Testing for COVID-19: A way to lift confinement restrictions

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This policy brief discusses the role of testing for COVID-19 as part of any plan to lift confinement restrictions and prepare for a possible new wave of viral infections. If all confinement restrictions are lifted before a vaccine or effective treatments are developed without other measures to suppress new infections, the infection rate is expected to rebound rapidly. Crucially, quick suppression of infections requires testing more people to identify who is infected; tracking them to make sure they do not spread the disease further; and tracing with whom they have been in contact. This brief discusses how testing strategies can be used to achieve three main goals: 1) suppressing the resurgence of local outbreaks; 2) identifying people who have developed some form of immunity and can safely return to work; and 3) gaining intelligence on the evolution of the epidemic, including on when a threshold for herd immunity has been reached. The brief discusses what tests can be used for each goal, as well as practical implementation issues with testing strategies, including the opportunities and risks of using digital tools in this context.

Key messages

- A key question behind any strategy to ease confinement restrictions and reopen economic activities is how to avoid a new spread of the SARS-CoV-2 virus that would necessitate further lockdowns. Once the number of infected people has successfully been brought sufficiently down, quick suppression of new waves of viral infections will be key. Testing strategies are central to achieve this.
- There are two types of tests. First, molecular diagnostic testing (RT-PCR) helps to identify those individuals who are infected at the time of the test. An effective strategy that tests, tracks people infected and traces their contacts (TTT), helps to reduce the spread of the virus and thus bring its reproduction number below one.
- Given the characteristics of this coronavirus– including the large number of asymptomatic cases and high reproduction number – to be effective at suppressing the spread of the virus, the TTT strategy should be used very widely, requiring a very large proportion of all cases (between 70 and 90%) to be traced to prevent a new outbreak of the virus. This would require increasing capacity for testing enormously; putting in place strict measures to prevent people who may be infectious from breaking quarantine; as well as identifying ways to trace contacts, which may push the limits of privacy concerns, unless new approaches to digital tracing, currently under development, are put in place.
- Significant logistics and capacity constraints – ranging from the availability of trained personnel to take accurate specimen, to the time required for laboratory analysis and the availability of reagents – have impeded more widespread diagnostic testing in many countries so far. Recent development of faster RT-PCR molecular diagnostic testing, which can be deployed at the point of care, should help scale-up capacity for effective TTT in countries. Digital enabled contact-tracing can help improve the speed and effectiveness of TTT strategies, as seen in some countries.
- A second type of test – so-called serologic test – detects people who have had a prior infection and thus developed antibodies. Such tests can be used for two purposes, namely to allow people who have acquired immunity to return to work safely, and to provide intelligence on the evolution of the epidemic across the population. Rapid serology test kits need to be developed and their clinical performance needs to be demonstrated before deployment at scale can happen.
- Despite the fact that a relatively low number of people have so far been infected and thus we are still far from herd immunity, the successful implementation of serologic testing strategies at large scale can help reduce the spread of the virus and complement the TTT strategy. This will also require major efforts, including: 1) verifying the clinical performance of tests, particularly for rapid serologic tests; 2) preparing procurement and logistics arrangements to scale up production and deployment of the tests, and train and deploy human resources, particularly for diagnostic RT-PCR tests; and 3) providing adequate safeguards to protect civil right and privacy of populations while deploying or apps-enabled tracking strategies.

1. The role of testing while waiting for a cure and a vaccine

Since the end of last year, the world has been in the grip of the SARS-CoV-2 virus, which has caused tens of thousands of deaths from the respiratory disease COVID-19. To combat the pandemic, many countries have put in place strict containment and mitigation strategies to minimise the risk of transmission, decrease the spread of the virus and 'buy time' for health care systems to cope with the huge numbers of patients and ultimately save as many lives as possible (OECD, 2020[1]).

As part of the response to COVID-19, virtually all OECD countries affected by the virus have introduced strict restrictions to social and economic life, including social distancing and even full lockdowns. The big question is now how to manage these restrictions, and how to go back to a *new normal of living with* SARS-CoV-2; a social and economic life that coexist with the virus. To avoid new peaks in the number of cases, overstretching health system capacities, infection rates need to remain suppressed until a vaccine or effective treatment are found. If all confinement strategies are lifted, however, the infection rate is expected to rebound in a matter of weeks (Ferguson et al., 2020[2]). A strategy is needed about when and how to relax confinement, and when and how to re-tighten some of them when necessary. This is needed to minimise the risk of further peaks of the outbreak or, at least, to win as much time as possible between the successive peaks.

> Once the number of people infected with the #Coronavirus has been successfully brought down, new waves of viral infections will need to be suppressed quickly. Testing strategies are central to achieve this. #COVID19

A number of factors need to be in place to achieve this goal.

First, healthcare capacity and resources need to be increased to ensure safe and effective management of future severe COVID-19 cases (OECD, 2020[3]).

Second, we need to understand the virus better, including: the incubation period and infectiousness of the disease at different stages; the extent of asymptomatic spread; immunity and its duration in those who contracted the virus; and the impact of changes in temperature on the disease spread.

Third – and the topic of this brief – information about the presence and propagation of SARS-CoV-2 in the population needs to improve significantly. For this, widespread testing and effective contact tracing, including cases with no or only mild symptoms, are key components of the post-lockdown strategy. Better information will help achieve three goals:

- Tracking of new cases to suppress the resurgence of local outbreaks as early as possible, aiming to avoid new peaks;
- Identifying previously infected people who can safely return to work, to revitalise the economy and to strengthen the health workforce;
- Gaining intelligence on the evolution of the epidemic, including on when a threshold for herd immunity has been reached. In the case of COVID-19, it has been estimated that 50% to 60% of the population needs to be immune to the virus to halt its spread (OECD, 2020[1]).

This brief discusses progress in testing for COVID-19, and how to use the information gathered.

2. Types and objectives of tests to detect COVID-19

Tests to detect the COVID-19 can be divided in two main categories:

- **Molecular diagnostic tests,** i.e. tests that will detect the presence of the virus; and
- **Serologic tests,** i.e. tests that will detect the immune response to the virus**.**

Two types of testing are key to tackle the #Coronavirus properly:

- Molecular testing to help identify people who are infected

- Serologic testing that detects those who have already had the infection & developed antibodies

2.1. Molecular diagnostic tests

RT-PCR is currently the only available means to detect the presence of the SARS-CoV-2, the viral agent responsible of the COVID-19 disease, in the organism. It tracks the presence of viral genetic material in a patient sample.

Samples are taken from places likely to have high virus concentration, using a swab to collect samples from the back of the nose or mouth, or via a bronchoalveolar lavage to collect samples from deep inside the lungs. The RT-PCR test involves binding sequences on the genetic material that only are found in the virus and repeatedly copying everything in between. This process is repeated many times, with a doubling of the target region with each cycle. A fluorescent signal is created when amplification occurs, and once the signal reaches a threshold, the test result is considered positive. If no viral genetic material is present, amplification cannot occur, resulting in a negative result (Hadaya, Schumm and Livingston, 2020[4]).

This **technique is generally very sensitive** (i.e. able to detect true positive cases) and **specific** (i.e. able to avoid false negative results). If an RT-PCR is positive, the result is most likely correct (the only case of false positive could be happening if a non-positive sample is contaminated by viral material, during test processing for instance). False negative results are also possible with RT-PCR, but are most frequently the result of a wrong patient sampling (swabs not pushed far enough in the patients' nasopharynx for instance) (Patel et al., 2020[5]).

The main constraints related to RT-PCR have to do with logistics. The procedure is labour intensive, and quite long (the procedure itself usually lasts a couple of hours but all the logistics around sampling, transport, and communication of results increases significantly the time it takes to get a result for one patient; this can take up to two days in some circumstances). A particular problem is that the collection of specimen depends on a lot of material (swabs, reagents) that are in short supply because of increased global demand (see Table 1). Various types of reagents can be used to perform RT-PCR to detect the presence of the viral agent. Different companies produce these reagents, which often target different sequences of the viral genetic material. Yet, regardless of the reagent used, the principle of an RT-PCR remains the same, as well as the constraints associated to it.

Some companies have developed RT-PCR techniques which are actually faster than the standard procedure and can also be used at the point of care, such as in a hospital, instead of being sent to a lab (see Box 1).

Other means to detect viral material are currently under development. For example, **direct viral antigen detection** is a technique that aims at detecting proteins of the virus called antigens. It requires the identification and production, in laboratories, of specific antibodies for the antigens of the virus, and their subsequent inclusion in testing kits. Once fully developed, these tests may be performed using swabs similar to those currently used in RT-PCR to collect patients' samples. The antibodies in the testing kit bind virus' antigens from the sample. Such tests would be quick to run (sometimes less than 15 minutes) and could be used at the point-of-care (no need for a lab). However, the complexity of identifying and producing the required antibodies for the kit means that development of the tests is long and very few of them have actually been developed and they still require to have their performance assessed (as of 8 April 2020, five viral antigen tests received a CE IVD[1] marking). Similarly to RT-PCR, direct viral antigen detection would also be used to detect the presence of the virus in patients, but would not give any information about whether they have had the disease and recovered.

Box 1. Some faster RT-PCR tests could help scaling-up testing capacities in countries

Fast RT-PCR tests can be done at point of care (emergency department, patient's bedside) in less than 30 minutes, without needing a laboratory.

Companies that develop these tests optimise the standard RT-PCR technique to speed up the amplification of the genetic material. The downside is that the tests have to be run on proprietary instruments, so they are only available in places that have invested in those instruments (conversely to the standard RT-PCR that can be run on any type of PCR machine). The most common example of the utilisation of these devices is the rapid flu test.

However, gains in speed are associated to a certain loss in accuracy. Some studies (Chartrand et al., 2012[6]; Chu et al., 2012[7]) report that rapid flu tests have low sensitivity, meaning that they miss a substantial fraction of positive patients. The performance of these tests against the COVID-19 has not been established yet, but a high level of false negatives would be problematic in case this technique started to be used more broadly as part of countries' testing strategies.

Several companies run these types of tests. As of 8 April 2020, the United States Food and Drug Administration (FDA) has issued Emergency Use Authorization (EUA)[2] for two fast RT-PCR tests, the first is called Xpert Xpress SARS-CoV-2 from Cepheid and the second is called ID Now COVID-19 from Abbott.

Source: https://time.com/5812664/5-minute-coronavirus-test/; https://a16z.com/2020/04/02/coronavirus-tests/.

[1] CE IVD marking means that the test is conform with the relevant EU legislation, Directive 98/79/EC on In Vitro Diagnostics.

[2] An in vitro diagnostic made (IVD) available under an EUA has not undergone the same type of review as an FDA-approved or cleared IVD. FDA may issue an EUA when certain criteria are met, which includes that there are no adequate, approved, available alternatives, and based on the totality of scientific evidence available, it is reasonable to believe that this IVD may be effective in the detection of the virus that causes COVID-19.

2.2. Serologic tests

Once a patient has recovered, the virus is eliminated from the patients' body and the molecular tests can no longer tell whether that person had been previously infected. The means to test patients for a prior infection is to check for their **immunological status *vis-à-vis* the virus**. Knowing both who has had the disease, and what proportion of the population has immunity, are both potential key pieces of information in managing the spread of the disease without widespread lockdowns.

The development of an antibody response to infection may still take some time and it may be host dependent (i.e. vary according to the general characteristics of the tested person, such as their health status and previous exposure to similar pathogen agents). In the case of SARS-CoV-2, early studies suggest that the majority of patients seroconvert (i.e. start producing antibodies) between 7 and 11 days post exposure to the virus, although some patients may develop antibodies sooner (Wölfel et al., 2020[8]). This means that, unlike molecular tests, serologic tests are not suitable to identify who should be in isolation to avoid spreading the disease.

Immunologic testing can be done via two different techniques: **ELISA (enzyme-linked immunosorbent assay)** and **immunochromatographic assays** (also known as lateral flow tests, such as those used for birth pregnancy test) (see Table 1). Both techniques require a blood sample and aim at detecting antibodies (IgG and IgM) produced by patients' immune systems in response to an infection by the SARS-CoV-2. The types of tests under development mainly correspond to immunochromatographic assays and are frequently referred to as "rapid tests". At the moment, these "rapid tests" are reserved for professional use, but it is possible that they could at some point be sold to the general public for personal use.

It is important to bear in mind that these tests have not been fully developed for SARS-CoV-2 and their true clinical performance is mostly unknown. A negative test does not therefore rule out the possibility that an individual has been infected, and vice-versa. The interpretation of these tests requires a substantial amount of further analysis before they can be considered ready for utilisation at scale. Despite this, some regulatory authorities have recently changed their guidance to allow the launch of tests without approvals, so long as they are not used as the sole diagnostic.

As of 8 April 2020, only one serologic rapid test received an Emergency Use Authorization from the United States Food and Drug Administration[3]. A further 64 manufacturers have notified the agency that they have validated similar tests and may market them in the near future. The FDA will not oppose the entry into the market of these tests[4], but will only review the tests offered if companies request an Emergency Use Authorization. In Europe, 86 rapid serologic tests received a CE IVD marking, so can in theory be sold for use. However, the CE IVD marking does not necessarily mean that those products will immediately be available to purchase on the EU market as the manufacturer may decide to market them in countries outside the EU, or there may not be distributors selling these devices in all Member States (European Centre for Disease Prevention and Control., 2020[9]).

[3] https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations#covid19ivd.

[4] As stated in FDA's Policy for Diagnostic Tests for Coronavirus Disease-2019, the FDA does not intend to object to the development and distribution by commercial manufacturers, or development and use by laboratories, of serology tests to identify antibodies to SARS-CoV-2, where the test has been validated, notification is provided to FDA. https://www.fda.gov/media/135659/download.

Table 1. What tests are available in the context of the COVID-19 outbreak?

	Molecular diagnostic tests		Serologic tests	
Objective of the test	Detection of the virus presence in the organism		Detection of the immune response to the virus	
Technique	RT-PCR	Direct SARS-CoV-2 antigen detection (still under development)	ELISA tests	Immunochromatographic assays (rapid tests)
What does it look for?	Looks for the presence of viral genetic material (RNA) in a sample taken from the patient (usually a nasopharyngeal swab).	Looks for the presence of viral antigens in a sample taken from the patient	Looks for the presence of an immune response (antibodies) against the virus in the patients' blood.	
What does a positive test mean?	The virus is present in the patient.		The patient has been exposed to the virus and is either recovering or has already recovered.	
What is the test used for?	To know whether a patient is currently infected by the SARS-CoV-2.		To know whether a patient has been exposed to the SARS-CoV-2 and is therefore protected against new infections (and may not spread the disease anymore).	
Pros	- If done properly, the technique is very sensitive and specific - "Fast RT-PCR" can be used at point of care	- Simple; - Rapid; - Could be used at point of care.	- More precise than immunochromatographic assays. - Provides a quantitative information (concentration in antibodies).	- Less resource intensive than ELISA tests; - Could be performed at point of care once the technique is fully validated (could potentially be sold to the general public). - Rapid (10 to 30 minutes)
Cons	- Labour intensive; - Majority of tests still need to be processed in a lab; - Risk of false negative (mainly bad sampling); - Not all labs can process RT-PCR (need the right device and a special authorization to handle hazardous materials); - Possible shortages of swabs and reagents.	- Complex to develop.	- Possible false negative (if performed too early in the infection process as antibodies have not yet been produced) - Possible false positives (interaction with other diseases); - Needs to be performed in a lab; - Resource Intensive (1 to 5 hours); - Kits being produced not tested yet; - Possible shortages of reagents.	- Provides only a qualitative information (presence or not of antibodies) - Kits being produced not tested yet; - Possible shortages of reagents;

3. How testing can be used to manage the COVID-19 disease

There are three ways that testing can be used to manage COVID-19:

- First, strong and effective **testing, tracking and tracing** (TTT, Section 3.1) is needed. If implemented properly, TTT is the most promising approach in the short-run to bringing – and keeping – the epidemic under control *without* resorting to widespread lockdowns of social and economic life. This sort of approach also provides key intelligence on the spread of the epidemic.
- Second, serologic tests among targeted priority population groups (e.g. health and other essential function workers) are needed to assess their immunity, so could be used to let them work without the need for repeated isolation. Potentially, this approach could also be extended to cover more of the population, assisting in restarting economic activity (Section 3.2).

- Third, once rapid serologic tests are reliable enough for utilisation at large scale, widespread testing will allow the estimation of how far away we are from herd immunity in the population. This is crucial information to inform how to adjust social distancing measures (Section 3.3).

> An effective strategy that tests suspected cases, tracks people infected and traces their contacts (TTT) will help to reduce the spread of the #Coronavirus virus

3.1. Testing, tracking, and tracing of new cases to suppress local outbreaks

Preventing transmission to control the spread of SARS-CoV-2 is the main objective of any containment strategy. The approach of testing, tracking and tracing (TTT) has become a central tool for achieving this objective as many countries have decisively implemented it or are in the process of scaling it up. Likewise, WHO has recommended to "Prioritize active, exhaustive case finding and immediate testing and isolation, painstaking contact tracing and rigorous quarantine of close contacts" (WHO, 2020[10]).

The TTT approach may be used to block the initial or recurrent spreads of a pathogen, aiming for a rapid extinction of local, well defined outbreaks that collectively can control an epidemic. For diseases where infectiousness begins simultaneously with at the onset of symptoms, TTT can be very effective. For instance, TTT was applied in recent disease outbreaks such as the severe acute respiratory syndrome (SARS) in 2003, the Middle East respiratory syndrome (MERS) in 2012, and the Ebola virus disease in 2014.

In the case of COVID-19, studies have shown that a substantial proportion of secondary transmission of the virus may occur prior to illness onset in asymptomatic or pre-symptomatic individuals (Nishiura, Linton and Akhmetzhanov, 2020[11]). Therefore, for the TTT strategy to be effective, contact tracing should be extended to some days before the onset of symptoms in every diagnosed patient; implementation needs to be at large scale, which poses a number of problems particularly in large countries; and it needs to be implemented quickly, to minimise the lag between the onset of symptoms and isolation of infected cases. Examples from South Korea and Singapore show how they have managed to control the initial COVID-19 outbreak in a relatively short period of time by implementing a package of initiatives that had TTT as a key component. Box 2 describes their TTT strategies in more detail.

In the context of COVID-19, TTT involves:

1. **Testing**: the use of diagnostic tests for identifying the infection of SARS-CoV-2 in a person. Currently, the gold standard is a RT-PCR test, but some countries have introduced molecular rapid-tests relying on the same principles of RT-PCR but being faster and less resource intensive (see Box 1). Fast molecular tests can be used as confirmatory, becoming a very good alternative to RT-PCR tests to speed up and ease testing procedures. In the case of SARS-Cov2, expanding testing to asymptomatic or pre-symptomatic cases such as people who have been in contact with a confirmed case is particularly important, given the delay until the onset of symptoms.

- **Tracking:** identifying where people infected are, in order to provide the most appropriate management of the case, and to prevent further spreading of the virus. In the case of COVID-19, management of mild cases requires isolation and/or the provision of symptomatic treatment for a self-resolution of the disease, while management of severe cases requires more extensive provision of symptomatic treatment and supportive care in a hospital, including intensive care as needed. Accurate tracking of infected patients and monitoring of compliance with isolation measures is key to limit contagion.

- **Tracing**; locating all the people that were in close contact with a person confirmed with COVID-19, at least since the onset of their disease and ideally some days before that. These contacts should ideally be placed in quarantine for at least 14 days (the upper bound of the incubation period of COVID-19), either in their homes or in a specific facility. This also implies following-up of the contacts to monitor for symptoms and signs of infection, and testing then to check for disease infection.

Because of the specific characteristic of the SARS-CoV-2 virus (high infectiousness, long incubation period, presence of asymptomatic cases), **the effectiveness of TTT depends on both high speed and the accuracy through which this approach is deployed**. A recent outbreak modelling study (Hellewell et al., 2020[12]), found that contact tracing and isolation might not contain outbreaks of COVID-19 unless very high levels of contact tracing are achieved. For instance, the majority of scenarios with a reproduction number (or ability to spread of the virus, so-called R0) of 1.5 were controllable within three months with less than 50% of contacts successfully traced, while for R0 of 2.5 and 3.5, more than 70% and 90%, of contacts, respectively, had to be traced. In the case of SARS-CoV-2, R0 was initially estimated to be about 2.2 and 2.7, but the evidence is still inconclusive and more recent studies have reported results around 3, or even as high as 5.7 (Sanche et al., 2020[13]), compared to 1.3 for seasonal flu. The probability of control decreases with long delays from symptom onset to isolation, fewer cases ascertained by contact tracing, and increasing transmission before symptoms.

> To reduce the risk of new "2nd wave" outbreaks of the #Coronavirus, 70%-90% of all people an infected person comes into contact with need to be traced, tested & isolated if infected. This would require a huge increase in testing. The challenges & costs of doing this pale in comparison to consequences of another lockdown.

TTT must be considered as one element of a package of interventions to control the epidemic and phase-out the confinement/lockdown measures in place in many countries. The main purpose is to find and suppress as much as possible the local outbreaks across territories, which will require continuous effort to conduct effective TTT. In addition, TTT helps monitor the evolution of the epidemic, since effective testing and digitally-enabled contact tracing allows the disease spread to be tracked. This can provide essential information to estimate in real-time the reproductive number of COVID-19 at a given point in time in a given community. Combined with other health system information (e.g. number of ICU beds), this can guide decisions about the lifting and reintroduction of social distancing measures[5].

[5] https://www.nytimes.com/2020/04/06/opinion/coronavirus-end-social-distancing.html.

Box 2. Applying the test-track-trace strategy to control the COVID-19 epidemic

South Korea's widespread and digital TTT strategy[6]

Following the lessons learned from previous SARS and MERS outbreaks in the Asian region, South Korea (hereafter, Korea) has made a remarkable effort to control the COVID-19 epidemic, with one of the strongest TTT strategies in the world.

- Testing: as of 6 April 2020, Korea had conducted almost ten RT-PCR tests per thousand inhabitants, only behind Germany and Italy among countries with populations over 50 million[7]. This pattern can be explained by a mix of strategic, logistic, capacity, regulatory, and even cultural considerations. Korea developed a strong infrastructure for test kit production, distribution and laboratory analysis, after a strategic early decision to track most possible cases very strictly. Innovative solutions were developed, such as drive-through COVID-19 testing centres, where samples are taken while people stay in their car. More than 600 testing centres were installed, some of them having transparent "phone booths" where health workers administered throat swabs using thick rubber gloves built into the chamber's walls. Many offices, hotels and other large buildings installed thermal image cameras to identify people with fevers and many restaurants check customers' temperatures before accepting them.
- Tracking: after testing suspected cases, the ones testing positive are tracked and provided with treatment free of charge. The cost is covered by central and local governments and the health insurance public corporation. Korea also provides a subsidy to individuals who need to be isolated (both self-isolation and hospitalisation) to support their living costs and penalises those who are suspected to be infected if they refuse to receive diagnostic test, subsequent treatment or go through self-isolation. People ordered into self-quarantine must download a mobile phone application, which alerts officials if a patient breaks isolation. All these tools allow for an effective tracking of patients.
- Tracing: Korea has developed a diverse digital crowd-sourced contact tracing strategy.
  - Mobile phone locations are automatically recorded making possible to trace nearly everyone by following the location of their phones, which is facilitated by the fact that phone companies require all customers to provide their real names and national registry numbers.
  - CCTV cameras are used to identify contacts of COVID-19 patients. In 2018, Korea had over 1 million CCTV cameras in public places[8].
  - Credit and debit cards transactions are used to draw a card user's movement on a map, since Korea has the highest proportion of cashless transactions in the world.
  - When a person tests positive and all contacts cannot be identified, then detailed information regarding her/his movements is sent by text message to residents living nearby.
  - The result of these tracing schemes are made public via national and local government websites, free smartphone apps that show the locations of infections, and text message updates about new local cases.

Fines for quarantine violations can reach around EUR 2 300.[2]

[6] https://www.nytimes.com/2020/03/23/world/asia/coronavirus-south-korea-flatten-curve.html; https://theconversation.com/coronavirus-south-koreas-success-in-controlling-disease-is-due-to-its-acceptance-of-surveillance-134068.

[7] Our World in Data COVID-19 Testing dataset. https://ourworldindata.org/covid-testing. Accessed on 13 April 13 2020.

[8] https://www.statista.com/statistics/651509/south-korea-cctv-cameras/.

A downside of this tracing system relates to privacy issues surrounding the measures, which may also prevent some infected people from coming forward (OECD, 2020[14]).

Singapore's universal TTT strategy

Singapore has also put in place a strong TTT strategy that managed to control the COVID-19 epidemic without major disruption to daily living (Lee, Chiew and Khong, 2020[15])[9].

- Testing: Singapore initiated a large testing strategy for all suspected cases since the early days of the outbreak, reaching 2 200 tests (RT-PCR) a day for a population of 5.7 million. Testing was deployed in primary care and hospital settings, and drive-through testing stations. In addition, people that died of a possible infectious cause and influenza-like illness were tested in sentinel clinics.
- Tracking: A network of more than 800 public health preparedness clinics was activated in the primary care setting, with subsidies extended to residents to incentivise them to seek care, allowing to track many cases. Doctors were instructed to provide medical leave of up to five days for patients with respiratory symptoms, allowing them to quarantine at home. All confirmed cases were immediately isolated in hospitals to prevent onward transmission. Treatment costs were borne by the government, including for patients from abroad.
- Tracing: All identified contacts presenting symptoms were referred to hospitals for isolation and testing, and then placed under 14 days quarantine from the last date of exposure. To facilitate compliance and reduce hardship, the Quarantine Order Allowance Scheme provides economic assistance and the Infectious Disease Act provides legal power to enforce contact tracing and quarantine, and to prosecute those who do not comply (penalties can be EUR 6 400 fine, six months jail, or both). Collaboration exists between public health officials, the armed forces and the police to trace people, for instance, using CCTV footage and data visualisation, conducting labour-intensive detective-like investigations. The latter includes direct interviews with the patient and all identified contacts, calling them by phone requesting several details to determine their movement history seven days prior to symptom onset. Through in-person visits, a legal quarantine order is handed to each person. Investigation also includes receipts and card payments investigation to trace the movements of the infected person.

3.2. Who should be tested?

Deploying diagnostic tests more broadly can generate critical information about the presence of SARS-CoV-2 in the population, and therefore likely patterns of transmission and propagation. For example, supposing that the test could be administered to a large majority of people say every two weeks, it would be possible to isolate all those infected, and others could conduct a normal life. This would be enormously expensive, but the cost would nevertheless be trivial compared to the costs of lockdown. However, there are huge logistical challenges. In practice even with fast RT-PCR that can be administered at the point of care (see Box 1), it is unlikely that testing capacity will be sufficient for population-wide exhaustive testing. This means that it is necessary for authorities to prioritise who should be tested.

Testing strategies have to be feasible within the constraints of testing capacity and taking into account the transmission scenarios that are likely to occur. The WHO provides laboratory testing strategy recommendations specific to the number of cases an outbreak has reached in a country, between no and sporadic cases, to sustained community transmission (WHO, 2020[16]). In other words, there is a clear sequence of whom should be tested first, depending on the stage of the epidemic.

[9] https://www.bbc.com/news/world-asia-51866102.

Given the number of cases reached in most OECD countries at this stage, the priority for **molecular laboratory tests** will initially remain for ensuring safe and appropriate medical care, and therefore testing of ***hospitalised patients, vulnerable people*** who are likely to require hospital care ***and health care workers***. Once testing capacity is increased sufficiently, tests can be expanded to ***suspected non-severe cases and*** to ***people who were in contact*** with confirmed cases. This can allow targeted isolation of people who are infected, including those who show no symptoms. Molecular tests are informative about whether a person is infected at the time of the test. As discussed above, RT-PCR-based tests represent the most accurate testing method but are also resource-intensive and capacity is therefore constrained.

Germany is an example where capacity for lab-based molecular tests was built early in the disease outbreak. Broad testing has allowed targeted isolation of confirmed cases, even if they were not symptomatic. At the same time, vulnerable people who were infected could be hospitalised and received respiratory support before the onset of severe symptoms, increasing the odds of survival. These factors may have contributed to relatively low mortality in Germany, although a number of other factors also played a role, including that many of the people initially infected were relatively young and healthy. As of 11 April, 27% of those infected by COVID-19 in Germany are over the age of 60; in Italy, 63% of those infected are over the age of 70.[10]

In the absence of reliable information about contacts between people who carry the virus and others, people at risk of being so-called ***super-spreaders*** can also be a priority group for repeated testing. These are people who come into contact with many other people as part of their daily activities. Beyond health professionals, people working in supermarkets and grocery stores, public transport and in delivery services may be at higher risk of spreading the virus to many other people.

Serologic testing, which identifies antibodies produced by the human immune system can serve a different purpose. Their use requires that accurate serologic tests are available (see above) but in addition, ideally we would also want to understand better the immunological response, and its duration. For example, whilst it seems clear that having had the disease once confers some immunity, how long this immunity might last is unclear (Petherick, 2020[17]). Serologic tests can also be conducted in ***priority groups*** such as super-spreaders. There is a particular interest in the potential for serologic tests as part of a strategy to support restarting economic activity. Most obviously, testing health professionals would limit unnecessary self-isolation, and increase the capacity of the health sector. Beyond this, testing occupational groups who cannot telework during lockdowns; and priority segments of the workforce, to identify those already immune, may be useful in allowing more people to safely (return to) work. In addition to targeted testing of priority groups, testing can also take place in ***random samples of people*** for estimating prevalence and assessing progress towards herd immunity, as discussed below.

If rapid serologic tests are to be used to support people re-engaging in economic and social activity, then their **immunity status could be recorded** in a personal record, such as the “passports” being considered in Germany and the United Kingdom or the WHO vaccination certificate required for some international travel. People who have an immune response could be released from restrictions to movement, preferably in conjunction with a molecular diagnostic test to confirm that the person does not have an active infection. If new cases can be tracked and isolated effectively and transmission reduced, restrictions can also more readily be eased gradually for people who are not immune.

However, the use of ‘passports’ may have serious unintended consequences. People who are *not* immune may seek to expose themselves to the virus in order to gain immunity and (re)gain a more normal life and work. This would be a very understandable response, given that many people have lost the chance to earn their living and support their families due to the lockdowns. Unfortunately, the risk of such behaviour is that the disease may start spreading very rapidly once again, with the possibility that health services are

[10] https://www.statista.com/statistics/1105465/coronavirus-covid-19-cases-age-group-germany/ accessed on 11 April 2020, and https://www.statista.com/statistics/1103023/coronavirus-cases-distribution-by-age-group-italy/ also accessed on 11 April 2020. Countries have reported age distribution of infected cases using different age groups.

overwhelmed. Such 'passports' may need to be applied with other restrictions on who can return to work, such as region, age, and type of occupation, if this risk is to be contained.

3.3. Gaining intelligence on the evolution of the epidemic: Testing for population surveillance

In addition to targeted testing of priority groups, testing can be used to **estimate the prevalence of immunity in the general population**, which is called 'herd immunity'. This represents the "degree to which the community is susceptible or not to an infectious disease as a result of members of the population having acquired active immunity from either previous infection or prophylactic immunization" (Reid and Goldberg, 2012[18]). In the case of COVID-19, since vaccines are not yet available the only current possibility of acquiring immunity is through getting the infection.

Herd immunity can be measured mainly in two ways (Reid and Goldberg, 2012[18]):

1. Indirectly from the age distribution and incidence pattern of the disease, if it is clinically distinct and reasonably common. This is an insensitive and inadequate method for infections that sometimes display no symptoms, which is the case of COVID-19.
2. Directly from assessments of immunity in defined population groups by application of serologic tests, as discussed above.

The assessment of immunity at the population level (also called sero-surveillance (Wilson et al., 2012[19])) can help to determine the level of antibodies required to achieve herd immunity, to identify groups of susceptible individuals ('immunity gaps') and to evaluate the persistence and duration of protective antibodies. Into the future, sero-surveillance could provide relevant information to plan vaccination strategies, avoiding the need to vaccinate those who already have immunity.

The term 'herd immunity for elimination' refers to the level at which an infection can no longer propagate effectively in the population (Williams, 2006[20]). At this level of immunity, there may be some secondary cases or even short chains of infection ("clusters"), but these chains are eventually broken, the spread of the virus stops and the outbreak is eradicated. In other words, the effective reproduction number at a given point in time (Rt) in these circumstances is less than 1.0. In the case of COVID-19, it was initially estimated that herd immunity can be reached when 50% to 60% of the population is immune to the virus, although this may go up to almost 75% in the case of a higher reproduction number (OECD, 2020[1]).

In order to get a better estimation of the immunity against SARS-CoV-19 in a population, sero-prevalence surveys of a probabilistic population sample per country or regions in a country can be deployed (Wilson et al., 2012[19]). This would help to assess progress towards herd immunity, at least for the period of time during which immunity is active (in the case of SARS-CoV-19, the exact duration of immunity is not yet known), along with providing a baseline for monitoring into the future. These are also key parameters to decide to what extent restrictions (e.g. social distancing measures) can be eased or lifted (in case, for instance, some groups of people were maintained into confinement longer than the rest of the population).

As mentioned in Section 2.2, since tests are gradually being developed (and tested/approved), some countries have already began planning such sero-epidemiological studies. For instance, researchers in Germany are proposing to regularly test immunity of 100 000 people[11] that can allow the provision of 'immunity certificates' in the future, while the UK government has bought 3.5 million rapid immunity tests and is ordering millions more[12]. However, serologic tests' reliability is still a major issue so governments are struggling to select the most appropriate one and are waiting for independent tests validations to come out.

[11] https://www.thelocal.de/20200327/germany-plans-mass-immunity-study-to-track-virus.

[12] https://www.theguardian.com/world/2020/mar/25/uk-coronavirus-mass-home-testing-to-be-made-available-within-days.

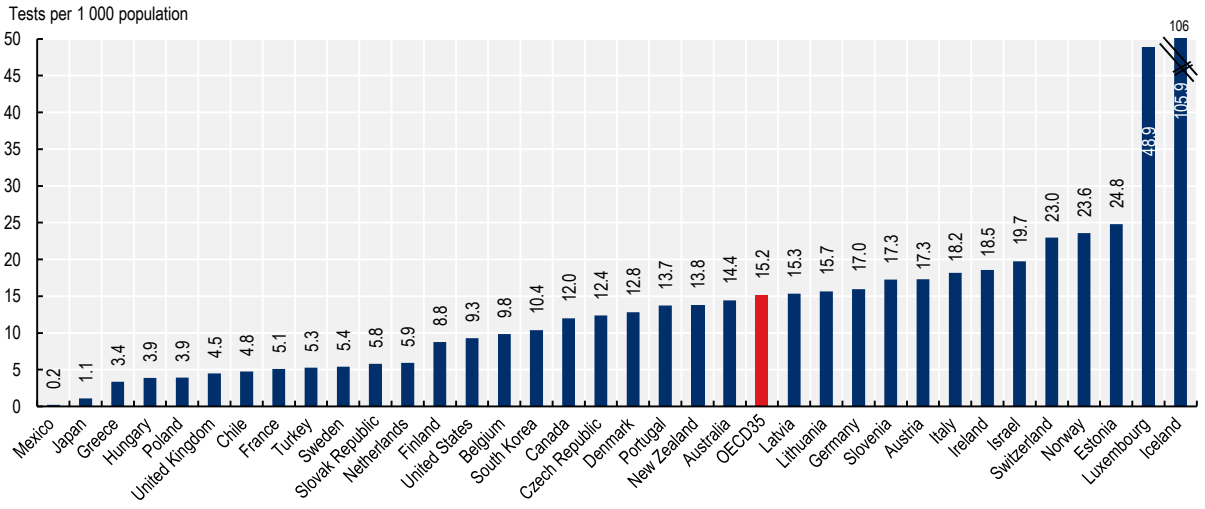
Another relevant factor has to do with better understanding the characteristics and evolution of the virus itself. So far, researchers have found that the virus is quite stable and does not mutate significantly[13]. However, this is another area where further research is desirable in order to inform policymaking.

Herd immunity is dynamic and can be lost over time through waning of immunological memory or deaths of immune individuals, and newly susceptible individuals arrive through births or migration (Reid and Goldberg, 2012[18]). Evidence from a survivor from the original SARS-CoV infection in 2002 indicates that, 17 years later, the person still has antibodies which are capable of neutralising the virus (Petherick, 2020[17]). Insofar as SARS-CoV-2 shares many characteristics with SARS-CoV-1, this gives hope that immunity for those who catch COVID-19 may be long lasting. However, immunity can also be diminished if the virus changes, as happens with influenza where a new vaccine is required every year. Therefore, the characteristics of immunity against SARS-CoV-19 still needs to be better understood, along with further rigorous assessment of serologic tests themselves.

4. Getting it done: Implementation aspects of testing strategies

Implementation of testing in OECD countries is varying rapidly. As of 15 April 2020, tests per 1 000 population in selected OECD countries varied from fewer than one to more than 100 tests per 1 000 population (see Figure 1).

Figure 1. Diagnostic testing for COVID-19 in selected OECD countries



Source: https://ourworldindata.org/covid-testing. Accessed 15 April 2020.

Successful implementation of testing strategies requires some practical problems to be overcome, and possible issues around data privacy to be addressed (OECD, 2020[14]).

> Testing for the #Coronavirus has varied widely across countries. To reduce the risk of new outbreaks, countries will need to greatly increase their testing capacity

13 https://www.washingtonpost.com/health/the-coronavirus-isnt-mutating-quickly-suggesting-a-vaccine-would-offer-lasting-protection/2020/03/24/406522d6-6dfd-11ea-b148-e4ce3fbd85b5_story.html.

4.1. The feasibility of testing strategies to inform management of COVID-19 restrictions

There are several **prerequisites for the feasibility of testing** as a key element for the transition away from current lockdown measures. These comprise scientific knowledge, planning demand for needed equipment and coordination in procurement, building capacity to execute tests, and managing information.

First, **scientific research on immunity** and how to test immunity needs to continue. It has to be entirely confirmed that immunity is indeed built for any person who got infected, and for how long such immunity lasts. So far, assumptions about immunity are based on animal models (Bao et al., 2020[21]), observational studies (Wölfel et al., 2020[8]) and what is known about immunological response to similar viruses (De Wit et al., 2016[22]). R&D towards producing accurate and reliable serologic assays for rapid testing of immunity has to be continued and recently developed tests need to be assessed by regulatory authorities using robust data. As stated in Section 2.2, although many tests are currently in development, and some are already commercially available,[14] anecdotal evidence suggests that many serologic tests currently available are not particularly accurate (Cassaniti et al., 2020[23]).

Second, governments need to make realistic **projections about the equipment necessary to execute large-scale testing strategies and coordinate procurement** at both national and international level. Demand projections and certainty about what will be purchased can help the manufacturing industry to build capacity. PCR-based tests require nasopharyngeal swabs for collecting samples, test kits with chemical reagents to isolate and prepare viral genetic material in the samples for analyses, laboratory machinery to conduct analyses, and protective equipment for personnel.

If procurement were coordinated at the international level, it would be easier to make sure supplies are available where needed most and to avoid shortages. The European Joint Procurement Agreement provides an example of how this can be done at the regional level. However, some governments have imposed export restrictions unilaterally and are engaging in buying practices that aim to secure priority access to supplies for their own populations.[15]

Third, **local capacity, including personnel, has to be built for executing tests**. PCR-based testing requires trained personnel to conduct the tests, defined procedures and laboratory infrastructure. Korea has shown how testing capacity can be called-up rapidly, including through the fast approval of test kits to be manufactured domestically, deploying resources to local manufacturers and using innovative solutions to make tests available to the population, such as drive-through testing facilities. Governments also need to monitor the pipeline of serologic tests that come to market, and assess if and how accurate tests can be scaled.

Finally, **information on infection and immunity status and contacts between people has to be managed efficiently** while respecting privacy. In addition to using more traditional methods, such as paper documents or personal "passports" that certifies infection and immunity status, digital solutions can play a key role here. They can allow for efficient tracking of contacts between people and integrate such information with infection and immunity status (Ferretti et al., 2020[24]). Governments have to move quickly to define data protection and governance frameworks, with proportionate protection of personal privacy while allowing for the use of personal information to protect public health. This issue is further discussed in the next section.

Successful implementation of testing strategies in developing countries requires addressing challenges, including higher budgetary restrictions, lower institutional capacity for procurement of equipment and

[14] A non-exhaustive but periodically updated list of tests and their development/regulatory status is available at https://www.finddx.org/COVID-19/pipeline/.

[15] See, for example, a regularly updated tracker of procurement actions by European governments published by MedTech Europe, the European trade association of medical device manufacturers, at https://www.medtecheurope.org/resource-library/covid-19-procurement-actions/.

supplies, lower installed laboratory capacity, fewer trained personnel to collect, analyse, and report results, and more complex logistics of reaching remote communities. The implementation of tracking and tracing strategies also involves challenges, given weaker data governance frameworks and less developed health information systems. Development assistance, both financial and technical, can play a key role to improve the feasibility of TTT in developing countries.

4.2. Balancing privacy and public health and security objectives

There is a tension between protecting privacy and civil liberties and providing public security in democratic societies. That tension becomes particularly acute in times of crisis. The SARS-CoV-2 is an invisible adversary that does not respect national boundaries. Limiting its spread and its impact upon the health of people and the functioning of health care systems is of utmost importance. While some degree of reduction of privacy protections may be necessary, this is not a given, and there are promising uses of digital tools and data that safeguard the right to privacy (OECD, 2020[14]).

The most comparable recent threat to public security in OECD countries is the threat of terrorism. In response to terrorist attacks, policy responses have impinged upon privacy to strengthen security (Jones, 2009[25]). For example, the use of closed-circuit television cameras (CCTV) in both public and private spaces rose markedly in many countries. The use of CCTV cameras became so pervasive in London that an individual's average city journey could result in hundreds of photos of them. In the United States, legal and procedural changes to search and surveillance after the 9/11 attacks empowered police to conduct on-going monitoring of citizens' physical movements and electronic footprint (Bloss, 2007[26]). Once new powers of surveillance are introduced, they tend to remain in place, even when the immediate threat abates.

For COVID-19, numerous surveillance technologies have emerged to monitor changes in the mobility of the population in response to social distancing and quarantine policies. In some cases, trackers utilise data from mobile phone apps where users have allowed the app to access location information. Examples are the Google COVID-19 Mobility Report and the Unacast Social Distancing Scoreboard (Google, 2020[27]) (Unacast, 2020[28]). The use of data from mobile apps raises concerns regarding informed consent, particularly when data uses and third party disclosures are explained within lengthy terms of service agreements that app users may not read. In Belgium, similar monitoring is enabled by aggregating de-identified data from three telecom providers (Cloot, 2020[29]).

Mobile data and associated technologies, such as GPS monitoring bracelets, are also being used to track specific individuals, either to ensure individuals maintain quarantine, or to identify individuals who have come in proximity to an infected person (Barrett, 2020[30]; Zastrow, 2020[31]). The European Commission has adopted a recommendation with steps and measures to develop a common EU approach for the use of mobile applications and mobile data[16]. For every 100 individuals living in OECD countries, there were 113 mobile broadband subscriptions in June 2019[17], suggesting the large majority of the population carries devices that can be used to create detailed logs of an individual's location over time. Location trails from various individuals can then be compared to enable contact tracing, and inform individuals who may have been exposed.

Informing individuals they may have been exposed to SARS-CoV-2 can be done in different ways (Raskar et al., 2020[32]), ranging from broad (i.e. the public) to targeted (i.e. specific groups or individuals) sharing of locations confirmed cases have visited while contagious. Location data can be shared with or without the consent of infected individuals. In principle, contact tracing using digital technologies and location data

[16] https://ec.europa.eu/commission/presscorner/detail/en/ip_20_626.

[17] OECD, Broadband Portal, www.oecd.org/sti/broadband/oecdbroadbandportal.htm.

can help with efforts to contain the spread of respiratory infections, but in practice there is significant uncertainty as to what are the true risks and benefits of such an approach.

There is a risk of public identification of individuals and resulting stigma, whether confirmed infected, suspected infected or susceptible, even with anonymised data (Rocher, Hendrickx and de Montjoye, 2019[33]). The identities of businesses visited by suspected or confirmed infected individuals may also be divulged, resulting in loss of revenues, even after these places have been closed and cleaned (Zastrow, 2020[31]). Extortionists can use digital contact tracing systems to demand ransoms from local businesses to not report themselves as sick and having visited the business (Raskar et al., 2020[32]). As with any information system, there are also cybersecurity risks and a potential for data breaches and ransomware attacks. Finally, without clear and actionable recommendations for individuals who have been exposed, there is a potential for misinformation, counterproductive behaviours or even panic.

Contact tracing may be possible, however, without sacrificing privacy. The Pan-European Privacy-Preserving Proximity Tracing (PEPP-PT) initiative aims to enable privacy-protective contact tracing (PEPP-T, 2020[34]). Individuals' mobile phones record Bluetooth handshakes with other mobile phones that have come into their proximity. The data are encrypted and stored on the phone. Should an individual test positive, health authorities will give them a code that they can voluntarily provide to a national trust service that runs the PEPP-PT app. The trust service sends an alert to the mobile phones that were in proximity to the infected case. Neither the infected person nor the exposed persons are identified. The Future of Privacy Forum has compiled information on various apps being used to track and trace SARS-CoV-2 infections.[18]

Crucially, there is limited real-world evidence of the cost-effectiveness of digital contact tracing, and several questions regarding its feasibility in the context of the current SARS-CoV-2 outbreak, as already discussed. Because digital contact tracing is still relatively novel, studies of its impact are either based on simulations (Ferretti et al., 2020[24]) or they are proof-of-concept pilots in low-resource settings (Danquah et al., 2019[35]). The simulations suggest that, given what we know about the COVID-19 epidemic, near-universal adoption and near-perfect compliance would be needed for digital contact tracing to be effective (Ferretti et al., 2020[24]). As mentioned above (Hellewell et al., 2020[12]), if the virus has a reproduction number of 3.5, contact tracing needs to be effective for some 90% of the cases for the effective reproduction number to come below one (indicating the epidemic is closer to being controlled).

As the number of cases rises, it becomes increasingly challenging to trace all the contacts of each suspected or confirmed case (ECDC, 2020[36]). The resources needed to follow up on each suspected case are significant, and there is a point at which extensive contact tracing may become unsustainable due to limited resources (ECDC, 2020[36]). This is all the more important given uncertainty in just how accurate underlying data used for digital contact tracing are. The precision of mobile location data is dependent on many factors, from cell tower positioning to skylines, and according to one estimate from the United States, the average distance between where a phone location is shown and where that phone is actually located is around 30 metres (PlaceIQ, 2016[37]). The accuracy may be worse when people are indoors and in densely populated areas, both of which are likely when countries are in lockdown. Bluetooth may be better and more privacy-protective (it is not location data), but not necessarily more accurate. Moreover, across OECD countries, only 63% of 55-74 year-olds actually used the internet in 2016[19], suggesting that some of the most important people to trace in the context of COVID-19 (i.e. the elderly) might not even be represented in the data.

In addition to mobile data, another privacy-intrusive technology is the use of drones (Doffman, 2020[38]). Some countries are using or considering deploying monitoring drones, to photograph people, to broadcast messages of the need to self-isolate and/or to take measurements of observed people including detection

[18] https://fpf.org/wp-content/uploads/2020/04/Privacy-Pandemics-The-Role-of-Mobile-Apps.pdf.

[19] OECD, ICT Access and Usage by Households and Individuals (database), http://oe.cd/hhind (accessed June 2017).

of fever, cough, and respiratory and heart rates (Pennic, 2020[39]). Both drones and CCTV cameras may be used with facial recognition algorithms (O'Donnell, 2020[40]).

All OECD countries either have existing legal provisions or may enact laws that enable infringement of privacy due to a threat to public security. In enacting new laws or provisions, individuals should have a right to a judicial remedy and the provisions should be time bound so that the surveillance does not become permanent. As United Nations experts (OHCHR, 2020[41]) have highlighted, "emergency responses to the coronavirus must be proportionate, necessary and non-discriminatory". Responses should align with the OECD Privacy Guidelines and with the OECD Council Recommendation on Health Data Governance, particularly with respect to public transparency of data uses (OECD, 2013[42]; OECD, 2019[43]). Ensuring a supervisory body or watchdog will monitor the implementation of surveillance technologies and inform the public of new surveillance technologies and of their rights is recommended.

As multiple countries move quickly to develop and roll out digitally enabled TTT, it is essential to weigh the prospective risks and benefits. Despite statements from international organisations and governments of the importance of data protection, many questions remain. For example, what type of data is being collected through these digital initiatives, with whom and how it is being shared, with what access and copy permissions, what algorithms are being used to analyse the data, with what robustness and validity, and what decisions are being taken based on these analyses. There is little to no clarity on these questions, notwithstanding numerous widely supported guidelines at international level for broad and inclusive oversight of digital tools with high potential for human rights abuse and violation. A digital approach to widespread use of TTT is likely to be a key part of a successful exit strategy, but for broad public trust, acceptance and use of such digital tools and data, the risks and benefits must be well understood and communicated to populations.

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