



Date: 20 October 2022

SARS-CoV-2 Variants of Concern Update

Circulating variants across Aotearoa New Zealand:

The Institute of Environmental Science and Research (ESR) reports there are four (sub)variants (BA.2.75.2, BQ.1, BQ.1.1 and XBB) that combined make up 4% or more of the sequenced community samples in Aotearoa New Zealand in the period of 1 to 14 October.

Note that changes in reporting of border and community cases makes the interpretation of latest trends in the proportion of variants difficult. However, these sequencing results correlate with wastewater variant analysis (with the exception of BQ.1.1 being at a higher proportion in some wastewater catchments).

BA.5	85%
BA.4	2%
BA.4.6	6%
BA.2	3%
BA.2.75	4%

For further information regarding the genomic report produced by ESR, please refer to the following. ([link](#))

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

Current overall variant risk status:

As of 14th October 2022, both XBB and BQ.1.1 have been detected in New Zealand. Due to both variants demonstrating substantial immune evasion compared to prior Omicron variants in lab tests, cases are likely to increase in the coming weeks.

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



Executive Summary

Section updated: 20 October 2022

Over the last month, a large number of new omicron variants has been reported over a relatively short period of time. These variants demonstrate convergence 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.

The European Centre for Disease Control (ECDC) is now reporting variants based on the identification of key mutations which have demonstrated important characteristics, in particular ACE2 binding affinity and immune escape from current vaccines or infection with previous variants. The change from tracking variants to monitoring mutations is significant and indicates a possible change in the pandemic to a phase of multiple circulating variants.

The assessment of severity through the analysis of mutations has not yet progressed to the point of clinical utility. The identification of increased severity for any specific mutation remains difficult to assess, especially in the short term.

Omicron remains the dominant SARS-CoV-2 variant globally. However, antigenic difference between circulating variants is now very wide, with greater differences between Omicron variants than between previously circulating named variants of concern (Alpha, Beta, Gamma and Delta).

BA.5 is the dominant variant in New Zealand with a slowly falling prevalence as other variants are replacing BA.5. There have been some methodological changes in reporting and genome sequencing, but the replacement of BA.5 by a range of other variants is almost certain and is being reported in multiple regions. In this respect, it is important to note that during periods of rapidly changing circulating variants, the time delays between the identification of cases and wastewater detection and reporting of genome sequencing can result in difficulties in interpreting the cause of case number fluctuations.

Currently, it is not possible to identify which of a range of variants will become dominant. While this may appear to hamper the prediction of case numbers and severity, it is clear that the new variants have a similar growth advantage due to immune escape. In addition, the new variants possess many similar mutations and in line with the discussion above, may be treated as a single variant.

New multivalent and Omicron specific vaccines are expected to provide improved protection against a wide range of Omicron variants, especially for hospitalisation. Antivirals continue to be effective at decreasing the severity of disease, but monoclonal antibodies have very little efficacy against the new variants.



Section 1 Key updates

Section updated: 20 October 2022

Growth advantage/transmissibility

BQ.1.X show a substantial growth advantage, but estimates have only been published for UK and are aggregated with other BE.1.1 lineages currently.

- BE.1.1 lineages (including BQ.1/BQ.1.1 sublineages) have an estimated growth advantage of 28.82% per week (95% CrI¹: 26.61 – 31.09) compared to BA.5 in the UK. (1)
- BF.7 variant have an estimated growth advantage of 17.95% per week (95% CrI¹: 16.58 – 19.44) compared to BA.5 in the UK. (1)
- BA.2.75.X lineages have an estimated growth advantage of 18.78% per week (95% CrI¹: 17.10 – 20.52) compared to BA.5 in the UK. (1)

Immune evasion, vaccine effectiveness

XBB and BQ.1.1 both have demonstrated substantial immune evasion in lab tests, compared to prior Omicron variants (i.e. BA.2, BA.5)

- A pre-print evaluating the *in vitro* neutralisation of variants from serum collected from individuals who were triple-vaccinated with CoronaVac and had either had a BA.1, BA.2 or BA.5 infection, or no infection, found that neutralisation titres were significantly lower against XBB and BQ.1.1 compared to BA.2 or BA.5. (2)
 - In those that had a BA.2 breakthrough infection, plasma neutralisation titres were 31-fold lower for XBB and 17-fold lower for BQ.1.1, compared to that of BA.2. (2)
 - In those that had a BA.5 breakthrough infection, plasma neutralisation titres were 19-fold lower for XBB and 6.7-fold lower for BQ.1.1, compared to that of BA.2. (2)

Disease course / Clinical features (symptoms and severity)

Further evidence analysing the spike protein between variants, supports the observation that the Omicron variant tends to be associated with less severe clinical outcomes compared to Delta/non-Omicron variants.

- A pre-print study investigating the role of the spike protein in pathogenicity and immune evasion of SARS-CoV-2, created a recombinant SARS-CoV-2 virus by encoding the spike gene from Omicron BA.1 in the backbone of an ancestral SARS-CoV-2 isolate and compared this to both the naturally occurring ancestral and Omicron BA.1 variants in a mouse infection model. The authors found that although immune escape by Omicron is mediated by mutations in the spike-protein, the viral determinants of pathogenicity are primarily conferred by genes that reside outside the spike gene. (3)

¹ 95% Credible Interval



- A separate study comparing the immune effects of the spike protein from WT and Omicron (BA.1), found that the spike protein from WT activates more pro-inflammatory immune pathways than the spike protein from Omicron and may be associated with the milder symptoms caused by Omicron infection. (4)

Therapeutics effectiveness

One lab study has shown a loss of efficacy for all currently approved monoclonal antibodies against BQ.1.1 and XBB, but there is currently no evidence to suggest these variants have antiviral resistance.

- One pre-print has assessed the neutralising abilities against Omicron variants and reported that all currently approved monoclonal antibody therapies including Evusheld and Bebtelovimab, have markedly reduced potency against the emerging Omicron sublineages BQ.1.1 and XBB in an *in vitro* study. (5) Although this is preliminary data, it indicates that current monoclonal antibody therapies may not be as effective against these variants, which may be significant if either of these variants becomes dominant. BQ.1.1 and XBB have a growth advantage compared to other variants but is not currently a dominant variant in New Zealand, with only three BQ.1.1 cases and one XBB case being detected in the most recent WGS report. (6)
- 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 a decrease in the performance of RATs to detect Omicron variants. However, data are limited.

- Currently there is some emerging evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant. (7, 8) Comparability between studies is limited by difference in study design and objectives. For these reasons it is difficult to compare the results between studies and evidence of reduced sensitivity may not be indicative of device performance.

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 documents

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

- UK Health Security Agency: SARS-CoV-2 Variants of Concern and Variants under Investigation in England, Technical Briefing 46, 7 October 2022 (1)

The UK Health Security Agency SARS-CoV-2 Variants of Concern and Variants under Investigation in England, Technical Briefing 46 on 7 October 2022 (1) reported that:



- A number of new variants have begun to circulate in the United Kingdom (UK) in recent weeks. The development of these additional lineages has been rapid. They have varying Omicron backbones but some convergent receptor-binding domain (RBD) mutations (notably at S:346) which are likely to produce a degree of escape from current immunity in the UK.



Section 2: Summary of Variants

Public Health Risk Assessment BA.5

Note: BA.4 and BA.5 have identical spike protein. Many results for these subvariants are reported as combined results on the basis of characterisation using S Gene Target Failure (SGTF).

Updated: 20 October 2022

	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><i>As at 20 October 2022, BA.5 is the predominant variant in New Zealand.</i></p> <p>BA.5 has a reported growth advantage of 11.2% over the previously dominant variant BA.2. The growth in BA.5 observed in the whole genome sequencing of individual testing is consistent with the growth observed in wastewater. As cases of BA.5 were increasing and displacing BA.2 in May and early June, the estimated growth rate of BA.5 for New Zealand was approximately 9% per day or 7 day doubling time. (9) This is consistent with growth advantages observed internationally.</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 BA.5 compared to prior Omicron variants, and BA.5 may have increased infectivity. (10)</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, but this is subject to revision. 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.(11-13)</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.(14-16)
Vaccine Effectiveness	Low	Low/ Moderate	<i>Vaccine effectiveness (VE):</i> Insufficient data for robust assessment of vaccine effectiveness but early data suggest there no indicators of a large change in VE against symptomatic infection from BA.2 to BA.5.(14, 17). One study has observed a decrease in VE against hospitalisation between BA.2 and BA.5, comparing people who had received the booster (3 dose with prior infection) to unvaccinated (with prior infection). No difference was seen for VE mortality. (18) The current epidemiological data, whilst incomplete, is consistent with the neutralisation findings.
Severity	Possible increase in risk of hospitalisation	Low/ Moderate	Booster vaccination reported to be associated with a lower risk reduction against BA.5 of hospitalisation (77%) and death (88%) compared to the risk reduction for BA.2 of 92% and 94% respectively.
Therapeutics	Low	Moderate	One <i>in vitro</i> study shows increased resistance to Evusheld compared to BA.2, (19) whilst another shows it retains activity. (20) 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. (21)
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 and is the variant associated with the current wave of cases in New Zealand.

*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 (Centaurus)

Updated: 20 October 2022

	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 community cases to 14 October in New Zealand is 4%</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>There are too few samples of BA.2.75 internationally or in New Zealand to determine if the observed growth advantage observed overseas will be replicated in New Zealand. The data requires continued close monitoring. Cases currently remain stable around 4-5% of all variants sequenced.</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 BA.2 infection and vaccination, compared to BA.4 or BA.5. (22-26) Potentially higher receptor binding compared to other Omicron lineages. There are no data on the ability of BA.2.75 to neutralise antibodies produced after BA.5 infection.</p>



Severity	Insufficient data	Insufficient data	No evidence of a change in severity compared to BA.5 Too few cases have been detected internationally or in New Zealand to evaluate severity. Lab and animal studies suggest mixed results for binding compared to BA.5, (26) but overall pathogenicity similar to BA.5. (27)
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.

**'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 (Aeterna)

Updated: 20 October 2022

	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 prevalence has slowly increased in NZ, now accounting for approximately 6% of genomes tested in the two weeks to 14 October.</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. (28)
Severity	Insufficient data	Insufficient data	
Therapeutics	Increased risk	Low	Some indication that Evusheld is less effective for this variant. (28)
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 (Cerberus)

Updated: 20 October 2022

	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) (29)</p> <p>Currently three cases have been detected in New Zealand as of 14 October 2022.</p> <p>Detected in wastewater in New Zealand as of 14 October 2022. (6)</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 BQ.1.1 compared to prior Omicron variants which may affect transmissibility/infectivity. (2)
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. (5)</p>
Severity	Insufficient data	Insufficient data	<p>No evidence of a change in severity compared to BA.5</p> <p>Too few cases have been detected internationally or in New Zealand to evaluate severity.</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. (5)
Testing	Insufficient data	Insufficient data	Currently there is some emerging evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant. (7, 8)



			However, 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 (Gryphon)

Updated: 20 October 2022

	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 one case has been detected in New Zealand as of 14 October 2022. (6)</p> <p>No detection of XBB in wastewater as of 14 October 2022. (6)</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. (2)
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. (5)</p> <p>Singapore reporting reinfections are making up 17-18% of new cases. (30)</p>
Severity	Insufficient data	Insufficient data	No evidence of increased severity, as there is a divergence and weakening of the correlation between the number of cases and new hospitalisations in Singapore. (34)
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. (5)



Testing	Insufficient data	Insufficient data	<p>Currently there is some emerging evidence that suggests a clinically relevant decrease in the performance of RATs for detection of the Omicron variant. (7, 8)</p> <p>However, it is uncertain how this will affect sensitivity specifically for XBB.</p>
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: 20 October 2022

The risk of clinically significant emerging variants is considered to be high, according to the WHO. (31) The WHO has expressed concern in early April, some countries have significantly reduced SARS-CoV-2 testing. They caution that unless robust surveillance systems are retained, countries may lose the ability to accurately interpret epidemiological trends, implement the appropriate measures necessary to reduce transmission and monitor and assess the evolution of the virus. (32)

Details of BQ.1.1, XBB, BA.4.6, BA.5 and BA.2.75 can be found above in the risk assessment.

Variants under monitoring

- As of October 14th 2022, the ECDC has designated Omicron lineages with mutations N460X and F490X, K444X and N460X, as a variant under monitoring (VUM). Among others, lineages BQ.1, BQ.1.1, XBB, BN.1 and BN.2 fall under either of these two designations. Data from GISAID EpiCoV shows a rapid increase of this VUM in Bangladesh, India, and Singapore, and it is present at low levels in the EU/EEA. The N460X and F490X substitutions are located near important antigenic sites, and there are some indications of a significant effect on neutralising activity. (33, 34)

XBB

- XBB is a recombinant Omicron variant, thought to have arisen in a single patient from a recombination event between the BJ.1 (from BA.2.10) and BM.1.1.1 (from BA.2.75) variants.
- A cluster of cases were flagged on 13 September 2022, from sequences originating from Singapore, India, Bangladesh and the USA in early September. (35)
- Spike mutational profile is related to BA.2 and BJ.1 but with the following mutations: 364T, 445P, 446S and 490V. (6)
- Currently driving an increase in cases in Singapore. As of 15 October reinfection rates are around 18% in Singapore. (30)
- No evidence of increased severity currently, as there is a divergence and weakening of the correlation between the number of cases and new hospitalisations. (30)
- One XBB *in vitro* study showed increased resistance to Evusheld and bebtelovimab. (2)

BQ.1.1

- An Omicron subvariant that is most closely related to the BA.5 subvariant. First flagged on 26 August 2022 with sequences from the USA, UK and Japan. First sequences uploaded onto GISAID from mid-July in Nigeria. (36)
- Spike protein mutational profile is the same as BA.5 with the following mutations: R346T, K444T and N460K. (6)
- Outside the spike protein, it has the following mutations: NSP12 protein (RNA-dependent RNA polymerase) mutation Y273H (also annotated as ORF1b:Y264H), NSP13 protein (helicase) mutation N268S (also annotated as ORF1b:N1191S). (36)
- One BQ.1.1 *in vitro* study showed increased resistance to Evusheld and bebtelovimab. (2)



BA.2.3.20

- A BA.2 and Delta recombinant that has a growth advantages over BA.5. (2) Variant has been detected in three countries distant from one another has rare 2-nucleotide mutation S:A484R. First detected in the United States and has since been detected in Singapore. (37)

BJ.1

- Detected on the 29 July 2022, is a BA.2 sub-lineage with 14 additional mutations in the spike protein, this variant has been mostly detected in India (70% of all BJ.1 cases) and has also been detected in Singapore, South Korea, Austria and the United States of America. (38, 39)

BA.2.10.X

- BA.2.10.X (also referred to as BA.2.10.1, BA.2.10.4 or BA.2.10+) is an Omicron subvariant, that has been identified due to its large collection of mutations. There is no observed evidence for phenotypic changes (transmission, severity, immune evasion), and there are very few reported cases of this variant to date. (38)

BA.2.75.2

- A pre-print study has found BA.2.75.2 to be resistant to neutralisation by Evusheld (tixagevimab and cilgavimab), but has remained sensitive to bebtelovimab. (40)
- Serum from blood donors in Sweden was on average five-fold less effective at neutralising BA.2.75.2 compared to BA.5. (40)
- BA.2.75.2 is carrying additional mutations, R346T, F486S, and D1199N that due to its growth advantage are suggestive of more extensive escape from neutralising antibodies than previous Omicron variants. (40)

BA.5.2.1

- A new subvariant of the Omicron BA.5 lineage detected in China on the 8 July 2022. (41) The first confirmed case of BA.5.2.1 was detected in Shanghai, with more cases since identified across multiple provinces in China.(41) There is limited scientific evidence around transmission potential, disease severity and other properties of this variant.



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