

Enhancing response to Omicron (COVID-19 variant B.1.1.529): Technical brief and priority actions for Member States

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A. Context

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 was 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 were likely to be associated with humoral immune escape potential and higher transmissibility.

B. Key current technical information: executive summary

B.1. Global 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. Second, current data indicate that Omicron has a significant growth advantage over Delta, leading to rapid spread in the community. The rapid increase in cases will lead to an increase in hospitalizations, may pose overwhelming demands on health care systems and lead to significant morbidity, particularly in vulnerable populations.

The overall **threat** posed by Omicron largely **depends on four key questions**: (i) how transmissible the variant is; (ii) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; (iii) how virulent the variant is compared to other variants; and (iv) how populations understand these dynamics, perceive risk and follow control measures, including public health and social measures (PHSM). This **global risk assessment**, and **public health advice**, are based on the currently best available evidence and will be updated frequently as more information becomes available in relation to these key questions.

B.2. Current evidence summary

This section contains an executive summary of the current best available evidence (as of 6 January 2021) regarding the potential impact of the Omicron variant. More detailed information is included in Section C.

Impact on epidemiology

- As of 6 January 2022, the Omicron variant had been identified in 149 countries across all six WHO Regions.
- There is consistent evidence that Omicron has a substantial growth advantage over Delta. The Omicron variant is spreading significantly faster than the Delta variant in countries with documented community transmission. Growth rates have declined or stabilized in many countries but remain significantly higher than for the Delta variant. While there is mounting evidence that immune evasion contributes to the rapid spread, more data are needed to better understand the relative contribution of intrinsic increased transmissibility and immune evasion in explaining transmission dynamics.
- Data on clinical severity of patients infected with Omicron are increasingly available. Early data from South Africa, the United Kingdom, Canada 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. Early data suggests that, as with all other variants of SARS-CoV-2, severity of Omicron increases with age and in the presence of underlying medical conditions, as well as among people who are not vaccinated. Moreover, current evidence about severity and hospitalization comes largely from countries with high levels of population immunity, and there remains uncertainty about the severity of Omicron in populations with different vaccination coverage and prior exposure to other variants.

Impact on *diagnostics and testing*

- The diagnostic accuracy of routinely used PCR and antigen-detection rapid diagnostic tests (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.

Impact on *immunity (following infection or vaccination)*

- Preliminary data from multiple 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, increased risk of reinfection has been reported in South Africa, the United Kingdom, Denmark, and Israel, all suggesting immune evasion against Omicron.
- There is growing (not peer-reviewed) evidence on vaccine effectiveness for Omicron, with data available from nine observational studies from four countries (United Kingdom, Denmark, Canada, South Africa), evaluating four vaccines (mRNA vaccines, Ad26.COVS.2.S, and AstraZeneca-Vaxzevria). 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. Early data suggests that the effectiveness of studied vaccines is significantly lower against Omicron infection and symptomatic disease compared to Delta, with homologous and heterologous booster doses increasing vaccine effectiveness. Based on data from two studies, vaccine effectiveness against hospitalization appears to be substantially higher than that against symptomatic disease, but nonetheless lower than against Delta. There is one study showing decreasing effectiveness of the booster dose against symptomatic disease over time. More data are needed to assess this preliminary finding across studies, vaccine platforms and dosing regimens. There are no effectiveness data for several vaccines, particularly the inactivated vaccines.

Impact on *host tropism, virus fitness and pathogenicity*

- Preliminary evidence suggests a potential shift in tropism of the Omicron variant towards the upper respiratory tract, as compared to Delta and the wild type (WT) virus that have a tropism for the lower respiratory tract. There is also evidence of less severe pathogenicity in the Syrian hamster (*M. auratus*) model, but this needs to be confirmed by peer-reviewed evidence and larger studies.

Impact on *therapeutics and treatments*

- 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 impaired neutralization against Omicron. Monoclonal antibodies will need to be tested individually for their antigen binding and virus neutralization, and these studies should be prioritized.

B.3. Priority actions for Member States

This section contains an executive summary of the current priority action for Member States. Further details are included in Section D. These recommended priority actions are based on the current global risk assessment (see Sections B.1. and C.5.) and the best available evidence (at 20 Dec 2021) regarding Omicron.

Surveillance and testing

- Because SGTF from commercial PCR kits is indicative for most isolates of Omicron, it can be used as a proxy marker for this variant. However, it should be noted that a minority of Omicron sequences lack this deletion and will be missed by this screening method. Once validated, other PCR-based screening assays (e.g. Single Nucleotide Polymorphism genotyping) may be useful proxy markers depending on the setting.
- 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.

Vaccination

- Efforts to rapidly accelerate COVID-19 vaccination coverage in at-risk populations in all countries should be intensified. Particular focus among [populations designated as high priority](#) (2) who remain unvaccinated or whose vaccination remains incomplete should be a priority for vaccination campaigns in all countries. In accordance with the SAGE review, the priority for booster doses is to maintain and optimize vaccine effectiveness against severe disease outcomes, especially for those at high risk for serious disease.

Public health and social measures

- 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 critical to reducing transmission of SARS-CoV-2. Enhanced surveillance with rapid testing, cluster investigations, contact tracing, isolation of cases and supported quarantine of contacts are strongly advised to interrupt chains of transmission. WHO continues to advise implementing the comprehensive, multi-layered and targeted use of public health and social measures (PHSM) to reduce the spread of all variants of SARS-CoV-2.

Travel-related measures

- 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](#) (3) for additional information.
- Blanket travel bans will not prevent international spread of any variants of SARS-CoV-2, including Omicron; and can 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.

Health system readiness and responsiveness

- WHO asks all Member States to regularly reassess and revise national plans based on their current situation and national capacities.
- 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 COVID-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.
- Clinical care of patients with COVID-19, infected with any SARS-CoV-2 variant, should be administered within health systems according to evidence-based guidelines, such as the WHO living guidelines for [clinical management](#) (4) and [therapeutics](#) (5), adapted appropriately for local context and resource settings.

Risk communication and community engagement

- 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.
- 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.

B.4. Priority research needed

- Enhance surveillance, including increasing testing and sequencing efforts to better understand circulating SARS-CoV-2 variants, including Omicron. Where capacity exists, countries should perform field investigations such as [household transmission studies](#) (6), studies of the “first few” cases [studies](#) (7), contact follow up and laboratory assessments to improve understanding of the characteristics of Omicron.
- 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-spreading events.
- More data, across different countries, are needed to understand how clinical markers of disease severity (such as oxygen use, mechanical ventilation, deaths) are associated with Omicron. WHO encourages countries to contribute to the collection and sharing of hospitalized patient data through the [WHO COVID-19 Clinical Data Platform](#) (8).
- The WHO Joint Advisory Group on COVID-19 Therapeutics [research agenda](#) (9) has identified urgent prioritization for more data regarding 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.
- Further research is needed to better understand Omicron's immune escape potential against vaccine- and infection-induced immunity, and Omicron-specific responses to vaccines. The Technical Advisory Group on Vaccine Composition (TAG-Co-VAC) regularly assesses the need for changes to vaccine composition and has recently provided this statement.
- Where capacity exists and in coordination with the international community, countries and partners are encouraged to perform studies to improve understanding of transmission parameters; vaccine effectiveness and impact; mechanisms of protection; disease severity; effectiveness of PHSM against Omicron; diagnostic methods; immune responses; antibody neutralization; population risk perception, knowledge, attitude and behavior towards PHSM, vaccines and tests; or other relevant characteristics. Generic [study protocols](#) (10) are available.
- Further studies that compare the relative sensitivity of diagnostic tests (i.e. antigen-detecting and PCR) to detect Omicron using clinically-relevant specimens are needed. Studies elucidating the impact of infection history and vaccine status on the performance of diagnostic tests should also be prioritized.

C. [Current evidence regarding Omicron](#)

This section contains a summary of the current best available evidence (at 5 January 2022) regarding the potential impact of the Omicron variant. A shorter executive summary of this evidence base is included in Section B.2.

C.1. Epidemiology

Incidence

- As of 6 January 2022 (4 pm CET), the Omicron variant had been confirmed in 149 countries. The variant is rapidly outpacing Delta in most countries and is now driving an upsurge in cases in most regions.
- In week 52 (26 December 2021 - 2 January 2022), the global weekly incidence of COVID-19 has increased by 71%

compared with the previous week, with the Region of the Americas and the South-East Asia Region reporting the highest increases of 100% and 78%, respectively. The South-East Asia region had previously seen a decline in the trend of new cases since July 2021.

- In South Africa, where Omicron was first reported and is now the dominant variant, there was a marked decline in reported case [numbers](#) (11) of infection caused by the Omicron variant in week 52, with a total of 60 142 COVID-19 cases reported, a 48% decrease compared to the previous week. The incidence of hospitalization is also decreasing significantly, suggesting that the Omicron epidemic may have peaked in South Africa.
- Similar trends have been reported in a few other Southern African countries where Omicron trends closely followed that of South Africa, including: Eswatini (1806 vs 4667 cases comparing week 52 to week 51, a 60% decrease); Namibia (4398 vs 7625 cases, a 42% decrease), Lesotho (2161 vs 2862 cases, a 24% decrease) and Zimbabwe (10 468 vs 12 073 cases, a 13% decrease). However, increases in the number of reported cases were seen in Mozambique (26 860 vs 6751 cases, a 298% increase) and Botswana (10 515 vs 9130 cases, a 15% increase).
- Large increases in the weekly incidence of cases of COVID-19 continue to be reported in other countries where Omicron is rapidly becoming the dominant variant. For example, [in the United Kingdom](#) (12), where the prevalence of Omicron was estimated at >95% on 30 December, over 1.1 million cases were reported in week 52, 2021, a 51% increase on the previous week. [In Denmark](#), where Omicron accounted for 90% of cases as of 28 December 2021, 116 331 new cases were reported during week 52, a 47% increase compared to the previous week (13). Similarly, [in the United States of America](#), where Omicron now accounts for 95% of cases (as of 1 January 2022), a 92% increase was observed in week 52, with over 2.5 million cases reported nationally (14).
- While South Africa reported a peak incidence of the Omicron wave similar to that of the previous Delta wave, incidence of Omicron in many countries has now far exceeded the incidence ever reported earlier in the pandemic. For example, the 7-day moving average of cases reached levels 232%, 409%, and 306% of the previous highest recorded incidence in the United States of America, France, and the United Kingdom respectively.
- Other notable large increases in the weekly incidence of cases have been reported in countries including: the Philippines (9124 vs 833 new cases, a 995% increase; Argentina (229 192 vs 58 783 new cases, a 290% increase; and Australia (138 240 vs 45 560 new cases, a 203% increase and India (102 330 vs 46 527 new cases, a 120% increase).

Transmission

- Omicron is showing a significant growth advantage, higher secondary attack rates and a higher observed reproduction number compared to Delta.
- [Studies of households and contacts in the United Kingdom](#) (15) 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. Similarly, a [study in Denmark](#) reported higher secondary attack rates when an index case was infected with the Omicron compared to the Delta variant (31% vs. 21%) in a household setting (16).
- The observed high growth rate is likely attributed to a combination of factors including immune evasion and potential intrinsic increased transmissibility (17). While there is growing evidence of immune evasion against transmission from natural and vaccine-derived immunity (see later sections), more data are needed to better understand the relative contribution of intrinsic increased transmissibility and immune evasion in explaining transmission dynamics.
- A recent analysis (non-peer reviewed) shows that immune evasion levels of 25% to 50% could explain the observed growth advantage observed in South Africa, even without an increase in intrinsic transmissibility (18). Another study from South Africa (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 (19).

- A study from Hong Kong University found that Omicron infects human bronchus tissue faster and better than Delta (20) and another study from the United Kingdom Genotype to Phenotype (G2P) consortium found that Omicron quickly outcompetes Delta in competition experiments using cells derived from the human nose, while this effect is not seen using lung-derived cells (21). This points at a growth advantage in the upper respiratory tract that may confer, at least to some extent, a transmission advantage independent of immune evasion.
- Other factors that may further contribute to higher growth rate are shorter serial intervals, as suggested by preliminary data from the Republic of Korea, where the serial interval of Omicron was 2.22 days (95%CI 1.48-2.97) (22) compared to Delta's 3.26 days (95%CI 2.92-3.6) (23). More data are required to corroborate such findings.
- Moreover, higher proportions of asymptomatic infection may also further contribute to transmission. This was suggested by a study including [vaccine trial participants](#) (24) in South Africa, which reported a higher proportion (16%) of routinely screened asymptomatic individuals were found to be infected with the virus during the period of Omicron dominance, compared to 2.6% during the period when the Beta and Delta variants were predominant.

Disease severity

- Data on case severity (including hospitalization, need for oxygen, mechanical ventilation, or deaths) are increasingly becoming available, improving our understanding of the impact of Omicron on severe cases, hospitalization and deaths. Several data sources on the Omicron variant suggest that the risk of hospitalization and the requirement for mechanical ventilation are lower than for the Delta variant. As such, a decoupling between case reports and hospitalizations is being observed in many countries, with proportionally lower incidence of hospitalization than what was observed with other variants given the level of community transmission. However, with very high levels of incidence, significant increases in hospitalization, severe disease and death are occurring and are continued to be expected to occur in the coming weeks, with significant pressure on health services. Moreover, current evidence about severity and hospitalization comes largely from countries with high levels of population immunity, and there remains uncertainty about the severity of Omicron in populations with different vaccination coverage and prior exposure to other variants.
- In South Africa, following a rapid increase in the number of hospitalizations in the public and private health sectors after the start of the Omicron wave, weekly hospital admissions continue to decline at a national level, with 6366 admissions in week 52, 2021 compared to 8900 admission during the previous week (a 28% reduction) (25). A [serological survey](#) (non-peer reviewed) in Gauteng province (26) 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](#) (27) found that laboratory-confirmed SARS-CoV-2 infected individuals with SGTF had a lower odds of severe disease (adjusted odds ratio 0.3, 95% CI 0.2-0.6).
- In the United Kingdom, reported hospitalizations with COVID-19 continue to increase, with 9218 new admissions reported in week 51, a 45% increase compared to the previous week, and over 14 000 in-patients as of 31 December. However, this is equivalent to only 36% of the maximum number of in-patients during the Alpha wave (18 January 2021; 39 254 in-patients). Additionally, the number of patients requiring mechanical ventilation has remained stable with a 7-day average of 850 patients on 26 December 2021 compared to 860 on 19 December 2021.
- The most recent analysis from the United Kingdom Health Security Agency with the Medical Research Council (MRC) Biostatistics Unit, University of Cambridge showed a 47% reduction in the risk of presentation to emergency care or hospital admission with Omicron compared to Delta (Hazard Ratio (HR) 0.53, 95%CI 0.50-0.57) and 66% reduction in the risk of admission from emergency departments (HR 0.33, 95%CI 0.3-0.37). [A report by Imperial College London on 22 December 2021](#) (28) calculated a 41% (95% CI: 37%-45%) reduced risk of a hospitalization resulting in a stay of one or more nights.

- In the United States of America, reported hospital admissions are rising rapidly, with a seven-day moving average of 14 776 admissions for COVID-19 between 27 Dec 2021 and 02 Jan 2022 (a 62.9% increase compared to the previous week). The 7-day admissions average is approaching the previous maximum of 16 497 admissions observed in early January 2021. While the proportional contribution of these hospitalizations between Omicron and Delta is not known, the US Centers for Disease Control and Prevention (CDC) have estimated that Omicron is associated with 95.4% (95% PI 92.9-97.0%) of all cases recorded between the 26 December 2021 and 01 January 2022. [A report from Case Western Reserve University](#) (29) compared electronic health records from a period of assumed Delta dominance (01 September 2021 to 15 November 2021) to a period of assumed Omicron dominance (15 December 2021 to 24 December 2021). This report found a reduced risk ratio (RR) of emergency department visit (RR 0.30 95% CI 0.28-0.33), hospital admission (RR 0.44, 95% CI 0.38-0.52), ICU admission (RR 0.33, 95% CI: 0.23-0.48), and ICU admission (RR: 0.16, 95% CI 0.08-0.32) in the Omicron period when compared to the Delta period.
- [Early data from Denmark](#) (13) showed that 0.9% of cases of Omicron have been hospitalized, compared with 1.1% of those with other variants, using data up to 28 December. However, the figures for Omicron hospitalizations should be interpreted with caution given the lag between disease onset and hospitalizations.
- Preliminary data from cohorts of patients in Ontario, Canada, with onset date between 22 November and 17 December 2021 also show a reduced risk of hospitalization and death for Omicron compared to Delta (HR 0.46 (95% CI 0.27 – 0.77) after adjusting for vaccination status.
- Using samples from the lower respiratory tract, [researchers at Hong Kong University found](#) (30) 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. In contrast, the Omicron variant showed relatively much slower replication in the lung. A similar finding reported by researchers from the United Kingdom in a preprint published on 3 January 2022 where Omicron showed a reduction in replication kinetics compared to Delta and the original strain (31). These observations could further support a reduction in intrinsic severe clinical presentation of patients infected with the Omicron variant.
- In summary, data from Denmark, South Africa, the United Kingdom, Canada and the USA and suggest a **reduced risk of hospitalization** for Omicron compared to Delta; and in the United Kingdom, a reduction in severity among hospitalized patients.
- Despite this, large upsurges in hospitalizations are observed, and are to be expected in the coming weeks given very high incidence rates of community transmission.
- However, further data are needed from more countries to better understand the full clinical picture of Omicron. WHO encourages countries to contribute to the collection and sharing of hospitalized patient data through the [WHO COVID-19 Clinical Data Platform](#) (8).

C.2 Host tropism, virus fitness and pathogenicity

- Two studies reported that cleavage efficiency of Omicron is lower than for WT and Delta (20,21), leading to impaired fusogenicity (particularly in lung tissue) and reduced syncytia formation, which may reduce pathogenicity (32,33).
- Efficient cleavage of the spike protein is especially important for the virus TMPRSS2 dependent entry into human cells; cells that express TMPRSS2 are more abundant in the lower respiratory tract, as compared to the upper respiratory tract (Meng et al). The Omicron variant seems to therefore preferentially enter cells via the endosomal (TMPRSS2 independent) pathway. This is confirmed by the observation that Omicron replicates less efficiently (10x) compared to Delta in freshly harvested human lung tissue (20).
- To date, two animal models have been used to assess severity; human ACE2 expressing mice have significantly less weight loss, recover faster and have less lung pathology when infected with Omicron compared to Delta or WT (34). A Syrian hamster (*M. auratus*) model similarly demonstrated weight gain rather than loss in Omicron-infected animals, as well as substantially reduced pathogenicity indicators compared to Delta or WT, associated with the poorer capability of Omicron to infect or spread in lung tissue (32).
- Additional studies on Syrian hamsters have yielded similar results, confirming that Omicron-infected animals show fewer clinical signs and have milder disease (35,36). Viral load in lung tissues is also lower in Omicron-infected animals compared to Delta or WT in both animal models.

C.3. Impact on diagnostics and testing

Assays

- 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 (37) and on the use of antigen-detection tests can be found [here](#) (38). 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 significantly 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) (39) 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](#) (40) 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 >98% of sequences submitted to GISAID as of 7 January, and BA.3 (only few dozen sequences), 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 over 80% 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 SGTF samples, because this deletion is also found in other VOCs (e.g. Alpha and subsets of Gamma and Delta), which are circulating at low levels worldwide.
- Depending on the context, other PCR-based assays are being developed to specifically detect Omicron (41–44). All four [WHO emergency use listing \(EUL\) approved](#) (45) 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 is under investigation.
- Statements from manufacturers indicate that most currently used Ag-RDTs, including three WHO EUL listed tests, have retained their ability to detect SARS-CoV-2 variants, including Omicron.
- Preliminary data are emerging demonstrating that dilutions of viral culture of Omicron are detected by several Ag-RDTs with similar sensitivity as the ancestral (wild-type) virus or (15,46,47) other VOCs although 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). In addition, a recent case report from the United States noted that two Ag-RDTs failed to detect Omicron cases early (days 0-3) in their disease course (48). 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 NAAT 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](#) (49).
- Laboratory personnel are encouraged to report any unusual findings to the manufacturer using this [form](#) (50). 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.

C.4. Impact on immunity (following prior infection or vaccination)

- 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 23 December 2021 (51).

Re-infection risk (immune evasion following prior infection)

- A meta-analysis from [A. Netzl, et al.](#), (52) aggregated all antibody neutralization studies against Omicron datasets until 22 December 2021. Here, with convalescent sera, the fold drop in neutralisation associated with Omicron was substantial (20x). This is complicated by the fact that the majority of titres associated with Omicron were below their individual assays' limit of detection. Conversely, individuals who were previously infected followed by two doses of vaccine, or thrice vaccinated, demonstrated a 7-fold reduction. Importantly, almost all samples from third dose vaccinees were obtained within one month of the last dose administration. Reduction in antibody titers to Omicron may contribute towards the increased risk for reinfection, as covered previously.
- Multiple datasets on cellular immunity have concluded that 70-80% of CD4+ and CD8+ responses were maintained for Omicron infection, in those that had been previously infected, and/or had been previously vaccinated (53–57). Well-preserved cellular immunity to Omicron may assist in protecting against severe disease and death, and likely underlies the observed reduced risk of hospitalisation for those with reinfection due to the Omicron variant (28).
- 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 (58). 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](#) (15) found that 5.9% of the confirmed cases between 1 November to 13 December 2021 resulted from reinfection, estimating the relative 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](#) (59). Similarly, an increase in reinfection cases classified by vaccination status was also reported by the [Israeli ministry of health](#) (60). These estimates are aligned with previous reports from South Africa that Omicron can evade immunity after natural infection. [Similar trends](#) (61) 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](#). (51)

Vaccine effectiveness (immune evasion following vaccination)

- Laboratory data on the immune response to Omicron is rapidly emerging, but most studies are not peer-reviewed. Most studies 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](#) (62) from 16 individuals who received the Pfizer vaccine predicts that 70% of Omicron epitopes may not be affected by T-cell recognition, suggesting a more preserved cellular-mediated protection against severe disease. Two [studies](#) (63,64) evaluated T-cell responses in vaccinated persons, showing that while neutralization responses are strongly reduced against Omicron, there is little effect on cellular immunity with durable CD8+ and CD4+ T cell responses that showed extensive cross-reactivity against both the Delta and Omicron variants. Two non-peer reviewed studies reported that, in 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.
- There are nine studies to date evaluating the effectiveness of the vaccines, though they are limited to data from only four (United Kingdom, Denmark, Canada, South Africa) countries, evaluating only four vaccines (mRNA vaccines, Ad26.COVS.2.S, and AstraZeneca-Vaxzevria). A summary of those studies is outlined below. The early data suggests that the studied vaccines do not perform as well against Omicron infection, disease, and hospitalization compared to Delta infection. There is evidence of lower vaccine effectiveness over time of the primary series, with homologous and heterologous booster doses increasing vaccine effectiveness. There is one study showing waning of the booster dose effectiveness over time; continuous monitoring is required to check if this finding is consistent across studies and vaccines. Only two studies evaluate the effectiveness against

hospitalization, which remains high but lower than against Delta; again waning of effectiveness against hospitalization needs to continue to be monitored.

- A test-negative design study in Scotland (65) (non-peer reviewed), United Kingdom, showed the third/booster vaccine dose was associated with a 57% (95% CI 55, 60) reduction in the risk of 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 (66) 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, 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, 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. These researchers also evaluated the risk of hospitalization (28) by comparing vaccination status among Omicron cases to vaccination status among Delta cases. Hazard ratios for hospitalization with Omicron among Pfizer BioNTech-Comirnaty and Moderna's mRNA-1273 as their primary series are similar to those seen for Delta in those vaccination categories, while Omicron hazard ratios are generally lower than for Delta for those who received AstraZeneca-Vaxzevria as their primary vaccination, though sample size was limited.
- In England, [vaccine effectiveness estimates](#) (67) have been calculated based on 204 036 symptomatic Omicron cases and 169 888 Delta cases. Among those who had received two doses of Pfizer BioNTech-Comirnaty, vaccine effectiveness was 63% (95%CI: 59-67%) two to four weeks after dose #2 for the Omicron variant, dropping to 10% (95%CI: 6 to 13%) after 25 weeks, compared with vaccine effectiveness of 64% (95%CI: 63 to 65%) against Delta in the same time period. Among those who had received two doses of AstraZeneca-Vaxzevria, there was no protective effect of vaccination against symptomatic disease with Omicron from 20 weeks after the second dose. Among those who had received two doses of mRNA-1273, vaccine effectiveness was 68% (95%CI: 55-78%) two to four weeks after dose #2 for the Omicron variant, dropping to 7% (95%CI: -48 to 41%) after 25 weeks, compared with vaccine effectiveness of 75% (95%CI: 39 to 90%) against Delta in the same time period. Vaccine effectiveness two to four weeks after a Pfizer BioNTech-Comirnaty booster dose was estimated at 64% (95%CI: 63 to 66%) in those who received AstraZeneca-Vaxzevria as the primary course and 69% (95%CI: 67 to 70%) in those who had received Pfizer BioNTech-Comirnaty as the primary course. However, this dropped to 43% (95%CI: 37 to 48%) and 49% (95%CI: 46 to 51%) respectively among those vaccinated with the booster dose at least 10 weeks prior.
- [A study from Denmark](#) (non-peer-reviewed) (68) 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 [published](#) (69) preliminary findings of vaccine effectiveness against hospitalization. They report a vaccine effectiveness of the Pfizer BioNTech-Comirnaty vaccine of 50% (95% CI: 35-62%) against hospitalization among an analysis restricted to those with COVID-like symptoms.
- A study from Denmark evaluated the odds of transmission among household members. Secondary attack rates were higher among vaccinated household members if the index case had Omicron when compared to Delta. They found that unvaccinated index cases, when compared to index cases vaccinated with the primary series of the mRNA vaccine or who had prior infection, had household members with a higher odds of infection (adjusted odds ratio 1.41 95% CI 1.27-1.57). The odds ratio was lower for those who had received a booster dose (aOR 0.72 95% CI 0.56-0.92).

- Caution should be used in interpreting vaccine effectiveness studies, and particularly for these early studies on Omicron. These studies are inherently subject to observational biases, some more than others. As a result, no single study result should be seen as definitive. Results across studies, consistency of findings, and trends in results are more relevant for drawing conclusions, and more such data are needed beyond these early studies.
- WHO is closely assessing the impact of the Omicron variant on vaccines through our research and development network by setting up and coordinating a live [repository](#) (70) of reagents to facilitate research focusing on the understanding of vaccine performance 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.
- Omicron neutralization and vaccine effectiveness data from studies in preprint or published are available at [View Hub](#).
- WHO guidance on best practices to conduct these types of studies and generic protocols can be found on this [website](#) (71). Such studies (72,73) are critical to understand the vaccine's impact on transmissibility of Omicron and its relative infectivity as compared with the currently prevalent Delta variant.

C.5. Impact on therapeutics and 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](#)) (74). Sotrovimab retained activity against Omicron but with a 3-fold lower potency in neutralization as measured by EC50 (75).
- WHO is working with its experts to prioritize the therapeutics [research agenda](#) (9) 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](#) (5).

C.6. Global risk assessment

This section summarizes the evidence presented in Sections C.1. - C.4. above), as of 5 January 2022, to arrive at an overall global risk assessment for the Omicron variant. The methods for assessing and including evidence in this technical brief are detailed in Annex E.2. of this document.

- At present, a total of 146 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 previously been observed during the COVID-19 pandemic.
- The clinical severity of Omicron appears lower than that of Delta, but increased transmission may nonetheless pose overwhelming demands on health care systems and lead to significant morbidity, particularly in vulnerable populations. In addition, little is known about the severity of Omicron in countries with low levels of pre-existing immunity, whether from vaccination or natural infection.
- 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. Very preliminary evidence suggests that vaccine protection against severe disease from Omicron is relatively maintained compared to performance against the Delta variant.

- The overall risk related to 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, despite signs of lower severity, is leading to significant surges in hospitalizations with severe consequences and burden on the health system and other sectors. Our understanding is still evolving, and this risk assessment will be updated as more information becomes available.
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D. [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 currently recommends the following priority actions:

D.1. Surveillance

Indicators

- 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 behavior towards PHSM, vaccines and tests; or other relevant characteristics. Generic [study protocols](#) (10) 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](#) (76) 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 (i) monitor Omicron introduction through targeted sequencing of suspected Omicron cases (see case definitions in the Annex E.1.), and (ii) detect Omicron community transmission through enhanced random sampling among SARS-CoV-2 confirmed cases (see case definitions in the Annex E.1.) in the community.

- In 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 (see case definitions in the Annex E.1.).
- 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 estimates.
- 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](#) (76). Additional guidance is available in [ECDC Guidance for representative and targeted genomic SARS-CoV-2 monitoring](#) (77).

D.2. Laboratory testing

Sequencing and PCR-based screening for variants

- 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.
- Reflecting the fact there are many mutations that may be suggestive of Omicron, and that the relative presence of Omicron sub-lineages or other VOCs including the del69-70 will vary by geography, different PCR-based methods (e.g. diagnostic tests that include SGTF or other gene target failure, or SNP-detection assays) may be considered by countries to screen for variants, including Omicron. These methods should be validated to reflect the national context and should not be the only method used for variant surveillance. Results of these assays may be used as a proxy marker of Omicron infection; samples with gene-target failure or SNP profiles compatible with Omicron should be considered suspected Omicron infection and prioritized for sequence confirmation.

Testing programs

- As part of routine quality assurance, testing programs should document and report any unexpected results, including using this [form](#) (50). 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 strategies be adaptable to the evolving epidemiological situation, resource availability and national context including adjusting testing and genomic sequencing capacities in anticipation of possible surges in testing demand from the community or international travelers (78).
- It is critical that SARS-CoV-2 testing is linked to public health actions to ensure appropriate clinical and supportive care, and Public Health and Social Measures.

D.3. Vaccination

Vaccination programs

- 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 whose vaccination remains incomplete. These include older adults, health care workers and those with underlying conditions putting them at risk of severe disease and death.
- In accordance with the SAGE review, the priority for booster doses is to maintain and optimize vaccine effectiveness against severe disease outcomes, especially for those at high risk for serious disease.
- 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 additional data will be available in the coming weeks.

D.4. 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 input, to the existing 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 the secondary impacts of restrictive measures can be better anticipated and mitigated.
- Guided by risk assessment, and 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 (79).

D.5. International travel-related measures

- 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 (80).
- 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 can 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.

D.6. Health system readiness and responsiveness

- As part of preparedness activities while studies are ongoing to better understand the phenotypic characteristics of Omicron, 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](#) (81) and that necessary resources are in place to respond to potential surges.
- Tools such as the [COVID-19 Essential Supplies Forecasting Tool](#) (82) 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/>) (83) should be continued on the COVID-19 care pathways ([Living guidance for clinical management of COVID-19 \(who.int\)](#)) (5).
- Clinical care of patients with COVID-19, caused by any variant version, should be administered within health systems according to evidence-based guidelines, such as the WHO living guidelines for [clinical management](#) (4) and [therapeutics](#) (5), adapted appropriately for local context and resource settings.

D.7. 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 analyzing 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, including 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 behaviors as a series of choices versus directive messages will enhance 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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E. Annexes

E.1. 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](#)) (84), who is a contact (as per [WHO contact definition](#)) (85) 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 case definitions

Suspected reinfection case

- Confirmed or probable COVID-19 case (as per current [WHO case definition](#))(84), 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 definitions

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 \geq 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 \geq 14 days after they have completed all recommended doses of the vaccine series.

Note: 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.

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