SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

MINISTRY OF HEALTH
MANATŪ HAUORA

COVID-19 Omicron Update

Contents

SCIENCE & TECHNICAL ADVISORY | RŌPŪ TOHUTOHU I TE PŪTAIAO ME TE HANGARAU

MINISTRY OF HEALTH
MANATŪ HAUORA

COVID-19 Omicron Update

Date: 03 February 2022

About this update

The Omicron variant is the focus of this update. Information is emerging at pace. New information included since the previous update is provided in red text.

Key points of new Omicron data

- Data on the Omicron sub-lineage BA.2 is emerging. BA.2 has now been reported in 57 countries and there has been a relative increase in BA.2 sequences according to WHO.
    - New data from the UKHSA and Denmark suggests BA.2 may have 30-50% greater transmissibility than BA.1.
    - UKHSA reports that the secondary attack rate (SAR) for BA.2 is 30% higher compared to BA.1 for household contacts. SAR analysis was unadjusted for vaccination status and only included close contacts named by the original case to NHS Test and Trace.
    - Vaccine effectiveness against symptomatic disease, including after boosters, appears similar for BA.1 and BA.2 on the basis of preliminary data which included Pfizer, Moderna and AstraZeneca vaccines (combined data). UKHSA plan further analysis of this data.
    - There is insufficient data to determine the severity of BA.2 infections. Danish Statens Serum Institut reported preliminary analysis of their data showed no differences in hospitalisations for BA.2 compared to BA.1.
    - ESR reporting indicates that 21 cases of BA.2 have been confirmed in Aotearoa New Zealand as of 12.00 am, 31 January 2022.
- The most common symptoms reported for Omicron infection are sore throat, cough, runny/stuffy nose, and fatigue. Recent data supports earlier reports that loss of smell and taste is less commonly reported.
    - Recent UK survey data suggests 25% of people with Omicron infection may be asymptomatic.
- Data continues to indicate a lower risk for hospitalisation and shorter hospital stay for individuals with Omicron infection. However, the high volume of cases leads to high hospital demand.
    - A newly reported US study comparing healthcare utilisation in high transmission periods of Omicron versus Delta found a relative increase in hospitalisations and Emergency Department visits for the Omicron period due to a higher volume of cases, but a relative decrease in the length of hospital stays.
- The UKHSA COVID-19 Vaccine Surveillance Report from 27 January notes that vaccine effectiveness against symptomatic disease is substantially lower for Omicron than Delta, with rapid waning. However, protection against hospitalisation remains high, particularly after 3 doses. For a Pfizer booster (after either Pfizer or AstraZeneca 2 doses), vaccine effectiveness against hospitalisation was estimated at around 90% dropping to around 75% after 10 to 14 weeks.
- Therapeutics – remdesivir and the oral antivirals molnupiravir and Paxlovid are expected to be effective against Omicron and this has been supported by recent evidence from *in vitro* studies. Paxlovid is now authorised for use across the European Union – in addition to previous authorisations in UK, US and Australia.

Omicron (B.1.1.529) Variant of Concern

Characteristic	Data
Growth advantage/ transmissibility	**Omicron is more transmissible and has a higher secondary attack rate than Delta** Using data from Denmark (to 18th Dec 2021), the effective (instantaneous) reproduction number of Omicron is 3.19 (95%CI 2.82–3.61) times greater than that of Delta under the same epidemiological conditions. [1] In Canada, initial modelling estimates of R_{eff} for Omicron is 1.5 (90%CI 0.78–2.34). [2] Data to 20 December 2021 reported by UKHSA show that, relative to Delta, Omicron is currently more concentrated in young adult age groups (20 to 29) and is less prevalent in children. [3] Of the 1,063 cases in one region of Canada, 59% of 1,063 cases were 18-24 years old and 27% were 25-39 years old, corresponding with the main outbreak environments being in post-secondary education and food/beverage settings. [2] Data from a US health provider in Houston, Texas, indicated a case-doubling time for Omicron of 1.8 days, three times faster than for Delta in this area. [4] Preprint data from South Africa found Omicron was more associated with asymptomatic infection and transmission than Beta and Delta. [5] In England, contact tracing data show a greater proportion of transmission happening outside the household for Omicron than for Delta. [3] Emerging data from the UK estimated a shorter generation time (interval between infection events in an infector-infectee pair) for Omicron during late November to December 2021, 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. [6] This translated to a transmission advantage of 160%-210% for Omicron. However, the study is subject to bias from factors such as differences in the populations the variants were present in, differences in immune escape between variants, and using test to test distribution as a proxy for the generation time distribution. <u>Secondary attack rate</u> Danish data [7]: • Overall, household SAR was 31% for Omicron and 21% for Delta. • Household SAR for unvaccinated individuals was 29% for Omicron and 28% for Delta. • Household SAR for fully vaccinated (defined according to each vaccine) individuals was 32% for Omicron and 19% for Delta. • Household SAR for booster-vaccinated individuals was 25% for Omicron and 11% for Delta. UK data [3]: The UKHSA Technical Briefing 33 (23 December 2021) reported that household SAR was 13.6% (95% CI: 13.1-14.1) for Omicron and 10.1% (95% CI: 10.0-10.2) for Delta. SAR in non-household settings was 7.6% (95% CI: 7.2-8.0) for Omicron and 2.8% (95% CI: 2.7-2.9) for Delta. However, this data has not been stratified by vaccination status. <u>Other data</u> Japan [8]: A study investigated the differences in viral environmental stability between the SARS-CoV-2 Wuhan strain and all VOCs on plastic and skin surfaces. The Omicron variant has the longest survival time of 21.1 hours (95% CI: 15.8–27.6) compared to 16.8 hours (95% CI: 13.1–21.1) for Delta. The high environmental stability of Omicron could increase the risk of contact transmission and contribute to its spread. Canada [9]: 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. On initial testing 196 of 475 HCWs were positive and were quarantined. Only 42 (15%) of 279 HCWs that were initially asymptomatic and allowed to work became positive a median of 4 days after the initial test, but no further transmission was detected. Absence of symptoms at initial evaluation (OR 3.8, 95% CI 2.5-5.7) and having received a third vaccine dose more than 7 days before (OR 1.88, 95% CI 1.3 – 2.8) were associated with increased odds of remaining negative.
Clinical features (symptoms and severity)	**Severity – data to date indicates hospitalisation and death rates are lower than Delta, taking into account vaccination status and risk for severe disease.** **Hospitalisation** <u>Hospitalisation frequency for Omicron relative to Delta</u> 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): • US study comparing healthcare utilisation in high transmission periods of Omicron vs Delta found a relative increase in ED visits (86%) and hospitalisations (76%) compared to the Delta period due to the higher volume of cases but a relative decease in the length of stay in hospitals (-27%). [10] • A preprint 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. [11] • A Norwegian study (n= 91005) found that cases infected with Omicron were 73% lower risk of hospitalisations compared with delta infection. [12] • A preprint study from France looked at 39 Hospitals in the Paris area to measure the risk of ICU admission. It found risk of hospitalisation with Omicron was reduced by 64% compared to Delta. [13] • Canadian data: risk of hospitalisation or death was 54% lower (Hazard Ratio =0.46, 95% CI: 0.27-0.77)[1]. [14]

[1] adjusted for vaccination status and region

Characteristic	Data

	• Scottish data: risk of hospitalisation 68% lower (observed/expected ratio of 0.32, 95% CI: 0.19-0.52).[2] [15]
	• UK data: risk of presentation to emergency care or hospital admission 50% lower than with Delta (Hazard Ratio 0.53, 95% CI: 0.50 to 0.57). The risk of hospital admission from emergency departments was approximately 67% lower than with Delta (Hazard Ratio 0.33, 95% CI: 0.30-0.37).[3] [16]
	• A pre-print 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. [17]
	• A US study in veterans found that infection by Omicron has a 45% (95% CI: 26-58) lower likelihood of resulting in hospitalisation than infection by Delta. [18]
	• UK data in long term care facility residents: risk of hospitalisation much lower, 10.8% for Delta and 4.0% for Omicron (Hazard Ratio 0.50, 95% CI: 0.29-0.87). [19] This paper by Krutikov and colleagues, part of the VIVALDI study, is also reported in the UKHSA Technical Briefing 35. [20]
	• Portugal data: risk of hospitalisation lower, 1.6% for Delta and 0.2% for Omicron (Hazard ratio 0.25, 95% CI: 0.15-0.43). [21]
	• Danish data [22] stratified rather than adjusted by vaccination status:
	  ○ Among those with <2 doses: 43% lower risk of hospitalisation (RR = 0.57, 95% CI: 0.44-0.75)
	  ○ Among those with 2 doses: 29% lower risk of hospitalisation (RR = 0.71, 95% CI: 0.60-0.86)
	  ○ Among those with 3 doses: 50% lower risk of hospitalisation (RR = 0.50, 95% CI: 0.32-0.76)
	
	Unadjusted for vaccination status (provides indication of burden on healthcare at the level of vaccination in country where study conducted):
	
	• UK data (adjusted to some extent for prior infection): reduction in hospitalisation of 38% (95%CI 31-45%) for emergency department attendance or admission, and 62% (95% CI 50-70%) for admission, [3] or (from a different group analysing same data, with different methods for prior infection) 20-25% lower for attendance at hospital, and 40-45% for hospital admission. [23]
	• US data (unclear if adjusted for vaccination/infection): 53% reduction in hospitalisation (hazard ratio for symptomatic hospital admission relative to Delta was 0.47 (95% CI: 0.35-0.62))[4] [24]
	• Danish data [22]: Overall, 36% lower risk of hospitalisation (RR = 0.64, 95% CI: 0.56, 0.75)
	
	<u>Hospitalisation frequency (not compared to Delta)</u>
	
	UK data:
	
	England: ICU admissions with a valid sequencing result for Omicron increased from 9% week commencing 15 December 2021 to 50% in week commencing 12 January 2022. [20]
	
	England: To 29th December, 815 Omicron hospitalisations had been reported. To the same date, around 650,000 Omicron cases had been reported, but there are lags in hospitalisation reporting and many recent cases are unlikely to have had sufficient observation time to be admitted to hospital (i.e., hospitalisation likely to be underestimated). [16] Some crude data available by day but vary substantially each day, and likely affected by lack of follow up time (people testing positive most recently only followed up for 7 days), and lack of adjustment for age or vaccination status. [23]
	
	Scotland: Did not report as numbers too small. [15]
	
	Canadian data:
	
	Ontario: 29,594 cases to December 25th, of whom 75 (0.25%) hospitalised (or died). Again this is likely to be an underestimate due to very short follow up of those diagnosed later. [14]
	
	US data:
	
	California: 52,297 cases to January 1, 2022, of whom 182 (0.35%) were admitted to hospital with symptoms. [24]
	
	Indian data:
	
	New Delhi: 82 cases to December 23rd, 3 (3.6%) of whom required hospitalisation. This could be biased due to the short follow up time since diagnosis, or underdiagnosis of cases. [25]
	
	French data:
	
	Marseille: 1,119 cases between November 28 to December 31, 21 (1.9%) of whom were admitted to the hospital. [26]
	
	<u>Paediatric data</u>

[2] adjusted for age, sex, socioeconomic status, vaccination status and clinical risk factors.
[3] 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.
[4] adjusted for age, sex, race/ethnicity, and neighborhood-level median household income, as well as clinical risk factors recorded within the prior year (including history of smoking, body mass index, Charlson comorbidity index, and healthcare utilization across outpatient, emergency department, and inpatient settings)

Characteristic	Data
	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). [27] US: According to news reports, the CDC says since mid-December the hospital admission rate for those under 5 has increased to more than 4 in 100,000 children, up from 2.5 per 100,000, while the rate among children aged 5 to 17 years is about 1 per 100,000 (link). However, the overall hospitalisation rate among children and teens is still lower than that of other age groups, and they account for less than 5 per cent of average new daily hospital admissions, according to the CDC. A US study in 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. [28] Risk for ED visits was 18.83% (vs 26.67%), hospitalisations was 1.04% (vs 3.14%), ICU admissions was 0.14% (vs 0.43%), and mechanical ventilation was 0.33% (vs 1.15%). UK: Pediatric admissions began to rise from 26 December 2021, with a 3-fold increase in 2 weeks. [29] The rise is most rapid among children under 5 years, and highest in infants aged under 1 year (based on data for all variants, but Omicron represents over 90% of sequenced samples in the UK). A clinical case review of a small number of Omicron admissions in infants found those admitted were not severely unwell. [29, 30] Preliminary data from the UK 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. [31] In the current wave, 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). Risk factors for hospitalisation with Omicron: In the UK, 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. [16] 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. [32] Of note, 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: no data found. Time in hospital with Omicron: median length of stay reported as 2.8 days but strong potential bias as included only those already discharged at 3 weeks after start of Omicron wave (i.e,. those with longer stays might not be included). [4] A South African study also found median hospital length stay was significantly lower for Omicron than other variants, but possibly suffers from similar bias. [33] Preliminary analysis of South African hospital admissions in Gauteng Province (includes Johannesburg and Tshwane) reported a median hospital stay of 4 days (inter-quartile range 2-6 days) during an Omicron-dominant period. [34] A US study estimated that the median duration of stay for patients with Omicron variant infections experiencing symptomatic hospitalisations was 1.5 (1.3-1.6) days, with 90% of patients expected to complete hospitalisations within 3.1 (2.7-3.6) days, corresponding to a 69.6% (95% CI: 64.0-74.5%) shorter median length of hospital stay compared to patients with Delta infections. [24] However, a key limitation in some of these studies is that longer stays will have been missed for Omicron (biasing median duration downward) due to short follow up times. A US study in veterans found that among COVID hospitalisations, Omicron is associated with a 2-day (95% CI: 1-2) shorter stay than Delta. The average length of stay was 6 days (95% CI: 5-7). [18] A Portuguese study found the length of stay in hospital for Omicron was significantly shorter than for Delta (confounding-adjusted difference[5] -4.0 days (95% CI -7.2 to -0.8). [21] **ICU admission** Severe/ICU/ventilated frequency relative to Delta Adjusted for vaccination status (important for understanding basic differences in severity as removes differences in vaccine effectiveness from assessment. However, residual confounding for vaccination status may still occur): • South African data: Among *hospitalised* individuals, after controlling for factors associated with severe disease[6], 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). [35] Compared to earlier Delta infections, after controlling for factors associated with severe disease[7], SGTF-infected individuals had lower odds of severe disease (aOR 0.3, 95% CI 0.2-0.5). • A US study in veterans found that Omicron is associated with a 73% (95% CI: 28-92) lower risk of ICU admission than Delta. [18] Unadjusted for vaccination status (provides indication of burden on healthcare at the level of vaccination in country where study conducted): • US data: Unadjusted hazard ratios for ICU admission associated with Omicron variant infection was 0.26 (95% CI: 0.10-0.73), a 74% reduction. [24] Severe/ICU/ventilated frequency (not compared to Delta)

[5] adjusted for sex, age, previous infection and vaccination status
[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.

Characteristic	Data

In Texas, among 862 people who tested positive for Omicron (mainly symptomatic people presenting to healthcare facilities), [4] 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. [34]

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).[24]

Risk factors for ICU/ventilation: no data.
Time to ICU/ventilation: no data.

Death

Death frequency relative to Delta

UK data: To 29 December 2021, a total of 57 people were reported to have died within 28 days of an Omicron COVID-19 diagnosis (198,348 confirmed cases of Omicron). [16]

South African data: After adjusting for age, sex, comorbidities, and subdistrict, the hazard ratio was 0.27 (95% CI: 0.19-0.38), a 73% reduction 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). [17]

US data: Unadjusted hazard ratios for mortality associated with Omicron variant infection was 0.09 (95% CI : 0.01-0.75) [24] 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). [19]

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. [21]

Risk factors for death: UK data: Of 57 people who died within 28 days of Omicron diagnosis (to 29th December 2021) the age of those dying ranged from 41 to 99 years. [16]

Time to death: UK data: median time from Omicron specimen date to death was 5 days (range 0 to 14). [16] Note that specimen date might not reflect date of symptom onset.

Other severity information

Non-peer reviewed studies (pre-prints) have shown that in hamster and mouse models, Omicron poorly infects the lung, leads to lower viral loads, and produces milder clinical signs of infection compared to those observed with previous strains. [36-38] Data from a study using ex-vivo human lung and bronchus tissue show similar results, with slower Omicron replication observed in the lung and faster in the bronchus compared to previous strains. [39] Clinical symptoms were largely absent in hamsters that were re-infected with Omicron, suggesting that immunity raised against the ancestral strain was protective against Omicron. [37] The characteristics of the antibody-mediated protection observed within this study is of interest while we wait for further studies in humans confirm the relevance of these findings.

Symptoms – Symptoms may be milder in previously infected and/or vaccinated individuals. Recent UK data suggests about 25% may be asymptomatic. 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.

Characteristic	Data
	The most common symptoms reported in early data were: cough; runny/stuffy nose; and fatigue. [40-43] The COVID Symptoms Study (by health science company Zoe and Kings College London) reports that headache and sneezing are also common symptoms of Omicron infection. [44] Preliminary information 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. [43] Symptoms reported in paediatric cases in South Africa have included fever, vomiting, diarrhoea and convulsions. [27] UKHSA Technical Briefing 34 compares Omicron to Delta symptoms. The report provides a recent analysis of NHS Test and Trace data of 182,133 confirmed Omicron cases and 87,920 confirmed Delta cases in the period between 01 December to 28 December 2021. Adjusted odds ratio analysis showed that Omicron cases were less likely to report loss of smell and taste compared to Delta cases (13% of Omicron cases, 34% of Delta cases, odds ratio 0.22, 95% CI: 0.21-0.23). However, Omicron cases were more likely to report a sore throat than Delta cases (53% of Omicron cases, 34% of Delta cases, odds ratio 1.93, 95% CI: 1.88-1.98). 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 [45] 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. [46] 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 the 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. [47] 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. [48] Recent 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.[49] Vaccine status of individuals within this group was not included in the report.
Disease course	**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): • Faroe Islands [50]: Observed incubation period was short, ranging from 2 to 6 days, with a mean incubation period of 3.24 days (95% CI 2.87-3.60). All had had 3 doses of Pfizer (2 primary, and booster in last 2.5 months) • Norway [40]: Estimated incubation period was 0 to 8 days, median of 3 days (interquartile range: 3–4). [40] Almost all participants interviewed had received 2 doses of an mRNA vaccine. The incubation period was consistent with another study (median 3 days for both Delta and Omicron variants) • USA [51]: Incubation period (6 cases only) of approximately 3 days (73 hours, range = 33–75 hours). [51] Serial Interval • Spain [52]: The mean serial interval was significantly shorter for Omicron (4.8 days) versus Delta (5.4 days), corresponding to a difference of -0.6 (95% CI: -1 to -0.15). • Netherlands [53]: Within households, a mean serial interval of 3.4 days was observed for SGTF (proxy for Omicron) and 3.9 days for non-SGTF (proxy for Delta) cases. Latent period: no data Duration of infectiousness Data predominantly from **vaccinated** people:

Characteristic	Data
	• Japan [54]: Preliminary data from the National Institute of Infectious Diseases suggest that the amount of viral RNA in specimens from Omicron infections (19 vaccinated and 2 unvaccinated cases) 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 [55]: A study investigating viral shedding dynamics included a small number of Omicron breakthrough infections (n=18) and showed similar infectious viral titres in nasopharyngeal samples for breakthrough Omicron and Delta (n=17 for this comparison) infections. Samples were gathered in the first 5 days post symptoms. • US [56]: Preliminary data from a longitudinal study (National Basketball Association's [NBA] occupational health programme) in a largely vaccinated cohort suggest that Omicron may have a lower peak viral load (Ct 23.3 for Omicron vs Ct 20.5 for Delta) and shorter clearance time (5.35 days for Omicron vs 6.23 days for Delta) than Delta. However, the rate of clearance (3.13 Ct/day for Omicron vs 3.15 Ct/day for Delta) and total mean duration of infection is similar (10 days for Omicron vs 11 days for Delta). These data are only from a small number of infections, so more is needed to understand the viral dynamics of Omicron and how they are affected by vaccination. • Singapore [47]: 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. Trough and illness onset median Ct values were similar for Omicron between those with primary vaccination or booster vaccination doses. • Switzerland [57]: A small study in Delta (n=17) and Omicron patients (n=18) found that Delta and Omicron have comparable genome copies (p=0.3345) but Omicron patients had slightly but not significantly lower infectious viral titres compared to Delta patients (p=0.1033). <u>Duration of illness</u> • Faroe Islands [50]: Time to resolution of symptoms varied, and at the end of follow-up, five individuals still reported symptoms, while the rest (16 individuals) reported symptoms lasting 1 to 9 days. • For time to hospitalisation and death, see "severity" section above. Data on the disease course remains limited at present, with few quantitative studies to date. • Singapore [47]: Negative viral cultures were obtained starting from day 2 of illness and no positive viral cultures were obtained for patients beyond day 5 of illness or with Ct values >26 based on 14 patients.
Immune evasion/vaccine effectiveness/therapeutics	**Vaccine effectiveness (VE) – some protection offered against symptomatic disease, however, VE is reduced compared to Delta. Rapid waning of VE occurs against Omicron but a booster dose restores protection. VE against hospitalisation appears to be 60-70% after a primary vaccine course but declines to ~45% from 25 weeks after second dose. VE against hospitalisation increases to ~90% after a booster dose (including in those over 65 years of age).** 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. (<u>link</u>) Pfizer is hoping to be able to deliver the vaccine in March 2022. (<u>link</u>) <u>VE against infection</u> A Danish cohort study has shown VE (Pfizer) against infection of 55% in the month after primary vaccination, [58] VE is significantly lower than for Delta infection and declines rapidly after the first month. [58] Booster vaccination increases VE back to 55%. [58] A study in the Netherlands also found an increased risk of infection with Omicron compared to Delta in vaccinated and previously infected individuals. [59] Emerging results from the US indicate that 2-dose VE for Moderna against Omicron infection (determined by S-gene status) was 30.4% (95% CI 5-49) at 14-90 days after vaccination and declines over time. [60] The 3-dose VE was 62.5% (95%CI: 56.2-67.9) against Omicron infection compared with 95.2% (95%CI: 93.4-96.4) for Delta. Among immunocompromised individuals, the 3-dose VE against Omicron infection was very low (11.5%; 95% CI: 0.0-66.5). The UKHSA reported unadjusted VE (all vaccines combined) against infection in healthcare workers (SIREN cohort): [29] • Those with no prior infection: 32% (95% CI: -6-57) after 2 doses and 62% (95% CI: 41-75) after 3 doses • Those with prior infection: 60% (95% CI: 36-75) after 2 doses and 71% (95% CI: 56-82) after 3 doses VE for US veterans (aged 65+ years) who received two doses of mRNA vaccines (vaccines not specified) was 25% (95% CI: 20-30) against Omicron infection, rising to 62% (95%CI: 59-65) after an mRNA vaccine booster. [18] <u>VE against symptomatic disease</u> VE data from South Africa [61, 62] the UK [3, 15, 16, 29, 63] and Denmark [58] all suggest reduced VE for 2-dose Pfizer vaccine regimens against symptomatic disease caused by Omicron compared with Delta. A booster dose of mRNA vaccine restores rapidly waning protection against symptomatic COVID-19 to levels similar to immediately after the primary course but early data from England suggest waning also occurs after the booster dose (e.g. VE against symptomatic disease dropped to ~50% 10 weeks after a Pfizer booster and ~65% 5-9 weeks after a Moderna booster following primary Pfizer course - see Figure 1). [3, 16, 29] A UK analysis

Characteristic	Data

conducted in the elderly aged 65+ years reported similar results. [64] Among those who received a primary course of Pfizer, VE after a Pfizer booster was 65% at 2 to 4 weeks but then dropped to 31% at 10+ weeks. For those who received a Moderna booster, VE was 70% at 2 to 4 weeks, dropping to 57% at 5 to 9 weeks.

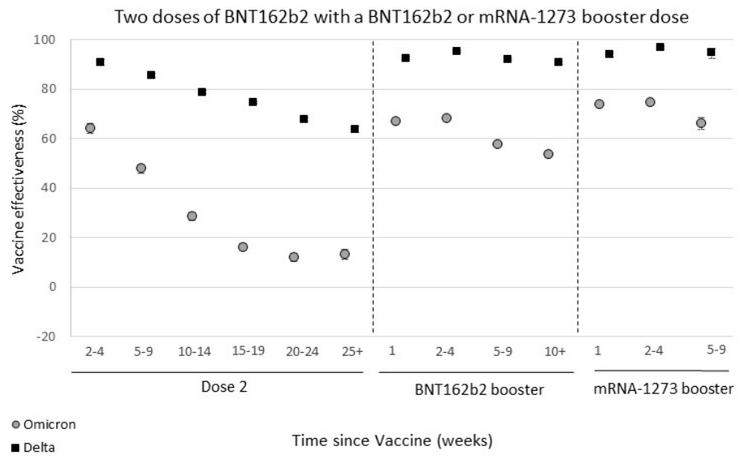

Figure 1: Pfizer vaccine effectiveness against symptomatic disease by period after 2 doses and after a booster. Note this is the updated figure, with more certainty about the data for boosters. [29]

Qatar: VE against symptomatic infection for a Pfizer booster dose relative to the primary course was 50.1% (95% CI: 47.3-52.8). [65]

<u>VE against hospitalisation</u>

UKHSA COVID-19 Vaccine Surveillance Report from 27 January reported estimates from a test-negative case control study:

- Protection against hospitalisation remained high, particularly after 3 doses**.** For a Pfizer booster (after either Pfizer or AstraZeneca primary 2 doses), VE against hospitalisation started at around 90% dropping to around 75% after 10 to 14 weeks. [66]

South African data for VE against hospitalisation:

- VE against hospitalisation for two doses of Pfizer was 70% (95%CI 62-76) during Omicron dominance (Delta dominance (93% [95%CI 90-94]) in South Africa.[67] Data were adjusted for age, sex, previous infection, surveillance week, geographic location, and CDC risk factors.
- Results from another South African study show that VE against hospitalisation for the Janssen vaccine increased over time since the second (booster) dose. [68]

UK data for VE against hospitalisation (all vaccines combined):

- For adults 18+ years, VE was 64% (95% CI: 54-71) 2 to 24 weeks after dose 2, declining to 44% (95%CI: 30-54) at 25+ weeks. VE increased to 92% (95% CI: 89-94) 2+ weeks after a booster dose, declining to 83% (95% CI: 78-87) at 10+ weeks. [29]
- For elderly aged 65+ years, booster VE was 94% (95% CI: 89-97) 2 to 9 weeks after a booster dose and 89% (95% CI: 80-95) at 10 weeks. VE after two doses was not reported in this analysis. [64]

US data:

- VE against Omicron-related hospitalisation for two doses of Pfizer was 68% (95% CI: 58−75), and VE for three doses of Pfizer was 89% (95% CI: 84−92). VE against omicron-related hospitalisation after two or three doses remained steady for several months. [69]
- VE against Omicron-related ED admission for two doses of Pfizer was 60% (95% CI: 43−72) at <3 months and declined to 41% (95% CI: 32−50) at ≥6 months. [69]
- VE against Omicron-related ED admission for three doses of Pfizer was 78% (95% CI: 73−82) at <3 months and declined to 48% (95% CI: 14−69) at ≥3 months. [69]
- VE against Omicron-related hospitalisation for mRNA vaccines was 81% 14–179 days after dose 2, 57% ≥180 days after dose 2, and 90% ≥14 days after dose 3. [70]
- VE against Omicron-related ED and UC encounters for mRNA vaccines was 52% 14–179 days after dose 2, 38% ≥180 days after dose 2, and 82% ≥14 days after dose 3. [70].

<u>VE against death</u>

Characteristic	Data
	Qatar: VE against any severe, critical, or fatal COVID-19 for a Pfizer booster dose relative to the primary course was estimated at 100.0% (95% CI: 71.4-100.0). [65] **Use of second booster dose** Israel: Initial news reports of a fourth Pfizer dose (second booster) trial in 150 medical personnel in Israel have noted minor side effects only and no safety signals. The fourth dose was given 4-5 months after the third dose. An additional 25,000 people over 60 years have now had a fourth Pfizer dose. (link) Israel's Health Ministry noted preliminary findings that a fourth dose of COVID-19 vaccine given to people over 60 in Israel made them three times more resistant to serious illness than thrice-vaccinated people in the same age group. The ministry also said the fourth dose, or second booster, made people over 60 twice as resistant to infection than those in the age group who received three shots of the vaccine. The fourth shot for people over 60 increases antibodies to even higher levels than the third, but it "probably" could not completely protect against infection by the highly transmissible Omicron variant. (link) On 25 January 2022, the Advisory Committee on Epidemic Control and the Advisory Board on COVID-19 Vaccination recommended a fourth dose to people under 60 and above 18 in Israel, if 5 months has passed from recovery or third dose administration date. This recommendation still needs to be approved by the Israeli Ministry of Health. (link) This follows the approval of a fourth vaccine dose to immunosuppressed individuals (link). Chile: From January 10, people over 12 years who are immunocompromised will be offered a fourth vaccine dose. From February 7 eligibility for a fourth dose will be extended to people over 55 years who had a 3rd vaccine dose at least 6 months previously. (link) The fourth vaccine regimen has not been specified. Third (booster) doses were Pfizer or AstraZeneca. (link) **Neutralising assays** Neutralisation studies provided initial data predicting lower vaccine effectiveness against Omicron. [71-76] These data have now been superseded by effectiveness data. **Cell-mediated responses** While data remain preliminary, an increasing number of studies indicate that vaccination provides a durable T-cell response to Omicron infection. [71, 77-80] **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. [47] **Prior Infection** A Qatar study estimated effectiveness of prior infection against preventing Omicron symptomatic re-infection at 61.9% (95% CI: 48.2-72.0) after excluding vaccinated individuals. Effectiveness against hospitalisation/death was 87.8% (95% CI: 47.5-97.1), however both vaccinated and unvaccinated individuals were included in this analysis. [81] The UKHSA reported an unadjusted effectiveness of 44% (95% CI: 4-67) against infection in unvaccinated healthcare workers (SIREN cohort) who had a prior infection. [29] **Therapeutics - Most monoclonal antibody products including Ronapreve appear ineffective against Omicron – sotrovimab an exception. Oral antivirals and remdesivir are expected to be effective and use is increasing internationally.** Antibody products The FDA (statement of 24 January) have revised authorisations for two monoclonal antibody treatments – bamlanivimab and etesevimab (administered together) and REGEN-COV (casirivimab and imdevimab; Ronapreve). These treatments are not authorised for use at present in any U.S. states, territories, or jurisdictions due to Omicron being estimated to comprise more than 99% of US COVID-19 cases as of January. (Link) *In vitro studies* In a non-peer reviewed study, only three of the tested 24 therapeutic antibody products (product names not revealed) retained their full potency against Omicron and high-level resistance was seen against fifteen. [82] Several other laboratory studies have shown Omicron is resistant to neutralisation by a number of monoclonal antibodies including casirivimab + imdevimab (Ronapreve). [82-87] Several other laboratory studies have shown Omicron is resistant to neutralisation by a number of monoclonal antibodies including casirivimab + imdevimab (Ronapreve). [82-87] Sotrovimab has been shown to retain some neutralisation activity. A preprint from the US found that Regeneron (REGN10933 and REGN10987), and Lilly (LY-CoV555 and LY37 CoV016) monoclonal antibodies were ineffective against Omicron, while Sotrovimab was partially effective. [74] An additional Australian study has also shown that of the mAbs tested, only sotrovimab retained neutralisation activity against Omicron in vitro. [88] *In vitro* data from Japan reported that sotrovimab and also the combination of cilgavimab + tixagevimab (marketed by AstraZeneca as Evusheld) showed some neutralisation activity against Omicron. [89] A preprint from the US found that Regeneron (REGN10933 and REGN10987),

Characteristic	Data
	and Lilly (LY-CoV555 and LY37 CoV016) monoclonal antibodies were ineffective against Omicron, while Sotrovimab was partially effective. [74] An additional Australian study has also shown that of the mAbs tested, only sotrovimab retained neutralisation activity against Omicron in vitro. [88] *Animal studies* An animal study (mice) from the University of Liverpool investigating the virological efficacy of casirivimab + imdevimab (Ronapreve) showed no reduction in viral RNA in lung and nasal turbinate tissue compared to saline for Omicron but a reduction for Delta. [90] Antivirals Antiviral agents including remdesivir and newer oral antivirals are expected to be effective against the Omicron variant on the basis of their mode of action. *In vitro* studies provide experimental evidence of preserved effect of remdesivir, molnupiravir and Paxlovid against Omicron. A non-peer reviewed cell-culture study showed that the antiviral drugs molnupiravir (Legevrio), Paxlovid, remdesivir, acriflavine, and AT-527 will likely retain efficacy for the omicron variant. [91] An *in vitro* study using live virus collected from nasal swab specimens demonstrated that the activity of the antivirals remdesivir, molnupiravir (specifically, its active metabolite EIDD-19331) and PF-07321332 (nirmatrelvir) was preserved against Omicron. [92] Antiviral assays completed in a Belgian study similarly reported retained effect of remdesivir, EIDD-19331 and nirmatrelvir against all variants studied, including Omicron. [93] Note that the oral antiviral Paxlovid is a combination of PF-07321332 and ritonavir, with the PF-07321332 responsible for blocking viral replication (whereas ritonavir acts to slow the breakdown of PF-07321332). Further *in vitro* studies supported by Pfizer showing that nirmatrelvir is effective against Omicron have also recently been reported as pre-prints. [94, 95] (Link) *In vitro* data from Japan reported in a January 26 NEJM editorial showed preserved effect of remdesivir, molnupiravir and PF-07394814 (active component of Paxlovid) against Omicron. Uraki and colleagues have demonstrated that molnupiravir reduced lung viral titres of Omicron in 4 infected laboratory hamsters. [96] Paxlovid is now authorised for use across the European Union following the granting of a conditional marketing authorisation by the European Commission on 28 January 2022. Link The Therapeutic Goods Administration (TGA) in Australia announced provisional approval for both molnupiravir and Paxlovid on 20 January 2022. (Link) The FDA and MHRA have authorised Pfizer's oral antiviral, Paxlovid (USA in those >12 years old, UK 18 years and over with risk of severe disease). [97] (link) The PANORAMIC (Platform Adaptive trial of Novel Antivirals for Early Treatment of COVID-19 in the Community) trial in the UK is currently investigating community use of molnupiravir in the UK and targeting enrolment from over-50 years and younger adults with underlying health conditions. (Link and Link)
Detection	**More PCR tests recognised as unable to detect Omicron. Saliva testing might offer advantages for Omicron over nasal swabs. RATs under spotlight but evidence is mixed for reduced analytical sensitivity, including two NZ approved RATs.** **PCR** PCR tests continue to be appropriate for diagnosis of SARS CoV-2. [98] On 23 December, the World Health Organization stated that PCR tests that include multiple gene targets are unlikely to be affected and should continue to be used to detect SARS-CoV-2 infection, including the Omicron variant. [99] However, the FDA has identified three COVID-19 molecular tests (from Applied DA Sciences, Meridian Bioscience and Tide Laboratories) that are not able to detect the Omicron variant because they target genes with deletions in Omicron. [100] ThermoFisher TaqPath PCR test can detect S gene target failure - an early marker to distinguish between Omicron and Delta, pending sequencing confirmation. [98] The PCR proxy marker RNA-dependent RNA polymerase (RdRp) target delay was associated with a lower risk of hospital admission. [101] To account for the changing receptor binding domain of the SARS-CoV-2 spike protein, assays capable of rapidly and accurately identifying variants including Omicron are being reported to have discriminated against a S-gene dropout Delta specimen. [102] A Malaysian study evaluated the Allplex SARS-Cov-2 Master Assay and Variant Assay and found that the assays should detect Omicron (B.1.1.529). [103] Two pre-print studies suggest saliva testing might detect more infections (and possibly earlier) than nasal swabs in PCR testing. [104, 105] **RATs** There are currently eleven RATs approved for use in New Zealand. The performance of four of the RATs currently approved in New Zealand have been reported as not affected by Omicron based on the manufacturers testing. [106-108] UKHSA reports initial laboratory validation of RATs in use by NHS Test and Trace shows similar sensitivity to detect Omicron compared to Delta [54]. A pre-print assessing 10 RATs (only 1 of the four in NZ), also found that all 10 had a sensitivity against Omicron consistent with prior variants. [97] However, a non-peer reviewed study using testing of seven RATs, three of them WHO-EUL approved and two approved for use in New Zealand, using cultured virus found a tendency towards lower sensitivity for Omicron compared to previous variants. [98] One small pre-print found RATs may not detect Omicron in its early phases although PCRs are positive (RATs positive 2 days later than PCR) [93] A pre-print from California assessed the BinaxNOW nasal rapid antigen test and reported decreased sensitivity with higher Ct values, suggesting that repeat testing may be required for those who are at high risk. [99] Sensitivity was 95.2% (95% CI 92-98) for Ct < 30, 82.1% (95% CI 77-87) for Ct < 35, and 65.2% (95% CI 60-70) overall (no threshold). BinaxNOW's clinical

Characteristic	Data
	sensitivity is influenced by the interaction between viral replication, the dynamics of tissue tropism, and the timing of sampling [100]. A pre-print study investigated the sensitivities of swabs compared to RT-PCR, found separate samples from nasal or throat swabs each detected 64.5% of 34 SARS-CoV-2 cases; combining the contributions of each swab for an individual increased the sensitivity to 88.7% . [109] A pre-print on 6 January 2022 reports a cost-effectiveness analysis of providing government-funded RATs for early detection of COVID-19 in Australia. The authors concluded that '*even only minor reductions in COVID-19 transmission rates due to early isolation would justify the additional costs associated with a policy of government-funded RATs*.' [110]
Effectiveness of infection prevention control/ public health measures	• A new modelling study suggests that in contrast to Delta, infection prevention control settings in South Africa and UK will be insufficient to control the Omicron outbreak in those countries. [111] • A French study discusses the implication of a higher viral load on airborne transmission within the context of COVID-19 with new variants and its implication for health policies. [112] The conclusion from their observations was that the present norms of ventilation, already insufficient, are not respected, especially in a variety of public premises, leading to high risk of contamination. Finally, the researchers insist that public health policy in the field of airborne transmission should be based on a multi parameter analysis, considering the whole complexity of dose evaluation.
Sub-lineages of interest	**The Omicron variant comprises four lineages including B.1.1.529, BA.1, BA.2 and BA.3. The lineage BA.2 was designated a variant under investigation (VUI) by UKHSA on 21 January 2022 due to increasing number of sequences. WHO have stated that a relative increase in BA.2 has been observed in multiple countries. BA.2 may have between 30-50% greater transmissibility compared to BA.1. UKHSA analysis shows similar vaccine effectiveness against symptomatic disease for BA.1 and BA.2 and evidence of a growth advantage for BA.2 compared to BA.1 in more than one country. Preliminary analysis from Danish Statens Serum Institut shows no differences in hospitalisations for BA.2 compared to BA.1** **Omicron lineage BA.2** BA.2 is a sub-lineage of Omicron (B.1.1.529) that was designated by Pangolin on 6 December 2021.[29] 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. (link) BA.2 was designated a variant under investigation (VUI) by UKHSA on 21 January 2022 due to increasing numbers of sequences in the UK and internationally. (link) UKHSA published a risk assessment for BA.2 on 26 January 2022. [113] Unlike BA.1, this sub-lineage does not have the spike deletion at 69-70 that causes S-gene target failure (SGTF).[29] Because of this, it is being called the "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. Data is emerging for BA.2. Most observational studies have relied on SGTF as a proxy for Omicron, which would only consider 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.1 accounts for 96.4% of sequences submitted to GISAID as of 31 January 2022, however, BA.2 has now been reported in 57 countries and there has been a relative increase in BA.2 sequences according to WHO.[114] In several countries, WHO reports that the weekly proportion of BA.2 relative to other Omicron sequences has risen to over 50% in the period 20 December 2021 to 1 February 2022. [114] In the UK, BA.2 accounts for an increasing proportion of S-gene positive (SGTP) tests. [29] BA.2 is increasing in prevalence in Philippines, India and particularly in Denmark, where it now accounts for almost half of Omicron cases. (link) [115] This may be relevant for testing of arrivals from these countries. ESR reporting indicates that 21 cases of BA.2 have been confirmed in Aotearoa New Zealand as of 12.00 am, 31 January 2022. UKHSA states that there is evidence of a growth advantage for BA.2 compared to BA.1 in more than one country. [113] The growth rate advantage observed in England, in areas where there are sufficient cases to assess, is supported by increased household SARs in preliminary UK data. [113] Scientists from Heidelberg University have shared data on Twitter which suggests a BA.2 growth advantage over Delta ~20% per day and BA.1 ~15% faster than Delta per day.(link) Virologists from Imperial College London have predicted that 'consistent growth across multiple countries is evidence BA.2 may be some degree more transmissible than BA.1' (link) however, further analysis is required. Based on early data BA.2 does not appear to be more immune evasive than BA.1. UKHSA states that a preliminary pseudovirus neutralisation study does not suggest a difference in neutralisation between BA.1 and BA.2, using sera from vaccinated individuals. [113] Preliminary analysis from the UKHSA found no statistical difference in the vaccine effectiveness for BA.1 and BA.2 at present.[20] Analysis included Pfizer, Moderna and AstraZeneca vaccines (combined data). After 2 doses effectiveness was 9% (7 to 10%) and 13% (-26 to 40%) respectively for BA.1 and VUI-22JAN-01 (BA.2), after 25+ weeks. This increased to 63% (63 to 64%) for BA.1 and 70% (58 to 79%) for VUI-22JAN-01 (BA.2) at 2 weeks following a booster vaccine. [20] UKHSA will continue to analyse this data. BA.2 may have between 30-50% greater transmissibility compared to BA.1. UKHSA reported that the crude SAR for BA.2 is 30% higher, compared to BA.1 for household contacts. Analysis of routine contact tracing data observed SAR for household contacts as 13.4% (10.7%-16.8%) for BA.2 and 10.3% (10.1%-10.4%) for BA.1. [20] SAR analysis was not adjusted for vaccination status and only included close contacts named by the original case to NHS Test and Trace are included, (household members, face-to-face contact, people within one metre of the case for one minute or longer, or people within 2 metres for 15 minutes). Contacts not named by the case but identified as part of contact tracing of international travellers on flights are excluded. [20] Non peer-reviewed analysis from the Danish Statens Serum Institut suggests a 50% increase in transmissibility for BA.2 compared to BA.1, with the estimated SAR of 29% for BA.1; and 39% SAR for BA.2 across households infected with Omicron. [116] Given the high SAR and lack of apparent immune evasion, it is plausible that a change in transmissibility is contributing to the growth advantage. [113]

Characteristic	Data
	Danish Statens Serum Institut has stated that preliminary analysis shows no differences in hospitalisations for BA.2 compared to BA.1 and that analyses are ongoing. [115] There is insufficient data available on the severity of BA.2. [113] Further analysis is required and UKHSA is undertaking laboratory and epidemiological investigations in order to understand more. **Omicron lineage BA.3** BA.3 is a sub-lineage of Omicron (B.1.1.529). [117] Preliminary investigation suggests that BA.3 has no specific mutations in the spike protein, but is a combination of the mutations found in BA.1 and BA.2. [118] Similar to BA.1, BA.3 has the SGTF deletion (Δ69-70) which means it can be detected using PCR tests that detect SGTF, such as Thermo Fisher's TaqPath and does not present the same issues as BA.2 discussed above in relation to PCR tests. (link) BA.3 is currently very rare, as of 24 January 2022, 85 sequences in the BA.3 lineage have been detected since the lineage was identified (link) and it is most commonly reported in Poland, South Africa and UK (link).

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.
R_0, 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.
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)	**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: • 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)	**WHO definition:** A SARS-CoV-2 variant:

	• 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)	**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).

Abbreviations

CDC: Centers for Disease Control and Prevention

GSAID: Global Initiative on Sharing Avian Influenza Data

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

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

R_0: 'R-naught', the baseline reproductive number

UKHSA: UK Health Security Agency

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

References

1. Ito, K., C. Piantham, and H. Nishiura, *Relative Instantaneous Reproduction Number of Omicron SARS-CoV-2 variant with respect to the Delta variant in Denmark.* J Med Virol, 2021.
2. Li, C., et al., *Broad neutralization of SARS-CoV-2 variants by an inhalable bispecific single-domain antibody*. 2021, bioRxiv.
3. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 33*. 23 Dec 2021; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1043807/technical-briefing-33.pdf.
4. Christensen, P.A., et al., *Early signals of significantly increased vaccine breakthrough, decreased hospitalization rates, and less severe disease in patients with COVID-19 caused by the Omicron variant of SARS-CoV-2 in Houston, Texas.* medRxiv, 2022: p. 2021.12.30.21268560.
5. Garrett, N., et al., *High Rate of Asymptomatic Carriage Associated with Variant Strain Omicron.* medRxiv, 2021: p. 2021.12.20.21268130.
6. Abbott, S., et al. *Estimation of the test to test distribution as a proxy for generation interval distribution for the Omicron variant in England*. medRxiv 2022; 2022.01.08.22268920]. Available from: http://medrxiv.org/content/early/2022/01/10/2022.01.08.22268920.abstract.
7. Lyngse, F.P., et al., *SARS-CoV-2 Omicron VOC Transmission in Danish Households.* medRxiv, 2021: p. 2021.12.27.21268278.
8. Hirose, R., et al., *Differences in environmental stability among SARS-CoV-2 variants of concern: Omicron has higher stability.* bioRxiv, 2022: p. 2022.01.18.476607.
9. Quach, C., et al., *Should healthcare workers with SARS-CoV-2 household exposures work? A Cohort Study.* medRxiv, 2022: p. 2022.01.23.22269719.
10. Iuliano AD, B.J., Boehmer TK, et al. , *Trends in Disease Severity and Health Care Utilization During the Early Omicron Variant Period Compared with Previous SARS-CoV-2 High Transmission Periods — United States, December 2020–January 2022.* MMWR Morb Mortal Wkly Rep 2022;71:146–152.
11. Fall, A., et al., *A Quick Displacement of the SARS-CoV-2 variant Delta with Omicron: Unprecedented Spike in COVID-19 Cases Associated with Fewer Admissions and Comparable Upper Respiratory Viral Loads.* medRxiv, 2022: p. 2022.01.26.22269927.
12. Veneti, L., et al., *Reduced risk of hospitalisation among reported COVID-19 cases infected with the SARS-CoV-2 Omicron BA.1 variant compared with the Delta variant, Norway, December 2021 to January 2022.* Eurosurveillance, 2022. **27**(4): p. 2200077.
13. Vieillard-Baron, A., et al., *EPIDEMIOLOGICAL CHARACTERISTICS AND SEVERITY OF OMICRON VARIANT CASES IN THE APHP CRITICAL CARE UNITS.* medRxiv, 2022: p. 2022.01.25.22269839.
14. Public Health Ontario. *Early Estimates of Omicron Severity in Ontario based on a Matched Cohort Study, November 22 to December 17, 2021*. Available from: https://www.publichealthontario.ca/-/media/documents/ncov/epi/covid-19-epi-enhanced-estimates-omicron-severity-study.pdf?sc_lang=en.
15. Sheikh, A., et al. *Severity of Omicron variant of concern and vaccine effectiveness against symptomatic disease: national cohort with nested test negative design study in Scotland*. 23 Dec 2021; Available from: https://www.pure.ed.ac.uk/ws/portalfiles/portal/245818096/Severity_of_Omicron_variant_of_concern_and_vaccine_effectiveness_against_symptomatic_disease.pdf.
16. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing: Update on hospitalisation and vaccine effectiveness for Omicron VOC-21NOV-01 (B.1.1.529)*. 31 December 2021; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1045619/Technical-Briefing-31-Dec-2021-Omicron_severity_update.pdf.
17. Davies, M.-A., et al. *Outcomes of laboratory-confirmed SARS-CoV-2 infection in the Omicron-driven fourth wave compared with previous waves in the Western Cape Province, South Africa*. medRxiv 2022;

2022.01.12.22269148]. Available from: http://medrxiv.org/content/early/2022/01/12/2022.01.12.22269148.abstract.

18. Young-Xu, Y., *Effectiveness of mRNA COVID-19 Vaccines against Omicron among Veterans.* medRxiv, 2022: p. 2022.01.15.22269360.
19. Krutikov, M., et al., *Outcomes of SARS-CoV-2 Omicron infection in residents of Long-Term Care.* medRxiv, 2022: p. 2022.01.21.22269605.
20. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 35. 28 January 2022.* . Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050999/Technical-Briefing-35-28January2022.pdf.
21. Peralta Santos, A., et al., *Omicron (BA.1) SARS-CoV-2 variant is associated with reduced risk of hospitalization and length of stay compared with Delta (B.1.617.2).* medRxiv, 2022: p. 2022.01.20.22269406.
22. Bager, P., et al., *Reduced Risk of Hospitalisation Associated With Infection With SARS-CoV-2 Omicron Relative to Delta: A Danish Cohort Study.* SSRN Electronic Journal, 2022.
23. Ferguson, N., et al. *Report 50: Hospitalisation risk for Omicron cases in England*. Available from: https://www.imperial.ac.uk/media/imperial-college/medicine/mrc-gida/2021-12-22-COVID19-Report-50.pdf.
24. Lewnard, J.A., et al. *Clinical outcomes among patients infected with Omicron (B.1.1.529) SARS-CoV-2 variant in southern California*. 11 Jan 2022; Available from: https://www.medrxiv.org/content/10.1101/2022.01.11.22269045v1.full.pdf.
25. Garg, R., et al. *Evidence of early community transmission of Omicron (B1.1.529) in Delhi- A city with very high seropositivity and past-exposure!* medRxiv 2022; 2022.01.10.22269041]. Available from: http://medrxiv.org/content/early/2022/01/13/2022.01.10.22269041.abstract.
26. Houhamdi, L., et al., *Characteristics of the first 1,119 SARS-CoV-2 Omicron variant cases, in Marseille, France, November-December 2021.* Journal of Medical Virology, 2022. **n/a**(n/a).
27. Cloete, J., et al. *Rapid rise in paediatric COVID-19 hospitalisations during the early stages of the Omicron wave, Tshwane District, South Africa*. 21 Dec 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.12.21.21268108v1.full.pdf.
28. Wang, L., et al. *COVID infection severity in children under 5 years old before and after Omicron emergence in the US*. medRxiv 2022; 2022.01.12.22269179]. Available from: http://medrxiv.org/content/early/2022/01/13/2022.01.12.22269179.abstract.
29. UK Health Security Agency. *SARS-CoV-2 variants of concern and variants under investigation in England. Technical briefing 34*. 14 January 2022; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1046853/technical-briefing-34-14-january-2022.pdf.
30. Torjesen, I., *Covid-19: Omicron variant is linked to steep rise in hospital admissions of very young children.* BMJ, 2022. **376**: p. o110.
31. UK Scientific Advisory Group for Emergencies. *CO-CIN: Child admissions and severity by epoch CO-CIN update*. 6 January 2022; Available from: https://www.gov.uk/government/publications/co-cin-child-admissions-and-severity-by-epoch-co-cin-update-january-2022-6-january-2022.
32. Public Health Scotland, *COVID-19 Statistical Report As at 5 January 2022.* Published 7 January 2022.
33. Goga, A., et al., *Breakthrough Covid-19 infections during periods of circulating Beta, Delta and Omicron variants of concern, among health care workers in the Sisonke Ad26.COV2.S vaccine trial, South Africa.* medRxiv, 2021: p. 2021.12.21.21268171.
34. Jassat W, K.S., Mudara C, et al., , *Clinical Severity of COVID-19 Patients Admitted to Hospitals in Gauteng, South Africa During the Omicron-Dominant Fourth Wave.* . Lancet Pre-print., December 29, 2021.
35. Wolter, N., et al., *Early assessment of the clinical severity of the SARS-CoV-2 omicron variant in South Africa: a data linkage study.* The Lancet.

36. Abdelnabi, R., et al., *The omicron (B.1.1.529) SARS-CoV-2 variant of concern does not readily infect Syrian hamsters*. 2021, bioRxiv.
37. Ryan, K., et al., *Convalescence from prototype SARS-CoV-2 protects Syrian hamsters from disease caused by the Omicron variant*. 2021, bioRxiv.
38. The Genotype to Phenotype Japan (G2P-Japan) Consortium. *Attenuated fusogenicity and pathogenicity of SARS-CoV-2 Omicron variant*. 26 Dec 2021; Available from: https://drive.google.com/file/d/1rhCazFav1pokFKmsZI5_oqIeH9ofFckR/view.
39. LKS Faculty of Medicine at The University of Hong Kong. *HKUMed finds Omicron SARS-CoV-2 can infect faster and better than Delta in human bronchus but with less severe infection in lung*. 15 December 2021; Available from: https://www.med.hku.hk/en/news/press/20211215-omicron-sars-cov-2-infection.
40. Brandal, L.T., et al., *Outbreak caused by the SARS-CoV-2 Omicron variant in Norway, November to December 2021.* Euro surveillance : bulletin Europeen sur les maladies transmissibles = European communicable disease bulletin, 2021. **26**(50).
41. Kuhlmann, C., et al., *Breakthrough Infections with SARS-CoV-2 Omicron Variant Despite Booster Dose of mRNA Vaccine.* SSRN Electronic Journal, 2021.
42. *SARS-CoV-2 B.1.1.529 (Omicron) Variant — United States, December 1–8, 2021.* MMWR. Morbidity and Mortality Weekly Report, 2021. **70**(50).
43. Li, A., et al., *Omicron and S-Gene Target Failure Cases in the Highest COVID-19 Case Rate Region in Canada - December 2021.* J Med Virol, 2021.
44. Iacobucci, G., *Covid-19: Runny nose, headache, and fatigue are commonest symptoms of omicron, early data show.* BMJ (Clinical research ed.), 2021. **375**: p. n3103.
45. Vihta, K.-D., et al., *OMICRON-ASSOCIATED CHANGES IN SARS-COV-2 SYMPTOMS IN THE UNITED KINGDOM.* medRxiv, 2022: p. 2022.01.18.22269082.
46. Kim, M.-K., et al., *Clinical Characteristics of 40 Patients Infected With the SARS-CoV-2 Omicron Variant in Korea.* J Korean Med Sci, 2022. **37**(3): p. 0.
47. Barnaby, Y., et al., Nature Portfolio, 2022.
48. Hajjo, R., et al., *The Epidemiology of Hundreds of Individuals Infected with Omicron BA.1 in Middle-Eastern Jordan.* medRxiv, 2022: p. 2022.01.23.22269442.
49. Elliott P., E.O., Bodinier B., et al. *Post-peak dynamics of a national Omicron SARS-CoV-2 epidemic during January 2022. REACT-1 study. Round 17.* 2022. ; Available from: https://www.imperial.ac.uk/media/imperial-college/institute-of-global-health-innovation/R17_final.pdf.
50. Gunnhild Helmsdal, et al., *Omicron outbreak at a private gathering in the Faroe Islands infecting 21 of 33 triple-vaccinated healthcare workers.* medRxiv, 23 Dec 2021.
51. Jansen, L., et al., *Investigation of a SARS-CoV-2 B.1.1.529 (Omicron) Variant Cluster — Nebraska, November–December 2021.* MMWR. Morbidity and Mortality Weekly Report, 2021. **70**(5152).
52. Águila-Mejía, J.D., et al., *Secondary Attack Rates, Transmission, Incubation and Serial Interval Periods of first SARS-CoV-2 Omicron variant cases in a northern region of Spain.* 2022.
53. Backer, J.A., et al., *Shorter serial intervals in SARS-CoV-2 cases with Omicron variant compared to Delta variant in the Netherlands, 13 – 19 December 2021.* medRxiv, 2022: p. 2022.01.18.22269217.
54. National Institute of Infectious Diseases, J. *Active epidemiological investigation on SARS-CoV-2 infection caused by Omicron variant (Pango lineage B.1.1.529) in Japan: preliminary report on infectious period. 5 January 2022.*; Available from: www.niid.go.jp/niid/en/2019-ncov-e/10884-covid19-66-en.html.
55. Puhach, O., et al. *Infectious viral load in unvaccinated and vaccinated patients infected with SARS-CoV-2 WT, Delta and Omicron*. medRxiv 2022; 2022.01.10.22269010]. Available from: http://medrxiv.org/content/early/2022/01/11/2022.01.10.22269010.abstract.
56. Hay J, K.S., Fauver JR, Mack C, et al. . *Viral dynamics and duration of PCR positivity of the SARS-CoV-2 Omicron variant. (Pre-print).* 2022.; Available from: https://nrs.harvard.edu/URN-3:HUL.INSTREPOS:37370587.
57. Benjamin, M., et al., Nature Portfolio, 2022.

58. Hansen, C.H., et al. *Vaccine effectiveness against SARS-CoV-2 infection with the Omicron or Delta variants following a two-dose or booster BNT162b2 or mRNA-1273 vaccination series: A Danish cohort study*. 22 Dec 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.12.20.21267966v2.full.pdf.
59. Eggink, D., et al., *Increased risk of infection with SARS-CoV-2 Omicron compared to Delta in vaccinated and previously infected individuals, the Netherlands, 22 November to 19 December 2021.* medRxiv, 2021: p. 2021.12.20.21268121.
60. Tseng, H.F., et al., *Effectiveness of mRNA-1273 against SARS-CoV-2 omicron and delta variants.* medRxiv, 2022: p. 2022.01.07.22268919.
61. Discovery Health. *Discovery Health, South Africa's largest private health insurance administrator, releases at-scale, real-world analysis of Omicron outbreak based on 211 000 COVID-19 test results in South Africa, including collaboration with the South Africa*. 14 Dec 2021; Available from: https://www.discovery.co.za/corporate/news-room.
62. Yang, W. and J. Shaman. *SARS-CoV-2 transmission dynamics in South Africa and epidemiological characteristics of the Omicron variant*. 21 Dec 2021; Available from: https://www.medrxiv.org/content/10.1101/2021.12.19.21268073v1.full.pdf.
63. Andrews, N., et al. *Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern*. 2021; Available from: https://khub.net/documents/135939561/430986542/Effectiveness+of+COVID-19+vaccines+against+Omicron+variant+of+concern.pdf/f423c9f4-91cb-0274-c8c5-70e8fad50074.
64. UK Health Security Agency. *Effectiveness of 3 doses of COVID-19 vaccines against symptomatic COVID-19 and hospitalisation in adults aged 65 years and older*. 2022; Available from: https://khub.net/documents/135939561/338928724/Effectiveness+of+3+doses+of+COVID-19+vaccines+against+symptomatic+COVID-19+and+hospitalisation+in+adults+aged+65+years+and+older.pdf/ab8f3558-1e16-465c-4b92-56334b6a832a.
65. Abu-Raddad, L.J., et al., *Effectiveness of BNT162b2 and mRNA-1273 COVID-19 boosters against SARS-CoV-2 Omicron (B.1.1.529) infection in Qatar.* medRxiv, 2022: p. 2022.01.18.22269452.
66. UK Health Security Agency. *COVID-19 Vaccine Surveillance Report. 27 January 2022.*; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1050721/Vaccine-surveillance-report-week-4.pdf.
67. Collie, S., et al., *Effectiveness of BNT162b2 Vaccine against Omicron Variant in South Africa.* New England Journal of Medicine, 2021.
68. Gray, G.E., et al., *Vaccine effectiveness against hospital admission in South African health care workers who received a homologous booster of Ad26.COV2 during an Omicron COVID19 wave: Preliminary Results of the Sisonke 2 Study.* medRxiv, 2021: p. 2021.12.28.21268436.
69. Tartof, S.Y., et al., *BNT162b2 (Pfizer–Biontech) mRNA COVID-19 Vaccine Against Omicron-Related Hospital and Emergency Department Admission in a Large US Health System: A Test-Negative Design.* SSRN Electronic Journal, 2022.
70. Thompson, M.G., et al., *Effectiveness of a Third Dose of mRNA Vaccines Against COVID-19–Associated Emergency Department and Urgent Care Encounters and Hospitalizations Among Adults During Periods of Delta and Omicron Variant Predominance — VISION Network, 10 States, August 2021–January 2022.* MMWR. Morbidity and Mortality Weekly Report, 2022. **71**(4).
71. GeurtsvanKessel, C., et al., *Divergent SARS CoV-2 Omicron-specific T- and B-cell responses in COVID-19 vaccine recipients*. 2021, medRxiv.
72. Nemet, I., et al., *Third BNT162b2 Vaccination Neutralization of SARS-CoV-2 Omicron Infection.* N Engl J Med, 2021.
73. Perez-Then, E., et al. *Immunogenicity of heterologous BNT162b2 booster in fully vaccinated individuals with CoronaVac against SARS-CoV-2 variants Delta and Omicron: the Dominican Republic Experience*.

2021 2021; Available from: https://www.medrxiv.org/content/medrxiv/early/2021/12/29/2021.12.27.21268459.full.pdf.

74. Tada, T., et al., *Increased resistance of SARS-CoV-2 Omicron Variant to Neutralization by Vaccine-Elicited and Therapeutic Antibodies*. 2021, bioRxiv.
75. Zeng, C., et al., *mRNA Booster Vaccines Elicit Strong Protection Against SARS-CoV-2 Omicron Variant in Cancer Patients*. 2021, medRxiv.
76. Zhang, L., et al., *The significant immune escape of pseudotyped SARS-CoV-2 variant Omicron.* Emerging Microbes & Infections, 2022. **11**(1): p. 1-5.
77. Keeton, R., et al., *SARS-CoV-2 spike T cell responses induced upon vaccination or infection remain robust against Omicron.* medRxiv, 2021: p. 2021.12.26.21268380.
78. Tarke, A., et al., *SARS-CoV-2 vaccination induces immunological memory able to cross-recognize variants from Alpha to Omicron.* bioRxiv, 2021: p. 2021.12.28.474333.
79. Liu, J., et al., *Vaccines Elicit Highly Cross-Reactive Cellular Immunity to the SARS-CoV-2 Omicron Variant.* medRxiv, 2022: p. 2022.01.02.22268634.
80. De Marco, L., et al., *Preserved T cell reactivity to the SARS-CoV-2 Omicron variant indicates continued protection in vaccinated individuals*. 2021, bioRxiv.
81. Altarawneh, H., et al., *Protection afforded by prior infection against SARS-CoV-2 reinfection with the Omicron variant.* medRxiv, 2022: p. 2022.01.05.22268782.
82. Lusvarghi, S., et al. *SARS-CoV-2 Omicron neutralization by therapeutic antibodies, convalescent sera, and post-mRNA vaccine booster*. 23 Dec 2021; Available from: https://www.biorxiv.org/content/biorxiv/early/2021/12/23/2021.12.22.473880.full.pdf.
83. Wilhelm, A., et al., *Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and monoclonal antibodies.* medRxiv, 2021: p. 2021.12.07.21267432.
84. Cao, Y., et al., *B.1.1.529 escapes the majority of SARS-CoV-2 neutralizing antibodies of diverse epitopes.* bioRxiv, 2021: p. 2021.12.07.470392.
85. Cathcart, A.L., et al., *The dual function monoclonal antibodies VIR-7831 and VIR-7832 demonstrate potent in vitro and in vivo activity against SARS-CoV-2.* bioRxiv, 2021: p. 2021.03.09.434607.
86. VanBlargan, L.A., et al., *An infectious SARS-CoV-2 B.1.1.529 Omicron virus escapes neutralization by several therapeutic monoclonal antibodies.* bioRxiv, 2021: p. 2021.12.15.472828.
87. Boschi, C., et al., *Omicron variant escapes therapeutic mAbs contrary to eight prior main VOC.* bioRxiv, 2022: p. 2022.01.03.474769.
88. Anupriya, A., et al., *SARS-CoV-2 Omicron: evasion of potent humoral responses and resistance to clinical immunotherapeutics relative to viral variants of concern.* Research Square, 2022.
89. Takashita, E., et al., *Efficacy of Antibodies and Antiviral Drugs against Covid-19 Omicron Variant.* New England Journal of Medicine, 2022.
90. Tatham, L., et al., *Lack of Ronapreve (REGN-CoV; casirivimab and imdevimab) virological efficacy against the SARS-CoV-2 Omicron variant (B.1.1.529) in K18-hACE2 mice.* bioRxiv, 2022: p. 2022.01.23.477397.
91. Dabrowska, A., et al. *Efficacy of antiviral drugs against the omicron variant of SARS-CoV-2*. 23 Dec 2021; Available from: https://www.biorxiv.org/content/biorxiv/early/2021/12/23/2021.12.21.473268.full.pdf.
92. Rosales, R., et al., *Nirmatrelvir, Molnupiravir, and Remdesivir maintain potent in vitro activity against the SARS-CoV-2 Omicron variant.* bioRxiv, 2022: p. 2022.01.17.476685.
93. Vangeel, L., et al., *Remdesivir, Molnupiravir and Nirmatrelvir remain active against SARS-CoV-2 Omicron and other variants of concern.* Antiviral Research, 2022. **198**: p. 105252.
94. Greasley, S.E., et al., *Structural basis for Nirmatrelvir in vitro efficacy against the Omicron variant of SARS-CoV-2.* bioRxiv, 2022: p. 2022.01.17.476556.
95. Rai, D.K., et al., *Nirmatrelvir, an orally active Mpro inhibitor, is a potent inhibitor of SARS-CoV-2 Variants of Concern.* bioRxiv, 2022: p. 2022.01.17.476644.
96. Ryuta, U., et al., *Therapeutic efficacy of antibodies and antivirals against a SARS-CoV-2 Omicron variant.* Nature Portfolio, 2022.

97. US Food and Drug Administration (FDA). *Coronavirus (COVID-19) Update: FDA Authorizes First Oral Antiviral for Treatment of COVID-19*. 22 Dec 2021; Available from: https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-fda-authorizes-first-oral-antiviral-treatment-covid-19.
98. UK Health Security Agency, *SARS-CoV-2 variants of concern and variants under investigation in England Technical briefing 32*

17 December 2021.
99. World Health Organisation. *Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States*. 23 Dec 2021; Available from: https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states.
100. US Food and Drug Administration (FDA). *SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests*. 15 Dec 2021; Available from: https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests.
101. Hussey, H., et al. *Assessing the clinical severity of the Omicron variant in the Western Cape Province, South Africa, using the diagnostic PCR proxy marker of RdRp target delay to distinguish between Omicron and Delta infections: a survival analysis*. medRxiv 2022; 2022.01.13.22269211]. Available from: http://medrxiv.org/content/early/2022/01/14/2022.01.13.22269211.abstract.
102. Mills, M.G., et al., *Rapid and Accurate Identification of SARS-CoV-2 Omicron Variants Using Droplet Digital PCR (RT-ddPCR).* medRxiv, 2022: p. 2022.01.11.22268981.
103. Fu, J.Y.L., et al., *SARS-CoV-2 multiplex RT-PCR to detect variants of concern (VOCs) in Malaysia, between January to May 2021.* Journal of Virological Methods, 2022. **301**: p. 114462.
104. Marais, G., et al. *Saliva swabs are the preferred sample for Omicron detection*. 24 Dec 2021; Available from: https://www.medrxiv.org/content/medrxiv/early/2021/12/24/2021.12.22.21268246.full.pdf.
105. Adamson, B.J., et al., *Discordant SARS-CoV-2 PCR and Rapid Antigen Test Results When Infectious: A December 2021 Occupational Case Series.* medRxiv, 2022: p. 2022.01.04.22268770.
106. Roche. *Media/roche.com statement in response to new Omicron variant of SARS-CoV-2 (B.1.1.529)*. 2021; Available from: https://www.roche.com/dam/jcr:0fe6a722-c127-4ed0-b6e8-0a7bd7d31ba9/en/reactive-media-statement-in-response-to-new-omicron-variant-of-covid-19.pdf.
107. Abbott. *Predicted Impact of Variants on Abbott SARS-CoV-2/COVID-19 Diagnostic Tests*. 26 Nov 2021; Available from: https://www.molecular.abbott/sal/COL-04232_v2.0_Cross_Division_COVID_Variant_Tech_Brief_June_Update_v2_clean_2.pdf.
108. Siemens. *CLINITEST® Rapid COVID-19 Antigen Test*. Dec 2021; Available from: https://www.siemens-healthineers.com/point-of-care-testing/covid-19-testing/covid-19-tests/clinitest-covid-19-antigen-test.
109. Goodall, B.L., et al., *Investigating sensitivity of nasal or throat (ISNOT): A combination of both swabs increases sensitivity of SARS-CoV-2 rapid antigen tests.* medRxiv, 2022: p. 2022.01.18.22269426.
110. Karnon, J., *Should rapid antigen tests be government funded in Australia? An economic evaluation.* medRxiv, 2022: p. 2022.01.03.22268709.
111. Bartha, F.A., et al., *Potential severity, mitigation, and control of Omicron waves depending on pre-existing immunity and immune evasion.* medRxiv, 2021: p. 2021.12.15.21267884.
112. Rowe, B.R., et al., *Increased airborne transmission of COVID-19 with new variants. Implications for health policies.* medRxiv, 2022: p. 2022.01.13.22269234.
113. UK Health Security Agency. *Risk assessment for SARS-CoV-2 variant: VUI-22JAN-01 (BA.2)*. 26 January 2022; Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1051013/26-january-2022-risk-assessment-for-VUI-22JAN-01_BA.2.pdf.
114. World Health Organization (WHO), *Weekly epidemiological update on COVID-19 - 1 February 2022*. 1 February 2022.

115. Institut, S.S. *Now, an Omicron variant, BA.2, accounts for almost half of all Danish Omicron-cases*. 20 January 2022; Available from: https://en.ssi.dk/news/news/2022/omicron-variant-ba2-accounts-for-almost-half-of-all-danish-omicron-cases.
116. Lyngse, F.P., et al., *Transmission of SARS-CoV-2 Omicron VOC subvariants BA.1 and BA.2: Evidence from Danish Households.* medRxiv, 2022: p. 2022.01.28.22270044.
117. World Health Organization (WHO). *Enhancing response to Omicron SARS-CoV-2 variant*. 21 January 2022; Available from: https://www.who.int/publications/m/item/enhancing-readiness-for-omicron-(b.1.1.529)-technical-brief-and-priority-actions-for-member-states.
118. Desingu, P.A., K. Nagarajan, and K. Dhama, *Emergence of Omicron third lineage BA.3 and its importance.* J Med Virol, 2022.