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Executive Summary

BA.2.86 has been reported in multiple countries, and the prevalence has been slowly increasing globally. However, based on the available limited evidence, the public health risk posed by BA.2.86 is currently evaluated as low at the global level. Current population immunity globally remains highly cross-reactive to this variant, especially against severe disease but also against symptomatic disease, and therefore the emergence of this variant will unlikely add increased burden to national public health systems. BA.2.86 was classified as variant under monitoring (VUM) on 17 August 2023 and based on updated information, BA.2.86 and its sublineages (including JN.1) are now being classified as a variant of interest (VOI).

Initial Risk Evaluation of BA.2.86 and its sublineages, 21 November 2023

BA.2.86 is a descendent lineage of BA.2, with the earliest sample collected on 24 July 2023 (1). This variant and its descendent lineages have a large number of mutations in the spike protein; the initially reported BA.2.86 sequences from Israel and Denmark had 34 amino acid substitutions relative to BA.2 and 36 substitutions relative to XBB.1.5 (the strain recommended for the updated COVID-19 vaccine [2]). The number of spike amino acid mutations in the BA.2.86 variant relative to BA.2 and XBB.1.5 is comparable to the number of mutations in the first Omicron strains relative to the SARS-CoV-2 index strain. BA.2.86 was designated as a VUM on 17 August 2023 (3).

As of 20 November 2023, there were 3 267 BA.2.86 sequences submitted to GISAID (1) from 46 countries, representing 8.9% of the globally available sequences in epidemiological week 44 (30 October to 5 November 2023). The largest proportion of BA.2.86 sequences are from the United Kingdom (19.7%, 643 sequences), France (11.9%, 389 sequences), Sweden (10.7%, 351 sequences), Spain (7.8% 254 sequences), Canada (6.8%, 223 sequences), Denmark (6.6%, 215 sequences) and the United States of America (6.3%, 208 sequences).

Globally, there has been a slow but steady increase in the proportion of BA.2.86 reported, with its global prevalence at 8.9% in epidemiological week 44, Table 1. This is a substantial rise from the data reported four weeks prior (week 40, 2 to 8 October 2023), when the global prevalence of BA.2.86 was 1.8%.

Table 1: Global proportions of SARS-CoV-2 Variants, week 40 to week 44 of 2023

Lineage	Countries[§]	Sequences[§]	2023-40	2023-41	2023-42	2023-43	2023-44
VOIs							
XBB.1.5*	128	308 614	8.5	8.2	8.3	7.2	8.3
XBB.1.16*	117	94 914	15.9	14.0	12.4	9.8	8.2
EG.5*	89	104 423	47.0	50.2	50.9	51.9	51.6
BA.2.86*	41	3 109	1.8	2.8	4.1	6.4	8.9
VUMs							
DV.7*	38	3 887	1.8	1.8	1.7	1.9	1.9
XBB*	142	88 309	3.4	2.9	2.7	2.8	2.3
XBB.1.9.1*	118	80 383	9.5	8.0	8.0	7.0	6.4
XBB.1.9.2*	95	36 685	2.4	2.3	1.8	2.1	1.9
XBB.2.3*	104	31 394	6.0	5.6	5.2	4.9	3.7
Unassigned	95	152 256	0.5	1.4	2.5	3.6	4.5
Other+	211	6 785 691	3.0	2.6	2.3	2.2	2.2

Table 2 below shows the BA.2.86 descendent lineages and the additional mutations relative to BA.2.86 in the spike and other proteins. A notable descendent lineage of BA.2.86 is JN.1 (BA.2.86 + S:L455S) with a global proportion of 3.2% in epidemiological week 44.

Table1: BA.2.86 descendent lineages and mutations

Variant	Parent Lineage	Additional Spike Mutations relative to BA.2.86	Additional Mutations in other proteins relative to BA.2.86
BA.2.86	BA.2	NA	NA
BA.2.86.1	BA.2.86	None	ORF1a:K1973R
JN.1	BA.2.86.1	S:L455S	ORF1a:F499L, ORF1a:K1973R, ORF1a:R3821K, ORF7b:F19L
JN.2	BA.2.86.1	None	ORF1a:Y621C, ORF1a:K1973R
JN.3	BA.2.86.1	None	ORF1a:K1973R, ORF1a:T2087I
BA.2.86.2	BA.2.86	None	ORF7a:E22D
BA.2.86.3	BA.2.86	None	None
JQ.1	BA.2.86.3	S:T95I	ORF1a:D1742N

As population immunity remains heterogenous globally due to differences in SARS-CoV-2 variants circulating around the world and in vaccination coverage, the immune escape potential of BA.2.86 will greatly depend on the immune background of the population tested. With this important caveat in mind, the immune escape of BA.2.86 relative to concurrently circulating variants appears to be limited, and certainly not as extensive as when Omicron emerged in the background of Delta (4-6). Sera from patients who had Omicron breakthrough infections (including XBB), exhibited robust neutralizing activity against BA.2.86, suggesting that upcoming XBB.1.5 monovalent vaccines could confer added protection, by triggering the expansion of existing B cells that will enhance cross-protection against BA.2.86 and its descendant lineages (7-8).

Importantly, T-cell memory has been reported to be highly durable and cross-reactive to BA.2.86 (9). This would suggest that there is sustained protection against severe disease caused by BA.2.86 infection as such protection is associated with T-cell memory (10). Initial observations of the reported BA.2.86 cases do not suggest a change in the clinical presentation or an increase in severity of this variant compared to other Omicron sublineages (11). Preliminary data from France also does not suggest differences with BA.2.86 in terms of age, sex, symptoms or other risk factors (12).

WHO and its Technical Advisory Group on SARS-CoV-2 Evolution (TAG-VE) continue to recommend that Member States prioritize specific actions to better address uncertainties relating to antibody escape and severity of BA.2.86. The suggested timelines are estimates and will vary from one country to another based on national capacities:

- Share information on the growth advantage of BA.2.86 in your country and/or provide sequence information (one to four weeks).
- Conduct neutralization assays using human sera, representative of the affected community(ies), and BA.2.86 live virus isolates (two to four weeks).
- Perform a comparative evaluation to detect changes in rolling or ad hoc indicators of severity (four to 12 weeks).

The WHO and its Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) continue to regularly assess the impact of variants on the performance of COVID-19 vaccines to inform decisions on updates to vaccine composition (2).

The risk evaluation below follows the WHO framework (13) and is based on currently available evidence. It will be revised regularly as more evidence and data from additional countries become available.

Overall risk evaluation: **Low**	Based on its genetic features, BA.2.86 may possess some antigenic advantage evading previous immunity in certain settings. With the available limited data at this stage, there is no evidence that BA.2.86 has additional public health risks relative to the other currently circulating Omicron descendent lineages. While BA.2.86 has the potential to cause surges in infections, there is currently no indication that the associated disease severity will be higher as compared to other circulating variants. The risk evaluation will be updated as more evidence arises.		
Indicator	Evidence	Level of risk	Level of confidence
Growth advantage	There are currently 3 267 BA.2.86 sequences available from 46 countries, representing 8.9% of the globally available sequences in epidemiological week 44 (30 October to 5 November 2023). Due to the low number of sequences, growth advantage has not been reliably estimated with the WHO's internal variant growth rate analysis method. However, there has been a steady increase in the global proportion of BA.2.86 from 1.8% in epidemiological week 40 (2 to 8 October 2023) to 8.9% in epidemiological week 44 (30 October to 5 November 2023). Similarly for countries with the highest proportion of BA.2.86 sequences, the prevalence of BA.2.86 in these countries rose from 3.6% to 14.2% for the United Kingdom, from 3.1% to 13.8% for France, and 5.5% to 12.0% for Sweden. BA.2.86 has been reported to have lower infectivity (pseudovirus) of HEK293T-hACE2 cells compared to XBB.1.5 and EG.5, but live virus experiments did not confirm such differences in viral properties in cell culture relative to XBB.1.5 (6). * see footnote for more explanations	Low	Low

Antibody escape	In some studies, BA.2.86 has been shown to have the potential to evade convalescent plasma from XBB breakthrough infection (BTI) and reinfections (4-5,14). However, in other studies, sera from patients who had Omicron breakthrough infections (including XBB) exhibited robust neutralizing activity against BA.2.86, suggesting that the upcoming XBB.1.5 monovalent vaccines could confer added protection (2). In general, the immune escape of BA.2.86 relative to concurrently circulating variants does not appear to be as extensive as when Omicron emerged in the background of Delta. Further, T-cell memory has been reported to be highly durable and cross-reactive to hypermutated BA.2.86 (10). ** see footnote for more explanations	Moderate	Moderate
Severity and clinical/diagnostic considerations	Initial observations of reported BA.2.86 cases do not suggest a change in the clinical presentation or an increase in severity of the disease (11). However, data is currently limited. BA.2.86 has been reported to be resistant to the clinically relevant monoclonal antibodies Evusheld, Bebtelovimab and Sotrovimab (12). *** see footnote for more explanations	Low	Low

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Annex:

*** Growth advantage**
Level of risk: Low, as there are other co-circulating variants with convergent mutations and equally growing proportions.

Confidence: Low, as the growth advantage can only be estimated in a few settings with limited data.

**** Antibody escape**
Level of risk: Moderate, as it is estimated that BA.2.86 might have similar immune evasion as XBB.1.5, the previous globally dominant variant that peaked at >50% prevalence.

Confidence: Moderate, as immune escape properties are inferred from studies using pseudoviruses and live viruses, and while there are differences depending on the immune background of the population tested, most studies concur that the immune escape of BA.2.86 relative to co-circulating variants appears to be limited, and certainly not as extensive as when Omicron emerged in the background of Delta. Additional laboratory studies from different regions of the world would be needed to further assess the risk of antibody escape in settings with different population immunity backgrounds.

***** Severity and clinical considerations**
Level of risk: Low, as currently there are no reports of elevated disease severity associated with this variant.

Confidence: Low. Although, there is regular co-ordination and data sharing between all WHO Regional colleagues, countries and partners, reporting of new hospitalizations and ICU data with the WHO has decreased substantially, therefore caution should be taken when interpreting severe cases due to this decrease in reporting. Further, additional studies would be needed to further assess the impact of this variant on clinical outcomes.

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