

Date: 01 July 2022

SARS-CoV-2 Variants of Concern Update

The purpose of this document is to provide an overview of recent developments with respect to the identification of new SARS-CoV-2 variants or further details about already identified variants. Characteristics of current circulating variants are monitored including: growth advantage/transmissibility; disease course/viral dynamics; clinical features (symptoms and severity); immune evasion, vaccine effectiveness and therapeutics effectiveness; and detection/testing.

All viruses, including SARS-CoV-2, change over time. Most of these changes have little to no impact on the properties of the virus, but some may affect properties such as: how easily it spreads, the associated disease severity, the performance of vaccines, therapeutic medicines, diagnostic tools, or the performance of other public health and social measures. Nomenclature systems for naming and tracking SARS-CoV-2 genetic lineages have been established by GISAID, Nextstrain and Pango. To assist with public discussions of variants, an expert group convened by WHO recommended using letters of the Greek Alphabet, i.e., Alpha, Beta, Gamma, Delta etc.

A selected sub-set of topic areas are comprehensively updated in each issue of this document. The dates stated for section updates relate to when a comprehensive update was performed, although additional data might have been added in the interim. New information included since the previous update is provided in red text.

This issue has been consolidated and condensed. Out-dated information has been removed as necessary.

Key documents published recently

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

- WHO: Weekly epidemiological update on COVID-19 – 29 June 2022 [[1](#)]
- UKHSA: SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 43, 24 June 2022 [[2](#)]

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Key new information

- Fewer CoV-2 sequences are being submitted to GISAID than earlier in 2022, with 94% of submitted sequences (globally) between 27 May and 27 June 2022 being the Omicron variant. Among Omicron sequences submitted between 13 and 19 June, BA.2 represented 25% of sequences, while BA.2.12.1 represented 11%, BA.4 represented 12%, and BA.5 represented 43%. This represents a decrease in the proportion of BA.2 and BA.2.12.1 sequences and an increase in BA.4 and BA.5.[\[1\]](#)
- At 24 June BA.4 and BA.5 are dominant in the UK, with an estimated 22% of cases being BA.4 and 39% BA.5.[\[2\]](#) Updated modelling shows the relative growth advantage for BA.5 is larger than BA.4 and it is therefore most likely that BA.5 will become the dominant variant in the UK. In the UK for the period 8 April to 8 June, the median weekly growth rate was 76% for BA.4 over BA.2 and 66% for BA.5 over BA.2.[\[2\]](#)
- Early adjusted analysis of BA.4/5 in the UK shows no reduction in vaccine effectiveness relative to BA.2. However, this is a preliminary analysis and does not take into account the time since last vaccination.[\[2\]](#)
- A longitudinal study in fully vaccinated UK health care workers showed that immune response varies depending on how and when individuals have previously encountered virus spike antigens (though vaccination and infection).[\[3\]](#) The study results most relevant to the New Zealand population (vaccinated, and either infection naïve or post-Omicron infection) were that Omicron infection in vaccinated people resulted in some enhancement of neutralising antibody and T-cell response against Omicron, but this enhancement was less than that observed against earlier variants (Alpha and Delta).
- Data from the UK COVID-19 Infection Survey found fewer people reported symptoms after reinfection than in their initial infection episode, suggesting reinfections are more likely to be asymptomatic (noting that these symptoms are self reported).[\[4\]](#)
- Many monoclonal antibodies show reduced efficacy against Omicron relative to Delta.[\[5\]](#) Additionally, although many of the newer Omicron subvariants (e.g. BA. 4 and BA.5) are derived from BA.2, there are significant mutations to in the spike.[\[6\]](#) As a result, it becomes likely that these variants will also have reduced sensitivity to therapeutic monoclonal antibodies.[\[6\]](#)
- On the 15 June, an FDA panel endorsed both Moderna and Pfizer COVID-19 vaccines for use in children aged 6 months to 4 years. In the US, five times as many children aged 0-4 years were hospitalised during the Omicron wave (Dec, 2021) than from the Delta wave [\[7\]](#) More than 200 deaths of 0–4 year olds have been reported in the US due to COVID-19 since Jan 2020, and this accounts for 1.7% of all deaths in this age group.[\[8\]](#) Approximately 3 out 4 children in the US have antibodies that show previous infection with SARS-CoV-2,[\[9\]](#) however, the CDC is still recommending vaccination in this group to prevent reinfection

Overview of variants

Section updated: *01 July 2022*

As of 16 May 2022, Delta and Omicron¹ were the only circulating Variants of Concern as designated by the WHO.[\(link\)](#) There were no currently circulating Variants of Interest as designated by the WHO at that time. As of 16 May, the WHO listed two variants under monitoring: B.1.640 and XD.[\[10\]](#)

Recently designated variants in the UK include the following, which were classified by the UKHSA Variant Technical Group (VTG) on 6 April 2022²[\[11\]](#):

- Recombinant XD was classified V-22APR-01
- Recombinant XE was classified V-22APR-02
- Omicron sub-lineage BA.4 was classified V-22APR-03
- Omicron sub-lineage BA.5 was classified V-22APR-04.
- Omicron sub-lineage BA.2.12.1 has yet to be classified as of 20 May 2022 [\[12\]](#)

Table 1 now also includes European Centre for Disease Prevention and Control (ECDC) classifications. The ECDC uses the label 'variant of concern' when clear evidence is available for a variant indicating a significant impact on transmissibility, severity and/or immunity that is likely to have an impact on the epidemiological situation in the EU/EEA.[\[13\]](#)

Note that whilst BA.4 and BA.5 were both first detected in South Africa, the country performs a high rate of whole genome sequencing, and it is possible the variants first emerged (but was not detected) somewhere else.[\[14\]](#)

Whole genome sequencing efforts are falling globally, potentially obscuring surveillance of VoCs as they emerge and become more prevalent.

The WHO Weekly Epidemiological Update on 29 June 2022 [\[1\]](#) reported that:

"There continues to be a decline in the number of SARS-CoV-2 sequences submitted to GISAID, as compared to January 2022 when 1,248,906 sequences were submitted. From 27 May to 27 June 2022, 146,183 SARS-CoV-2 sequences were submitted to GISAID. Among these sequences, the Omicron VOC remains the dominant variant circulating globally, accounting for 94% of sequences reported in the past 30 days. Among Omicron sequences, as of epidemiological week 24 (13 to 19 June 2022) BA.2 represents 25%, while BA.2.12.1 represents 11%, BA.4 represents 12%, and BA.5 represents 43%. Comparing the proportion of Omicron sequences submitted during epidemiological weeks 23 (6 to 12 June) and 24, BA.2 declined from 30% to 25%, BA.2.12.1 declined from 18% to 11%, while BA.4 increased from 9% to 12% and BA.5 increased from 28% to 43%."

¹ Includes BA.1, BA.2, BA.3, BA.4, BA.5 and descendent lineages. It also includes BA.1/BA.2 circulating recombinant forms such as XE.

² Whilst recombinant lineages generally are monitored through horizon scanning, UKHSA has classified XD and XE recombinant lineages as variants V-22APR-01 and V-22APR-02, respectively. XD has been classified a variant (V) on the basis of the data published from France, suggesting that it may be biologically distinct. XE has been classified a variant (V) based on apparent continued growth within the UK.

SARS-CoV-2 Variants of Concern Update

Table 1: Overview of SARS-CoV-2 variants of public health interest

Table updated: 04 July 2022

| Pango lineage | WHO label | UKHSA label | UKHSA designation | ECDC designation | Earliest documented samples | Distribution |
|--|--------------------------|-----------------|---|---|-----------------------------------|--|
| BA.2.75 | Not yet defined | Not yet defined | Not yet defined | Not yet defined | India, 02 June 2022 | Detected in India, UK, Canada, USA, Germany and Japan |
| B.1.1.529/ BA.4 | Omicron sub-lineage BA.4 | V-22APR-03 | Variant | Variant of Concern as of 12 May 2022 (previously variant of interest)[15] | South Africa, January 2022. [14] | Detected in the UK in the past 12 weeks as at 6 May.[16] Dominant in South Africa along with BA.5.[15] |
| B.1.1.529/ BA.5 | Omicron sub-lineage BA.5 | V-22APR-04 | Variant | Variant of Concern as of 12 May 2022 (previously variant of interest)[15] | South Africa, February 2022. [14] | Detected in the UK in the past 12 weeks as at 6 May.[16] Dominant in South Africa along with BA.4. Increasing trend in the variant proportions for BA.5 observed in Portugal in recent weeks.[15] As of 6 May UKHSA reported it had been detected in 17 countries, with highest numbers in South Africa, Portugal, Germany and the UK.[16] |
| BA.2.12.1 | | | Signal in monitoring | | | Detected in the UK in the past 12 weeks as at 6 May.[16] |
| B.1.1.529/BA.2 | Omicron | VOC-22JAN-01 | Variant of concern (previously a variant under investigation) | Variant of Concern[13] | | Detected in the UK in the past 12 weeks as at 6 May.[16] |
| BA.3 | - | - | Signal in monitoring (previously Variant in monitoring) | Variant under monitoring [13] | South Africa [13] | Detected in the UK in the past 12 weeks as at 6 May.[16] As of 16 May 2022, most BA.3 cases reported were in South Africa (81%) and the US (5%).(link) |
| B.1.1.529/BA.1 | Omicron | VOC-21NOV-01 | Variant of concern | Variant of Concern[13] | | Detected in the UK in the past 12 weeks as at 6 May.[16] |
| Delta and Omicron recombinant lineages (UK) | - | | Signal in monitoring (previously Variant in monitoring) | | United Kingdom, Feb-2022 [17, 18] | Detected in the UK in the past 12 weeks as at 6 May.[16] |

| Pango lineage | WHO label | UKHSA label | UKHSA designation | ECDC designation | Earliest documented samples | Distribution |
|--|-----------|---|---|--|--|---|
| AY.119.2/BA.1.1 Recombinant | | | Signal under monitoring | | | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| XD Recombinant (Delta x BA.1) | | V-22APR-01 | Variant (<i>previously signal under monitoring</i>) | | France, Jan-2022 [10] | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| XE Recombinant (BA.1 x BA.2) | | V-22APR-02 | Variant | | First case detected on 19 January 2022. [17, 18] | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| AY.119.2/BA.1.1 Recombinant | | | Signal under monitoring | | | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| BA.1/BA.2 Recombinant (with unique mutation C3583T) | | | Signal in monitoring | | | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| XF Recombinant | | | Signal in monitoring | | | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| B.1.617.2 and sub-lineages | Delta | V-21APR-02 (<i>previously VOC-21APR-02</i>) | Variant (<i>previously a variant of concern</i>) | Variant of Concern [13] | India, Oct-2020 [10] | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| B.1.1.7 | Alpha | V-20DEC-01 (<i>previously VOC-20DEC-01</i>) | Variant (<i>previously a variant of concern</i>) | De-escalated variant | United Kingdom, Sep-2020 [10] | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| B.1.351 | Beta | V-20DEC-02 | Variant of Concern (<i>last report unclear designation</i>) | | South Africa, May-2020 [10] | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| AY.4.2 | | V-21OCT-01 (<i>previously VUI-21OCT-01</i>) | Variant (<i>previously a variant under investigation</i>) - AY.4.2 is a sub-lineage within Delta that has been assigned as a distinct variant by UKHSA. | De-escalated but monitored under Delta VOC | | Detected in the UK in the past 12 weeks as at 6 May. [16] |
| B.1.640 | - | - | Signal in monitoring (<i>previously Variant in monitoring</i>) | | Multiple countries, Sep-2021 [10] | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| B.1.617.3 | | V-21APR-03 | Variant | | | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| B.1.621 | Mu | V-21JUL-01 (<i>previously VUI-21JUL-01</i>) | Variant (<i>previously Variant under Investigation</i>) | | Colombia, Jan-2021 [10] | Detected in GISAID, but not in the UK, in the past 12 weeks as at 6 May. [16] |
| P.1 | | Removed from UKHSA list | Removed from UKHSA list | | Brazil, Nov-2020 [10] | |

Table updated: 16 May 2022

Omicron Overview

Section updated: 01 July 2022

- Omicron variant is dominant across the world, and has displaced the Delta variant. [19]
 - Spread has been rapid even in regions with high levels of population immunity. [20]
- Omicron first detected in November 2021 causing a rapid resurgence of COVID-19 cases in South Africa. [20]
 - Within three days of the first genome being uploaded, the WHO had designated it as the fifth variant of concern of SARS-CoV-2 (Omicron, B.1.1.529). [20]
 - Within three weeks the variant had been identified in 87 countries. [20]
- Compared to the Alpha, Beta, Gamma, and Delta VoCs, Omicron variant has the greatest number of mutations; 50 mutations accumulated throughout the genome. [21]
 - At least 32 mutations in the spike protein (twice as many as Delta), [21] enabling highly efficient evasion from neutralising antibodies. [19]
 - Omicron has continued to evolve, leading to further variants with slightly different genetic constellations of mutations. [22]
- The Omicron variant (B.1.1.529) comprises a number of lineages and sub-lineages. [23]
 - Major descendant lineages include BA.1, BA.2, BA.3, BA.4, BA.5
 - BA.2 and BA.3 are evolutionarily linked to BA.1 [24] and BA.4 and BA.5 are evolutionarily linked to BA.2. [11]
 - Recombinant lineages (Table 3) include XE, a BA.1/BA.2 recombinant [10]
 - There are a large number of mutations differentiating Omicron variants from other known SARS-CoV-2 lineages. [20]
- **BA.1 and BA.2**
 - In December 2021, Pango announced designation of two genetically distinct sub-lineages of B.1.1.529 as BA.1 (B.1.1.529.1) and BA.2 (B.1.1.529.2) [25]. BA.1 for the original globally distributed lineage, and BA.2 for the new outlier lineage. The prefix BA was then an alias for B.1.1.529. [25].
 - BA.2 was designated a variant under investigation (VUI) by UKHSA on 21 January 2022. BA.2 contains 29 mutations in the spike protein and a deletion at 25-27. Some of the mutations in the spike protein are shared with BA.1. [26]
 - Differentiation of BA.1 from BA.2 requires whole genome sequencing (WGS). BA.1 contains the spike deletion at position 69-70 which is associated with S-gene target failure (SGTF) in some widely used PCR tests.
 - SGTF patterns have been used to assess the spread of Omicron lineage BA.1.
 - The BA.2 genome generally is S-gene target positive, but as of 30 March 2022, the UKHSA reported that 0.16% of BA.2 samples sequenced had the deletion at position 69-70. [11].
 - UKHSA is no longer reporting SGTF patterns. UK testing policy on 1 April resulted in a substantial reduction in tests processed through assays which can report SGTF. SGTF is no longer a reliable representation of variants in the population, and the UKHSA will not be reporting it going forward. [16]
- **BA.3**
 - BA.3 has the SGTF deletion ($\Delta 69-70$) so can be detected using PCR tests that detect SGTF, and has a combination of mutations found in BA.1 and BA.2 spike proteins. [27]
 - As of 01 June 2022, the proportion of sequences submitted to GISAID that were BA.3 in the past 30 days, has declined to <1%. [28]
- **BA.4 and BA.5**
 - These were classified by the VTG on 6 April 2022 as V-22APR-03 and V-22APR-04, respectively. [1] WHO announced that BA.4 and BA.5 had been added to their list of variants for monitoring on 12 April 2022. The ECDC classified both as variants of concern on 12 May. [15]

- BA.4 and BA.5 have many mutations in common with the BA.2 variant,[\[14\]](#) as well as a number of additional mutations. The BA.4 and BA.5 sub-variants tend to be discussed together because the mutations in their spike protein gene are identical (but differ in mutations elsewhere in the genome).[\[14\]](#)
- As of **19 June 2022**, the proportion of Omicron sequences submitted to GISAID that were BA.4 and BA.5 has risen from 9% to 12% and 28% to 43% respectively, compared to the previous week. [\[1\]](#)
- At June 24th BA.4 and BA.5 are dominant in the UK, with an estimated 22% of cases being BA.4 and 39% BA.5. [\[2\]](#) Updated modelling shows the relative growth advantage for BA.5 is larger than BA.4 and it is therefore most likely that BA.5 will become the dominant variant in the UK. In the UK for the period 8th April to 8th June, the median weekly growth rate was 76% for BA.4 over BA.2 and 66% for BA.5 over BA.2. [\[2\]](#)
- Early UK analysis of BA.4/5 shows no reduction in vaccine effectiveness relative to BA.2 after previous positivity, testing pillar, health and social care worker status, clinical risk status, age, gender, and week of test were adjusted for. However, this is a preliminary analysis and does not take into account the time since last vaccination. [\[2\]](#) There are insufficient data for a robust assessment of the effectiveness of COVID-19 vaccines against mild or severe disease with BA.4 and BA.5. [\[2\]](#)
- No increase in severity of disease has been observed with BA.4/BA.5 compared to previous Omicron sub-lineages.[\[29, 30\]](#)
- **BA.2.12.1**
 - As of 01 June 2022, the proportion of sequences submitted to GISAID for BA.2.12.1 in the past 30 days, has risen from 11% to 16%. [\[28\]](#)

Characteristics of Omicron

Omicron: Growth advantage/ transmissibility

Section updated: 16 May 2022

Omicron is more transmissible and has a higher secondary attack rate than Delta

- A study estimated that Omicron had a growth advantage that corresponds to a 5.4-fold (95% CI = 3.1–10.1) weekly increase in cases compared with Delta. [20]
- Data from Denmark (to 18th Dec 2021), the effective reproduction number of Omicron is 3.19 (95%CI 2.82–3.61) times greater than Delta under the same epidemiological conditions. [31]
- Data from Texas, USA, indicated a case-doubling time for Omicron of 1.8 days, three times faster than for Delta in this area. [32]
 - Omicron is more associated with asymptomatic infection and transmission than Beta and Delta. [33]
 - Contact tracing data show a greater proportion of transmission happening outside the household for Omicron than for Delta. [34]
- Data from the UK estimated a shorter generation time (interval between infection events) for Omicron with a mean of 1.5-3.2 days (standard deviation [SD] 1.3-4.6 days), compared to a mean of 2.5-4 days (SD 1.9-3 days) for Delta. [15]
- UKHSA analysis of contact-tracing data shows the mean serial interval for BA.1 is 3.72 days (95% CI: 3.62 - 3.80). [35]

Household transmission

- Secondary Attack Rate (SAR) of 29% for BA.1 compared with an SAR of 39% for BA.2 across households infected with Omicron. [36]
- SAR for Omicron ranges from 7.6% to 50% depending on country and setting. [34, 37, 38]

Other data

- The Omicron variant has a survival time in the environment of 21.1 hours (95% CI: 15.8–27.6) compared to 16.8 hours (95% CI: 13.1–21.1) for Delta. [39] The high environmental stability of Omicron could increase the risk of contact transmission and contribute to its spread. However, convincing evidence of fomite transmission has not been demonstrated for any variant to date.
- A study found that initial testing of HCWs if they had a household positive case in majority of instances, was sufficient to prevent nosocomial transmission to patients. [40]
- A human challenge study using **wild-type virus** found that a dosage of 10 TCID50 (very low dose) was sufficient to result in an infection. Also, they found that viral shedding occurs in both the nose and throat at high levels irrespective of symptom severity. [41]

BA.2-specific growth advantage/ transmissibility information

UK data gives a mean serial interval for BA.2 of 3.27 days, with 95% of serial intervals expected to be less than or equal to 7.56 - 8.40 days after primary case symptom onset.

Serial interval

- Mean serial interval for BA.2 is 3.27 days around half a day shorter than BA.1 (3.72 days).[\[35\]](#)
- BA.2 has a shorter median serial interval of 2.68 days compared to BA.1 (3.27 days).
- 95% of BA.2 serial intervals are expected to be less than or equal to 7.56 - 8.4 days after primary case symptom onset.
- 95% of BA.1 serial intervals expected to be less than or equal to 8.21 - 8.57 days after primary case symptom onset.[\[35\]](#)

Viral load

- Studies have found evidence of higher viral loads from BA.2 than BA.1. [\[42, 43\]](#) This suggests that the increased viral load in the upper pharynx may explain the growth advantage of BA.2 over BA.1.
- However, other studies have found no correlation between increased viral loads with infection with BA.2 over BA.1.[\[44\]](#) [\[45\]](#)

Omicron: Disease course/ viral dynamics

Section updated: 16 May 2022

Median or mean incubation period 3-4 days, maximum incubation unclear (6-8 days reported). Omicron may have a shorter serial interval than Delta.

NOTE: Incubation period refers to the time from infection until symptom development. The serial interval refers to the time from illness onset in the primary case to illness onset in the secondary case. The latent period refers to the time from infection until the person becomes infectious (and more likely to test positive)

Incubation period

Single exposure event data (assumes participants infected at event):

- Incubation periods are short, ranging from 0 to 8 days, with a mean or median incubation period of around 3 days days [46-49]

Human challenge studies (non-Omicron, novel transmission data)

- Incubation period of 2 to 4 days after inoculation with **wild-type virus**. [41] Viral load (VL) rose steeply and peaked around day 4-5.

Serial Interval

- The mean serial interval ranges from 2.5 to 4.8 days. [37, 49-51]

Latent period:

Human challenge studies (non- omicron, novel transmission data)

- Viral shedding by qPCR became quantifiable in throat swabs from 40 hours post-inoculation, significantly earlier than in the nose, where initial viral quantifiable detection occurred at 58 hours post-inoculation. [41]

Duration of infectiousness

Data predominantly from **vaccinated** people:

- Japan [52]: Viral RNA from Omicron infection samples was highest 3-6 days after diagnosis or symptom onset and then decreased gradually, with a marked decrease 10 days after diagnosis or symptom onset. A similar trend was seen for viral isolates, with no infectious virus detected in the respiratory samples 10 days post diagnosis or symptom onset.
- Switzerland [53]: A study investigating viral shedding dynamics included a small number of Omicron breakthrough infections and showed similar infectious viral titres in nasopharyngeal samples for breakthrough Omicron and Delta infections. Samples were gathered in the first 5 days post symptoms.
- Singapore [54]: Ct value at presentation was significantly higher for Omicron compared with Delta infections (20.7 [IQR 17.9 – 28.5] vs. 19.1 [15.4 – 21.1], $p < 0.001$). Pattern of viral shedding was comparable for Omicron and Delta, with an increase in viral load over the first 2-3 days of illness, and significant decline from Day 8. Illness onset median Ct values were similar for Omicron between those with primary vaccination or booster vaccination doses.
- Switzerland [55]: Found that Delta and Omicron have comparable genome copies ($p = 0.3345$).

Human challenge studies (non- omicron, novel transmission data)

- Some clinical participants still shed culturable virus ~10 days after symptom onset but the sample size is small ($n = 36$). [41]

Duration of illness

- Time to resolution of symptoms varies, and at the end of follow-up, five individuals still reported symptoms, while the rest (16 individuals) reported symptoms lasting 1 to 9 days. [46]
- One study found positive viral cultures obtained from day 2 of infection but were cleared and negative by day 5 of illness. [54]

Omicron: Clinical features (symptoms and severity)

Section updated: 16 May 2022

Hospitalisation

Hospitalisation frequency for Omicron relative to Delta

Adjusted for vaccination status (important for understanding basic differences in severity as it can remove differences in vaccine effectiveness from assessment. However, residual confounding for vaccination status may still occur):

- A Swedish study found risk of severe disease was lower with Omicron by 40% for unvaccinated and 71% less for vaccinated individuals, compared to Delta. [56]
- US study found a relative increase in ED visits (86%) and hospitalisations (76%) from Omicron compared to the Delta period due to the higher volume of cases but a relative decrease in the length of stay in hospitals (-27%). [57]
- US study comparing Omicron period vs Delta period found that among hospitalised omicron patients (41% vaccinated) they were less likely to require ICU or die. [58]
- A Norwegian study found that cases infected with Omicron were 73% lower risk of hospitalisations compared with delta infection.[59]
- A French study found risk of hospitalisation with Omicron was reduced by 64% compared to Delta. [60]
- Canadian data: risk of hospitalisation or death was 54% lower³. [61]
- Scottish data: risk of hospitalisation 68% lower.⁴[62]
- UK data: risk of presentation to emergency care or hospital admission 50% lower than with Delta. The risk of hospital admission from emergency departments was approximately 67% lower than with Delta.⁵ [63]
- A study from South Africa showed that much of the severity reduction observed for Omicron relative to Delta was due to prior infection and vaccination. Intrinsically reduced virulence accounted for a ~25% reduced risk of hospitalization/death compared to Delta. [64]
- A US study in veterans found that infection by Omicron has a 45% lower likelihood of resulting in hospitalisation than infection by Delta. [65]
- UK data in long term care facility residents: risk of hospitalisation much lower, 10.8% for Delta and 4.0% for Omicron. [66, 67]
- Portugal data: risk of hospitalisation lower, 1.6% for Delta and 0.2% for Omicron. [68]
- Danish data [69] stratified rather than adjusted by vaccination status:
 - Among those with <2 doses: 43% lower risk of hospitalisation

³ adjusted for vaccination status and region

⁴ adjusted for age, sex, socioeconomic status, vaccination status and clinical risk factors.

⁵ Controlled for date of specimen and area of residence and further adjusted for age, sex, ethnicity, local area deprivation, international travel, vaccination status. Also adjusted for whether the current infection is a known reinfection, although as reinfections are substantially under-ascertained, the adjustment may not have fully accounted for the effect of reinfections.

- Among those with 2 doses: 29% lower risk of hospitalisation
- Among those with 3 doses: 50% lower risk of hospitalisation

Unadjusted for vaccination status (provides indication of burden on healthcare at the level of vaccination in country where study conducted):

- Reduction in hospitalisation of 38% for emergency department attendance or admission, and 62% for admission [34]
- Reductions in hospitalisation compared to Delta range from 36% to 53% depending on country. [69-71]

Hospitalisation frequency (not compared to Delta)

Hospitalisation frequency varies depending on country/region but ranges from 0.25% in [61]Canada to 3.6% in [72]India, with many countries reporting values between these two values. [70, 73]

Paediatric hospitalisation

- South Africa: Rapid increases in paediatric COVID-19 cases and hospitalisations were reported in the Tshwane District, mirroring high community transmission of SARS-CoV-2 (Omicron variant). [74]
- US study of Children under 5 years found a significantly lower risk for severe clinical outcomes in the 3-day time-window following initial Omicron infection compared to Delta. [75] Risk for an ED visit was 18.83% (vs 26.67%), hospitalisation was 1.04% (vs 3.14%), ICU admissions was 0.14% (vs 0.43%), and mechanical ventilation was 0.33% (vs 1.15%).
- UK: Paediatric admissions began to rise from 26 December 2021, with a 3-fold increase in 2 weeks. [76]
 - The rise is most rapid among children under 5 years, and highest in infants aged under 1 year based on period of 90% Omicron prevalence determined via WGS.
 - A clinical case review of a small number of Omicron admissions in infants found those admitted were not severely unwell. [76, 77]
 - UK data during the Omicron wave (14 December 2021 to 6 January 2022) indicate less severe outcomes in children aged under 1 year compared to previous waves. [78] In this wave period, 12.7% required oxygen use compared to 22.5% in the first wave of the pandemic. 16% required admission to intensive care (vs 14%), 3.9% required use of mechanical ventilation (vs 5.8%), 1.3% required use of non-invasive ventilation (vs 7.2%), and mean length of stay was 1.9 days (vs 6.6 days).
- A study from the US states that paediatric acute upper airway infection (UAI) cases have increased during the Omicron variant surge, with many developing severe disease. [79]
 - The retrospective cohort study suggests that Omicron replicates more efficiently in the conducting airways, increasing the risk of a croup phenotype in children as they have smaller airways.

Risk factors for hospitalisation with Omicron

- A UK study found the age range of individuals admitted with Omicron to 29 December 2021 was 0 to 100 years (median: 45.5 years); 496 (60.9%) were aged 40 years or more; 30.8% were aged 70 years or more. [63]
- Public Health Scotland data reported on hospital admissions for COVID-19 (week of 22-28 December 2021) shows approximately 44% were in people 60 plus years of age, and 21% of admissions were in people aged 80 plus. [80]

- Most cases of COVID-19 at this time in Scotland were Omicron but the proportion of cases of the Omicron variant for each age-group hospitalised are not reported.

Time to hospitalisation with Omicron

Currently, there is no studies to date that have investigated this

Time in hospital with Omicron

- Hospital stays from Omicron infection range from 1 to 6 days and this varies depending on country and demographic but the mean time in hospital tends to be 3 to 4 days.[\[32, 70, 81\]](#) Overall, hospital stays for Omicron infections are significantly shorter compared to that of Delta infections.[\[65, 68, 82\]](#)

ICU admission

Severe/ICU/ventilated frequency relative to Delta

- ICU admission from Omicron infection is around 70-74% lower than from Delta infection.[\[65, 70\]](#)
- South African data: Among *hospitalised* individuals, after controlling for factors associated with severe disease⁶, the odds of severe disease did not differ between S-Gene Target-Failure (SGTF, interpreted as Omicron) infected individuals compared to non-SGTF individuals diagnosed during the same time period (aOR 0.7, 95% CI 0.3-1.4).[\[83\]](#) Compared to earlier Delta infections, after controlling for factors associated with severe disease⁷, SGTF-infected individuals had lower odds of severe disease (aOR 0.3, 95% CI 0.2-0.5).

⁶ controlled for factors known to be associated with severity (age, presence of comorbidity, sex, province and healthcare sector) and adjusted for the number of days between the date of specimen collection and date of hospital admission, known prior SARS-CoV-2 infection and SARS-CoV-2 vaccination status.

⁷ Controlled for factors known to be associated with disease severity (age, presence of co-morbidity, sex, province and healthcare sector), and adjusted for number of days between date of specimen collection and date of hospital admission, known prior SARS-CoV-2 infection and SARS-CoV-2 vaccination status.

Severe/ICU/ventilated frequency (not compared to Delta)

In Texas, among 862 people who tested positive for Omicron (mainly symptomatic people presenting to healthcare facilities),^[32] the maximum ventilatory support required was:

| | |
|-------------------------------------|--|
| Extracorporeal membrane oxygenation | 1 (0.7% of 134 hospitalised, 0.1% of 862 testing positive for Omicron) |
| Mechanical ventilation | 6 (4.5%, 0.7%) |
| Non-invasive ventilation | 9 (6.7%, 1.0%) |
| High flow oxygen | 12 (9.0%, 1.4%) |
| Low flow oxygen | 42 (31%, 4.9%) |
| Room air (but hospitalised) | 64 (48%, 7.4%) |

- A total of 19.7% (875/4438) of hospital admissions required supplemental oxygen (not further specified) and 6.9% were treated in ICU (308/4438) in an analysis of data from Gauteng Province, South Africa during an Omicron-dominated period. ^[81]

Californian data: The daily risk of mechanical ventilation among patients (unclear if analysis restricted to hospital inpatients) with Omicron infections was significantly lower than for Delta (0 vs 0.04 per 1000 person-days at risk).^[70]

Death

Death frequency relative to Delta

South African: A 73% reduction in death relative to Delta, but the extent of reduction was attenuated when prior infections and vaccination were also considered (HR: 0.72, a 28% reduction relative to Delta).^[64]

US: Unadjusted hazard ratios for mortality associated with Omicron variant infection was 0.09 (95% CI : 0.01-0.75)^[70] but unadjusted ratios could be confounded by many factors, and the short follow up time might bias results.

UK data in long term care facility residents: Reduced risk of death within 28 days of a new diagnosis in the Omicron dominant period (1.1 deaths / 1000 person-days, 95% CI: 0.6-2.2) compared to the pre-Omicron period (3.8 deaths / 1000 person-days, 95% CI: 2.8-5.2).^[66]

Portugal data: The odds of death were 0.14 (95% CI: 0.0011-1.12), representing a reduction in the risk of death of 86% for Omicron compared with Delta.^[68]

Time to death

UK data: median time from Omicron specimen date to death was 5 days (range 0 to 14).^[63] Note that specimen date might not reflect date of symptom onset.

Symptomatology

Symptoms may be milder in previously infected and/or vaccinated individuals. Recent UK data suggests a substantial proportion of Omicron cases may be asymptomatic – estimates range from 25-54%. The most common symptoms reported are sore throat, cough, runny/stuffy nose, and fatigue. Additional data supports earlier reports that loss of smell and taste is less commonly reported by Omicron cases than for Delta, and that sore throat is more commonly reported.

- The most common symptoms reported in early data were: cough; runny/stuffy nose; and fatigue.^[47, 84-86]
- The COVID Symptoms Study reports that headache and sneezing are also common symptoms of Omicron infection. ^[87]

- Data suggests no difference in symptoms between vaccinated and unvaccinated cases of COVID-19 infection but milder and of shorter duration in vaccinated cases (data likely to include both Omicron and Delta cases). ([link](#))
- A study from Canada of 1,063 cases of Omicron (confirmed or suspected) found that only 10% reported shortness of breath. [\[86\]](#)
- Symptoms reported in paediatric cases in South Africa have included fever, vomiting, diarrhoea and convulsions. [\[74\]](#)
- UKHSA comparison of Omicron to Delta symptoms from confirmed Omicron cases and confirmed Delta cases in the period between 01 December to 28 December 2021.
 - Omicron cases were less likely to report loss of smell and taste compared to Delta cases (13% of Omicron cases compared to 34% of Delta cases).
 - However, Omicron cases were more likely to report a sore throat than Delta cases (53% of Omicron cases, 34% of Delta cases).
 - Adjustments were made for age group, sex, ethnicity, self-reported vaccination status (two or more doses, one or no dose, or missing data), geographical region of residence, and the week in which symptoms began.
 - UKHSA states that the findings relating to reports of sore throat could be incidental and suggests that sore throat may not be a specific predictor of Omicron infection, as another recent study led by Oxford University and the Office for National Statistics [\[88\]](#) found increased reports of sore throat in both PCR-positives and symptomatic PCR-negative cases. More data are required to understand which symptoms may be used to identify Omicron infections.
- A study from Korea investigated the clinical and epidemiological characteristics of 40 patients with Omicron (42.5% were fully vaccinated) and found that half of the patients (19, 47.5%) were asymptomatic, while the others had mild symptoms. [\[89\]](#)
 - The most common symptoms were sore throat (25%), fever (20%), headache (15%), cough (12.5%), and sputum production (12.5%).
 - While these findings are consistent with recent reports of mild symptoms from other sources, given the small size and low median age of the study (39.5), more data are required to understand symptoms and determine the severity of Omicron.
- A Singapore study compared symptoms between Omicron and Delta found having sore throat was significantly more common in Omicron patients (sore throat 46.0 vs 23.0%, $p=0.005$) and less likely to develop pneumonia (3.4 vs 16.1%, $p=0.005$).
 - Median neutrophil count, C-reactive protein and lactate dehydrogenase levels were lower in Omicron infections.
 - Patients with booster vaccination were significantly older and had higher anti-spike antibody but were similar in clinical and laboratory features including median initial and lowest PCR cycle threshold values. [\[54\]](#)
- A study from Jordan showed that the most frequent symptoms for Omicron were fever, cough, sore throat, runny nose, joint and muscle pain, and general fatigue. Loss of taste and smell was only reported in 1.2% of patients. [\[90\]](#)
- UK data reported from the Real-time Assessment of Community Transmission-1 (REACT-1) survey (Round 17; 99% Omicron cases) found a substantial proportion (approximately 25%) of positive tests were in asymptomatic people. [\[91\]](#)
 - Vaccine status of individuals within this group was not included in the report.

- Data from the UK COVID-19 Infection Survey found fewer people reported symptoms within 35 days following the first observed positive test from reinfection than in their initial infection episode, suggesting reinfections are more likely to be asymptomatic, (noting that these symptoms are self reported). [4]
 - Viral load, indicated by Ct Value, was on average lower in reinfections (Ct value of 25.15) than initial infections (Ct Value of 26.91), in data collected from 20 December 2021 onwards.
 - There has been a further reduction in reports of loss of taste/smell, previous present 16% of cases in November dropping to 11-12% of cases with a string positive.
 - The UK COVID-19 Infection Survey collects data on characteristics of people testing positive for COVID-19, including data on symptoms for those who had strong positive tests - Ct value under 30 (see imbedded table below). These data are provisional, reflect infections reported in the community, and exclude infections reported in hospitals, care homes, or other institutional settings.
 - While the December data provide an indication of the common symptoms of the Omicron variant, Omicron was not dominant for the whole of December, so these data are not a complete representation and further information is required. Data from the UK COVID-19 Infection Survey which reported on what can be considered the beginning of the 'Omicron period' (20 December 2021 23 January 2022) indicates that approximately 54% of participants did not report any symptoms (within 35 days after first observed positive test), considered asymptomatic.[92]

| Symptoms | Percentage of people with this symptom within 35 days of a positive PCR, among those people with a Ct value under 30 | |
|--|--|----------|
| | January 2022 | May 2022 |
| Any symptoms | 61.27 | 59.71 |
| No symptoms (asymptomatic) | 38.73 | 40.29 |
| Classic symptoms (cough, fever, shortness of breath, loss of taste, loss of smell) | 49.46 | 51.73 |
| Loss of taste or smell | 11.1 | 11.89 |
| Gastrointestinal symptoms (abdominal pain, nausea or vomiting, diarrhoea) | 14.46 | 13.9 |
| Cough | 40.49 | 46.34 |
| Fatigue (weakness) | 34.13 | 37.14 |
| Headache | 36.63 | 34.54 |
| Sore throat | 35.71 | 37.64 |
| Fever | 21.12 | 22.77 |
| Loss of smell | 7.58 | 8.01 |
| Muscle ache (myalgia) | 23.25 | 22.82 |
| Loss of taste | 9.14 | 9.6 |
| Shortness of breath | 11.53 | 11.19 |
| Nausea or vomiting | 8.19 | 7.7 |
| Abdominal pain | 6.23 | 4.66 |
| Diarrhoea | 5.46 | 6.39 |

The above table is taken from the 22 June 2022 edition of UK COVID-19 Infection Survey. [4]

BA.2-specific clinical features (symptoms and severity) information

Preliminary analyses show no differences in frequency of hospitalisation for BA.2 compared to BA.1.

- Multiple studies have failed to show a difference in frequency of hospitalisations or severity between BA.1 and BA.2. [\[93-96\]](#)
- Data on Omicron in children suggested that symptoms were less severe than previous variants, and paediatric deaths were rare. However, these data were from populations in which a majority were already protected from past infection, vaccination or both. [\[97\]](#)
- A large study of an uninfected and unvaccinated population of children investigated severe outcomes among 1,147 children aged 11 years or below who were hospitalised between 5 February and 28 February 2022 (a BA.2-dominant period). Intrinsic severity of BA.2 in children who had no past COVID-19 or vaccination was determined to be not mild. [\[97\]](#)
 - Children hospitalised during the BA.2 dominant period had higher odds of PICU admissions, mechanical ventilation and oxygen use.
 - BA.2 was reported to be more neuropathogenic than previous SARS-CoV-2 variants, influenza and parainfluenza viruses, resulting in more seizures.

Omicron: vaccine effectiveness

Section updated: 16 May 2022

Vaccine effectiveness (VE)

Data described below relate to the original “wild type” vaccines (not an Omicron-based vaccine)

2 doses of Pfizer (primary course): VE against infection with Omicron is approximately 50% soon after 2 doses of Pfizer. Within 5-6 months of the second dose VE wanes to levels unlikely reduce transmission and the initial VE against hospitalisation of around 60-70% after a primary vaccine course declines to ~45%.

Booster dose: VE against infection with Omicron is around 55-70% after a booster dose of Pfizer, but also wanes. VE against hospitalisation increases to ~90% after a Pfizer booster dose (including in those over 65 years of age) and remains at above 70% 3 months after the booster. Duration of effectiveness of Pfizer vaccine against hospitalisation after a booster dose has not been fully established, but effects remain higher for longer than for protection against infection.

(Note: Pfizer and BioNTech have begun enrolment for a clinical trial to test the safety, tolerability, and immunogenicity of an Omicron-based vaccine candidate in 1,420 healthy adults aged 18-55 years. ([link](#)) Pfizer is hoping to be able to deliver the vaccine in (southern hemisphere) Spring 2022. However, testing in primates has shown no advantage of an Omicron specific mRNA (Moderna) booster over a booster with the regular Moderna vaccine ([link](#))).

Data from individual studies (Pfizer where available)

VE against infection, symptomatic infection and onward transmission

Summary of the international data:

- VE against infection with Omicron is 40- 55% soon after 2 doses of Pfizer. This represents an epidemiologically important reduction in transmission.
- VE against infection with Omicron wanes to levels unlikely reduce transmission within 5-6 months of the second dose
- VE against infection with Omicron is around 55-69% after a booster dose of Pfizer. Although there is some indication of waning after a booster dose, data about symptomatic infection in the UK suggests this occurs more slowly after a booster dose than after a primary course of Pfizer, with VE against symptomatic infection remaining above 50% in those that had received a booster more than 10 weeks prior.
- Data about onward transmission are scarce and are only available for “all vaccines” and not Pfizer alone. Non-peer-reviewed data from a small study suggest that vaccinated people infect fewer people in their household (a setting where many “exposure events” are likely to occur, generally resulting in lower “vaccine efficacy” than in settings with less intense contact.

SARS-CoV-2 Variants of Concern Update

Table 2: Vaccine effectiveness on transmission related parameters (Omicron)

| Vaccine | Outcome | 2 doses (95% CI in brackets) | | | 3 doses (95% CI in brackets) | | |
|--------------------|--------------------------------|---|---|--|---|---|---|
| | | Soon after | Later effect | Data not reported by time since 2nd dose | Soon after | Later effect | Data not reported by time since 3rd dose |
| Pfizer (all doses) | Infection | Denmark[103]*: 1-30 days 55% (24- 74%) 31-60 days 16% (-21 – 42%) 61-90 days 10% (-10 – 26%) Denmark [104] 14-30 days 40% (38-41%) | Denmark[103]*: 91-150 days -76% (-95 - -60) Denmark [104] >120 days 13% (13-14%) | Portugal[105]*: 28% (12-41%)† | Denmark[103]*: 1-30d 55% (30- 70%) Denmark [104] 14-30 days 55% (55-56%) | Denmark [104] >120 days 50% (47-53%) | Portugal[105]*: 69% (46-82%)† |
| | Symptomatic infection** | UKHSA [76]: 14-28d¥ 64% (62-66%) | UKHSA [76]: 70-98d¥ 29% (27-30%) >180d¥ 14% (12-16%) | | UKHSA [76]: 14-28d¥ 68% (66-70%) | UKHSA [76]: >70d ¥ 54% (52-56%) | USA [106]: 65% (62-68%), estimate vs. 2 doses almost identical. Qatar[107]*: Only VE relative to primary course (shows booster prevents 50% (47-53%) of symptomatic infections |

SARS-CoV-2 Variants of Concern Update

| Vaccine | Outcome | 2 doses (95% CI in brackets) | | | 3 doses (95% CI in brackets) | | |
|--|------------------------------|--|--|---|--|---|---|
| | | Soon after | Later effect | Data not reported by time since 2nd dose | Soon after | Later effect | Data not reported by time since 3rd dose |
| | | | | | | | that occur with only a primary course). |
| | Onward transmission | No Data | | | No Data | | |
| mRNA (Moderna, or Moderna and Pfizer) | Infection | USA [108]: 14-90 days 44% (35-52%) | USA [108]: 91-180 days 24% (16-30%) 181-270 days 14% (10-17%) >270 days 6% (0.4 - 11%) | USA [108]: 14% (11 – 17%) USA [65]*: 25% (20 – 30%) | USA [108]: 14-60 days 72% (70-73%) | USA [108]: >60 days 47% (41- 54%) | USA [108]: 70% (68% - 79%) USA [65]*: 62% (59 – 65%) |
| | Symptomatic infection | No data | | | No Data | | |
| | Onward transmission | No data | | | No Data | | |
| All vaccines | Infection | | | UKHSA (SIREN study) [76]: 32% (-6-57%)§ Netherlands: [109]* 33% (31-35%) Norway[110]*: 27% (6 – 49%)‡ | | | UKHSA (SIREN study) [76]: 62% (41-75%)§ Netherlands: [109]* 68% (67-69%) Norway[110]*: 45% (26 – 57%)‡ |

SARS-CoV-2 Variants of Concern Update

| Vaccine | Outcome | 2 doses (95% CI in brackets) | | | 3 doses (95% CI in brackets) | | |
|---------|------------------------------|------------------------------|--------------|--|------------------------------|--------------|---|
| | | Soon after | Later effect | Data not reported by time since 2nd dose | Soon after | Later effect | Data not reported by time since 3rd dose |
| | | | | | | | Spain [111]*: Only VE relative to primary course (shows booster prevents 51% (50- 52%) of infections that occur with only a primary course). |
| | Symptomatic infection | No Data | | | No Data | | |
| | Onward transmission | | | Norway[110]*: % house contacts infected by: Unvaccinated 57% (51 - 62%) Partial primary 42% (34 – 49%) Full primary 51% (47 – 55%) | | | Norway[110]*: % house contacts infected by: Unvaccinated 57% (51 – 62%) Boosted 46% (36 – 55%) ‡ |

* pre-print. Findings not peer reviewed so may change

**additional data available from Hong Kong but appears to exclude those with severe disease. [112] VE 31% (2%-52%) after 2 doses, VE after 3 doses 20-59 years 72% (55-82%), 60+ years 72% (43%-86%)

† Indirect calculation of VE by multiplication of estimates

‡pre-print with substantial changes in estimates since first posted. Note that study looks at transmission within households, where frequency of contact is higher, often resulting in lower VE estimates than for “per contact” VE estimates (for “leaky vaccines”)

¥ Data points not reported in text. Estimates read from graph, below (Figure 1)

§ Data reported are for those with no prior COVID-19 infection. For those with prior infection these values are 60% (95% CI: 36-75) after 2 doses and 71% (95% CI: 56-82) after 3 doses

In terms of VE against Omicron in comparison to VE against Delta, data from multiple studies [34, 62, 63, 76, 103, 113-115] all suggest reduced VE for 2-dose Pfizer vaccine regimens against symptomatic disease caused by Omicron compared with Delta.

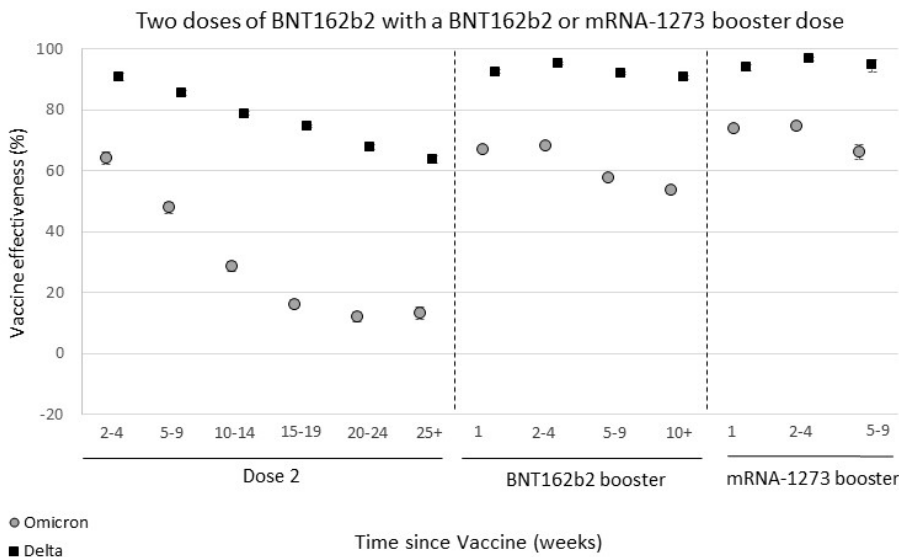


Figure 1: Pfizer vaccine effectiveness against symptomatic disease by period after 2 doses and after a booster.[76]

VE against hospitalisation / severe disease

VE after receiving a booster dose:

Data from multiple countries (UK, South Africa, USA, Denmark, and Hong Kong) show high vaccine effectiveness (VE) of 89% - 92% against hospitalisation for people aged 18-59+ years >2 weeks after receiving a booster including for those people aged 65 years or older. [104] [116] [117] [118] [119] After 10 or more weeks the VE wanes to approximately 75-83%. [116] [117]

A study from Hong Kong found that relative VE against severe disease compared to primary course is highest for people aged 60+ years. [112]

VE after receiving two doses (primary course):

Data from multiple countries show a vaccine effectiveness of 62% - 70% >2 weeks after receiving the second dose. [76, 118] [118] A US study with mRNA vaccines reported a higher VE of 81%. [119]

After 5-6 months the VE declined to 44% and 57% in the US mRNA study [76] [119], whereas a Danish study reported an increase to 66% after 4 months. [104]

VE against death

Qatar: relative VE (compared to the primary course) against any severe, critical, or fatal COVID-19 for a Pfizer booster dose was estimated at 100.0% (95% CI: 71.4-100.0). [107]

Hong Kong: relative VE (compared to the primary course) against mortality for 20-59 years was 83% (-29-98%), 60-69 years 82% (20-96%), 80+ years 66% (-1.3-89%).[112]

VE of second booster dose (fourth dose)

Some countries recommend the administration of a second booster dose to elderly populations or individuals at increased risk of severe disease or exposure.

Compared to people vaccinated with 1 booster dose of Pfizer, the marginal VE against infection of a fourth dose peaks at 64% (62-66%) during the third week [\[120\]](#) and provides significantly enhanced protection against severe illness with adjusted rate ratios ranging from 3.4 (2.5-4.7) to 4.3 (2.6-7.1) after week 4 to 6 weeks. [\[121\]](#) For people aged 60+ year VE peaks after 3-4 weeks at an adjusted rate of 2.1 [\[121\]](#)

A study on efficacy showed the VE 14 to 30 days after the receiving the second booster dose was 52% against PCR confirmed infection, 61% against symptomatic infection, 68% against hospitalisation, and 76% against death compared to one booster dose. [\[122\]](#)

However, marginal VE (relative to the first booster dose) begins to decline four weeks after inoculation, dropping to 29% (18-39%) after nine weeks. [\[120\]](#)

Data from reviews (all vaccines)

A WHO weekly epidemiological report (22 June 2022) included an updated summary of evidence on Omicron, including for vaccine effectiveness. [\[124\]](#)

The WHO notes that results of vaccine effectiveness (VE) studies should be interpreted with caution because estimates vary with the type of vaccine administered and the number of doses and scheduling (sequential administration of different vaccines). [\[124\]](#)

Some key points from the WHO interpretation of results of VE for the Omicron variant include:

- To date, 23 studies from ten countries have assessed the duration of protection against the Omicron variant of five vaccines.
- Findings from these studies show reduced VE of primary vaccine series against the Omicron variant than has been observed for previous variants, for all outcomes (severe disease, symptomatic disease, and infection).
- However, in the majority of studies, VE estimates against the Omicron variant remain higher for severe disease.
- VE estimates against symptomatic disease and infection within the first three months of primary series vaccination tended to be lower than those against severe disease, and VE decreased more substantially over time.
- Booster vaccination substantially improves VE for all outcomes, but studies that assess VE of booster vaccination beyond 6 months are needed to evaluate the longer duration of protection.

SARS-CoV-2 Variants of Concern Update

A more detailed summary of the WHO VE interpretation is below, highlighting results particularly for mRNA vaccines and AstraZeneca.

| Outcome | Timing | WHO summary of VE results for Omicron (as at 22 June 2022) |
|----------------------------|---|--|
| Severe disease | Within first three months of primary series vaccination | mRNA vaccines: seven of 13 (54%) VE estimates were $\geq 70\%$ AstraZeneca: one study reported VE of $< 70\%$ |
| | Beyond three months after vaccination | mRNA vaccines: 13 of 29 (45%) VE estimates for the mRNA vaccines were $\geq 70\%$ while 20 (69%) were $\geq 50\%$ AstraZeneca: one of the 12 (8%) VE estimates was $\geq 70\%$ while eight (67%) were $\geq 50\%$ |
| | Between 14 days and three months after receipt of booster | A booster dose improved VE estimates against severe disease in all studies, with only one estimate for Pfizer as the booster dose below 70%. |
| | Three to six months post mRNA booster | 17 of 20 (85%) estimates showed VE $\geq 70\%$ (an mRNA vaccine was given as the primary series in 13 of the 20 estimates while AstraZeneca-Vaxzevria and Sinovac-CoronaVac were given as the primary series for six and one of the twenty estimates, respectively). |
| Symptomatic disease | Within first three months of primary series vaccination | Only three of 13 (23%) VE estimates for the mRNA vaccines were $\geq 70\%$, and seven (54%) were $\geq 50\%$; all the three (100%) VE estimates for AstraZeneca were below 50%. |
| | Beyond three months after vaccination | Only 1 of 29 (3%) of the VE estimates were $\geq 50\%$ (21 estimates evaluated mRNA vaccines, six evaluated AstraZeneca) |
| | Between 14 days and three months post booster | An mRNA booster after completion of a primary series of an mRNA vaccine, AstraZeneca-Vaxzevria, or Sinovac-CoronaVac, improved VE estimates against symptomatic disease, with five of 21 (24%) VE estimates $\geq 70\%$ and 16 (76%) estimates $\geq 50\%$, between 14 days and three months post booster. |
| | Three to six months following receipt of an mRNA booster dose | Booster dose protection declined with time since vaccination, with only 2 of 13 (15%) available estimates indicating a VE of $\geq 50\%$ at three to six months following receipt of an mRNA booster dose. Estimates for a booster dose of AstraZeneca-Vaxzevria (one estimate) and Sinovac-CoronaVac (one estimate) three to six months post vaccination indicated VE of $< 50\%$. |
| Infection | | VE estimates against infection showed a similar pattern as those against symptomatic disease. |

Vaccine response in T-cells & B cells

Section updated: 01 July 2022

A longitudinal study in vaccinated UK health care workers showed that immune response varies based on previous infection and vaccination. [3]

- The study found that different infection histories alongside different timings of vaccination had an impact on immune response against Omicron.
- The study results most relevant to the New Zealand population (vaccinated, and either infection naïve or post-Omicron infection) were that Omicron infection in vaccinated people resulted in some enhancement of neutralising antibody and T-cell response against Omicron, but this enhancement was less than that observed against earlier variants (Alpha and Delta).
- The study cohort contained only vaccinated participants, so the magnitude of immune response to Omicron infection could not be compared to the response in people naïve to any SARS-CoV-2 antigen exposure.
- The study investigators hypothesise that previous order of exposure to SARS-CoV-2 antigens (through vaccination or infection) results in immune imprinting, which affects response to subsequent SARS-CoV-2 exposures.

Vaccine effectiveness/efficacy in Children

Vaccination in children is generally split into different age groups. **Note: age categories are different between Pfizer-BioNTech and Moderna COVID-19 vaccines:**

| Pfizer | | Moderna | |
|------------------|---------------------------------|------------------|---------------------------------|
| Age Group | Eligible for vaccination in NZ* | Age Group | Eligible for vaccination in NZ* |
| 6 month –4 years | Not yet | 6 month –5 years | Not yet |
| 5-11 years | Yes | 6-11 Years | Not yet |
| 12-17 years | Yes | 12-17 years | Yes |

*As of June 2022

Risks to Children under 5 years

- Children are less at risk of becoming severely ill with COVID-19 compared to adults. [7] However, according to the CDC:
 - Five times as many children aged 0-4 years were hospitalised during the Omicron wave (Dec, 2021) than from the Delta wave [7]
 - more than 200 deaths of 0-4 year olds have been reported in the US due to COVID-19 since Jan 2020. This accounts for 1.7% of all deaths in this age group [8]
 - multisystem Inflammation Syndrome (MIS-C) is being seen in children after a SARS-CoV-2 infection with no alternative diagnosis. This is categorised as severe illness, with multisystem organ involvement, fever and inflammation. Although relatively uncommon, MIS-C can present approximately 2-6 weeks following acute infection and generally requires intensive care treatment, with 1-2% of patients dying [8, 125]
 - long COVID has had impacts on children in this age group with known histories of SARS-CoV-2 infection experiencing symptoms such as fatigue, loss of smell and loss of taste at higher frequencies than children without prior infections [8]
- On the 15 June, an FDA panel endorsed both Moderna and Pfizer COVID-19 vaccines for use in children aged 6 months to 4 years. This was endorsed by the FDA's Vaccine and Related Biological

Products Advisory Committee who voted unanimously to recommend the use of either vaccines which they deemed to be safe and effective in young children against COVID-19. CDC official Sara Oliver says the agency is not favouring one vaccination (Moderna or Pfizer) over the other but that either vaccine is better than none ([Washingtonpost](#)).

- Both vaccines are mRNA based and have the potential to generate antibody levels like those induced in young adults following vaccination.
- These levels are considered to be protective although this is speculative as the link between antibodies and level of protection is unknown.
- A study (April 2022) suggests that approximately 3 out of 4 children in the US have antibodies that show previous infection with SARS-CoV-2, [9] however, the CDC is still recommending vaccination in this group to prevent reinfection

Pfizer COVID-19 Vaccine (Children 6 months- 4 years)

- Pfizer has submitted an amended Emergency use Authorization (EUA) to the FDA for the use of the Pfizer-BioNTech COVID-19 vaccine in children 6 months to under 5 years. [126] Details of the primary course are:
 - a three-dose series of 3 µg each (compared to two doses of 10 µg in 5-11 and 30 µg doses for all older age groups)
 - intervals of 3 weeks between first and second dose and at least 8 weeks between the second and third dose.
- Overall Pfizer noted that the three doses in 6 month-4 year olds elicited a strong immune response (discussed below with clinical results) and was well tolerated, presenting mild to moderate side effects.
- The data submitted to support the EUA was from an ongoing Phase II/III trial (C4591007). Only data analysed before the 29 April 2022 was included in the EUA, this encompassed safety data from 1,678 children under 5 years old. The trials was a randomised, double blinded trial with 2:1 (placebo control: vaccination). [126]
 - The trial split the participants into two cohorts by age, 6-23 months and 2- 4 years. Patients with a history of past SARS-CoV-2 infection were not excluded from the study.
 - Safety and effectiveness data was collected following the second dose for both age groups. This measured neutralizing geometric mean titres (GMTs) and seroresponse rates were assessed against a reference strain.
 - Following analysis of safety and effectiveness data after the first two doses, the protocol was amended to include a third primary dose. After the third dose the trials end points and success criteria were met. [126]
- Trial efficacy:
 - The 2–4 year old cohort had vaccine efficacies of 30% (first dose only) and 40% (second dose). This did not meet that the pre-specified immunobridging success criteria in the 2–4 years cohort.
 - Preliminary analysis of efficacy after a third dose was reported as follows:
 - 6 -23 month cohort: 75.6% (95% CI: -369.1%, 99.6%)
 - 2-4 year old cohort: 82.4% (95% CI: -7.6%, 98.3%)
 - Combined analysis of both age groups: 80.4% (95% CI: 14.1%, 96.7%).
 - Exploratory analysis for immunogenicity against Delta and Omicron variants was performed. This noted similar GMT against Delta (Using B.1.617.2) although significantly lower for Omicron (using BA.1 strain). As this was exploratory, the sensitivity of the assay is unknown. [126]
- Trial Safety:

- Serious adverse effects (SAE) were reported in similar frequencies in the vaccinated and the placebo groups.
 - 6-23 months cohort: 3.1% reported SAE after vaccination and 2.3% after placebo. The most reported SAE included respiratory illnesses, gastrointestinal or infections, all of which are common within this age group.
 - 2-4 years cohort: 0.7% reported SAE after vaccination and 0.9% after placebo. [\[126\]](#)
- The risk of SAEs was lower in 6 month-4 year olds what is generally seen in all other age groups (likely due to the lower dose of mRNA). [\[126\]](#)
- This clinical trial did not indicate any new safety concerns compared to the safety profile of vaccination in older people. [\[126\]](#)
- Limitations leading to risk in vaccinating 6 month-4 year olds includes uncertainties in:
 - incidence of myocarditis/pericarditis in this age group
 - safety data available in subpopulations (i.e., immunocompromised children or previously infected children). [\[126\]](#)

Moderna COVID-19 Vaccine (Children 6 months – 5 years)

Moderna has received FDA authorization for emergency use of COVID-19 vaccine for children 6 months of age and older. [\[127\]](#)

- The Moderna vaccine for 6 month to 5 year olds is a two-dose primary vaccination (25 µg doses, 1 month apart). This is again a lower dose than provided to adults (100 µg/dose). [\[127\]](#)
- The two dose schedule means that the primary course is completed in approximately 1/3 of the time frame required to complete the Pfizer primary course.
- Moderna submitted clinical data from the KidCOVE trial supporting the use of vaccine in 6month to 5 year olds. This was a randomised, observer blind, placebo control study designed to evaluate the safety, immunogenicity and tolerability of the vaccination. Data from approximately 6,700 children was included in the FDA submission. [\[127\]](#)
- Data was separated by the following age groups:
 - 6 months – 23 months
 - 2 years – under 6 years
- KidCOVE that meet the following objectives:
 - Safety (Primary objective)
 - The vaccine was tolerated by the 6month to 5 year olds in a consistent way to all other age groups, including adults.
 - Adverse effects were mainly mild or moderate, with more reported following the second dose than the first. Less than 0.2% on participants were reported to have fevers over 40°C following vaccinations.
 - No new safety concerns were raised
 - No reports of myo/pericarditis, MIS-C or deaths.
 - Immunogenicity (Primary objective)
 - Interim results, released on 23 March 2022, showed a robust neutralising antibody results in children aged 6 months - 5 year old which was comparable the response in young adults (despite the lower dose vaccine).
 - Efficacy (Secondary objective)
 - Vaccine efficacy was 51% and 37% for 6-23 month and 2-5 year olds respectively.
 - This was considered as satisfactory to the studies primary objective and comparable to adult efficacy to Omicron.

Children aged 5-11 years

- Since January 2022, children [aged 5 - 11 years](#) have been eligible for two doses of Pfizer, with 8 week intervals between doses in New Zealand. Children are not currently eligible for third doses, unless severely immunocompromised.
- Currently, only the Paediatric dose of Pfizer is offered to this age group in New Zealand.

Pfizer COVID-19 Vaccine (Children 5-11 years)

- The primary series for two dose this age group is 10 µg per vaccination (compared to three doses of 3 µg in 6month-4 years and two doses of 30 µg doses for 12 years and older age groups)
- Prevention of infection from Omicron after two doses of Pfizer in children aged 5-11 ranges from 31% to 68%.[\[128, 129\]](#) Multiple studies have evidence of a significant reduction in the efficacy of the Pfizer vaccine in 5 to 11 years in preventing infection against Omicron compared to the 90.7% reported before the emergence of Omicron during a high Delta prevalence.[\[130\]](#)
- A preprint study has shown evidence that the effectiveness of the Pfizer vaccine may wane more rapidly in 5–11 year olds than other age groups.[\[131\]](#)
- The study reported a 65% vaccine efficacy against infection within 14 days of vaccination, but this declined rapidly to just 12% within 28-34 days.[\[131\]](#) Adolescents are afforded a greater level of protection against infection from Omicron by the Pfizer vaccine. [\[128\]](#)
- One study found a vaccine efficacy against infection from Omicron for 12-15 year olds remains >59% 150 days after vaccination. [\[128\]](#) Similarly, it was found that vaccine efficacy against infection in 12-17 year olds was 66% within 14 days of vaccination but only decreased to 56% within 28-34 days.[\[131\]](#)

Omicron: immune evasion

Section updated: 16 May 2022

Neutralising assays

- Neutralisation studies provided initial data predicting lower vaccine effectiveness against Omicron than for previous variants.[\[132-137\]](#) These data have now been superseded by effectiveness data.
- BA.2 does not appear to have a greater capacity for immune evasion by antibody neutralisation than BA.1. [\[138-140\]](#)

Cell-mediated responses

While data remain preliminary, an increasing number of studies indicate that vaccination provides a durable T-cell response to Omicron infection.[\[132, 141-144\]](#)

Immunopathological characteristics

Omicron breakthrough patients had a more robust IFN-γ response (critical for viral clearance) and lower concentration of proinflammatory cytokines at the acute phase of infection. They also had lower frequency of immature neutrophils indicating milder inflammatory response.[\[54\]](#)

Reinfection

Reinfection after previous infection with a “pre-Omicron” variant

- Two studies have reported a estimated effectiveness of prior infection with a pre-Omicron variant against Omicron reinfection ranges from 19% to 61.9% [\[76, 145, 146\]](#). Effectiveness against hospitalisation/death was 87.8%. [\[145\]](#)

- Omicron was associated with a 5.41-fold (95% CI: 4.87-6.00) higher risk of reinfection than Delta, controlling for vaccination, age, and ethnicity. Reinfection risk is slightly higher at 6.36-fold for unvaccinated individuals vs 5.02-fold for vaccinated. [\[146\]](#)
- A New Zealand study investigated neutralising antibody activity over time using sera from a cohort of Southern District Health Board PCR-confirmed cases infected between 11 March and 5 April 2020.
 - Neutralising antibody activity was assessed to Omicron and earlier variants, including Delta, at 11 months post infection, with a key finding being the limited cross-neutralisation of Omicron from a previous non-Omicron infection. [\[147\]](#)
- UK data from the COVID-19 Infection Survey reported in February 2022 that there were more reinfections in a month when Omicron became the dominant variant (764 reinfections), than in the previous 18 months (586 reinfections). Unvaccinated people were approximately twice as likely to be re-infected than people who had their second vaccine 14 to 89 days previously. [\[148\]](#)
 - The reinfection rate was reported as increasing from 11.7 to 180.3 per 100,000 people since Omicron became the dominant variant (proportion vaccinated not specified).

Reinfection after previous Omicron infection

- Data from Qatar indicate strong protection against Omicron sub-lineage reinfection provided by a previous Omicron infection (regardless of the sub-lineage causing the primary infection) with an effectiveness of over 85%. [\[149\]](#).
- UK data on BA.2 reinfection is being monitored as part of the SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study of NHS healthcare workers and is summarised in UKHSA reports. [\[17, 150\]](#)
 - A small number of sequence-confirmed BA.2 reinfections after BA.1 infection have been identified and that these reinfections have been predominantly in unvaccinated people. [\[150\]](#)
 - The SIREN study defines reinfection as: new PCR positive infections 90 days after a previous PCR positive date or 28 days after antibody positivity consistent with prior infection. [\[17\]](#)
- Neutralisation studies support protection from BA.2 reinfection after BA.1 infection in those vaccinated. [\[150\]](#)
 - A cross-neutralisation study using human sera from unvaccinated individuals infected with BA.1 showed similar, but slightly lower neutralisation activity of BA.1 sera against BA.2 (and BA.3). [\[151\]](#)

Omicron: effectiveness of therapeutics

Section updated: 30 June 2022

Therapeutic use for treatment of COVID-19

- Most people can safely manage their own COVID-19 symptoms at home. However, for people with increased risk factors or comorbidities, different therapeutic options may provide improved outcomes for the patient.
- The Ministry of Health has an overview [about COVID-19 therapeutics](#) and [advice for healthcare professionals](#) websites.
- Therapeutic options currently include antiviral medications (paxlovid, remdesivir, molnupiravir), anti-SARS-CoV-2 monoclonal antibodies (evusheld, sotrovimab), immunomodulators (bara tocilizumab) and anti-inflammatory drugs (dexamethasone, budesonide) available as EUA for COVID-19 management.[98] The utility, effectiveness and need for each of these options is different between individuals, and criteria for each is specific, based on disease severity and individual risk factors.
- The emergence of new variants produces challenges to the therapeutics as adaptive mutations can completely alter the viral genome and pathogenic potential. New variants that become VOC are often associated with increased virulence, pathogenicity and transmissibility which may help them evade the immune response and have decreased effectiveness to current therapeutics. [6, 98]

Therapeutics in relation to BA.4 and BA.5

- Many monoclonal antibodies showed reduced efficacy against Omicron variants relative to Delta.[5]
- Additionally, although many of the newer Omicron subvariants are derived from BA.2, there are significant mutations to in the spike.[6] It has been established that this reduces the sensitivity to vaccine-induced neutralising antibodies.[99, 100] As a result, it becomes likely that these variants will also have reduced sensitivity to therapeutic monoclonal antibodies.[6]
- Evusheld is a long-acting antibody combination (tixagevimab and cilgavimab) derived from the B cells of individuals previously infected by SARS-CoV-2. There are conflicting data supporting its effectiveness against BA.4/5.
 - A [press release](#) by AstraZeneca (who manufacture the drug) reports data from multiple sources showing neutralising against BA.2, the global dominant variant currently, and all other variants tested to date (May, 2022). One study, [101] based at the University of Oxford, has in vitro data showing that Evusheld retains neutralisation efficacy against Omicron variants including BA.4 and BA.5.
 - In contrast, another study reported that BA.4/5 showed an increased resistance to Evusheld compared to BA.2 variant. This was estimated at an increase of approximately 20-fold times resistant.[6]
- A preprint study suggested that among the therapeutic antibodies authorized for clinical use, only bebtelovimab (LY-COV1404) retains full potency against both BA.2.12.1 and BA.4 and BA.5. [102]

Omicron: Detection

Section updated: 16 May 2022

PCR

Most observational studies have relied on SGTF as a proxy for Omicron, which identify BA.1 but not BA.2. Therefore, caution is required when interpreting comparative analyses which use S-gene target results as the only determinant of Omicron and Delta.

- BA.2 lineage generally does not have the spike deletion at 69-70 that causes S-gene target failure (SGTF).^[76] Nicknamed “stealth” version of Omicron as it cannot be detected using PCR tests that detect SGTF, such as Thermo Fisher’s TaqPath. ([link](#))
- This has implications on using PCR tests that detect SGTF as a proxy for rapidly detecting Omicron cases. It should be noted that as at 30 March 2022, the UKHSA reported that 0.16% of BA.2 samples sequenced had the deletion at position 69-70.^[11]

RATs

Evidence on the performance of RATs is of two main types: analytical studies that use stored/’spiked’ samples of the virus; and clinical studies that measure real-world performance. It is generally understood that laboratory experiments cannot fully replicate the real-world application of a test kit and clinical performance studies are required.

Due to the time needed to establish and perform research studies the current evidence base contains more analytical than clinical studies, refers to the BA.1 variant, and is mostly from pre-print sources. Summary of current evidence on detection of the Omicron variant:

- Published analytical studies - four investigated the performance of various RATs. Three found similar sensitivities for both Omicron and Delta ^[152-154], and one found reduced sensitivity for Omicron.
- Pre-print analytical studies - four (one using CareStart, and one using Clinitest RATs that are authorised in NZ,) found no change in sensitivity between Omicron and Delta ^[155-158], and one reported some reduced sensitivity. ^[159]
- Pre-print clinical performance study - a good quality study using BinaxNOW (not currently authorised in NZ) found sensitivity of only 52.1% compared to RT-PCR in Omicron cases confirmed by whole genome sequencing. ^[160] However, sensitivity could be improved to 75.7% by changing the RT-PCR positivity threshold from Ct of 40 to Ct of 30. Unfortunately, this study did not compare sensitivity with other variants. A low quality study found two RATs (neither authorised in NZ) yielded higher false negative rates. ^[161] A moderate quality study found the performance of 3 RATs (including BD Veritor that is authorised in NZ) in detecting Omicron was not inferior to Delta.^[162]
- Pre-print studies on swab sample site - four addressed the issue of whether sensitivity varies by swab sample site. All assumed cases were Omicron during large community outbreaks. Three studies used the Abbott Panbio RAT (which is authorised in NZ) and found that mid-turbinate swabs perform better than buccal. ^[163] The second study used a RAT not currently authorised in NZ and found oral cheek specimen was significantly less sensitive than nasal swab. The third study compared nasal, throat, and combined nasal/throat swabs and found support for the combined method is self-perceived asymptomatic individuals.^[164] The fourth compared sensitivity for MT (66.7%), OP (82.2%) and saliva (72.5%) specimens, concluding the data do not support a preferred sample type for Omicron ^[165].
- Government reports – The UKHSA published a preliminary analysis of the performance of four RATs with Omicron on 17 December 2021. ^[166] One of these is authorised in NZ (Orient Gene). They

reported the RATS “all of which target the nucleocapsid protein, have detected the new Omicron variant that contains 4 amino acid changes from the original viral sequence.” The FDA state they are working on the issue of Rat performance [167], the ECDC’s latest guidance is pre-Omicron [168], and the WHO reported in December 2021 that no reduction in RAT sensitivity has been reported so far.[169]

- Manufacturer statements - most RAT manufacturers have issued statements about the ability of their products to detect Omicron.[170-172] Unfortunately, these tend to lack supporting evidence, and can therefore be considered very low quality.

New signals

Section updated: 01 July 2022

The risk of clinically significant emerging variants is considered to be high, according to the WHO.^[173] The WHO has expressed concern that during recent months, 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.^[174]

This section covers BA.4/BA.5 and then BA.2.12/ BA.2.12.1/ BA.2.12.2, followed by recombinant variants.

BA.4 and BA.5

- BA.4 and BA.5 are Omicron sub-lineages that were first detected in South Africa in January and February 2022 respectively.^[175] The WHO began tracking these sub-variants in mid-April. Both BA.4 and BA.5 had been identified at the NZ border as of 4 May 2022.^[176] The number of countries reporting detection of the BA.4 and BA.5 variants is rising, along with the number of cases.^[14]
- BA.4 and BA.5 have many mutations in common with the BA.2 variant.^[14] They also have a number of additional mutations. The BA.4 and BA.5 sub-variants tend to be discussed together because the mutations in their spike protein gene are identical (though they differ in mutations found elsewhere in the genome).^[14]
- Both lineages contain the amino-acid substitutions L452R, F486V, and R493Q in the spike receptor binding domain compared to BA.2.^[13] SGTF is present in BA.4 and BA.5.^[22]
- Preliminary studies suggest that BA.4 and BA.5 have a significant change in antigenic properties compared to BA.1 and BA.2, especially compared to BA.1.^[175]
- As of 19 June 2022, the proportion of Omicron sequences submitted to GISAID that were BA.4 and BA.5 has risen from 9% to 12% and 28% to 43% respectively, compared to the previous week. ^[1] BA.4/BA.5 prevalence in the EU ranges from 53% in Belgium to 93% in Portugal as of 02 July 2022. ^[177] At June 24th BA.4 and BA.5 are dominant in the UK, with an estimated 22% of cases being BA.4 and 39% BA.5. ^[2] Updated UK modelling shows the relative growth advantage for BA.5 is larger than BA.4 and it is therefore most likely that BA.5 will become the dominant variant in the UK.
- In the UK for the period 8th April to 8th June, the median weekly growth rate was 76% for BA.4 over BA.2 and 66% for BA.5 over BA.2. ^[2] For the week of 8-14th May, the estimated daily growth advantage for BA.5 over BA.2 was 13% in Portugal, similar to the 12% daily growth advantage previously reported by South Africa.^[175]
- Early UK analysis of BA.4/5 shows no reduction in vaccine effectiveness relative to BA.2 after previous positivity, testing pillar, health and social care worker status, clinical risk status, age, gender, and week of test were adjusted for. However, this is a preliminary analysis and does not take into account the time since last vaccination.^[2] There are insufficient data for a robust assessment of the effectiveness of COVID-19 vaccines against mild or severe disease with BA.4 and BA.5. ^[2]
- A preprint study that used sera from both vaccinated and boosted individuals, found BA.4 and BA.5 to be significantly more (4.2-fold) resistant to neutralization than BA.2. This suggests that breakthrough infections of vaccinated individuals may be more likely than with BA.2. ^[102]

- A study investigating neutralizing immunity using blood samples from participants previously infected with BA.1 and with or without vaccination against live virus. [178] The vaccinated group (3 doses) showed 5-fold increased neutralization capacity of BA.4/BA.5 when compared to the unvaccinated group. This indicates better protection in vaccinated individuals, although it is likely this protection will decrease over time with waning. [178]
- Both BA.4 and BA.5 are capable of escaping immune protection induced by infection with BA.1. [175]
- **No increase in severity of disease has been observed with BA.4/BA.5 compared to previous Omicron sub-lineages.** [13, 29, 30]

BA.2.12 and BA.2.12.1

- New York State Department of Health announced the emergence of two Omicron subvariants in New York State, BA.2.12 and BA.2.12.1 on 13 April 2022, both sub-lineages of BA.2. [179]
 - Estimated to have a 23% – 27% growth advantage above BA.2. New York Department of Health reported no evidence of increased disease severity by these subvariants. [179]
 - The CDC estimated 36.5% (95% PI 28.9-44.9%) of COVID-19 cases in the United States to be BA.2.12.1 as of 30 April 2022.
- BA.2.12.1 has a substitution mutation at the L452 location (L452Q). This is similar to BA.4/B.5 which have L452R. [180]
 - A mutation to L452 location has arisen independently in other variants including Delta, Epsilon, Kappa. This mutation is linked to immune evasion and cell binding, making it a mutation of interest in new variants. [181]
- BA.2.12.1 has been shown to have increased immune evasion abilities compared to BA.2. [181]
 - BA.2.12.1 has strong neutralising evasion against plasma taken from people with previous BA.1 infection (both 3-dose vaccinated and unvaccinated). [181].
- A preprint study that used sera from both vaccinated and boosted individuals, found BA.2.12.1 to be modestly more (1.8-fold) resistant to neutralization than BA.2. [102]
- Cell culture experiments showed increased replication efficiency of BA.2.12.1 in human alveolar epithelial cells than BA.2, producing viral titres that were 61-fold higher than cells infected with BA.2. [182]

Recombinants

- Viruses naturally evolve and are continuously changing as a result of genetic selection. [183] They can undergo minor genetic changes through mutation, as well as major genetic changes through recombination. [183]
 - The frequency of creation of recombinants between two variants depends on the duration of their co-circulation, the time until viral clearance, and the number of people exposed to both viruses. [184]
- The WHO continues to closely monitor and assess the public health risk associated with recombinant variants, alongside other SARS-CoV-2 variants, and will provide updates as further evidence becomes available. [173]
 - The Pango dynamic nomenclature system gives recombinant viruses a two-letter abbreviation starting with X.

- Three SARS-CoV-2 recombinant variants with evidence of person-to-person transmission have been reported: XD (AY.4/BA.1 recombinant, where AY.4 is Delta), XE (BA.1/BA.2 recombinant) and XF (another AY.4/BA.1 recombinant).
- XE was first reported in New Zealand on 23 April 2022. [\[185\]](#) Sequencing data from ESR had not found any of the other known recombinant variants, or an original recombination variant, in New Zealand.

Delta Overview

Section updated: 20 May 2022

- UKHSA no longer classifies Delta as a Variant of Concern, however the WHO does.
- A study has raised concerns that Delta could continue to pose a threat. ([link](#))
 - Variants tend to disappear when dominated by the next variant.
 - Wastewater surveillance in Israel found that even at the height of the Omicron wave, the Delta variant was still detected at low levels. [\[186\]](#)
 - Modelling suggests that Omicron levels may decrease until it is eliminated, while the Delta variant could maintain its 'cryptic circulation', possibly resulting in the re-emergence of a Delta wave or generation of a new variant.

Glossary of Terms

| | |
|---|---|
| The AstraZeneca vaccine | AZD1222 or ChAdOx1 |
| The Pfizer/BioNTech vaccine | Comirnaty/BNT162b2 |
| Global Initiative on Sharing Avian Influenza Data (GISAID) | This is a consortium that promotes and provides open access to SARS-CoV-2 genomic sequence data. Its original purpose was for sharing data on avian (bird) flu. |
| Immune escape | The ability of the virus to evade our body's immune response. See also Immune response. |
| Immune response | The response of our immune system to an infection. It includes development of specific antibodies to the virus and also cell-mediated responses (triggered by T cells). |
| Mutation | Small change made to the pattern of nucleotides that make up the virus. These occur as the virus spreads and replicates. Most do not confer a benefit to the virus. |
| Naming mutations | Mutation nomenclature (i.e., how they are named), describes what occurred at a specific location of the genome. For example, the 'E484K' mutation means that at the position 484, the amino acid changed from glutamic acid (E) to lysine (K). When a deletion occurs, the location is provided (e.g., deletion 144). |
| N-terminal domain | Part of the spike protein of the SARS-CoV-2 virus. |
| R₀, Reproductive number | The reproductive number R ₀ (R-naught), is a measure of how contagious a disease is. It is the average number of people who would catch a disease from one infected individual when there are no control measures in place, e.g., vaccination, lockdowns. |
| R_{eff}, Effective reproductive number | The 'effective R' (R _{eff}) is the R observed when control measures are in place. R _{eff} can therefore change depending on the control measures currently enacted in a particular population. In general, whenever R is less than 1, i.e., an infected person goes on to infect less than one person on average, then the prevalence of the disease would be expected to decrease. |
| Secondary attack rate | The probability that an infection occurs among persons within a reasonable incubation period after known contact with an infectious person in household or other close-contact environments. |
| Serial interval | The time from symptom onset of a case to symptom onset in their identified contacts. |
| SGTF / SGTP | "The Omicron genome (lineage BA.1) contains the spike deletion at position 69/70 which is associated with S-gene target failure (SGTF) in some widely used PCR tests. Such PCR tests evaluate the presence of 3 SARS-CoV-2 genes: Spike (S), nucleocapsid (N) and ORF1ab. SGTF is defined as a PCR test where the N and ORF1ab genes are detected (with Ct values less than or equal to 30) but the S-gene is not. SGTF patterns can be used to assess the spread of Omicron lineage BA.1. The Omicron lineage BA.2, VOC-22JAN-01, does not generally contain the spike gene deletion and is S-gene target positive (SGTP)." [11] |
| Variant | Viruses with mutations are referred to as variants of the original virus. New variants of SARS-CoV-2 have been emerging as the virus has spread and evolved. |

| | |
|--|---|
| Variant of Concern (VOC) | <p>WHO definition: A SARS-CoV-2 variant that meets the definition of a VOI (see below) and, through a comparative assessment, has been demonstrated to be associated with one or more of the following changes at a degree of global public health significance:</p> <ul style="list-style-type: none"> • Increase in transmissibility or detrimental change in COVID-19 epidemiology; OR • Increase in virulence or change in clinical disease presentation; OR • Decrease in effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics. |
| Variant of Interest (VOI) | <p>WHO definition: A SARS-CoV-2 variant:</p> <ul style="list-style-type: none"> • with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; AND • Identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health. |
| Variant under Investigation (VUI) | <p>UKHSA definition: SARS-CoV-2 variants, if considered to have concerning epidemiological, immunological or pathogenic properties, are raised for formal investigation. At this point they are designated Variant Under Investigation (VUI) with a year, month, and number. Following a risk assessment with the relevant expert committee, they may be designated Variant of Concern (VOC).</p> |

Abbreviations

CDC: Centers for Disease Control and Prevention

Ct: Cycle Threshold

E: Glutamic Acid

GISAID: Global Initiative on Sharing Avian Influenza Data

ICU: Intensive Care Unit

IPC: Infection Prevention and Control

L: Lysine

mRNA: messenger RNA

N: Nucleocapsid (Protein)

NPI: Non-pharmaceutical intervention

PCR: Polymerase Chain Reaction

RBD: Receptor binding domain (of the virus spike protein)

RAT: Rapid Antigen Test

R_{eff}: 'Effective R', the effective reproductive number

R₀: 'R-naught', the baseline reproductive number

RNA: Ribonucleic Acid

S: Spike (Protein)

UKHSA: UK Health Security Agency

UAI: Upper Airway Infection

VE: Vaccine effectiveness

VTG: Variant Technical Group

WHO: World Health Organisation

Useful Links

| | |
|---|---|
| US CDC – SARS CoV-2 variant classifications and definitions | CDC classification of variants |
| Outbreak Info | Outbreak Info |
| WHO - Tracking SARS-CoV-2 variants | WHO Variant Tracking |
| UK Health Security Agency Technical Briefings (from October 2021 onwards) | Investigation of SARS-CoV-2 variants: technical briefings |
| Public Health England Technical Briefings | Investigation of SARS-CoV-2 variants: technical briefings |

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