World Health Organization

XBB.1.5 Updated Risk Assessment, 20 June 2023

XBB.1.5 was first reported on 5 January 2022, and designated a Variant of Interest (VOI) on 11 January 2023.

XBB.1.5 is a descendent lineage of XBB, and a recombinant of two BA.2 descendent lineages. Previous risk assessments can be found here [1,2,3].

As of 20 June 2023, 294 872 sequences of the Omicron XBB.1.5 variant have been made available from 112 countries. A majority of the XBB.1.5 sequences are from the United States of America (47.1%, 138 829 sequences). The other countries include the United Kingdom (8.6%, 25 403 sequences), Canada (8.5%, 25 031 sequences), Austria (4.9%, 14 457 sequences), Germany (4.2%, 12 379 sequences), France (3.4%, 9 891 sequences), and Spain (2.3%, 6 653 sequences).

XBB.1.5 began rising in prevalence in late 2022, attaining a prevalence of 3% in week 51-2022, and peaking in week 12-2023 with a prevalence of 55%. Since week 14-2023, there has been a decline in the prevalence of XBB.1.5. During epidemiological week 18 (1 to 7 May 2023) the global prevalence was 36.7% and during epidemiological week 22 (29 May to 4 June 2023) the global prevalence of XBB.1.5 was 23.3.

The global risk assessment for XBB.1.5 is comparable to the other currently co-circulating XBB variants with available evidence (see risk assessment table below). While growth advantage and immune escape properties have been observed in different countries and immune backgrounds, differences in severity have not been reported in countries where XBB.1.5 is/was reported to be circulating.

Taken together, available information does not suggest that XBB.1.5 has additional public health risk relative to the other currently co-circulating Omicron descendent lineages. However, XBB.1.5 may continue to circulate in some countries, and descendent lineages with additional escape mutations observed in other co-circulating lineages may continue to emerge.

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 [4].

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

Variants with substantial growth advantage and a spike protein profile similar to XBB.1.5

WHO is tracking other XBB lineages with similar Spike protein profiles as XBB.1.5 such as XBB.1.9.1 (no differences in the Spike), XBB.1.9.2 (no differences in the Spike), and XBB.2.3 (XBB.1.5+S:D253G,S:P521S). These variants have been increasing in prevalence and in week 22-2023 had a prevalence of 18.3% for XBB.1.9.1, 12.4% for XBB.1.9.2, and 6.6% for XBB.2.3. The three lineages are designated variants under monitoring (VUM).

Overall risk assessment: Low	Based on its genetic features, immune escape characteristics and growth rate estimates, XBB.1.5 may continue to circulate globally, albeit to low levels as the prevalence has continued to decline over the past seven weeks. No increases in COVID-19 disease severity have been observed. Taken together, available evidence does not suggest that XBB.1.5 has additional public health risks relative to the other currently co-circulating Omicron descendent lineages.		
Indicator	Evidence	Level of Risk	Level of Confidence
Growth advantage	Comparing the month of April and the month of May 2023, the global proportion of XBB.1.5 relative to other circulating variants declined from 50% (51 791/103 557) to 36.6% (21 623/59 154). Similarly, for countries with more than 5000 sequences, the prevalence of XBB.1.5 declined from 79.9% to 62% for the United States of America (USA), 53.5% to 39.6% for the United Kingdom, 73.5% to 56.5% for Canada, 53.9% to 38% for Austria, 53.1% to 42.7% for Germany, 52.1% to 42.3% for France and 60.2% to 47.9% for Spain. From WHO's internal variant growth rate analysis, similarly used by the UK Health Security Agency (UKHSA), XBB.1.5's growth rate has continued to decline globally and across all the WHO [5]. US Centers for Disease Control and Prevention (CDC) Nowcast model-based projections predict a decline of the XBB.1.5 variant to 39.9% (95% predictive interval 36.7-43.2%) by 10 June 2023 [6]. * see footnote for more explanations	Low	High
Antibody escape	Using pseudotyped virus neutralization assays, XBB.1.5 was 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 had recently received a bivalent (BA.5) vaccine booster, and highest in individuals with hybrid immunity [8–10]. Neutralization data using live virus isolates were consistent with pseudovirus neutralization 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. However, cross-reactive T cell responses, which were present prior to boosting, are likely to continue to provide protection against severe disease [13].	Moderate	High

	On 18th May 2023, TAG-CO-VAC recommended an update to the composition of COVID-19 vaccines to use as the vaccine antigen a monovalent XBB.1 descendent lineage, such as XBB.1.5 (e.g., hCoV-19/USA/RI-CDC-2-6647173/2022, GenBank: OQ054680.1, GISAID: EPI_ISL_16134259 or WHO Biohub: 2023-WHO-LS-01, GenBank: OQ983940, GISAID EPI_ISL_16760602), or XBB.1.16 given the small genetic and antigenic differences from XBB.1.5 (e.g., hCoV-19/USA/MI-CDC-LC1038976/2023, GenBank: OQ931660 GISAID: EPI_ISL_17619088) [15]. ** see footnote for more explanations		
Severity and clinical considerations	An analysis from India did not report any differences in clinical severity of XBB and its descendent lineages, as compared to other Omicron lineages [16]. A preliminary analysis from the US reported that there was no difference in number of deaths per hospital admissions of patients with XBB.1.5 compared to other Omicron lineages (Source: US CDC internal analysis). To date, XBB.1.5 has not acquired carry any known mutation(s) associated with potential changes in severity (such as S:P681R) [17,18]. A study of SARS-CoV-2 antivirals and monoclonal antibodies reported that the antivirals remdesivir, molnupiravir, nirmatrelvir, and ensitrelvir remained 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]. *** see footnote for more explanations	Low	High

Annex:

*** Growth advantage**

Level of risk: Low, as over the past 10 weeks, the prevalence of XBB.1.5 and growth rates have continued to decline. In addition, the VOI XBB.1.16 and VUMs such as XBB.1.9.1, XBB.1.9.2, and XBB.2.3 are rapidly growing whereas there is no XBB.1.5 descendent lineage that appears capable of outcompeting these variants to sustain the previous global dominance.

Confidence: High, as the prevalence and growth advantage estimates have been monitored over several months and by several groups of experts in several countries and WHO regions.

**** Antibody escape**

Level of risk: Moderate, due to a similar immune evasion profile as XBB.1.16, a VOI whose prevalence is on the increase.

Confidence: High, as immune escape results are based on work from several laboratories and using both pseudoviruses and live virus isolates.

***** Severity and clinical considerations**

Level of risk: Low, as the country with the highest number of cases of XBB.1.5, the US, in addition to other countries such as India have reported no differences in the number of deaths per hospital admissions of patients with XBB.1.5 compared to other Omicron lineages.

Confidence: High, as there is regular coordination and data sharing with all WHO Regional colleagues, countries and partners continue, and as such we continue to receive early signals from countries if and when severity is rising.

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