

Executive Summary

JN.1 is currently the most prevalent SARS-CoV-2 variant globally. Considering the available evidence, the additional public health risk posed by JN.1 is still evaluated as low at the global level. Current population immunity globally as well as immunity generated by the XBB.1.5 booster vaccination is expected to remain cross-reactive to this variant against symptomatic and severe disease. Therefore, the continued spread of this variant alone is unlikely to increase the burden on national public health systems compared to other Omicron sub-lineages.

Updated Risk Evaluation of JN.1, 15 April 2024

JN.1 is a descendent lineage of BA.2.86, with the earliest sample collected on 25 August 2023 (1).

As of 6 April 2024, there were 162 773 JN.1 sequences submitted to GISAID (1) from 121 countries, representing 93.7% of the globally available sequences in epidemiological week 12 (18 to 24 March 2024). This is a rise in prevalence from 91.8% four weeks prior in epidemiological week 8 (19 to 25 February 2024, Table 1). The JN.1 variant is also the most prevalent SARS-CoV-2 variant in all four WHO regions with consistent sharing of SARS-CoV-2 sequences at epidemiological week 12 (93.9% for the Western Pacific region (WPR), 85.7% for the South East Asia region (SEAR), 94.7% for the European region (EUR), and 93.2% for the region of the Americas (AMR)).

| Lineage | Countries§ | Sequences§ | 2024-08 | 2024-09 | 2024-10 | 2024-11 | 2024-12 |
|------------|------------|------------|---------|---------|---------|---------|---------|
| VOIs | | | | | | | |
| XBB.1.5 | 143 | 377836 | 0.2 | 0.3 | 0.3 | 0.0 | 0.1 |
| XBB.1.16 | 131 | 126607 | 0.2 | 0.1 | 0.2 | 0.2 | - |
| EG.5 | 112 | 213938 | 1.9 | 1.8 | 1.2 | 1.1 | 1.1 |
| BA.2.86 | 88 | 21221 | 2.3 | 1.9 | 1.6 | 1.3 | 1.4 |
| JN.1 | 119 | 157686 | 91.8 | 92.1 | 93.0 | 93.2 | 93.7 |
| VUMs | | | | | | | |
| XBB | 147 | 108373 | 0.1 | 0.1 | 0.0 | 0.1 | - |
| XBB.1.9.1 | 128 | 99354 | 0.1 | 0.1 | 0.1 | 0.1 | - |
| XBB.2.3 | 121 | 52137 | 0.2 | 0.2 | 0.3 | 0.3 | 0.2 |
| Unassigned | 75 | 30446 | 0.1 | 0.1 | 0.1 | 0.1 | 0.2 |

Table 1: Global proportions of SARS-CoV-2 Variants, weeks 8 to 12 of 2024

Figures by WHO, data from GISAID.org, extracted on 06 March 2024.

Number of countries and sequences are since the emergence of the variants.

The operation of the second and lineages, except those individually specified elsewhere in the table.

The VOI and the VUMs that have shown increasing trends are highlighted in orange, those that have remained stable are highlighted in blue, while those with decreasing trends are highlighted in green.

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). VUMs

The risk evaluation below follows the WHO framework (3) and is based on currently available evidence.



| Overall risk evaluation: Low | Based on its genetic features, JN.1 possesses some antigenic advantage evading previous immunity. The available evidence on JN.1 does not suggest additional public health risks relative to the other currently circulating Omicron descendent lineages. Available limited evidence does not suggest that the associated disease severity is higher as compared to other circulating variants. | | | | | | |
|------------------------------------|---|---------------|---------------------|--|--|--|--|
| Indicator | Evidence | Level of risk | Level of confidence | | | | |
| Growth advantage | There are currently 162 773 JN.1 sequences available from 121 countries, representing 93.7% of the globally available sequences in epidemiological week 12 (18 to 24 March 2024). This is a significant rise in prevalence from 91.8% four weeks prior in epidemiological week 8 (19 to 25 February 2024). | High | High | | | | |
| | JN.1 is also the most prevalent SARS-CoV- 2 variant in all four WHO regions with consistent sharing of SARS-CoV-2 sequences at epidemiological week 12, i.e. 93.9% for the Western Pacific region (WPR), 85.7% for the South East Asia region (SEAR). 94.7% for the European region (EUR), and 93.2% for the region of the Americas (AMR). | | | | | | |
| | Rapid expansion of JN.1 was detected in wastewater surveillance in South and Southeast Asia between October and December 2023 (4). | | | | | | |
| | The factors driving the high transmissibility of JN.1 remain unclear. * see footnote for more explanations | | | | | | |
| Immune escape | • | Moderate | High | | | | |
| | The majority of these studies have found JN.1 to be more evasive than other recently circulating Omicron sublineages, such as EG.5 or XBB.1.5. However, several studies have found similar neutralization of JN.1 and one or several recent Omicron sublineages. Where JN.1 | | | | | | |

| | has been found to be more immune evasive, the drop in neutralization titer is typically modest and many individuals retain some neutralization. Vaccination with an XBB.1.5 monovalent booster has been shown by multiple studies to increase neutralization titers against JN.1 (5-6, 11-17). Effectiveness of the XBB.1.5 monovalent booster at protecting from symptomatic JN.1 infection has been estimated at between 19% to 49% in different studies from the US (26-27). Pre-existing SARS-CoV-2-specific T cells are predicted to cross-recognize BA.2.86, whereby 72% and 89% of CD4 and CD8 SARS-CoV-2 responses are still conserved in BA.2.86 (28). | | |
|---|--|-----|----------|
| Severity and clinical/diagnostic considerations | ** see footnote for more explanations There have been no reports of changes in disease severity in studied patients. The infectivity of JN.1 pseudo-virus in CaLu-3 cells has been shown to be similar to XBB.1.5 and lower than BA.2.86 (20). Further, a study examining ICU patients in France found no difference in severity of illness, requirement for mechanical ventilation or mortality at 28 days between JN.1 and XBB (29). One study showed no activity of the monoclonal antibody Sotrovimab against JN.1 (30). The same study found similar <i>in vitro</i> activity of Nirmatrelvir, Remdesivir and Molnupiravir against BA.2.86.1 as against XBB.1.16.1 and EG.5.1.3 (30). *** see footnote for more explanations | Low | Moderate |



Annex:

* Growth advantage

Level of risk: High, as the variant is dominant across all WHO regions with consistent SARS-CoV-2 sequence data sharing and contains sub-variants that are the fastest growing among the currently circulating SARS-CoV-2 variants.

Confidence: High, as the variant is dominant across all WHO regions and its expansion is reflected in wastewater surveillance.

** Antibody escape

Level of risk: Moderate, as it is estimated that JN.1 has increased immune evasion relative to cocirculating variants.

Confidence: High, as there are increasing data on cross neutralization of JN.1 from varied 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: Moderate. There have been several studies looking at disease severity in SARS-CoV-2 infected patients, and JN.1 has been the dominant variant for several months with no reports of elevated disease severity. However, additional studies would be needed to further assess the impact of this variant on clinical outcomes. 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.



References

- 1. GISAID. Available from: <u>https://gisaid.org/hcov19-variants/</u>
- World Health Organization Technical Advisory Group on COVID-19 Vaccine Composition. Available from: <u>https://www.who.int/news/item/13-12-2023-statement-on-the-antigen-composition-of-covid-19-vaccines</u>
- 3. WHO. SARS-CoV-2 variant risk evaluation, 30 August 2023. Available from: https://apps.who.int/iris/rest/bitstreams/1528680/retrieve
- 4. Wannigama, D. L. et al. Wastewater-based epidemiological surveillance of SARS-CoV-2 new variants BA.2.86 and offspring JN.1 in South and Southeast Asia. Journal of Travel Medicine taae040 (2024) doi:10.1093/jtm/taae040.
- 5. Jeworowski, L. M. et al. Humoral immune escape by current SARS-CoV-2 variants BA.2.86 and JN.1, December 2023. Eurosurveillance 29, 2300740 (2024).
- Jain, S. et al. XBB.1.5 monovalent booster improves antibody binding and neutralization against emerging SARS-CoV-2 Omicron variants. 2024.02.03.578771 Preprint at <u>https://doi.org/10.1101/2024.02.03.578771</u> (2024).
- Peled, Y. et al. Sixth monovalent XBB.1.5 vaccine elicits robust immune response against emerging SARS-CoV-2 variants in heart transplant recipients. The Journal of Heart and Lung Transplantation (2024) doi:10.1016/j.healun.2024.03.014.
- Cheng, S. M. S. et al. Cross-neutralizing antibody against emerging Omicron subvariants of SARS-CoV-2 in infection-naïve individuals with homologous BNT162b2 or BNT162b2(WT + BA.4/5) bivalent booster vaccination. Virology Journal 21, 70 (2024).
- Coombes, N. S. et al. Evaluation of the cross reactivity of neutralising antibody response in vaccinated human and convalescent hamster sera against SARS-CoV-2 variants up to and including JN.1 using an authentic virus neutralisation assay. 2023.10.21.563398 Preprint at <u>https://doi.org/10.1101/2023.10.21.563398</u> (2024).
- 10. Bekliz, M. et al. Immune escape of Omicron lineages BA.1, BA.2, BA.5.1, BQ.1, XBB.1.5, EG.5.1 and JN.1.1 after vaccination, infection and hybrid immunity. 2024.02.14.579654 Preprint at https://doi.org/10.1101/2024.02.14.579654 (2024).
- Roederer, A. L. et al. Ongoing evolution of SARS-CoV-2 drives escape from mRNA vaccine-induced humoral immunity. 2024.03.05.24303815 Preprint at <u>https://doi.org/10.1101/2024.03.05.24303815</u> (2024).
- Chalkias, S. et al. Interim Report of the Reactogenicity and Immunogenicity of Severe Acute Respiratory Syndrome Coronavirus 2 XBB–Containing Vaccines. The Journal of Infectious Diseases jiae067 (2024) doi:10.1093/infdis/jiae067.
- 13. Wang, Q. et al. XBB.1.5 monovalent mRNA vaccine booster elicits robust neutralizing antibodies against XBB subvariants and JN.1. Cell Host & Microbe 32, 315-321.e3 (2024).
- 14. Lasrado, N., Rössler, A., Rowe, M., Collier, A. Y. & Barouch, D. H. Neutralization of SARS-CoV-2 Omicron subvariant BA.2.87.1. Vaccine (2024) doi:10.1016/j.vaccine.2024.03.007.
- 15. Sheward, D. J. et al. Neutralisation sensitivity of the SARS-CoV-2 BA.2.87.1 variant. 2024.03.21.586176 Preprint at <u>https://doi.org/10.1101/2024.03.21.586176</u> (2024).
- 16. Wang, Q. et al. SARS-CoV-2 Omicron BA.2.87.1 Exhibits Higher Susceptibility to Serum Neutralization Than EG.5.1 and JN.1. 2024.03.10.584306 Preprint at https://doi.org/10.1101/2024.03.10.584306 (2024).
- 17. Abul, Y. et al. Broad immunogenicity to prior SARS-CoV-2 strains and JN.1 variant elicited by XBB.1.5 vaccination in nursing home residents. 2024.03.21.24303684 Preprint at https://doi.org/10.1101/2024.03.21.24303684 (2024).
- 18. Kaku, Y. et al. Virological characteristics of the SARS-CoV-2 JN.1 variant. The Lancet Infectious Diseases 24, e82 (2024).

- 19. Yang, S. et al. Fast evolution of SARS-CoV-2 BA.2.86 to JN.1 under heavy immune pressure. The Lancet Infectious Diseases 24, e70–e72 (2024).
- 20. Li, P. et al. Distinct Patterns of SARS-CoV-2 BA.2.87.1 and JN.1 Variants in Immune Evasion, Antigenicity and Cell-Cell Fusion. 2024.03.11.583978 Preprint at <u>https://doi.org/10.1101/2024.03.11.583978</u> (2024).
- 21. Song, X.-D. et al. Seroprevalence of SARS-CoV-2 neutralising antibodies and cross-reactivity to JN.1 one year after the BA.5/BF.7 wave in China. Lancet Reg Health West Pac 44, 101040 (2024).
- 22. Yang, S. et al. Antigenicity assessment of SARS-CoV-2 saltation variant BA.2.87.1. 2024.03.07.583823 Preprint at <u>https://doi.org/10.1101/2024.03.07.583823</u> (2024).
- 23. Zhang, L. et al. Virological traits of the SARS-CoV-2 BA.2.87.1 lineage. 2024.02.27.582254 Preprint at https://doi.org/10.1101/2024.02.27.582254 (2024).
- 24. Wang, Q. et al. Robust SARS-CoV-2 Neutralizing Antibodies Sustained through Three Months Post XBB.1.5 mRNA Vaccine Booster. 2024.02.16.580687 Preprint at https://doi.org/10.1101/2024.02.16.580687 (2024).
- 25. He, X. et al. Heterogeneous hybrid immunity against Omicron variant JN.1 at 11 months following breakthrough infection. 2024.03.02.583082 Preprint at <u>https://doi.org/10.1101/2024.03.02.583082</u> (2024).
- 26. Link-Gelles, R. Early Estimates of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccine Effectiveness Against Symptomatic SARS-CoV-2 Infection Attributable to Co-Circulating Omicron Variants Among Immunocompetent Adults — Increasing Community Access to Testing Program, United States, September 2023–January 2024. MMWR Morb Mortal Wkly Rep 73, (2024).
- 27. Shrestha, N. K., Burke, P. C., Nowacki, A. S. & Gordon, S. M. Effectiveness of the 2023-2024 Formulation of the Coronavirus Disease 2019 mRNA Vaccine. Clinical Infectious Diseases ciae132 (2024) doi:10.1093/cid/ciae132.
- Alessandro Sette, John Sidney, Alba Grifoni. Pre-existing SARS-2-specific T cells are predicted to cross-recognize BA.2.86. Cell Host & Microbe. Volume 32, Issue 1, 2024. Pages 19-24.e2. ISSN 1931-3128. <u>https://doi.org/10.1016/j.chom.2023.11.010</u>..
- 29. Prost, N. de et al. Clinical phenotypes and outcomes associated with SARS-CoV-2 Omicron variant JN.1 in critically ill COVID-19 patients: a prospective, multicenter cohort study. 2024.03.11.24304075 Preprint at https://doi.org/10.1101/2024.03.11.24304075 (2024).
- 30. Planas, D. et al. Distinct evolution of SARS-CoV-2 Omicron XBB and BA.2.86/JN.1 lineages combining increased fitness and antibody evasion. Nat Commun 15, 2254 (2024).