COVID-19: Point-of-Care (POC) Testing

A Rapid Guidance Summary from the

Penn Medicine Center for Evidence-based Practice

Last updated April 30, 2020 4:00 pm All links rechecked April 29 unless otherwise noted.

Key questions answered in this summary

- What are the characteristics of currently available COVID-19 tests that can be interpreted at the point of care?

Assessment of the comparative effectiveness of saliva samples vs. swab samples for detection of SARS-CoV-2 infection is outside the scope of this report.

Summary of major findings

- There are presently no FDA-approved tests for SARS-CoV2 or COVID-19 disease. All tests in current use are being used under an Emergency Use Authorization from FDA.
- There are three authorized tests that can be performed using a point-of-care PCR testing device in a clinic or other care setting. They require a specialized analyzer and trained operator. The devices can only perform one test at a time so throughput is limited by the number of devices available. Results are available in 13 to 45 minutes.
- Test results submitted as part of the FDA authorization process suggest that these point-of- care PCR tests have good sensitivity for detecting the SARS-CoV-2 virus. Direct evidence on the clinical effectiveness of these tests is lacking.
- The current point-of-care tests require a swab specimen from the nose or throat. Some approved laboratory tests can be performed on samples of saliva or sputum. The effectiveness of any test is also dependent on obtaining a good-quality specimen.
- While some of those laboratory tests are described as “real time,” they typically take a minimum time of 2 to 3 hours to complete.

Public health agency and professional society guidelines on point of care testing

Source	Recommendations
CDC April 27	For initial diagnostic testing for COVID-19, CDC recommends collecting and testing upper respiratory tract specimens (nasopharyngeal swab). CDC also recommends testing lower respiratory tract specimens, if available. No guidance for what type of test to use.
IDSA April 29	Guideline for diagnostics remains under development.
NIH April 29	No guidelines for diagnostic testing.

Health technology assessment reports on point of care testing

Source	Recommendations

ECRI	No reports relating to point of care testing for SARS-CoV-2. ECRI has issued a policy paper on antibody testing. ECRI has also issued a technology briefing on point of care molecular analyzers which includes pricing data and purchasing considerations for this device. Availability of the report is limited to subscribers to ECRI's services.

CADTH (Canada)	No reports relating to COVID-19 testing. A 2016 report on point of care influenza testing may be of interest.
NICE (UK)	No reports relating to COVID-19 testing.
INAHTA	A search of the Health Technology Assessment database (currently in pre-release status) found no reports on COVID-19 testing
HIQA (Ireland) April 22	Pathogen detection tests (such as RT-PCR) and tests to detect an immune response to the virus (development of SARS-CoV-2-specific antibodies) should not be considered competing alternatives. Both testing approaches are clinically relevant, but must be deployed at different time points during the clinical course of infection taking consideration of their relevant diagnostic windows. PCR is the 'gold standard' recommended for use by the WHO and ECDC for the diagnosis of COVID-19 cases during the acute phase of infection. It is indicated for the detection of SARS-CoV-2 RNA early in the clinical course of infection. False negative results can occur if testing takes place in the initial incubation period following infection. The minimum duration from infection to a positive test remains uncertain. Using PCR, SARS-CoV-2 viral RNA can be detected one-to-two days prior to symptom onset in upper respiratory tract samples. Microfluidic lab-on-chip technologies and genetic sequencing do not appear to be used at a national level in any country for the detection of COVID-19. Although not yet CE-marked, a microarray respiratory panel incorporating SARS-CoV-2 is reported to be in use in the UK. New technologies for the diagnosis of COVID-19 are rapidly emerging and regulatory agencies are responding quickly to this emerging pathogen. Forty-two laboratory-based RT-PCR tests were identified, 17 of which were identified as being CE-marked by the manufacturer. Of the 17 devices, five manufacturers reported diagnostic test accuracy results. Clinical sensitivity ranged from 89% to 100%, and clinical specificity ranged from 98% to 100%. Given the need for specialised equipment and reagents, technically skilled staff and potential long turnaround times with RT-PCR, alternative diagnostic methods with comparable accuracy and reduced operational requirements are needed. There is evidence to suggest that nucleic acid detection-based methods such as CRISPR and RT-LAMP may have comparable diagnostic test accuracy to RT-PCR, and may have operational advantages in terms of ease-of-use and turnaround time. Many of these devices are still in the development stage. In our initial review, commercially available CE-marked tests using these methodologies were not identified. The pre-analytical phase can be a major source of errors in diagnostic testing. To mitigate such risks, training and quality assurance procedures are required to ensure that test samples are appropriately identified and reported (right result, right patient), and to ensure adequate procedures for correct specimen (for example, swab) collection, handling, transport, and storage. Point of care tests are not suitable for high-throughput testing. RT-LAMP is a faster and more convenient method for SARS-CoV-2 RNA detection requiring fewer laboratory resources and has the potential to extend the capacity of laboratories to process 2.5 more clinical samples relative to qRT-PCR. No CE-marked RT-LAMP technologies have been identified, although a number are reported to be in development. Many of the rapid tests available and in development for the detection of SARS-CoV-2 are based on antigen and antibody immunoassays. The majority of rapid tests are based on lateral flow assays, cellulose-based devices intended to detect the presence of a target analyte in a liquid sample. As highlighted previously, with antibody and antigen-based tests there is a potential for cross-reactivity to proteins common to other types of coronavirus. Reliable measures of the diagnostic test accuracy of newly developed tests will require independent validation studies. *CEP NOTE: This report includes a comprehensive list of tests being marketed in various countries.*

CEP NOTE: Health technology assessment agencies provide guidance on drugs, devices, and other products used in health care. Their reports may include reviews of clinical evidence as well as information on suppliers, pricing, the state of development of the technology, and potential impact of the technology on the health care system.

Evidence reviews on point of care testing

Reviewer	Findings
Wales April 23	Health Technology Wales (HTW) Researchers searched for, appraised and summarised all published evidence on the diagnostic performance, effectiveness or economic impact of tests used to detect the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus to inform COVID-19 diagnosis. We identified 22 studies reporting diagnostic accuracy, detection rates and the time taken to obtain test results. The majority of studies (20/22) tested hospitalised, symptomatic patients with a strong clinical suspicion of COVID-19. Studies in people with milder symptoms are comparatively limited in number (two studies). All the tests studied used laboratory-based polymerase chain reaction (PCR) protocols, with one exception; a single study of loop-mediated isothermal amplification assay. The majority of studies investigated tests at an early stage in their development, before any wider deployment and commercialisation. We did not identify any evidence on the effectiveness of any specific commercially available tests for the presence of SARS-CoV-2. Tentatively, it appears the type of sample obtained, the part of the body sampled, and the timing of test relative to symptom onset could be influential on test results and accuracy, but we did not identify evidence with enough certainty to guide how these factors could be used to optimise testing. There are important gaps in the available evidence on the effectiveness of tests for the presence of SARS-CoV-2. We did not identify any studies of virus testing in asymptomatic patients, or in any specific populations such as healthcare workers. Furthermore, no evidence is available for any point-of-care tests. We did not identify any evidence on the economic impact of any test, or how any test influences subsequent patient management.
CEBM (Oxford) April 20	Many diagnostic tests for coronavirus disease 2019 (COVID-19) are available so far, with more gaining emergency approval every day. These tests are largely based on four different techniques, 1) reverse transcription polymerase chain reaction (RT-PCR) – the current standard test for COVID-19, 2) loop-mediated isothermal amplification (LAMP) – a simple, but less developed testing method, 3) lateral flow – hand-held single-use assays providing results for an individual patient in as short as 15 minutes, and 4) enzyme-linked immunosorbent assay (ELISA) – quick and technically simple assays that are easily read and offer relatively high throughput.
CEBM April 7	Moving diagnostic testing for COVID-19 from laboratory settings to the point of care is potentially transformative in the rate and quantity of testing that could be performed. Eleven diagnostic tests that are potentially suitable for testing for COVID-19 at the point-of-care are described: six molecular tests, and five antibody-based tests. Some devices show high diagnostic accuracy during controlled testing, but performance data from clinical settings, and a clear understanding of the optimal population and role for these tests in the care pathway, are currently lacking. Each of the point of care tests presently available in the US had sensitivity of 100% and specificity of 100% in small trials of laboratory samples (known viral content) reported to FDA. [Click here for evidence table] *CEP NOTE: the CEBM report makes reference to the possibility of using saliva samples in the MicrosensDx COVID-19 Point-of-Care Test. However, this device has not received marketing approval or emergency use authorization yet. The manufacturer is seeking CE marking to permit sale of the device in Europe: no plans for marketing in the US have been announced.*

Description of FDA-authorized tests

Point of care reverse PCR tests

As of April 29, FDA has granted Emergency Use Authorization for three commercial products with COVID-19 tests that can be run in patient care settings (i. e. point of care tests). All three of these tests require nasal or throat specimens on swabs: they cannot test saliva or blood. The tests come in single-use cartridges that include the reagents and substrates necessary to carry out a reverse polymerase chain reaction (PCR) test (please see below for explanation of the process). The sample is placed in the cartridge and the cartridge is loaded into a machine that automates the testing process. These machines are used for other PCR tests, so they are

already situated in settings like hospitals, doctors' offices, and pharmacies.

- Xpert Xpress SARS-CoV-2 test (Cepheid Corp., Sunnyvale CA)
- Accula SARS-CoV-2 Test (Mesa Biotech Inc., San Diego CA)
- ID NOW COVID-19 (Abbott Diagnostics, Scarborough ME)

Note: please click the name of the test for the FDA authorization, and the name of the manufacturer for the manufacturer's site.

Cepheid states that its system can provide results in 45 minutes. Only one sample can be tested at a time but up to 16 test modules can be connected to a GeneExpert hub, so total daily throughput depends on the number of modules. Mesa states that its system takes 30 minutes to complete a test: daily throughput was not reported. Abbott states that its system can give results in 13 minutes or less and process up to 470 patient samples in 24 hours, but CEP believes that actual throughput will be less if some tests are negative or are positive with lower viral levels that take longer to detect.

Each of the manufacturers reported results from trials of their systems as part of their FDA filings. Samples of known viral content and known virus-free samples were analyzed with the devices. For each device, sensitivity and specificity were both 100%, but the trials included only 30 to 50 positive and negative samples each so the 95% confidence intervals on sensitivity and specificity could be as broad as 86% to 100%.

Laboratory reverse PCR tests

FDA is granting Emergency Use Authorization to individual laboratories for molecular-based tests developed in those laboratories for detection of nucleic acid from SARS-CoV-2. Each laboratory intending to perform these tests must develop their own protocol and apply for authorization. Laboratories must be previously certified to perform high-complexity tests. As of April 29, there are 22 such authorized laboratories, including the C hildren's Hospital of Philad elphia (CHOP). Emergency Use Authorization has also been granted for various commercial in vitro diagnostic products working on the same principle.

The CHOP test appears to be typical of the real-time reverse PCR assays. It can test respiratory specimens supplied either from nasal or pharyngeal swabs, nasopharyngeal or tracheal aspirates, or bronchial lavage specimens. It is not authorized for testing of saliva samples, but some other tests of this type are. RNA is extracted from the specimen using an automated extraction device (available from several suppliers). The RNA is then reverse-transcribed to cDNA and amplified using an automated PCR device (also available from several suppliers). It is used with a primer/probe set specific to a gene of the SARS-CoV-2 virus and a control primer/probe set. If the target gene RNA is present in the specimen, the probe is cleaved during the PCR, which makes the fluorescent marker detectible.

According to the FDA summaries, the analytical sensitivity of these tests is on the order of 10 to 20 RNA copies per microliter (cp/µl). The turnaround time is not reported in the FDA summaries, but other PCR assays require approximately 2 to 3 hours to complete.

Serologic tests

Serologic tests identify antibodies specific to the SARS-CoV-2 virus. They do not identify the virus itself. Those antibodies indicate that a person has been previously been exposed to the virus and has had an immune response, but at present, it is not known whether or not those antibodies confer immunity to future COVID-19 disease. Serologic tests are being offered by commercial suppliers under FDA Emergency Use Authorization. None are presently authorized for point of care use.

Guidance sources

CADTH–Canadian Agency for Drugs and Technologies in Health CEBM–Centre for Evidence-Based Medicine (Oxford, UK) ECRI–ECRI Institute (non-profit health services research company) HIQA–Health Information and Quality Authority (Ireland) IDSA–Infectious Disease Society of America

INAHTA–International Network of Agencies for Health Technology Assessment NICE–National Institute for Health and Care Excellence (UK)

Wales–Health Technology Wales

About this report

A Rapid Guidance Summary is a focused synopsis of recommendations from selected guideline issuers and health care systems, intended to provide guidance to Penn Medicine providers and administrators during times when latest guidance is urgently needed. It is not based on a complete systematic review of the evidence. Please see the CEP web site (http://www.uphs.upenn.edu/cep) for further details on the methods for developing these reports.

Lead analyst: Matthew D. Mitchell, PhD (CEP) Evidence team leader: Emilia J. Flores, PhD, RN (CEP) Reviewer: Nikhil K. Mull, MD (CEP)