

COVID-19 CADTH HORIZON SCAN

COVID-19 Testing: A Summary of Testing Methods

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To produce this report, CADTH used a modified approach to the selection, appraisal, and synthesis of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

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Methods

This report presents an overview of emerging health technologies related to COVID-19 monitoring or diagnostic testing, a description of some of the published clinical studies, and a summary of some important considerations related to the potential implementation of these tests. This report was not prepared using systematic review methods and did not involve a critical appraisal or analysis of relevant study findings. This report is not intended to provide recommendations for or against the use of a particular technology.

Literature Search Strategy

A limited literature search was conducted by an information specialist on key resources including PubMed, MEDLINE and Embase via Ovid, the Cochrane Library, the University of York Centre for Reviews and Dissemination databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were COVID-19 and diagnostic testing. No filters were applied to limit the retrieval by study type. The search was limited to English-language documents published between January 1, 2019 and October 19, 2020. Conference abstracts were removed from the search results.

Study Selection

One author screened the literature search results and reviewed the full text of all potentially relevant studies. Studies were considered for inclusion if the intervention was a test related to COVID-19 monitoring or diagnosis. Conference abstracts and grey literature were included when they provided additional information to that available in the published studies.

Peer Review

A draft version of this bulletin was reviewed by a clinical expert.

Summary

- Tests for COVID-19 can detect signs of an active or past infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) — the virus that causes COVID-19.
- There are currently three main categories of COVID-19 tests: reverse transcription-polymerase chain reaction (RT-PCR), antigen, and serology.
- A variety of methods can be used to collect samples for COVID-19 testing.
- Testing is one component of a comprehensive public health strategy to combat the COVID-19 pandemic.
- The availability of tests, and the evidence to support their use, is rapidly changing.

Background

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 19 (COVID-19), was first detected in late 2019. Since then, there have been more than 46 million cases and 1.2 million deaths from COVID-19 worldwide.¹ In Canada, there have been more than 236,000 cases and 10,000 deaths reported.² The actual number of SARS-CoV-2 infections may be up to 10 times greater than reported, as not everyone who becomes infected gets tested for the virus.

Testing is an important part of a comprehensive public health strategy. Tests for SARS-CoV-2 can either detect the presence of the virus in the body (to diagnose a current infection) or can detect the presence of antibodies that have been developed after infection with the virus (indicating a past infection).³ The early diagnosis of COVID-19 plays a critical role in optimizing supportive care for individuals with severe illness⁴ and in containing the transmission of the infection through case identification, isolation, and contact tracing.⁴

In Canada, as of this writing, more than 9.5 million SARS-CoV-2 tests have been administered. This corresponds with a test rate of more than 250,000 tests per million people. The average overall test positivity rate has been approximately 2.4%,² with pockets of the country at times reaching positivity rates greater than 12%.⁵ Testing criteria and strategies vary across the country and within provinces depending on the directives of local health authorities.

The Technology

There are three main types of tests used in relation to COVID-19 monitoring and diagnosis: reverse transcriptase-polymerase chain reaction (RT-PCR), antigen, and serology. Each one identifies a different target and can best be used at different points in the course of infection. These tests can be evaluated based on their sensitivity (a test's ability to correctly identify the target that is indeed present in a person's sample) and specificity (the test's ability to correctly identify when there is no target in a sample). The higher the sensitivity and specificity values, the more confident we can be in the accuracy of the results of the test.

RT-PCR (Nucleic Acid Technology)

Polymerase chain reaction (PCR) testing is considered the "gold standard" for diagnosing an active SARS-CoV-2 infection.⁶ Reverse transcription-polymerase chain reaction (RT-PCR) testing looks for the presence of viral genetic material in the diagnostic sample and is usually done by trained professionals in a lab.³ These tests convert single-strand samples of ribonucleic acid, or RNA, into double-stranded DNA and then amplify the DNA into larger quantities that are easier for the test to detect.⁷

In general, swab samples are taken from the nose or throat, or saliva samples are collected, and then are shipped to a lab and processed.³ The turnaround time to receive the test results ranges from one to three days and may depend on testing volume.³ A positive test means that the person tested currently has the virus.³ RT-PCR tests are most often conducted in a lab, but some point-of-care (PoC) RT-PCR tests are available in some rural, remote, and isolated communities or in some high-risk areas, where faster test results are required.³

The FDA has published a list of the sensitivities of many of the RT-PCR tests that have received Emergency Use Authorization (EUA) relative to the FDA SARS-CoV-2 reference panel as a way to compare the tests' performances against each other.⁸ Not all manufacturers have submitted the reference panel data.

Antigen

Antigen tests for SARS-CoV-2 generally use lateral flow immunoassays to detect the presence of viral proteins and identify a current infection.^{9,10} The tests require a sample to be collected with a swab from inside the nasopharynx. After collection, the swab is mixed⁹ in a liquid reagent, which is then applied to the testing device.⁹ These types of tests are used for PoC diagnoses of other respiratory illnesses such as influenza, respiratory syncytial virus, and pneumonia, as well as other infections such as group A *Streptococcus* and malaria.¹¹ Antigen tests are generally less sensitive than RT-PCR testing. For this reason, they may be more likely to miss a case of COVID-19 and may be more appropriate for screening and monitoring the spread of SARS-CoV-2 rather than diagnosing COVID-19.⁶

There are different ways of interpreting the results of rapid antigen tests. Some use devices similar to pregnancy tests that visually display a positive or negative result,¹²⁻¹⁶ while others require the use of bench-top¹⁷ or hand-held¹⁸ analyzers to display and interpret the results of the test.

These tests are mainly being developed for rapid use at the PoC, which means that they can be used in a health care setting like a doctor's office, pharmacy, or assessment centre, and the samples do not need to be sent to a lab to be analyzed.¹⁹ The tests are generally easy to use, can be done by trained health care workers at the site, and results can be obtained quickly, usually in about 30 minutes.¹⁹ Faster results mean people with positive tests can be isolated more quickly and contact tracing can begin in a shorter time span.¹⁹ More information about rapid antigen testing is available in an earlier [CADTH](#) Horizon Scanning Report.

Serology

Serological testing measures the presence of antibodies in the blood. Antibodies are proteins produced by the immune system to protect the body from infection.²⁰ Serology tests are not meant to detect a current SARS-CoV-2 infection; instead they are used to detect antibodies that have been developed after the immune system has responded to the virus. This usually happens about seven to 14 days after the initial infection.^{21,22} Serology tests have been shown to be most able to detect antibodies about 14 days after infection.²³

There are three main types of serology tests: lateral flow immunoassay, chemiluminescence immunoassay, and enzyme-linked immunosorbent assay. More details regarding each of these test types is available in an additional [CADTH](#) Horizon Scanning Report on serological tests for COVID-19.

At this time, there is still uncertainty regarding immunity to COVID-19, as well as concerns around the accuracy of some serological tests. For this reason, in Canada, the role of serology tests in clinical care is limited.²⁴ The current focus of serology tests is on research on immunity and population-based studies to guide public health policies.²⁴

A government-funded COVID-19 immunity task force has been established to oversee the coordination of a series of country-wide serological test surveys. Data from these surveys will provide insight into the extent of the spread of the virus, its impact on populations at higher risk, and potential immunity.²⁵ As of November 2020, 28 research projects have been funded through the task force.²⁶

Summary

Table 1: Summary of Testing Methods for The Detection of SARS-CoV-2

Type of test	Looks for	Currently authorized sampling methods	Used for	Setting
Nucleic acid technology	Viral genetic material	Nasopharyngeal, oropharyngeal, nasal, oral, saliva	Screening, diagnosis	Lab and PoC
Antigen testing	Viral proteins	Nasopharyngeal, nasal, oral, saliva	Screening, monitoring	Lab and PoC
Serological testing	Antibodies	Blood (serum or finger prick)	Identification of past infection, immune response	Lab and PoC

PoC = point-of-care; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Sample Collection

There are a variety of methods for obtaining samples for SARS-CoV-2 testing using different collection techniques or different fluid for sampling. These samples can also be collected by different people depending on the test. Currently, most samples are taken by health care professionals in a clinical setting, but some self-collection methods are being studied. The type of sample collected will depend on the type of test being used.

It is the responsibility of the manufacturer of the test to properly assess the effectiveness and accuracy of sampling methods in combination with their tests. For example, if a manufacturer claims that their test works with nasopharyngeal samples, they must provide evidence of this prior to regulatory authorization.²⁷ The manufacturer would have to do more investigation to provide the necessary evidence that the same accuracy of results can be obtained from the test using another method of sample collection.²⁷

The same applies to who can perform a test. The regulator can only authorize a test to be administered by the groups of people who administered the tests in the clinical studies.²⁸ Just because a test seems straightforward to conduct does not mean the regulator can choose to allow at-home use or self-sampling for reasons of convenience to people wishing to get tested. If the manufacturer thinks its test can be used by lay people, and wants to market the test for that use, it is the responsibility of the manufacturer to provide evidence of the test's effectiveness when conducted by a user who is not a trained professional.

Sampling Sites

Nasopharyngeal

Nasopharyngeal samples are collected from the nasopharynx using a long swab that reaches where the nasal passages meet the throat (about as far back as your ear).²⁹ The swab is swirled around and then held in place for a few seconds to make sure enough secretions have been absorbed into the swab. The swab is then removed and placed into a sterile container and sent to a lab for processing or used immediately for a PoC test.²⁹ These samples are generally taken by health care workers, as they require a degree of skill to obtain an adequate sample.³⁰ This method of sample collection also involves a high risk of disease transmission and health care workers must wear appropriate personal protective equipment (PPE) to ensure

their own safety.³⁰ Nasopharyngeal sampling has so far been considered the standard for SARS-CoV-2 testing.

Oropharyngeal

Oropharyngeal samples are taken by swabbing the back of the throat around the tonsils.²⁹ The potential for disease transmission using this sampling method is the same as described for nasopharyngeal testing, since the proximity and exposure to the person being tested are the same for both methods.³⁰

Nasal

Nasal samples are taken by swabbing around the inside of the nostril for about 15 seconds to collect sample material.²⁹ These samples can be collected by health care professionals, but there is also the potential for self-collection.³⁰ Cross-sectional studies comparing the accuracy of nasal samples with nasopharyngeal samples for RT-PCR found that positive agreement of detection by nasal specimens relative to the nasopharyngeal specimens ranged from 81.0% to 100%.³⁰ Similar or greater detection of SARS-CoV-2 infection was found with self-collected nasal swabs versus clinician-collected nasopharyngeal swabs for RT-PCR.³⁰

Sample Types

Saliva

Saliva samples are collected by having an individual produce one to five millilitres of saliva and depositing it into a sterile collection tube.²⁹ There are different methods possible for producing a saliva sample. Saliva may be collected by pooling saliva in the mouth before spitting, repeatedly spitting into a container, coughing and pooling in the mouth before depositing the sample in the container, or by a passive drooling technique.³⁰ SARS-CoV-2 can likely be found in saliva samples within seven to ten days after symptom onset.³¹

Evidence from cross-sectional studies has been mixed regarding the accuracy of saliva sampling. Some research has shown that saliva samples have the potential to produce similar or higher SARS-CoV-2 detections rates with RT-PCR when compared with nasopharyngeal sampling³⁰ and others have shown saliva sampling to be less accurate, particularly in non-hospitalized patients.³² Some studies have shown that saliva samples collected early in the morning before eating breakfast and the brushing of teeth are able to produce the most accurate results.^{33,34}

In British Columbia, they have developed a “swish and spit” test for the detection of SARS-CoV-2 that has eliminated the need for swabs in some sample collections.³⁵ The method is intended for school-aged children. A sterile saline solution is swished for five seconds and gargled for five seconds, and repeated for a total of three swish-and-gargle cycles. The solution is then spit into a collection tube and sent for testing.³⁵ This method of sample collection and testing did not undergo Health Canada review or authorization, as it was developed by a lab, for use in that lab. Lab-developed and administered testing methods do not require the same review as those being marketed for sale.²⁸ More details about the use of saliva-based testing are available in an earlier [CADTH Horizon Scanning Report](#); however, due to the rapidly evolving evidence base and regulatory environment related to COVID-19 testing, some regulatory and evidence-based information may no longer be accurate.

Blood

Blood sampling is used for serological testing to detect antibodies. Samples for lab-based tests are usually taken from blood serum, whereas PoC tests may use a finger prick sample.³⁶

Self-Collected Samples

As sample collection can put a health care worker at risk for infection, efforts have been made to validate the accuracy of methods that allow people to take their own samples to provide for testing.³⁷ Self-sampling may also reduce the burden of sample collection on the health care system by reducing the resources required — both people and equipment.³⁷ It may also reduce the stigma for those being tested. Self-sampling may not work for everyone. It relies on an individual to have the physical capability to obtain the sample and transfers the burden of sample integrity and transport to the individual in cases where the sample needs to be mailed to a lab for processing. The agreement between clinician-collected oropharyngeal or nasopharyngeal swabs and self-collected lower nasal,³⁸⁻⁴⁰ throat,⁴⁰ and saliva samples^{39,41} was generally reported as sufficient to support the use of either sampling method.

Laboratory Techniques

Pooled Sampling

In pooled testing, samples from a group of people are mixed and processed by RT-PCR testing as one sample. If the pooled sample returns a negative result, everyone in the group will be considered negative for SARS-CoV-2. If the pooled sample produces a positive result, all samples that were a part of that group would be retested to determine where the positive result came from.^{42,43} Researchers have successfully evaluated pools of five, eight, and 10 samples, but indicated that the appropriate size of the sample pool may depend on the prevalence of SARS-CoV-2 in the testing population.^{42,43} Since about 98% of SARS-CoV-2 tests conducted in Canada have produced negative results,² pooled testing may be a way to reduce the number of tests, speed up testing times, minimize resource usage, and reduce waste associated with negative tests while still accurately capturing positive test results.^{42,43}

Regulatory Availability

The first test for SARS-CoV-2 that was used in Canada was developed by the National Microbiology Laboratory.²⁸ The nucleic acid-based testing method was validated and shared for use within public health labs across Canada.²⁸ Lab-developed tests are regulated in Canada by the provincial colleges of medicine, not Health Canada, and currently have a large role in COVID-19 testing. Labs can create their own sample collection and testing methods for SARS-CoV-2, and are responsible for ensuring that those tests are both safe and effective.²⁸

There are currently approximately 100 different commercial tests for SARS-CoV-2 identified as under consideration by Health Canada.⁴⁴ As of the end of November 2020, more than 45 commercial tests have received authorization for use under the interim order for importing and selling medical devices for uses related to COVID-19.⁴⁵ This includes laboratory- and PoC-based RT-PCR, antigen, and serology tests. The decision of how and where to implement each test in practice remains with the provinces and territories.

Health Canada has indicated it is open to reviewing all testing solutions, including self-collected or at-home tests.¹⁹ These types of tests would allow people with or without symptoms to assess and monitor their infection status as often as they felt necessary.¹⁹ The current

priority review areas of interest are rapid PoC PCR or antigen-based testing and tests using saliva samples.²⁸

Cost and Administration

In Canada, most tests for the detection of SARS-CoV-2 are publicly funded and the costs associated with procurement and administration are not clearly reported. The total cost of administering RT-PCR and serology tests would include the combined cost of testing equipment, testing supplies, and health care worker resources required to take the samples, ship the samples to the lab, and pay the salaries of lab workers to run the tests.

As an example of testing costs, an RT-PCR swab kit and test processing at government-run assessment centres in Ontario costs \$47.50, which does not include the additional costs associated with swab collection, patient assessment, and required PPE.⁴⁶ Pharmacies in Ontario that collect samples for RT-PCR testing on asymptomatic people are reimbursed \$42 per test for patient assessment and sample collection.⁴⁶ The province of Nova Scotia has made a deal with a private lab to provide COVID-19 testing for asymptomatic people who require a negative test result prior to essential travel or for compassionate reasons, such as visiting an ill relative or attending a funeral, at a cost of \$287.50 to be paid by the person requesting the test.⁴⁷ The Government of Nova Scotia is covering the cost of testing for people who are symptomatic or who have had close contact with someone with confirmed COVID-19.⁴⁷ Serology testing is available through some private labs in Ontario at an out-of-pocket cost of \$70 per test.⁴⁸

Tests administered at the PoC may be less expensive on a per-test basis because there is generally less equipment involved, there is no longer a cost associated with getting the patient samples to a lab for processing, and there may not be a need for health care workers to collect the samples or administer the tests depending on the test's design. The equipment is often simpler and costs less to produce than what is required in a lab. When used for screening purposes, tests are administered more frequently per individual, and could result in an overall higher cost of testing per person.

In the US, the rapid Abbott BinaxNOW COVID-19 Ag Card costs US\$5 per test.¹² This test can be used in combination with a free mobile app that provides the individual with access to their most current test results.⁴⁹ The BD Veritor System for antigen testing costs approximately US\$300 and an additional US\$20 per test conducted.⁵⁰ A rapid serological test by BTNX Inc. sells for approximately US\$10 per test.⁵¹

Who Might Benefit?

The ability to quickly and accurately test and diagnose people with COVID-19 is necessary to slow the spread of SARS-CoV-2. Testing benefits everyone. When a person is diagnosed with COVID-19, they can isolate themselves immediately and minimize the chances of the virus being spread to others. Isolating those who test positive early in the infectious period, and initiating contact tracing immediately, could potentially decrease the rate of community transmission.

Testing requirements vary by jurisdiction, but testing may be required for anyone who needs to confirm the diagnosis of COVID-19 due to symptoms or known exposure to a confirmed case. Testing may also be used for people who require tests for screening or monitoring for SARS-CoV-2 because they work (e.g., health care facilities, schools, factories, and so forth) or live in group settings that can put them at higher risk of infection.

The ease of use and short turnaround time of rapid testing means more people could be tested more quickly, potentially resulting in less productive time lost to waiting for tests and for results. More rapid testing could also lead to more frequent testing, allowing people with positive results to be identified in the earlier stages of infection.¹⁰ Using PoC testing has the potential to free up labs to do confirmatory RT-PCR diagnostic testing rather than it being used to monitor broad populations of asymptomatic people who want to get tested as a precaution before returning to school or work, or before travel. Overall, more testing options provide the opportunity for a greater proportion of the population to be tested and help to curb the spread of the virus.

Current Practice

RT-PCR testing is the current standard for the diagnosis of COVID-19 in Canada.³ Pan-Canadian COVID-19 testing and screening guidance was published on October 7, 2020.⁶ The intention of the guidance was to inform the best use of test resources and to suggest which test is most relevant in specific situations.⁶

Testing guidance suggested that PCR-based tests with high sensitivity should be used to provide a definitive diagnosis of COVID-19.⁶ Using PCR testing for people who are not showing any symptoms, or who have not had close contact with a confirmed case of COVID-19, is not recommended.⁶ There is the potential to explore alternative sampling methods, like saliva, for use with PCR tests. These tests are not ideal for high-frequency testing because of their cost and high requirements for both personnel and equipment.⁶

Screening is intended to indicate SARS-CoV-2 infection status. Screening can be done using more rapid testing techniques and may have lower sensitivity than diagnostic testing.⁶ Rapid tests typically require fewer resources and may allow for a higher frequency of testing and are more easily scaled to be able to efficiently test large numbers of people.⁶ Because of their lower sensitivity and specificity in relation to PCR testing, antigen tests may be best used in scenarios where both positive and negative results will be appropriately interpreted within the context of the setting.⁶ Health Canada released interim guidance on the use of rapid antigen detection for disease monitoring in October 2020.⁵²

Surveillance methods may be undertaken to monitor the levels of infection at a community level. Traditional and non-traditional (e.g., wastewater testing) data sources are used in combination with diagnostic and screening test data to provide a high-level overview of how SARS-CoV-2 cases are changing in a community.⁶

Each Canadian province and territory is responsible for determining how testing for SARS-CoV-2 will take place in that jurisdiction. Testing requirements may change as new evidence emerges about accuracy, speed, and availability of the tests. Links are provided in Table 2 to sites providing more information about COVID-19 and testing in each region.

Table 2: Links to Provincial and Territorial Testing Strategies

Province or Territory	Public Health Bodies
Alberta	Alberta Health Services
British Columbia	BC Centre for Disease Control
Manitoba	Manitoba Government
New Brunswick	Government of New Brunswick
Newfoundland and Labrador	Government of Newfoundland and Labrador
Nova Scotia	Nova Scotia Health Authority
Ontario	Public Health Ontario
Prince Edward Island	Government of Prince Edward Island
Quebec	Government of Quebec
Saskatchewan	Government of Saskatchewan
Northwest Territories	Government of Northwest Territories
Nunavut	Nunavut Department of Health
Yukon	Government of Yukon

Safety

No safety issues have been reported related to the collection of testing samples, although some people do experience discomfort from the deep nasal swab.⁵³

Harms

The rapid PoC antigen tests have been shown to have a lower sensitivity than the RT-PCR test. That means there is a higher chance of a false-negative result, which is a negative test result in a person who is positive for the virus.³ One of the ways this can happen is when the test is performed too soon after exposure to the virus and there is not enough viral antigen in the sample to result in a positive test.³ False-negative tests may result in further spread of the virus by people who have received a negative test result despite being unknowingly infectious to others.³

A risk of providing people with more frequent results from tests with lower sensitivity is the potential for behaviour modification based on those results. Compliance with public health measures may be decreased due to a false sense of security in the receipt of a negative test result that may be incorrect.⁵²

Concurrent Developments

On November 17, 2020, the FDA granted EUA for the Lucira COVID-19 All-In-One Test Kit — the first at-home self-test for SARS-CoV-2.⁵⁴ The test has been authorized for home use for people aged 14 years and older who are suspected of having COVID-19. The test is currently only available by prescription from a physician.⁵⁴ A self-collected nasal swab sample is placed in a vial, which is then placed into the testing unit. The results are available within 30 minutes and are displayed on the testing unit.⁵⁴ The Lucira test is also authorized for PoC use for people of all ages, but samples from people less than 14 years of age cannot be self-collected and must be obtained by a health care professional.⁵⁴

A rapid PoC antigen test that is able to detect both influenza A and influenza B, and SARS-CoV-2, at the same time has received EUA in the US.⁵⁵ A rapid PoC PCR test for the same purpose was authorized by Health Canada in November 2020.⁴⁵ Since COVID-19 and influenza present with some similar symptoms, this kind of test might be helpful to differentiate the source of infection as North America enters flu season.

Clustered regularly interspaced short palindromic repeats (CRISPR) technology is making its way into SARS-CoV-2 testing. These tests can produce results in about 20 minutes and do not need to be completed in a laboratory setting.⁵⁶ CRISPR pairs a protein with an RNA guide that looks for viral RNA. If RNA is detected, the protein starts slicing up the viral RNA into small strands. The sample can then be run through a flow detection system, similar to a pregnancy test. If there is no virus, the long RNA guide fragments will all be stopped in one location by the filter. If there is virus present, shorter bits of viral RNA will flow through the filter to stop at a different place on the test.⁵⁶ These tests also have the potential to test for other viruses at the same time as SARS-CoV-2, which could increase their potential usefulness.⁵⁶ Two lab-based CRISPR tests have received EUA from the FDA for the detection of SARS-CoV-2.⁵⁶ Regulators in India authorized a CRISPR-based test, FELUDA, in September 2020.⁵⁷ The test is paper strip-based, costs about US\$6.75, and can produce results in less than one hour.⁵⁷

Researchers at Oxford University are developing what might be described as a vending machine for COVID-19 testing.⁵⁶ A self-collected cheek swab or saliva sample is inserted into the stand-alone machine, where the test is run on the swab itself, and results can be reported in a few minutes. The researchers expect the test to be inexpensive and hope to bring it to market by mid-2021.⁵⁶

Researchers at the University of Miami are evaluating a rapid test that detects SARS-CoV-2 by analyzing droplets from a person's breath.⁵⁸ They intend to ask a random selection of students, staff, and faculty to volunteer a breath sample at the same time as getting their mandatory nasal swab for PCR testing and will compare the swab and breath results to each other.⁵⁸ The person breathes into a sterile tube that is then placed into a scanner that can then detect the presence of SARS-CoV-2. The device works similarly to a Breathalyzer used to detect blood alcohol content.⁵⁸ The test can return results in about one minute and is expected to cost "less than a cup of coffee."⁵⁸

In Taiwan, a company has modified surgical robots to be able to obtain nasal swab samples for SARS-CoV-2 testing.⁵⁹ The robot uses 3-D imaging to determine how deep to insert the swab and is guided by a nasal clip.⁵⁹ The intention of using robots to collect SARS-CoV-2 samples is to reduce the amount of exposure for health care workers.⁵⁹

Looking Forward

Screening and Monitoring

Researchers at the University of Ottawa and CHEO have undertaken a wastewater tracking project to measure and monitor the levels of shed virus in Ottawa's wastewater.⁶⁰ Clinical studies have shown that most people with COVID-19 shed SARS-CoV-2 in their stool, sometimes before they are even showing symptoms. The virus is then flushed into the wastewater system, where levels for the whole city can be monitored.⁶⁰ This surveillance method could prove to be a good signal of the actual level of COVID-19 in the community, as it incorporates data from everyone, not just people who are tested, and can show increases in

community infection days before the testing numbers catch up.⁶⁰ Other cities around the world have started similar monitoring programs.⁶¹

An artificial intelligence (AI) model has been developed at the MIT–Massachusetts Institute of Technology that detects asymptomatic COVID-19 by analyzing forced coughs that are recorded with a smartphone.⁶² The researchers have trained the AI using a database of tens of thousands of recorded coughs, including people who were diagnosed with COVID-19. The model was able to correctly identify 98.5% of all the coughs from people diagnosed with COVID-19 and 100% of the coughs from people with an asymptomatic diagnosis.⁶² The team is working to transform the model into an app for submission to the FDA. If it is approved, the app could provide a simple way for people to screen themselves daily for possible infection with SARS-CoV-2 and quickly alert them to seek out confirmatory diagnostic testing.⁶²

Over two days at the beginning of November 2020, Slovakia tested two-thirds of its population for SARS-CoV-2 using rapid antigen tests.⁶³ Testing was free and voluntary, but anyone who was unwilling or unable to be tested, or received a positive result, was required to self-quarantine for two weeks. A total of 3,625,332 tests were administered, with 38,359 returning a positive result, or a positivity rate of 1.06%.⁶³ The intention of the testing push was to get control over the recent increase in cases without having to institute country-wide lockdown measures.⁶³

The city of Liverpool, England started testing everyone who lives or works in the city for SARS-CoV-2 in November 2020.⁶⁴ The city has recorded one of the highest rates of coronavirus-related deaths in England.⁶⁴ Tests will be provided regardless of whether a person is showing any symptoms of COVID-19 and will be administered every two weeks. The testing program will use a mix of rapid antigen testing and RT-PCR testing.⁶⁴

Travel

Beginning in November 2020, cruise ships were once again departing from US ports. The cruise ship industry has agreed to mandatory SARS-CoV-2 testing prior to boarding for all ships carrying more than 250 passengers.⁶⁵ One cruise line has installed a full-scale testing lab onboard one of its ships in preparation for its return to sailing. The lab has the capacity to test all passengers and crew onboard each day using saliva samples and PCR testing.⁶⁶

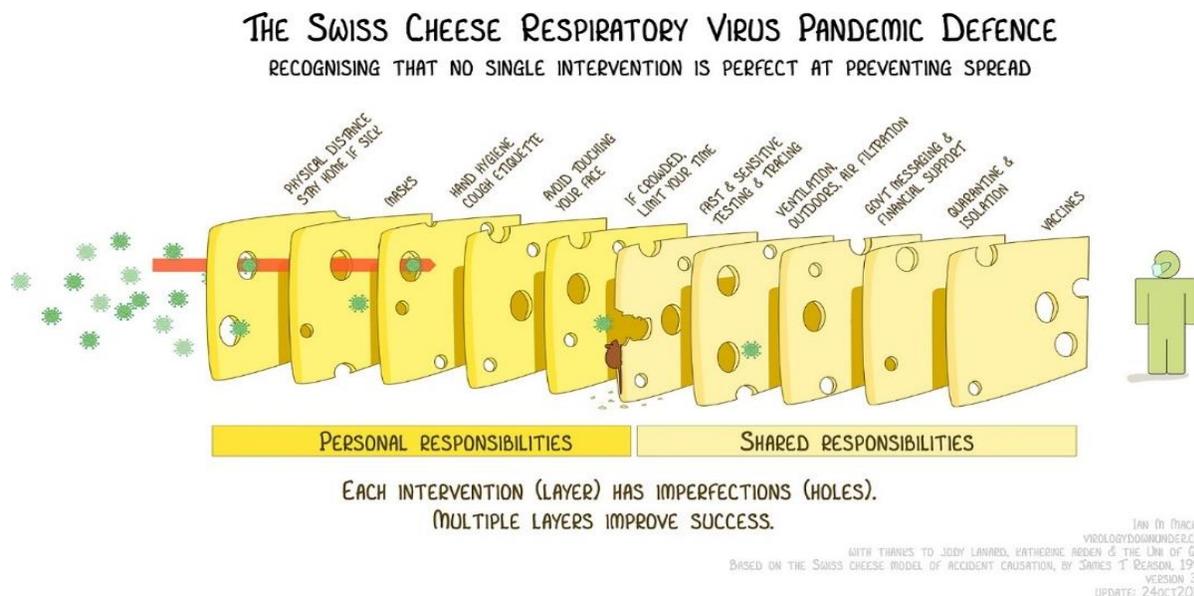
Testing has begun at airports prior to travel or upon arrival at the airport. In Finland and the United Arab Emirates, COVID-19–sniffing dogs have been seen in airports screening travellers.⁶⁷ There are additional studies underway in the UK and the US to assess the accuracy and training requirements necessary to make dogs useful in this capacity.⁶⁷ Dogs may not be able to diagnose an active SARS-CoV-2 infection, but the method could be used to screen large numbers of people quickly and identify people who should undergo further testing.⁶⁷ Some airlines have started offering free rapid COVID-19 testing to all passengers and crew at the airport before boarding.⁶⁸

A pilot project to reduce the currently required 14-day quarantine period for Canadians who have travelled internationally was launched in Alberta on November 2, 2020.⁶⁹ Canadians showing no symptoms of COVID-19 returning to Canada at the Calgary International Airport and the Coutts land border crossing will have the option of providing a sample for a test upon entry. They will then be required to quarantine until they receive their test results in one or two days.⁶⁹ If the results come back negative, they will be allowed to leave quarantine and take another test at a local pharmacy six or seven days after arrival. All participants in the pilot must stay in Alberta for 14 days, report on their health daily, and adhere to a list of conditions.⁶⁹

Issues to Consider

Testing is just one part of a comprehensive public health strategy. There are multiple layers to public health. While no one intervention is 100% effective, the more layering of them together, the better overall chance there is of the interventions working. This is sometimes referred to as the “Swiss cheese model” (Figure 1).⁷⁰ Each intervention is represented as a piece of Swiss cheese — they all have holes but, when stacked on top of one another, the slices overlap and the holes get blocked.⁷¹ When it comes to the COVID-19 pandemic, the slices fall into two categories: personal and shared responsibilities.⁷¹ Personal responsibilities include: physical distancing, staying home when feeling unwell, wearing masks, hand hygiene, cough etiquette, avoiding touching one’s face, and limiting time in crowded spaces. Shared responsibilities include: fast and sensitive testing and contact tracing, adequate ventilation and air filtration, government messaging and financial supports, quarantine and isolation measures, and effective vaccines.⁷¹

Figure 1: The Swiss Cheese Respiratory Virus Pandemic Defence



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Under laboratory conditions, the RT-PCR test is quite accurate. However, that reflects a perfect analytic environment. In reality, testing is conducted in the real world, in overburdened clinical and community settings, where test result accuracy may be influenced by inefficient sampling, lab contamination, sample degradation, contamination during sampling or swab extraction, contamination in the lab, or other sources of error.⁷²

There have been some hesitations about adopting lower-sensitivity tests as a diagnostic tool because of the potential for false-negative results and the unintentional spread of SARS-CoV-2. While antigen testing is generally less sensitive than RT-PCR RNA testing, these tests might be useful as a screening or monitoring tool, as they are inexpensive, fast, and could be administered often.⁷³ The CDC—Centers for Disease Control and Prevention has indicated that the tests are sensitive to high viral loads and people with asymptomatic infection are likely at the highest risk of spreading SARS-CoV-2 without realizing it.⁷³ More frequent testing of

asymptomatic individuals could result in infectious cases being isolated sooner and potentially preventing further spread, although no rapid tests are currently authorized for this use. Screening tests for SARS-CoV-2 could be especially helpful in large group settings such as long-term care homes, correctional facilities, workplaces, or schools.¹⁰ More than 3.8 million rapid COVID tests were distributed to Canadian provinces and territories starting in November 2020, but they have not yet been fully incorporated into testing programs because of hesitations regarding their accuracy.⁷⁴ Many rapid results are still being verified using PCR testing.⁷⁴

Information from antibody testing, if accurate, could provide insight into the transmission of COVID-19 and may inform policy decisions on return to work, the use of PPE, the continuation of social distancing practices, and attendance at large gatherings.⁷⁵ The loosening of restrictions put into place due to the COVID-19 pandemic will be influenced by the characteristics of different community populations and will be linked to their vulnerability and immunity to the infection.⁷⁶

As with all things related to COVID-19, testing is evolving rapidly. More tests for the screening and diagnosis of SARS-CoV-2 are under development and will likely be submitted to regulators in the near future.

Final Remarks

Testing is an important and evolving factor in the management of the pandemic. For testing to be an effective part of public health strategy, it must be easily and equitably available to all who need it. This would include both the location of, and access to, testing locations and ensuring enough tests, equipment, and people have been secured to provide an adequate number of tests relative to demand. The COVID-19 pandemic has magnified existing direct and indirect societal inequities. Public health measures like quarantine, physical distancing, and testing do not have the same impacts on everyone. These factors are important when assessing interventions related to COVID-19.

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