World Health Organization

XBB.1.5 Updated Risk Assessment, 24 February 2023

XBB.1.5 is a descendent lineage of XBB, which is a recombinant of two BA.2 descendent lineages. Previous risk assessments can be found here.[1,2]

From 22 October 2022 to 21 February 2023, 45 193 sequences of the Omicron XBB.1.5 variant have been made available from 74 countries. Most of these sequences are from the United States of America (72.2%). The other countries include the United Kingdom (7.3%), Canada (5.0%), Germany (2.7%), Austria (1.8%). Denmark (1.1%), and France (1.0%).

Based on its genetic characteristics and available growth rate estimates, XBB.1.5 is likely to further contribute to increases in case incidence globally. There is high-strength of evidence for increased risk of transmission and moderate-strength of evidence for immune escape. The number of cases associated with XBB.1.5 is still low in many countries, and from reports by several countries, no early signals of changes or increases in severity have been observed. At this time, because there is limited data currently available globally, a full assessment of the severity of XBB.1.5 cannot yet be confidently assessed. Taken together, available information does not suggest that XBB.1.5 has additional public health risk relative to the other currently circulating Omicron descendent lineages.

WHO and its Technical Advisory Group on SARS-CoV-2 Evolution (TAG-VE) continue to recommend Member States prioritize the following studies to better address uncertainties relating to antibody escape, and severity of XBB.1.5. The suggested timelines are estimates and will vary from one country to another based on national capacities:

- Neutralization assays using human sera, representative of the affected community(ies), and live XBB.1.5 virus isolates (2-4 weeks, see below table for results of studies that were performed)
- Comparative assessment to detect changes in rolling or ad hoc indicators of severity (4-12 weeks, see below table for results of studies that were performed)

The WHO Technical Advisory Group on COVID-19 Vaccine Composition (TAG-CO-VAC) continues to regularly assess the impact of variants on the performance of COVID-19 vaccines to inform decisions on updates to vaccine composition.[3]

This updated risk assessment below is based on currently available evidence and will be revised regularly as more evidence and data from additional countries become available.

Indicator	Evidence	Confidence in the assessment
Growth advantage	In the United States of America (USA), XBB1.5 currently represents 23-86% of circulating variants across the different regions within the country.[4] From 1 February 2023 to date and for countries with more than 100 sequences, such as the United Kingdom (UK), Canada, Germany, Austria and Denmark, XBB.1.5 represents 13-36% of submitted sequences to GISAID. In the EURO region, between week 01-2023 and week 05-2023, the median proportion of all nationally sequenced XBB.1.5 virus isolates was 5.0% (range: 0.3-13.9%, from 16 countries or areas).[5] In the AFRO region, South Africa has reported a strong increase in XBB.1.5 from 1% in December 2022, to 10% in January 2023, and 76% as of the latest report from February 2023.[4–6] In addition, an *in silico* analysis indicated that the mutation S:F486S (present in XBB.1) abrogated the local hydrophobic interaction with ACE-2 whereas 486P (present in XBB.1.5) restored it. The amino acid change to 486P contributes to a higher ACE-2 binding affinity, and suggests a mechanism for XBB.1.5 to have a higher growth advantage as compared to its parent lineage XBB.1.[7]	High
Antibody escape	Using pseudotyped virus neutralization assays, XBB.1.5 is shown to be as immune evasive as XBB.1, and one of the Omicron subvariants with the highest immune escape to date.[7–13] Antibody titers against XBB.1 were mostly absent in individuals with a history of vaccination with index virus-based vaccines (2-4 doses), were higher in those who recently received a bivalent (BA.5) vaccine booster, and highest in individuals with hybrid immunity.[8–10] Neutralisation data using live virus isolates were consistent with pseudovirus neutralisation data in showing that bivalent mRNA boosting restores the antibody response.[14] Another pseudovirus neutralization study reported that antibody titers to XBB.1.5 in bivalent mRNA boosted individuals declined to pre-booster levels after 3 months, while antibody titers to other Omicron lineages declined less strikingly. However, cross-reactive T cell responses, which were present prior to boosting, are likely to continue to provide protection against severe disease.[13]	Moderate
Severity and clinical considerations	Severity assessments in human populations are ongoing. An analysis from India did not report any differences in clinical severity of XBB and its descendent lineages, as compared to other Omicron lineages.[15] A preliminary analysis from the US reports that there is no difference in number of deaths per hospital admissions of patients with XBB.1.5 compared to other Omicron lineages. Indicators such as the number of hospital admissions per case and the number of deaths per case are	Low

	difficult to estimate and interpret because of the current case under-ascertainment in most countries, and which tend to overestimate severity of currently circulating variants as compared to previously circulating variants (Source: US CDC internal analysis). There are currently no data on real world vaccine effectiveness against severe disease or death. XBB.1.5 does not carry any known mutation(s) associated with potential changes in severity (such as S:P681R).[16,17] A recent study reported that antivirals remdesivir, molnupiravir, nirmatrelvir, and ensitrelvir remain efficacious against both XBB.1.5 and XBB *in vitro*, while monoclonal antibodies imdevimab–casirivimab, tixagevimab–cilgavimab, sotrovimab, and bebtelovimab might not be effective against XBB.1.5 in the clinical setting.[14]	
Risk assessment conclusion	Based on its genetic characteristics and growth rate estimates, XBB.1.5 is likely to contribute to further increases in case incidence globally. There is high-strength of evidence for increased risk of transmission and moderate-strength of evidence for immune escape. From reports by several countries, no early signals of increases in severity have been observed. **Taken together, available information does not suggest that XBB.1.5 has additional public health risks relative to the other currently circulating Omicron descendent lineages.**	

Risk assessment framework and indicators used to assess risk and confidence given available evidence

Rapid indicators: 0-4 weeks		Confidence in the assessment		
		LOW	**MODERATE**	**HIGH**
Growth advantage	Evidence of a growth advantage likely to lead to global predominance A. An increase in variant specific Rt B. Logistic growth (compared to currently circulating variant) (Nb variants with subnational-limited growth are not assessed).	All data derived from one country	At least two models; data from two countries not linked by close travel	At least two models and at least three countries in three regions, over more than two weeks
Immune escape	• Genomic (predictive) and structural biology assessment • Pseudovirus neutralization using vaccinee sera or pre-banked population serosurveys • Reinfection rate through a cohort study or surveillance system • Signals from outbreak investigations (Rapid VE is unlikely by 28 days so the rapid RA cannot reach high confidence).	One indicator (reinfection, neutralization or structural model)	Two indicators including neutralization data	[rapid VE]
Severity and clinical considerations	• Change in a rolling surveillance metric for severity synchronized with increase in variant e.g. o Infection hospitalization ratio o Indicators from sentinel hospital network (e.g. surveillance of severe acute respiratory infections) o Comparison of admission trends with previous variants • Change in the demographic profile of who is admitted to hospital • Change in clinical phenotype • Major tests/therapeutics issues	One metric, one country	Multiple metrics, one country OR same method in multiple countries	Multiple metrics, multiple countries in multiple regions
Risk assessment	Including overall view of threat in the wider context, confidence level in the assessment, and identification of urgent priority work.			

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