XBB.1.5 Rapid risk assessment, 11 January 2023

The Omicron XBB.1.5 variant is a sublineage of XBB, which is a recombinant of two BA.2 sublineages. From 22 October 2022 to 11 January 2023, 5 288 sequences of the Omicron XBB.1.5 variant have been reported from 38 countries. Most of these sequences are from the United States of America (82.2%), the United Kingdom (8.1%), and Denmark (2.2%).

WHO's Technical Advisory Group on Virus Evolution (TAG-VE) met on 5 January 2023 to discuss the latest evidence on XBB.1.5 and assess the public health risk associated with this variant. Based on its genetic characteristics and early growth rate estimates, XBB.1.5 may contribute to increases in case incidence. To date, the overall confidence in the assessment is low as growth advantage estimates are only from one country, the United States of America.

WHO and the TAG-VE recommend Member States to prioritize the following studies to better address uncertainties relating to the growth advantage, antibody escape, and severity of XBB.1.5. The suggested timelines are indicative and will vary from one country to another based on national capacities:

- Analysis of growth advantage from additional countries where XBB.1.5 has been detected (1-3 weeks).
- Neutralization assays using human sera representative of the affected community(ies) and XBB.1.5 live virus isolates (2-6 weeks).
- Comparative assessment to detect changes in rolling or *ad hoc* indicators of severity (see table below, 4-12 weeks)

The rapid 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	Confidence in the assessment
Growth advantage	National weekly growth advantage in the United States of America, but within-country regional differences reported, with an increase in proportions from 1% (95% CI 0.3-2.2%) in week 47 to 8% (95% CI 3.4-15.3%) in week 50, and a rapid increase in proportion in the north-east part of the United States of America.[1] As of the date of publication, available data are available only from one country, and therefore confidence in a global assessment is low.	Low
Antibody escape	Along with BQ.1* variants, XBB* variants are the most antibody-resistant variants to date. [2–4] Using pseudotyped virus neutralization assays, XBB.1.5 is shown to be equally immune evasive as XBB.1, the Omicron subvariant with the highest immune escape to date.[7] These data reported that sera from individuals with a) BA.1, b) BA.5 or c) BF.7 breakthrough infection and three doses of the inactivated vaccine (Coronavac) or d) BA.5 infection following three or four doses of mRNA vaccine (BNT162b2 or mRNA-1273) do not induce high neutralization titers against XBB.1.5.[5] There is currently no data on real world vaccine effectiveness against severe disease or death.	Moderate
Severity and clinical considerations	No data. Severity assessments are ongoing. XBB.1.5 does not carry any mutation known to be associated with potential change in severity (such as S:P681R). [6,7]	Low
Risk assessment	Based on its genetic characteristics and early growth rate estimates, XBB.1.5 may contribute to increases in case incidence globally. To date, the overall confidence in the assessment is low as growth advantage estimates are only from one country, the United States of America.	

References

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3. Tamura, T. *et al. Virological characteristics of the SARS-CoV-2 XBB variant derived from recombination of two Omicron subvariants*. http://biorxiv.org/lookup/doi/10.1101/2022.12.27.521986 (2022) doi:10.1101/2022.12.27.521986.

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5. Yue, C. *et al. Enhanced transmissibility of XBB.1.5 is contributed by both strong ACE2 binding and antibody evasion*. http://biorxiv.org/lookup/doi/10.1101/2023.01.03.522427 (2023) doi:10.1101/2023.01.03.522427.

6. Mlcochova, P. *et al.* SARS-CoV-2 B.1.617.2 Delta variant replication and immune evasion. *Nature* **599**, 114–119 (2021).

7. Saito, A. *et al.* Enhanced fusogenicity and pathogenicity of SARS-CoV-2 Delta P681R mutation. *Nature* **602**, 300–306 (2022).

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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. • infection hospitalization ratio • indicators from sentinel hospital network (e.g. surveillance of severe acute respiratory infections) • comparison of admission trends with previous variants	One metric, one country	Multiple metrics, one country OR same method in multiple countries	Multiple metrics, multiple countries in multiple regions

	• change in the demographic profile of who is admitted to hospital • Change in clinical phenotype • Major tests/therapeutics issues			
Risk assessment	Including overall view of threat in the wider context, confidence level in the assessment, and identification of urgent priority work.			