

Date: 21 November 2022

SARS-CoV-2 Variants of Concern Update

Executive Summary

Section updated: 16 November 2022

In the second half of 2022, many new Omicron sub-variants have been reported. These variants demonstrate convergent evolution which is a process whereby variants from different lineages accumulate similar mutations. Mutations in the spike protein appear to be responsible for the enhanced characteristics of these variants, compared to previous Omicron variants.

Although many of these new sub-variants demonstrate a transmission advantage over earlier sub-variants (which can come from increases in innate transmissibility or from immune evasion), there is currently no evidence of an increase in severity of disease caused by these variants.

New information in this report includes:

- A number of convergent subvariants displaying a growth advantage relative to BA.5 in the UK.[1] BQ.1.1 shows the greatest growth advantage (relative to BA.5) at 63% per week (at 20 October 2022), followed by BQ.1 and BQ.1.X sub-lineages at 53% per week.
- Evidence from a surge of cases of BQ.1.1 in France suggests it is not causing increased rates of hospitalisations and deaths.[2]
- During BA.4/5-dominant period, mRNA vaccines showed VE against hospitalisation or urgent care visit was 68% (95% CI: 50 - 80) at 7-119 days (1 week to 4 months) post-vaccination and 36% (95% CI: 29 - 42) at >120 days (more than 4 months) post-vaccination.[3]
- Immunogenicity data for BA.4/5 bivalent vaccines are mixed: some studies show little difference between bivalent vaccine and monovalent Wild Type (original formulation) vaccines, while others show suggested BA.4/5 bivalent vaccines elicit greater neutralisation titres against Omicron variants than the Wild Type (WT) monovalent vaccines.
- Antivirals: There is currently no evidence to suggest any currently emerging variants have become resistant to Nirmatrelvir/ritonavir (Paxlovid).

New signals:

- BR.2.1 (a BA.2.75 sub-lineage, with 3 extra spike mutations [4]) has been making up an increasing proportion of community samples in New South Wales, Australia. There has been a marked increase in NSW of the proportion of community samples that are BA.2.75 (mostly BR.2 sub-lineage): proportion of samples that were BA.2.75 (mostly BR.2 sub-lineage) were for week ending 15th October 7.7%, and for the week ending 29th October 20.1% [5]



- XBC is a recombinant lineage that combines sequences from the Delta and Omicron variants.[6] In the fortnight ending 11 November 2022, eight cases caused by XBC have been detected in New Zealand.[6] These have been from non-hospitalised cases. [6] The XBC lineage has been present in Australia and South East Asia for some time, with no indication of increased disease severity (albeit this is based on small case numbers). [6]
- CH.1.1 is derived from BM.4.1.1 (and consequently BA.2.75) and is defined by the S:L452R mutation.[7] The growth in BA.2.75 in New Zealand in October and November may be driven by an increase of CH.1.1 (46% of BA.2.75 cases in week ending 11 November).[6]
- BR.2.1 is BA.2.75 with 3 extra spike mutations.[4] The majority of BR.2 sequences reported internationally to early November 2022 have originated from New South Wales (NSW) in Australia.[5] Also in other countries including Japan.[7] Marked increase in NSW of the proportion of community samples that are BA.2.75 (mostly BR.2 sub-lineage): week ending 15th October 7.7%, week ending 29th October 20.1% [5]
- BN.1 is a descendant of BA.2.75.5 (and consequently BA.2.75), with S:R346T and S:490S mutations. [7] As of 11 November 2022, BN.1.X accounts for 4.3% of USA national cases.[8] The growth advantage and characteristics of disease it causes (e.g. severity) are not yet well defined.



Circulating variants across Aotearoa New Zealand:

The Institute of Environmental Science and Research (ESR) COVID-19 Genomics Insights (CGI) report was last produced on 16 November 2022, with data from the period of 29 October - 11th November).[6] The percentage of sequenced cases (community, including hospital, and “border” cases combined) that were of each variant in this period are shown in figure 1 (noting that ~2.0% of all cases were sequenced in this fortnight, and only variants with a frequency above 1% are shown). Additionally, of the 835 cases sequenced, there were 8 XBC cases identified (non-hospitalised).[6]

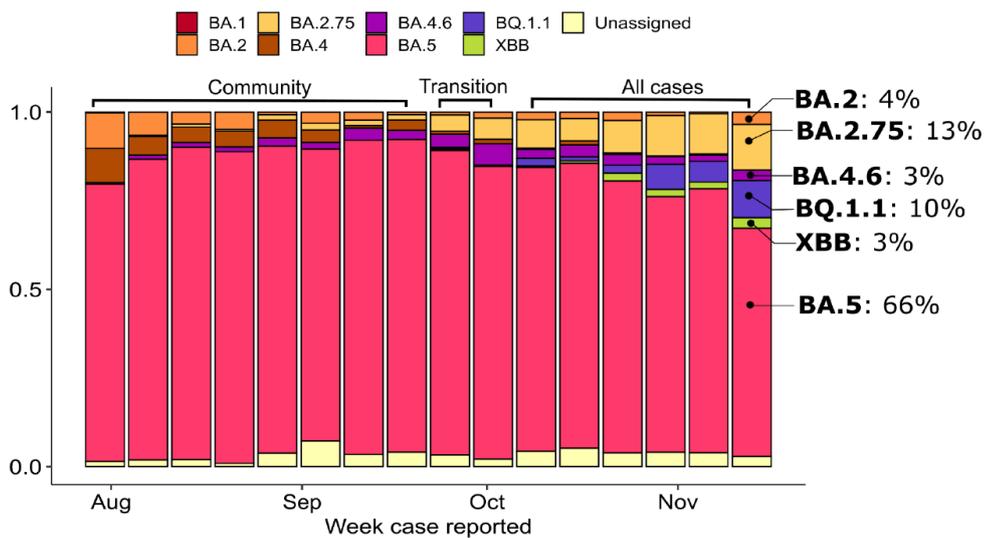


Figure 1: Frequency of SARS-CoV-2 variants in New Zealand each week. Only variants with a frequency above 1% are shown. Data is subject to change as samples may still be added to the most recent two-week period. Only data from community cases were used until September 2022, while in the “transition” period, cases known to be associated with the border are removed. Data from all cases (community, including hospital, and border) are used since October. Source: ESR [link](#)

BA.2.75 and BQ.1.1 have grown relative to BA.5 in recent weeks, and the growth of BA.2.75 is driven by several distinct descendants of the original BA.2.75 lineage (including CH.1.1, BA.2.75.8 and BM* (BM sub-lineages)).[6]

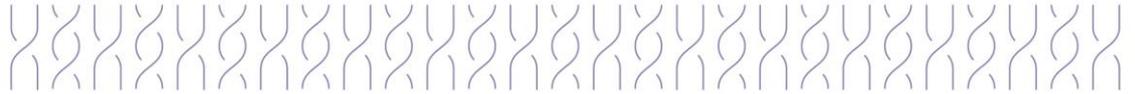
A publicly accessible version of the genomic report produced by ESR is available [here](#).

Wastewater surveillance (31 October – 13 November 2022) has seen similar patterns in variants to that seen in cases. BA.4/5 remains the dominant strain detected in wastewater with detection of BA.2.75 and BQ.1.1 increasing and XBB detected also. [6] The publicly accessible ESR Wastewater surveillance dashboard can be accessed [here](#).

Current overall variant risk status

Subvariants detected in cases in New Zealand such as BQ.1.1, BA.2.75 sub-lineages (including CH.1.1), XBB and XBC. BQ.1.1 and XBB have demonstrated substantial immune evasion in laboratory testing compared to prior Omicron variants. Cases of these subvariants are likely to increase relative to BA.5 in the coming weeks. CH.1.1 may have driven growth in BA.2.75 and its sub-variants in New Zealand in November and is likely to further increase (relative to BA.5). However, it is unknown if one or more variants will cause a wave or produce overall higher baseline incidence.

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



Section 1 Key Omicron information

Section updated: 09 November 2022

Features of Omicron

Growth advantage/transmissibility

A number of convergent subvariants (that is, different subvariants that have accumulated similar mutations) are displaying a growth advantage relative to BA.5 in the UK.[1] BQ.1.1 shows the greatest growth advantage (relative to BA.5) at 63% per week (at 20 October 2022), followed by BQ.1 and BQ.1.X sub-lineages at 53% per week. See “Section 2: Summary of Variants” and for available estimates of growth advantage for each variant.

Vaccine effectiveness, immune evasion

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.

Vaccine effectiveness

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

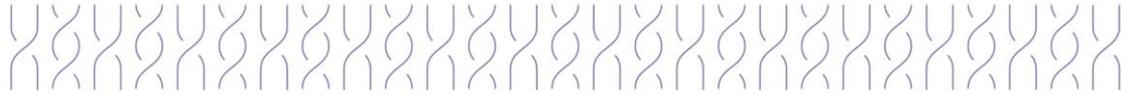
Three doses: Moderna vaccine showed VE (against BA.2, BA.2.12.1, BA.4 and BA.5) was 61.0% - 90.6% at 14 – 30 days post-third dose. [9] However, this diminished to levels below 20% against all subvariants after 5 months. [9]

Four doses: Moderna vaccine showed 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. [9]

VE against severe disease

Two doses: mRNA vaccines during a BA.4/5 dominant period showed VE against hospitalisation or urgent care visit was 25% (95% CI: 17 - 32) at >150 days post-vaccination. [3]

Three doses: Moderna vaccine showed 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. [9] During a BA.4/5 dominant period, mRNA vaccines showed VE against hospitalisation or urgent care visit was 68% (95% CI: 50 - 80) at 7-119 days post-vaccination [3] and 36% (95% CI: 29 – 42 at >120 days post-vaccination.[3]



Four doses: Moderna vaccine showed VE against hospitalization (time since vaccination unclear) for BA.4/BA.5 was 88.5%. [9]

Protection from vaccination plus prior Omicron infection

Previous Omicron infection in triple-vaccinated individuals provides a high level of protection against BA.5 and BA.2 infections. The study assessed outcomes across the period of 10 April to 30 June 2022. [10]

- Protection against BA.5 infection was estimated to be 92.7% (95% CI: 91.6 – 93.7).
- Protection against BA.2 infection was estimated to be 97.1% (95% CI: 96.6 – 97.5).
- High levels of protection against hospitalisation were conferred by infection with BA.5 at 96.4% (95% CI: 74.2 - 99.5) and BA.2 at 91.2% (95% CI: 76.3 – 96.7).

Evidence from laboratory testing

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 vaccine), and are higher after a booster (third) dose, than after the primary course.[11-14]

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

Immunogenicity data for BA.4/5 bivalent vaccines are mixed.

Some studies show little difference between bivalent vaccine and monovalent Wild Type (original formulation) vaccines. [15, 16]

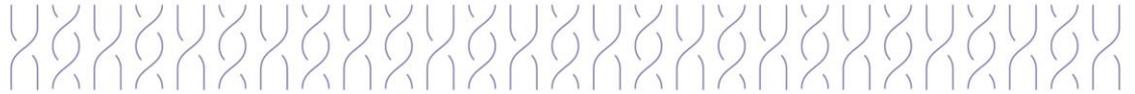
However, some pre-print studies have suggested BA.4/5 bivalent vaccines elicit greater neutralisation titres against Omicron variants than the Wild Type (WT) monovalent vaccines (however, activity against Omicron variants were substantially lower than against WT virus):

- One study assessed neutralising activity against WT virus and Omicron variants including BA.1, BA.5, BA.2.75.2, and BQ.1.1. [17]
- Another assessed activity against WT virus and Omicron variants including BA.4/5, BA.4.6, BA.2.75.2, BQ.1.1 and XBB.1). [18]
- A small sub-study in Moderna's clinical trial showed similar positive results for the BA.4/5 bivalent vaccine (including robust neutralizing activity against BQ.1.1, despite an approximately 5-fold drop in titres for BQ.1.1 compared to BA.4/BA.5. [19]

Disease course and clinical features (symptoms and severity)

Various studies continue to indicate a reduction in severity and lower mortality for the Omicron variant (and subvariants) as compared with the Delta variant. [20-22] 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.[23]

Several studies have indicated that Omicron exhibits enhanced replication in nasal epithelial cells and reduced replication in pulmonary cells, which may contribute to reduced severity of disease.[21]



Therapeutics effectiveness

Monoclonal antibody treatment: Bebtelovimab remains authorised for use (Emergency Use Authorization) in the USA due to being effective against most circulating variants (excluding BQ.1 and BQ.1.1). [24] A pre-print laboratory-based study has suggested it may be ineffective against some variants that are not currently (at 16 November 2022) predominant in New Zealand (e.g. BQ.1.1 and XBB). [25]

Antivirals: There is currently no evidence to suggest any currently emerging variants have become resistant to Nirmatrelvir/ritonavir (Paxlovid).

Detection/testing

There is some evidence to suggest changes in the performance of RATs to detect Omicron variants. However, data are limited and appears 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. [26-30] 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, the data supports the continued use of RATs for self-testing. [26-30] Emerging evidence also highlights the need for techniques such as serial testing to maximise sensitivity against new Omicron variants of concern. [28, 30]

Associated documentation

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

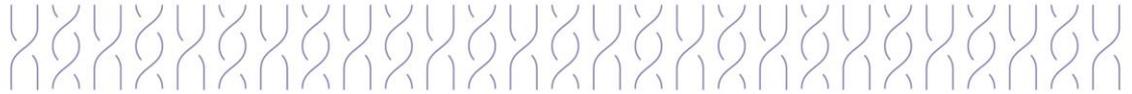
- New Variants of Concern Monitoring and preparedness
- Outlook Strategy Group
- New Variant Public Health Risk Assessments

Key recent international documents

Section updated: 09 November 2022

In addition to selected recent pre-prints and published studies, key reports used in this update include:

1. World Health Organization (WHO) Weekly epidemiological update on COVID-19:
 - 16 November 2022 [31]
 - 9 November 2022 [32]
 - 2 November 2022 [33]
 - 26 October 2022 [34]
2. UK Health Security Agency: SARS-CoV-2 Variants of Concern and Variants under Investigation in England, Technical Briefing 47, 28 October 2022 [1]



World Health Organization updates

The WHO Weekly Epidemiology Updates on 16 November 2022 [31] and 9 November 2022 [32] reported the status of circulating variants. The most recent report reported that: [31]

- The global variant circulation indicates a replacement of previously dominating BA.5 descendent lineages by the most recently emerging variants, notably by BQ.1, and BA.5 + R346X.
 - BQ.1 rose from 13.3% to 16.2%
 - BA.5 with additional mutations (R346X, K444X, V445X, N450D and/or N460X) continued to increase, rising from 22.4% to 23.3%;
 - BA.2.75 showed a rise in sequence prevalence from 4.1% to 5.4%.
 - XBB and its descendent lineages rose from 1.5% to 2.0%.

The WHO Weekly Epidemiology Update on 2 November 2022 [33] reported that:

- The WHO TAG-VE (Technical Advisory Group on SARS-CoV-2 Virus Evolution) met again on 24 October 2022 to further discuss Omicron subvariants XBB and BQ.1.
- According to the TAG-VE statement, based on currently available evidence—which at present is limited—the expert group advises that the overall phenotypes of XBB and BQ.1 (and their sublineages) do not diverge sufficiently from each other, or from other Omicron lineages with additional immune escape mutations, in terms of the necessary public health response, to warrant the designation of new variants of concern and assignment of a new label.
- XBB and BQ.1 remain Omicron VOC. So far, available information does not indicate an increase in severity.

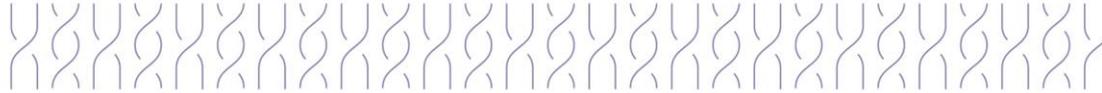
The WHO Weekly Epidemiology Update on 26 October 2022 [34] reported that:

- The relevant Spike protein (S) amino acid positions and substitutions under monitoring are S:R346X, S:K444X, S:V445X, S:N450X and S:N460X. BA.2, BA.4 and BA.5 and their various subvariants have in many cases acquired the same mutations at the same position, indicating convergent evolution.
- Convergent evolution refers to the independent genetic adaptation of two or more different variants at the same genomic position, i.e., the same nucleotide or amino acid change is observed in multiple variants, with these variants not being direct descendants of each other. Areas of convergent evolution point to a potential role in the adaptation and further evolution of the virus.

UK Health Security Agency updates

The UK Health Security Agency SARS-CoV-2 Variants of Concern and Variants under Investigation in England, Technical Briefing 47 on 28 October 2022 [1] reported that (at 20 October 2022):

- BA.5, including all sub-lineages, remains the dominant parent lineage in the UK at greater than 75% of all sequenced samples in the UK.
- In the most recent week, logistic growth of variants with 1, 2 or 3 convergent and antigenically significant RBD mutations was respectively 23%, 47%, and 66% per week.
 - The category with 3 RBD mutations consisted largely of BQ.1.1 (59%) with the remainder consisting primarily of a mixture of BA.2.75 sub-lineages (29%).



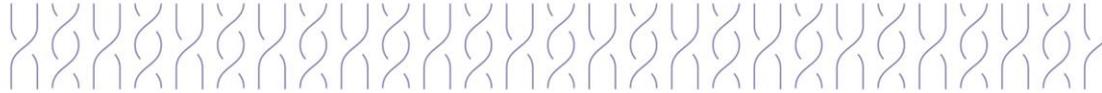
Section 2: Summary of Variants

Public Health Risk Assessment BA.5

Updated: 16 November 2022

BA.5 has key spike mutations at positions: L452R, F486V, and R493Q. [35] Note: BA.4 and BA.5 have identical spike protein.

	Overall Risk Assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	High	<p>Evidence of a growth advantage compared to BA.2.</p> <p>As at 16 November 2022, BA.5 remains the predominant variant in New Zealand, but makes up a declining proportion of sequenced cases (75% in fortnight ending 11 November.[6] A model estimating the relative growth rates of variants in New Zealand predicts BA.5 will make up less than 50% of cases by mid-December.[6] BA.5 has a reported growth advantage of 11.2% over the previously dominant variant BA.2.</p>
Transmissibility	Insufficient data	Insufficient data	<p>No direct data on intrinsic transmissibility. There is some laboratory evidence that ACE2 binding is increased for BA.5 compared to prior Omicron variants, and BA.5 may have increased infectivity. [36]</p>
Immune evasion	Increased risk	High	<p>There is evidence of increased immune evasion compared to BA.2, based on laboratory data; however, preliminary data suggest no substantial decrease in vaccine effectiveness. Growth advantage is likely mostly due to immune evasion properties, rather than changes to intrinsic transmissibility.</p> <p><i>Laboratory data:</i> BA.5 has moderate drop in neutralising antibodies compared to BA.1 and BA.2, and lower protection conferred from vaccination with 3 doses. Less of an impact was associated with 'hybrid' protection, e.g., by 'breakthrough' infections after vaccination.[37-39]</p>



			<i>Reinfection:</i> Limited evidence on the rates of reinfection in New Zealand or internationally, including after prior Omicron variant infection. Prior infection with BA.1 or BA.2 provides some protection against BA.5; prior infection with non-Omicron variants is lower.[40-42]
Vaccine Effectiveness	Low	Low/ Moderate	<p><i>Vaccine effectiveness (VE) relative to BA.2:</i> Early data suggest there no indicators of a large change in VE against symptomatic infection from BA.2 to BA.5.[40, 43]. Booster vaccination reported to be associated with a lower risk reduction against BA.5 for hospitalisation (77%) and death (88%) compared to the risk reduction for BA.2 of 92% and 94% respectively. [44]</p> <p><i>Vaccine effectiveness (VE):</i> Three doses of an mRNA vaccine confer a VE against infection for BA.5 that is initially high (~90%) but diminishes over time to levels unlikely to prevent infection >150 days post-vaccination. [9] There is evidence of a decrease in VE against hospitalisation as time elapses since third dose of a mRNA vaccine, however a fourth dose may restore this. [3, 9] VE against severe disease at more than 120 days appears to be half that at less than 120 days. [3]</p>
Severity	Possible increase in risk of hospitalisation	Low/ Moderate	Evidence regarding the severity of BA.5/BA.4 compared to BA.2 has been mixed. [20] Some studies have found no clear indication of a change in severity whilst at least one study suggested an increased risk of hospitalisation with BA.5 infections compared with BA.2. [20]
Therapeutics	Low	Moderate	One <i>in vitro</i> study shows increased resistance to Evusheld compared to BA.2, [45] whilst another shows it retains activity. [46] Real-world evidence has indicated that Evusheld, when given to vaccinated people, provides an increased protection against symptomatic and severe COVID-19 compared to booster vaccination alone. [47]
Testing	Insufficient Data	Insufficient data	
Overall Assessment			There is an increase in overall risk from the previous predominant variant, BA.2. BA.5 is more transmissible compared to BA.2. BA.5 produced a wave of cases in New Zealand but is now making up a declining proportion of sequenced cases.



**The 'Overall risk assessment' is presented in comparison to the prior or current predominant variant, in this case BA.2. 'Increased risk' indicates the assessed variant as worse than the previous predominant variant 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 predominant variant.*

***'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.*

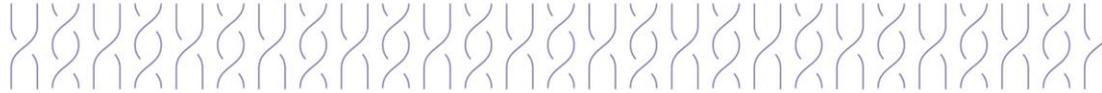


Public Health Risk assessment for BA.2.75

Updated: 16 November 2022

BA.2.75 has 8 key mutations from BA.2: 147E, 152R, 157L, 210V, 257S, 339H, 446S, 460K. [35]

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased Risk	Moderate	<p>Evidence of a growth advantage compared to BA.5.</p> <p>Prevalence in New Zealand is increasing gradually.</p> <p>There is evidence that BA.2.75 has a growth advantage against BA.4/5 in some countries (India, Austria, Singapore).</p> <p>BA.2.75 (and its descendant sub-lineages) are making up an increasing proportion of sequenced cases in New Zealand.[6] In the fortnight ending 11 November 2022 it made up 13% of sequenced cases and 11% of isolates from hospital cases.[6]</p>
Transmissibility	Insufficient data	Insufficient data	There is no direct data on intrinsic transmissibility and there is no current ability to measure this directly from surveillance data.
Immune evasion	No change in risk	Low	<p>No evidence of increased immune evasion.</p> <p>Mutations suggest that BA.2.75 may have immune evasion potential. However, there is 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 neutralise antibodies produced after vaccination and BA.2 infection, compared to BA.4 or BA.5. [48-</p>



			52] Potentially higher 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.
Severity	Insufficient data	Insufficient data	No evidence of a change in severity compared to BA.5 No formal evaluations of BA.2.75 severity are available. Lab and animal studies suggest mixed results for binding compared to BA.5, [52] but overall pathogenicity similar to BA.5. [53] Some <i>in vitro</i> evidence to suggest an increases in cell-cell fusion and ability to infect lower airways compared to BA.2 which could alter pathogenicity. [54]
Therapeutics	Insufficient data	Insufficient data	
Testing	Insufficient data	Insufficient data	
Overall Assessment	No change in risk		

*The 'Overall risk assessment' is presented in comparison to the prior or current predominant variant, in this case BA.5 'Increased risk' indicates the assessed variant as worse than the previous predominant variant 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 predominant variant.

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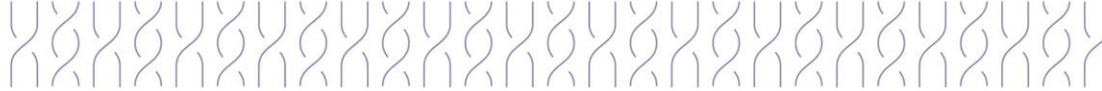


Public Health Risk assessment for BA.4.6

Updated: 02 November 2022

BA.4.6 has an identical spike to BA.5. However, BA.4.6 has an additional mutation at R346T. [35]

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Low	<p>Evidence of a growth advantage compared to BA.4/5.</p> <p>BA4.6 has made up a relatively stable proportion of sequenced isolates (from wastewater and cases) in New Zealand since September 2022.[6] In the fortnight ending 11 November 2022 it made up 3% of all sequenced cases and less than 3% of isolates from hospital cases.[6]</p> <p>BA.4.6 variant has an estimated growth advantage of 4.2% per week (95% Credible Interval: 3.6 – 4.9) compared to BA.5 in the UK (at 20 October 2022). [1]</p>
Transmissibility	Insufficient data	Insufficient data	
Immune evasion	No change in risk	Low	Early data shows that BA.4.6 has greater immune escape from vaccine serum than BA.5, showing on average 2.4 to 2.6-fold decrease in antibody neutralisation. [55]
Severity	Insufficient data	Insufficient data	
Therapeutics	Increased risk	Low	Some indication that Evusheld is less effective for this variant. [55]



Testing	Insufficient Data	Insufficient Data	
Overall Assessment	No change in risk		

**The 'Overall risk assessment' is presented in comparison to the prior or current predominant variant, in this case BA.5. 'Increased risk' indicates the assessed variant as worse than the previous predominant variant 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 predominant variant.*

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Public Health Risk assessment for BQ.1.1

Updated: 16 November 2022

BQ.1.1 is related to BA.5.3 but with Spike protein mutations 444T, 460K, 346T [35]

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Moderate	<p>Evidence of a growth advantage compared to BA.5. [1, 56, 57]</p> <p>BQ.1.1 variant has an estimated growth advantage of 63% per week (95% Credible Interval: 59 – 68) compared to BA.5 in the UK (at 20 October 2022). [1]</p> <p>Currently present in New Zealand and is growing relative to BA.5. [6] In the fortnight ending 11 November 2022 it made up 10% of sequenced cases and 5% of isolates from hospital cases.[6]</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. [25]</p>
Immune evasion	Increased risk	Moderate	<p>Evidence of increased immune evasion.</p> <p>More resistant to neutralisation from sera of vaccinated and breakthrough infected individuals. [25]</p> <p>At least 2 small studies show that mRNA bivalent BA.4/5 vaccine produces robust neutralising activity against BQ.1.1 compared to monovalent wild type vaccine. [17, 19]</p>
Severity	Insufficient data	Insufficient data	<p>No evidence of a change in severity compared to BA.5</p> <p>Evidence from a surge of cases of this variant in France suggests it is not causing increased rates of hospitalisations and deaths.[2]</p>



Therapeutics	Increased risk	Low	One <i>in vitro</i> study showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. [25]
Testing	Insufficient data	Insufficient data	Evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), [26-30] but it is uncertain how this will affect sensitivity specifically for BQ.1.1
Overall Assessment	There is an increase in overall risk from the previous predominant variant, BA.5. (Moderate confidence) BQ.1.1 is increasing in frequency overseas and appears to be more transmissible and immune evasive.		

**The 'Overall risk assessment' is presented in comparison to the prior or current predominant variant, in this case BA.5. 'Increased risk' indicates the assessed variant as worse than the previous predominant variant 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 predominant variant.*

***'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.*

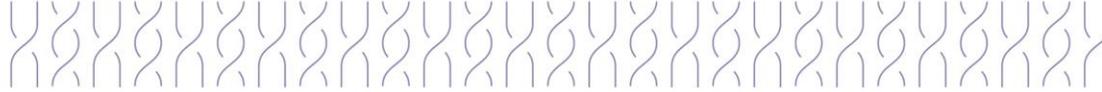


Public Health Risk assessment for XBB

Updated: 16 November 2022

XBB is a recombinant virus (related to BA.2 and BJ.1) with additional spike protein mutations 364T, 445P, 446S and 490V. [35]

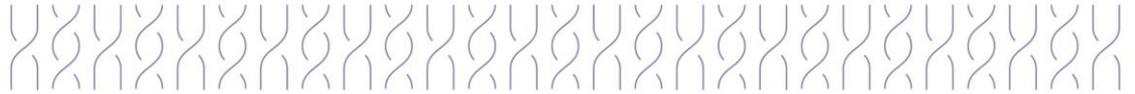
	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Low	<p>Evidence of a growth advantage compared to BA.5</p> <p>Cases are increasing in Singapore against a background of BA.5.</p> <p>Currently present in New Zealand and is growing. [6] In the fortnight ending 11 November 2022 it made up 3% of all sequenced cases and 2% of isolates from hospital cases.[6]</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 XBB compared to prior Omicron variants which may affect transmissibility/infectivity. [25]</p>
Immune evasion	Increased risk	Moderate	<p>Evidence of increased immune evasion.</p> <p>More resistant to neutralisation from sera of vaccinated and breakthrough infected individuals. [25]</p>
Severity	Insufficient data	Insufficient data	<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. [33]</p>
Therapeutics	Increased risk	Low	<p>One <i>in vitro</i> study showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. [25]</p>



Testing	Insufficient data	Insufficient data	Evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant (varies by device), [26-30] but it is uncertain how this will affect sensitivity specifically for XBB.
Overall Assessment	No change in risk		

**The 'Overall risk assessment' is presented in comparison to the prior or current predominant variant, in this case BA.5. 'Increased risk' indicates the assessed variant as worse than the previous predominant variant 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 predominant variant.*

***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: 17 November 2022

In the second half of 2022, many new Omicron sub-variants have been reported. These variants demonstrate convergent evolution which is a process whereby variants from different lineages accumulate similar mutations. For example, the 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 variants under monitoring (VUM). The location of these mutations might produce a significant effect on neutralising activity. [58, 59]

For many BA.2.75 sub lineages, mutations on N-Terminal domain (NTD) can cause reduction in neutralisation titres. [25]

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.

XBC

- XBC is a recombinant lineage that combines sequences from the Delta and Omicron variants.[6]
- In the fortnight ending 11 November 2022, eight cases caused by XBC have been detected in New Zealand.[6] These have been from non-hospitalised cases. [6]
- The XBC lineage has been present in Australia and South East Asia for some time, with no indication of increased disease severity (albeit this is based on small case numbers). [6]

BA.2.75.2

- BA.2.75.2 is a BA.2.75 sub-lineage with mutations at 346T, 486S, and 1199.[35]
- These mutations may allow additional escape from neutralising antibodies with serum from blood donors in one study being five-fold less effective at neutralising BA.2.75.2 compared to BA.5. [60]
- BA.2.75.2 variant has an estimated growth advantage of 37% per week (95% Credible Interval: 33 – 42) compared to BA.5 in the UK (at 20 October 2022). [1]
- BA.2.75.2 may be (from one study) resistant to neutralisation by Evusheld (tixagevimab and cilgavimab), but has remained sensitive to bebtelovimab. [60]
- BM.4.1.1BM.4.1.1 is a BA.2.75 sub-lineage with R346T, F486S, and R346T mutations in the spike protein.
- First emerged in India in early October ([link](#)). As of 13 November 2022, it makes up 2.5% of all sequenced cases in India. ([link](#))
- The mutational profile of the spike protein for BM.4.1.1 is predicted to likely render Evusheld ineffective by authors of a preprint paper. [25]



CH.1.1

- CH.1.1 is derived from BM.4.1.1 (and consequently BA.2.75) and is defined by the S:L452R mutation.[7]
- In New Zealand, the BA.2.75 and sub-lineages accounted for 13% of sequenced for the fortnight ending 11 November 2022. [6] The growth in BA.2.75 October and November may be driven by an increase of CH.1.1 (46% of BA.2.75 cases in week ending 11 November).[6]
- The additional mutations are predicted to potentially render bebtelovimab ineffective (in addition to Evusheld) by authors of a preprint paper [25]

BR.2.1

- BA.2.75 with 3 extra spike mutations (L452R, F486I, R346T (sometimes reversed). [4]
- The majority of BR.2 sequences reported internationally to early November 2022 have originated from New South Wales (NSW) in Australia. [5] Also in other countries including Japan.[7]
- Marked increase in NSW of the proportion of community samples that are BA.2.75 (mostly BR.2 sub-lineage): week ending 15th October 7.7%, week ending 29th October 20.1% [5]

BN.1

- BN.1 is a descendant of BA.2.75.5 (and consequently BA.2.75), with S:R346T and S:490S mutations. [7]
- As of 11 November 2022, BN.1.X accounts for 4.3% of USA national cases.[8] The growth advantage and characteristics of disease it causes (e.g. severity) are not yet defined.
- BA.2.75.5 variant has an estimated growth advantage of 45% per week (95% Credible Interval: 40 – 50) compared to BA.5 in the UK (at 20 October 2022), but an estimate specific for BN.1 is not yet available. [1]

CK.2.1.1

- Sub-lineage of BA.5, defined by S:S255F mutation
- Some sources note transmission advantage, but not yet confirmed by official sources.



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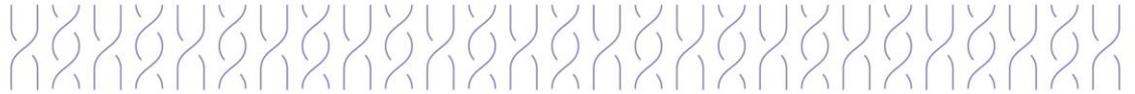
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