HOW READY IS THE US TO DIAGNOSE COVID-19?

By Kristen Cook, Bob Lavoie, Joe Bernardo, Laura Furmanski, Barry Rosenberg, and Josh Kellar

This is the first in a series of short articles on the role of testing in combating the COVID-19 outbreak. While the responsibility for diagnosis falls primarily on medical professionals and the companies that support them with equipment and supplies, business leaders need a baseline of knowledge on how testing works, what it is used for, and how it can help them restore operations and public confidence once the immediate emergency has passed.

No subject related to COVID-19 has received more attention than diagnostic testing. Wall-to-wall media coverage, combined with concern over the availability of diagnostic kits, has led to confusion and sometimes fear.

The ability to accurately diagnose the disease is a prerequisite for treating it and ultimately for overcoming the public health emergency. There is also an urgent need to move beyond the immediate medical priority of testing—determining whether individuals require treatment—to the ability to aggregate test data on a population-wide basis (in a region or segment of people, for example) in order to get our arms around how the virus is evolving. Even once the peak is well in the past, the need for testing will continue as governments and businesses look to reestablish public confidence and bring staff back to work safely. (A rapid mobile field test could aid in the recovery of industries such as travel and transportation, for example.)

Recognizing that the situation is changing extremely fast, here is our assessment of the current state of testing capability in the US and its likely evolution in the near and medium term. Our analysis and conclusions (which do not cover diagnostic imaging) are based on our work with leading international and national test manufacturers and lab services providers as well as our own internal team of more than 500 medical professionals and life scientists.

A Complex Landscape

Diagnostic testing for viruses has three main components:

- The instrument platform—the testing equipment that is already installed in hospitals and labs across the country
- The test kits themselves, the cartridges that contain the reagent or chemicals needed to test each sample
- The sample collection kits, which are needed to collect, preserve, and transport the patient sample for testing

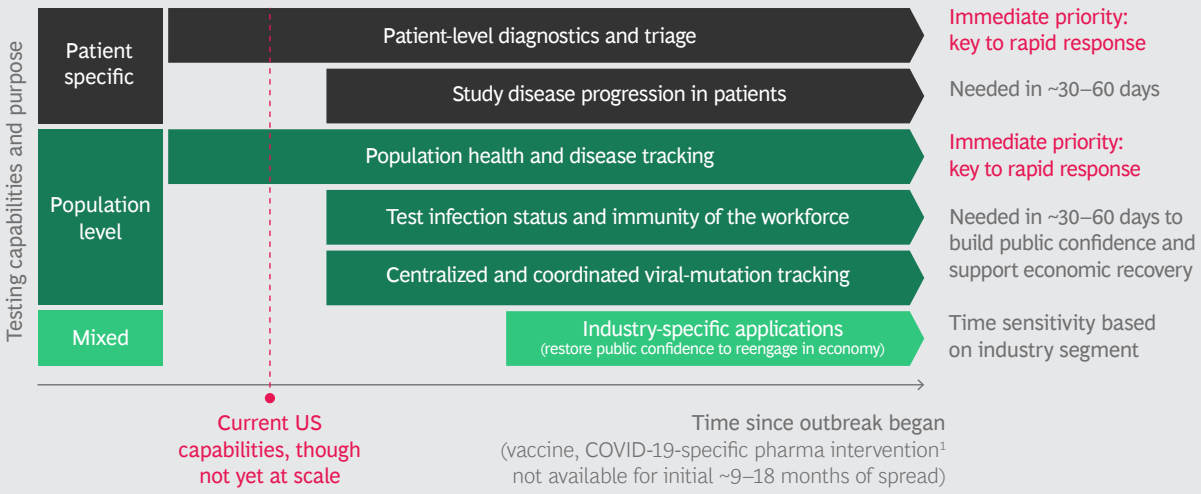
No single diagnostic test is perfect for all uses. There are tradeoffs across four key dimensions that need to be considered:

- **Speed.** The time from "sample to answer," including sample collection, the logistics to move the sample to the lab, sample processing, and the level of automation involved, which affects the time it takes to run and interpret the test results.
- **Accuracy.** The fidelity to detect COVID-19 when and only when it is present (avoiding false negatives and false positives).
- **Sample Type.** The type of clinical sample, such as oral or nasal swab, blood sample, or sputum. There are implications for access, cost, and accuracy.
- **Cost and Pricing.** The cost per test, which is a factor of the reagents (chemical ingredients) needed as well as the labor to collect and process the samples. Typically, the level of automation, proximity to the patient, and sample-to-answer speed determine pricing.

In the early days of a pandemic such as this one, testing provides essential information on the scale, location, and trajectory of the disease. As the pandemic evolves, diagnostic testing will be required for evaluating the infection status of symptomatic patients, identifying asymptomatic carriers, and confirming the immunity of exposed populations. (See Exhibit 1.) In addition, we will need to track how COVID-19 might mutate; if it does, diagnostics will need to adapt. Ultimately, tests will help ensure that people can get back to work and will help reestablish public confidence in various sectors of the economy.

When we talk of "tests," however, we are actually referring to a couple of different types of diagnostic tools and processes. The initial US response to rapidly increasing demand was a test developed by the

EXHIBIT 1 | Testing Needs Will Evolve Through the Course of the COVID-19 Outbreak



Source: BCG analysis.
[1]Only supportive and symptomatic therapies are currently available; R&D activities ongoing to develop COVID-19-specific novel drugs and repurpose existing drugs.

CDC as well as a series of tests developed by others and approved under the FDA's Emergency Use Authorization (EUA). The majority of currently approved tests are lab-developed tests (LDTs), which are deployed at large academic medical centers and reference laboratories and cannot be scaled up quickly.

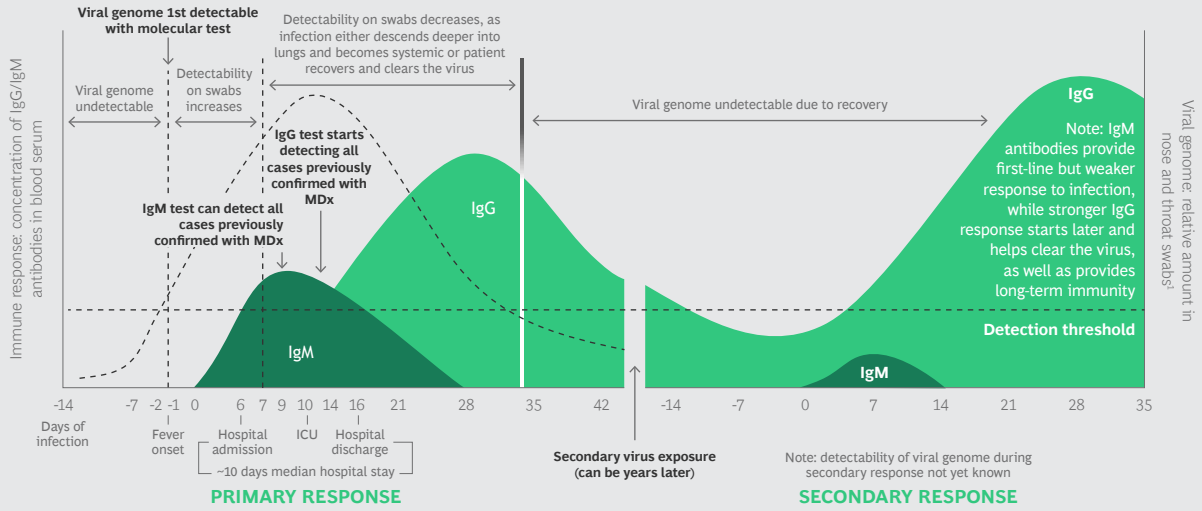
In vitro diagnostic (IVD) tests, which can be deployed more broadly than LTDs by tapping into the extensive installed base of testing platforms at hospitals and labs throughout the country, are now in accelerated development. The widespread use of IVDs will make timely, onsite testing available at most large hospitals. It also will enable consistent comparison from one lab to another—which is important for assessing and building a database of results—and will speed and expand our ability to diagnose individual patients, track and predict hot spots of the outbreak, and monitor how the virus itself mutates to create different strains.

Within each of these broad test categories, there are multiple types of tests appropriate for various use cases. One type, which is becoming more widely available now, is molecular diagnostic testing that detects the presence of the viral genome. These tests are particularly useful for the diagnosis and triage of patients, monitoring the spread of disease, identifying strains and mutations (including next-generation sequencing), testing the infection status of a workforce segment, and producing industry-specific apps to rebuild customer trust. Viral-genome tests can detect COVID-19 one to two days before symptoms appear. (See Exhibit 2.)

Another type of test, which is expected to appear soon on the market, assesses the development of the immune response to the virus in patients by detecting the presence of two different types of antibodies (IgG and IgM) that the body produces in response to the infection. Immune-response tests don't achieve the same detection rate as viral-genome diagnoses until 9 to 12 days later. While they are less useful in the immediate response, they can still help track disease development and will be essential in the event of a secondary recurrence of the virus (as occurred with the Spanish flu in 1918), because the viral genome is no longer detectable after patient recovery. These tests can help detect the immunity

EXHIBIT 2 | Two Types of Tests Have Different Strengths and Use Cases

Viral-genome test detects COVID-19 1–2 days before symptoms; immune response (IgG/IgM rapid) tests take 9–12 days longer



Sources: Wang et al., *JAMA* (2020); IgG/IgM product insert materials; expert interviews; BCG analysis.
Note: Detectability of viral particle not shown as test currently does not exist.
[1]Current tests detecting presence of viral genome are qualitative and are not meant to measure absolute amount of viral genome present (i.e., viral load).

of an exposed population, monitor the spread of disease, test the infection status of a workforce segment, and study disease progression. They can also be used for industry-specific diagnostic apps.

Two other types of viral test are not yet available for clinical use for COVID-19. Viral-load diagnoses assess the amount of viral genome in patient samples and can be used to monitor disease progression and predict whether a patient is still infectious. They require large amounts of data to link test results and patient outcomes. Tests for the presence of viral particles have the potential to enable rapid, point-of-care testing but require a validated antibody against the virus. Both tests typically take 6 to 12 months or longer to develop.

The Current State of Testing

The FDA, using its EUA authority, has approved several tests for the detection of COVID-19 viral genomes and continues to review and approve other tests for various COVID-19 uses. More than 30 viral-genome tests are available now, and efforts are scaling up. (See Exhibit 3.) The nation's full infrastructure of qualified labs and diagnostic-testing platforms is being activated and expanded to meet testing demand, including about 7 IVD tests from the CDC and diagnostics companies and more than 25 LDTs from reference and hospital labs.

More of both types of test are expected to launch in the coming weeks. While the FDA is rapidly approving tests, there can still be a lag of up to three weeks from approval to full deployment of IVDs because of the time needed for shipping as well as setup and validation within each clinical lab. Given the proliferation of testing, the FDA and the industry need to ensure that appropriate quality control mechanisms are put in place to maintain accuracy and comparability.

No immune-response tests have been authorized to date, although the first could be available in the next two weeks. Several tests are pending in—or preparing for—EUA review, and more companies have announced their intent to develop similar products. The utility of these tests, however, is limited to determining previous exposure and subsequent recovery from the disease. They are not intended to diagnose ongoing infection or screen asymptomatic carriers in the general population.

A major factor in testing is the time that it takes to get results. This depends in large part on the distance that patients or samples must travel to test facilities. Results

EXHIBIT 3 | More Than 30 Tests for Viral Genomes Are Available Today Including Both LDTs and IVDs

	DESCRIPTION	ADVANTAGES	DISADVANTAGES	PROVIDER EXAMPLES
Laboratory-developed tests (LDTs) 26+ launched to date	• "Home brew" that is designed, manufactured, and used within a single lab • Individual labs responsible for certification and approval • Not meant for distribution to other labs	• Individual labs able to start development immediately • Standardized use for each LDT/lab	• Many different LDTs needed for broad testing coverage • Lot-to-lot variability in reagents • Certification and filing for approval needed for each lab • Each lab needs access to viral material to develop and validate the test • Instrument access and staffing limitations	New York State Department of Health University of Washington Virology LabCorp NorthShore University Diagnostic Solutions Stanford Health Care UNC Health Arup Laboratories Quest Diagnostics BioReference Laboratories Viracor Eurofins
In vitro diagnostic tests (IVDs) 11 approved to date	• Off-the-shelf commercial test kits • Designed and manufactured by a commercial supplier for use by multiple customer labs • Manufacturer responsible for validation and approval • Labs responsible for certification for use	• Scalable: a single test can be broadly distributed • Internal resources and infrastructure for logistics and regulatory approval • Can get large batches of reagents from same lot to reduce variability	• Individual tests often compatible only with specific platforms • Time required to scale production and distribution	CDC Roche Danaher/Cepheid Quidel BioFire Defense DiaSorin GenMark Abbott Thermo Fisher Scientific Hologic Novacyt/ Primerdesign Mesa Biotech

Needed to achieve reliable testing at scale

Source: BCG analysis.

from reference labs, for example, can take one to four days from collection to results, depending on the distance. Packaging and transporting samples increase the overall time required. The range of time needed for hospital lab results depends on the distance between the collection site and the laboratory. Even if the sample is taken onsite, results can take 24 hours. High-performing onsite molecular labs can achieve sample to answer in less than 12 hours to inform triage in hospital emergency rooms.

Clinical testing performed at the time of care delivery with fast (near-patient) or instant (point-of-care) results is essential to make immediate decisions about patient care, but this capability has the furthest to scale up. Some rapid near-patient tests have just been approved for use in hospital and clinical settings, and many more new tests are expected to launch in the coming weeks, including much-needed rapid near-patient and point-of-care solutions. Near-patient testing comes with tradeoffs, including higher costs and the need for operators with technical skills. For instance, one technical operator can either process four cartridges at a time on a 35-pound near-patient platform, such as Cepheid's GeneXpert IV, or run hundreds of samples a day on a Roche Cobas system in a centralized hospital lab.

In time, we will need to get testing still closer to patients—in pharmacies and potentially remote sites for some industries (such as airports and large workplaces). As we learned from the H1N1 flu experience, however, many rapid tests launched and approved under EUA during outbreaks are later pulled off the market by regulators because of poor performance.

Other Factors to Consider

Several labor and materials considerations, occurring at multiple stages of the diagnostic process, will also affect our ability to realize universal testing coverage and capacity. At the sample collection stage, for example, there are potential shortages of swabs, collection tubes, and personal protective equipment—as well as of skilled technicians and nurses. The *New York Times* reported on March 20 that the company that supplies 50% of the sample-collection swab market in the US is based in Italy and struggling to keep up with demand at home while operating in lockdown conditions.

There are other requirements as well. Transporting samples needs a robust logistics infrastructure, insulated packaging, and dry ice. It also involves nontechnical and clinical logistics workers, such as handlers and drivers. At the lab, sample preparation requires lab staff, RNA isolation kits, sample tubes, pipettes, and pipette tips. And running the actual tests involves more qualified technical personnel, testing kits, reaction reagents, as well as reaction tubes and microplates. In practice, actual testing capacity is often about one-third of the theoretical maximum, after accounting for workflow timing, equipment maintenance, quality control, and fluid refills. Additionally, many machines require batches that run for three to six hours, while other machines permit "random access" of individual urgent samples.

What Does the Future Hold?

Much remains to be learned about COVID-19, including the impact of non-pharma interventions to slow the disease spread and "flatten the curve" and how the virus could mutate, which will affect infection and mortality rates and the ability to diagnose illness through testing. If history is any indicator, though, we know that all tests are not created equal and that the testing landscape will evolve toward fewer, more reliable tests even as it sees the introduction of new tests for new use cases. For instance, not every patient presenting with symptoms is necessarily infected with COVID-19. We are likely to see broader respiratory panels, such as Qiagen's QiaStat-Dx Respiratory Panel, approved in Europe. Such equipment can be used to diagnose more than 20 respiratory viruses, including the virus that causes COVID-19, in one test. Such capabilities typically come at higher costs and are generally available only on dedicated instruments.

The medical community will begin to pick winners and losers as COVID-19 test comparability data becomes available. This will be a positive development so long as winners can manufacture and distribute tests quickly and at sufficient scale. At the same time, innovation will continue to enable new uses, such as COVID-19 tests as part of broader respiratory panels, tests for patient antibodies to COVID-19 that can prove immunity (or resistance), and rapid tests (less than one hour) that can detect the virus outside of a clinic setting.

As a result, we expect testing platforms to consolidate around fewer validated providers. Once the FDA lifts EUA, test providers will need formal regulatory clearance (or will need to withdraw their test from the market). As testing scales up, priorities will quickly shift to securing the full supply chain including critical inputs such as test supplies and collection inputs (swabs) and an adequate supply of qualified technical labor.

Given the unprecedented number of tests coming to market, there is an urgent need for quality control and quality assurance infrastructure, especially while the FDA EUA is in force. Until we know that the available tests are of similar quality and deliver comparable results, the onus will be on business leaders to carefully scrutinize test suppliers that come to market with point-of-care tests but that lack strong track records in the industry.

As everyone looks for the silver bullet that will get the general population back to work and restart industries, we are already seeing unscrupulous players (mostly from outside the US) make dubious claims, including touting head-to-head "comparable results" with approved US tests. We expect to see a rise in such purported solutions as industry subsegments from airlines to hospitality to law enforcement to education search for answers to their particular needs. Once the immediate public health crisis has passed, navigating the selection of near-customer testing options will fall on the shoulders of business executives looking to restore confidence and climb the recovery curve.

Testing capabilities and capacity need to catch up with COVID-19: the virus is spreading exponentially while diagnostic testing is scaling at a linear rate. The industry is on the case—more than 20 companies have new solutions under active development. The immediate shortfalls between demand and supply will start to close. But it is more and more evident that the COVID-19 emergency has a good while to run. As we move more deeply into the crisis, and eventually contemplate recovery, executives in all sectors will confront the need for some type and extent of testing. It is not too soon to start contemplating what each industry's and company's specific testing needs might be, to outline the parameters, and to begin working with test manufacturers to develop solutions that go beyond traditional testing in hospitals and labs. We will need to test in easy-to-access sites, such as pharmacies and mobile locations, until vaccines or other therapies are available.

We are only 100 days into understanding the biological behaviors of COVID-19. Expanded testing, along with clinical interpretation, will enable physicians to treat COVID-19 patients and will allow executives to get their companies back in business.

About the Authors

Kristen Cook is a principal in the Chicago office of Boston Consulting Group. You may contact her by email at cook.kristen@bcg.com.

Bob Lavoie is a managing director and partner in the firm's New York office. You may contact him by email at lavoie.bob@bcg.com.

Joe Bernardo is a senior advisor in BCG's Boston office. You may contact him by email at bernado.joe@advisor.bcg.com.

Laura Furmanski is a managing director and partner in the firm's Bay Area–Silicon Valley office. You may contact her by email at furmanski.laura@bcg.com.

Barry Rosenberg is a managing director and senior partner in BCG's Chicago office. You may contact him by email at rosenberg.barry@bcg.com.

Josh Kellar is a managing director and partner in the firm's Chicago office. You may contact him by email at kellar.josh@bcg.com.

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