Enhancing response to Omicron SARS-CoV-2 variant: 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 are associated with humoral immune escape potential and higher transmissibility. The Omicron variant comprises four lineages including B.1.1.529, BA.1, BA.2 and BA.3.

B. Key current technical information: executive summary

B.1. Global risk assessment

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).

Based on the currently available evidence, the **overall risk related to Omicron remains very high**. Omicron has a significant growth advantage over Delta, leading to rapid spread in the community with higher levels of incidence than previously seen in this pandemic. Despite a lower risk of severe disease and death following infection than previous SARS-CoV-2 variants, the very high levels of transmission nevertheless have resulted in significant increases in hospitalization, continue to pose overwhelming demands on health care systems in most countries, and may lead to significant morbidity, particularly in vulnerable populations.

B.2. Current evidence summary

This section contains an executive summary of the current best available evidence (as of 20 January 2022) regarding the potential impact of the Omicron variant. More detailed information is included in Section C.

Impact on *epidemiology*

- As of 20 January 2022, the Omicron variant had been identified in 171 countries across all six WHO Regions.
- Omicron has a substantial growth advantage over Delta, and it is rapidly replacing Delta globally. There is now significant evidence that immune evasion contributes to the rapid spread of Omicron, but further research is needed to better understand the relative contribution of intrinsic increased transmissibility and immune evasion in explaining transmission dynamics. While the BA.1 lineage has previously been the most dominant, recent trends from India, South Africa, the United Kingdom, and Denmark suggest that BA.2 is increasing in proportion. Drivers of transmission and other properties of BA.2 are under investigation but remain unclear to date.

- Data on clinical severity of patients infected with Omicron are increasingly available. Epidemiological trends continue to show a decoupling between incident cases, hospital admissions and deaths, compared to epidemic waves due to previous variants. This is likely due to a combination of the lower intrinsic severity of Omicron, as suggested by a number of studies from different settings, and that vaccine effectiveness is more preserved against severe disease than against infection. However, high levels of hospital and ICU admission are nevertheless being reported in most countries, given that levels of transmission are higher than ever seen before during the pandemic. Moreover, more data are needed to better understand how clinical markers of severity – such as the use of oxygen, mechanical ventilation, and number of deaths are associated with Omicron. This is particularly important given that current evidence about severity and hospitalization has largely been shared from countries with high levels of population immunity, and there remains uncertainty about the severity of Omicron in populations with both lower vaccination coverage and lower prior exposure to other variants.

Impact on *diagnostics and testing*

- The diagnostic accuracy of routinely used PCR and the WHO emergency use listing (EUL) approved antigen-detection rapid diagnostic tests (Ag-RDT) assays does not appear to be significantly 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. As a growing minority of publicly shared sequences (including all BA.2 sub-lineage sequences) lack this deletion, using SGTF as proxy marker to screen for Omicron will miss Omicron lineages lacking this deletion.

Impact on *immunity (following infection or vaccination)*

- Current evidence consistently shows a reduction in neutralizing titres 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 by South Africa, the United Kingdom, Denmark, and Israel.
- There is a growing body of evidence on vaccine effectiveness (VE) for Omicron, with data available from 15 observational studies from five countries (the United Kingdom, Denmark, Canada, South Africa, and the United States of America), evaluating four vaccines (mRNA vaccines, Ad26.COV2.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 suggest 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. Despite this, follow-up time after booster doses for most studies is short, and there is evidence of waning of VE in months following booster doses. VE estimates against severe outcomes, usually defined as hospitalization, are lower for Omicron than Delta, but mostly remain greater than 50% after the primary series and improve with a booster dose to above 80%. More data are needed to assess these preliminary findings 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. Preliminary in vitro data suggests that antivirals retain activity against Omicron.

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 (as of 20 January 2022) regarding Omicron.

Surveillance and testing

- PCR-based screening assays (e.g. Single Nucleotide Polymorphism (SNP) genotyping) may be useful proxy markers of Omicron and should be validated for a given setting.
- SGTF from commercial PCR kits is indicative for most Omicron isolates and may also be considered as a proxy marker for this variant. However, it should be noted that a minority of Omicron sequences (including all BA.2 lineage) lack the 69-70 deletion, and will therefore be missed by this screening method. An increasing trend in the proportion of BA.2 is currently being observed in a number of countries, including in Denmark, India and the United Kingdom, and therefore use of SGTF-based screening should be interpreted with caution. Drivers of transmission of BA.2 are under investigation but remain unclear to date. PCR-based screening assays (e.g. Single Nucleotide Polymorphism genotyping) may be useful proxy markers depending on the setting.
- Member States' initial cases/clusters associated with the 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 applicable, the number of PCR-based screening method positive (genotyping or 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 position of the Strategic Advisory Group of Experts on Immunization (SAGE), 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.

Infection Prevention and Control

- Health care facilities should have an infection prevention and control (IPC) programme or at least a dedicated and trained IPC focal point; engineering and environmental controls; administrative controls; standard and transmission based -precautions; screening and triage for early identification of cases and source control; and COVID-19 surveillance and vaccination of health workers. In contexts with community transmission, universal masking by all persons in health facilities, using a well-fitted medical mask, is recommended.

Public health and social measures

- With the emergence of the Omicron variant, physical distancing, the use of well-fitting masks (in conjugate indoor settings and outdoors when distancing can't be maintained), ventilation of indoor spaces, hand hygiene and avoidance of crowds where appropriate PHSM measures are not in place 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 to reduce the spread of all variants of SARS-CoV-2.

Contact tracing and Quarantine

- WHO recommends a risk-based, pragmatic approach for Member States to consider when introducing any changes to existing CT and quarantine measures, taking into account the continuity of the critical functions in society and the public health risks and benefits in relation to the pandemic. Any curtailing of CT or quarantine will increase the risk of onward transmission and must be weighed against pragmatic needs.

- Prioritization for identification and follow-up of contacts should be given to those at highest risk of getting infected and highest risk of spreading the virus to vulnerable people; and those at highest risk for development of severe disease. Shortening of quarantine of contacts may be considered, in particular for essential workers, including health workers, when combined with rigorous application of infection prevention and control and public health and social measures; and with SARS-CoV-2 testing, when possible.

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 variant 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. Communication should emphasise the likelihood that we will learn more and the guidance may change.
- Individuals and communities should be provided with timely, accessible and accurate information about how to protect themselves and others from Omicron and other variants, with an emphasis on getting fully vaccinated and continuing to practice protective behaviours to reduce transmission and infection.

B.4. Priority research needed

- Studies are needed to better understand the properties of BA.2, including comparative assessments of BA.2 and BA.1 for key characteristics such as transmissibility, immune escape and virulence.
- Surveillance should continue to be enhanced, including increasing testing and sequencing efforts to better understand circulating SARS-CoV-2 variants, including Omicron and its sub-lineages. Where capacity exists, countries should perform field investigations such as household transmission studies (6), "first few" cases studies (7), contact follow up, and laboratory assessments, to improve understanding of the epidemiological characteristics of Omicron in various settings. 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, including among unvaccinated individuals and individuals without prior infection. 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, especially for inactivated vaccines where no evidence is currently available. The Technical Advisory Group on Vaccine Composition (TAG-Co-VAC) regularly assesses the need for changes to vaccine composition and has recently issued an interim statement on COVID-19 vaccines in the context of the circulation of Omicron.
- 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 behaviour 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 (as of 20 January 2022) regarding the potential impact of the Omicron variant.

C.1. Epidemiology

Incidence

- As of 20 January 2022, the Omicron variant has been identified in 171 countries. The variant has rapidly outpaced Delta in most countries, driving an upsurge of cases in all regions.
- The case incidence of COVID-19 continues to increase globally with a 20% weekly increase in week 2 (10-16 January 2022) compared to the previous week. However, the global rate of increase does appear slower given that there was a 55% increase that was reported for week 1 (3-9 January) compared to week 52 (27 December 2021–2 January 2022).
- During week 2, the South-East Asia Region and the Eastern Mediterranean Region reported the highest increases in case incidence of 145% and 68%, respectively. However, a decrease of 27% was reported in the African Region following a peak in week 52, 2021.
- The large increase in the South-East Asia Region is mainly driven by the increase in the number of cases in India which reported 1 594 160 million new cases compared to 638 872 cases the previous week (a 150% increase). In the Eastern Mediterranean Region, the highest numbers of new cases were reported from Morocco (46 104 vs 31 701 new cases, a 45% increase); Lebanon (45 231 vs 38 112 new cases, a 19% increase) and Tunisia (39 487 vs 13 416 new cases, a 194% increase).
- In the WHO European Region, the increase in weekly case incidence has slowed, with a 10% increase in week 2 compared to 31% in week 1 (2 – 9 January 2022). However, differences within the Region are reported; while a decline or plateauing is starting to be observed in a few countries in Western Europe, many Eastern European and Central Asian countries are seeing high growth rates, with the highest increases seen in week 2 in Kazakhstan

(54 927 vs 6672 new cases in week 1, a 723% increase), Uzbekistan (4744 vs 1223 new cases, a 288% increase) and Kosovo[1] (2990 vs 842 new cases, a 255% increase).

- The increase in weekly case incidence has also slowed in the WHO Region of the Americas, with a 17% increase as of 16 January compared to 78% as of 9 January, mainly driven by the decrease in the number of new cases in the United States of America. However, large increases in case incidence continued to be seen in Central and South America and the Caribbean and Atlantic Ocean Islands, with the largest increases in cases in week 2 reported in Martinique (13 540 vs 1835 new cases, a 638% increase), El Salvador (1343 vs 289 new cases, a 365% increase) and Ecuador (42 992 vs 10 532 new cases, a 308% increase).
- In the WHO Western Pacific Region, the rate of increase in case incidence has begun to slow, mainly driven by the trend in Australia. During week 2 of 2022, an increase of 38% was reported while in week 1, a 122% increase compared to their previous week was reported.
- In South Africa, where Omicron was first reported and is now the dominant variant, there has been a sustained decrease in reported cases since the peak was reported in mid-December 2021. Moreover, the decline in the incidence of cases seen in much of the southern Africa is now starting to be seen in other countries, particularly those which reported an early introduction of Omicron and rapid replacement of Delta.

Transmission

- Omicron has been found to have a significant growth advantage, higher secondary attack rates and a higher observed reproduction number compared to Delta.
- An analysis of GISAID data following a previously published methodological approach (11) shows a growth rate advantage of Omicron over Delta in all countries with sufficient sequence data, translating to a pooled mean transmission advantage (i.e. relative difference in effective reproduction numbers) of 189% (95% Confidence Interval: 162% – 217%) across epidemiological contexts under the assumption of an unchanged generation time. However, early evidence for a reduced generation time of Omicron (12) suggests the transmission advantage may be lower; for a 20% shorter generation time, the estimated pooled mean transmission advantage of Omicron over Delta is 163% (139% – 186%) (13–15).
- Household transmission studies further corroborate the transmission advantage of Omicron. For example, household secondary attack rates for Omicron consistently show higher values compared to Delta: 13.6% (95% CI: 13.1%-14.1%) vs 10.1% (95% CI: 10.0%-10.2%) in the UK (16), and 31% vs. 21% in Denmark (17).
- The transmission advantage of Omicron appears to be largely driven by immune evasion, but also potential increased intrinsic transmission fitness (18). While there is significant evidence of immune evasion against transmission from infection and vaccine-derived immunity (see later sections), more data are needed to better understand the relative contribution of intrinsic increased transmission fitness and immune evasion in explaining transmission dynamics.
- There is evidence that the Omicron variant infects human bronchus tissue faster and more efficiently than Delta (19) and outcompetes Delta in competition experiments using cells derived from the human nose, but not in lung-derived cells (20). This points at a predominance of viral replication in the upper respiratory tract that may confer, at least to some extent, a transmission advantage independent of immune evasion.
- Preliminary results from South Africa have suggested that if there is intrinsic higher transmission fitness, it is likely modest, with some analyses suggesting that immune evasion levels of 25% to 50% could explain the observed growth advantage, even without an increase in intrinsic transmissibility (21). 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 (22).
- Further studies are required to better understand the drivers of transmission, and of declining incidence in various settings. These factors include the intrinsic transmission fitness properties of the virus, degree of immune evasion, the level of vaccine-derived and post-infection immunity, levels of social mixing and degree of application of public health and social measures.

[1] *All references to Kosovo should be understood to be in the context of the United Nations Security Council resolution 1244 (1999).*

Disease severity

- Globally, there has been a 4% increase in the number of new deaths from in week 2 (10 – 16 January 2022) compared to the previous week, with highest increases in the South-East Asia Region (12%) and the Region of the Americas (a 7% increase).
- 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, hospitalisation and deaths.
- Surveillance trends from most countries show a decoupling between incident cases and hospitalisations in many countries, with proportionally lower incidence of hospitalisation, given the level of community transmission, than what was observed with other variants. This decoupling appears to be driven partially by a lower intrinsic severity of Omicron compared to Delta (see below), as well as by more preserved vaccine effectiveness against severe disease than against infection.
- Several studies have looked at the risk of hospitalization and severe disease with Omicron compared to Delta. 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) (23). A report by Imperial College London on 22 December 2021 (24) calculated a 41% (95% CI: 37%-45%) reduced risk of a hospitalization resulting in a stay of one or more nights. Similarly, using a record linkage approach (25), a study in South Africa found that laboratory-confirmed SARS-CoV-2 infected individuals with SGTF, as a proxy for Omicron, had lower odds of severe disease (adjusted odds ratio 0.3, 95% CI 0.2-0.6). In the USA, a recent report from Case Western Reserve University (26) compared electronic health records from a period of assumed Delta dominance (1 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. Another study conducted in the USA (27) reported better clinical outcomes for Omicron compared to Delta, with a 52% (HR 0.48, 95%CI; 0.36-0.64), 53% (HR 0.47 95%CI; 0.35-0.62), 74% (HR 0.26, 95%CI; 0.10-0.73), and 99.1% (HR 0.01, 95%CI; 0.01-0.75) reductions in risk of any subsequent hospitalization, symptomatic hospitalization associated with COVID-19, ICU admission, and mortality respectively, for cases infected with the Omicron relative to the Delta variant. In Canada, preliminary data from cohorts of patients with onset date between 22 November and 25 December 2021 also show a reduced risk of hospitalization and death for Omicron compared to Delta (HR 0.35, 95%CI: 0.26, 0.46) after adjusting for vaccination status, further suggesting a reduction in intrinsic severity (28).
- Furthermore, using samples from the lower respiratory tract, researchers at Hong Kong University found (29) that the Omicron variant replicates up to 70 times faster in the human bronchi compared to the Delta variant and the wild-type SARS-CoV-2 virus. In contrast, the Omicron variant showed relatively much slower replication in the lung. A similar finding was reported in the United Kingdom where Omicron showed a reduction in replication kinetics compared to Delta and the original SARS-CoV-2 strain (30). These observations could further support a reduction in intrinsic severe clinical presentation of patients infected with the Omicron variant.
  In terms of symptoms, preliminary data from the United Kingdom show that Omicron infections appear to be associated with more frequent sore throat than for Delta, and reduction in frequency in loss of smell and taste (31), although these findings need to be interpreted with caution given increase circulation of other respiratory viruses, and potential co-infection.
- Nevertheless, despite lower severity, significant increases in hospitalization, severe disease and death are occurring and likely to continue in the coming weeks, with significant pressure on health services, given the high incidence levels of community transmission. Moreover, current evidence about severity and hospitalization comes largely from countries with high levels of population immunity (post-infection and vaccine-derived), and there remains uncertainty about the severity of Omicron in populations with lower vaccination coverage and prior exposure to other SARS-CoV-2 variants.

- 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 (19,20), 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 TMRPRSS-2 dependent entry into human cells; cells that express TMPRSS-2 are more abundant in the lower respiratory tract, as compared to the upper respiratory tract (33). The Omicron variant seems to therefore preferentially enter cells via the endosomal (TMRPSS-2 independent) pathway. This is confirmed by the observation that Omicron replicates less efficiently (10x) compared to Delta in freshly harvested human lung tissue (19).
- 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). 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 four Pango lineages: the parental B.1.1.529 and the descendent lineages BA.1, BA.2 and BA.3. The BA.1 lineage, which accounts for 97.4% of sequences submitted to GISAID as of 19 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 nearly 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 considered as a marker suggestive of Omicron, but depending on which Omicron lineages are circulating locally, will miss cases of BA.2 or other isolates lacking the 69-70 deletion. As well, 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) and may be useful to screen for Omicron.

- 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 investigating the sensitivity of Ag-RDTs to detect Omicron: several groups have demonstrated that dilutions of viral culture of Omicron or of clinical samples are detected by several Ag-RDTs with similar sensitivity as the wild-type virus or other VOCs (46–51). On the other hand, a recent study suggests that the analytical sensitivity of seven Ag-RDTs trended slightly lower for detection of Omicron compared to the wild-type virus or other VOCs and that four Ag-RDTs showed significantly lower sensitivity to detect Omicron compared to Delta (52). In addition, a recent case report from the United States noted that two Ag-RDTs (using nasal swabs) failed to detect Omicron cases early (days 0-3) in their disease course despite high viral loads detected in the saliva (53). 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 are EUL approved 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 (54).
- Laboratory personnel are encouraged to report any unusual findings to the manufacturer using this form (55). 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 (56).

Re-infection risk (immune evasion following prior infection)

- A meta-analysis from A. Netzl, et al., (57) 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 or three doses of vaccine 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 (58–62). 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 (24).
- The risk of reinfection in England with the Omicron variant was estimated to be 5.4fold 95% CI: 4.87-6.00) higher in comparison the Delta variant (63). 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%. A report by UKSHA (46) 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. A report from the UK Office of National Statistics found that the risk of reinfection was 16 times higher in the Omicron dominant period (20 Dec 2021 to 8 Jan 2022) than the Delta dominant period (17 May 2021 to 19 Dec 2021) (64). Increased risk of reinfection was also associated with unvaccinated individuals. In addition, those who were asymptomatic during their primary infection, or had high Ct values in their primary infection were at a higher risk of reinfection. An increased trend in reinfection case count was observed in Denmark (65). Similarly, an increase in reinfection cases classified by vaccination status was also reported by the Israeli ministry of health (66). These estimates are aligned with previous reports from South Africa that Omicron can evade immunity after infection. Similar trends (67) 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(56). As of now, there are no data on the risk of reinfection with Omicron following a prior Omicron infection.

- A pre-print by researchers in Qatar have shown that protection afforded by prior infection in preventing symptomatic reinfection with Omicron was 56%, a drop from around 90% protection against reinfection with Alpha, Beta, or Delta (68).

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 (8-to-128 fold reductions compared to the ancestral strain) in sera collected within six months of vaccination (69). Booster doses following primary series with multiple vaccines increase the geometric mean titers of neutralizing antibodies, but still show a 2-to-16 fold reduction compared to the ancestral strain. In contrast to findings about the humoral immune response, CD8+ and CD4+ T cell responses seem to be >80% preserved in the majority of studies (60,70,71).
- As of January 20, there are 14 studies evaluating the vaccine effectiveness from five countries (United Kingdom, Denmark, Canada, South Africa, USA), evaluating four vaccines (both mRNA vaccines, Ad26.COV2.S, and AstraZeneca-Vaxzevria). Only one appears in a peer-reviewed publication (72); the others are preprints. Overall, there is accumulating evidence of lower vaccine effectiveness against infection and symptomatic disease soon after vaccination compared to Delta. There is also evidence of accelerated waning of VE over time of the primary series against infection and symptomatic disease for the studied vaccines, with some studies showing no effectiveness against these outcomes several months after vaccination. Homologous and heterologous booster doses increase vaccine effectiveness against Omicron, although follow-up time after booster for most studies is short, precluding a long-term evaluation of waning. VE estimates against severe outcomes, usually defined as hospitalization, are lower for Omicron than Delta, but mostly remain greater than 50% after the primary series and improve with a booster dose to over 80%.
- A brief summary of the evidence of vaccine performance against Omicron to date is given below.

Infection/symptomatic disease

United Kingdom

- In England, using a test-negative design, VE for symptomatic infection dropped to under 20% by 20 weeks after vaccination (completion of the primary series) for Pfizer BioNTech-Comirnaty, Moderna mRNA-1273, and AstraZeneca-Vaxzevria. An mRNA booster dose for all three vaccines following a primary two dose series restored VE to >60%, with some evidence of waning of VE by 10 weeks post-booster (73).
- Using a different design than the previously mentioned study, estimates of VE against symptomatic infection from Omicron were between 0% and 19% following two doses of Pfizer BioNTech-Comirnaty or AstraZeneca-Vaxzevria, and between 54% and 77% after a booster dose (63).
- In Scotland (74), a third/booster mRNA vaccine dose was associated with a 57% (95% CI 55, 60) reduction in symptomatic infection relative to ≥25 weeks post second dose (Pfizer BioNTech-Comirnaty, Moderna mRNA-1273, and AstraZeneca-Vaxzevria), as compared to a relative VE of 88% (95% CI 86,89) for presumed Delta infection.

- Another Scottish study found the VE for symptomatic infection a median of five months post-vaccination to be 5% for AstraZeneca-Vaxzevria and approximately 25% for both mRNA vaccines, with an increase to 59-64% after an mRNA booster dose (75).
- The SIREN cohort study among health care workers found the VE against any infection for the two mRNA vaccines and AstraZeneca-Vaxzevria combined was 32% after two doses among those without previous infection and 60% among those with previous infection, increasing to 62% and 71%, respectively after a booster dose (31).

Denmark

- A nationwide cohort estimated a VE against infection of 55% (95% CI 24-74%) and 37% (95% CI -70-76%) for Pfizer BioNTech-Comirnaty and Moderna- mRNA 1273, respectively, in the month after vaccination, with evidence of waning VE to negligible VE by two to three months. A booster dose among those who received a primary series of Pfizer BioNTech-Comirnaty was found to restore the VE to 55% in the first month post-booster.

Canada

- In Ontario, there was negligible VE against infection among recipients of a primary series that included at least one mRNA vaccine. The VE increased to >40% after an mRNA booster (76). Subsequent analysis with more cases suggests that confounding bias among early Omicron cases likely lowered early VE estimates.

U.S.A.

- In a study among members of a large health maintenance organization in California, the VE for two doses of the Moderna mRNA-1273 vaccine was 30% (5%-49%) within three months of full vaccination and dropped to 0% by 6 months (77). The VE increased to 64% (58-90%) within six weeks after a third dose among immunocompetent persons; the VE was 49% (13%-70%) among persons boosted >6 weeks before. Immunocompromised persons had negligible VE after a booster dose (VE= 11.5% [0-66.5]).

Severe disease/hospitalization

South Africa

- An insurance company study reported a VE of the Pfizer BioNTech-Comirnaty vaccine of 50-70% against (72) hospitalization.
- The Sisonke trial of health care workers showed that a second dose of the Janssen-Ad26.COV2.S vaccine had 85% (54-95) VE against hospitalization through two months post-vaccination (78).
- In a cohort study from Western Cape Province that was a case-only analyses (i.e., VE was not calculable), persons vaccinated with the primary series either Pfizer BioNTech-Comirnaty or Janssen-Ad26.COV2.S vaccine, had a 55% reduced probability to progress from SARS-CoV-2 infection to hospital admission or death, and a 76% reduced probability to progress to death, than did persons who were unvaccinated (79).

United Kingdom

- Combined data from England/Wales for three vaccines (Pfizer BioNTech-Comirnaty, Moderna mRNA-1273, and AstraZeneca-Vaxzevria) showed that the VE against hospital admission fell to 44% (95% CI 30-54) by 25 weeks post-full vaccination, and increased to >80% through 10 weeks after booster vaccination (80). There was approximately a 70% reduction in progression from symptomatic infection to hospital admission after the booster dose.

Caution should be used in interpreting vaccine effectiveness studies. Observational studies are inherently subject to biases, and these biases might be exaggerated when evaluating the early cases of Omicron in a geographic area, as early cases likely have differences in exposure risk and vaccination status compared to the general population. While 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. More such data are needed beyond these early studies to establish a more complete picture of vaccine performance against Omicron variant.

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 (81) of reagents to facilitate research focusing on the understanding of vaccine performance through animal model studies, antibody neutralization activity and cellular protection. Omicron neutralization and vaccine effectiveness data from studies in preprint or published are available at View Hub.

C.5. Impact on therapeutics and treatments

1. 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 (82–85). On 16 December 2021, Roche issued a statement on diminished potency of casirivimab and imdevimab against Omicron *in vitro* studies (2021216_Roche statement on Ronapreve Omicron.pdf) (86). Sotrovimab retained activity against Omicron but with a 3-fold lower potency in neutralization as measured by EC50 (84).
2. Preliminary in vitro data suggests that antivirals retain activity against Omicron (87–90).

- 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 Global Risk Assessment is based on the evidence provided (in Sections C.1. - C.4. above), as of 20 January 2022. The methods for assessing and including evidence in this technical brief are detailed in Annex E.2.
Based on the currently available evidence, the **overall risk related to Omicron remains very high**. Omicron has a significant growth advantage over Delta, leading to rapid spread in the community with higher levels of incidence than previously seen in this pandemic. Despite a lower risk of severe disease and death following infection than previous SARS-CoV-2 variants, the very high levels of transmission nevertheless result in a significant increases in hospitalization, continue to pose overwhelming demands on health care systems in most countries, and may lead to significant morbidity, particularly in vulnerable populations.

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. 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 behaviour 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

3. Countries should continue to undertake targeted sampling of specific populations, as outlined in the guidance for surveillance of SAR-CoV-2 variants (91) for sequencing.
4. 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.).

- Once evidence from representative sequencing demonstrates that Omicron is the dominant strain circulating, it can be assumed that SARS-CoV-2 infections detected are most probably due to Omicron. Routine surveillance should continue to ensure early detection of newly emerging variants.
- 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 (e.g. 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.
- Countries in which sequencing shows that Omicron is the dominant variant, should continue representative and targeted sequencing to understand which Omicron lineages are circulating and to enable detection of other potentially emerging variants.
- 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 (91). Additional guidance is available in ECDC Guidance for representative and targeted genomic SARS-CoV-2 monitoring (92).

D.2. Laboratory testing

Sequencing and PCR-based screening for variants

1. 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.
2. 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. Of note, the increase in BA.2 in recent weeks,

which lacks del69-70, must be taken into account when developing such proxy screening strategies.

3. PCR-based screening 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

4. The use of either molecular tests (NAAT, PCR) or antigen-detection assays are both appropriate to diagnose SARS-CoV-2 infection as per existing Interim guidance on diagnostic testing for SARS-CoV-2 (37) and on the use of antigen-detection tests here (38). No test is perfect, and negative results should be interpreted within the clinical/epidemiological context.
5. As part of routine quality assurance, testing programs should document and report any unexpected results, including using this form (55). 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).
6. 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 (93).
7. 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 (PHSM)

- Crowd avoidance, physical distancing, the use of well fitted masks, ventilation of indoor space, and hand hygiene remain key to reducing transmission of SARS-CoV-2, especially in the context of emerging variants. Acceptable mask types for use by the general public include reusable, non-medical masks that comply with standards (the ASTM F3502 standard or CEN Working Agreement 17553), or disposable medical masks. With reduced vaccine effectiveness against Omicron, increasing adherence to protective behaviours is essential to reduce transmission. Risk reduction Policies should be strengthened, and implemented to encourage appropriate adherence to a comprehensive package of prevention and control measures.
- PHSM may need to be enhanced to further limit interpersonal contact to control transmission with a more transmissible variant. RCCE activities should be expanded to emphasize the importance of the six protective behaviours.
- The use of established PHSM in response to individual cases or clusters of cases, including contact tracing, quarantine of contacts and isolation of cases 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 behaviours, knowledge and perceptions (as well as uncertainties related to the rapidly evolving situation of Omicron), countries should be ready to escalate PHSM in a timely manner to avoid overwhelming demands on health care services.
- For further guidance on risk-based calibration of PHSM, please see WHO's interim guidance (94).

D.5. Infection prevention and control (IPC)

- Health facilities should have an IPC programme or at least a dedicated and trained IPC focal point, engineering and environmental control, administrative controls, standard and transmission based -precautions, screening and triage for early identification of cases and source control, and COVID-19 surveillance and vaccination of health workers (95).
- Health facilities should continue to adhere to and strengthen key WHO-recommended IPC measures, in particular, adhering to respiratory etiquette and hand hygiene best practices, contact, droplet and airborne precautions, adequate environmental cleaning and disinfection; ensuring adequate ventilation; isolation facilities of COVID-19 patients; in addition, where possible, maintaining a physical distance among all individuals in health facilities of at least 1 meter (increasing it whenever feasible), especially in indoor settings.
- In areas of known or suspected community or cluster SARS-CoV-2 transmission, masking by all health workers, including community health workers and caregivers, other staff, visitors, outpatients and service providers using a well-fitted medical mask, is strongly recommended at all times. This is important in all contexts, including where caring for non-COVID-19 patients, and in any common area (e.g., cafeteria, staff rooms). In areas with known or suspected sporadic transmission, targeted continuous medical mask use is recommended in health facilities.
- Either a respirator or a medical mask should be used by health workers when caring for a suspected or confirmed COVID-19 patient (96). Additionally, all health workers should wear a respirator in the following circumstances:
    - When ventilation is known to be poor or cannot be assessed or the ventilation system is not properly maintained
    - Based on health workers' values and preferences and on their perception of what offers the highest protection possible to prevent SARS-CoV-2 infection.
- A respirator should always be worn along with other PPE (gloves, gowns, eye protection) by health workers performing aerosol-generating procedures (AGPs) and by health workers on duty in settings where AGPs are regularly performed on patients with suspected or confirmed COVID-19, such as intensive care units, semi-intensive care units or emergency departments
- Appropriate mask fitting should always be ensured (for respirators through initial fit testing and seal check and for medical masks through methods to reduce air leakage around the mask) as should compliance with appropriate use of PPE and other precautions (96).

D.6. Contact tracing and quarantine in a high caseload environment in the context of Omicron

- The available scientific evidence around contact tracing (CT) and quarantine measures for Omicron is currently limited . WHO therefore continues to recommend a risk-based, pragmatic approach for Member States to consider when introducing any changes to existing CT and quarantine measures, taking into account the continuity of the critical functions in society and the public health risks and benefits in relation to the pandemic.
- Any curtailing of CT or shortening of the duration of quarantine will increase the risk of onward transmission and must be weighed against healthcare capacity, population immunity, and socio-economic priorities.

Prioritizing contact tracing in a high caseload environment

- WHO recognizes that in scenarios in which case numbers are high, it may not be possible to identify, monitor and quarantine all contacts. Prioritization for identification and follow-up of contacts should therefore be given to:
    - contacts at highest risk of getting infected and highest risk of spreading the virus to vulnerable people, health and care staff, particularly those working in nursing homes long-term care facilities and hospitals; and other frontline essential workers
    - contacts at highest risk for developing severe disease: people with co-morbidities, the immunocompromised, the elderly, and unvaccinated adults with no known prior SARS-CoV-2 infection
- When a contact develops COVID-19 symptoms, they should be considered as a suspected case of COVID-19 and, as such, a referral pathway to testing should be available and recommended as per existing guidance (93). In resource-constrained settings and/or when testing capacity is limited and thus, testing of all symptomatic contacts is not possible, highest-risk contacts should be prioritized, as above (93)

Quarantine in a high caseload environment

- When the number of cases and the number of identified contacts requiring quarantine are high and impacting essential societal functions, changes to the duration of the quarantine period (the current WHO recommendation is 14 days) may be considered. However, they need to recognize that changes will have risks and benefits. These changes should always be combined with rigorous application of infection prevention and control and public health and social measures, and with an adequate testing strategy based on RT-PCR or Rapid Antigen Test, when possible.
- When rapid and accurate testing is available and as a measure to exit quarantine earlier, modelling and observational studies based on data for previous variants (97–100) have shown that quarantine maybe shortened, if the contact has no symptoms and presents a negative PCR or antigen test, performed in an accredited laboratory or by a qualified professional, at the end of the shortened quarantine period. WHO does not recommend self-administered antigen tests to shorten quarantine.
- Where testing to shorten quarantine is not possible, the absence of symptom development after a certain number of days can be used as a proxy. For example, the post-quarantine transmission risk for 10 days quarantine (based on pre-Omicron data) is estimated to be around 1%, with an upper limit of about 10% (100).
- If the quarantine period is shortened WHO recommends individuals to continue to wear a well-fitted mask at all times, during all indoor and outdoor activities where interaction with other people may occur, along with other infection prevention and control measures including physical distancing, appropriate ventilation of indoor spaces, and hand hygiene for the remainder of the total 14 days. These individuals should also continue to carefully self-monitor for symptoms, and seek testing if symptoms arise.

D.5. International travel-related measures

- National authorities should lift or ease international traffic bans, as they do not provide added value and continue to contribute to the economic and social stress in countries. The failure of travel bans introduced after the detection and reporting of the Omicron variant to limit the international spread of Omicron demonstrates the ineffectiveness of such measures over time. 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 (3).

- National authorities should continue to apply an evidence-informed and risk-based approach when implementing international travel measures in accordance with the statement from the 10th meeting of the IHR Emergency Committee and WHO's interim guidance published in July 2021 (101).
- 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.
- 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 (102) and that necessary resources are in place to respond to potential surges.
- Tools such as the COVID-19 Essential Supplies Forecasting Tool (103) 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/) (104) 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.
- Protecting health workers remains a priority, including by training (or refreshers) for health workers on infection, prevention, and control (https://openwho.org/courses/ipc-health-workers), as well as appropriate respiratory protection equipment, in light of Omicron (95,96).

D.7. Risk communication and community engagement (RCCE)

- National all-hazard or COVID-19 specific RCCE plans and activities should be updated to incorporate changing needs in light of Omicron, in the context of the broader pandemic response.
- RCCE activities in response to Omicron should be well coordinated between partners.
- Authorities should communicate information related to Omicron and potential implications for individuals and communities in a timely, transparent, empathetic and accessible manner to maintain and strengthen trust and increase acceptance of response measures and authorities. Targeted communication and engagement should be designed for high-risk individuals and communities who may not perceive the nuanced risks of Omicron or who may be more at risk (e.g., people who are older, who have existing health conditions or who have not been vaccinated, minority groups, those in fragile, conflict and violent states etc.).
- One of the most important and effective interventions in the 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. All RCCE efforts related to Omicron should emphasise that the scientific evidence is growing and recommendations may change.
- Listening to community perceptions through online or offline methods and socio-behavioural surveys and analysing this data are key to responding with effective communication and engagement interventions. This should be done in an ongoing manner, with RCCE and other public health interventions being iteratively adapted based on findings. Social and behavioural data should be a key component of multi-source surveillance systems.
- RCCE plans, strategies and activities should be targeted to specific populations based on social, cultural, behavioural, demographic and environmental data to encourage vaccine uptake and adherence to protective measures by all individuals and communities, including among individuals who are fully vaccinated who may perceive the risk to be lower.

- 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, health workers and other influential members of society who are well respected by the target audience). There should be an information monitoring system in place to capture emerging trends, rumours and misinformation to enable delivery of a targeted communication package.
- Two way communication systems should be established or existing platforms utilized to facilitate community dialogue and incorporate community voices in the design and implementation of the response.
- When PHSM are adjusted, communities should be fully and regularly informed, engaged and enabled before changes are made. Clear, concise and transparent risk communication, including an evidence-based rationale for adjusting measures, should be developed with communities targeted for PHSM 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 enhance uptake.
- RCCE activities should emphasise the continued importance of getting fully vaccinated and of continuing to practice the protective behaviours (avoiding crowds, keeping a safe distance, wearing a well-fitting mask, keeping indoor spaces well ventilated, cleaning hands regularly and covering coughs and sneezes).

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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) (105), who is a contact (as per WHO contact definition) (106) 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., 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)(105), 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 ≥ 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.

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.

E.2 References

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