

Date: 20 December 2022

SARS-CoV-2 Variants of Concern Update

Executive Summary

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

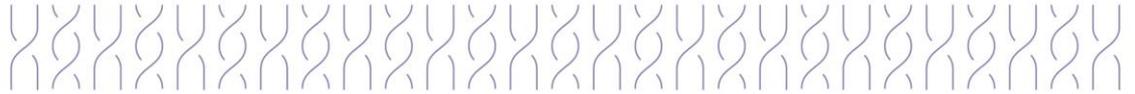
Section updated: 15 December 2022

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:

- BA.5 is no longer the predominant variant in New Zealand and made up 33% of all sequenced cases (and 38% of hospital case isolates) in the fortnight ending 9 December 2022. (1) BA.4/5 now accounts for less than 20% of sequences detected in wastewater but remains widespread over wastewater sampling sites across New Zealand. (1)
- The current increase in incidence of SARS-CoV-2 infections in New Zealand is not driven by a single variant but is consists of a number of Omicron subvariants with increased immune evasion characteristics. In the week ending 9 December 2022, BA.2.75 and associated sub-lineages represented the largest group in New Zealand, making up 39% of all sequenced cases (and 34% of sequenced hospitalised cases). (1)
- The recent growth of BA.2.75 in recent weeks has been driven by several distinct descendants of the original BA.2.75 lineage, including CH.1.1, BN, BR.2. (1) However, at present it is not clear if BQ.1.1, XBC or newly emerging lineages will be displaced or be able to co-circulate with BA.2.75 sub-lineages.
- 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. (2-5)
- New Signal: BF.7
 - BF.7 is a sub-lineage of BA.5 and has a mutation on the spike protein, R346T, which may confer increased immune evasion properties compared to BA.5. (7)
 - BF.7 is an emerging variant in China. (6) It is not currently considered to be of particular concern since there is no evidence of an increase in severity or transmissibility over variants currently circulating in New Zealand. However, BF.7 is being monitored as it is potentially the dominant variant in China's current wave of infection. It currently appears to be growing rapidly in China, but this is in a population with relative lack of acquired immunity. BF.7 is appearing to be remaining steady elsewhere. For example, in the US it was estimated to account for 5.7% of infections up to 10 December 2022, down from 6.6% the week prior.



Section 1 Key Omicron information

Circulating variants across Aotearoa New Zealand

Section updated: 15 December 2022

The Institute of Environmental Science and Research (ESR) COVID-19 Genomics Insights (CGI) report was last produced on 15 December 2022, with data from the period of 26 November – 9 December 2022. (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 ~2.0% of all cases were sequenced in this fortnight, and only variants with a frequency above 1% are shown). (1)

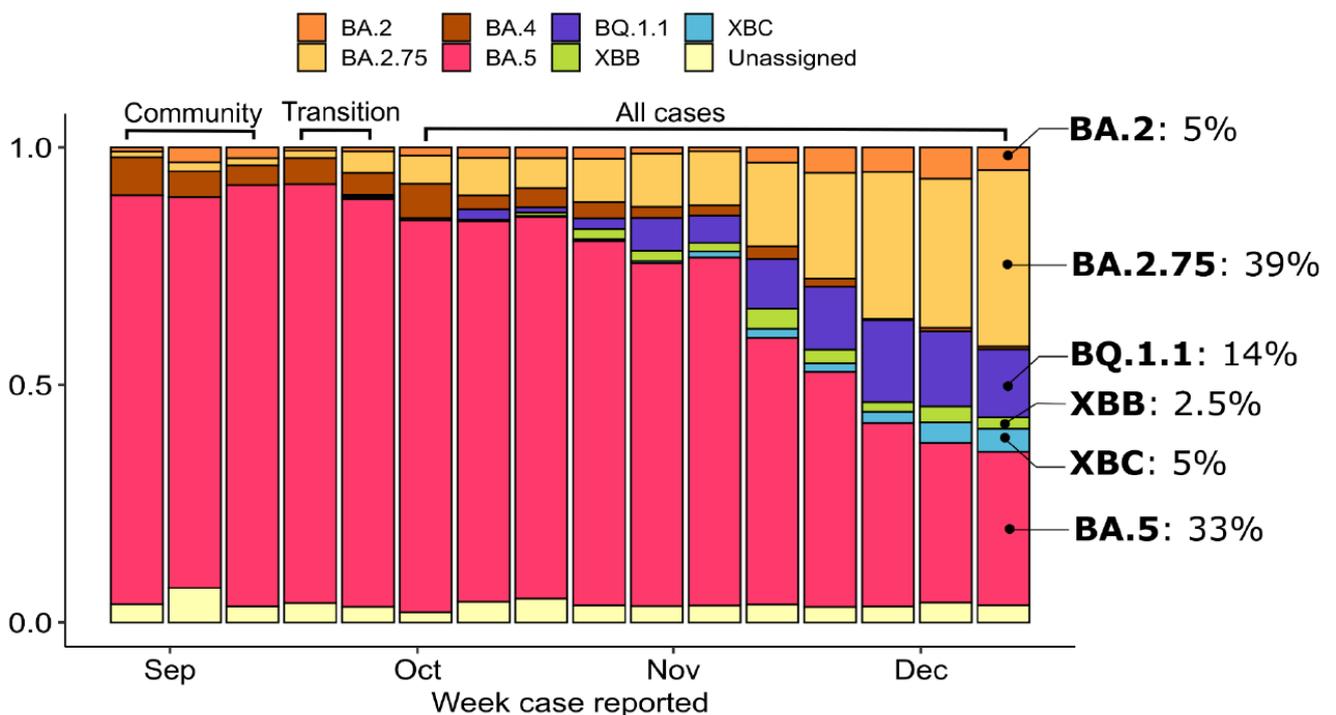
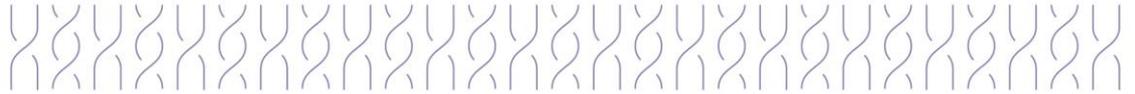


Figure 1: Frequency of SARS-CoV-2 variants in New Zealand each week. Only variants with a frequency above 1% are shown. Data is subject to change as samples may still be added to the most recent two-week period. Only data from community cases were used until September 2022, while in the “transition”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

The recent growth of BA.2.75 in recent weeks is driven by several distinct descendants of the original BA.2.75 lineage, including CH.1.1, BN, BR.2. (1) These fast-growing lineages mean that BA.2.75 may quickly become the dominant subvariant in Aotearoa. However, at present it is not clear if BQ.1.1, XBC or newly emerging lineages will be displaced or be able to co-circulate with BA.2.75 sub-lineages. (1)

Genomic surveillance has identified a set of CH.1.1 genomes containing an additional spike protein



mutation (S255P). (1) This mutation is present in approximately 10% of CH.1.1 genomes and is very rare in publicly available genomes from overseas, suggesting the mutation may have arisen in New Zealand. (1)

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). Wastewater surveillance from 28 November – 11 December 2022 has seen similar patterns in variants to that seen in cases. BA.2.75 sequences now are the dominant variants detected in wastewater (making up ~62% and ~53% of isolates in the first and second weeks of the reporting period, respectively) and are now being detected at all sentinel sites. However, detections of BQ.1.1 are trending upward (~13% and ~22% in the two weeks), and BQ.1.1 is being detected at more sentinel sites. BA.4/5 now accounts for less than 20% of sequences detected in wastewater but remains widespread over sites. (1)

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

Current overall variant risk status

Section updated: 15 December 2022

Subvariants detected in cases in New Zealand such as BQ.1.1, BA.2.75 sub-lineages (including CH.1.1), XBB and XBC have demonstrated substantial immune evasion in laboratory testing compared to prior Omicron variants. Cases of these subvariants are likely to increase (as a proportion of cases) in the coming weeks. The current increase in incidence of SARS-CoV-2 infections is not driven by a single variant but it consists of a number of Omicron subvariants with increased immune evasion characteristics.

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

Features of Omicron

Section updated: 15 December 2022

Growth advantage/transmissibility

Growth advantage is becoming 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.

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

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. (9) However, this diminished to levels below 20% against all subvariants after 5 months. (9)

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. (9)

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

A single study from the USA has estimated the VE against symptomatic infection of bivalent Omicron BA.4/5 mRNA vaccines (as a third, fourth or fifth dose). (10) Absolute VE (that is, 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. (10) 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. The study did not have a comparison group receiving the dose as an original formulation monovalent vaccine, so these data do not show whether the effect of the BA.4/5 dose is superior to the original formulation. It should be noted that this study was conducted in the USA from mid-September to mid-November 2022 so in a setting with frequent prior infection (i.e., these estimates show additional protection provided by vaccination in a population that has experienced previous waves of infection), with numerous circulating Omicron sub-lineages.

VE against severe disease

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. (11) **Two doses also provide high VE against death for adolescents and children, but data about duration of this effect in young people are limited.** (12)

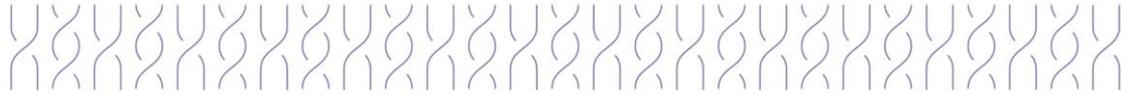
Three doses: Moderna vaccine shows VE against hospitalisation (time since vaccination unclear) was 97.5%, 82.0%, and 72.4% for BA.1, BA.2 and BA.4/5 respectively. (9) **During a BA.4/5 dominant period, mRNA vaccines show VE against hospitalisation or urgent care visit was 68% (95% CI: 50 - 80) at 7-119 days post-vaccination, and 36% (95% CI: 29 – 42 at >120 days post-vaccination.**(11)

Four doses: Moderna vaccine shows VE against hospitalisation (time since vaccination unclear) for BA.4/BA.5 was 88.5%. (9) **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.** (11)

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. (13)

- 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).

Immunological data

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. (14-17) 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. (18)

Immunological data suggest hybrid immunity after monovalent vaccine and (Delta or Omicron) infection is likely to be robust. (19)

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). (20)

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

Immunogenicity data for BA.4/5 bivalent vaccines are mixed. Some studies have shown little difference between bivalent vaccine and monovalent WT (original formulation) vaccines, (21-23) while others suggest BA.4/5 bivalent vaccines elicit greater neutralisation titres against Omicron variants than the monovalent WT vaccines. (24-27)

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

Bivalent vaccines for children

There are no publicly available safety, immunogenicity or efficacy data (at 15 December 2022) for bivalent vaccines for 5- to 11-year-olds. 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. (28, 29)

Immunological response from vaccination plus prior Omicron infection

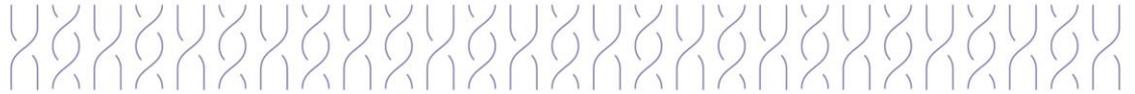
There is some evidence to suggest that an individual's first exposure to a variant (either through infection or vaccination) shapes the immune response to future infections (how well the antibody produced neutralises a variant not previously encountered). (30, 31)

Safety of second booster

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.(32)

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. (33-35) 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. (36)

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. (37)

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. (34, 38)

A study published in November 2022 reported an increased risk of death, hospitalisation, and sequelae with reinfection compared to no reinfection. (39) 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

Monoclonal antibody treatments: laboratory-based studies suggest that monoclonal antibody treatments (such as Evusheld) are ineffective against some emerging variants. (40-43) **The proportion of variants that Evusheld cannot neutralise is greater than 50%. (1)** Clinical effectiveness data for Evusheld (Aotearoa New Zealand's most used monoclonal antibody treatment) are available for a period of BA.1 predominance, (44) 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. (2-5).

Detection/testing

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. (45-49) 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. (45-49) Emerging evidence also highlights the need for techniques such as serial testing to maximise sensitivity against new Omicron variants of concern. (47, 49)

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: 15 December 2022

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

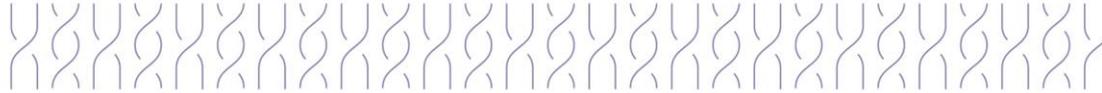
1. World Health Organization (WHO) Weekly epidemiological update on COVID-19: **14 December 2022 (50)**
2. UK Health Security Agency: SARS-CoV-2 Variants of Concern and Variants under Investigation in England, Technical Briefing 48, 25 November 2022. (8)

World Health Organization update

The WHO Weekly Epidemiology Update on 14 December 2022 reported the status of circulating variants compared to the previous week. (50) Sequences submitted globally continue to show similar trends to recent weeks with BA.5 descendent lineages remaining dominant (73.7% of sequences) followed by BA.2 descendent lineages (10.4%). BA.4 descendent lineages continued to decline in prevalence (2%). There was a rise in BQ.1 sequences to 33.9% of sequences, and XBB sequences also increased, rising to 3.38%.

UK Health Security Agency update

The UK Health Security Agency update on 25 November 2022 reported estimated weekly growth rates for variants in the UK (relative to BA.5.2 at 9 November 2022). (8) Details are reported in section "Growth advantage/transmissibility"



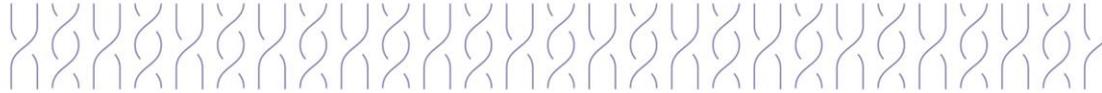
Section 2: Summary of Variants

Public Health Risk Assessment BA.5

Updated: 15 December 2022. *This section will be substantially revised in the next update*

BA.5 has key spike mutations at positions: L452R, F486V, and R493Q. (51) 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>BA.5 is no longer the predominant variant in New Zealand and now makes up 33% of all sequenced cases for the week ending 9 December 2022. In the fortnight to the week ending 9 December 2022, BA.5 made up 38% of hospital isolates. (1)</p>
Transmissibility	Insufficient data	Insufficient data	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. (52)
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 three doses. Less of an impact was associated with 'hybrid' protection, e.g., by 'breakthrough' infections after vaccination.(53-55)</p> <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. (56-58)</p>



Vaccine Effectiveness	Low	Low/ Moderate	<p><i>Vaccine effectiveness (VE) relative to BA.2:</i> Early data suggest there are no indicators of a large change in VE against symptomatic infection from BA.2 to BA.5. (56, 59) Booster vaccination is 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. (60)</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. (9, 11) VE against severe disease at more than 120 days appears to be half that at less than 120 days. (11)</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. (33) Some studies 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. (33)
Therapeutics	Low	Moderate	One <i>in vitro</i> study shows increased resistance to Evusheld compared to BA.2, (43) whilst another shows it retains activity. (61) 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. (44)
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.

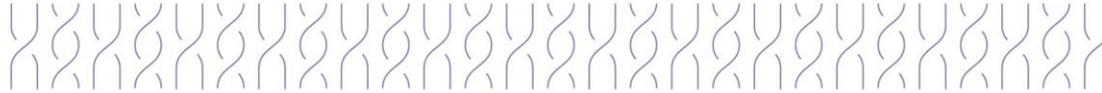


Public Health Risk assessment for BA.2.75

Updated: 15 December 2022

BA.2.75 has 8 key mutations from BA.2: 147E, 152R, 157L, 210V, 257S, 339H, 446S, 460K. (51)

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased Risk	Moderate	<p>Evidence of a growth advantage compared to BA.5. 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). BA.2.75 and sub-lineages (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). (8)</p> <p>In the fortnight ending 9 December 2022, BA.2.75 (and associated sub-lineages) made up 39% of all sequenced cases in New Zealand (more than any other group of associated variants), and 34% of sequenced hospital cases.(1)</p>
Transmissibility	Insufficient data	Insufficient data	There are 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>There is evidence of increased immune evasion by BA.2.75 sub-lineages in the form of increased representation in reinfection cases.</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. (62-66) 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.</p> <p>BA.2.75 growth in New Zealand has been driven by several descendants of the original lineage, this includes CH1.1 BR.2 and BN.(1) During the fortnight ending 9 December, CH.1.1 was strongly over-represented in reinfection cases, accounting for 29% of reinfection cases.(1)</p>
Severity	Insufficient data	Insufficient data	<p>No evidence of a change in severity compared to BA.5</p> <p>Few formal evaluations of BA.2.75 severity are available. An early assessment of the severity of BA.2 sub-lineages 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. (67) Lab and animal studies suggest mixed results for binding compared to BA.5, (66) but overall pathogenicity similar to BA.5. (68) 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. (69)</p>
Therapeutics	Insufficient data	Insufficient data	
Testing	Insufficient data	Insufficient data	
Overall Assessment	<p>There is an increase in overall risk from the previous predominant variant, BA.5. (Moderate confidence)</p> <p>BA.2.75 and associated sub-lineages are increasing in frequency in New Zealand and appear to be more transmissible and immune evasive.</p>		

*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 BA.4.6

Updated: 15 December 2022

BA.4.6 has an identical spike to BA.5. However, BA.4.6 has an additional mutation at R346T. (51)

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Low	Evidence of a growth advantage compared to BA.4/5. BA.4.6 has an estimated growth advantage of 4.4% per week (95% Credible Interval: 3.1 to 5.7%) compared to BA.5.2 in the UK (at 9 November 2022). (8) It has made up a relatively stable proportion of sequenced isolates (from wastewater and cases) in New Zealand since September 2022. (1) In the fortnight ending 9 December 2022, BA.4 made up less than 1% of all sequenced cases and less than 1% of isolates from hospital cases. (1)
Transmissibility	Insufficient data	Insufficient data	
Immune evasion	No change in risk	Low	Early data show 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. (70)
Severity	Insufficient data	Insufficient data	
Therapeutics	Increased risk	Low	Some indication that Evusheld is less effective for this variant. (70)
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.

**'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 BQ.1.1

Updated: 15 December 2022

BQ.1.1 is related to BA.5.3 but with Spike protein mutations 444T, 460K, 346T (51)

	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Moderate	<p>Evidence of a growth advantage compared to BA.5. (71-73)</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).(8)</p> <p>Currently present in New Zealand. <i>In the week ending 9 December 2022, BQ.1.1 made up 14% of all sequenced cases. In the fortnight ending 9 December 2022 it made up 17% of sequenced isolates from hospital cases. (1)</i></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. (40)</p>
Immune evasion	Increased risk	Moderate	<p>Evidence of increased immune evasion.</p> <p>More resistant to neutralisation from sera of vaccinated and infected individuals. (40, 74) 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. (24, 26, 74)</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. (75)</p>



Therapeutics	Increased risk	Low	<i>In vitro</i> studies showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. (40, 74)
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), (45-49) but it is uncertain how this will affect sensitivity specifically for BQ.1.1
Overall Assessment	<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.</p>		

*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.

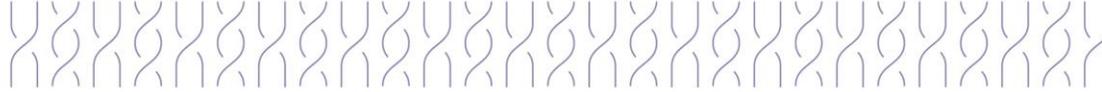


Public Health Risk assessment for XBB

Updated: 15 December 2022

XBB is a recombinant virus (related to BA.2 and BJ.1) with additional spike protein mutations 364T, 445P, 446S and 490V. (51)

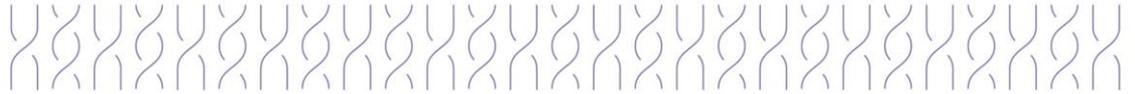
	Overall risk assessment*	Confidence level **	Assessment and rationale
Overall growth advantage	Increased risk	Low	<p>Evidence of a growth advantage compared to BA.5</p> <p>XBB has an estimated growth advantage of 56.9% per week (95% Credible Interval: 46.9 to 67.2%) compared to BA.5.2 in the UK (at 9 November 2022).(8)</p> <p>Currently present in New Zealand and is continuing to fluctuate between 1-4% of sequenced cases. In the week ending 9 December 2022, it made up 2.5% of all sequenced cases and 2% of isolates from hospital cases. (1)</p>
Transmissibility	Insufficient data	Insufficient data	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. (40)
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. (40, 74)</p>
Severity	Insufficient data	Insufficient data	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. (76)
Therapeutics	Increased risk	Low	<i>In vitro</i> studies showed loss of efficacy of all currently approved clinical monoclonal antibody therapies including Evusheld and Bebtelovimab. (40, 74)



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), (45-49) 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: 15 December 2022. *This section will be substantially revised in the next update*

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 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 variants under monitoring (VUM). The location of these mutations might produce a significant effect on neutralising activity. (77, 78)

For many BA.2.75 sub-lineages, mutations on N-terminal domain (NTD) can cause reduction in neutralisation titres. (40)

In Australia and New Zealand, there is currently no single variant driving case numbers. (79)

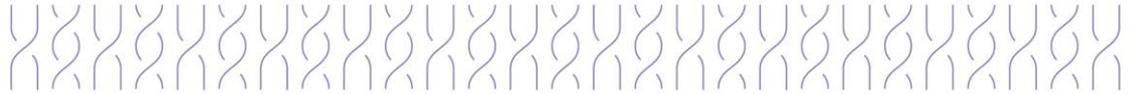
Details of BA.5, BA.2.75, BQ.1.1, BA.4.6, and XBB can be found above in the risk assessment section. Short summaries are provided here of newer variants which are not covered in the risk assessment section but are of heightened concern because of their growth rate in New Zealand or internationally, or 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.

BF.7

- BF.7 is a sub-lineage of BA.5 and has a mutation on the spike protein, R346T, which may confer increased immune evasion properties compared to BA.5. (7)
- BF.7 is an emerging variant in China. (6) It is not currently considered to be of particular concern (no evidence of an increase in severity or transmissibility over variants currently circulating in New Zealand) but is being monitored as it is potentially the dominant variant in China's current wave of infection. It currently appears to be growing rapidly in China, but this is in a population with relative lack of acquired immunity. BF.7 is appearing to be remaining steady elsewhere. For example, in the US it was estimated to account for 5.7% of infections up to 10 December 2022, down from 6.6% the week prior.
- BF.7 has been detected in several other countries around the world including India, US, UK and several European countries such as Belgium, Germany, France and Denmark.

XBC

- XBC is a recombinant lineage that combines sequences from the Delta and Omicron variants. (80) Some studies suggest that chronic infections may be contributing to the emergence of such recombinant variant lineages. (81)
- In the fortnight ending 9 December 2022, XBC made up 5% of all sequenced cases in New Zealand and 4% of sequenced hospitalised cases. (1)
- XBC appears to be most common in the Philippines and Brunei, circulating at a prevalence of around 5%. Sub-lineage XBC.1 (S:L452M) has been rising in Australia.(82)
- 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). (80)



XBF

- Sub-lineage from a BA.5.2.3 and CJ.1 (a BA.2.75 sub-lineage) recombinant. Spike identical to CJ.1, additional mutations (from BA.2.75) S:486P, S:R346T, S:F490S. (82)
- Growing in Australia and Denmark. (82) Appears to be growing less rapidly in South Asia than CH.1.1 (another BA.2.75 sub-lineage),(82) but epidemiology could be different in New Zealand.
- No data have yet emerged about the severity of XBF disease.

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. (83)
- In the fortnight ending 9 December 2022, BA.2.75 (and associated sub-lineages) made up 39% of all sequenced cases in New Zealand (more than any other group of associated variants), and 34% of sequenced hospital cases. (1)
- The growth of BA.2.75 sub-lineages in New Zealand in recent weeks has been driven by several distinct descendants including CH.1.1, BN (and sub-lineages), and BR.2 (and sub-lineages). (1)
- During the fortnight ending 9 December 2022, CH.1.1 was strongly over-represented in reinfection cases in New Zealand, accounting for 29% of reinfection cases (and only 14% of first infections). (1)
- Approximately 10% of sequenced CH.1.1 genomes sequenced in New Zealand have an additional spike mutation (S255P). This is very rarely seen in publicly available genomes and may have arisen in Aotearoa New Zealand. (1)
- The additional mutations have been reported in a preprint to be likely to reduce neutralising ability of monoclonal antibodies, including Evusheld (40)

BR.2.1

- BA.2.75 with three extra spike mutations (L452R, F486I, R346T (sometimes reversed)). (84)
- The growth of BA.2.75 sub-lineages in New Zealand in recent weeks has been driven by several distinct descendants including CH.1.1, BN (and sub-lineages), and BR.2 (and sub-lineages). (1)
- The majority of BR.2 sequences reported internationally to early November 2022 have originated from New South Wales (NSW) in Australia. (85) Also in other countries including Japan. Marked increase in NSW of the proportion of BA.2.75 (mostly BR.2 sub-lineage) in community samples from 7.7% in week ending 15 October to 20.1% in week ending 29 October 2022. (85)

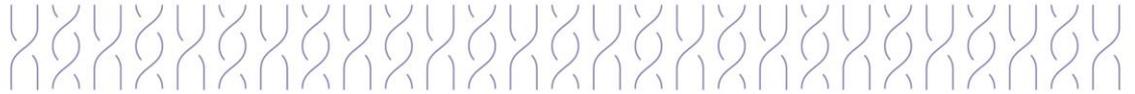
BN.1

- BN.1 is a descendant of BA.2.75.5 (and consequently BA.2.75), with S:R346T and S:490S mutations. (83) BN.1 is a descendant of BA.2.75.5 (and consequently BA.2.75), with S:R346T and S:490S mutations. (83)
- The growth of BA.2.75 sub-lineages in New Zealand in recent weeks has been driven by several distinct descendants including CH.1.1, BN (and sub-lineages), and BR.2 (and sub-lineages). (1)
- Appears to be growing less rapidly in South Asia than CH.1.1 (another BA.2.75 sub-lineage), (82) but epidemiology could be different in New Zealand.



BA.2.75.2

- BA.2.75.2 is a BA.2.75 sub-lineage with mutations at 346T, 486S, and 1199. (51) These mutations may allow additional escape from neutralising antibodies (in one study, five-fold less effective at neutralising BA.2.75.2 compared to BA.5). (86)
- BA.2.75.2 had an estimated growth advantage of 37% per week (95% Credible Interval: 33 – 42) compared to BA.5 in the UK (at 20 October 2022). (73)
- BA.2.75.2 may be resistant to neutralisation by Evusheld (tixagevimab and cilgavimab).(40, 86)

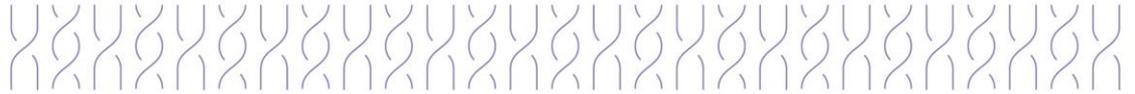


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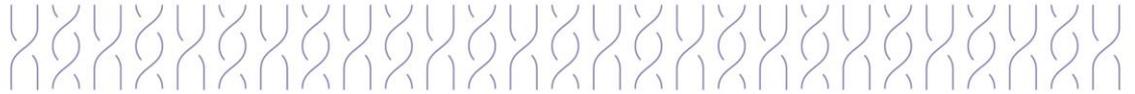
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