

COVID-19 testing strategies and objectives

15 September 2020

Key messages

- Implementation of objective-driven and sustainable testing strategies for COVID-19 supports the overall public health response to the pandemic and helps mitigate its impact on vulnerable populations and healthcare systems, while ensuring that societies and economies can continue to function.
- ECDC proposes five main objectives for testing in order to control transmission; reliably monitor SARS-CoV-2 transmission rates and severity; mitigate the impact of COVID-19 in healthcare and social care settings; detect clusters or outbreaks in specific settings and maintain sustained control of COVID-19 once achieved.
- Testing strategies should be flexible and rapidly adaptable to change, depending on the local epidemiology, transmission, population dynamics and resources.
- Ideally, all people with COVID-19 symptoms should be tested as soon as possible after symptom onset. This requires easy access to testing for all, including non-residents. Test turnaround time should be minimised, people testing positive should isolate and timely contact tracing should be carried out, ensuring that all close contacts are tested, irrespective of symptoms.
- All patients with acute respiratory symptoms in hospitals and other healthcare settings, and all specimens from sentinel primary care surveillance should be tested for both SARS-CoV-2 and influenza during the influenza season to monitor incidence and trends over time.
- Healthcare and social care settings require intensive testing when there is documented community transmission. Periodic and comprehensive testing of all staff and residents/patients is recommended to prevent nosocomial transmission. Furthermore, all patients/residents should be tested upon or immediately prior to admission.
- Clusters or outbreaks may occur in certain settings, such as workplaces, educational facilities, prisons, and migrant detention centres. Testing policies and systems should be in place for rapid detection and control to protect the relevant populations in these settings and to protect the community from amplified transmission.
- Countries experiencing high SARS-CoV-2 transmission in a local community should consider testing the whole
 population of the affected area. This would enable identification of infectious COVID-19 cases and allow for
 their prompt isolation to interrupt chains of transmission. Depending on the epidemiological situation, size and
 population density of the affected area, such an approach could be less disruptive for society than having to
 introduce and ensure compliance with more stringent public health measures.
- To prevent re-introduction, countries or sub-national areas that have achieved sustained control of SARS-CoV-2 circulation should, in addition to quarantine measures, consider targeted testing and follow-up of individuals coming from other areas within the same country, or from other countries that have not yet achieved sustained control of the virus.

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European Commission request

The European Commission requested the European Centre for Disease Prevention and Control (ECDC) to develop an overview document on testing strategies for COVID-19.

Target audience

Public health authorities in the European Union and European Economic Area (EU/EEA) and the United Kingdom (UK).

Definitions

Asymptomatic case: a person with laboratory-confirmed SARS-CoV-2 who has not shown any clinical symptoms during a 14-day follow-up period since the last possible exposure to an index case, or in the seven days since collecting the sample which gave the first RT-PCR positive result.

Pauci-symptomatic case: a person with laboratory-confirmed SARS-CoV-2 showing very mild clinical symptoms.

Pre-symptomatic: a person that is asymptomatic when testing positive SARS-CoV-2, but who develops COVID-19-compatible symptoms during the seven-day-period after collecting the sample which tested positive.

Contact person: individual who has had exposure to a symptomatic or asymptomatic case. For detailed definitions please see ECDC guidance on contact tracing, including tracing of high-risk (close) or low-risk exposure contacts [1].

Population-wide testing (or 'mass testing') refers to carrying out a high volume of tests for SARS-CoV-2 in individuals, irrespective of symptoms, in a given population to identify cases with laboratory-confirmed SARS-CoV-2 infection and inform prevention and control measures. Population-wide testing is also referred to as mass screening, universal testing and population-based screening.

This document uses ECDC's case definition [2] for the classification of possible, potential and confirmed cases of COVID-19.

Scope of this document

This document outlines strategies and objectives for sustainable SARS-CoV-2 testing of populations to achieve specific public health objectives in various epidemiological situations. General population-wide testing, as well as targeted testing of individuals, or specific populations related to particular settings, are presented on the basis of country experiences and information collected from scientific literature.

Background

ECDC has progressively updated its recommendations for SARS-CoV-2 PCR testing, taking into account the epidemiological situation in the EU/EEA countries and the UK and their testing capacities [3-5].

From a public health perspective, testing strategies should aim to ensure that reliable epidemiological data are rapidly available to guide prevention and control measures (e.g. isolation of cases, contact tracing and quarantine, introduction/adjustment/lifting of non-pharmaceutical interventions, risk communication to the population). Furthermore, appropriate testing and efficient processes should ensure that outbreaks are prevented or promptly detected and controlled, particularly in settings where there are high-risk groups, such as hospitals and long-term care facilities.

Objectives for testing

The implementation of objective-driven and sustainable testing strategies for COVID-19 supports the overall public health response to the pandemic and helps mitigate its impact on vulnerable populations and healthcare systems, while ensuring that societies and economies continue to function. Various testing strategies have been identified for use in countries, or in regions within a country, and for different epidemiological situations according to the following objectives:

- A Control transmission.
- B Monitor incidence and trends and assess severity over time.
- C Mitigate the impact of COVID-19 in healthcare and social-care settings.
- D Rapidly identify all clusters or outbreaks in specific settings.
- E Prevent (re-)introduction into regions/countries with sustained control of the virus.

Depending on the epidemiological situation, more than one strategy may be employed simultaneously to meet the objectives. This applies when countries and/or regions within a country are experiencing a variety of epidemiological situations or when there are certain populations that could be disproportionately affected (ethnic minorities, specific age groups, etc.). Table 1 provides an overview of the testing guidance to achieve the objectives listed above depending on the epidemiological situation in the general population.

The speed of testing and reporting of results to individuals and health authorities is critical for isolating cases and initiating contact tracing activities and other public health measures. Minimising the time between testing and the communication of results will help to maximise the impact of the respective testing strategy and facilitate timely contact tracing and contact management in order to limit ongoing transmission. Determinants for successful implementation of a testing strategy include access to testing, supply and logistics. However, it is also important to communicate to the public the need to test as soon as possible after symptom onset and provide them (and also visitors/tourists) with clear instructions on how to access testing. The general public should be informed of the rationale for quarantining and testing close contacts, irrespective of symptoms, and why this strategy may change, depending on available data and resources.

Timely notification of results should be available via automated processes, mobile apps, and/or other electronic means. ECDC recommends that the reasons for testing an individual are always reported to the local/national public health authorities. This information is necessary to interpret the data, plan proportionate response measures, and communicate effectively with the population.

An overriding principle for each testing approach is to test people with COVID-19-compatible symptoms. However, testing approaches based on the objectives described below might increase and enhance testing for particular populations or in specific situations - e.g. testing individuals irrespective of symptoms.

Testing objective A - Control transmission

To reduce the spread of SARS-CoV-2 and control transmission within the population, all individuals with COVID-19compatible symptoms should be identified and tested for SARS-CoV-2 as soon as possible after symptom onset. Individuals testing positive need to be isolated in a timely manner and their contacts identified for systematic contact tracing. This approach enables sporadic cases and clusters to be rapidly identified, thus limiting further transmission in the community. Testing could be prioritised for those contacts that have developed COVID-19compatible symptoms, but expanded to include testing and follow-up testing of asymptomatic close contacts, if resources allow. Contact tracing should even continue during widespread transmission, to the extent possible.

Control widespread community transmission

Local areas of very intense SARS-CoV-2 transmission have been reported in Europe and elsewhere [6-8]. These areas have often had high population density and the initial chains of transmission went undetected until widespread transmission was occurring. In most instances, controlling such epidemics was challenging and required disruptive interventions such as 'stay-at-home' measures or severe mobility restrictions for extended periods of time.

In such situations, testing an entire community would enable public health authorities to identify most of the infectious COVID-19 cases at a given point in time (e.g. including pre-symptomatic, pauci-symptomatic, and asymptomatic cases), enabling their prompt isolation and the interruption of chains of transmission. Depending on the size and population density of the affected area, the capacity to reach, test and isolate cases, and to trace and quarantine contacts, this approach could be more cost effective than introducing and ensuring long-term compliance to more stringent public health measures.

Possible objectives of population-wide testing:

- To reduce the incidence to manageable levels, prevent or reduce the need for stringent non-pharmaceutical interventions, or shorten their duration during widespread transmission.
- To estimate prevalence and understand the epidemiological characteristics of infected individuals at a given point of time to help control the epidemic.
- To understand what is driving transmission in areas or settings with high incidence to guide implementation of more targeted measures.

Population-wide testing strategies which test all individuals irrespective of symptoms, may be appropriate for local areas with high incidence. However, the effectiveness and cost-effectiveness of this approach remains unknown and the testing approach should not compromise accessibility or cause delays to the testing of those who are symptomatic. Without timely analysis and notification in order to isolate cases, population-wide testing on its own will not be effective in reducing transmission.

Household testing

The objective of selective or comprehensive testing of households within a country or region is to control transmission by identifying cases that often go undetected. This may provide more accurate epidemiological information on clinical presentations by age, risk factors for transmission and secondary attack rates. Rates of transmission are known to be higher in the household setting than in non-household settings and household cases potentially represent a large proportion of undetected cases in any given population [9].

Population-wide individual-initiated testing

Some countries permit individual-initiated testing for SARS-CoV-2 to address the public demand to know SARS-CoV-2 infection status, irrespective of the presence of symptoms. There are no specific public health objectives that can be achieved by adopting this approach and therefore it should not be implemented if testing resources are limited. The opportunity for individual-initiated testing tends to be taken up if testing is easily accessible, free, if there are low/no barriers to entry (e.g. not requiring registration or prescription), and if case notification turnaround times are fast (<24 hours).

Testing objective B - Monitor incidence and trends, and assess severity over time

Ongoing, population-based surveillance of COVID-19 is essential throughout all phases of the pandemic in order to inform prevention and mitigation strategies. A description how to carry out population-based COVID-19 surveillance is available in ECDC and WHO surveillance guidance documents [4,10-12].

Primary care

Respiratory symptoms for COVID-19 cases are often indistinguishable from those for influenza and other respiratory viruses. Therefore, where there is ongoing widespread transmission of respiratory infections across a country or region, monitoring the number of consultations involving people with COVID-19-compatible symptoms, influenza-like illness (ILI) or acute respiratory infection (ARI), (i.e. performing comprehensive syndromic surveillance) is critical in order to identify all possible cases for testing. If testing capacity is insufficient to test all identified individuals, as a minimum, a representative, systematic sample should be tested for SARS-CoV-2 and, depending on the time of the year, for influenza. The proportion of possible cases with COVID-19-compatible symptoms, ILI or ARI testing positive for SARS-CoV-2 or influenza gives an indication of the positive predictive value of the syndrome for these infections. When multiple respiratory viruses (SARS-CoV-2, influenza, respiratory syncytial virus (RSV), and other viruses) are co-circulating, testing should be expanded to cover these pathogens and understand their relative contribution to consultation rates in primary care. If there is a continuous high proportion of SARS-CoV-2-positive cases detected and no other major respiratory viruses, such as influenza, are circulating, the syndromic data can reliably be used to monitor trends.

The ongoing COVID-19 situation will influence the resources available for influenza testing during the influenza season, and it might not be possible to test all specimens from primary-care patients with respiratory symptoms for both influenza and SARS-CoV-2 at the same time. Therefore, all those with compatible symptoms should be tested for SARS-CoV-2 in the first instance, while all individuals with underlying conditions and the elderly should be tested for both influenza and SARS-CoV-2. Based on testing capacities, clinical judgement and the level of influenza circulation (from sentinel and hospital data), specific patient groups, or a random sample of all patients could be considered for parallel influenza testing in all primary care settings.

Existing sentinel surveillance systems based on syndromic case definition for influenza (both primary care and secondary care) complement the comprehensive syndromic system described above and should continue to operate according to standard procedures to ensure historical data comparability. For influenza, a subset of patients fulfilling the ILI or ARI case definition, based on a national sampling strategy, is swabbed by sentinel practitioners and the specimens sent to the national influenza centres (NICs) or reference laboratories for virological testing (influenza and other respiratory viruses). In addition to influenza, clinical respiratory population-representative primary-care sentinel surveillance is a good proxy of the incidence and circulation of SARS-CoV-2 and sentinel specimens should therefore be tested both for influenza and SARS-CoV-2. This will increase the number of specimens that national reference laboratories or NICs need to test for both viruses. Should capacity in the NICs be insufficient to test all specimens from sentinel sites, a selected number of specimens should be sent to the NICs in accordance with the selection scheme for previous years. All other specimens need to be sent to other diagnostic laboratories for SARS-CoV-2 testing. Multiplex RT-PCR tests are available to detect multiple respiratory viruses in the same specimen including SARS-CoV-2 and influenza [13]. Influenza-positive specimens from sentinel sources should be characterised genetically, antigenically and for antiviral susceptibility. Documents on how to operate this system during the COVID-19 pandemic, including testing approaches, will be published jointly with WHO's Regional Office for Europe.

Hospitals settings

As with primary care, syndromic surveillance systems for severe acute respiratory infections (SARI) in hospitals or surveillance systems for severe COVID-19 cases are critical for rapidly identifying possible cases that should undergo SARS-CoV-2 testing and initiating prevention and control measures. Furthermore, in the absence of a robust population-based surveillance system for the monitoring of milder cases in the community, hospitalisation rates represent a solid indicator for monitoring COVID-19 trends, as it is likely that most individuals with SARI are tested for SARS-CoV-2 when admitted to hospital. Therefore, ECDC recommends that throughout the pandemic all individuals presenting to healthcare facilities with SARI are tested for both SARS-CoV-2 and influenza during the influenza season. Testing for other respiratory viruses, such as RSV, should continue as before, taking the local testing capacities and clinical judgement into consideration. Early identification of other pathogens (e.g. influenza or *Legionella*) in risk groups should inform clinical treatment, as well as infection prevention and control (IPC) measures and public health action that might be different to those for COVID-19. The use of multiplex molecular testing systems should be considered in these settings, if available.

Testing objective C - Mitigate the impact of COVID-19 in healthcare and social care settings

Transmission in healthcare and social care settings has contributed to a significant amount of the COVID-19 burden worldwide. A significant number of healthcare workers have acquired SARS-CoV-2 infection while performing their duties. Many have tested positive without symptoms or with only very mild symptoms [14]. Similarly, outbreaks in acute and long-term care settings have been reported involving staff, patients and residents and these have been characterised by an increased morbidity and mortality. For these reasons, healthcare and social care services have been targeted for more extensive COVID-19 testing than the general population. Additionally, this approach was designed to protect healthcare workers from being exposed to unidentified cases admitted to healthcare for other reasons [15-22].

Almost all countries within the EU/EEA and UK have indicated that they regularly test healthcare workers and residents in LTCFs irrespective of symptoms. The majority of clusters and outbreaks in occupational settings reported by EU/EEA countries were from the health and social care settings, which might also result from the prioritisation of testing [15].

Healthcare workers

To mitigate the impact of COVID-19, ECDC recommends that healthcare workers and staff working in social care and other high-risk settings are tested periodically, irrespective of symptoms. To achieve effective prevention and control, screening should be repeated regularly, (e.g. at least once a week or every two weeks). This should be accompanied by appropriate use of personal protective equipment (PPE) and daily monitoring of symptoms in staff who must be sent home if COVID-19-compatible symptoms appear. This approach applies at most COVID-19 transmission levels in the community, with the exception of communities where the virus has been consistently eliminated or where transmission has only been documented in sporadic clusters which have been promptly controlled and where measures are in place to reduce the risk of re-introduction.

Different screening approaches have been reported (e.g. regular weekly testing of healthcare workers over a period of several weeks, testing of symptomatic staff and symptomatic household contacts or comprehensive testing of all healthcare workers in a hospital or ward. Modelling studies estimated that weekly PCR testing to screen healthcare workers and other high-risk groups, irrespective of symptoms, would reduce their contribution to SARS-CoV-2 transmission by 23% (95% UI 16–40), in addition to the reduction achieved by self-isolation following the appearance symptoms, assuming results are available within 24 hours [23]. ECDC therefore recommends this approach.

Hospitals

With the exception of wards dedicated to the treatment of COVID-19 patients, all other areas of the hospital should be COVID-19-free. The testing approach needs to consider the epidemiological situation in the community served by the hospital. The general testing approach, to test all people with COVID-19-compatible symptoms, also included patients admitted to hospital and staff as well as all contacts of confirmed cases.

When there is documented community transmission and if testing capacity allows, all patients should be tested for SARS-CoV-2 on admission to the facility and managed as possible COVID-19 cases until the test result is available. Given the 14-day incubation period and the possibility of asymptomatic disease course, patients admitted to the hospital should be monitored daily for COVID-19 compatible signs and symptoms, and tested again on Days 3–5 after admission if no signs and symptoms have developed before. Planned admissions, such as admissions for elective surgery, should be tested 24–72 hours before admission and admitted only after a confirmed negative result.

If the level of SARS-CoV-2 transmission in the community served by the hospital is very low or absent, as demonstrated by applying the testing approach described under Objectives A and B, patients should be checked

for COVID-19 compatible symptoms on admission and monitored daily during their hospital stay. Testing needs to be done when symptoms develop.

If it is impossible to screen all patients on admission due to insufficient testing capacity, screening of specific patient populations in healthcare settings can be considered to prevent virus introduction to sensitive areas where vulnerable populations are treated. This may also protect staff in these settings working with vulnerable groups, maintaining a safe working environment and limiting healthcare-associated infections and spread. Specific wards have been included in screening programmes for COVID-19, including oncological or delivery wards, neonatal intensive care units and organ transplantation units.

As an alternative to universal screening of all patients, including children, upon admission to hospital [24, 25], more targeted approaches have been suggested for vulnerable groups, such as general screening before entering wards for specific healthcare services (e.g. on oncological wards to protect cancer patients and enable them to continue their treatment) [26]. Another option involved the testing of patients receiving systemic therapy, radiation, all transplant and immunotherapy patients and donors. Scheduled surgical patients were tested 24-48 hours pre-surgery, then advised to self-isolate until surgery [26,27]. Another reported approach involved the screening of all in-patients and newly-admitted patients at an organ transplant unit located in a region with significantly high community-based transmission, with tested patients being kept in a separate specific ward while awaiting results [28]. To protect neonates and neonatal intensive care patients, all neonates admitted, their parents and all staff were tested [22,29]. One approach involved the screening of patients for orthopaedic surgery, including acute trauma patients, and patients undergoing surgical procedures in surgical departments within hospitals or primary care specialty clinical practices upon admission to hospital wards [30-33]. Other hospitals or primary care specialty clinical practices tested patients, their caregivers and staff in electrophysiology units, along with the emergency medical service staff [34] or patients scheduled to undergo surgical procedures (with a view to saving on PPE/limiting exposure of healthcare workers) [31]. The screening of pregnant women for COVID-19 can help to calibrate PPE requirements for healthcare staff during and following delivery, as well as minimising the risk of mother-to-child transmission [35]. It should be noted that the number of positive tests in pregnant women has been low, and some hospitals have therefore discontinued such screening [36]. Although a screening test may be scheduled for the expected week of delivery, a more effective approach for COVID-19 prevention and control in this population would be to reduce the number of contacts during the 2-4 weeks before the expected delivery date. If the delivery is scheduled, ideally the test should be performed 24-72 hours in advance, depending on the time needed to obtain a laboratory result.

Long-term care facilities (LTCF)

LTCF have been severely affected by COVID-19, causing high morbidity in residents and staff as well as mortality in residents due to the vulnerability of the population within these facilities. Systematic monitoring of all residents and staff for COVID-19 symptoms at such facilities, testing of possible cases, isolation, meticulous IPC measures and COVID-19 surveillance have been key elements to limiting the spread across facilities and preventing severe disease and deaths [10].

In a number of studies worldwide, early and comprehensive testing of staff and residents following identification of a case [37-39] at a facility has proven effective in supporting control efforts and facilitating outbreak response measures (i.e. to group residents accordingly) [37,38,40-47]. ECDC recommends the testing strategy below for use among LTCF residents and visitors, regardless of the epidemiological situation in the community served by the facility.

- New and returning residents should be tested with RT-PCR for COVID-19 between 24 and 72 hours before admission, depending on the time required to obtain the test result, and monitored for COVID-19 symptoms daily. If testing capacity allows, repeated testing can be considered 3–5 days after admission.
- All staff at LTCFs, including those who do not have direct contact with residents, should be tested regularly. In areas with community transmission, this could be weekly or every other week.
- Possible cases i.e. those with clinical symptoms compatible with COVID-19 should be isolated and tested as soon as possible, with laboratories prioritising these specimens. Ideally, there should be comprehensive testing of all staff.
- When a first case is confirmed in an LTCF resident or member staff, or if a confirmed case has been observed at the facility, comprehensive testing of all residents and staff should be considered, including testing of those without symptoms.
- Persons with atypical¹ or mild symptoms of COVID-19 at an LTCF (residents or staff) should be tested for COVID-19. Depending on the epidemiological situation in the community served by the facility, this should also trigger preparation for comprehensive testing of all residents and staff.

¹ Atypical presentations in older adults and people with underlying conditions include anorexia, anosmia, apathy, conjunctivitis, diarrhoea, disorientation, lethargy, loss of weight, nausea, rash, respiratory distress, somnolence, stuffed nose or vomiting.

Social protection services including home care

Healthcare workers providing home care have been at increased risk of testing positive for COVID-19 [48]. These healthcare workers often provide care to individuals who are vulnerable for severe disease. Therefore, social workers or carers working with the elderly or people with relevant co-morbidities in the community, such as those working in home care or social assistance, should be tested at regular intervals (e.g. weekly or every other week), in line with the recommendations for long-term care facilities.

Testing objective D - Rapidly identify all clusters or outbreaks in specific settings

Large outbreaks of COVID-19 have been detected in a variety of settings, sometimes causing spill-over infections in the local community or across borders. Clusters or outbreaks of COVID-19 occurring in certain settings may go unnoticed for some time, posing a risk to the individuals in the setting, particularly those who are more vulnerable to SARS-CoV-2, and to the wider community. Early identification of clusters, isolation of cases and notification of contacts can prevent further spread within these settings and to the wider community.

Occupational settings and schools usually host a higher proportion of individuals who, if infected with SARS-CoV-2, may only develop a mild or asymptomatic form of the disease, and who may have links to many other members of the community through household contacts [15]. Prisons and migrant detention centres are closed settings containing large numbers of individuals where SARS-CoV-2 has the potential to spread rapidly.

In all epidemiological situations, all those with COVID-19 compatible symptoms and high-risk contacts should be tested, irrespective of symptoms. Furthermore, in all epidemiological situations, all contacts (high-risk and low-risk) exposed in specific settings or during events prone to cause the spread of SARS-CoV-2 (e.g. choir performances, weddings, funerals, bars and other social events) should be tested. Similarly, if a case has been identified in a prison, migrant detention or reception centre or in certain occupational settings, all contacts should be tested. In the event of widespread community transmission, incoming prisoners or migrants at detention centres, or prisoners or migrants returning to a facility following a hospital stay or medical procedure, should be tested, irrespective of symptoms.

In order to rapidly detect outbreaks and confirm them through PCR testing, where possible, it is essential that monitoring systems are in place to detect signals of possible COVID-19 infection in these settings. This can include daily monitoring of symptoms in individuals attending or working in a given setting and verification of the health status of those absent from schools or workplaces, where feasible.

Additional considerations related to disease burden and testing which may help with the early identification of clusters or outbreaks in some of these specific settings are listed below.

Occupational settings

A review of occupational outbreaks and clusters carried out by ECDC found that 95% were reported to have occurred in indoor settings, often in confined spaces where physical distancing could not be maintained or where workers shared transportation and/or accommodation [15]. The different occupational settings where clusters were observed varied widely and included food packaging and processing plants, offices, construction sites, military and law enforcement institutions, industry, educational facilities and health and social care services.

Workplace-based testing schemes may support the early identification of COVID-19 and prevent occupational transmission, however, testing without additional accompanying measures will not prevent clusters or outbreaks in the workplace. Challenges related to the implementation of wider screening or testing approaches in these settings are outlined in ECDC's report on population-wide testing [49].

All employees showing symptoms compatible with COVID-19 in accordance with the case definition should be tested for SARS-CoV-2. Asymptomatic persons identified as high-risk exposure (close) contacts of confirmed cases could be considered for testing. In some workplaces, where mitigation measures are hard to ensure due to the nature of the work performed, all staff (high and low risk contacts of confirmed cases) may need to be prioritised for testing.

Schools

School settings bring children and young adults of different age groups together at close quarters, in shared teaching rooms, and at sports and other community facilities. It has been shown that children have more social contacts than adults and this fact is also relevant for school settings [50]. Similarly, school staff have a large number of contacts with pupils and other staff. Several investigations have focussed on the role of children in the transmission of COVID-19 within schools and other educational settings as a possible location for outbreaks that might cause spill-over to the general population, or vice versa. More details are outlined in previously published documents on COVID-19 in children and in school settings [51,52].

Children are more likely to have a mild or asymptomatic COVID-19 infection, and are much less prone to be hospitalised or have fatal outcomes than adults. Outbreaks of COVID-19 in schools have been documented, however child-to-child transmission in these settings has been limited [51].

Testing for SARS-CoV-2 in school settings can promote the identification of cases among students and staff in order to conduct contact tracing and initiate prevention and control measures, thereby reducing further transmission. All pupils and staff showing symptoms compatible with COVID-19 in accordance with the case definition should be tested for SARS-CoV-2. Asymptomatic individuals identified as high-risk exposure (close) contacts of cases could also be considered for testing [2].

Prisons

It is estimated that 1.5 million inmates were in penal institutions in the European Region in 2019 [53]. There are challenges to the successful control of COVID-19 clusters in prisons which include unavoidable close human tohuman contact, poor ventilation, sub-optimal healthcare services, multi-morbidities of those in prison and the often high turnover of people coming in and out of the prison from the community, including prison staff. Outbreaks in prison settings have been reported in Europe and these can have serious consequences for public health as they can quickly overburden prison and community health services. Moreover, given the high turnover in many prisons, such outbreaks can result in increased transmission within, or reintroduction into, marginalised communities [54].

All inmates with COVID-19-compatible symptoms should be tested for SARS-CoV-2, as should all potential COVID-19 case contacts (low- and high-risk, irrespective of symptoms). This includes situations where the symptoms occur upon entry to prison, during detention or before release [12].

The following groups could also be considered/prioritised for testing, given the potential for outbreaks in prison settings which can then have a significant effect on the prison population, especially if there is widespread community transmission:

- incoming prisoners (new, transferred from other institutions or going in and out of the premises) irrespective
 of symptoms, to reduce the risk of COVID-19 being introduced into the prison. Reverse cohort units should be
 considered to quarantine new arrivals or transferred inmates for a period of 14 days to detect any cases
 before allowing them to enter the general prison population, as a negative test on reception does not exclude
 the possibility of infection subsequently developing;
- all prisoners and staff to be tested, irrespective of symptoms, either after a case is detected in staff/inmates
 or to identify asymptomatic cases and those in the early stages of infection. This will help guide isolation,
 contact tracing and infection control and can be useful for implementing 'cocooning' strategies and early
 clinical care to minimise severe disease and fatal outcomes.

Migrant detention and reception centres

Outbreaks of COVID-19 have been detected in several migrant detention and reception centres [55-58]. Given the transmission potential of a respiratory virus such as SARS-CoV-2, migrants and refugees living in reception and detention centres may be particularly vulnerable to the impact of COVID-19 [59,60]. Providing free and equitable screening for infectious and chronic diseases to migrants and refugees at reception and detention centres in a non-discriminatory and non-stigmatised manner is vital, particularly in the context of COVID-19 [61,62], as there are specific sub-populations of migrants and refugees who are affected by underlying diseases, making them particularly vulnerable to COVID-19 [61,63]. Health services need to be able to detect cases early and link people to care, ensuring that measures are taken to protect those at increased risk of COVID-19.

Residents of reception and detention centres in areas with widespread COVID-19 transmission should be screened for vulnerabilities based on the risk of developing severe disease or complications. This screening should be conducted upon admission to a reception or detention centre. After identification, a 'cocooning' strategy, to move these vulnerable groups to less crowded settings, may assist in reducing transmission, improving health outcomes and alleviating the pressure on local healthcare services.

All people in migrant detention and reception centres with COVID-19-compatible symptoms should be tested for SARS-CoV-2, as should asymptomatic persons identified as close contacts of detected cases. This includes situations where the symptoms occur upon entry to the facility, during detention or before release. Possible or confirmed COVID-19 cases not requiring hospitalisation should be isolated or separated from others. The following groups could also be considered/prioritised for testing, given the potential for outbreaks in these settings:

- Incoming residents (new, transferred from other institutions or going in and out of the premises) irrespective
 of symptoms, to reduce the risk of introducing COVID-19 cases into the facility.
- New arrivals could be quarantined or housed in a separate area on entry as a negative test does not exclude the possibility of their becoming infectious in the 14 days following exposure.
- Wider testing of all residents and staff after a case is detected, to identify asymptomatic cases and those in the early stages of infection in order to guide isolation, contact tracing and infection control. Implementation of 'cocooning' strategies can also be helpful, along with early clinical care to minimise severe disease and fatal outcomes.

Other populations at risk

Following the relaxation of measures, many clusters have been reported associated with social events, particularly clusters involving young people participating in late-night outdoor leisure activities [64]. There have been some suggestions that projecting the voice to be heard over loud music or noise, often associated with alcohol intake, and not observing physical distancing, may be linked to increased transmission [64]. Furthermore, clusters associated with choir practice and large outbreaks associated with religious gatherings have been reported in several settings worldwide [65-67].

Homeless people are at increased risk of infection due to their living conditions, with many also having an increased risk of severe disease outcome [68,69]. Several rapidly spreading outbreaks of COVID-19 have been reported in homeless shelters, some with fatal outcomes [70-72]. People with COVID-19-compatible symptoms should be tested and provided with separate accommodation at housing shelters.

In all epidemiological situations, all contacts (high-risk and low-risk) exposed in the above-mentioned settings should be tested, irrespective of symptoms if a case has been found in the setting.

Testing objective E - Prevent (re-)introduction into regions/countries with sustained control of the virus

In the current epidemiological situation ECDC does not recommend that travellers should be systematically tested when crossing internal or external administrative borders [5,73]. The testing approach proposed in this chapter has a specific objective and applies to an exceptional situation, when a country or region has achieved consistent sustained control of the virus, as demonstrated by the effective implementation of population-based surveillance described above.

The implementation of non-pharmaceutical interventions together with comprehensive testing of possible cases and intense contact tracing could result in sub-national areas or entire countries experiencing no circulation of SARS-CoV-2 for extended periods. This situation would enable social, educational, commercial, and other activities to recommence, offering overall benefits for people's well-being and for the economy. Any countries or areas that are experiencing this very exceptional status should consider testing individuals coming from other areas within the same country or other countries that have not yet achieved sustained control of the virus. For this approach to be effective, all incoming individuals should be tested before entering the COVID-19 free areas. Given the 14-day incubation period and the possibility of asymptomatic disease, these individuals should self-monitor daily for COVID-19 compatible signs and symptoms and be tested rapidly if they develop such symptoms. In the absence of symptoms, and if they are in quarantine, they should be tested again at the end of the quarantine period on Day 14 after arrival.

In all other epidemiological situations, including the current situation in the EU/EEA and in the UK (September 2020), screening of travellers is not considered a cost-effective strategy for substantially preventing the crossborder transmission of COVID-19.

The challenges of this testing strategy are outlined in detail in ECDC's document on population-wide testing [49]. Detailed requirements on protocols for screening via health declaration forms and/or temperature screening and individual screening (usually by a health professional) require defined mechanisms, clear case definitions, an adequate number of trained primary and secondary screeners, adequate personal protective equipment for personnel, and a way in which to safely isolate suspected cases from other travellers [74]. In addition to logistical and technical requirements, communication with travellers about testing procedures and protocols concerning any requirements for entry to a country needs to take place well in advance of travel.

Relevant ECDC guidance documents

Testing objectives A and B - Control transmission and monitor incidence and trends, and assess severity over time

European Centre for Disease Prevention and Control (ECDC). Strategies for the surveillance of COVID-19. ECDC; [updated 9 April 2020]. Available from: https://www.ecdc.europa.eu/en/publications-data/strategies-surveillance-covid-19

European Centre for Disease Prevention and Control (ECDC). Methodology for estimating point prevalence of SARS-CoV-2 infection by pooled RT-PCR testing [updated 28 May 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-</u>data/methodology-estimating-point-prevalence-sars-cov-2-infection-pooled-rt-pcr

European Centre for Disease Prevention and Control (ECDC). Population-wide testing of SARS-CoV-2: country experiences and potential approaches in the EU/EEA and the United Kingdom [updated 19 August 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/population-wide-testing-sars-cov-2-country-experiences-and-potential-approaches</u>

Under development: Strategies for the surveillance of influenza and COVID-19 in primary care.

Testing objective C - Mitigate the impact of COVID-19 in healthcare and social care settings

European Centre for Disease Prevention and Control (ECDC). Surveillance of COVID-19 at long-term care facilities in the EU/EEA [updated 19 May 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/surveillance-COVID-19-long-term-care-facilities-EU-EEA</u>

European Centre for Disease Prevention and Control (ECDC). Infection prevention and control and preparedness for COVID-19 in healthcare settings - fourth update. ECDC [updated 3 July 2020]. Available from:

https://www.ecdc.europa.eu/en/publications-data/infection-prevention-and-control-and-preparedness-covid-19-healthcaresettings

Testing objective D - Identify outbreaks in specific settings

European Centre for Disease Prevention and Control (ECDC). Guidance on the provision of support for medically and socially vulnerable populations in EU/EEA countries and the United Kingdom during the COVID-19 pandemic. ECDC [updated 3 July 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/guidance-medically-and-socially-vulnerable-populations-covid-19</u>

European Centre for Disease Prevention and Control Infection prevention and control and surveillance for coronavirus disease (COVID-19) in prisons in EU/EEA countries and the UK – July 2020. ECDC: Stockholm; 2020. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/IPC-and-surveillance-for-coronavirus-disease-in-prisons.pdf

European Centre for Disease Prevention and Control. Guidance on infection prevention and control of coronavirus disease (COVID-19) in migrant and refugee reception and detention centres in the EU/EEA and the United Kingdom – June 2020. ECDC: Stockholm; 2020. <u>https://www.ecdc.europa.eu/en/publications-data/covid-19-guidance-prevention-control-migrant-refugee-centres</u>

European Centre for Disease Prevention and Control (ECDC). COVID-19 clusters and outbreaks in occupational settings in the EU/EEA and the UK [Internet]. ECDC [updated 11 Aug 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/covid-19-clusters-and-outbreaks-occupational-settings-eueea-and-uk.</u>

European Centre for Disease Prevention and Control (ECDC). COVID-19 in children and the role of school settings in COVID-19 transmission [Internet]. ECDC [updated 6 August 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/children-and-school-settings-covid-19-transmission</u>

European Centre for Disease Prevention and Control (ECDC). Objectives for COVID-19 testing in school settings. ECDC [updated 10 August 2020]. Available from: <u>https://www.ecdc.europa.eu/en/publications-data/objectives-covid-19-testing-school-settings</u>

Testing objective E - Prevent (re-)introduction into regions/countries with sustained control of the virus

European Centre for Disease Prevention and Control (ECDC). Population-wide testing of SARS-CoV-2: country experiences and potential approaches in the EU/EEA and the United Kingdom [updated 19 August 2020]. Available from: https://www.ecdc.europa.eu/en/publications-data/population-wide-testing-sars-cov-2-country-experiences-and-potential-approaches

Table 1. Testing guidance depending on objectives and epidemiological situation

Objective	Epidemiological situation	Population to test
Control transmission	All situations	 All possible cases*. All high-risk exposure (close) contacts of confirmed cases, irrespective of symptoms**. If resources allow, Re-test high-risk exposure (close) contacts that test negative and remain asymptomatic**.
	Widespread community transmission	 All population of a country/region/municipality/neighbourhood/community. Possible approaches include household testing, inviting everyone to present for testing and facilitating access to voluntary testing. All high-risk exposure (close) contacts of confirmed cases, irrespective of symptoms**. If resources allow, Re-test high-risk exposure (close) contacts that test negative and remain asymptomatic**.
Monitor incidence and trends, and assess severity over time	No local transmission	 ILI/ARI (sentinel primary care) SARI (hospital)
	Sporadic cases, cluster of cases or community transmission	 All possible cases* (comprehensive surveillance) ILI/ARI (sentinel primary care) SARI (hospital) All high-risk exposure (close) contacts irrespective of symptoms, depending on testing capacities**. If testing capacity is exceeded, A systematic sample of all detected possible cases and their symptomatic contacts**.
Mitigate the impact of COVID-19 in healthcare and social-care settings	No local transmission	All possible cases* among staff, patients/residents and visitors. This implies that the presence of signs and symptoms among patients/residents is verified upon admission and during the first 14 days of hospitalisation/residence.
	Sporadic cases, clusters of cases or community transmission	 All staff periodically, irrespective of symptoms. All patients/residents, upon or just prior to admission; All possible cases*. All contacts (high-risk and low-risk) of confirmed cases in all health-and social-care settings**. If a case is detected in an LTCF or in certain hospitals or hospital wards hosting patients at high risk of severe COVID-19, all staff and residents of the LTCF and hospital or hospital ward should be tested, irrespective of symptoms. If resources allow and it is logistically feasible, All patients/residents that test negative upon admission to the hospital should have a follow-up test on Day 3–5. This should be in combination with daily checks for the presence of COVID-19 signs and symptoms during the first 14 days of hospitalisation.
Identify clusters or outbreaks in specific settings	No local transmission or sporadic cases, clusters of cases	 All possible cases*. All high-risk exposure (close) contacts, irrespective of symptoms**. All contacts (high-risk and low-risk) exposed in specific settings or events known to cause the virus to spread, such as choir performances, weddings, funerals, bars, other social events**. Wider testing in prisons, detention and reception centres and certain occupational settings where a case has been identified.
	Community transmission	 All possible cases*. All high-risk exposure (close) contacts, irrespective of symptoms**. All contacts (high-risk and low-risk) exposed in specific settings or events known to cause the virus to spread, such as choir performances, weddings, funerals, bars, other social events**. Wider testing in prisons, detention and reception centres and certain occupational settings where a case has been identified. Incoming prisoners or migrants at detention centres, and prisoners or migrants returning to a facility following a hospital stay or medical procedure. This objective implies that monitoring systems are in place to detect symptoms of possible COVID-19 infection in settings where people congregate. If resources allow: Re-test high-risk exposure (close) contacts that test negative and remain asymptomatic**.
Prevent (re-)introduction into regions/countries with sustained control of the virus.	No locally acquired cases in community	 Testing individuals coming from other areas that have not yet achieved sustained control of the virus on arrival, plus quarantine. Re-test at Day 14 to lift quarantine with two negative tests

* according to case definition [2]; LTCF: long-term care facility; ILI: influenza-like illness; ARI: acute respiratory infection; SARI: severe acute respiratory infection;

** Please see section 'Testing of contacts' for details on testing of contact persons.

Methods for testing and limitations

Incubation period

Current estimates suggest a median incubation period of five to six days for COVID-19, with a range from one to 14 days. In a study involving 425 patients, the mean incubation period for COVID-19 was 5.2 days (CI: 4.1 to 7.0 days), with 95% of cases having an incubation period less than 12.5 days [75]. Another study on 181 cases arrived at very similar numbers, with a median incubation period of 5.1 days (CI: 4.5 to 5.8 days) and 97.5% of cases having an incubation period of 5.1 lays (CI: 4.5 to 5.8 days) and 97.5% of cases having an incubation period of less than 11.5 days [76]. In addition, fewer than 2.5% of cases were estimated to show symptoms within 2.2 days (CI: 1.8 to 2.9 days) of exposure. Taken together, the large majority of symptomatic cases are expected to have an incubation period of between two and 12 days. This is important for determining the timing of testing.

Test types

There are three main types of detection assays relevant for COVID-19 diagnostic testing, depending on what the test is trying to detect:

- nucleic acid tests detect the presence of viral RNA typically, these use an amplification step based on reverse transcriptase polymerase chain reaction (RT-PCR), and are called Nucleic Acid Amplification Tests (NAATs);
- antigen tests detect the presence of a viral antigen, typically part of a surface protein;
- antibody tests detect the presence of antibodies generated against SARS-CoV-2.

Both NAATs and antigen tests can be used to detect ongoing infection, and WHO's interim guidelines specify using an NAAT to confirm a COVID-19 case [77]. Antibodies against SARS-CoV-2 become detectable typically 10–14 days after infection, meaning that antibody tests are only useful to confirm a prior infection, and a positive result does not imply protective immunity against SARS-CoV-2 reinfection [78].

Two other important aspects of detection assays are their rapidity and ease of use. The common technical specifications for in vitro diagnostic medical devices (IVDs, Commission Decision 2002/364/EC) [79] define rapid tests as 'those tests which can only be used singly or in a small series and which have been designed to give a rapid result for near patient testing'. The draft WHO target product profile for a point-of-care test (POCT) for diagnosis of suspected COVID-19 cases and their close contacts, specifies the following requirements for such a test [80].

- Target use setting:
 - acceptable: the tests can be performed outside of laboratories, at routine and ad-hoc triage/screening points run by healthcare facilities, such as emergency units, mobile units and in the community (contact tracing) by healthcare workers or laboratory technicians with appropriate training in sample collection, biosafety and the use of the test;
 - desirable: same as acceptable but can be performed by trained lay workers (volunteer/community health workers).
- Time to result:
 - acceptable: ≤40 minutes;
 - desirable: ≤20 minutes.

Testing algorithms

In addition to testing a single sample once, it is possible to use a combination of tests (i.e. a testing algorithm) to improve the testing process overall and the efficiency of testing. The three algorithms set out below are particularly relevant.

Rapid test, potentially followed by a confirmatory test on the same sample

When a rapid test is used, the intention is to detect a substantial proportion of the cases in a timely manner in order to allow for rapid implementation of control measures. Such a test requires high specificity to avoid false positives, but in practice usually has a lower sensitivity. There this is a substantial probability that the negative results from the rapid antigen test are false negatives, while the positive results are very likely to be true positives. A second confirmatory test with high sensitivity and specificity, typically a non-rapid molecular test executed in a laboratory, can then be run on these negative samples to detect additional cases, while positive results need to be confirmed by RT-PCR, according to the case definition.

Sample pooling

Pooling or group testing of specimens is faster than individual testing and saves resources in situations where the proportion of positive samples is expected to be very small (up to 5%) [11,81]. Several samples are combined and tested once, typically with a leftover or second sample kept from each individual. If the combined result is positive, which may occur rarely or more frequently depending on the epidemiological situation, the individual samples are then tested.

Alternatively, samples may be put into several pools, the results of which together identify the sample that was positive. For infection rates from 0–2.5%, binary splitting pooling seems to be the best method [81] while others have suggested a single stage non-adaptive group-testing approach for up to 1.3% positivity without the need to subsequently test individual samples [81]. ECDC has provided a methodology for estimating the point prevalence of SARS-CoV-2 infection through pooled RT-PCR testing [11].

Follow-up testing and timing of testing

Follow-up testing refers to the performing of more than one test on an individual at different points in time to increase the probability of detection. This testing algorithm is used for the detection of asymptomatic or presently pre-symptomatic cases, and not primarily for detection of symptomatic cases. Cases do not immediately test positive after infection, but only after the virus has replicated sufficiently and sufficient RNA or viral antigen is present in the specimen that was collected. This also depends on the sensitivity of the test used. However, in many scenarios it is not possible to know if sufficient time has elapsed since infection to be able to detect the virus with the chosen test. This may be due to the variation in the incubation period for each individual, or an unknown exposure time. The earlier the case is detected, the more potential there is to prevent further transmission (e.g. through contact tracing). Therefore, the rationale for performing follow-up tests is that a first test might be negative because the case is at the stage of infection where the virus still cannot be detected using the test in question, particularly if this is a rapid test with lower sensitivity.

As shown in the average infectiousness profile (Figure 1), there is a sharp increase in infectiousness, assessed as a proportion of inferred transmission and thus viral load and detectability, from around four days before onset of symptoms [82,83]. However, detection of viral RNA has been shown to be possible during the incubation period by RT-PCR assay one to three days before symptom onset [82,84,85].

Given that the incubation period is up to 12 days for the large majority of the cases (see 'Incubation period' section above), for most cases this leaves a period of several days between being infected and being detectable. Therefore, in situations where asymptomatic or pre-symptomatic individuals are tested and there is no information or only unreliable information on the possible date of exposure, one or several follow-up tests after a first negative test can substantially improve case finding. When taken together with the incubation period of 12 days for the majority of cases and the detectability of the virus 1–3 days prior to symptom onset, based on the current evidence we assess that testing around Day 10 after exposure would be able to identify the majority of those infected with SARS-CoV-2. ECDC is continuously reviewing the evidence and also conducting internal modelling work in this area and will update this assessment based on new information.

If the date of exposure is known, and a single test is planned, this test should not be taken before Day 2 following exposure, given the low probability of detection. If the exposure date is unknown, the first test should be taken as soon as possible. If a single follow-up test is taken after the first test, it should be taken around 10 (i.e. 12 minus two) days after the first test to detect as many cases as possible. If resources allow, additional follow-up tests before Day 10 can be done to improve the timeliness of detection. If the individual develops symptoms before a planned follow-up test, a test should be taken as soon as possible in accordance with the applicable strategy for testing symptomatic cases. The use of follow-up testing to detect asymptomatic or pre-symptomatic cases should not be confused with testing to discharge a patient from isolation, which typically requires two consecutive negative tests [86].



Figure 1. Average inferred proportion of transmission as a function of days after symptom onset

Adapted from He et al. [82,83]

An estimated 44% (95% confidence interval, 30–57%) of transmissions occurred before the onset of symptoms in this study. The density (%) can be considered to be in arbitrary units; the area under the curve represents 100%.

Specimen types

Samples for diagnostic tests for SARS-CoV-2 can be taken from the upper (nasopharyngeal/oropharyngeal swabs, nasal aspirate, nasal wash or saliva) or lower respiratory tract (sputum or tracheal aspirate or bronchoalveolar lavage). Data comparing the accuracy of RT-PCR testing suggest that test sensitivity may vary depending on the type of specimen. Nasopharyngeal or oropharyngeal swabs are considered sensitive specimen types for the diagnosis of SARS-CoV-2, while the combination of nasopharyngeal/oropharyngeal swab samples has proven more sensitive than nasopharyngeal swabs in three different studies [84,87,88]. In a situation where a nasopharyngeal or other upper respiratory tract specimen (as mentioned above) is not acceptable to the person being tested, saliva could be considered as an alternative specimen [89,90]. Saliva is a non-invasive specimen that can also be considered for self-sampling.

Contact tracing

The aim of contact tracing is to promptly identify and manage contacts of laboratory-confirmed COVID-19 cases in order to reduce the risk of their contributing to further onward transmission before they have been identified and quarantined. Rigorous contact tracing, when accompanied by extensive testing, is an effective strategy for the control of COVID-19. ECDC has published guidance on how to perform contact tracing [1] and guidance on how to increase capacity and maintain operations even during more widespread transmission, or if resources are stretched [1,91]. In order to ensure that contact tracing reaches contacts before they are able to transmit infection to others it is vital that people with COVID-19-compatible symptoms are tested as soon as possible after symptom onset. This includes emphasising to the public the need to test as soon as symptoms develop and ensuring that testing is easily accessible (also for overseas visitors/non-residents). Test turnaround time should be minimised, and both individuals and public health authorities notified promptly after a positive result so that contact tracing can be initiated, the case interviewed and the contact persons reached. ECDC has identified indicators for monitoring contact tracing and countries should be encouraged to collect and analyse relevant data [92].

Testing of contacts

All symptomatic contacts (high-risk and low-risk exposure contacts) should be tested as quickly as possible to allow for further contact tracing. It is also recommended that high-risk exposure contacts without symptoms and low-risk exposure contacts in special settings are tested as soon as possible after being traced, in order to facilitate early identification of any secondary cases among contacts and to initiate further contact tracing of those who may have been exposed before quarantine began.

If the first test taken is negative and a subsequent test, taken on or after Day 10 following the last exposure to the case, is negative, the contact person may be discharged from quarantine before the recommended 14-day period. However, a small proportion of contact persons may still develop infection at the very end of the incubation period

and not have symptoms or a detectable viral load at Day 10. Consequently, early release from quarantine needs to be assessed on a case-by-case basis and testing later than Day 10 could be considered for contacts working with vulnerable populations or contacts in high-risk settings, such as prisons².

If possible, testing should also be done as part of case investigation work to understand where the index case acquired the infection from. This would facilitate further contact tracing to interrupt chains of transmission.

Role of asymptomatic and pre-symptomatic cases

As of May–June 2020, some Member States began to gradually expand their testing strategies to include people, irrespective of symptoms and also those with mild presentations. Asymptomatic people or contacts of cases were tested as part of screening activities (population at risk, airports, before admission to hospital), contact tracing, prevalence surveys and other population-wide testing approaches [49].

Broader testing strategies and population-wide studies that included individuals irrespective of symptoms have been able to analyse the proportion of asymptomatic or pre-symptomatic cases on the day of testing within the tested population and have shown that between 5% and 80% of those infected with SARS-CoV-2 remain asymptomatic [93]. A study by Sermet et al [94] observed that more than 50% of the seropositive children tested did not report any symptoms, a proportion similar to a study by Oran et al [95] in adults. In Spain during a population-based seroprevalence study, 22–36% of past infections were asymptomatic [96].

A study in the Republic of Korea, in March 2020, reported that 110 (36%) of the 303 patients with SARS-CoV-2 were asymptomatic during the period of isolation and 21 of those developed symptoms during isolation [97]. This study did not include assessment of further transmission from asymptomatic individuals but indicates that viral RNA levels in asymptomatic cases are at the same levels as in symptomatic patients. The study showed prolonged detection of viral RNA for up to 17 days in asymptomatic patients and 19.5 days in symptomatic (including pre-symptomatic) patients [97]. As healthcare workers in hospitals and long-term care facilities are at high risk of exposure, these individuals are tested more often than other individuals without symptoms in the general population and a high proportion of these laboratory-confirmed cases have been identified as asymptomatic at the time of testing [10,98].

Cases that remain asymptomatic throughout the duration of their infection might undermine prevention and control measures that rely on identifying symptomatic cases. In a symptom-based monitoring system, such individuals would not be tested or detected, contributing to transmission in a country. However, the proportion of the asymptomatic cases among all positive tested cases is variable and seems to depend on the context. Although the overall prevalence of asymptomatic cases still remains uncertain, asymptomatic individuals represent a substantial proportion of all cases.

Long term carriers and re-infection

Since the beginning of the pandemic, patients with laboratory-confirmed COVID-19 have been identified as being PCR-positive over longer periods of time following infection [99,100]. In recent weeks a few cases, both symptomatic and asymptomatic, have been identified with a second confirmed SARS-CoV-2 infection after a first laboratory-confirmed infection. These cases have been confirmed by virus sequence data identifying different SARS-CoV-2 strains in the patients [101-103]. Additional cases with reinfections are under investigation in several countries, however, the magnitude and the contributing factors are currently not understood. Testing strategies and other public health measures need to take into account people remaining PCR positive over extended periods of time, as well as re-infections. These two issues also need additional further investigation in order to better understand the evolution of immune responses and the likelihood of re-infection.

Limitations

The proportion of people infected but showing no symptoms or very mild symptoms while contributing to the transmission of the virus is still not fully understood and seems to vary in different situations and populations. This poses a particular challenge for any effective testing approach that is mainly based on symptomatic people, since asymptomatic or pauci-symptomatic cases will normally not seek medical attention, and thus would not be tested and detected.

The relationship between infectivity, virus concentration in a particular body site (i.e. throat, lung, gastro-intestinal tract), and detectability via test on a specimen taken from that site is not well characterised as yet. In addition, the infectious dose is as yet unknown for SARS-CoV-2. Detectability using any test was taken to start at the point when infectious viral load increases exponentially and, by analogy, to end at the point where infectious viral load decreases to the same level. More data on the relationship between these variables is needed, followed by the

² ECDC is carrying out an ongoing assessment of empirical and other evidence on optimal testing time for risk management.

modelling of scenarios, in particular with respect to follow-up testing. In addition to all of the above, testing is dependent on access and the success of the approach relies on a short turnaround time for test results. The reliability of the test result is dependent on the overall epidemic situation (i.e. prevalence of the disease in the population), quality of the sample collected, transportation, quality of the laboratory, test specifications including thresholds and reference standards.

In addition to those currently infected, there is also a proportion of people who have developed an immune response against SARS-CoV-2 but may become infected again. This is currently an area requiring substantial research and it is not possible to determine this proportion to within a very high degree of confidence or to determine the level of protection provided by the immune responses against re-infection.

Conclusions

This document outlines different testing strategies that could be applied by countries based on their epidemiological situation, available testing capacities, infrastructure and objectives. The testing approaches have been published in several previous ECDC documents, including the most recent (eleventh) update of the Rapid Risk Assessment [5], where ECDC recommends that testing efforts be maximised, with the aim of offering timely testing to all symptomatic cases in order to ensure isolation of the case and tracing and quarantine of their contacts. An expanded, but targeted testing approach is outlined, based upon active surveillance and early detection of all symptomatic cases, developed and adapted through ongoing assessment of the local epidemiological situation. Robust, easy-to-access testing is crucial in order to identify localised resurgence early on. This may facilitate the implementation of targeted mitigation measures rather than applying burdensome blanket mitigation measures for an entire population. Member States within the EU/EEA and the UK should maintain the core capacity to test all symptomatic cases and their symptomatic contacts, and focus on optimising testing strategies to ensure quick turnaround times and robust contact tracing efforts.

ECDC also suggests taking a more comprehensive approach, with a low threshold for testing asymptomatic people in specific settings where there are known high-risk populations (e.g. in LTCFs and prisons). Consideration should be given to testing irrespective of symptoms for those in healthcare and social-care settings (staff, patients, residents) or for other vulnerable populations. If resources permit, people who have had a high-risk exposure to a confirmed case (close contacts) [1] could also be included in this testing approach. Such testing should not compromise the accessibility or timeliness of testing for those who are symptomatic, and should be regularly evaluated to provide evidence on the effectiveness of the strategy. Testing strategies should remain flexible and should be adapted to the local epidemiological situation, population dynamics, and resources at the local level.

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Annex 1. Literature search methodology and results

Literature search methodology

Searches were performed on 27 July 2020, in a COVID-19 EndNote reference library database, maintained by ECDC's Library, and included 42 837 records at the time of search. The EndNote library database is designed to retrieve all new publications related to COVID-19 in PubMed from the start of the epidemic and is updated daily. It is complemented by the monitoring of journal websites, COVID-19-specific publishers' portals for new publications and pre-print portals for upcoming publications.

Natural vocabulary (i.e. keywords) was used in all fields, in title and abstract field search combinations to represent the concept of universal testing; truncation was applied. The keywords included terms for universal, population, asymptomatic testing and screening, antibody testing, symptom recall, PCR, risk population.

Google (Scholar)

mass testing strateg* covid OR sars-cov-2

Google

Asymptomatic screening "universal population" strategy covid-19 OR Sars-cov-2 – 181 "universal population screening" strategy covid-19 OR Sars-cov-2 – 38 strategy "covid 19" OR "Sars cov 2" "universal population screening" – 15 sars cov 2 covid asymptomatic screening strategy OR strategies "universal population"- 56 sars cov 2 covid asymptomatic screening strategy OR strategies "general population"-169.