

Enhancing readiness for Omicron (B.1.1.529): Technical brief and priority actions for Member States

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Executive summary and background

- On 26 November 2021, [WHO designated the variant B.1.1.529 a variant of concern \(VOC\)](#) (1), following advice from the WHO's Technical Advisory Group on Virus Evolution. The variant has been given the name Omicron. Omicron is a highly divergent variant with a high number of mutations, including 26-32 mutations in the spike protein, some of which may be associated with humoral immune escape potential and higher transmissibility.
- As of 22 December 2021, the Omicron variant had been identified in 110 countries across all six WHO Regions. Current understanding of the Omicron variant continues to evolve as more data become available. This technical brief provides updated early evidence on key aspects of Omicron related to transmission, severity and impact on interventions such as diagnostics, therapeutics and vaccines, and outlines a set of priority actions for Member States.
- The overall threat posed by Omicron largely depends on four key questions: (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 (PHSM). 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 of 2-3 days. Growth rate estimates in South Africa are now declining, driven largely by the declining rates in Gauteng province. It remains uncertain to what extent the observed rapid growth rate since November 2021 can be attributed to immune evasion or intrinsic increased transmissibility, but is likely a combination of both. At the time of writing, estimates of generation times for Omicron are still needed to better understand the observed dynamics.
- Data on clinical severity of patients infected with Omicron is growing but is still limited. Early data from South Africa, the United Kingdom (UK) and Denmark suggest a reduced risk of hospitalization for Omicron compared to Delta. However, the risk of hospitalization is only one aspect of severity, which may be altered by admission practices. More data across different countries are needed to understand how clinical markers of severity—such as the use of oxygen, mechanical ventilation and deaths—are associated with Omicron. At the present time, it is still unclear to what extent the observed reduction in risk of hospitalization can be attributed to immunity from previous infections or vaccination and to what extent Omicron may be less virulent.
- Preliminary data from several non-peer reviewed studies suggest that there is a reduction in neutralizing titers against Omicron in individuals who have received a primary vaccination series or in those who have

had prior SARS-CoV-2 infection. In addition, the increased risk of reinfection reported in England, UK, as well as a growing trend of reinfection cases in Denmark and Israel, can be potentially attributed to immune evasion against Omicron.

- To date, there are still limited available data, and no peer-reviewed evidence, on vaccine efficacy or effectiveness for Omicron. Preliminary findings of vaccine effectiveness studies (test-negative design) have been released from South Africa and the United Kingdom. Available preliminary data should be interpreted with caution because the designs may be subject to selection bias and the results are based on relatively small numbers. Results from the UK 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 African 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; studies of the comparative sensitivity of Ag-RDTs are ongoing. 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. Although 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, since this deletion can also be found in other VOCs (e.g. Alpha and subsets of Gamma and Delta) that are circulating at low frequencies worldwide.
- Therapeutic interventions for the management of patients with severe or critical Omicron-associated COVID-19 that target host responses (such as corticosteroids, and interleukin 6 receptor blockers) are expected to remain effective. However, preliminary data from non-peer reviewed 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 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. The increases in cases, particularly rapidly, have and will continue to subsequently increase hospitalizations and burden health systems where Omicron circulates. Our understanding is still growing, 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 their current situation and national capacities.
- With the emergence of the Omicron variant, 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. Enhanced surveillance with rapid testing and stricter cluster investigations and 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 (many of which are significantly overburdened after two years of the COVI-19 pandemic), ensure mitigation plans

are in place to maintain essential health services and that 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 in all countries should be reinforced. Particular focus among [populations designated as high priority](#) (2) who remain unvaccinated or are not yet fully vaccinated should be a priority for vaccination campaigns in all countries. Delta is still by far the predominant variant worldwide, causing significant transmission and disease. Vaccines are highly effective against Delta and are likely to have some effectiveness against Omicron, particularly for preventing severe disease, even if performance is lower than with other variants. Finally, in some countries with high COVID-19 hospitalizations and deaths, boosters could play an important role, especially for individuals at highest risk of severe disease and death.
- 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](#) (3), studies of the "first few" cases [studies](#) (4), contact follow up and laboratory assessments to improve understanding of the characteristics of Omicron.
- Because SGTF from commercial PCR kits is indicative for Omicron, it 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.
- Member States are further 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, the 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 remains unknown and what is being done by responsible authorities.

Current state of knowledge on Omicron

Epidemiologyⁱ

- As of 23 December 2021 (4 pm CET), the Omicron variant had been confirmed in 110 countries. In several countries where there is evidence of widespread local transmission, the Omicron variant has become dominant.
- In South Africa, where Omicron was first reported and is now the dominant variant, the case incidence of COVID-19 is now declining. In week 50 (13-19 December) (6), a total of 162 987 COVID-19 cases were reported, a 1.5 fold increase compared to the previous week. However, data from 15-21 December show a 5% decrease in the weekly case incidence. As of 18 December, Gauteng province continued to see the highest number of weekly cases. However, a 46% decrease in the number of cases per 100 000 compared to the previous week was reported.
- Between 13 and 19 December, increases in the incidence of cases compared to the previous week continued to be observed in countries neighbouring South Africa with the exception of Zimbabwe, which showed similar numbers (26 671 vs 26 479). The majority of these countries however, reported smaller increases compared to the previous week. These include Lesotho (1.3x increase, 1631 vs 1264 cases); Eswatini (1.6x increase, 7540 vs 4806 cases); Namibia (2.7x increase, 4721 vs 1722 cases) and Mozambique (3.1x increase, 4703 vs 1540 cases). Only Botswana reported a larger increase (4.8x increase, 3774 vs 788 cases).
- Nevertheless, large increases continue to be seen in other African countries, where cases of Omicron are either confirmed or awaiting confirmation. These countries include Kenya (8.5x increase, 6201 vs 726 cases); Malawi (8.3x increase, 2182 vs 264 cases);
- the Democratic Republic of the Congo (3.3x increase, 5825 vs 1767 cases) and Rwanda (4.6x increase, 829 vs 180 cases). It is possible that either the spread of Omicron or enhanced testing following the declaration of a VOC contribute to these increases.
- In the European Region, Omicron has been confirmed as the dominant variant in the United Kingdom (UK) with 71.5% of cases for which the S gene status of COVID-19 cases was known to have SGTF in specimens collected between 18 and 19 December 2021. Omicron is expected to replace Delta and become the dominant variant in a number of other countries in this Region at the start of 2022 (7).
- In the United States of America, Omicron became the dominant variant the week ending 18 December, accounting for approximately 73% of cases. A 1.1x decrease in weekly cases (823 415 vs 725 750) as of 19 December was reported. However, data from 15-21 December has shown a 13% weekly increase, suggesting an impact of Omicron on case incidence (8).

ⁱ Note: Data from Mauritius. The increase in the number cases reported in the Technical Brief published 17 December was the result of batch-reporting rather than true increase, the data has been adjusted. Data from Mauritius included both PCR and RDT confirmed cases from 25 October.

Transmission

- The most [recent daily Omicron overview by the UK Health Security Agency \(UKHSA\)](#) on 22 December 2021 (9) reports that between 19 and 20 December, 90% of cases in London and 76% of cases in England were Omicron cases, with an estimated doubling time of less than 2.5 days across all regions.
- Preliminary findings from [studies of households and contacts in the UK](#) (10) found a higher risk of

transmission to contacts from an Omicron index case, when compared to Delta index cases. The most recent 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 2.9 (95% CI 2.4-3.5)] and the increased risk of a close contact becoming a secondary case [adjusted odds ratio 1.96 (95% CI: 1.77-2.16)]. The household secondary attack rate estimated using routine contact tracing data for Omicron is 15.8% (95% CI: 14.3%-17.5%) and 10.3% (95% CI: 10.1%-10.5%) for Delta.

- Growth estimates of Omicron in the United States of America, as well as those for other countries experiencing recent surges in cases due to Omicron in Europe such as Denmark, Ireland, Germany, Netherlands and Switzerland are consistent with earlier estimates of a doubling time of between 2 and 3 days. Daily reported case numbers of Omicron in the Gauteng province of South Africa are now declining, which is reflected in [recent estimates](#) of declining growth rate at a national level (11), but the reasons for this are currently unclear.
- The growth advantage of Omicron over Delta has now been confirmed across many settings. Evidence from neutralization studies, early estimates of vaccination effectiveness against symptomatic disease and studies of reinfection risk suggest this is at least partly due to immune evasion against infection. However, it is still unclear whether Omicron also exhibits increased intrinsic transmissibility. Furthermore, more data are needed to inform generation time estimates for Omicron, which may differ from those observed for Delta and previous variants.
- [A recent analysis](#) (non-peer reviewed) shows that assuming 80% population immunity in South Africa, immune evasion levels of 25-50% could explain the observed growth advantage without an increase in transmissibility (12) (12). [Another study](#) (non-peer reviewed) estimates that Omicron is 36.5% (95% CI 20.9-60.1) more transmissible than Delta and that Omicron erodes 63.7% (95%CI 52.9-73.9) of the population immunity accumulated from prior infection and vaccination in Gauteng province (13). [A third recent study](#) (non-peer reviewed) bounds the plausible ranges for estimates of immune escape and transmissibility, highlighting that both immune escape and increased transmissibility could be responsible for the growth advantage of Omicron (14). Although increases in transmissibility in addition to immune evasion are possible due to the increased affinity to bind to the ACE2 receptor, more data are needed to better understand these characteristics.

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. Several data sources on the Omicron variant suggest that the risk of hospitalization is lower than for the Delta variant. However, 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.

- Following a rapid increase in the number of hospitalizations in the public and private health sectors since the start of the Omicron wave, weekly hospital admissions appear to be declining at a national level in South Africa. The trends in hospitalization during this fourth wave in South Africa are driven primarily by Gauteng province (15). A [serological survey](#) (non-peer reviewed) in Gauteng province of South Africa (16) found that infection rates during the fourth wave, which is predominantly driven by the Omicron variant, increased more rapidly compared to previous waves (driven by previously identified variants including Delta) but that hospitalization and deaths remained relatively low. Another study (non-peer reviewed) using a record linkage approach (17) found that laboratory-confirmed SARS-CoV-2 infected individuals with SGTF had a lower odds of severe diseases (aOR 0.3, 95% CI 0.2-0.6). This is in agreement with earlier data from a private health insurance provider in South Africa suggesting a reduced risk of hospitalization

for Omicron compared to Delta (18). 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 England, reported hospitalizations and deaths continue to increase, with [195 hospitalizations and 18 deaths reported](#) as of 22 December (9). [A report by Imperial College London on 22 December 2021](#) (19) (non-peer reviewed) based on hospitalization data in England for cases with specimen dates between 1 – 14 December 2021, indicates a reduction in the risk of hospitalization for infection with the Omicron relative to the Delta variant. Omicron cases were estimated to have a 15-20% reduced risk of any hospitalization and a 41% (95% CI: 37%-45%) reduced risk of a hospitalization resulting in a stay of 1 or more nights.
- [Early data reported from Scotland](#) (20) (non-peer reviewed) based on hospital admissions from 1 November 2021 to 19 December 2021 suggest that Omicron is associated with a two-thirds reduction in the risk of COVID-19 hospitalization when compared to Delta.
- [Data from Denmark published on 21 December 2021](#) (21) show that 0.6% of cases of Omicron have been hospitalized, compared with 1.6% of those with other variants, using data up to 15 December. However, the figures for Omicron hospitalizations should be interpreted with caution given the lag between disease onset and hospitalizations. It is still unclear whether the observed reduction is only due to the protection offered from prior infection and vaccination or additionally due to an intrinsic reduction in severity.
- Using samples from the lower respiratory tract, [researchers at Hong Kong University found](#) that the Omicron variant replicates faster (up to 70 times faster) in the human bronchi compared to the Delta variant and the original SARS-CoV-2 virus (22). In contrast, the Omicron variant showed relatively much slower replication in the lung. This replication pattern is thought to explain the less severe clinical presentation of patients infected with the Omicron variant.
- In summary, early data from Denmark, South Africa and the UK and suggest a reduced risk of hospitalization for Omicron compared to Delta. However, the risk of hospitalization is only one aspect of severity, which may be altered by admission practices, and so it is important to understand more about clinical markers of severity, such as the use of oxygen, invasive mechanical ventilation and deaths associated with Omicron, for which more data is needed. WHO encourages countries to contribute to the collection and sharing of hospitalized patient data through the [WHO COVID-19 Clinical Data Platform](#) (23).

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](#) (24). 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](#)) (25) based on sequence analysis and preliminary laboratory evidence. An overview of the predicted [impact](#) of Omicron on several commercially-available PCR kits can be found [here](#) (26) and demonstrates limited impact.
- The Omicron variant includes Pango lineages B.1.1.529, BA.1, BA.2 and BA.3. BA.1, which accounts for >99% of sequences submitted to GISAID as of 23 December, and BA.3 have the 69-70 deletion in the spike protein, while BA.2 does not. Knowledge of B.1.1.529 is still developing, but this lineage is more diverse, with the 69-70 deletion present in about half of all currently available sequences.
- 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, because this deletion is found in other VOCs (e.g. Alpha and subsets of Gamma and Delta), which are circulating at low levels worldwide.

- All four [WHO emergency use listing \(EUL\) approved](#) (27) 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.
- Statements from manufacturers indicate that most currently used Ag-RDTs, including 2 WHO EUL approved tests, have retained their ability to detect SARS-CoV-2 variants, including Omicron.
- Preliminary laboratory data is emerging demonstrating that dilutions of viral culture of Omicron are detected by several Ag-RDTs as the ancestral virus or other VOCs (10,28), though there is also one report that suggests that analytical sensitivity of seven Ag-RDTs trended slightly lower for detection of Omicron compared to the ancestral virus or other VOCs (29). More data are needed to better understand if there are any differences in antigen-based detection of 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](#) (30).
- Laboratory personnel are encouraged to report any unusual findings to the manufacturer using this [form](#) (31). This may include increased discrepancies in cycle threshold (Ct) values between different gene targets and 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 related to Omicron.

Immune evasion

- Immune evasion after past infection or vaccination plays a significant role in the rapid growth in Omicron cases as described in the WHO technical brief published on 17 December 2021 (32).
- The [risk of reinfection in England with the Omicron variant was estimated to be 5.4](#) (95% CI: 4.87-6.00) fold higher in comparison the Delta variant (33). The relative risks were 6.36 (95% CI: 5.23-7.74) and 5.02 (95% CI: 4.47-5.67) for unvaccinated and vaccinated cases, respectively. This implies that the protection against reinfection by Omicron after a past infection may be as low as 19%. The recent [report by UKSHA](#) (10) found that 5.9% of the confirmed cases between November 1st to December 13th resulted from reinfection, estimating the risk for reinfection with Omicron at 3.3 (95%CI: 2.8 to 3.8) compared to other variants. An increased trend in reinfection case count was observed in [Denmark](#) (34). Similarly, an increase in reinfection cases classified by vaccination status was also reported by the [Israeli ministry of health](#) (35). These estimates are aligned with previous reports from South Africa that Omicron can evade immunity after natural infection. [Similar trends](#) (36) were also reported in South Africa in earlier technical briefs. Further definition on reinfection can be found in the [technical brief published on 10 December](#) (37). In a peer-reviewed manuscript by [X. Zhang et al](#), convalescent plasma samples from previously infected individuals with the Delta variant were tested with Omicron Spike pseudo virus (38). A 39-fold decrease in neutralization capacity of patients previously infected with Delta was observed, implying on a significant immune escape of the Omicron against previous immunity to Delta. A 10-fold increase affinity of Omicron spike to ACE2 receptor suggested increased infectivity.
- Laboratory data on the immune response to Omicron is rapidly emerging, but most studies are not peer-reviewed (39–49). They report 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](#) (50) from 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. Two non-peer reviewed studies reported that comparison to other VOCs and the ancestral virus, there was a reduction in binding antibodies levels against the Omicron recombinant receptor binding domain (51) and the N Protein N-terminal domain (NTD) (52) in convalescent non-vaccinated individuals. However, binding was mostly retained in vaccinated individuals.

Impact on vaccines

- Results of vaccine effectiveness based on clinical outcomes in England, UK and South Africa indicate a reduction in vaccine effectiveness for Omicron against infection, symptomatic disease and hospitalization compared to earlier variants.
- A test-negative design study in Scotland (20) (non-peer reviewed), UK, showed the third/booster vaccine dose was associated with a 57% (95% CI 55, 60) reduction in the risk of symptomatic S gene negative (presumably Omicron) symptomatic infection relative to ≥ 25 weeks post second dose, as compared to a VE of 88% (95% CI 86,89) among S gene positive cases (presumably Delta).
- Another analysis by researchers at Imperial College London (53) compared the hazard ratio 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, UK 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, after two doses and three doses of vaccine. Using the estimated vaccine

effectiveness against Delta, this elevated hazard ratio translates into estimates of vaccine effectiveness against symptomatic infection from Omicron between 0% and 19% following two doses, and between 54% and 77% after a booster dose.

- In a [non-peer-reviewed study](#) (54), a multinational team investigated antibody neutralization activity using a pseudo virus assay with Omicron receptor binding domain (RBD) in sera from individuals vaccinated with a range of vaccines was assessed. No neutralization activity was detected in individuals vaccinated with Ad26.COV2.S or Sputnik V or BBIBO-CorV against the Omicron spike. A 33-, 44- and 36-fold reduction in neutralization was recorded in those vaccinated with mRNA 1273, Pfizer BioNTech-Comirnaty and AstraZeneca-Vaxzevria, respectively. This study was in alignment with previously reported datasets on neutralization reduction against Omicron. Nonetheless, because of differences in the testing methods it remains challenging to evaluate overall estimates for neutralization reduction.
- In England, [vaccine effectiveness estimates](#) (53) have been calculated 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 at 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 study from Denmark](#) (non peer-reviewed) using a nationwide cohort estimated a VE of 55% (95% CI 24,74) and 37% (95% CI -70,76) for Pfizer BioNTech-Comirnaty and Moderna- mRNA 1273, respectively, against Omicron SARS-CoV-2 infection, with evidence of waning VE with time; VE against Delta infections was substantially higher.
- In South Africa, the insurance company Discovery Health [posted a press release](#) (18) 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, but uncertainty estimates around these figures and details of methods were not included.
- WHO is closely assessing the impact on vaccines through our research and development network by setting up and coordinating a live [repository](#) (55) 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](#) (56). Such studies are critical to understand 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. On 16 December 2021, ROCHE issued a statement on diminished potency of casirivimab and imdevimab against Omicron in *in vitro* studies ([2021216 Roche statement on Ronapreve Omicron.pdf](#)) (57). Sotrovimab retained activity against Omicron but with a 3-fold lower potency in neutralization as measured by EC50.
- WHO is working with its experts to prioritize the [research agenda](#) (58) and collect further data regarding the efficacy of monoclonal antibodies and antivirals. Urgent prioritization is for 1) antigen binding and virus neutralization by antiviral monoclonal antibodies and 2) 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 \(who.int\)](#)) (59).

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 110 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, 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

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 unfolds worldwide. Countries should optimize their response to Delta, which will benefit responses to Omicron and any future variants.

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](#) (60) 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 guidance for surveillance of SARS-CoV-2 [variants](#) (61) 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 permit 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](#) (61). Additional guidance is available in [ECDC Guidance for representative and targeted genomic SARS-CoV-2 monitoring](#) (62).

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 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 uptake of COVID-19 vaccination in all eligible populations but prioritizing individuals at risk (41) 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 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.

- Omicron may have a high likelihood of immune evasion from antibody-mediated protection, especially protection directed at the spike protein. 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.
- Further research is needed to better understand Omicron's escape potential against vaccine- and infection-induced immunity. Research efforts are ongoing, and it is anticipated that data will 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 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 (5) 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, considering 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's interim guidance (5) (63).

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](#) (64) and that necessary resources are in place to respond to potential surges. Tools such as the [COVID-19 Essential Supplies Forecasting Tool](#) (65) 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/>) (66) should be continued on the COVID-19 care pathways ([Living guidance for clinical management of COVID-19 \(who.int\)](#)) (59)

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 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 especially critical to build and foster trust 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 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).

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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. Samples tested through these methods should therefore 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. Alternatively, 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-19-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-19-like symptoms ≥ 14 days after they have completed all recommended doses of the vaccine series.

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