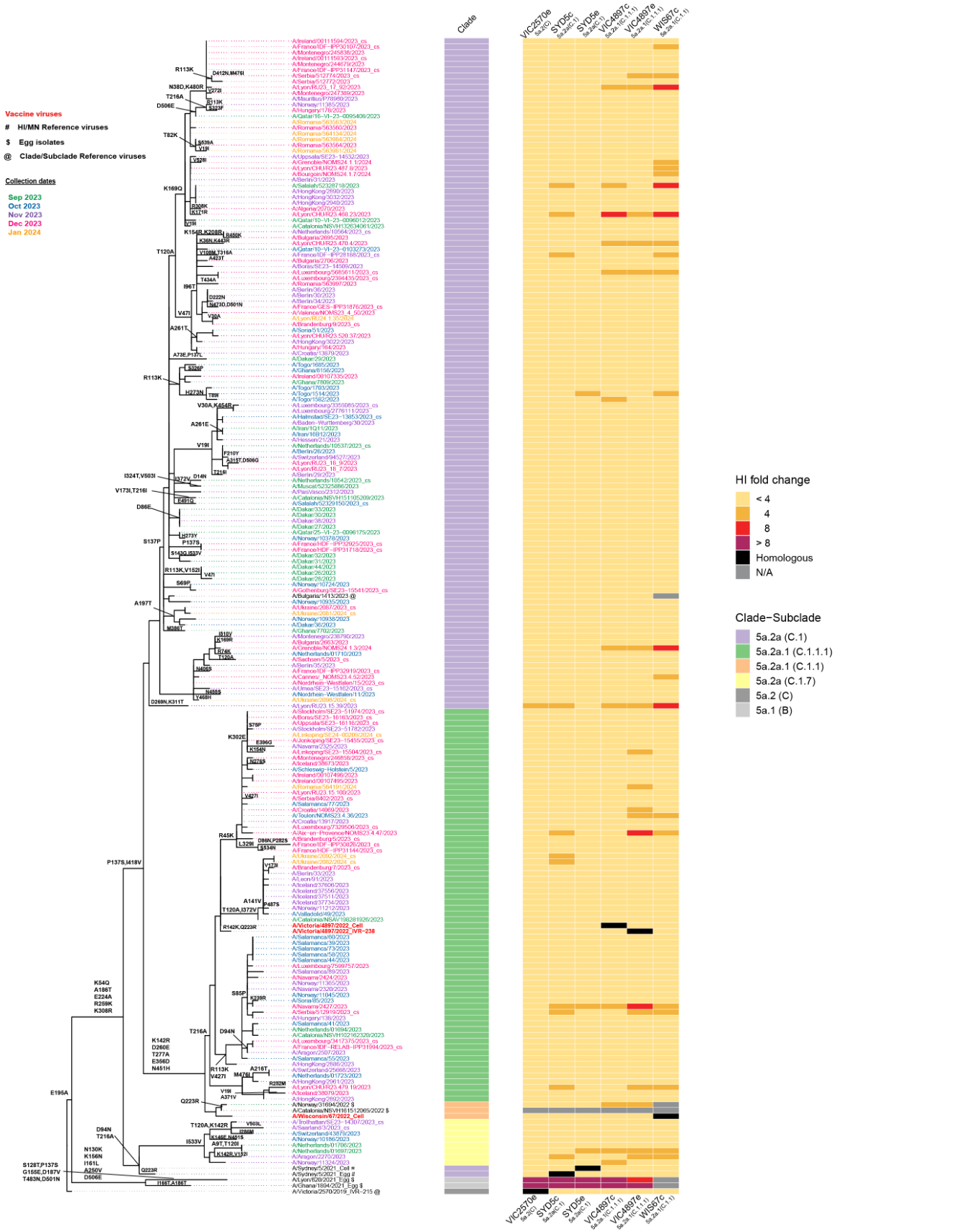
For 944 A/H1N1, 664 A/H3N2 and 269 B/Victoria viruses where PA gene sequencing was successful, no markers associated with reduced inhibition by baloxavir marboxil were identified, except for one A/H1N1 virus with substitution I38T and another with substitution E23K (NI), one A/H3N2 and one B/Victoria virus, both with substitution I38V (virus isolation and phenotypic test in process).

Annex

Heatmapped phylogenetic trees represent the combined genetic and antigenic analyses where the correlation between genetic groups, signature amino acids and their antigenic profile (including microneutralisation for A/H3N2) can be observed.

These outputs were generated by the London WHO Collaborating Centre at the WIC for the NH 2024–2025 February VCM with influenza viruses with collection dates between 1 September 2023 and 31 February 2024.

A/H1N1


Vaccine viruses
HI/MN Reference viruses
$ Egg isolates
@ Clade/Subclade Reference viruses
Collection dates
Sep 2023
Oct 2023
Nov 2023
Dec 2023
Jan 2024
Clade
VIC2570e 5a.2(C)
SYD5c 5a.2a(C.1)
SYD5e 5a.2a(C.1)
VIC4897c 5a.2a.1(C.1.1.1)
VIC4897e 5a.2a.1(C.1.1.1)
WIS67c 5a.2a.1(C.1.1)
HI fold change
< 4
4
8
> 8
Homologous
N/A
Clade−Subclade
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5a.2a.1 (C.1.1.1)
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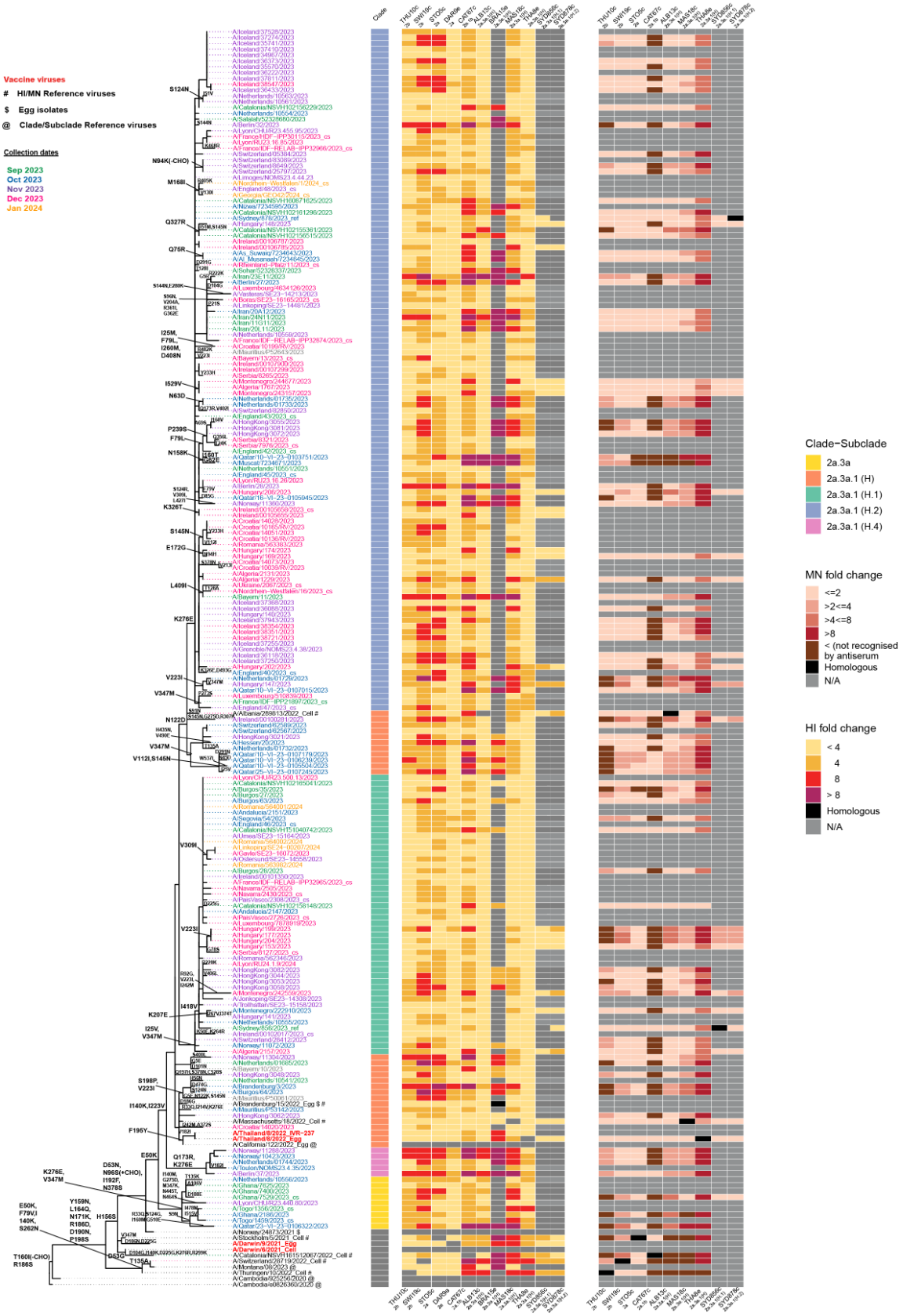
5a.2a (C.1.7)
5a.2 (C)
5a.1 (B)

A/H3N2


Vaccine viruses
HI/MN Reference viruses
$ Egg isolates
@ Clade/Subclade Reference viruses
Collection dates
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Oct 2023
Nov 2023
Dec 2023
Jan 2024
Clade
Clade−Subclade
2a.3a
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2a.3a.1 (H.1)
2a.3a.1 (H.2)
2a.3a.1 (H.4)
MN fold change
<=2
>2<=4
>4<=8
>8
< (not recognised by antiserum
Homologous
N/A
HI fold change
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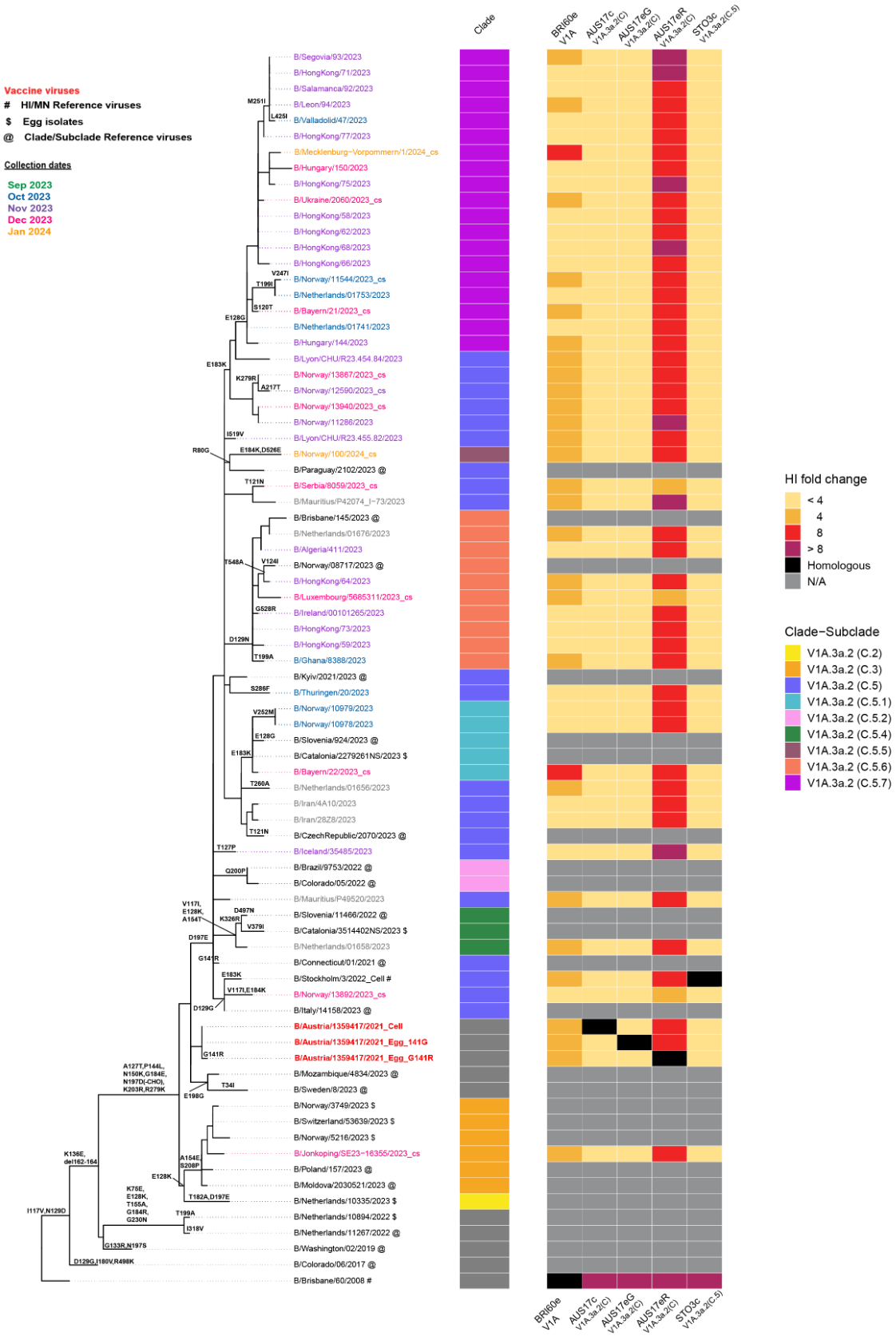
4
8
> 8
Homologous
N/A

B/Victoria


Vaccine viruses
HI/MN Reference viruses
$ Egg isolates
@ Clade/Subclade Reference viruses
Collection dates
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Oct 2023
Nov 2023
Dec 2023
Jan 2024
Clade
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AUS17c V1A.3a.2(C)
AUS17eG V1A.3a.2(C)
AUS17eR V1A.3a.2(C)
STO3c V1A.3a.2(C-5)
B/Segovia/93/2023
B/HongKong/71/2023
B/Salamanca/92/2023
B/Leon/94/2023
B/Valladolid/47/2023
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B/Norway/3749/2023 $
B/Switzerland/53639/2023 $
B/Norway/5216/2023 $
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B/Netherlands/11267/2022 @
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B/Colorado/06/2017 @
B/Brisbane/60/2008 #
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L425I
V247I
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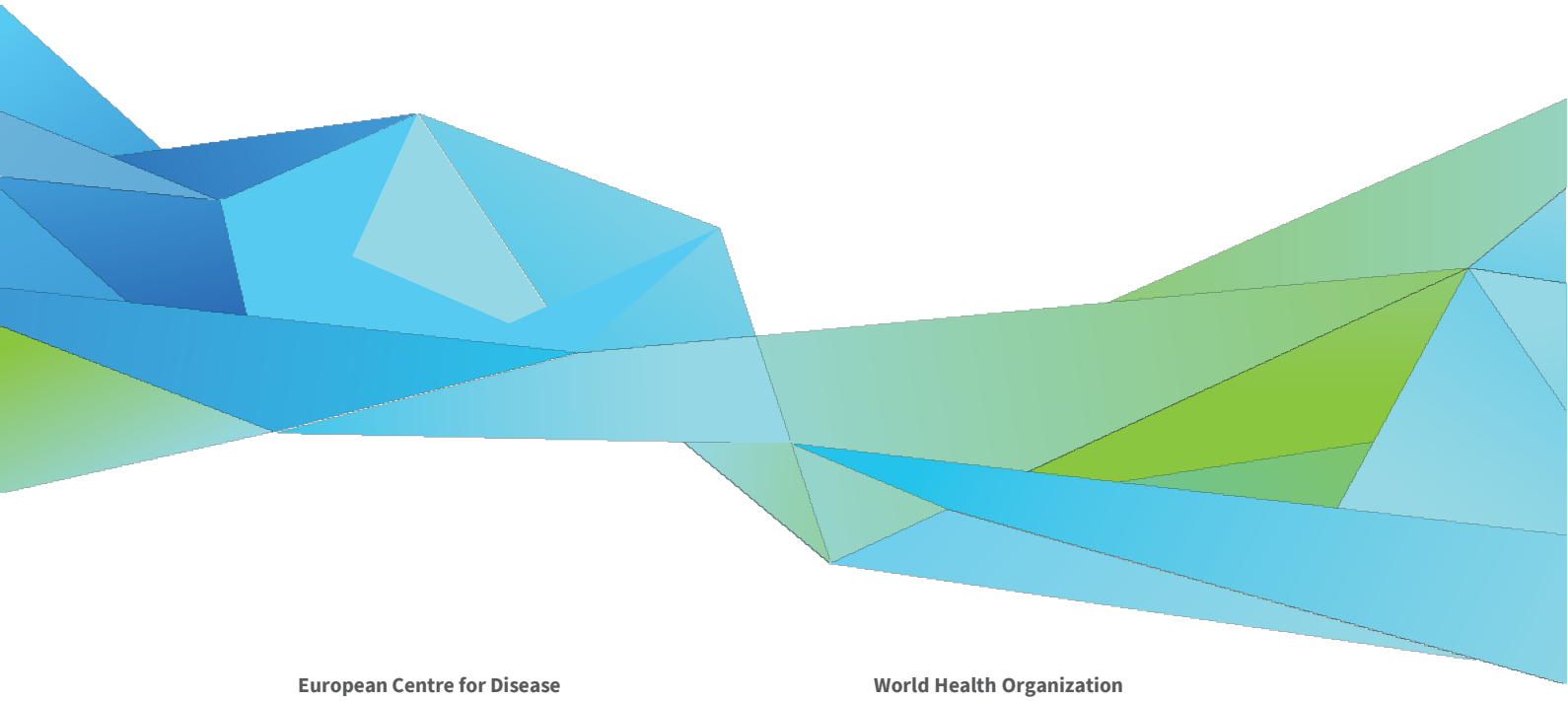
S120T
E128G
E183K
K279R
A217T
I519V
R80G
E184K,D526E
T121N
T548A
V124I
G528R
D129N
T199A
S286F
V252M
E128G
E183K
T260A
T121N
T127P
Q200P
V117I, E128K, A164T
D497N
K326R
V379I
D197E
G141R
E183K
V117I,E184K
D129G
G141R
A127T,P144L, N150K,G184E, N197D(-CHO), K203R,R279K
T34I
E198G
K136E, del162-164
A154E, S208P
E128K
K75E, E128K, T155A, G184R, G230N
T182A,D197E
I117V,N129D
T199A
I318V
G133R,N197S
D129G,I180V,R498K
HI fold change
< 4
4
8
> 8
Homologous
N/A
Clade−Subclade
V1A.3a.2 (C.2)
V1A.3a.2 (C.3)
V1A.3a.2 (C.5)
V1A.3a.2 (C.5.1)
V1A.3a.2 (C.5.2)
V1A.3a.2 (C.5.4)
V1A.3a.2 (C.5.5)
V1A.3a.2 (C.5.6)
V1A.3a.2 (C.5.7)

WHO Collaborating Centre reports

A full description of results generated by the London WHO Collaborating Centre at the WIC and used at the September 2024 WHO VCM, and previous ones, can be found at https://www.crick.ac.uk/partnerships/worldwide-influenza-centre/annual-and-interim-reports



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