

Enhancing Readiness for Omicron (B.1.1.529): Technical Brief and Priority Actions for Member States

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Summary

Background

- On 26 November 2021, [WHO designated the variant B.1.1.529 a variant of concern \(VOC\)](#), (1) on the basis of advice from WHO's Technical Advisory Group on Virus Evolution. The variant has been given the name Omicron. Omicron variant is a highly divergent variant with a high number of mutations, including 26-32 in the spike protein, some of which are concerning and may be associated with humoral immune escape potential and higher transmissibility.
- As of 16 December 2021, the Omicron variant has been identified in 89 countries across all six WHO regions. Current understanding of the Omicron variant will continue to evolve as more data becomes available.
- The overall threat posed by Omicron largely depends on four key questions, including: (1) how transmissible the variant is; (2) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; (3) how virulent the variant is compared to other variants; and (4) how populations understand these dynamics, perceive risk and follow control measures, including public health and social measures. Public health advice is based on current information and will be tailored as more evidence emerges around those key questions.
- There is consistent evidence that Omicron has a substantial growth advantage over Delta. It is spreading significantly faster than the Delta variant in countries with documented community transmission, with a doubling time between 1.5–3 days. Omicron is spreading rapidly in countries with high levels of population immunity and it remains uncertain to what extent the observed rapid growth rate can be attributed to immune evasion, intrinsic increased transmissibility or a combination of both. However, given current available data, it is likely that Omicron will outpace Delta where community transmission occurs.
- There are still limited data on the clinical severity of Omicron. More data are needed to understand the severity profile and how severity is impacted by vaccination and pre-existing immunity. Hospitalizations in the UK and South Africa continue to rise, and given rapidly increasing case counts, it is possible that many healthcare systems may become quickly overwhelmed.
- Preliminary data suggest that there is a reduction in neutralizing titres against Omicron in those who have received a primary vaccination series or in those who have had prior SARS-CoV-2 infection, which may suggest a level of humoral immune evasion.
- There are still limited available data, and no peer-reviewed evidence, on vaccine efficacy or effectiveness to date for Omicron. Preliminary findings of vaccine effectiveness studies (test-negative design) were obtained from South Africa and England, the United Kingdom. Available preliminary data to be interpreted

with caution as the designs may be subject to selection bias and the results are based on relatively small numbers. Results from England indicate a significant reduction in vaccine effectiveness against symptomatic disease for Omicron compared to Delta after two vaccine doses of either Pfizer BioNTech-Comirnaty or AstraZeneca-Vaxzevria vaccines. There was, however, higher effectiveness two weeks after a Pfizer BioNTech-Comirnaty booster, which was slightly lower or comparable to that against Delta. A non-peer-reviewed study by South Africa researchers using private health insurance data reported reductions in vaccine effectiveness of the Pfizer BioNTech-Comirnaty vaccine against infection, and to a lesser degree against hospitalization. Details about the methods or results were not available at the time of writing.

- The diagnostic accuracy of routinely used PCR and antigen-based rapid diagnostic test (Ag-RDT) assays does not appear to be impacted by Omicron. Most Omicron variant sequences reported include a deletion in the S gene, which can cause an S gene target failure (SGTF) in some PCR assays. Though a minority of publicly-shared sequences lack this deletion, SGTF can be used as a proxy marker to screen for Omicron. However, confirmation should be obtained by sequencing, as this deletion can also be found in other VOCs (e.g. Alpha and subsets of Gamma and Delta) circulating at low frequencies globally.
- Therapeutic interventions for the management of patients with severe or critical COVID-19 associated with the Omicron variant that target host responses (such as corticosteroids, and interleukin 6 receptor blockers) are expected to remain effective. However, preliminary data from preprint publications suggest that some of the monoclonal antibodies developed against SARS-CoV-2 may have decreased neutralization against Omicron. Monoclonal antibodies will need to be tested individually for their antigen binding and virus neutralization, and these studies should be prioritized.

Risk Assessment

- The overall risk related to the new variant of concern Omicron remains very high for a number of reasons. First, the global risk of COVID-19 remains very high overall, and second, current data indicate that Omicron has a significant growth advantage over Delta, leading to rapid spread in the community and subsequent increase in hospitalizations. Our understanding is still evolving, and the risk assessment will be updated as more information becomes available.

Priority actions for Member States

- WHO is asking all member states to regularly reassess and revise national plans based on current situation and national capacities.
- The use of well-fitting masks, physical distancing, ventilation of indoor spaces, crowd avoidance, especially during holiday periods, and hand hygiene remain key to reducing transmission of SARS-CoV-2 with the emergence of the Omicron variant. Enhanced surveillance with rapid testing and stricter contact tracing of cases suspected to be infected with a variant of concern (VOC) are strongly advised to interrupt chains of transmission.
- In anticipation of increased COVID-19 caseloads and associated pressure on the health system, ensure mitigation plans are in place to maintain essential health services and necessary health care resources are in place to respond to potential surges. This would include surge capacity plans for health workers as well as plans for providing additional practical support to health workers, with particular attention to the needs of mothers and single parent families.
- Efforts to accelerate COVID-19 vaccination coverage in at risk populations as rapidly as possible should continue. Particular focus among [populations designated as high priority](#) (4) who remain unvaccinated or are not yet fully vaccinated should be a priority for vaccination campaigns. Delta is still by far the predominant variant worldwide causing significant disease and transmission against which vaccines are highly effective, and vaccines are likely to have some effectiveness against Omicron, particularly for severe disease, even if performance is reduced compared with other variants. Finally, in some countries with high COVID-19 hospitalizations and deaths, [boosters could play an important role, especially for those at](#)

[highest risk of severe disease and deaths](#)

- Ensure early warning systems are in place to inform efficient and rational adjustment of public health and social measures, with effective approaches for engaging affected communities and communicating these adjustments while anticipating populations' concerns.
- Enhance surveillance, including increasing testing and sequencing efforts to better understand circulating SARS-CoV-2 variants, including Omicron. Where capacity exists, perform field investigations such as [household transmission studies](#),⁽²⁾ first few cases [studies](#),⁽³⁾ contact follow up and laboratory assessments to improve understanding of the characteristics of Omicron.
- Because SGTF from commercial PCR kits is indicative for Omicron, this can be used as a proxy marker for this variant. However, it should be noted that a small minority of Omicron sequences lack this deletion and will be missed by this screening method.
- All initial cases/clusters associated with Omicron variant infection should be reported to WHO through the International Health Regulations (IHR) mechanism.
- Thereafter, Member States are encouraged to report (publicly or through IHR) the weekly relative prevalence of Omicron as the number of sequences of Omicron (numerator) divided by the total number of sequences generated through routine surveillance (denominator) and/or, where available, number of SGTF out of the number tested in the same unit of time, according to sampling date.
- A risk-based approach to adjust international travel measures in a timely manner is recommended. See [WHO advice for international traffic in relation to the SARS-CoV-2 Omicron variant](#) ⁽⁵⁾ for additional information.
- Authorities should regularly communicate evidence-based information on Omicron and other circulating variants and potential implications for the public in a timely and transparent manner, including what is known, what is unknown and what is being done by responsible authorities.

Background

On 26 November 2021, following advice from WHO's Technical Advisory Group on Virus Evolution, WHO designated the SARS-CoV-2 variant B.1.1.529 a variant of concern (VOC). This variant was named Omicron.

The overall threat posed by Omicron largely depends on three key questions, including: (1) how transmissible the variant is; (2) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; (3) how virulent the variant is compared to other variants; and (4) how populations understand these dynamics, perceive risk and follow control measures, including public health and social measures.

This technical brief addresses early evidence around those key aspects, and outlines a set of priority actions for Member States.

Epidemiology

- As of 16 December 2021 (4 pm CET), the Omicron variant has been confirmed in 89 countries. In several countries where there is evidence of widespread local transmission, the Omicron variant is expected to become dominant in the coming week(s).
- In South Africa, where Omicron was first reported, the case incidence of COVID-19 has continued to rise since the second week of November. [In week 49](#), (6) a total of 109 053 COVID-19 cases were reported, a 1.6-fold increase compared to the previous week, with the highest incidence still reported in Gauteng province where some of the initial cases of Omicron were identified. Omicron is now the dominant variant sequenced in South Africa.
- Between 6 and 12 December large increases in the incidence of cases compared to the previous week were observed in countries neighboring South Africa including Lesotho (15.2x increase, 1264 vs 83 cases); Zimbabwe (5.8x increase, 26479 vs 4572 cases) Eswatini (5.7x increase, 4806 vs 840 cases); Namibia (4.6x increase, 1722 vs 375 cases) and Mozambique (4.4x increase, 1540 vs 353 cases). Additionally, large increases are now starting to be seen in other African countries reporting cases of Omicron, including Mauritius (8.8x increase (6415 vs 733 cases); the Democratic Republic of the Congo (4.4x increase, 1388 vs 314 cases); Nigeria (4.3x increase, 2496 vs 585 cases) and Zambia (4.3x increase, 665 vs 156 cases). While the reasons for those increases remain unclear, it is possible that the spread of Omicron, in combination with enhanced testing following the declaration of a VOC, play a role.
- In the European Region, Delta remains the dominant variant in most countries. [Modelling predictions](#) (7) suggest that Omicron may rapidly become dominant within the first two months of 2022. As of 16 December 2021, a total of 27 EU/EEA countries have reported confirmed cases of Omicron
- In the United Kingdom, as of 16 December, there have been 11 708 confirmed cases (by sequencing or genotyping) of cases of Omicron and 37 430 cases with S-gene target failure (SGTF). Between 13-14 December, 41% of the cases in England with known S gene status were SGTF (9587/23393), with the highest proportion seen in London (73.5%, 2406/3274).
- In the United States, the Centers for Disease Control and Prevention (CDC) reports that the Delta variant still accounts for over 99.9 % of all COVID-19 cases in the USA. The Omicron variant has been detected in 36 states with no reported deaths to date.

Transmission

- The daily reproductive number (Rt) [estimated by the National Institute for Communicable Diseases \(NICD\)](#) (8) in South Africa using reported cases was below 1 in October and early November 2021. These estimates increased from the start of November and reached [2.56 \(95% CI 2.23, 2.96\)](#) (8) based on case data up until 4 December. A recent pre-print study by Grabowski et al. (non-peer reviewed) estimates a doubling time

in Gauteng province of South Africa of between 3.2 and 3.6 days based on data from 8 November to 5 December 2021.

- In the latest technical brief by UK Health Security Agency (UKHSA), the estimated growth rate of S gene target failure (SGTF) cases compared with S gene target positive (SGTP) using data up until 6 December was 0.35 per day, corresponding to a doubling time of 2 days. These estimates are based on non-travel related cases and account for the probability that an SGTF originates from an Omicron case. This also corresponds to an R_t of 3.7 (3.3, 4.2), assuming a generation time of 5.2 days. The most recent [daily overview of Omicron by UKHSA](#) (9) reports that between 12 and 13 December, 74% of cases in London and 41% of cases in England were Omicron cases. Central estimates of doubling times are now less than two days across all regions in England, except the South West.
- Preliminary findings from [studies of households and contacts in UK](#) (9) have found a higher risk of transmission to contacts from an Omicron index case, when compared to Delta index cases. The initial findings show the increased risk of household transmission using routine testing data (adjusted odds ratio of transmission from an Omicron index case compared to a Delta index case 3.2 (95% CI 2.0-5.0)) and the increased risk of a close contact becoming a secondary case (adjusted odds ratio 2.09 (95% CI: 1.54-2.79)). The household secondary attack rate estimated using routine contact tracing data for Omicron is 21.6% (95% CI: 16.7%-27.4%) and 10.7% (95% CI: 10.5%-10.8%) for Delta. These findings describe overall growth advantage rather than intrinsic transmissibility.
- A paper published by the Scottish Government based on SGTF data in Scotland up until 6 December estimates a doubling time of 2.18-2.66 days. Based on this, Omicron is projected to constitute the majority of cases in Scotland between mid-December and early January 2022.
- [A preliminary report by researchers at London School of Hygiene and Tropical Medicine \(LSHTM\)](#) (10) (non-peer reviewed) published on 11 December, estimates a 2.4-day doubling time of Omicron in England and anticipates that it will become the dominant variant in England in a matter of weeks. The authors estimate that, for a 12.8-fold reduction in neutralization relative to Delta, Omicron exhibits a 5–10% lower transmission rate than Delta, while for a 5.1-fold reduction in neutralization relative to Delta, Omicron exhibits a 30–35% higher transmission rate than Delta.
- An analysis by researchers at [Imperial College London](#) (46) based on SGTF data between 29/11/2021 and 11/12/2021 and genotyping result of specimen dates between 23/11/2021 and 11/12/2021 in England, suggests a rapid growth of Omicron relative to Delta, with doubling time of about two days.
- [Other preliminary estimates](#) (11) of growth rates based on variant frequencies on 14 December, by researchers at the Fred Hutchinson Cancer Research Center, correspond to estimated doubling times of: 3.0 (2.6, 3.6) days in South Africa; 1.8 (1.6, 2.2) days in the United Kingdom; 1.6 (1.3, 1.9) days in Denmark and 2.0 (1.8, 2.4) days in the United States of America. However, these are preliminary estimates and need to be interpreted with caution.
- In summary, recent evidence from multiple geographies indicates that Omicron has a significant growth advantage over Delta, spreading fast through communities, with a doubling time of between 1.5 and 3 days. A higher risk of transmission compared to Delta has been confirmed by household and contact studies in the United Kingdom.
- How much of the growth advantage of Omicron is due to immune evasion or to increased transmissibility remains unclear at present. Neutralization studies, early estimates of vaccination effectiveness against symptomatic disease, and studies of reinfection risk suggest substantial humoral immune evasion against infection (See page 8).

Clinical severity

- Data on case severity (including hospitalization, need for oxygen, mechanical ventilation or deaths) are still limited, and our understanding is expected to evolve in the coming weeks owing to the time lag between an increase in the incidence of cases and that of severe cases, hospitalization and deaths.
- South Africa has seen a rapid increase in the incidence of hospitalization in the public and private health sectors since the start of the Omicron wave. On average, admissions in the Gauteng Province in weeks 47 and 48 have increased by over 450% compared to the average admission rate in weeks 45 and 46, and a 68% increase in COVID-19 hospital deaths has been observed over the same period. Other provinces in South Africa are also seeing steady increases in the number of hospitalized cases, with a national Rt for admissions estimated at [1.70 \(1.54,1.87\)](#) (8) based on data up until 28 November 2021. The number of in-hospital deaths reported by the COVID-19 [hospital surveillance platform](#) (12) increased in all provinces in week 49, with the exception of the Northern Cape and Western Cape Provinces.
- [Preliminary data](#) (13) from a private health insurance provider suggest that the risk of hospitalization may be moderately reduced with Omicron compared to previous epidemic waves in South Africa, with a 25% reduction in hospitalizations, compared to the Delta variant, and proportionally fewer patients in intensive care units. This, in addition to a lower growth rate in hospitalizations compared to that of cases, suggests that the increase in hospitalizations is driven by high levels of transmission, rather than increased severity. However, these preliminary data need to be interpreted with caution, particularly in the context of a high level of population immunity and limited understanding of the protection of infection- and vaccine-derived immunity against severe disease.
- In the United Kingdom, trends in hospitalization have been increasing since the end of November. Cases [with confirmed SGTF](#) (9) are increasing in all regions of the United Kingdom, and one Omicron death has so far been reported.
- Denmark has reported a steep rise in Omicron cases since it was first identified on 28 November 2021. The first 785 cases [reported](#) (14) ranged in age from 2 to 95 years old (median: 32); 433 (55%) were male; 599 (76%) were fully vaccinated; and 56 (7.1%) were fully vaccinated with a booster. Of those 785, 9 (1.2%) were hospitalized, one required treatment in the intensive care unit (ICU) and no deaths were reported.
- In an [outbreak related to a Christmas party in Norway](#), (15) 80 out of 111 participants were diagnosed with SARS-CoV-2 infection, 66 of whom were confirmed Omicron cases. One case was asymptomatic and 74 (91%) reported at least three symptoms. Among the 81 cases, the most common symptoms were cough (83%), runny/stuffy nose (78%), fatigue/lethargy (74%), sore throat (72%), headache (68%) and fever (54%). Symptom onset was on average three days after the party. No hospital admissions have been reported as of 13 December. However, severe outcomes generally take several weeks to observe and so no conclusions on severity can be drawn at this stage.
- As of week 49, a of 1366 case-level data were reported for Omicron and 7 for S-gene target failure through [the European Surveillance System \(Tessy\)](#), including cases from Austria (78; 6%), Finland (28; 2%), Ireland (18; 1%), Italy (15; 1%), Liechtenstein (1; 0%), Luxembourg (1; 0%), Norway (1 160; 84%), Portugal (21; 2%), Romania (8; 1%), Slovakia (3; 0%) and Sweden (40; 3%). The median age of these 1 373 cases was 32 (range: 0-92) years and 715 (52%) were male. Among 463 (34%) cases with complete data on symptom status, 410 (89%) cases were reported as symptomatic and 53 (11%) as asymptomatic. Status of severe COVID-19 outcomes was known for 547 (40%) cases for hospitalization, 545 (40%) for ICU admission or respiratory support and 1 218 (89%) for death (some incomplete reporting of these variables is expected for more recent cases). Among these cases, four (1%) were hospitalized, none required ICU or respiratory support and none died.
- It is too early to conclude if Omicron is more or less severe than other VOCs. However, early data suggest that the severity may be potentially lower than for the Delta variant and even if this is the case, it is expected that hospitalizations will increase as a result of significant increases in transmission. More

hospitalizations will put a burden on health systems and lead to more deaths, particularly with short doubling times requiring rapid scale up.

- Further information is needed to fully understand the clinical picture of those infected with Omicron, and WHO encourages countries to contribute to the collection and sharing of hospitalized patient data through the [WHO COVID-19 Clinical Data Platform](#) (16).

Impact on diagnostics

- SARS-CoV-2 infection can be diagnosed using either molecular tests (NAAT, PCR) or antigen-detection assays. Interim guidance on diagnostic testing for SARS-CoV-2 and on the use of antigen-detection tests can be found [here](#) (17). No test is perfect, and negative results should be interpreted within the clinical/epidemiological context.
- PCR tests that include multiple gene targets, as recommended by WHO, are unlikely to be affected and should continue to be used to detect SARS-CoV-2 infection, including the Omicron variant. This has been confirmed by statements issued by manufacturers as well as the United States Food and Drug Administration ([US FDA](#)) (18), based on sequence analysis and preliminary laboratory evidence.
- The Omicron variant (parent Pango lineage B.1.1.529) includes 3 descendent lineages (BA.1, BA.2 and BA.3). BA.1 and BA.3 have the 69-70 deletion in the spike protein, while BA.2 does not. As of 15 December 2021, BA.1 accounts for 99% of sequences submitted to GISAID, and overall, over 95% of Omicron variant sequences reported include a 69-70 deletion in the S gene.
- Presence of the 69-70 deletion in the spike protein causes a negative signal for the S gene target in certain PCR assays This S-gene target failure (SGTF) can be used as a marker suggestive of Omicron. However, confirmation should be obtained by sequencing for at least a subset of samples, as this deletion is found in other VOCs (e.g. Alpha and subsets of Gamma and Delta), which are circulating at low-levels globally.
- All four [WHO emergency use listing \(EUL\) approved](#) (19) antigen-detection rapid diagnostic tests (Ag-RDTs), target the Nucleocapsid protein of SARS-COV-2. Omicron has G204R and R203K mutations in the Nucleocapsid protein, which are also present in many other variants currently in circulation. So far, these mutations have not been reported to affect the accuracy of Ag-RDTs to detect SARS-CoV-2. In addition, Omicron sequences contain a 3 amino acid deletion at positions 31-33 and the P13L mutation in the Nucleocapsid protein. The specific impact of these mutations on the performance of Ag RDTs (e.g. on sensitivity) is under investigation.
- Preliminary evidence from multiple laboratories and from manufacturers point at the retained ability of most currently used Ag-RDTs, including 2 WHO EUL approved tests, to detect SARS-CoV-2 variants, including Omicron.
- WHO is assessing the risk posed by Omicron on diagnostics that have Emergency Use Listing by reviewing summarized risk assessments conducted by manufacturers, conducting independent in-silico analysis for NAT assays and considering the results of independent laboratory testing using clinical specimens, clinically-derived isolates or synthetic constructs/recombinant antigen. Any urgent safety information would be communicated by the manufacturers using field safety notices and/or by WHO via posting a WHO Information Notice for Users [here](#) (20).
- Laboratory personnel are encouraged to report any unusual findings to the manufacturer using this [form](#). This may include increased discrepancies in cycle threshold (Ct) values between different gene targets, failure to detect specific gene targets, including those containing gene sequences that coincide with documented mutations or misdiagnosis (for example, false negative results).
- To date, there have been no reported misdiagnoses (false negative results) for any WHO EUL approved diagnostic product in relation to Omicron.

Immune evasion

- Preliminary evidence from epidemiological, modelling and laboratory studies suggests that humoral immunity is less protective against infection by Omicron than against other variants.
- A [study in South Africa](#) showed that the likelihood of reinfection with Omicron was higher than what would have been expected with previous variants, and early findings from unpublished modelling studies (personal communication), also suggest that some level of immune evasion against infection is likely.
- Similar findings have also been found in a [recent analysis](#) (46) on data from England, United Kingdom, where the risk of reinfection with Omicron was estimated to be 5.41 (95% CI: 4.87-6.00) fold higher than for Delta.
- Laboratory data on humoral immune response to Omicron is rapidly emerging, with available results from 11 non-peer reviewed studies looking into the antibody neutralization activity against Omicron. (21–31) While these reports capture a small number of samples and use different testing methods (e.g. live virus, pseudo virus), making the comparability between studies challenging, all have reported a substantial fall in neutralizing titers against Omicron compared to other VOCs and the ancestral virus both in vaccinated and convalescent samples. In contrast to findings about humoral immune response, [preliminary in-silico data](#) (32) (among 16 individuals who received the Pfizer vaccine) predicts that 70% of Omicron epitopes may not be affected by T-cell recognition, which may suggest a more preserved cellular-mediated protection against severe disease.
- A [study](#) (24) of samples from a longitudinal cohort of previously infected individuals who subsequently received an mRNA vaccine and individuals who received two doses of mRNA vaccines followed by a third dose of Pfizer BioNTech-Comirnaty vaccine, had high levels of neutralization against Omicron one month after the final dose, suggesting that waning immunity may account for some of the reduction in neutralization activity observed.
- Similar trends were [reported by the Ministry of Health in Israel](#) (29) for the third dose of Pfizer BioNTech-Comirnaty vaccine. It is important to note these samples were tested one month post Pfizer BioNTech-Comirnaty booster dose, and monitoring of longer-term effects is therefore still needed.
- A study in the United Kingdom reported a reduction in neutralization titres in individuals vaccinated with 2 doses of either Pfizer BioNTech-Comirnaty or AstraZeneca-Vaxzevria vaccine at day 28 post second dose, suggesting an increased risk for breakthrough infections due to circulating Omicron, and in line with early [vaccine effectiveness estimates](#) (33) from England (see below).
- It is essential that COVID-19 vaccination among at-risk groups in all countries is prioritized and accelerated urgently.

Impact on vaccines

- Preliminary results of vaccine effectiveness based on clinical outcomes in England and South Africa have emerged over the last week, indicating a reduction in vaccine effectiveness for Omicron against infection, symptomatic disease and hospitalization compared to earlier variants.
- In England, [vaccine effectiveness estimates](#) (33) were based on 581 symptomatic Omicron cases, 56 439 eligible Delta cases and 130 867 test-negative controls. Among those who had received 2 doses of Pfizer BioNTech-Comirnaty, vaccine effectiveness was 88.0% (95%CI: 65.9 to 95.8%) 2-9 weeks after dose 2 for the Omicron variant, dropping to 34% (95%CI: -7.0 to 59.0%) after 25 weeks, compared with vaccine effectiveness of 63.5% (95%CI: 61.4 to 65.5%) against Delta in the same time period. Among those who had received 2 doses of AstraZeneca-Vaxzevria, there was no protective effect of vaccination against symptomatic disease with Omicron from 15 weeks after the second dose. However, these estimates are

based on relatively small numbers and are likely to reflect an older population and a population with more co-morbidities than those given the Pfizer BioNTech-Comirnaty vaccine. Vaccine effectiveness two weeks after a Pfizer BioNTech-Comirnaty booster dose was estimated as 71.4% (95%CI: 41.8 to 86.0%) in those who received AstraZeneca-Vaxzevria as the primary course and 75.5% (95%CI: 56.1 to 86.3%) in those who had received Pfizer BioNTech-Comirnaty as the primary course.

- [A more recent analysis](#) (46) by researchers at Imperial College London compared the relative risk of symptomatic infection with Omicron compared to Delta for different vaccine schedules (two doses of Pfizer BioNTech-Comirnaty or AstraZeneca-Vaxzevria, with or without an mRNA vaccine booster), based on PCR-confirmed symptomatic infections in England, United Kingdom excluding international travellers, and matching by day, age, sex, region and ethnicity. The preliminary results suggest a higher risk of infection for Omicron, compared to Delta, translating into estimates of vaccine effectiveness against symptomatic infection between 0% and 20% following two doses, and between 55% and 80% after a booster dose.
- In South Africa, the insurance company Discovery Health [posted a press release](#) (13) on preliminary findings of vaccine effectiveness against infection and hospitalization. They report a vaccine effectiveness of the Pfizer BioNTech-Comirnaty vaccine of 33% against infection and 70% against hospitalization, however uncertainty estimates around these figures and details of methods were not included.
- [A meta-analysis](#) (34) across four datasets reported a 9.7-fold fall (95%CI 5.5-17.1) in neutralization titre against Omicron. Vaccine efficacy for Omicron was estimated based on a model, six-month post vaccination with mRNA vaccine, to be 40% and 80% against symptomatic and severe disease, respectively. Vaccine efficacy for Omicron after a Pfizer BioNTech-Comirnaty booster dose may increase to 86.2% (95% CI: 72.6-94) and 98.2% (95% CI: 90.2-99.7) against symptomatic and severe disease, respectively.
- WHO is closely assessing the impact on vaccines through our research and development network by setting up and coordinating a live [repository](#) (35) of reagents to facilitate research focusing on the understanding of vaccine effectiveness through animal model studies, antibody neutralization activity and cellular protection.
- Clinical vaccine effectiveness estimates require continued and ideally improved surveillance and epidemiological studies. Hence, countries with confirmed cases of Omicron are encouraged to consider conducting vaccine effectiveness studies, especially against severe disease and death.
- WHO guidance on best practices to conduct these types of studies and generic protocols can be found on this [website](#). Such studies are critical to compare the vaccine's impact on transmissibility of Omicron and its relative infectivity as compared with the currently prevalent Delta variant.

Impact on therapeutics/treatments

- WHO continues to work with researchers to understand the effectiveness of therapeutics against the Omicron variant. Interleukin-6 receptor blockers and corticosteroids are expected to remain effective in the management of patients with severe and critical disease since they mitigate the host inflammatory response to the virus.
- Preliminary in vitro data published in preprints suggests that some of the monoclonal antibodies developed against SARS-CoV-2 may have decreased neutralization against Omicron.^{16,17,40-43} On 16 December 2021, ROCHE issued a statement on casirivimab and imdevimab diminished potency versus Omicron from in vitro studies ([2021216 Roche statement on Ronapreve Omicron.pdf](#)) (36). Sotrovimab retained activity against Omicron but with a 3-fold lower potency in neutralization as measured by EC50.¹⁷
- WHO is working with its experts to prioritize the [research agenda](#) (37) and collect further data regarding the efficacy of monoclonal antibodies and antivirals. Urgent prioritization is for a) antigen binding and virus neutralization by antiviral monoclonal antibodies and b) characterization of the COVID-19 phenotype caused by infection with the Omicron variant in a diverse patient population.

- For the most up-to-date guidelines, see the WHO website on COVID-19 Therapeutics ([Therapeutics and COVID-19 \(who.int\)](#)) (38).

Global risk assessment

This section summarizes the evidence presented above to arrive at an overall global risk assessment for the Omicron variant.

- At present, a total of 89 countries across all six WHO Regions have reported Omicron cases.
- Omicron is rapidly outpacing the Delta variant where community transmission occurs, with a higher growth rate than has been observed in the COVID-19 pandemic.
- The clinical severity of Omicron remains uncertain, but increased transmission, with similar or even lower severity than Delta, could nonetheless pose overwhelming demands on health care systems and lead to significant morbidity. The impact on vulnerable populations would be substantial, particularly in countries with low vaccination coverage and low population immunity.
- Preliminary evidence from epidemiological studies on reinfection, neutralization studies, modelling estimates and the considerably altered antigenic profile of the Omicron spike protein suggests a significant degree of humoral immune evasion. Furthermore, early results from vaccine effectiveness against symptomatic disease have shown significant reductions in protection from Omicron compared to the Delta variant.
- The overall risk related to the new variant of concern Omicron thus remains very high for a number of reasons. First, the global risk of COVID-19 remains very high overall, and second, Omicron spreads faster in communities than Delta, which could lead to further surges with severe consequences. Our understanding is still evolving, and the risk assessment will be updated as more information becomes available.

Priority Actions for Member States

Based on the risk assessment, the following priority actions are recommended to enhance readiness for the new variant of concern Omicron. All countries should regularly reassess and revise national plans based on the current situation, public risk perceptions and national capacities. The Delta variant is still dominant worldwide, and enhanced efforts to control Delta will benefit the control of Omicron, regardless of how the situation with Omicron worldwide unfolds. Countries should optimize their response for Delta which will benefit responses to any future variants as well as Omicron.

WHO recommends the following priority actions:

Enhanced Surveillance

- Ensure early warning systems are in place, composed of multiple indicators such as growth (e.g. growth rate, effective reproduction number), case incidence and test positivity proportion. It is also crucial to monitor indicators related to disease severity and pressure on health care systems (e.g. bed occupancy of general ward and intensive care units and health care worker exposure and burnout).
- Where capacity exists and in coordination with the international community, perform studies to improve understanding of transmission parameters, vaccine effectiveness, severity, effectiveness of public health and social measures (PHSM) against Omicron, diagnostic methods, immune responses, antibody neutralization, population risk perception, knowledge, attitude and behaviour towards PHSM, vaccines and tests or other relevant characteristics. Generic [study protocols](#) (39) are available. Specimens collected during such investigations may warrant prioritization for sequencing. The epidemiological studies and sequencing of specimens can be targeted to those with particular individual-level characteristics (e.g. suspected reinfections, clinical characteristics; immunocompromised patients and selective sequencing of vaccine breakthrough) as well as regular clusters and super-spreader events.
- When recording case data, particular attention should be paid to cases' vaccination status, including dates and vaccine products; history of previous SARS-CoV-2 infection; symptoms/clinical presentation; and clinical severity/outcome.

Sampling strategies

- Countries should continue to undertake targeted sampling of specific populations, as outlined in the variant guidance for surveillance of SARS-CoV-2 [variants](#) (40), for sequencing.
- To assess whether Omicron may already have been circulating in the past, countries should consider the following
 - Where available, conduct a retrospective review of available genomic sequences and S gene target failure (SGTF) data from October 2021 onwards at the country level. If not already done, sequence specimens with SGTF in the recent past, preferably from October 2021 through the present.
 - For countries with capacity, wastewater sampling may serve as an additional tool for the retrospective and prospective investigation of Omicron in the community.
- To enhance prospective detection of Omicron, the following should be considered.
 - **Countries that have not yet detected Omicron** should (1) monitor Omicron introduction through targeted sequencing of suspected Omicron cases (see definition in the Annex), and (2) detect Omicron community transmission through enhanced random sampling among SARS-CoV-2 confirmed cases (see case definitions) in the community.

- **For countries with confirmed community transmission of Omicron**, emphasis should be put on enhanced random sampling for sequencing among confirmed cases of SARS-CoV-2 infection in the community.
- Case definitions are provided in the Annex.
- Importantly, countries should ensure genomic sequences are reported in a timely manner, including sharing via databases in the public domain (e.g. GISAID) to facilitate analysis.
- All countries should report the numerator and denominator of Omicron samples detected through sequencing or PCR screening (SNP-based assays or SGTF) to allow calculation of the prevalence of circulating Omicron variant. This can be done through the IHR mechanism, public reporting or direct report sharing with WHO.
- Sampling strategies for detection of Omicron (random or targeted) should be reported adjoining the relative prevalence reports of Omicron to allow an understanding of the representativeness of the prevalence of Omicron.
- For further details on surveillance in the context of emerging variants, including sampling strategy, please refer to [WHO guidance for surveillance of SARS-CoV-2 variants Interim guidance 9 August 2021](#) (40). Additional guidance is available in [ECDC Guidance for representative and targeted genomic SARS-CoV-2 monitoring](#) (41).

Laboratory Testing for Omicron

- Suspected and probable cases of Omicron infection should be confirmed by sequencing. Both targeted sequencing of the spike gene (using Sanger sequencing or Next Generation Sequencing) or whole genome sequencing are appropriate to confirm the presence of Omicron.
- For countries using diagnostic tests that include SGTF, or SNP-detection assays to screen for variants, samples that include SGTF or with a SNP profile compatible with Omicron should be considered suspected Omicron infection and should be prioritized for sequence confirmation.
- In addition, all countries are recommended to enhance surveillance and sequencing to characterize circulating SARS-CoV-2 variants, including detection of Omicron.
- As part of routine quality assurance, testing programs should document and report any unexpected results. This may include increased discrepancies in cycle threshold (Ct) values between different gene targets, failure to detect specific gene targets, including those containing gene sequences that coincide with documented mutations or misdiagnosis (for example, false negative results).
- WHO recommends that national testing capacity and genomic sequencing capabilities should be appropriately planned for possible surges in testing demand for community and international travelers, based on national testing strategy.
- It is critical that SARS-CoV-2 testing be linked to public health actions to ensure appropriate clinical and supportive care, and linkage with contact tracing activities to break chains of transmission.

Vaccination

- Efforts should be intensified by public health authorities to accelerate COVID-19 vaccination coverage in all eligible populations, but with priority for populations at high risk for serious disease who remain unvaccinated or are not yet fully vaccinated. These include older adults, health care workers and those with underlying conditions putting them at risk of severe disease and death. Delta is still by far the predominant variant globally against which vaccines are highly effective, and vaccines are likely to have some effectiveness against Omicron, particularly for severe disease, even if the performance is reduced compared with other variants.

- Omicron may have a high likelihood of immune evasion from antibody-mediated protection, especially protection directed at the spike protein. However, immune evasion potential from cell-mediated immunity is more difficult to predict.
- Despite uncertainties, it is reasonable to assume that currently available vaccines offer some protection against Omicron, particularly against severe disease and death.
- The presence of multiple mutations of the spike protein in the receptor-binding domain suggests that Omicron may have a high likelihood of immune evasion from antibody-mediated protection, especially protection directed at the spike protein. However, immune evasion potential from cell-mediated immunity is more difficult to predict. Overall, further research is needed to better understand the escape potential against vaccine- and infection-induced immunity. Research efforts are ongoing, and the data are expected to be available in the coming weeks.

Risk-based approach in adjusting international travel measures

- Use a risk-based approach to adjust international travel measures in a timely manner.
- WHO advises the following:
 - Countries should continue to apply an evidence-informed and risk-based approach when implementing international travel measures in accordance with the IHR and WHO's interim guidance published in July 2021 (5).
 - National authorities may apply a multi-layered risk mitigation approach to potentially delay the exportation or importation of the new variant, including via the use of entry/exit screening, testing or quarantine of travellers. These measures should be informed by a risk assessment process and be commensurate with the risk; time-limited; and applied with respect to travellers' dignity, human rights and fundamental freedoms.
 - Blanket travel bans will not prevent the international spread, and they place a heavy burden on lives and livelihoods. In addition, they can adversely impact global health efforts during a pandemic by disincentivizing countries to report and share epidemiological and sequencing data.
 - All travellers should remain vigilant for signs and symptoms of COVID-19, get vaccinated when it is their turn and adhere to public health and social measures at all times.
- See *WHO advice for international traffic in relation to the SARS-CoV-2 Omicron [variant](#) published on 30 Nov 2021* (5) for additional information.

Public health and social measures (PHSMs)

- The use of well fitted masks, physical distancing, ventilation of indoor space, crowd avoidance and hand hygiene remain key to reducing transmission of SARS-CoV-2, even in the context of emerging variants. However, PHSMs may need to be enhanced to further limit interpersonal contact, to control transmission with a more transmissible variant.
- The use of established PHSMs in response to individual cases or clusters of cases, including contact tracing, quarantine and isolation, must continue to be adapted with community involvement and to the epidemiological and social context. This can be most effective when working through community leaders, civil society and community-based organizations to understand the impacts of PHSM on different population groups. In this way, practical, relevant and acceptable advice can be provided and secondary impacts of restrictive measures can be anticipated and mitigated.
- Guided by risk assessment, taking into account the epidemiological situation, response capacities, vaccination coverage and public perception—as well as uncertainties related to the rapidly evolving situation of Omicron—countries should be ready to escalate PHSMs in a timely manner to avoid overwhelming demands on health care services.
- For further guidance on risk-based calibration of PHSMs, please see [WHO guidance](#) (42).

Health care system readiness

- As part of preparedness activities while studies are ongoing to better understand the phenotypic characteristics of the new VOC, and in the anticipation of possible increase in COVID-19 case-load and associated pressure on the health system, countries are advised to ensure mitigation plans are in place to [maintain essential health services](#) (43) and that necessary resources are in place to respond to potential surges. Tools such as the [COVID-19 Essential Supplies Forecasting Tool](#) (44) are available for use to estimate needs in personal protective equipment (PPE), diagnostics, oxygen and therapeutics. Training and re-training of workforce with standardized materials (<https://openwho.org/>) (45) should be continued on the COVID-19 care pathways ([Living guidance for clinical management of COVID-19 \(who.int\)](#)) (38)

Risk communication and community engagement

- Authorities should communicate information related to Omicron and potential implications for the public in a timely and transparent manner to further foster trust and increase acceptance of response measures. Targeted communication and engagement should be designed for high-risk individuals who may not perceive the nuanced risks of Omicron.
- One of the most important and effective interventions in a public health response to any event is to maintain trust and credibility by proactively communicating with the population what is known, what is unknown and what is being done by responsible authorities to reduce risk.
- Listening to community perceptions through online or offline methods or socio-behavioral surveys and analysing this data are key to responding with effective communication and engagement interventions. Target communication and engagement to specific populations to encourage vaccine uptake and use of protective measures by all, even among individuals who are fully vaccinated.
- COVID-19 information overload and misinformation should be managed at all stages of the response by providing the right information at the right time to the right people through trusted channels (e.g. community and faith leaders, family doctors and other influential members of society). There should be an information monitoring system in place to capture emerging trends to enable delivery of a targeted communication package.
- When PHSMs are adjusted, communities should be fully and regularly informed, engaged and enabled before changes are made, to allow them to take ownership of the selected PHSMs. It is critical to build and foster trust, especially in contexts where there is little or no involvement of the local population in decision-making. Clear, concise and transparent risk communication, including an evidence-based rationale for adjusting measures, should be developed with communities targeted for PHSMs and explained consistently through several information sources that specified communities regularly use (e.g. local radio, hotlines, community networks). Communicating the benefits of these measures and framing the protective behaviours as a series of choices versus directive messages will enable uptake.
- Communities will be critical to implementing population-wide PHSMs and contributing to the mitigation of the social and economic impact of certain measures (e.g. disrupting availability of food and other needed supplies).

References

1. World Health Organization. Classification of Omicron (B.1.1.529): SARS-CoV-2 Variant of Concern [Internet]. 2021 [cited 2021 Dec 10]. Available from: [https://www.who.int/news/item/26-11-2021-classification-of-omicron-\(b.1.1.529\)-sars-cov-2-variant-of-concern](https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern)
2. World Health Organization. Household transmission investigation protocol for coronavirus disease 2019 (COVID-19) [Internet]. World Health Organization; 2020 [cited 2021 Dec 17]. Available from: [https://www.who.int/publications/i/item/household-transmission-investigation-protocol-for-2019-novel-coronavirus-\(2019-ncov\)-infection](https://www.who.int/publications/i/item/household-transmission-investigation-protocol-for-2019-novel-coronavirus-(2019-ncov)-infection)
3. World Health Organization. The first few X cases and contacts (FFX) investigation protocol for coronavirus disease 2019 (COVID-19), version 2.2 [Internet]. World Health Organization; 2020 [cited 2021 Dec 17]. Available from: [https://www.who.int/publications/i/item/the-first-few-x-cases-and-contacts-\(-ffx\)-investigation-protocol-for-coronavirus-disease-2019-\(-covid-19\)-version-2.2](https://www.who.int/publications/i/item/the-first-few-x-cases-and-contacts-(-ffx)-investigation-protocol-for-coronavirus-disease-2019-(-covid-19)-version-2.2)
4. World Health Organization. WHO SAGE Roadmap For Prioritizing Uses Of COVID-19 Vaccines In The Context Of Limited Supply [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://www.who.int/publications/i/item/who-sage-roadmap-for-prioritizing-uses-of-covid-19-vaccines-in-the-context-of-limited-supply>
5. World Health Organization. WHO advice for international traffic in relation to the SARS-CoV-2 Omicron variant (B.1.1.529) [Internet]. 2021. Available from: <https://www.who.int/news-room/articles-detail/who-advice-for-international-traffic-in-relation-to-the-sars-cov-2-omicron-variant>
6. National Institute for Communicable Diseases. South African COVID-19 Weekly Epidemiology Brief [Internet]. National Institute for Communicable Diseases (NICD) South Africa; 2021 [cited 2021 Dec 17]. Available from: <https://www.nicd.ac.za/wp-content/uploads/2021/12/COVID-19-Weekly-Epidemiology-Brief-week-49-2021.pdf>
7. European Centre for Disease Prevention and Control. Assessment of the further emergence of the SARS-CoV-2 Omicron VOC in the context of the ongoing Delta VOC transmission in the EU/EEA, 18th update [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://www.ecdc.europa.eu/en/publications-data/covid-19-assessment-further-emergence-omicron-18th-risk-assessment>
8. National Institute for Communicable Diseases. The Daily COVID-19 Effective Reproductive Number (R) in South Africa [Internet]. 2021 [cited 2021 Dec 9]. Available from: <https://www.nicd.ac.za/wp-content/uploads/2021/12/COVID-19-Effective-Reproductive-Number-in-South-Africa-week-48.pdf>
9. UK Health Security Agency. Omicron daily overview: 15 December 2021 [Internet]. UK Health Security Agency; 2021 [cited 2021 Dec 17]. Available from: https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1041210/20211215_OS_Daily_Omicron_Overview.pdf
10. Barnard RC, Davies NG, Pearson CA, Jit M, Edmunds J. Modelling the potential consequences of the Omicron SARS-CoV-2 variant in England [Internet]. London School of Hygiene and Tropical Medicine; 2021 [cited 2021 Dec 17] p. 1–21. Available from: https://cmmid.github.io/topics/covid19/reports/omicron_england/report_11_dec_2021.pdf

11. Figgins M, Bedford T. SARS-CoV-2 variant dynamics across US states show consistent differences in effective reproduction numbers [Internet]. 2021 [cited 2021 Dec 27]. Available from: <https://github.com/blab/rt-from-frequency-dynamics>
12. National Institute for Communicable Diseases. South African COVID-19 Hospital Surveillance Update: week 49, 2021 [Internet]. National Institute for Communicable Diseases (NICD) South Africa; 2021 [cited 2021 Dec 17]. Available from: <https://www.nicd.ac.za/wp-content/uploads/2021/12/NICD-COVID-19-Daily-Sentinel-Hospital-Surveillance-Report-National-20211216.pdf>
13. Discovery Health. Real-world analysis of Omicron outbreak based on 211 000 COVID-19 test results in South Africa [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://www.discovery.co.za/corporate/news-room>
14. Espenhain L, Funk T, Overvad M, Edslev SM, Fonager J, Ingham AC, et al. Epidemiological characterisation of the first 785 SARS- CoV-2 Omicron variant cases in Denmark, December 202. :7.
15. Brandal LT, MacDonald E, Veneti L, Ravlo T, Lange H, Naseer U, et al. Outbreak caused by the SARS-CoV-2 Omicron variant in Norway, November to December 2021. Eurosurveillance [Internet]. 2021 Dec 16 [cited 2021 Dec 17];26(50). Available from: <https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2021.26.50.2101147>
16. World Health Organization. The WHO Global Clinical Platform for COVID-19 [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19/data-platform>
17. World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection: Interim guidance, 06 October 2021 [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2infection-using-rapid-immunoassays>
18. U.S. Food and Drug Administration. SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicron>
19. World Health Organization. WHO Emergency Use Listing for In vitro diagnostics (IVDs) Detecting SARS-CoV-2 [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://extranet.who.int/pqweb/key-resources/documents/who-emergency-use-listing-vitro-diagnostics-ivds-detecting-sars-cov-2-2>
20. World Health Organization. Safety information for medical devices including in vitro diagnostics [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://www.who.int/teams/regulation-prequalification/incidents-and-SF/safety-information-for-medical-devices-including-in-vitro-diagnostics>
21. Cele S, Jackson L, Khan K, Khoury DS, Moyo-Gwete T, Tegally H, et al. SARS-CoV-2 Omicron has extensive but incomplete escape of Pfizer BNT162b2 elicited neutralization and requires ACE2 for infection [Internet]. Infectious Diseases (except HIV/AIDS); 2021 Dec [cited 2021 Dec 10]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.08.21267417>
22. Wilhelm A, Widera M, Grikscheit K, Toptan T, Schenk B, Pallas C, et al. Reduced Neutralization of SARS-CoV-2 Omicron Variant by Vaccine Sera and monoclonal antibodies [Internet]. Infectious Diseases (except HIV/AIDS); 2021 Dec [cited 2021 Dec 10]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.07.21267432>

23. Sheward DJ, Kim C, Pankow A, Dopico XC, Martin D, Dillner J, et al. Quantification of the neutralization resistance of the Omicron Variant of Concern. :3.
24. Schmidt F, Muecksch F, Weisblum Y, Silva JD, Bednarski E, Cho A, et al. Plasma neutralization properties of the SARS-CoV-2 Omicron variant [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2021 Dec [cited 2021 Dec 17]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.12.21267646>
25. Dejnirattisai W, Shaw RH, Supasa P, Liu C, Stuart AS, Pollard AJ. Reduced neutralisation of SARS-COV-2 Omicron-B.1.1.529 variant by post-immunisation serum. 2021;7.
26. Businesswire. Pfizer and BioNTech Provide Update on Omicron Variant [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://www.businesswire.com/news/home/20211208005542/en>
27. Rössler A, Riepler L, Bante D, Laer D von, Kimpel J. SARS-CoV-2 B.1.1.529 variant (Omicron) evades neutralization by sera from vaccinated and convalescent individuals [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2021 Dec [cited 2021 Dec 17]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.08.21267491>
28. Zhang L, Li Q, Liang Z, Li T, Liu S, Cui Q, et al. The significant immune escape of pseudotyped SARS-CoV-2 Variant Omicron. *Emerg Microbes Infect.* 2021 Dec 10;1–11.
29. Nemet I, Kliker L, Lustig Y, Zuckerman NS, Erster O, Cohen C, et al. Third BNT162b2 vaccination neutralization of SARS-CoV-2 Omicron infection [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2021 Dec [cited 2021 Dec 17]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.13.21267670>
30. Hong Kong University. HKUMED-CU Medicine Joint Study Finds COVID-19 Variant Omicron Significantly reduces virus neutralization ability of BioNTech vaccine [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://sph.hku.hk/en/News-And-Events/Press-Releases/2021/HKUMed-CU-Medicine-joint-study-finds-COVID-19-variant>
31. Gruell H, Vanshylla K, Tober-Lau P, Hillus D, Schommers P, Lehmann C, et al. mRNA booster immunization elicits potent neutralizing serum activity against the SARS-CoV-2 Omicron variant [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2021 Dec [cited 2021 Dec 17]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.14.21267769>
32. Burgers W, Riou C. Preliminary experimental data on T cell cross-reactivity to Omicron [Internet]. 2021 [cited 2021 Dec 17]. Available from: https://cdn.who.int/media/docs/default-source/blue-print/wendy-burgers_c19_whoconsultation_15dec2021.pdf?sfvrsn=2a2a7479_7
33. Andrews N, Stowe J, Kirsebom F, Toffa S, Rieckard T, Gallagher E. Effectiveness of COVID-19 vaccines against the Omicron (B.1.1.529) variant of concern [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://khub.net/documents/135939561/430986542/Effectiveness+of+COVID-19+vaccines+against+Omicron+variant+of+concern.pdf/f423c9f4-91cb-0274-c8c5-70e8fad50074>
34. Khoury DS, Steain M, Triccas JA, Sigal A, Davenport MP, Cromer D. Analysis: A meta-analysis of Early Results to predict Vaccine efficacy against Omicron [Internet]. *Infectious Diseases (except HIV/AIDS)*; 2021 Dec [cited 2021 Dec 17]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.12.13.21267748>
35. World Health Organization. SARS-CoV-2 Omicron variant assays and animal models study tracker [Internet]. 2021 [cited 2021 Dec 17]. Available from: <https://www.who.int/publications/m/item/repository-of-omicron-biological-materials-for-in-vitro-and-in-vivo-studies>

36. Roche. Ronapreve does not retain neutralising activity against the Omicron variant [Internet]. 2021 [cited 2021 Dec 17]. Available from: https://www.roche.com/dam/jcr:df6dcb4-d787-45d6-9b1d-ffc17d667e4c/2021216_Roche%20statement%20on%20Ronapreve%20Omicron.pdf
37. WHO Joint Advisory Group on COVID 19 Therapeutics Prioritization - DRAFT Statement on the possible effects of the new SARS CoV-2 Omicron variant on treatment of hospitalized COVID-19 patients [Internet]. 2021 [cited 2021 Dec 17]. Available from: https://cdn.who.int/media/docs/default-source/blue-print/joint-advisory-group-on-covid-19-therapeutics-prioritization_draft-statement-on-omicron_2021.12.01r.pdf?sfvrsn=524c2f1f_7&download=true
38. World Health Organization. Therapeutics and COVID-19: Living guideline [Internet]. World Health Organization; [cited 2021 Dec 17]. Available from: <https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.4>
39. World Health Organization. The Unity Studies: WHO Sero-epidemiological Investigations Protocols [Internet]. 2020 [cited 2021 Dec 17]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations>
40. World Health Organization. Guidance for surveillance of SARS-CoV-2 variants: Interim guidance, 9 August 2021 [Internet]. [cited 2021 Dec 10]. Available from: https://www.who.int/publications/i/item/WHO_2019-nCoV_surveillance_variants
41. European Centre for Disease Prevention and Control. Guidance for representative and targeted genomic SARS-CoV-2 monitoring [Internet]. European Centre for Disease Prevention and Control; 2021 May [cited 2021 Dec 10]. Available from: <https://www.ecdc.europa.eu/en/publications-data/guidance-representative-and-targeted-genomic-sars-cov-2-monitoring>
42. Considerations for implementing and adjusting public health and social measures in the context of COVID-19: interim guidance, 14 June 2021 [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://apps.who.int/iris/handle/10665/341811>
43. World Health Organization. Maintaining essential health services during the COVID-19 outbreak [Internet]. 2021 [cited 2021 Dec 10]. Available from: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/related-health-issues>
44. World Health Organization. COVID-19 Essential Supplies Forecasting Tool [Internet]. 2021 [cited 2021 Dec 10]. Available from: https://www.who.int/publications/i/item/WHO-2019-nCoV-Tools-Essential_forecasting-Overview-2020.1
45. World Health Organization. Welcome to OpenWHO [Internet]. [cited 2021 Dec 17]. Available from: <https://openwho.org/>
46. Ferguson N, Ghani A, Cori A et al. Growth, population distribution and immune escape of the Omicron in England. Imperial College London (16-12-2021), doi: <https://doi.org/10.25561/93038>.

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Annex: Working definitions

Interim Omicron-specific case definitions

Suspected case of SARS-CoV-2 Omicron variant infection

- Confirmed COVID-19 case, irrespective of symptoms (as per current WHO case definition), who is a contact (as per WHO contact definition) of a probable or confirmed Omicron case
- Confirmed COVID-19 case (as per current WHO case definition), residing in or travelling from an area with detection of Omicron anytime within the 14 days prior to symptom onset.

Probable case of SARS-CoV-2 Omicron variant infection

- Confirmed COVID-19 case positive for S-gene Target Failure (SGTF) or a PCR-based SNP-detection assay suggestive of Omicron*

*Note: the target deletions/mutations may not be unique to Omicron and may be missing from certain minority Omicron sequences, therefore samples tested through these methods should be confirmed through sequencing.

Confirmed case of SARS-CoV-2 Omicron variant infection

- A person with a confirmed sequencing result for SARS-CoV-2 Omicron (can be through targeted spike or whole genome sequencing)

Note: Clinical and public health judgment should determine the need for further investigation in patients who do not strictly meet clinical or epidemiological criteria. Surveillance case definitions should not be used as the sole basis for guiding clinical management.

SARS-CoV-2 Reinfection

Suspected reinfection case: Confirmed or probable COVID-19 case (following WHO case definition), with a history of a primary confirmed, or probable COVID-19 infection, with at least 90 days between the episodes.

Probable reinfection case: Positive RT-qPCR testing results for both episodes or equivalent positive antigen tests fitting the WHO Case Definition with episodes occurring at least 90 days apart, based on the sampling date. OR - Genomic evidence for the second episode is available and includes lineage that was not submitted to SARS-CoV-2 genomic databases at the time of first infection.

Reinfection confirmed by sequencing: Samples available for both primary and secondary episodes allowing for full genomic sequencing, whereby samples must be shown to be phylogenetically distinct from one another. Evidence should be generated at clade/lineage, as defined by genomic classification of SARS-CoV-2 between the first and second infection. If evidence of different clades is demonstrated in episodes less than 90 days apart, this also constitutes evidence of confirmed reinfection. If there are more than two nucleotide differences for every month separating the samples between the sequences for first and second infections, i.e., exceeding the expected single nucleotide variation, these would be considered as different lineages/clades. The 90-day cut off should ideally be determined between onset dates (for probable cases), or sampling dates (for confirmed cases) of primary and secondary episodes.

Vaccine breakthrough

Vaccines should be authorized by a stringent regulatory authority or listed under WHO Emergency Use Listing.

Cases and infections are expected in vaccinated persons, albeit in a small and predictable proportion, in relation to vaccine efficacy values. The following definitions should be used to characterize infections and cases in vaccinated persons:

- **Asymptomatic breakthrough infection:** detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person without COVID-like symptoms ≥ 14 days after they have completed all recommended doses of the vaccine series.
- **Symptomatic breakthrough case:** detection of SARS-CoV-2 RNA or antigen in a respiratory specimen collected from a person with COVID-like symptoms ≥ 14 days after they have completed all recommended doses of the vaccine series.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Apart from limited exceptions, the names of proprietary products are distinguished by initial capital letters.