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# WHO TAG-VE Risk Evaluation for SARS-CoV-2 Variant Under Monitoring: NB.1.8.1

## Executive Summary

NB.1.8.1 has been designated a SARS-CoV-2 variant under monitoring (VUM) with increasing proportions globally, while LP.8.1 is starting to decline. Considering the available evidence, the additional public health risk posed by NB.1.8.1 is evaluated as low at the global level. Currently approved COVID-19 vaccines are expected to remain effective to this variant against symptomatic and severe disease. Despite a concurrent increase in cases and hospitalizations in some countries where NB.1.8.1 is widespread, current data do not indicate that this variant leads to more severe illness than other variants in circulation.

## Initial Risk Evaluation of NB.1.8.1, 23 May 2025

NB.1.8.1 is a SARS-CoV-2 variant derived from the recombinant variant XDV.1.5.1, with the earliest sample collected on 22 January 2025. NB.1.8.1 is one of six VUMs tracked by the WHO and was designated as a VUM on 23 May 2025 [1,2]. In comparison to the currently dominant SARS-CoV-2 variant, LP.8.1, NB.1.8.1 has the following additional Spike mutations: T22N, F59S, G184S, A435S, V445H, and T478I. When compared to JN.1, NB.1.8.1 has the following mutations: T22N, F59S, G184S, A435S, F456L, T478I, and Q493E. Spike mutations at position 445 have been shown to enhance binding affinity to hACE2, which could increase the variant's transmissibility, mutations at position 435 shown to reduce the neutralisation potency of class 1 and class 1/4 antibodies [3], and mutations at position 478 shown to enhance the evasion of Class 1/2 antibodies [4]. Using pseudoviruses and plasma from BA.5 breakthrough infections with JN.1 or XDV+F456L infection, NB.1.8.1 showed 1.5–1.6-fold reduction in neutralization compared to LP.8.1.1 [4]. In mice previously immunized with SARS-CoV-2 variants, further immunisation using monovalent KP.2 or monovalent LP.8.1 mRNA vaccines elicited similar or modestly lower neutralising antibody titres against NB.1.8.1 than those elicited by immunising KP.2 or LP.8.1 antigens [5,6].

As of 18 May 2025, there were 518 NB.1.8.1 sequences submitted to GISAID [7] from 22 countries, representing 10.7% of the globally available sequences in epidemiological week 17 of 2025 (21 to 27 April 2025). While still low numbers, this is a significant rise in prevalence from 2.5% four weeks prior in epidemiological week 14 of 2025 (31 March to 6 April 2025), Table 1. Between epidemiological weeks 14 and 17 of 2025, NB.1.8.1 increased in prevalence in all the three WHO regions that are consistently sharing SARS-CoV-2 sequences, i.e. an increase from 8.9% to 11.7% for the Western Pacific region (WPR), from 1.6% to 4.9% for the Region of the Americas (AMR), and from 1.0% to 6.0% for the European Region (EUR). There are only 5 NB.1.8.1 sequences from the South East Asia Region (SEAR), and none from the from the African Region (AFR) and the East Mediterranean Region (EMR).

Table 1: Global proportions of SARS-CoV-2 Variants, epidemiological week 14 to 17 of 2025

| Lineage* | Countries§ | Sequences§ | 2025-14 | 2025-15 | 2025-16 | 2025-17 |
|---|---|---|---|---|---|---|
| **VOIs** | | | | | | |
| JN.1 | 143 | 339570 | 12.0 | 12.1 | 11.5 | 9.7 |
| **VUMs** | | | | | | |
| KP.3 | 85 | 61526 | 2.7 | 2.2 | 0.8 | 1.5 |
| KP.3.1.1 | 89 | 117331 | 9.5 | 10.8 | 10.2 | 8.5 |
| LB.1 | 99 | 25457 | 2.4 | 2.5 | 1.7 | 0.9 |
| XEC | 73 | 52366 | 22.3 | 20.0 | 18.8 | 17.8 |
| LP.8.1 | 51 | 15993 | 42.0 | 41.4 | 40.9 | 39.0 |
| NB.1.8.1 | 22 | 518 | 2.5 | 4.1 | 7.1 | 10.7 |
| Recombinant | 144 | 513365 | 6.6 | 6.9 | 8.9 | 11.8 |
| Others | 111 | 35263 | 0.1 | 0.1 | - | 0.1 |

Figures by WHO, data from GISAID, extracted on 18 May 2025.

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

*The variants listed include descendant lineages, except those individually specified elsewhere in the table.

The VOI and the VUMs that have shown increasing trends are highlighted in yellow, 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 Virus Evolution (TAG-VE) continue to recommend that Member States prioritize specific actions to better address uncertainties relating to antibody escape and severity of NB.1.8.1:

- Conduct neutralization assays using human sera, representative of the affected community(ies), and sera from naive animal models infected with NB.1.8.1 live virus isolates.
- Perform a comparative evaluation to detect changes in rolling or ad hoc indicators of severity.

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. In the latest recommendation published on 15 May 2025, the WHO TAG-CO-VAC advised that monovalent JN.1 or KP.2 remain appropriate COVIID-19 vaccine antigens; monovalent LP.8.1 is a suitable alternative vaccine antigen [8].

The risk evaluation below follows the published WHO framework for risk evaluation of SARS-CoV-2 variants [9] and is based on currently available evidence. This risk evaluation will be revised regularly as more evidence and data from additional countries become available. With declining prevalence of VOIs, and VUMs increasingly unable to meet the VOI definition, WHO, on 29 November 2024, began conducting risk evaluations for VUM designations in addition to VOI designations.

Considering the evolution of the global epidemiological situation in relation to COVID-19 and to support member states in addressing the continuous risk posed by COVID-19 during the transition from the response to a public health emergency of international concern to its management within broader disease prevention and control programmes, the IHR Standing Recommendations for COVID-19 issued by the WHO Director General's originally set to expire on 30 April 2025, have been extended for an additional year with the same content, until 30 April 2026 [10].

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| Overall risk evaluation:<br><br>**Low** | NB.1.8.1 is growing rapidly compared to co-circulating variants. However, NB.1.8.1 exhibits only marginal additional immune evasion over LP.8.1. While there are reported increases in cases and hospitalizations in some of the WPR countries, which has the highest proportion of NB.1.8.1, there are no reports to suggest that the associated disease severity is higher as compared to other circulating variants.<br><br>The available evidence on NB.1.8.1 does not suggest additional public health risks relative to the other currently circulating Omicron descendent lineages. | | |
| Indicator | Evidence | Level of risk | Level of confidence |
| Growth advantage | There are currently 518 NB.1.8.1 sequences from 22 countries, representing 10.7% of the globally available sequences in epidemiological week 17 of 2025 (21 to 27 April 2025). While still low numbers, this is a significant rise in proportion from 2.5% four weeks prior in epidemiological week 14 of 2025 (31 March to 6 April 2025).<br><br>While NB.1.8.1 is increasing in proportion, LP.8.1, the most frequent SARS-CoV-2 variant tracked by the WHO, is decreasing in proportion and represented 39.0% in epidemiological week 17 of 2025, compared to 42.0% in epidemiological week 14 of 2025.<br><br>Using a logistic regression model [11], compared to LP.8.1.1, NB.1.8.1 was estimated to have a higher relative growth advantage than co-circulating variants BA.3.2, NB.1, NB.1.8, LF.9, LF.7.2.1, LF.7.7.2, XFH and XEC.25.1 [4]. Only XFG had a higher relative growth advantage than NB.1.8.1.<br><br>NB.1.8.1 pseudovirus exhibits robust engagement of soluble human ACE2; this engagement is lower than that of LP.8.1.1 but higher than other expanding variants including XFG and XFH [4]. Furthermore, NB.1.8.1 pseudoviruses exhibits robust infectivity of Vero cells *in vitro* [4].<br><br>* see footnote for more explanations | Moderate | Low |
| Immune escape | Using pseudoviruses, and plasma from BA.5 breakthrough infections with either JN.1 or JN.1/XDV+F456L infection, NB.1.8.1 showed 1.5–1.6-fold reduction in neutralization compared to LP.8.1.1 [4]. Neutralization data from other cohorts is not currently available. | Low | Low |

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|---|---|---|---|
| | Antigenic cartography employing serum samples from naive mice immunized with two doses of spike mRNA vaccine indicates that NB.1.8.1 pseudovirus antigenically clusters with other JN.1 sublineages [4].<br><br>NB.1.8.1 pseudovirus exhibits enhanced evasion of several RBD-targeting neutralizing monoclonal antibodies from class 1/2 (likely due to spike mutation K478I), while spike mutation A435S reduces monoclonal antibody neutralization potency across all epitopes [4].<br><br>** see footnote for more explanations | | |
| Severity and clinical/diagnostic considerations | There are no reported or published studies on the impact of NB.1.8.1 on clinical outcomes.<br><br>The detection of NB.1.8.1 is increasing in several countries from WPR concurrently experiencing a rise in SARS-CoV-2-related cases and hospitalizations. However, routine clinical surveillance data do not indicate any signs of increased severity associated with NB.1.8.1, compared to previously circulating variants. Currently there is no evidence of increases in indicators like COVID-19-related ICU admissions and deaths per hospitalizations, or all-cause mortality.<br><br>NB.1.8.1 does not contain any additional protease substitutions compared to XBB.1.16.1, EG.5.1.3 and BA.2.86.1 and is therefore unlikely to exhibit elevated resistance to Nirmatrelvir compared to these variants [12].<br><br>NB.1.8.1 exhibits the Nsp12 (polymerase) substitution D284Y (Orf1b: D275Y); the potential impact of this substitution on activity of remdesivir and molnupiravir has not been examined.<br><br>*** see footnote for more explanations | Low | Low |

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# Annex:

*** Growth advantage**

*Level of risk*: Moderate, as NB.1.8.1 is growing substantially across all WHO regions with consistent SARS-CoV-2 sequence data sharing.

*Confidence*: Low, as NB.1.8.1 expansion has only begun recently, there are low levels of sequencing data and therefore variant proportions exhibit spikes, and the variant has not been detected in some regions.

**** Antibody escape**

*Level of risk*: Low, as the immune evasion of NB.1.8.1 in available data is of a similar magnitude to prior JN.1 sublineages upon their emergence. Additionally, NB.1.8.1 clusters with other JN.1 sublineages within antigenic cartography data based on sera from immunised mice.

*Confidence*: Low, as NB.1.8.1 antigenicity has only been assessed in a single study using pseudoviruses with serological data from two cohorts. Additional laboratory studies using sera from different cohorts and regions are needed to further assess the risk of antibody escape.

***** Severity and clinical considerations**

*Level of risk*: Low, as currently there are no reports of elevated disease severity associated with this variant. Available evidence doesn't suggest resistance to Nirmaltevir.

*Confidence*: Low. Currently there are no studies assessing the impact of this variant on clinical outcomes. Although, there is regular co-ordination and data sharing between all WHO Regional Offices, countries, and partners, reporting of new hospitalizations, ICU admission data with the WHO has been decreased substantially, therefore caution should be taken when interpreting trends in routine surveillance of severe cases. No studies have been conducted yet on the potential impact of the variant on the activity of antivirals like remdesivir and molnupiravir.

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## References


1. World Health Organization Tracking SARS-CoV-2 Variants Available online: https://www.who.int/activities/tracking-SARS-CoV-2-variants/ (accessed on 5 December 2024).
2. Coronavirus Disease (COVID-2019) Situation Reports: Coronavirus Disease (COVID-19) Weekly Epidemiological Updates and Monthly Operational Updates Available online: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports.
3. Liu, J.; Yu, Y.; Yang, S.; Jian, F.; Song, W.; Yu, L.; Shao, F.; Cao, Y. Virological and Antigenic Characteristics of SARS-CoV-2 Variants LF.7.2.1, NP.1, and LP.8.1. *Lancet Infect Dis* **2025**, *25*, e128–e130, doi:10.1016/S1473-3099(25)00015-5.
4. Guo, C.; Yu, Y.; Liu, J.; Jian, F.; Yang, S.; Song, W.; Yu, L.; Shao, F.; Cao, Y. Antigenic and Virological Characteristics of SARS-CoV-2 Variant BA.3.2, XFG, and NB.1.8.1. *bioRxiv* **2025**, doi:10.1101/2025.04.30.651462.
5. Pfizer/ BioNTech. (2025-2026 COVID-19 Vaccine Formula: Pfizer/BioNTech Supportive Data) 22 May 2025. US FDA Vaccines and Related Biological Products Advisory Committee Meeting. Available from: https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-may-22-2025-meeting-announcement (accessed 23 May 2025).
6. Moderna, Inc. (Moderna COVID-19 Vaccines Update) 22 May 2025. US FDA Vaccines and Related Biological Products Advisory Committee Meeting. Available from: https://www.fda.gov/advisory-committees/advisory-committee-calendar/vaccines-and-related-biological-products-advisory-committee-may-22-2025-meeting-announcement (accessed 23 May 2025)
7. Khare, S.; Gurry, C.; Freitas, L.; Schultz, M.B.; Bach, G.; Diallo, A.; Akite, N.; Ho, J.; Lee, R.T.C.; Yeo, W.; et al. GISAID's Role in Pandemic Response. *China CDC Wkly* **2021**, *3*, 1049–1051, doi:10.46234/ccdcw2021.255.
8. WHO World Health Organization Technical Advisory Group on COVID-19 Vaccine Composition: Statement on the Antigen Composition of COVID-19 Vaccines 15 May 2025.
9. World Health Organization *SARS-CoV-2 Variant Risk Evaluation, 30 August 202*; World Health Organization: Geneva, 2023;
10. Standing Recommendations for COVID-19 Issued by the Director-General of the World Health Organization (WHO) in Accordance with the International Health Regulations (2005) (IHR) Available online: https://www.who.int/publications/m/item/standing-recommendations-for-covid-19-issued-by-the-director-general-of-the-world-health-organization-(who)-in-accordance-with-the-international-health-regulations-(2005)-(ihr).
11. Chen, C.; Nadeau, S.A.; Topolsky, I.; Manceau, M.; Huisman, J.S.; Jablonski, K.P.; Fuhrmann, L.; Dreifuss, D.; Jahn, K.; Beckmann, C.; et al. Quantification of the Spread of SARS-CoV-2 Variant B.1.1.7 in Switzerland. *Epidemics* **2021**, *37*, 100480, doi:10.1016/j.epidem.2021.100480.
12. Planas, D.; Staropoli, I.; Michel, V.; Lemoine, F.; Donati, F.; Prot, M.; Porrot, F.; Guivel-Benhassine, F.; Jeyarajah, B.; Brisebarre, A.; 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* **2024**, *15*, 2254, doi:10.1038/s41467-024-46490-7.