



Date: 7 February 2022

# SARS-CoV-2 Variants of Concern Update

## Executive Summary

*Note: New information in this report is shown in red text.*

*Section updated: 7 February 2023*

Since mid-2022, many new Omicron subvariants have been reported. These variants demonstrate convergent evolution whereby variants from different lineages accumulate similar mutations. Mutations in the spike protein appear to be responsible for many of the enhanced characteristics of these variants.

### **New information in this report includes:**

- The variant landscape in New Zealand is similar to previous reports with no single variant accounting for more than 50% of genomically sequenced samples from COVID-19 cases. However, BA.2.75 and its subvariants (including CH.1.1) together account for just over 50% of sequences from cases and 84% of wastewater sequencing reads (wastewater includes XBF in BA.2.75 data). XBB and its subvariants (including XBB.1.5) remain stable, accounting for 2-3% of sequenced cases and wastewater reads in January 2023. Two other recombinant variants, XBF and XBC, account for 15% and 8% of sequenced cases respectively. They have been present and growing in New Zealand since late 2022.
- XBB.1.5 is a sublineage of XBB that is now dominant in the United States and has been associated with a rise in case numbers. XBB.1.5 is also increasing in Europe and Australia. It has been present in New Zealand since December 2022. XBB.1.5 has a growth advantage over XBB, with mutations associated with both immune evasion and enhanced ACE-2 binding. Despite the reported growth advantage, there has not yet been an observed increase in XBB detections in New Zealand. However, the increase in cases of XBB.1.5 cases in Australia, as well as Europe, suggests that a rise in XBB.1.5 cases is likely to occur in New Zealand. The impact on overall case numbers is yet to be determined.
- BA.5.2.48 and BF.7.14 (both BA.5 sublineages) continue to dominate sequences from China, together with other BA.5 descendants that represent a smaller proportion of cases. None of the lineages dominating in the rest of the world (e.g. BA.2.75, XBB or their subvariants) have yet been found in large clusters in China. However, given the limited number of sequences from China, there is potential for undetected spread. There is no evidence to date that the wave of infections in China has yet produced a novel variant with concerning mutations.
- Molnupirivir is unlikely to be associated with a decrease in the rate of hospitalisation or other severe outcomes for the treatment of COVID-19 but may decrease the duration of illness. It is possible that further research will identify a use for Molnupirivir in selected clinical situations.
- Current monoclonal antibody therapies are ineffective for the prevention of COVID-19 for almost all currently circulating variants.



# Section 1 Key Omicron information

## Circulating variants across Aotearoa New Zealand

Section updated: 02 February 2023

The Institute of Environmental Science and Research (ESR) COVID-19 Genomics Insights (CGI) report was last produced on 02 February 2023, with data from the period of 14 January – 28 January 2023. (1)

The percentage of sequenced cases (community, including hospital, and "border" cases combined) of each variant in this period are shown in figure 1 (noting that ~1.5% of all cases were sequenced in this reporting period, and only variants with a frequency above 1% are shown). (1)

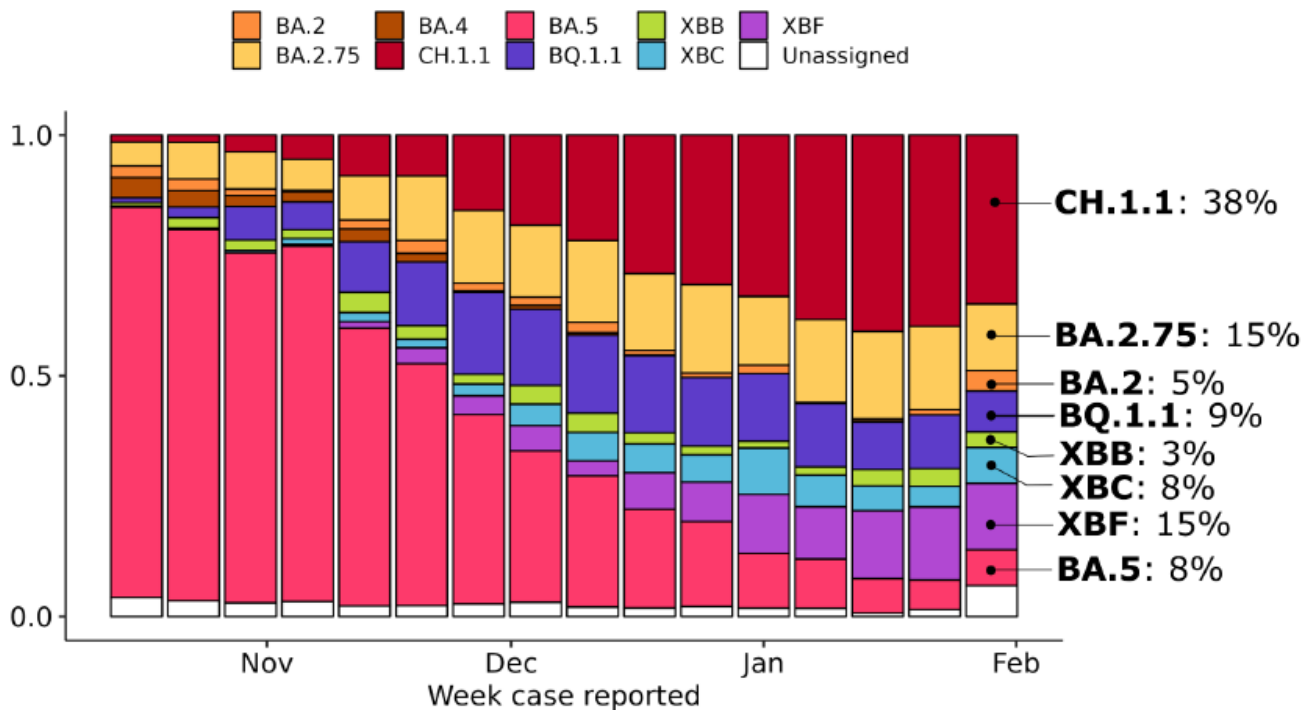


Figure 4. Frequency of variants/lineages in the past 16 weeks. Frequencies > 1% are annotated in the last week. Note, data for the most recent fortnight is preliminary, as it will be updated as additional cases reported within these weeks are converted into genomes. Cases classified as 'Unassigned' are typically partial genomes where it is difficult to be definitive regarding variant/lineage. Source: [ESR link](#)

A publicly accessible version of the genomic report produced by ESR is available [here](#).

Wastewater sampling is less prone to selection bias than samples from cases (which, for example, overrepresents hospitalised cases and under-represent some regions in New Zealand). CH.1.1 was the most widespread and common variant in wastewater in the last week of January 2023, being detected at 89% of sites and comprising 53% of sequencing reads nationally. Other sublineages in the BA.2.75 group (including BM.4, BR.2, XBF and BA.2.75) accounted for another 32% of sequencing reads nationally, being detected at



80% of sites. Thus, as a whole, the BA.2.75 group (including CH.1.1) represented 84% of sequencing reads nationally. XBB variants (including XBB.1.5) accounted for 2-3% of reads in January 2023. XBB detections remain steady and at low levels, suggesting that XBB.1.5 has yet to spread widely in the community. (1)

The publicly accessible ESR Wastewater surveillance dashboard can be accessed [here](#).

## Current overall variant risk status

*Section updated: 7 February 2023*

### Unchanged from previous report

Despite the development of a large range of Omicron variants demonstrating convergent evolution, there has been relatively little change in the overall variant landscape. The large outbreak of cases in China and the development of XBB.1.5 in the United States could change the current situation. The potential development of concerning new variants from China has been identified as an ongoing risk and the growth advantage of XBB.1.5 has the potential to cause an increase in cases in New Zealand.

There is no strong evidence of an increase in disease severity associated with these variants.

## Features of Omicron

### Growth advantage/transmissibility

*Section updated: 19 January 2023*

Growth advantage has become challenging to estimate with the backdrop of numerous circulating variants. In particular, estimates will vary with each country's specific prior variant mix and are specific to a point in time. Consequently, applying international estimates to New Zealand is unlikely to be informative. Additionally, fewer data are now available as whole genome sequencing surveillance is being less thoroughly conducted worldwide. For data about estimates of growth advantage, see previously published versions of this report. This report provides information on XBB.1.5 which appears to have a significant growth advantage. Details are presented in the Risk assessment table.

### Vaccine effectiveness, immune evasion

*Section updated: 19 January 2023*

Formal estimates of vaccine effectiveness (VE) require cases to accumulate (usually requiring some time) before estimates can be calculated. VE estimates are therefore currently not available for most variants that emerged after BA.2 and BA.5. Where VE estimates are not available, laboratory testing can provide some information by, for example, measuring how well antibodies in the serum from vaccinated people neutralise each variant. However, results from such laboratory tests need to be confirmed by epidemiological data. The development of bivalent vaccines has added further difficulties to reporting the VE of circulating variants.



## Vaccine effectiveness

Section Updated: 2 February 2023

Vaccine effectiveness reported here is only for periods including BA.4/5 waves, as variants prior to BA.4/5 are now not often seen. VE for previous variants such as BA.1 are included in previous Variants of Concern Updates and so are not repeated here. VE is also only reported here for mRNA vaccines.

### VE against infection

#### Monovalent (Wild Type) original formulation vaccines

Three doses: Moderna vaccine shows VE (against BA.2, BA.2.12.1, BA.4 and BA.5) was 61.0% - 90.6% at 14 – 30 days post-third dose. (2) However, this diminished to levels below 20% against all subvariants after 5 months.(2)

Four doses: Moderna vaccine shows VE ranged between 64.3%-75.7% for BA.2, BA.2.12.1, and BA.4 and was 30.8%) against BA.5 at 14-30 days post-fourth dose. VE was low beyond 90 days for all subvariants. (2)

#### Bivalent (BA.4/5, Wild type) mRNA vaccines

Absolute VE (compared to those who have received no doses of any COVID-19 vaccine) against symptomatic SARS-CoV-2 infection ranged from 22% (95% CI: 15-29) in those aged 65 and older, to 43% (95% CI: 39-46) in those aged 18-49 years at a maximum of 2.5 months after the bivalent vaccine dose. (3) Relative VE (that is, compared to those who have received the same number of previous monovalent doses but not the bivalent booster) increased in all age group with the time since the most recent previous dose. (3) Due to lack of a comparison group these data do not show whether the effect of the BA.4/5 dose is superior to the original formulation.

### VE against severe disease

#### Monovalent (Wild Type) original formulation vaccines

Two doses: mRNA vaccines during a BA.4/5 dominant period show VE against hospitalisation or urgent care visit was 25% (95% CI: 17 - 32) at > 150 days post-vaccination. (4) Two doses provide high VE against death for adolescents and children, but data about duration of this effect in young people are limited. (5)

Three doses: Moderna vaccine shows VE against hospitalisation (time since vaccination unclear) was 97.5%, 82.0%, and 72.4% for BA.1, BA.2 and BA.4/5 respectively. (2) During a BA.4/5 dominant period, mRNA vaccines show VE against hospitalisation or urgent care visit was 68% (95% CI: 50 - 80) at 7-119 days post-vaccination, and 36% (95% CI: 29 – 42 at > 120 days post-vaccination.(4)

Four doses: Moderna vaccine shows VE against hospitalisation (time since vaccination unclear) for BA.4/BA.5 was 88.5%. (2) During a BA.4/5 dominant period, a second mRNA booster dose yielded a VE against hospitalisation to 66% (95% CI: 53-75%) at 7-59 days post-vaccination in those aged 65 years or older, and 57% (95%CI 44-66%) at more than 60 days post-vaccination.(4)

#### Bivalent (BA.4/5, Wild type) mRNA vaccines

There **are limited data** from studies directly comparing the clinical efficacy of a recent bivalent vaccine booster to the clinical efficacy of a recent WT vaccine booster:

- A US study estimating vaccine effectiveness (VE) against severe disease and death for BA.4/5 bivalent mRNA vaccines (Moderna and Pfizer–BioNTech) and monovalent mRNA vaccines, found that VE for one monovalent booster dose was 24.9% (95% CI: 1.4 - 42.8), and for one bivalent booster dose 61.8% (95% CI: 48.2 - 71.8). The difference in VE against this outcome between the bivalent booster and the monovalent booster was 36.9 percentage points (95% CI: 12.6 - 64.3). (6) VE estimates were similar when the analysis was restricted to: 1) participants who were 18



years and over or 65 years and over, 2) participants who received an mRNA vaccine as their primary vaccine, or 3) previously uninfected participants. In addition, estimates of VE were similar for the Moderna and Pfizer–BioNTech boosters and similar among the first, second, and third booster doses. However, there is a risk of bias in this study as two separate time periods were used for comparing the efficacy of bivalent to monovalent vaccines.

- A Nordic study compared BA.4/5 bivalent boosters mainly to BA.1 bivalent boosters, and to no booster dose. Although the study did compare BA.4/5 bivalent boosters to monovalent vaccine, it was underpowered to estimate differences in level of protection on severe disease. The results had very wide confidence intervals crossing, or close to, null effect. Specifically, VE of -3.2% (-129.9% to 100%) against hospitalisation and 64.1% (0.6% to 100.0%) against death was reported. Additionally, there is a risk of bias due to varying results between the four countries, different cohort sizes and different age limits for participants (with lower age limit ranging from 50-64 years). (7)

Other studies generally support BA.4/5 mRNA booster being more effective at preventing severe disease and death than continuing with **no** additional booster dose. (8-13)

### **Protection from vaccination plus prior Omicron infection**

A systematic review (of studies to mid-2022) found that hybrid immunity provides higher protection against severe COVID-19 related outcome than infection or vaccination alone. (14) Prior infection and hybrid immunity both provided greater and more sustained protection against Omicron than vaccination alone. However, individuals with hybrid immunity had the highest magnitude and durability of protection against all outcomes, reinforcing the global imperative for vaccination. (14)

More recent publications on this topic include:

- Previous Omicron infection in triple-vaccinated individuals provides a high level of protection against BA.5 and BA.2 infections (92.7 - 97.1%) and hospitalisation (91.2 -96.4%). (15)
- Hybrid immunity following infections from BA.1 or BA.5 when compared with vaccine-only immunity leads to substantially increased protection against BA.5 reinfection for up to 8 months.(16)

## **Immunological data**

*Section Updated: 1 February 2023*

### **Monovalent (Wild Type) original formulation vaccines**

Evidence continues to accumulate that neutralising antibody levels against Omicron decline after a primary course of Pfizer vaccine (original monovalent, wild type (WT) vaccine), and are higher after a booster (third) dose, than after the primary course. (17-20) Similar results from a phase II clinical suggest that antibody titres increased following a booster (third or fourth) dose of Novavax (NVX-CoV2373) without increasing reactogenicity. (21)

Immunological data suggest hybrid immunity after monovalent vaccine and (Delta or Omicron) infection is likely to be robust. (22)

Data show that the memory T cell response generated by monovalent WT (original formulation) remains robust and is mostly unaffected by the mutations in Omicron (B.1.1.529). (23)

### **Bivalent (BA.4/5, Wild type) mRNA vaccines**

Immunological data for bivalent vaccines will be superseded by clinical data (see section Vaccine Effectiveness, above) as clinical data becomes available.



This section summarises immunological data available for BA.4/5 bivalent mRNA vaccines up to 31 January 2023.(24-37) Most studies show that BA.4/5 mRNA bivalent boosters generate neutralising antibody against emerging Omicron subvariants, including BA.2.75, BQ.1.1 and XBB. Among studies with a comparison to WT monovalent vaccine, the neutralising antibody response was greater for the BA.4/5 bivalent vaccine. Specific information includes:

- a. BA.4/5 mRNA bivalent booster vaccines elicit neutralising antibody against emerging Omicron subvariants that are not contained in the vaccine. (24, 29-35)
- b. Multiple studies support a greater increase in neutralising antibody titres to XBB when compared to the WT monovalent vaccine. (24, 29-33, 35)
- c. However, a few studies have found boosting with BA.4/5 bivalent mRNA vaccines did not elicit a superior neutralising antibody response but instead was comparable to that of the original WT monovalent vaccines. (28, 37)
- d. One pre-print study found that neutralising antibody titres elicited by the BA.4/5 bivalent boosters against XBB, declined over time and by three months were at similar levels to that prior to boosting. (36)

#### Bivalent vaccines for children

Preliminary safety findings from the first 11 weeks of bivalent booster vaccination in children aged 5–11 years are reassuring and similar to those described for monovalent booster vaccination. (38)

Emergency use authorisations (USA) or recommendation for marketing authorisation (EU) have been made on data including safety, immunogenicity, efficacy, and observational effectiveness data for the monovalent WT (original formulation) vaccine, and immunogenicity data from other Pfizer bivalent vaccines.(39, 40)

#### **Immunological response from vaccination plus prior Omicron infection**

There is some evidence to suggest that an individual's first exposure to a variant (either through infection or vaccination) shapes the immune response to future infections (how well the antibody produced neutralises a variant not previously encountered). (41, 42)

A US Study assessing the extent of antibody response against the original WT strain as well as Omicron sublineages BA.2.75 and BA.2.75.2 found that GMTs were highest in the group of people who had a breakthrough infection after receiving three or four monovalent doses. (28)

#### **Safety of second booster**

*Section Updated: 1 February 2023*

A pre-print of a study (including 250,000 people in Israel) about the safety of a second booster of Pfizer's BNT162b2 vaccine, found no significant differences in frequency of self-reported adverse events after the second booster compared with the first booster dose. (43) Similarly to a primary course, a booster of Pfizer vaccine is associated with an increased risk rate of myocarditis in 12- to 39-year-old males (Relative Risk of 2.28 (95% CI, 0.77 to 6.80), however, compared to a primary course the risk appears to be lower. (44)

#### Bivalent vaccines

Data generally continues to support the safety profile of BA.4/5 mRNA bivalent vaccines being similar to that of the original formulation monovalent mRNA vaccines. (33, 45) However, a signal has been detected in a single database in the US (CDC's Vaccine Safety Datalink (VSD) for ischemic stroke after the Pfizer bivalent vaccine in people ages 65 and older. This signal is being investigated but has not yet been observed in any other US study/database (including VAERS) or in other countries. (46) This signal will continue to be monitored. The CDC states that no change is recommended in COVID-19 vaccination practice. (46) The CDC



presented an update to the Vaccines and Related Biological Products Advisory Committee (VRBPAC) meeting on January 26, 2023, suggesting that the safety signal for ischemic stroke has weakened since its initial identification. However, it remains statistically significant, and it is unclear what the cause is. The CDC and Food and Drug Administration (FDA) are investigating whether a possible role of concomitant high-dose or adjuvanted flu vaccination with COVID-19 vaccination are the cause. (21)

## Disease course and clinical features (symptoms and severity)

*Section Updated: 5 December 2022*

Various studies continue to indicate a reduction in severity and lower mortality for the Omicron variant (and subvariants) as compared with the Delta variant. (47-49) However, Omicron infections still contribute to excess total mortality. A study from Italy found that excess total mortality persisted during the circulation of the Omicron variant in Italy (although data only available to 31 January 2022), contributing to a reversal in the long-term trend towards increasing life expectancy. (50)

Analysis from a large study in England from 1 May 2020 to 31 March 2022 showed some changes in symptom profiles associated with the different variants over that period, such as lower reporting of loss of sense of smell or taste for Omicron compared to previous variants. (51)

Laboratory studies have also been conducted to investigate pathogenicity of variants on cells. Such studies have supported Omicron severity being lower than previous variants (with one researcher suggesting that descendants of BA.5 and BA.2 (including BQ.1 and BQ.1.1) could cause slightly more severe disease than BA.1 or the original Omicron). However, these findings require validation from clinical data. (48, 52)

A study published in November 2022 reported an increased risk of death, hospitalisation, and sequelae with reinfection compared to no reinfection. (53) These results have been widely reported; however, the results should be interpreted very carefully as the follow-up time after symptom onset is not the same in the comparison groups, introducing bias.

## Therapeutics effectiveness

*Section Updated: 01 February 2023*

Monoclonal antibody treatments: laboratory-based studies suggest that monoclonal antibody treatments (such as Evusheld) are ineffective against some emerging variants. (54-57) **The proportion of variants that Evusheld cannot neutralise is now greater than 90%. (1)** Clinical effectiveness data for Evusheld (Aotearoa New Zealand's most used monoclonal antibody treatment) are available for a period of BA.1 predominance, (58) but not for later variants.

Real-world evidence suggests that Paxlovid, New Zealand's most prescribed antiviral, remains effective against Omicron variants (including BA.4 and BA.5) in vaccinated populations. (59-62). Initial clinical data (February 2022) reported that molnupiravir caused a 30% reduction in hospitalisations and deaths in unvaccinated adults with mild-to-moderate COVID-19 symptoms and at least one risk factor. (63) In contrast, recent clinical data (December 2022) suggests that that molnupiravir treatment may not be associated with any meaningful clinical benefit in vaccinated adults. (64) However it remains unclear if changes in efficacy are due to methodological differences between the studies or changes in the SARS-CoV-2 virus.



## Detection/testing

*Section Updated: 5 December 2022*

There is some evidence to suggest changes in the performance of RATs to detect Omicron variants. However, data are limited, and changes appear to be dependent on both the individual device and subvariant. Use of techniques such as serial testing may maximise sensitivity.

Growing international evidence suggests that clinically relevant changes in RAT performance for detection of Omicron variants differ on an individual device basis. (65-69) Comparability between studies is limited by difference in study design and objectives. The results are also dependent on which Omicron variant was assessed, making it difficult to determine whether evidence of reduced sensitivity is indicative of real-world device performance. Studies indicate that despite reports of reduced sensitivity, data support the continued use of RATs for self-testing. (65-69) Emerging evidence also highlights the need for techniques such as serial testing to maximise sensitivity against new Omicron variants of concern. (67, 69)

## Associated documentation

The following documents or ongoing work programmes draw upon the evidence in this document:

- New Variants of Concern Monitoring and preparedness
- Outlook Strategy Group
- Variant Risk Assessments

## Key recent international documents

*Section updated: 23 January 2023*

In addition to selected recent pre-prints and published studies, key reports used in this update include the following risk assessments for XBB.1.5 from key peak bodies.

### **World Health Organization update**

The WHO's Technical Advisory Group on Virus Evolution (TAG-VE) met on 05 January 2023 to discuss the Omicron XBB.1.5 variant, which has been reported in 38 countries with most of the sequences coming from the United States (82.2%), the United Kingdom (8.1%), and Denmark (2.2%). Based on its genetic characteristics and early growth rate estimates, XBB.1.5 may contribute to increases in case incidence. However, the overall confidence in the assessment is currently low as growth advantage estimates are only from one country, the United States.

The WHO and the TAG-VE recommend Member States to prioritize studies to better address uncertainties relating to the growth advantage, antibody escape, and severity of XBB.1.5, with suggested timelines varying based on national capacities. The rapid risk assessment will be revised regularly as more evidence and data from additional countries become available. (70)

### **UK Health Security Agency update**

The UK currently has high incidence of the BQ.1 variant and its sublineages. Two other variants, CH.1.1 and XBB.1.5, are showing positive growth compared to BQ.1. CH.1.1 is at moderate prevalence and XBB.1.5 is at low prevalence. The growth advantage of XBB.1.5 is biologically plausible due to its immune escape properties and ACE-2 affinity. CH.1.1 and XBB.1.5 are currently the most likely variants to predominate in the





UK following BQ.1. However, there is high uncertainty in the growth estimates for XBB.1.5 due to the small number of sequenced samples.

There is no increase in risk of hospitalization for people with BQ.1 compared to BA.5, but further analysis is ongoing. A preliminary analysis of vaccine effectiveness against hospitalization for BQ.1 compared to BA.5 has been undertaken, but the numbers of sequences in the available data are too small to make a confident assessment. (71)



# Section 2: Summary of Variants

Public Health Risk Assessments for the Omicron subvariants BA.5 and BA.4.6, can be found in the previous SARS-CoV-2 Variant of Concern Update [here](#).

## Variant Risk Assessment for XBB.1.5

*Updated: 02 February 2023*

XBB.1.5 is a sublineage of XBB, with additional spike protein mutations 252V, S486P (72)

|                                 | Overall risk assessment* | Confidence level **      | Assessment and rationale  |
|---------------------------------|--------------------------|--------------------------|---|
| <b>Overall growth advantage</b> | <b>Increased risk</b>    | <b>Low</b>               | <p><b>Evidence of a growth advantage compared to Omicron subvariants including BA.5 and BQ.1.1 (70, 73)</b></p> <p>Informal analyses suggest XBB.1.5 has a growth advantage over BQ.1 and associated sublineages, (74) of approximately 10% per day in early January 2023.(75) However, growth advantage is context specific (e.g. to the immune landscape) and it is not yet clear how this will translate to the New Zealand setting.</p> <p><i>XBB.1.5 is currently present in New Zealand, with only small numbers of sequences reported (12 identified between 14 to 17 January 2023). (1) In the week ending 29 January 2023, XBB sublineages made up 2-3% of wastewater samples. Less than 1% of hospitalised sequenced isolates were XBB or its sublineages in this period.</i></p> |
| <b>Transmissibility</b>         | <b>Increased risk</b>    | <b>Low</b>               | <p><b>Evidence of increased transmissibility</b></p> <p>There is laboratory evidence that ACE2 binding is increased for XBB.1.5 compared to prior Omicron variants, which is likely to affect transmissibility/infectivity by increasing the ability of the variant to attach and enter cells. (35, 72, 74)</p>   |
| <b>Immune evasion</b>           | <b>Insufficient data</b> | <b>Insufficient data</b> | <p><b>Limited data available about immune evasion.</b></p>  |



|                           |   |                          |   |
|---------------------------|---|--------------------------|---|
|                           |   |                          | Early laboratory studies suggest there is an ability to evade antibody that is similar to XBB (that is, more resistant to neutralisation by antibody than all other variants to date).(70, 72, 74) There are currently no data on real world vaccine effectiveness against severe disease or death.(70) |
| <b>Severity</b>           | <b>Insufficient data</b>  | <b>Insufficient data</b> | <b>No evidence of a change in severity compared to previous Omicron subvariants</b><br>XBB.1.5 does not carry any mutation known to be associated with potential change in severity. Severity assessments are ongoing. No early signals from informal sources of marked increase in severity.           |
| <b>Therapeutics</b>       | <b>Increased risk</b>   | <b>Low</b>               | <b>Currently no evidence of resistance to Paxlovid or Molnupiravir.</b><br><i>In vitro</i> studies showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. (72)   |
| <b>Testing</b>            | <b>Insufficient data</b>  | <b>Insufficient data</b> | There is some evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device),(65-69) but it is uncertain how this will affect sensitivity specifically for XBB.1.5.   |
| <b>Overall Assessment</b> | <b>Based on its genetic characteristics and early growth rate estimates there is an increase in overall risk compared to the New Zealand variant landscape of late December 2022. XBB.1.5 may contribute to increases in cases in New Zealand. Differences in immune landscape between New Zealand and USA populations mean effects seen in parts of the USA might not directly translate to the New Zealand setting.</b> |                          |   |

\*The 'Overall risk assessment' is presented in comparison to the prior variant landscape in Aotearoa New Zealand. 'Increased risk' indicates the assessed variant as worse than the previous variant landscape with regards to that characteristic; 'no change' means that the assessed variant poses equivalent risk; and 'decreased risk' means that the assessed variant is better than the previous variant landscape.

\*\*'Confidence level' indicates the overall quality of data that are available to make the risk assessment: 'High' (high quality, robust data); 'Moderate' (good data with limitations); 'Low' (very little data available). 'Insufficient data' indicates that there are no data of reasonable quality on which to base an assessment at this time.



# Variant Risk assessment for XBB

Updated: 02 February 2023

XBB is a recombinant virus ( related to BA.2 and BJ.1) with additional spike protein mutations 364T, 445P, 446S and 490V. (76)

|                                 | Overall risk assessment* | Confidence level **      | Assessment and rationale  |
|---------------------------------|--------------------------|--------------------------|---|
| <b>Overall growth advantage</b> | <b>Increased risk</b>    | <b>Low</b>               | <p><b>Evidence of a growth advantage compared to BA.5</b></p> <p>XBB has an estimated growth advantage of 56.9% per week (95% Credible Interval: 46.9 to 67.2%) compared to BA.5.2 in the UK (at 9 November 2022).(77)</p> <p>In the week ending 29 January 2023, XBB and its sublineages made up 2-3% of wastewater samples. (1) Less than 1% of hospitalised sequenced isolates were XBB or its sublineages in this period.</p> |
| <b>Transmissibility</b>         | <b>Insufficient data</b> | <b>Insufficient data</b> | <p>No direct data on intrinsic transmissibility and there is no current ability to measure from surveillance data. There is some laboratory evidence that ACE2 binding is increased for XBB compared to prior Omicron variants which may affect transmissibility/infectivity. (54)</p>  |
| <b>Immune evasion</b>           | <b>Increased risk</b>    | <b>Moderate</b>          | <p><b>Evidence of increased immune evasion.</b></p> <p>More resistant to neutralisation from sera of vaccinated and breakthrough infected individuals. (54, 78)</p>   |
| <b>Severity</b>                 | <b>Insufficient data</b> | <b>Insufficient data</b> | <p>In late October 2022 the World Health Organization Technical Advisory Group on SARS-CoV-2 Virus Evolution noted that current (limited) information does not indicate an increase in severity for XBB. (79)</p>   |
| <b>Therapeutics</b>             | <b>Increased risk</b>    | <b>Low</b>               | <p><i>In vitro</i> studies showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. (54, 78)</p>   |



|                           |                          |                          |  |
|---------------------------|--------------------------|--------------------------|--|
| <b>Testing</b>            | <b>Insufficient data</b> | <b>Insufficient data</b> | Evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), (65-69) but it is uncertain how this will affect sensitivity specifically for XBB. |
| <b>Overall Assessment</b> | <b>No change in risk</b> |                          |  |

*\*The 'Overall risk assessment' is presented in comparison to the prior variant landscape in Aotearoa New Zealand. 'Increased risk' indicates the assessed variant as worse than the previous variant landscape with regards to that characteristic; 'no change' means that the assessed variant poses equivalent risk; and 'decreased risk' means that the assessed variant is better than the previous variant landscape.*

*\*\*\*Confidence level' indicates the overall quality of data that are available to make the risk assessment: 'High' (high quality, robust data); 'Moderate' (good data with limitations); 'Low' (very little data available). 'Insufficient data' indicates that there are no data of reasonable quality on which to base an assessment at this time.*



# Variant Risk Assessment for BF.7

Updated: 02 February 2023

BF.7 is a sublineage of BA.5.2.1 but with spike protein mutations R346T

|                                 | Overall risk assessment* | Confidence level **      | Assessment and rationale  |
|---------------------------------|--------------------------|--------------------------|---|
| <b>Overall growth advantage</b> | <b>Insufficient data</b> | <b>Insufficient data</b> | <p><b>Insufficient data to assess growth advantage</b></p> <p>Sequences uploaded by China to GISAID between 01 December 2022 to 03 January 2023, show 33% of all sequences were BF.7.(80) BF.7 has been observed to have a growth advantage compared to BA.5 in the UK,(81) but comparison of growth estimates suggest it is unlikely to outcompete other circulating variants such as BQ.1 and associated sublineages.</p> <p>BF.7 has been present in New Zealand at low levels since October 2022, (82) <b>but has not been detected in New Zealand since the beginning of 2023. (1)</b></p> |
| <b>Transmissibility</b>         | <b>Insufficient data</b> | <b>Insufficient data</b> | <b>No evidence of increased intrinsic transmissibility compared to prior Omicron subvariants</b>  |
| <b>Immune evasion</b>           | <b>Increased risk</b>    | <b>Low</b>               | <p><b>Evidence of increased immune evasion.</b></p> <p>Some laboratory data suggests a higher resistance to neutralisation from sera of vaccinated and infected individuals,(83, 84) whilst one study found a similar resistance to neutralisation as BA.4/5. (85)</p>  |
| <b>Severity</b>                 | <b>Insufficient data</b> | <b>Insufficient data</b> | <b>No evidence of a change in severity compared to previous Omicron subvariants</b>   |
| <b>Therapeutics</b>             | <b>Increased risk</b>    | <b>Moderate</b>          | Currently there is no evidence of resistance to antivirals Paxlovid or Molnupiravir. <i>In vitro</i> studies showed loss of efficacy of Evusheld.(85)   |



|                           |   |                          |   |
|---------------------------|---|--------------------------|---|
| <b>Testing</b>            | <b>Insufficient data</b>  | <b>Insufficient data</b> | There is some evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), (65-69) but it is uncertain how this will affect sensitivity specifically for BF.7. |
| <b>Overall Assessment</b> | <b>No change in risk compared to the New Zealand variant landscape of late December 2022.</b> |                          |   |

*\*The 'Overall risk assessment' is presented in comparison to the prior variant landscape in Aotearoa New Zealand. 'Increased risk' indicates the assessed variant as worse than the previous variant landscape with regards to that characteristic; 'no change' means that the assessed variant poses equivalent risk; and 'decreased risk' means that the assessed variant is better than the previous variant landscape.*

*\*\*'Confidence level' indicates the overall quality of data that are available to make the risk assessment: 'High' (high quality, robust data); 'Moderate' (good data with limitations); 'Low' (very little data available). 'Insufficient data' indicates that there are no data of reasonable quality on which to base an assessment at this time.*



# Variant Risk assessment for BA.2.75

Updated: 02 February 2023

BA.2.75 has 8 key mutations from BA.2: 147E, 152R, 157L, 210V, 257S, 339H, 446S, 460K. (76)

Sublineages of BA.2.75 include BA.2.75.2, BN.1, BR.2.1 and CH.1.1 all of which have been discussed in previous [variant updates](#)

|                                 | Overall risk assessment* | Confidence level **      | Assessment and rationale   |
|---------------------------------|--------------------------|--------------------------|--|
| <b>Overall growth advantage</b> | <b>Increased Risk</b>    | <b>Moderate</b>          | <p><b>Evidence of a growth advantage compared to BA.5. Prevalence in New Zealand is increasing gradually.</b></p> <p>There is evidence that BA.2.75 has a growth advantage against BA.4/5 in some countries (India, Austria, Singapore). BA.2.75 and sublineages (excluding BN.1) have an estimated growth advantage of 22.5% per week (95% Credible Interval: 19.1 to 26.0%) compared to BA.5.2 in the UK (at 9 November 2022). (77)</p> <p><i>In the fortnight ending 27 January 2023, BA.2.75 made up 15% and CH.1.1 made up 38% of all sequenced cases in New Zealand. (1) BA.2.75 made up of 18% and CH.1.1 made up 44% of all sequenced hospitalised cases. (1)</i></p>                  |
| <b>Transmissibility</b>         | <b>Insufficient data</b> | <b>Insufficient data</b> | There are no direct data on intrinsic transmissibility and there is no current ability to measure this directly from surveillance data.  |
| <b>Immune evasion</b>           | <b>No change in risk</b> | <b>Low</b>               | <p><b>There is evidence of increased immune evasion by BA.2.75 lineages in the form of increased representation in reinfection cases.</b></p> <p>Mutations suggest that BA.2.75 may have immune evasion potential. However, there are very limited data to evaluate immune evasion against vaccination, prior infection with BA.5, or a combination of the two (hybrid immunity). There are no estimates of vaccine effectiveness against BA.2.75.</p> <p>Laboratory data: Neutralisation studies found that BA.2.75 was similar or slightly less able to be neutralised by antibodies produced after vaccination and BA.2 infection, compared to BA.4 or BA.5. (86-90) Potentially higher</p> |





|                           |  |                          |   |
|---------------------------|--|--------------------------|---|
|                           |  |                          | <p>receptor binding compared to other Omicron lineages. There are no data on the ability of antibodies produced after BA.5 infection to neutralise BA.2.75.</p> <p>A pre-print study found CH.1.1 to have a higher resistance to neutralisation from sera of vaccinated and infected individuals. (35)</p> <p>During the fortnight ending 13 January 2023, CH.1.1 was strongly over-represented in reinfection cases, accounting for 41% of reinfection cases and also represented 19% of first-time sequenced infections. (91)</p>   |
| <b>Severity</b>           | <b>Insufficient data</b>   | <b>Insufficient data</b> | <p><b>No evidence of a change in severity compared to BA.5</b></p> <p>Few formal evaluations of BA.2.75 severity are available. An early assessment of the severity of BA.2 sublineages in India indicates that BA.2.74, BA.2.75, and BA.2.76 are causing 'mild' disease with no evidence of an increased risk of hospital admission or severe disease. (92) Lab and animal studies suggest mixed results for binding compared to BA.5, (90) but overall pathogenicity similar to BA.5. (93) Some <i>in vitro</i> evidence suggest an increase in cell-cell fusion and ability to infect lower airways compared to BA.2 which could alter pathogenicity. (94)</p> |
| <b>Therapeutics</b>       | <b>Insufficient data</b>   | <b>Insufficient data</b> | Currently there is no evidence of resistance to antivirals Paxlovid or Molnupiravir.  |
| <b>Testing</b>            | <b>Insufficient data</b>   | <b>Insufficient data</b> | There is some evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), (65-69) but it is uncertain how this will affect sensitivity specifically for CH.1.1.   |
| <b>Overall Assessment</b> | <p><b>There is an increase in overall risk from the previous predominant variant, BA.5. (Moderate confidence)</b></p> <p><b>BA.2.75 and associated sublineages, particularly CH.1.1, are increasing in frequency in New Zealand and appear to be more transmissible and immune evasive. BA.2.75 and CH.1.1 combined currently account for 50% of sequenced genomes in New Zealand.</b></p> |                          |   |

\*The 'Overall risk assessment' is presented in comparison to the prior variant landscape in Aotearoa New Zealand. 'Increased risk' indicates the assessed variant as worse than the previous variant landscape with regards to that characteristic; 'no change' means that the assessed variant poses equivalent risk; and 'decreased risk' means that the assessed variant is better than the previous variant landscape.

\*\*'Confidence level' indicates the overall quality of data that are available to make the risk assessment: 'High' (high quality, robust data); 'Moderate' (good data with limitations); 'Low' (very little data available). 'Insufficient data' indicates that there are no data of reasonable quality on which to base an assessment at this time.



# Variant Risk assessment for BQ.1.1

Updated: 02 February 2023

BQ.1.1 is related to BA.5.3 but with Spike protein mutations 444T, 460K, 346T (76)

|                          | Overall risk assessment* | Confidence level ** | Assessment and rationale  |
|--------------------------|--------------------------|---------------------|---|
| Overall growth advantage | Increased risk           | Moderate            | <p><b>Evidence of a growth advantage compared to BA.5. (81, 95, 96)</b></p> <p>BQ.1.1 variant has an estimated growth advantage of 48.5% per week (95% Credible Interval: 43.3 to 54.1%) compared to BA.5.2 in the UK (at 9 November 2022).(77)</p> <p>Currently present in New Zealand. In the week ending 27 January 2023, BQ.1.1 made up 9% of all sequenced cases. In the fortnight ending 27 January 2023 it made up 8% of sequenced isolates from hospital cases. (1)</p> |
| Transmissibility         | Insufficient data        | Insufficient data   | <p>No direct data on intrinsic transmissibility and there is no current ability to measure from surveillance data. There is some laboratory evidence that ACE2 binding is increased for BQ.1.1 compared to prior Omicron variants which may affect transmissibility/infectivity. (54)</p>   |
| Immune evasion           | Increased risk           | Moderate            | <p><b>Evidence of increased immune evasion.</b></p> <p>More resistant to neutralisation from sera of vaccinated and infected individuals. (54, 78) At least two small studies show that mRNA bivalent BA.4/5 vaccine produces robust neutralising activity against BQ.1.1 compared to monovalent wild type vaccine. (25, 29, 78)</p>  |
| Severity                 | Insufficient data        | Insufficient data   | <p><b>No evidence of a change in severity compared to BA.5</b></p> <p>Evidence from a surge of cases of this variant in France suggests it is not causing increased rates of hospitalisations and deaths. (97)</p>  |



|                           |   |                          |  |
|---------------------------|---|--------------------------|--|
| <b>Therapeutics</b>       | <b>Increased risk</b>   | <b>Low</b>               | <i>In vitro</i> studies showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. (54, 78)   |
| <b>Testing</b>            | <b>Insufficient data</b>  | <b>Insufficient data</b> | Evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), (65-69) but it is uncertain how this will affect sensitivity specifically for BQ.1.1 |
| <b>Overall Assessment</b> | <p>There is an increase in overall risk from the previous predominant variant, BA.5. (Moderate confidence)</p> <p>BQ.1.1 is increasing in frequency overseas and appears to be more transmissible and immune evasive. The frequency in NZ has remained relatively stable at approximately 15%</p> |                          |  |

\*The 'Overall risk assessment' is presented in comparison to the prior variant landscape in Aotearoa New Zealand. 'Increased risk' indicates the assessed variant as worse than the previous variant landscape with regards to that characteristic; 'no change' means that the assessed variant poses equivalent risk; and 'decreased risk' means that the assessed variant is better than the previous variant landscape.

\*\*'Confidence level' indicates the overall quality of data that are available to make the risk assessment: 'High' (high quality, robust data); 'Moderate' (good data with limitations); 'Low' (very little data available). 'Insufficient data' indicates that there are no data of reasonable quality on which to base an assessment at this time.



# New signals

*Section updated: 02 February 2023*

*With the rapid development of new variants with convergent mutations, future variant updates will focus on the mutations present in the variant landscape rather than specific variants. Any variants with markedly different clinical features will be monitored and reported.*

In the second half of 2022, many new Omicron subvariants have been reported. These variants demonstrate convergent evolution which is a process whereby variants from different lineages accumulate similar mutations. For example, the European Centre for Disease Prevention and Control (ECDC) has designated Omicron lineages with mutations at N460X and at either F490X or K444X (these include BQ.1, BQ.1.1, XBB, BN.1 and BN.2) as a variant under monitoring (VUM). The location of these mutations might produce a significant effect on neutralising activity. (98, 99)

For many BA.2.75 sublineages, mutations on N-terminal domain (NTD) can cause reduction in neutralisation titres. (54)

In Australia and New Zealand, there is currently no single variant driving case numbers. (100)

Details of BA.5, BA.2.75, BQ.1.1, BA.4.6, and XBB can be found above in the risk assessment section. Short summaries are provided here of newer variants which are not covered in the risk assessment section but are of heightened concern because of their growth rate in New Zealand or internationally, or because there are other features of concern (e.g., if increased severity was suspected). Because these variants have only been recently detected, the growth advantage, immune escape potential, and characteristics of disease they cause (e.g., severity) is often not yet well understood.

Details of the Omicron subvariants BR.2.1, BN.1 and BA.2.75.2, can be found in the previous SARS-CoV-2 Variant of Concern Update [here](#).

## XBP

- XBP is a recombinant lineage of BA.2.75 and BQ.1 (without S:R346T spike mutation). (101)
- Earliest sequence detected in GISAID was on 04 November 2022, from Texas, USA, and detected in Europe in late January 2023. (101) No further epidemiological data yet available.

## XBC

- XBC is a recombinant lineage that combines sequences from the Delta and Omicron variants. (102) Some studies suggest that chronic infections may be contributing to the emergence of such recombinant variant lineages. (103)
- In the week ending 27 January 2023, XBC made up 8% of all sequenced cases in New Zealand, and 3% of wastewater samples. (1) In the fortnight ending 27 January 2023 it made up 6% of sequenced isolates from hospital cases. (1)
- XBC appears to be most common in the Philippines and Brunei, circulating at a prevalence of around 5%. Sublineage XBC.1 (S:L452M) has been rising in Australia.(104)
- The XBC lineage has been present in Australia and Southeast Asia for some time, with no indication of increased disease severity (albeit this is based on small case numbers). (102)

## XBF

- Sublineage from a BA.5.2.3 and CJ.1 (a BA.2.75 sublineage) recombinant. Spike identical to CJ.1, additional mutations (from BA.2.75) S:486P, S:R346T, S:F490S. (104)



- Growing in Australia and Denmark. (104) Appears to be growing less rapidly in South Asia than CH.1.1 (another BA.2.75 sublineage),(104) but epidemiology could be different in New Zealand.
- In the week ending 27 January 2023, XBF made up 15% of all sequenced cases in New Zealand. (1) In the fortnight ending 27 January 2023 it made up 12% of sequenced isolates from hospital cases.(1)
- No data have yet emerged about the severity of XBF disease.



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