Executive Summary

Previously, JN.1 was tracked as part of BA.2.86, the parent lineage that is classified as a variant of interest (VOI). However, in recent weeks, JN.1 continues to be reported in multiple countries, and its prevalence has been rapidly increasing globally and now represents the vast majority of BA.2.86 descendent lineages reported to GISAID. Due to its rapidly increasing spread, WHO is classifying JN.1 as a separate variant of interest (VOI) from the parent lineage BA.2.86.

Considering the available, yet limited evidence, the additional public health risk posed by JN.1 is currently evaluated as low at the global level. It is anticipated that this variant may cause an increase in SARS-CoV-2 cases amid surge of infections of other viral and bacterial infections, especially in countries entering the winter season. Following discussions with the WHO Technical Advisory Group for Virus Evolution (TAG-VE) and considering the data at hand, current population immunity globally as well as immunity generated by XBB.1.5 booster vaccination is expected to remain cross-reactive to this variant, against symptomatic and severe disease. Therefore, the spread of this variant will unlikely increase the burden on national public health systems compared to other Omicron sublineages. However, countries approaching the winter season should be aware that, altogether, SARS-CoV-2 and co-circulating pathogens may exacerbate the respiratory disease burden.

Initial Risk Evaluation of JN.1, 19 December 2023

JN.1 is a descendent lineage of BA.2.86, with the earliest sample collected on 25 August 2023 (1). In comparison with the parent lineage BA.2.86, JN.1 has the additional L455S mutation in the spike protein.

As of 16 December 2023, there were 7344 JN.1 sequences submitted to GISAID (1) from 41 countries, representing 27.1% of the globally available sequences in epidemiological week 48 (27 November to 3 December 2023). The countries reporting the largest proportion of JN.1 sequences are France (20.1%, 1552 sequences), the United States of America (14.2%, 1072 sequences), Singapore (12.4%, 934 sequences), Canada (6.8%, 512 sequences), the United Kingdom (5.6% 422 sequences), and Sweden (5.0%, 381 sequences).

Globally, there has been a rapid increase in the proportion of JN.1 reported, with its global prevalence at 27.1% in epidemiological week 48, Table 1. This is a substantial rise from the data reported four weeks prior (week 44, 30 October to 5 November 2023), when the global prevalence of JN.1 was 3.3%. This rapid growth is observed across all the three WHO regions with consistent sharing of SARS-CoV-2 sequences, i.e. the region of the Americas (AMR), the Western Pacific (WPR) and the European (EUR) regions, with the largest increase seen in WPR from 1.1% in epidemiological week 44 to 65.6% in epidemiological week 48. BA.2.86.1 (JN.1's parent lineage) replication kinetics on primary nasal epithelial cells (hNEC) have been observed to not be higher than other XBB-derived variants (2). However, it remains to be determined whether the high transmissibility of JN.1 in humans is also associated with enhanced fitness in primary hNECs and other cell types, and how much of that is linked to non-spike mutations.

Table 1: Global proportions of SARS-CoV-2 Variants, week 44 to week 48 of 2023

Lineage	Countries[§]	Sequences[§]	2023-44	2023-45	2023-46	2023-47	2023-48
VOIs							
XBB.1.5*	128	316 888	8.2	7.9	8.6	7.4	7.3
XBB.1.16*	119	103 516	9.6	9.0	6.6	5.6	4.2
EG.5*	93	143 675	53.7	54.1	51.7	46.5	36.3
BA.2.86*	49	5 972	4.4	4.8	5.8	7.1	5.9
JN.1*	41	7 344	3.3	5.3	10.1	16.7	27.1
VUMs							
DV.7*	40	4 635	1.2	0.9	0.9	1.0	0.6
XBB*	143	90 441	2.3	2.0	1.8	1.2	1.0
XBB.1.9.1*	118	85 640	6.7	5.4	5.5	4.3	3.3
XBB.1.9.2*	95	37 764	1.7	1.1	0.7	0.5	0.2
XBB.2.3*	107	34 573	3.5	3.4	2.5	2.3	1.6
Unassigned	95	155 778	3.4	4.2	4.2	6.4	11.9

§ Number of countries and sequences are since the emergence of the variants.
* Includes descendant lineages, except those specified on the table. For example, XBB* does not include XBB.1.5, XBB.1.16, EG.5, XBB.1.9.1, XBB.1.9.2, and XBB.2.3.

Due to differential vaccine coverage and circulation of SARS-CoV-2 variants around the world, population immunity remains heterogenous globally and therefore, the immune escape potential of JN.1 depends on the immune background of the population tested. Whereas the immune escape of BA.2.86.1 (JN.1's parent lineage) from XBB.1.5 and EG.5.1, breakthrough infection appears to be similar to concurrently circulating variants such as HK.3, JN.1 displays a higher immune evasion property (2,3). However, there are limited data on cross neutralization of JN.1 and despite the reduction in JN.1 neutralization, protection by XBB.1.5 monovalent vaccines are likely to be effective against JN.1 (4). WHO technical advisory groups, with scientists from around the world, are actively monitoring this (5).

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 and JN.1. The suggested timelines are estimates and will vary from one country to another based on national capacities:

- Conduct neutralization assays using human sera, representative of the affected community(ies), and JN.1 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).

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 (6).

The risk evaluation below follows the WHO framework (7) 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, JN.1 may possess some antigenic advantage evading previous immunity. With the limited data at this stage, the available evidence on JN.1 does not suggest additional public health risks relative to the other currently circulating Omicron descendent lineages. While there is a rapid increase in JN.1 infections, and likely increase in cases, available limited evidence does not suggest that the associated disease severity is 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 7344 JN.1 sequences available from 41 countries, representing 27.1% of the globally available sequences in epidemiological week 48 (27 November to 3 December 2023). This is a rapid increase in the global proportion of JN.1 from 3.3% in epidemiological week 44 (30 October to 5 November 2023). Similarly for the same period and for countries with the highest proportion of JN.1 sequences, the prevalence of JN.1 in these countries rose from 10.9% to 45.5% for France, from 2.1% to 19.9% for the United States of America, from 1.4% to 72.7% for Singapore, from 1.0% to 9.9% for Canada, from 1.8% to 20.4% for the United Kingdom, and from 1.8% to 22.9% for Sweden. This rapid growth is observed across all the three WHO regions with consistent sharing of SARS-CoV-2 sequences, i.e. WPR, EUR and AMR, with the largest increase seen in WPR from 1.1% in epidemiological week 44 to 65.6% in epidemiological week 48. Wastewater data from multiple countries approaching the winter season points at a large wave of SARS-CoV-2 infections in the community (8), however that has not resulted yet into pressure on health care systems despite significant co-circulation of other viral and bacterial infections. BA.2.86.1 (JN.1's parent lineage) replication kinetics on primary nasal	High	High

	epithelial cells (hNEC) have been observed to not be higher than other XBB-derived variants (2). However, it remains to be determined whether the high transmissibility of JN.1 in humans is also associated with enhanced fitness in primary hNECs and other cell types, and how much of that is linked to non-spike mutations. * see footnote for more explanations		
Antibody escape	JN.1 in comparison with parent BA.2.86 lineage carries the additional spike mutation L455S that significantly enhances immune evasion capabilities (9). Variants such as HK.3 that carry the L455F mutation have been shown to possess increased transmissibility and immune escape ability compared to the parental EG.5.1 variant (10). Neutralization assay using rodent sera infected with BA.2.86 showed that NT50 against JN.1 was comparable to that against BA.2.86. However, the NT50 of XBB.1.5 and EG.5.1 breakthrough infection sera against JN.1 were significantly lower than that of HK.3 (2.6-to 3.1-fold) and BA.2.86 (3.8-fold) (3). In another study, whereas XBB.1, EG.5.1 and BA.2.86.1 neutralization were globally similar in individuals who experienced XBB breakthrough infections, JN.1 displayed higher immune evasion properties compared to BA.2.86.1 (2). JN.1 was 2.9-to-4.3-fold resistant to sera from individuals vaccinated with an XBB.1.5 mRNA vaccine booster (4). ** see footnote for more explanations	Moderate	Low
Severity and clinical/diagnostic considerations	A study from Belgium in ≥65-year-old patients has reported no difference in the odds of hospitalization with JN.1 compared to non-BA.2.86 variant (OR: 1.15 [0.74-1.78]) (11). On the contrary, preliminary data from Singapore indicated lower risk of hospitalization and severity in BA.2.86 elderly and younger cases (12). However, data are currently limited. *** see footnote for more explanations	Low	Low

Annex:

* Growth advantage
Level of risk: High, as the variant is fast growing across all WHO regions with consistent SARS-CoV-2 sequence data sharing and has become the most prevalent variant in some countries.

Confidence: High, as the rapid growth has been reported by several countries in different WHO regions.

** Antibody escape
Level of risk: Moderate, as it is estimated that JN.1 has increased immune evasion relative to its parent BA.2.86.1 lineage that had a similar immune evasion as EG.5 the current most prevalent variant globally.

Confidence: Low, as there are only limited data on cross neutralization of JN.1. 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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