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

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Summary

Background

- On 26 November 2021, WHO designated the variant B.1.1.529 a variant of concern (VOC), on the basis of advice from WHO's Technical Advisory Group on Virus Evolution. The variant has been given the name Omicron. Omicron variant is a highly divergent variant with a high number of mutations, including 26-32 in the spike protein, some of which are concerning and may be associated with immune escape potential and higher transmissibility. However, there are still considerable uncertainties. As of 9 December 2021, cases of human infections with this variant have been identified in 63 countries across all six WHO regions. Current understanding of the Omicron variant from recent data are likely to evolve as more data becomes available.
- The overall threat posed by Omicron largely depends on three key questions, including: (1) how transmissible the variant is; (2) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; and (3) how virulent the variant is compared to other variants. Public health advice is based on current information and will be tailored as more evidence emerges around those key questions.
- Based on current limited evidence Omicron appears to have a growth advantage over Delta. It is spreading faster than the Delta variant in South Africa where Delta circulation was low, but also appears to spread more quickly than the Delta variant in other countries where the incidence of Delta is high, such as in the United Kingdom. Whether Omicron's observed rapid growth rate in countries with high levels of population immunity is related to immune evasion, intrinsic increased transmissibility, or a combination of both remains uncertain. However, given the current available data, it is likely that Omicron will outpace the Delta variant where community transmission occurs.
- There are still limited data on the clinical severity of Omicron. While preliminary findings from South Africa suggest it may be less severe than Delta, and all cases reported in the EU/EEA to date have been mild or asymptomatic, it remains unclear to what extent Omicron may be inherently less virulent. More data are needed to understand the severity profile.
- There are limited available data, and no peer-reviewed evidence, on vaccine efficacy or effectiveness to date for Omicron. Preliminary evidence, and the considerably altered antigenic profile of the Omicron spike protein, suggests a reduction in vaccine efficacy against infection and transmission associated with Omicron. There is some preliminary evidence that the incidence of reinfection has increased in South Africa, which may be associated with humoral (antibody-mediated) immune evasion. In addition,

preliminary evidence from a few studies of limited sample size have shown that sera obtained from vaccinated and previously infected individuals had lower neutralization activity (the size of the reduction ranges considerably) than with any other circulating VOCs of SARS-CoV-2 and the ancestral strain.

- The diagnostic accuracy of routinely used PCR and antigen-based rapid diagnostic test (Ag-RDT) assays does not appear to be influenced by Omicron. Most Omicron variant sequences reported include a deletion in the S gene, causing some S gene targeting PCR assays to appear negative. Although some publicly shared sequences lack this deletion, this remains a minority of currently available sequences, and S gene target failure (SGTF) can therefore be used as a useful proxy marker of Omicron, for surveillance purposes. However, confirmation should be obtained by sequencing, as this deletion can also be found in other VOCs (e.g., Alpha and subsets of Gamma and Delta).
- Therapeutic interventions for the management of patients with severe or critical COVID-19 associated with the Omicron variant that target host responses (such as corticosteroids, and interleukin 6 receptor blockers and prophylaxis with anticoagulation) are expected to remain effective. However, monoclonal antibodies will need to be tested individually, for their antigen binding and virus neutralization and these studies should be prioritized.

Risk Assessment

- The overall risk related to the new variant of concern Omicron remains very high for a number of reasons. First, the global risk of COVID-19 remains very high overall, and second, preliminary evidence suggests potential humoral immune escape against infection and high transmission rates, which could lead to further surges with severe consequences. Our understanding is still evolving, and the risk assessment will be updated as more information becomes available.

Priority actions for Member States

- Enhance surveillance and sequencing efforts to better understand circulating SARS-CoV-2 variants, including Omicron. Where capacity exists, perform field investigations such as household transmission studies, contact follow up and laboratory assessments to improve understanding of the characteristics of Omicron.
- As SGTF from a widely used PCR test (ThermoFisher TaqPath) is indicated for Omicron, the SGTF can be used as the marker for this variant, which may lead to efficient detection of Omicron. However, it should be noted that some sequences are lacking this deletion.
- All initial cases/clusters associated with Omicron variant infection should be reported to WHO through the IHR mechanism.
- Thereafter, Member States are encouraged to report (publicly or through IHR) the weekly relative prevalence of Omicron as the number of sequences of Omicron (numerator) divided by the total number of sequences generated through routine surveillance (denominator) and/or, where available, number of SGTF out of the number tested in the same unit of time, according to sampling date.
- Efforts to accelerate COVID-19 vaccination coverage as rapidly as possible should continue, particularly among populations designated as high priority who remain unvaccinated or are not yet fully vaccinated. Delta is still by far the predominant variant worldwide causing significant disease and transmission against which vaccines are highly effective, and vaccines are likely to have some effectiveness against Omicron, particularly for severe disease, even if the performance is reduced compared with other variants.
- 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* for additional information.
- The use of well-fitting masks, physical distancing, ventilation of indoor space, crowd avoidance, and hand hygiene remain key to reducing transmission of SARS CoV-2 even with the emergence of the

Omicron variant. Enhanced surveillance with rapid testing and stricter contact tracing of cases suspected cases to be infected with a Variant Of Concern is strongly advised to interrupt chains of transmission.

- Ensure early warning systems are in place to inform efficient adjustment of public health and social measures.
- In anticipation of increased COVID-19 caseloads and associated pressure on the health system, ensure mitigation plans are in place to maintain essential health services and necessary health care resources are in place to respond to potential surges.
- Authorities should regularly communicate evidence-based information on the Omicron and other circulating variants and potential implication for the public in a timely and transparent manner, including what is known, what is unknown and what is being done by responsible authorities.

Background

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

The overall threat posed by Omicron largely depends on three key questions, including: (1) how transmissible the variant is; (2) how well vaccines and prior infection protect against infection, transmission, clinical disease and death; and (3) how virulent the variant is compared to other variants.

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

Epidemiology

- In South Africa, where Omicron was first reported, the case incidence of COVID-19 continues to rise since the second week of November. In week 48, a total of 67 507 cases were reported, a nearly 5-fold increase on the previous week, with the highest incidence reported in Gauteng province.
- Since the last update published on 7 December 2021 (Weekly Epidemiological Update), additional countries across all six WHO Regions have reported confirmed cases of the Omicron variant. As of 9 December 2021 (2 pm CET), the Omicron variant has been confirmed in 63 countries. Community transmission has been confirmed in South Africa and the United Kingdom and cases with no epidemiological link to travel outside the European Union or European Economic Area have been reported in Belgium, Denmark, Finland, Spain and Iceland. Between 29 November and 5 December large increases in the incidence of cases compared to the previous week were seen in countries neighbouring South Africa including Eswatini (20x increase (840 vs 42 cases)); Zimbabwe (14.6x increase (4572 vs 313 cases)) (); Mozambique (13.1x increase (353 vs 27 cases), Namibia (7.8x increase (375 vs 48 cases)) and Lesotho (3.2x increase(83 vs 26 cases)). While drivers of these increases remain unconfirmed, some of these countries are now reporting confirmed cases with the Omicron variant and it is therefore plausible that spread of Omicron, in combination with enhanced testing following the declaration of a VOC, play a role.

Transmission

Estimates from case reports

- The daily reproductive number (Rt) estimated by the National Institute for Communicable Diseases (NICD) in South Africa using reported cases remained below 1 in October and early November 2021. These estimates increased from the start of November and reached 2.55 (95% CI 2.26, 2.86) at a national level based on case counts up to 29 Nov 2021. In Gauteng Province, where most cases have been reported in South Africa, the most recent estimates of Rt are 3.06 (95% CI 2.59, 3.62). Estimates based on GISAID sequencing data suggest an Rt of approximately 1.5. However, targeted sampling and lagged data mean that current estimates based on these data are likely to be biased.
- Using SGTF as a proxy for Omicron, analyses from the UK Health Security Agency (UKHSA) have shown a growth of cases with SGTF compared with S gene target positive (SGTP) of 141% in week 48, compared to the previous week suggesting a significant growth advantage of Omicron over Delta. More recent evidence from the UKHSA released on 08 Dec 2021 indicates that SGTF cases continue to grow and account for 1% of all cases as of the end of November. Furthermore, data from household transmission risk, secondary attack rates and growth rates from the UK also suggest that Omicron has a growth advantage over Delta, with some evidence of higher humoral immune evasion than Delta.
- Finally, early data published on the 9 December 2021 by the Statens Serum Institute in Denmark showed

796 confirmed Omicron cases, with case counts increasing by at least 50% per day in recent days, accounting for over 3% of all cases in Denmark.

Estimates from modelling

- Preliminary unpublished estimates from many research groups worldwide have suggested that Omicron has a growth advantage over Delta in South Africa. Based on data reported data, researchers have estimated a 1.4 to 3.1 higher Rt for Omicron than Delta (personal communications). However, these estimates are based on early SGTF and sequencing data that has not been randomly sampled, and hence need to be interpreted with caution.
- The European Centre for Disease Prevention and Control, illustrated, through modelling, how the Omicron variant could become the dominant variant in Europe within the next few months, based on hypothetical scenarios of growth advantage. For example, assuming the proportion of Omicron variant circulating in Europe in December was at 0.1%, a 1.5 times higher transmission compared to Delta could result in the Omicron variant being dominant by March 2022.

Clinical severity

- Data on hospitalization remain limited, and more time will be needed to understand the impact of Omicron on severity and death, particularly in the context of vaccination. As of 9 December, all 402 confirmed cases identified in 21 European Union and European Economic Area (EU/EEA) countries for which information was available on severity were asymptomatic or had mild symptoms, and no deaths have been reported. However, given the low number of reported cases, these data should be interpreted with caution and conclusions on severity cannot yet be drawn.
- While South Africa reported an 82% increase in hospital admissions due to COVID-19 (from 502 to 912) during the week 28 November – 4 December 2021, the proportion of those hospitalizations that are due to the Omicron variant, compared to the proportion of community transmission due to Omicron is not yet known
- In addition, given that Omicron is circulating in populations with high levels of pre-existing immunity, it is not yet clear to what extent these early observations of lower severity may stem from lower severity following prior infection or vaccination or due to lower virulence of the virus.
- Even if the severity is potentially lower than for the Delta variant, it is expected that hospitalisations will increase as a result of increasing transmission. More hospitalizations can put a burden on health systems and lead to more deaths. More information on case severity is expected in the coming weeks due to the time lag between an increase in the incidence of cases and an increase in the incidence of severe cases, and deaths. Further information is needed to fully understand the clinical picture of those infected with Omicron and WHO encourages countries to contribute to the collection and sharing of hospitalized patient data through the WHO COVID-19 Clinical Data Platform.

Immune evasion

- Preliminary evidence from epidemiological, modelling and laboratory studies, suggests that humoral immunity is less protective against infection by Omicron than against other variants. A study in South Africa showed that the likelihood of reinfection with Omicron was higher than what would have been expected with previous variants, and early findings from unpublished modelling studies (personal communication), also suggest some level of immune evasion against infection is likely. However, there remains significant uncertainty around the extent to which immune evasion or intrinsic increased transmissibility explain current trends.

- As of 9 December 2021, results from four non-peer reviewed studies of the effect of neutralizing antibodies on sera from naturally infected and vaccinated individuals have been made available.[16,22-24] While results differ, all studies show significant reductions in neutralization against Omicron by different sets of plasma samples when compared to the ancestral strain and other VOCs, including samples from ChAdOx1-S [recombinant] vaccine, COVID-19 mRNA Vaccine (nucleoside modified), tozinameran vaccinees and convalescent plasma. These are preliminary findings based on low numbers of samples, and further evidence from larger studies is needed. The effect of booster doses is also not sufficiently addressed, however analyses posted by Pfizer suggests that a booster dose provides neutralization of Omicron one month after the third dose. Neutralizing activity of sera from vaccinated plus infected or infected plus vaccinated individuals (also called hybrid immunity) holds well against Omicron, according to these very preliminary data. If confirmed, this may have important implications in settings that experienced high levels of infection and still have low vaccine coverage, as vaccination remains crucial. Moreover, how this translated into vaccine effectiveness estimates, especially against severe disease, remains unclear, particularly since cell-mediated immunity also confers protection.
- Overall, preliminary evidence suggests some degree of immune evasion against infection, but much more evidence is needed.
- It is essential that COVID-19 vaccination among at risk groups in all countries is prioritized and accelerated urgently.

Impact on diagnostics

- SARS-CoV-2 infection can be diagnosed using either molecular tests (NAAT, PCR) or antigen-detection assays. Interim guidance on diagnostic testing for SARS-CoV-2 can be found here and on the use of antigen-detection tests can be found here.
- PCR tests that include multiple gene targets are unlikely to be affected and should continue to be used to detect SARS-CoV-2 infection, including the Omicron variant. This has been confirmed by statements issued by suppliers as well as the US FDA, based on sequence analysis.
- The majority of Omicron variant sequences reported include a 69-70 deletion in the S gene. While some publicly shared sequences lack this deletion, these represent a minority of currently available sequences. Presence of the 69-70 deletion causes a negative signal for the S gene target in certain PCR assays, such as with the TaqPath COVID-19 Kits (Thermo Fisher Scientific). This S-gene target failure (SGTF) can be used as a marker suggestive of Omicron. However, confirmation should be obtained by sequencing for at least a subset of samples, as this deletion is found in other VOCs (e.g., Alpha and subsets of Gamma and Delta) which are circulating at low-levels globally.
- All four WHO emergency use listing (EUL) approved antigen-detection rapid diagnostic tests (Ag-RDTs), target the Nucleocapsid protein of SARS-COV-2. The vast majority of Omicron sequences include the G204R and R203K mutations in the Nucleocapsid protein, which are present in many other variants currently in circulation. These mutations have not been reported to affect the accuracy of Ag-RDTs to detect SARS-CoV-2. In addition, the majority of 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 currently unclear.
- Official statements from several Ag-RDT suppliers, including two with EUL-approved assays, indicate that based on sequence analysis, the performance of their tests is not expected to be impacted by the Omicron variant. Preliminary laboratory evidence is emerging that independently confirms that Ag-RDTs can accurately diagnose infection with the Omicron variant.
- To date, there have been no reported misdiagnoses (false negative results) for any WHO EUL approved diagnostic product in relation to Omicron.

Impact on vaccines

- There is a need for more data to assess whether the mutations present on the Omicron variant may result in reduced protection from vaccine derived immunity. WHO will continue to work with partners to monitor and evaluate these data once they become available.
- Assessment of the threat will be facilitated by key laboratory studies, including animal studies. Neutralization activity of plasma collected from vaccinated and previously infected individuals would be tests against Omicron. While it will take some time to have sufficient stocks of the virus to be shared broadly , it will also be important to develop and share pseudo-neutralizing assays. Animal studies will help to evaluate virulence and ability to evade immune responses to previous variants. Laboratory research coordination with sharing of reagents and knowledge will be just as critical in evaluating the threat from the Omicron variant as it was in facilitating development of the original vaccines.
- Full assessment of the threat will also require continued and ideally improved surveillance and epidemiological studies. Through these studies, a clearer picture of the transmissibility of Omicron and its relative infectivity as compared with the currently prevalent Delta variant will emerge.
- Another key clinical input will be information about how well current vaccines are performing against the Omicron variant. These studies will help to determine the degree to which previous vaccination or infection protects against infection, mild disease, or severe disease caused by the Omicron variant. This will require studies of vaccine effectiveness which specify the variant(s) of the cases, and will be most quickly conducted in places with higher incidence of the Omicron variant to provide a first indicator of clinical vaccine performance.
- WHO guidance on best practices to conduct these types of studies can be found on this website.

Impact on therapeutics/treatments

- WHO continues to work with researchers to understand the effectiveness of therapeutics against the Omicron variant. Interleukin-6 Receptor Blockers and corticosteroids are expected to remain effective in the management of patients with severe and critical disease since they mitigate the host inflammatory response to the virus.
- Preliminary data published in preprints suggests that some of the monoclonal antibodies developed against SARS-CoV-2 may have decreased neutralization against Omicron.[16,17] WHO is working with its experts to prioritize the research agenda and collect further data regarding the efficacy of monoclonal antibodies and antivirals. Urgent prioritization is for a) antigen binding and virus neutralization by antiviral monoclonal antibodies and b) characterization of the COVID-19 phenotype caused by infection with the Omicron variant, in a diverse patient population.
- For most up to date guidelines, see WHO website on COVID-19 Therapeutics (Therapeutics and COVID-19 (who.int)

Global risk assessment

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

- At present, a total of 63 countries have identified Omicron cases in all six WHO regions.
- Omicron is spreading fast in South Africa, where the incidence of Delta is low, but also appears to be spreading faster than the Delta variant in other countries with high incidence of Delta circulation, suggesting that Omicron will likely outpace the Delta variant where community transmission occurs.

- The clinical severity of Omicron remains uncertain, but increased transmission, with similar or even lower severity than Delta could pose overwhelming demands on health care systems and lead to significant morbidity. The impact on vulnerable populations would be substantial, particularly in countries with low vaccination coverage.
- Preliminary evidence from epidemiological studies on reinfection, neutralization studies, modelling estimates, and the considerably altered antigenic profile of the Omicron spike protein, suggests some degree of humoral immune evasion and a likely reduction in vaccine efficacy and effectiveness against infection and transmission associated with Omicron.
- The overall risk related to the new variant of concern Omicron thus remains very high for a number of reasons. First, the global risk of COVID-19 remains very high overall, and second, there is concerning preliminary evidence on Omicron suggesting both potential immune escape and higher transmissibility that could lead to further surges with severe consequences. Our understanding is still evolving, and the risk assessment will be updated as more information becomes available.

Priority Actions for Member States

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

Enhanced Surveillance

- Ensure early warning systems are in place, composed of multiple indicators such as growth (e.g. growth rate, effective reproduction number), case incidence, and test positivity proportion. It is also crucial to monitor indicators related to disease severity and pressure on health care systems (e.g. bed occupancy of general ward and intensive care unit).
- 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, or other relevant characteristics. 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 usual clusters and super-spreader events.
- When recording case data, particular attention should be paid to cases' vaccination status including dates and products of vaccination; history of previous SARS-CoV-2 infection; symptoms/clinical presentation; and clinical severity/outcome.

Sampling strategies

- Countries should continue to undertake targeted sampling of specific populations , as outlined in the variant guidance for surveillance of SAR-CoV-2 variants, for sequencing.
- In order 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 dropout 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 present.
    - For countries with capacity, wastewater sampling may serve as an additional tool for the retrospective and prospective investigation of Omicron in the community.
- In order 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 (definition in Appendix),and (ii) detect Omicron community transmission through enhanced random sampling among SARS-CoV-2 confirmed cases (see case definitions) in the community.
    - **For countries with confirmed community transmission of Omicron**, emphasis should be put on enhanced random sampling for sequencing among SARS-CoV-2 confirmed SARS-CoV-2 cases in the community.

- 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 sequenced Omicron samples to allow calculation of the prevalence of circulating Omicron variant.
- Case definitions are shown in Appendix.
- 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; additional guidance is available from ECDC Guidance for representative and targeted genomic SARS-CoV-2 monitoring.

Laboratory Testing for Omicron

- Suspected and probable cases of Omicron infection should be confirmed by sequencing; targeted sequencing of the Spike gene (using Sanger sequencing or Next Generation Sequencing) or whole genome sequencing are both appropriate to confirm the presence of Omicron.
- For countries using diagnostic tests which include SGTF, samples that include SGTF are considered suspected Omicron infections and should be prioritized for sequence confirmation of the Omicron variant.
- In addition, all countries are recommended to enhance surveillance and sequencing to characterize the circulating SARS-CoV-2 variants, including detection of Omicron.
- WHO recommends that national testing capacity, genomic sequencing capabilities should be appropriately planned for possible surges in testing demand for community and international travelers, based on national testing strategy.
- It is critical that all SARS-CoV-2 testing be linked to public health actions to ensure appropriate clinical care and support and to carry out contact tracing to break chains of transmission.

Vaccination

- Efforts should be intensified by public health authorities to accelerate COVID-19 vaccination coverage in all eligible populations, but with priority for populations at high risk for serious disease in all countries who remain unvaccinated or not yet fully vaccinated. These include older adults, health care workers and those with underlying conditions putting them at risk of severe disease and death. Delta is still by far the predominant variant globally against which vaccines are highly effective, and vaccines are likely to have some effectiveness against Omicron, particularly for severe disease, even if the performance is reduced compared with other variants.
- The presence of multiple mutations of the spike protein in the receptor-binding domain suggests that Omicron may have a high likelihood of immune evasion from antibody-mediated protection., especially protection directed at the spike protein. However, immune evasion potential from cell-mediated immunity is more difficult to predict. Overall, further research is needed to better understand the escape potential against vaccine- and infection-induced immunity. Research efforts are ongoing, and the data are expected to be available in the coming weeks.

- Despite uncertainties, it is reasonable to assume that currently available vaccines offer some protection, particularly against severe disease and death.

Risk-based approach in adjusting international travel measures

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

Public health and social measures (PHSMs)

- The use of well fitted masks, physical distancing, ventilation of indoor space, crowd avoidance, and hand hygiene remain key to reducing transmission of SARS-CoV-2, even in the context of emerging variants. However, PHSMs may need to be enhanced, to further limit interpersonal contact, to control transmission with a more transmissible variant.
- The use of established PHSMs in response to individual cases or clusters of cases, including contact tracing, quarantine and isolation, must continue to be adapted to the epidemiological and social context and enforced.
- Guided by risk assessment, taking into account the epidemiological situation, response capacities, vaccination coverage and public perception, as well as uncertainties related to the rapidly evolving situation of Omicron, countries should be ready to escalate PHSMs in a timely manner to avoid overwhelming demands on health care services.
- For further guidance on risk-based calibration of PHSMs, please see WHO guidance.

Health care system readiness

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

Risk communication and community engagement

- Authorities should communicate information related to Omicron and potential implication for the public in a timely and transparent manner to further foster trust and increase acceptance of response measures.
- One of the most important and effective interventions in a public health response to any event is to proactively communicate with the population what is known, what is unknown and what is being done by responsible authorities to get more information and to reduce risk.
- COVID-19 information overload and misinformation should be managed at all stages of the response by providing the right information at the right time to the right people through trusted channels (e.g. community and faith leaders, family doctors and other influential members of society). There should be an information monitoring system in place to capture emerging trends to enable delivery of a targeted communication package.
- When PHSMs are adjusted, communities should be fully and regularly informed, engaged and enabled before changes are made, to allow them to take ownership of the selected PHSMs. It is critical to build and foster trust, especially in contexts where there is little or no involvement of the local population in decision-making. Clear, concise and transparent risk communication, including an evidence-based rationale for adjusting measures, should be developed with communities targeted for PHSMs.
- Communities will be critical to implementing population-wide PHSMs and contributing to the mitigation of the social and economic impact of certain measures (e.g. disrupting availability of food and other needed supplies).

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Annex: Working definitions

Interim Omicron-specific Case definitions

Suspected case of SARS-CoV-2 Omicron variant infection

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

Probable case of SARS-CoV-2 Omicron variant infection

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

*note these methods may under-detect Omicron as the target deletions/mutations may not be present in all Omicron sequences, and must be confirmed by sequencing as deletions/mutations may not be unique to Omicron

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 be used to determine the need for further investigation in patients who do not strictly meet the clinical or epidemiological criteria. Surveillance case definitions should not be used as the sole basis for guiding clinical management.

SARS-CoV-2 Reinfection

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

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

Reinfection confirmed by sequencing: Samples available for both primary and secondary episodes allowing for full genomic sequencing, whereby samples must be shown to be phylogenetically distinct from one another. Evidence should be generated at clade/lineage, as defined by genomic classification of SARS-CoV-2 between the first and second infection. If evidence of different clades is demonstrated in episodes less than 90 days apart, this also constitutes evidence of confirmed reinfection. If there are more than two nucleotide differences for every month separating the samples between the sequences for first and second infections, i.e., exceeding the expected Single Nucleotide Variation, these would be considered as different linages/clades.

The 90-day cut off should ideally be determined between onset dates (for probable cases), or sampling dates (for confirmed cases) of primary and secondary episodes.

Vaccine breakthrough

Vaccines should be authorized by a Stringent Regulatory Authority or listed under WHO Emergency Use Listing.

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

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

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