Recommendations for national SARS-CoV-2 testing strategies and diagnostic capacities

Interim guidance

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Key points

- Diagnostic testing for SARS-CoV-2 is a critical component to the overall prevention and control strategy for COVID-19.
- Countries should have a national testing strategy in place with clear objectives that can be adapted according to changes in the epidemiological situation, available resources and tools, and country specific context.
- It is critical that all SARS-CoV-2 testing is linked to public health actions to ensure appropriate clinical care and support and to carry out contact tracing to break chains of transmission.
- All individuals meeting the suspected case definition for COVID-19 should be tested for SARS-CoV-2, regardless of vaccination status or disease history (1).
- Individuals meeting the suspected case definition for COVID-19 should be prioritized for testing. If resources are constrained and it is not possible to test all individuals meeting the case definition, the following cases should be prioritized for testing:
    - individuals who are at risk of developing severe disease
    - health workers
    - inpatients in health facilities
    - the first symptomatic individual or subset of symptomatic individuals in a closed setting (e.g. long-term care facilities) in the setting of a suspected outbreak.
- Nucleic acid amplification tests (NAAT) are the reference standard for diagnosis of acute SARS-CoV-2 infection.
- Countries can use high quality antigen-detection lateral flow or rapid diagnostic tests (Ag-RDTs), which are simple to use and offer rapid results, to achieve high coverage of testing, ideally testing all symptomatic individuals meeting the COVID-19 case definition as soon as possible from disease onset (within the first week of illness). Information on the use of Ag-RDTs can be found here and here. Interim guidance on the use of Ag-RDTs can be found here (2).
- Testing of asymptomatic individuals with NAAT or Ag-RDTs is currently recommended only for specific groups including contacts of confirmed or probable COVID-19 cases and frequently exposed groups such as health care workers and long-term care facility workers.
- Widespread screening of asymptomatic individuals is not a currently recommended strategy due to the significant costs associated with it and the lack of data on its operational effectiveness.
- Considerations for the use of self-testing should include improved access to testing and potential risks that may affect outbreak control. The potential benefits and harms of self-testing with SARS-CoV-2 Ag-RDTs will be addressed in a separate guidance document.
- Mutation-detecting NAAT assays may be used as a screening tool for SARS-CoV-2 variants, but the presence of a specific variant should be confirmed through sequencing. Such tests should be appropriately validated for their purpose.
- The network of SARS-CoV-2 testing facilities should leverage and build on existing capacities and capabilities, be able to integrate new diagnostic technologies and adapt capacity according to the epidemiological situation, available resources and country specific context.

Version Control

This interim guidance replaces the WHO guidance entitled "Laboratory testing strategy recommendations for COVID-19", originally published on 21 March 2020.

Updates from previous version

This version provides updated guidance on diagnostic testing strategy in the context of updated transmission classifications, public health and social measures, public health surveillance and the WHO case definitions for COVID-19. The use of new tools such as antigen detection rapid diagnostic tests (Ag-RDTs) and considerations for testing vaccinated individuals and testing for genetic mutations associated with variants have been integrated. Annexes including a compilation of relevant resources and the 10 components of expansion of subnational testing have also been developed for this version.

Background

COVID-19 has put enormous demand on laboratory infrastructure and required an unprecedented rapid scale-up of testing capacity for its causative agent, SARS-CoV-2, at all levels of the health care system. More recently, the identification of variants with mutations that may confer changes in phenotypic properties, designated as variants of interest (VOIs) or variants of concern (VOCs), further highlights how detection of SARS-CoV-2 remains a critical element in the global strategy to control COVID-19 (3). More information on variants can be found on the WHO website here.

Laboratory capacity is one of the core capacities required to detect, assess, notify and report public health events under the International Health Regulations (IHR) 2005 (4). Testing is a critical tool in detecting the etiological agent, understanding virus transmission, and guiding and monitoring public health control measures and the clinical management of patients. Several different diagnostic techniques for SARS-CoV-2 are available, as follows:

i. **Detection of viral RNA**, through manual or automated nucleic acid amplification tests (NAAT), such as real time reverse-transcription polymerase chain reaction (rRT-PCR);
ii. **Detection of viral antigens** through immunodiagnostic techniques, such as lateral flow assays (LFAs), commonly called rapid diagnostic tests or Ag-RDTs.
iii. **Detection of host antibodies** through serological techniques, such as LFAs, enzyme linked immunosorbent assays (ELISAs), or chemiluminescent immunoassays (CLIAs).

WHO interim guidance on the technical requirements of diagnostic testing for SARS-CoV-2 can be found here (5). NAAT is the most sensitive and specific and is therefore recommended as the reference standard. Ag-RDTs offer an opportunity to increase the availability and speed of testing in appropriate scenarios. Full guidance on the use of Ag-RDTs can be found here (2). Antibody detection is not recommended for diagnosis of COVID-19, as it may take up to two weeks for host antibodies to be produced, but it plays an important role in the detection of past infection for research and surveillance (6-9). More information on natural immunity to SARS-CoV-2 can be found here (10).

Response plans and testing strategies should be adapted and responsive to evolving epidemiological situations, the addition of approved[1] new diagnostic tests and available resources at national and local levels. Testing should always be linked to public health actions such as clinical care (11), isolation of cases (12), contact tracing (13), supported quarantine of contacts (14) and provision of information to the individual undergoing testing. Testing for SARS-CoV-2 should be carried out as part of a multi-layered public health response strategy and clear time bound consequences of testing should be defined.

To be most effective, SARS-CoV-2 testing should be implemented within a strong national system comprising the public health laboratory network and clinical diagnostic laboratories, and include mechanisms to coordinate with other relevant sectors, such as veterinary, academic and private stakeholders. Although not directly linked to clinical management, leverage of existing sentinel surveillance sites and networks such as the Global Influenza Surveillance and Response System (GISRS) continues to play an important role in SARS-CoV-2 surveillance (15).

This updated interim guidance aims to provide guidance to countries on testing strategies and the expansion and prioritization of national and subnational diagnostic testing capacity and capability for SARS-CoV-2 to meet existing and anticipated needs, while acknowledging resource constraints. It is primarily intended for laboratory and diagnostic stakeholders across Member States and national public health authorities involved in the scale up of SARS-CoV-2 testing and improvement of integrated testing services, particularly in resource constrained areas.

[1] Approved, recommended or validated by the national regulatory authority.

Testing strategy recommendations

Testing is a critical element to the overall prevention and control strategy for COVID-19 (4). National testing strategies should set clear objectives and be adaptable according to the current and evolving epidemiological situation, available resources and the country specific context. By addressing these components, countries can develop a risk-based approach to the scaling up or focusing of testing, including a plan to consider the components of expansion of subnational testing described in Annex I and where and how additional testing capacity can be accessed or leveraged. Frequent reviews and changes to the testing strategy should be undertaken periodically or when there are situational changes. This process should be led by the national public health authority laboratory leadership and counterparts from epidemiological, surveillance and clinical management teams should be engaged when developing and implementing any testing strategy.

WHO recommends that all individuals meeting the case definition for COVID-19, irrespective of vaccination or disease history, be tested for the presence of SARS-CoV-2 in respiratory specimens (1). While the testing of symptomatic individuals should be prioritized over testing asymptomatic individuals, testing of asymptomatic individuals can be informative in instances such as follow up of contacts of confirmed or probable cases or testing of health care and long-term care facility workers that are frequently exposed. Widespread testing of asymptomatic populations, including through self-testing, is not currently recommended, based on lack of evidence on impact and cost-effectiveness of such approaches and the concern that this approach risks diverting resources from higher priority testing indications.

Member States that consider policies to test outside these recommendations should do so only if the following conditions are met:

- timely and reliable testing of suspected cases is maintained as the priority strategy
- there are available human and financial resources for testing, reporting, isolation, contact tracing and follow-up of all test-positive individuals

If asymptomatic individuals are tested with Ag-RDTs and do not have an epidemiological link to a confirmed case or working in an area where COVID-19 patients are cared for, results should be treated as presumptive and ideally confirmed by NAAT. More information on addressing screening of specific populations is available for contacts, healthcare workers, workplaces, long term care facilities, schools and travelers (13, 16).

Confirmatory testing with NAAT

NAAT is considered as the reference standard for diagnosis of SARS-CoV-2 infection. Ag-RDTs are not meant to replace NAAT but can be implemented as a complementary strategy as there are many that are highly reliable (see WHO Emergency Use Listing), easy to use, and offer rapid turnaround of results. Ag-RDTs can be used where NAAT is not available or where results will be delayed by more than 48 hours. Ag-RDT uptake is encouraged to expand accessibility of testing and can be considered as follows:

- In **symptomatic individuals in high prevalence settings** confirmation of positive Ag-RDT results by NAAT is not necessary. Negative Ag-RDT results may be confirmed by NAAT at clinical discretion[2].
- In **symptomatic individuals in low prevalence settings** confirmation of negative Ag-RDT results by NAAT is not necessary. Positive Ag-RDT results may be confirmed by NAAT at clinical discretion[2].
- In **asymptomatic individuals** that are contacts of confirmed cases or are frequently exposed, such as health care and long-term care facility workers, Ag-RDT results are not required to be confirmed by NAAT but may be confirmed using NAAT, at clinical discretion[2].

Epidemiological situation

Different testing strategies should be considered according to differing epidemiological situations, availability of resources and other factors such as very remote or hard to access areas (17). The extent of transmission of SARS-CoV-2 in the population being tested will affect the positive and negative predictive values (PPV and NPV) of the tests. In populations with few or no cases, it is preferable to use the reference standard NAAT to diagnose cases, as it is the most specific. Where the number of cases is increasing and laboratories and health facilities are under heavy burden, it may be more effective to use tests that can be carried out closer to the patients and are less resource intensive, such as Ag-RDTs. Scale-up of testing should be accompanied by increased capacity to manage the clinical care, contact tracing and isolation measures associated with test results.

If testing is being done in a setting with widespread community transmission, the priority may be to reduce transmission through cluster detection and implementation of public health and social measures (PHSM). In a setting with limited transmission, the goal may be more targeted to the early detection of cases and identification of their contacts, such as in the reintroduction of the virus through imported cases to areas that had previously suppressed transmission. Capacity for COVID-19 surveillance and SARS-CoV-2 testing should be retained during periods of low or no transmission in case of a resurgence of cases and rapid increase in demand. Once new sporadic cases or clusters are detected the priority is to limit further transmission and reduce the spread of the virus through public health interventions.

[2] More information on how high and low prevalence affects interpretation of test results can be found in Annex I of the Ag-RDT guidance here.

Countries should track the quantity and results of testing and report to WHO on a weekly basis as outlined in the WHO interim guidance on public health surveillance for COVID-19 (18). Indicators and targets should be defined when developing a testing strategy and may be adapted according to the epidemiological situation. Informative indicators include the test positivity rate and the case incidence (see below). Useful additional measures of the impact of testing include the turnaround time for testing (the time from sampling to result availability for the patient), and the frequency of implementation of measures to interrupt transmission among test-positive cases.

The test positivity rate is the percentage of SARS-CoV-2 tests performed that are positive. This can be collated at national or subnational levels at either designated diagnostic facilities or sentinel sites. It is dependent on both the amount of testing and the testing strategy and therefore both factors must be considered in parallel. For example, test positivity rates amongst individuals with suspected COVID-19 are likely to be much higher than among asymptomatic people. The case incidence is the number of cases detected per proportion of the population, per administrative area. This is also influenced by the testing strategy and the population being tested.

Transmission scenarios

WHO has defined transmission scenarios and associated recommendations for countries, territories and areas, hereafter referred to as countries (19). The interim guidance on critical preparedness, readiness and response actions for COVID-19 outlines seven SARS-CoV-2 transmission scenarios: countries with no cases (no cases); countries with 1 or more cases, imported or locally detected (sporadic cases); countries experiencing clusters of cases related in time, geographical location or common exposure (clusters of cases); and countries experiencing community transmission (CT), which is divided into four levels, from low incidence (CT1) to very high incidence (CT4) (17). Countries may simultaneously experience differing transmission or extents of CT across subnational levels, requiring local adaptation of testing strategy.

Suggestions for SARS-CoV-2 testing and expansion based on these transmission scenarios, as described in WHO guidance on public health criteria to adjust public health and social measures in the context of COVID-19, are shown in Table 1 below (19)

Table 1 *SARS-CoV-2 transmission scenarios and their suggested implications for subnational expansion of SARS-CoV-2 testing.*

Transmission Scenario	Testing strategy guidance and key actions
No cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases, to allow for identification of new clusters or importation of new cases. Test patients with unexpected clinical presentation or an increase in hospital admissions in a specific demographic group that could be COVID-19. Strengthen or sustain capacity and expertise at the national public health laboratory. Establish a laboratory contingency plan including mapping of national testing resources and capacities and identify potential sources of infection (e.g. imported cases, zoonotic spillover events). Prepare for the possibility of increasing transmission and plan for surge SARS-CoV-2 testing capacity, including through the revision of SOPs and simulation exercises. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Sporadic cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Establish a laboratory contingency plan including mapping of national testing resources and capacities and identify potential sources of infection (e.g. imported cases, zoonotic spillover events). Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Clusters of cases	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Activate laboratory contingency plan in localized areas. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.
Community transmission (CT1 to CT4)	Test all individuals meeting the case definition and, as capacities allow, asymptomatic contacts of confirmed or probable cases. Activate laboratory contingency plan. Consider expansion of testing capacity through the following: • Activate localized surge capacity. • Expand localized testing facilities. • Increase accessibility of testing facilities. • Expand testing product options, including expanding the use of approved point of care NAAT and Ag-RDTs. • Introduce mobile testing facilities. • Introduce mobile sampling facilities. • Deploy laboratory staff from other fields, including veterinary and academic laboratories, to backstop COVID-19 laboratory staff. Test all or a subset of samples from SARI/ARI/ILI surveillance for SARS-CoV-2.

SARI, severe acute respiratory syndrome; ARI, acute respiratory infection; ILI, influenza like illness; SOP, standard operating procedure; NAAT, nucleic acid amplification test; Ag-RDT, antigen-detecting rapid diagnostic test.

Available resources and prioritization of testing strategy

The national SARS-CoV-2 testing strategy should address the use of available resources to maintain the highest level of public health impact. When faced with community transmission over large areas of the country, the national testing strategy may be adapted to consider testing constraints and prioritization, whilst assuring national standards are consistently met. Regardless of constraints, prioritization for testing should be given to:

- Individuals meeting the suspected case definition who are at risk of developing severe disease; and vulnerable populations, who may require hospitalization and advanced care for COVID-19;
- Health and care workers (including emergency services and non-clinical staff) and long-term care facility workers meeting the suspected case definition;
- Testing of symptomatic inpatients (to ensure that infection prevention and control measures can be correctly implemented such that vulnerable patients who do not have COVID-19 are protected from nosocomial SARS-CoV-2 infection); and
- The first symptomatic individuals or a subset of individuals affected in a closed setting (e.g. schools, long-term living facilities, prisons, hospitals) to quickly identify outbreaks and ensure containment measures. All other individuals with symptoms related to the close settings may be considered probable cases and isolated without additional testing if testing capacity is limited (20).

Alternative measures and public health interventions can be taken if testing capacity is low. Quarantine measures for contacts of confirmed cases and isolation of individuals showing symptoms should be implemented in all situations. Specific situations are described in Table 2, below, along with diagnostic testing approaches when capacity is over-stretched in areas with ongoing community transmission.

Table 2 *Example situations and management alternatives if testing capacity is outstretched, in areas with ongoing community transmission.*

Situation where testing and response capacity is outstretched	Alternative measures
Individual meeting case definition for COVID-19, mild, with no risk factors	Test when possible. If Ag-RDT or NAAT is not available, register as a suspected case and home isolate according to WHO guidance (21).
Individual meeting case definition for COVID-19, requiring admission to health care facility	Strongly recommended to test using Ag-RDT or NAAT, where available. If testing is not possible, implement isolation measures warding against nosocomial transmission.
Symptomatic health care worker identified as a contact	Recommended to test using Ag-RDT or NAAT. If not possible, register as a suspected case and home isolate according to WHO guidance (21).
Symptomatic health care worker with no known COVID-19 contact	Strongly recommended to test using Ag-RDT or NAAT.
Increased number of suspected cases in a specific group (potential cluster)	Test a subset of the cases using Ag-RDT or NAAT. Consider all other symptomatic individuals as probable cases and isolate (1).
Symptomatic individuals in closed settings, including schools, hospitals, long-term living facilities	Test a subset of the cases using Ag-RDT or NAAT. Consider all other symptomatic individuals as probable cases and isolate (1).
Recovering patient	Not necessary to test. Symptomatic patients and confirmed cases can be released from isolation following 10 days after symptom onset plus 3 additional days without symptoms. Asymptomatic convalescent individuals can be released following 10 days after positive test (22).
Asymptomatic contacts of confirmed or probable cases, including health care workers	Quarantine contacts for 14 days. If contacts become symptomatic, assume COVID-19 and isolate (19). Viral confirmation with Ag-RDT or NAAT not required as a negative result would not remove the need for 14 day quarantine. (14) Positive results of testing would, however, allow contact investigation of the newly confirmed case.
Other asymptomatic individuals	Testing is not required.

Ag-RDT, antigen-detecting rapid diagnostic test; NAAT; nucleic acid amplification test.

Context specific considerations for testing

Broadened use of diagnostics in widespread asymptomatic population screening and self-testing for SARS-CoV-2

The measurable impact and cost-effectiveness of widespread asymptomatic population screening, including through self-testing for SARS-CoV-2 are under review by WHO. Considerations include unclear specific impact of testing on disease control, the considerable financial cost of these programmes, and potential negative implications for outbreak management such as reduced centralized capacity to monitor disease trends and diminished PPV (the likelihood that a positive test result is a true positive).

Further applications of self-testing are being explored, such as home testing of symptomatic individuals, and may be complementary to national testing strategies. Research into potential benefits and harm are under review, and at the present time there is not sufficient evidence to make recommendations. WHO is reviewing evidence and will release interim guidance on the use of self-testing separately. In addition, a systematic review and a rapid review of available evidence each show limited evidence that mass screening in combination with other PHSM such as stringent movement restrictions may reduce incidence and noted that much of the evidence base is reliant on modelling studies (23, 24). At the present time, the evidence base on effectiveness of widespread asymptomatic population screening and self-testing for SARS-CoV-2 is currently lacking and therefore is not sufficient to make recommendations. WHO will publish evidence-based interim guidance on widespread asymptomatic population screening separately.

The behavior of individuals and adherence to public health measures following positive results on self-testing, also requires additional evidence generation. WHO urges the research community to carry out studies to help clarify the programmatic utility and cost-effectiveness of such mass-screening approaches.

Testing individuals with immunity for SARS-CoV-2

Any individuals meeting the suspected case definition, regardless of vaccination status, or previous infection with SARS-CoV-2, should also be tested if SARS-CoV-2 infection is suspected. There is currently limited evidence available on the extent to which partially or fully vaccinated individuals or previously infected individuals may contribute to transmission. In addition, there is ongoing risk of vaccine escape and reinfection due to SARS-CoV-2 variants with altered immunogenic properties. It is recommended that suspected cases among individuals with immunity are tested using NAAT with subsequent referral for sequencing if positive.

If it is routine practice to test contacts, asymptomatic contacts who are fully vaccinated or have history of prior infection may also be tested at clinical discretion.

Testing for SARS-CoV-2 variants

General guidance on testing strategy recommendations for the purpose of patient management remain the same. PHSM should be implemented for all known circulating SARS-CoV-2 variants and the goal continues to be to suppress SARS-CoV-2 transmission. However, VOCs may impact on the effectiveness of countermeasures, including diagnostics. For example, B.1.1.7 and other variants contain a mutation that results in Spike gene target amplification failure in some assays (25, 26). The possibility of further impacts on commercial NAAT test kits is under continual review by WHO through the Prequalification and Post Market Surveillance programs. Early identification, detection, monitoring and reporting of emerging variants is therefore important. WHO has published definitions of VOIs and VOCs and recommended actions for Member States to take when they are identified here.

Characterization of variants has led to recommendations on increased uptake of sequencing technologies and associated sampling strategies to detect and monitor variants in space and time (3). Sequencing is a tool for characterization, rather than a diagnostic tool and not covered in this interim guidance. WHO has published interim guidance for SARS-CoV-2 sequencing for public health goals, including recommendations on prioritization of samples for sequencing. NAATs that can identify specific mutations have been developed and commercialized. These assays should be used for screening purposes only, following a positive validated diagnostic test for SARS-CoV-2. Depending on the context, positive results from mutation screening assays may be indicative of a specific variant but are not confirmatory as they only detect mutations or deletions, which may be associated with other known or novel variants. Therefore, all or at least a subset of positive samples should be referred for sequencing to confirm the presence of a specific variant.

Country specific factors

Demographic factors including population density and the presence of vulnerable groups such as refugee and migrant or displaced populations may impact the type and availability of testing resources. Specific country contexts also affect decision-making, such as in low- and middle-income countries (LMICs), small island developing states and countries with complex and/or protracted emergencies.

More information

The network of SARS-CoV-2 testing facilities should leverage and build on existing capacities and capabilities, be able to integrate new diagnostic technologies and adapt capacity according to the epidemiological situation, available resources and country specific context. The 10 components of subnational expansion of testing have been developed to support countries to expand their diagnostic networks for SARS-CoV-2, in order to increase capacity. They can be found in Annex I.

Additional resources and training packages relevant to diagnosis of SARS-CoV-2 can be found in Annex II.

Conclusion

COVID-19 has highlighted the importance of a well-resourced, resilient and reliable laboratory network and presents an opportunity to leverage resources and strengthen country capacity for detection of SARS-CoV-2 and other epidemic prone diseases. Timely and accurate testing is an essential tool in preventing and controlling the spread of SARS-CoV-2 and must be implemented strategically, resulting in the cost-effective implementation of clearly defined public health countermeasures. This document presents the main elements to be considered in the expansion of domestic SARS-CoV-2 testing, and how to appropriately prioritize testing capacity when resources are constrained. It provides a summary of the tools available and considerations for how and where to apply them. However, the situation is highly dynamic and likely to change. This interim guidance will be updated considering future developments such as the epidemiological situation and availability of therapeutics or vaccines. Surveillance and readiness for COVID-19 response should be maintained at all times.

Methods