HARVARD MEDICAL SCHOOL | BLAVATNIK INSTITUTE GLOBAL HEALTH & SOCIAL MEDICINE

The COVID Collaborative*
INTERSTATE ACTION TO SOLVE THE TESTING CRISIS

OVERVIEW

The Immediate Crisis

The United States stands to lose the war on COVID19 due to an acute testing backlog and delays in processing and reporting of diagnostic tests for SARS-CoV-2 (the virus that causes COVID19). With cases surging, efforts to slow the spread of the virus, in the absence of large-scale lockdowns, are dependent on the robust identification of cases through widespread testing and tracing of contacts. Without timely case finding (diagnosis), and tracing and testing potential exposures (contact tracing), halting chains of transmission is an exercise in futility.

As a result, we are at a unique moment of vulnerability: While innovations in testing at scale are on the horizon, we are still dependent on one type of SARS-CoV-2 test (i.e., RT-qPCR) that is run on a limited number of platforms by a small number of commercial and other laboratories with an insufficient supply of testing materials and reagents. While many states had hoped to reduce transmission enough to rely on broad surveillance testing by the fall, surging caseloads across the country are undermining that strategy. This crisis affects all states because uncontrolled viral spread in one area of the country poses a threat to all areas of the country.

The Solution: The Governors' COVID Action Alliance

Cross-state, collective action can solve the testing crisis, which is why we propose the establishment of the Governors' COVID Action Alliance. This Alliance would expand and surge states' existing and latent testing capacity and allocate it as a common resource across states according to need. States that need tests will be able to access excess capacity elsewhere, while states that have already made significant investments in testing capacity will have an insurance policy against future outbreaks and surges.

The immediate goal is to expand testing capacity and resource utilization of member states so as to eliminate > 24-hour delays in testing within the next 4-6 weeks. The Alliance will do this by setting testing priorities; funneling testing resources to where they can save the most lives; pooling resources to address supply deficiencies; ensuring interoperability among state testing protocols and laboratories, and measuring progress using a common set of metrics.

Building on the Interstate Compact

These efforts would complement the recently announced Interstate Compact.[1] While that initiative expands point-of-care testing for individual states, the Alliance would also create a shared supply of point-of-care tests, expand multiple types of testing, and enable *cross-state sharing* of capacity to respond to urgent testing needs. The Alliance will ensure that testing capacity reaches the right person, at the right time, in the right place. The COVID Collaborative can provide negotiations support, technical assistance, and a real time problem-solving platform.

* The COVID Collaborative, powered by UNITE.us, is a consortium of health, education, and economic leaders and institutions designed to develop consensus action plans to contain SARS-CoV-2, and safely and sustainably reopen schools, businesses, and communities. The COVID Collaborative has commissioned Harvard Medical School's Program in Global Public Policy to consult with the nation's leading public health experts and institutions and produce a consensus action plan to alleviate the nationwide surge in demand for COVID testing over the next 2-12 weeks (see Appendix B for explanation of Harvard Program)

THE NEED FOR A COORDINATED INTERSTATE TESTING STRATEGY

Statement of the Problem

Testing is the backbone of any public health intervention to combat the spread of an infectious disease. Testing facilitates basic medical and public health interventions (treatment and breaking of transmission chains), but also provides visibility into where the disease has spread and where it might be going.

Over recent weeks, increases in testing wait times have been widely reported, with many patients waiting up to 14 days for SARS-CoV-2 testing results. By the time an individual receives these delayed results, they may no longer be infectious, rendering the results useless and allowing local outbreaks to initiate and spread undetected. This undermines the benefits of any test and trace strategy, imperiling our efforts to contain the epidemic and limit the economic and social damage it is doing. This crisis is compounded by the lack of a nationwide understanding of testing, reagent, and processing gaps, and the fact that states do not report testing data using common metrics.

The Imperative for Interstate Action

Without a cross-state coordinated approach to surge testing capacity and relieve testing backlogs, the COVID19 crisis is likely to continue well into 2021 and possibly beyond. The impact of reopening economies, schools, and travel is causing states where spread had been deemed to be "controlled" to observe increases in SARS-CoV-2 cases, requiring increased testing to cope with suspected new cases. However, the lack of adequate testing capacity and the existence of major testing backlogs pose risks to all states, whether transmission is currently contained or uncontrolled. In states and communities where viral spread is contained, testing backlogs still result in transmission before diagnoses can be made. In states experiencing uncontrolled spread, testing backlogs may put health systems at risk and expose health care professionals to infection. The dependence on commercial testing companies means that all states experience testing backlogs once their local capacity, consisting of state and hospital labs, is exceeded.

Seizing the Opportunity: The Governors' COVID Action Alliance

The Governors' COVID Action Alliance will establish a coordinated testing strategy and address testing shortages by pooling resources to maximize existing and expanded testing capacity. Several factors create the opportunity for the Alliance to be successful in these efforts:

- There is excess SARS-CoV-2 diagnostic testing capacity that is not being utilized currently at both state labs and academic centers.[2]
- State labs have demonstrated an ability to expand testing capacity through collaboration with local private partners, which could be replicated across states.[3,4]
- The Interstate Compact and federal efforts, such as NIH's Rapid Acceleration of Diagnostics (RADx) initiative, have the potential to increase the availability of point-of-care testing in the coming weeks to months.[5]

However, even as capacity is expanded, NIH officials note that "managing the distribution and implementation of tests into the appropriate venues and geographic localities will be critical" and that a plan for achieving this does not necessarily exist.[6] The Governors' COVID Action Alliance will fill this void.

Alliance Functions and Membership

As a first order of business, the Alliance will serve as a vehicle for setting testing priorities, expanding testing capacity, managing national testing surge needs, and ensuring interoperability between state testing protocols. These elements will form a national testing strategy that will, in the immediate term, reduce or eliminate the testing backlog and prepare the United States to adopt a medium and longer-term strategy to control the virus.

In order to promote decisions made in the interest of public health, the Alliance should consist of states that are committed to evidence-based public health interventions to contain the spread of SARS-CoV-2. Member states would be incentivized to adopt these interventions because of the additional testing capacity and support the Alliance will provide.

Urgent Actions

To resolve the immediate testing crisis, the Alliance must act rapidly to:

- Expand testing capacity by mobilizing third party, academic, and veterinary research labs; optimizing existing capacity by ensuring interoperability among state public health laboratories; creating surge capacity for point-of-care tests, reagents and supplies; and lessening the need for testing.

- Facilitate interoperability of testing systems by developing guidelines and standards to manage logistics and prioritize needs.

- Stand up an operations center that can rapidly provide information on testing capacity, coordinate logistics to ensure capacity is utilized, and ensure interoperability of testing centers and systems across state lines.

Simultaneously, the Alliance should work to promote a set of common metrics that can enable state and local leaders to better understand how to target scarce testing resources in their communities. Common metrics would encourage and facilitate a data-driven approach to testing that could drive down cases and deaths.† Groups such as COVID Local, Harvard's Global Health Institute, and Resolve to Save Lives have created metrics frameworks to consider. [7]

† Five possible metrics that would indicate actions need to be taken and resources surged include: > 3% positive test rate; less than 90-95% of close contacts elicited, located and tested in < 24 hours; testing turnaround times > 24 hours; increase in the number of people in quarantine or isolation outstrips the ability of the state to offer social and financial support; and stay at home recommended for > 25 cases per 100,000 population.

EXPANDING TESTING CAPACITY AND LESSENING THE NEED FOR TESTING

There is no single solution to the current testing crisis, but there is a set of inter-related solutions readily available that, if organized, can rapidly alleviate testing backlogs and maximize efficient use of our collective testing capacities. The solutions below share the following criteria:

- They can be deployed within 2-12 weeks
- They make use of current capabilities, without relying on in-development innovations
- They will help relieve the testing crisis
- They provide a technical foundation for delivering testing innovations and programs in the medium and longer term
- They provide a governance foundation for cross-state management of other problems related to the COVID crisis, such as contact tracing, PPE provision, vaccine deployment

Expand Capacity by Mobilizing Third Party, Academic, and Veterinary Labs

A key way to rapidly expand our national testing capabilities overall involves helping every state to mobilize third party, academic, and veterinary research laboratories to do SARS-CoV-2 testing. Capacity can be expanded by:

- Building partnerships with third party labs and suppliers, including not-for-profit and commercial vendors, to directly expand state testing capacity. These partnerships can include links between the state, universities, and medical centers (as in Minnesota), directly provide test kits and equipment to expand state lab capacity (as in Maine), or leverage a network of smaller labs to coordinate testing at the state level (as in New York). [8,9,10] These efforts enable states to run thousands of additional tests per day.

- Standing up and expanding SARS-CoV-2 testing at academic facilities and academic medical centers (such as the Broad Institute and UCSF/Chan Zuckerberg Biohub).[11,12] These centers have the preexisting capacity and expertise to conduct SARS-CoV-2 molecular testing by surging equipment and personnel to support their transition to high-throughput testing. The Innovative Genomics Institute at UC Berkeley published a blueprint for rapidly setting up additional high-throughput SARS-CoV-2 testing labs.[13] The Alliance will work to ensure that these labs are not only utilizing their full current capacity, but also expanding that capacity by tens of thousands to a 100,000 or more tests per day per testing center.‡

- Mobilizing veterinary schools that have latent, but underutilized, high-throughput testing platforms that can be converted to conducting SARS-CoV-2 testing.[14]

States can directly aid efforts to expand testing capacity by implementing regulatory changes, as California has done.[15] These regulatory changes allow testing laboratories to utilize trained

‡ The Broad Institute reports completing 4,000-12,000 SARS-CoV-2 RT-PCR tests daily on average using their high-complexity CLIA-certified platform out of an advertised capacity of 35,000-40,000 tests. It is reported that their testing capacity can be scaled to at least 100,000 tests per day using their existing testing platform with sufficient demand.

academic workers who lack medical technician certifications to expand the laboratory workforce. Moreover, they allow new laboratory spaces to operate under a preexisting CLIA license, meaning they can be set up rapidly without needing a new CLIA certification.

The Alliance would support every member state in expanding its internal testing capacities, drawing from one or a combination of these models.

Supporting an Alliance of states to implement these measures involves:

- Helping states identify the attributes of labs that indicate they could quickly increase testing capacity
- Offering technical assistance to states as they integrate testing capabilities of these labs
- Improving cross-lab communication and encouraging rapid data sharing
- Providing training for laboratory staff
- Advising states on ways to maintain quality control

Optimize Existing Capacity by Ensuring Interoperability of State Public Health Labs

The epidemic is playing out unevenly across states, with some experiencing exponential growth, some with very few cases, and yet others with declining caseloads after a large spike in cases. The unevenness of the epidemic has meant that some states with robust testing capacities have been underutilized while others are overwhelmed – a dynamic we can exploit by redistributing testing samples from places with high caseloads to those with low ones. If states in the Alliance agree on a prioritization plan for testing, combining their testing stock would reduce pressure on the system by improving allocative efficiency across the public health lab network as a whole.

Currently there is no formal mechanism for interstate transport and processing of testing samples. Nor is there a coordinated effort to procure and distribute reagents, testing supplies, and workforces to those labs that are most in need of support. Understanding how to match unused capacity with needs across state lines will require standardized data about the capacities of state labs and their affiliates, such as testing platforms in use and deficiencies in their supply chains.

Supporting an Alliance of states to implement this measure involves:

- Creating a standardized, granular catalogue of the capacities of each member state's public health lab and affiliates
- Facilitating negotiations that produce a testing prioritization scheme, with metrics, that specifies the conditions under which each state in the Alliance would be willing to donate a portion of their public health system testing stock to others
- Working with IT partners to build, or expand existing, digital platforms that allow for interoperability across labs by facilitating sample bar coding, sample tracking, lab processing, billing, and results reporting

Create Surge Capacity by Establishing a Shared Supply of Point-of-Care Tests and Reagents

Point-of-care and point-of-use antigen testing is particularly useful in places experiencing exponential growth in cases. (See Appendix A for an overview of testing methods and strategies.) Hospitals that typically rely on now-backlogged centralized commercial labs to conduct testing benefit from having on-site point-of-care capacity that allows them to rapidly identify patients who are infected before they are assigned to a clinical ward. Likewise, when there is runaway community transmission and the numbers of contacts per case are growing exponentially, repeated point-of-use testing like antigen tests offer a quick, easy way to identify and disrupt chains of transmission. Accordingly, the Alliance would facilitate the creation of a shared supply of point-of-care and point-of-use testing capacities, and the reagents and supplies they require, that could be directed to communities that have lost control of the epidemic.

Supporting an Alliance of states to implement this measure involves:

- Facilitating negotiations to produce a prioritization scheme that specifies when and under which conditions states that are Alliance members would receive surge testing capabilities
- Supporting procurement of surge capacity testing kits and machines
- Supporting development of surge capacity testing deployment protocols

Lessen the Need for Testing Via Public Health Measures & Sparing RT-qPCR Capacity

The major way to reduce stress on our collective testing stock is to implement strict rules to implement conventional public health measures like:

- Mask wearing
- Hand washing
- Social distancing measures, including stay-at-home orders when daily cases increase beyond 25 per 100,000 people[16]
- Environmental modification measures like improving ventilation in enclosed spaces
- Undertaking robust contact tracing

States that collaborate to both implement public health measures *and* strategically improve their collective testing capacities will be best positioned to control the epidemic.

Beyond these public health measures, there are diagnostic strategies that can serve to prioritize SARS-CoV-2 tests where most needed – particularly the most commonly used test, the RT-qPCR, which the commercial labs employ. For example, the sensitivity of molecular tests decreases after seven days of symptoms, so they are less effective at diagnosing severely ill patients who present to hospitals toward the end of their disease course.[17] Other modalities like chest CT scans, combined with patient history and bloodwork results, are likely better at confirming COVID19 diagnosis in severely ill patients.[18] RT-qPCR capacity can be further

conserved through pooled testing, and by using point-of-care and point-of-use capacity for surveillance testing, which is critical to resuming economic and social activity. Research is currently underway to develop other RT-qPCR-sparing strategies in a variety of other contexts as well. Coordinated implementation of test-sparing diagnostic protocols across states may offload testing demand in the short, medium, and longer term.

Supporting an Alliance of states to implement this measure involves:

- Facilitating joint development of test-sparing COVID19 diagnostic strategies and protocols based on the latest surveillance research
- Facilitating negotiation on public health measures that all Alliance members agree to implement

OVERCOMING THE CHALLENGES TO INTEROPERABILITY

Many of the solutions offered above require, or are greatly enhanced by, interoperability across state laboratories and Departments of Public Health. While challenges exist, there are solutions the Alliance can employ to overcome them.

***Tagging and Barcoding of Samples*:** In order to ensure that samples can be transferred between labs, they need to be able to be "read in" to a number of systems, including state department of health databases and electronic medical records. A standardized barcoding system is required that would allow all tests to be entered and tracked across digital systems and databases.

Medical Billing and Payment: Payment for tests could be accomplished via billing third-party insurance, public insurance programs like Medicare or Medicaid, or dedicated federal funding given to states for SARS-CoV-2 testing.

Reporting Coordination: As testing expands, it is vital that cases are reported to state public health agencies and the CDC in order to inform public health decision making. Currently, reporting is performed by the ordering institution, not the reference lab performing the test. We propose that technological solutions be adopted to ensure that the relevant agencies be informed of test results. In particular, as uniform barcodes are adopted, those barcodes could include information as to the origin of the test and contain hardwired information regarding the relevant agency to report to.

Establishment of SOPs and Reagents: A primary barrier to interoperability is ensuring that the sample collected is compatible with all downstream testing platforms. Fortunately, SARS-CoV-2 diagnostic samples are relatively uniform, public health labs largely use the same testing platforms, and workflows are similar between non-point-of-care tests. However, this standardization presents an additional problem of platforms using similar reagents and testing materials that are in short supply. Coordination across states to purchase supplies in bulk and prioritize allocation may help manage these supply chain issues. Another possibility is for labs to work together to diversify approaches, creating tests with a variety of reagents and materials so collectively the testing stock is less dependent on a single approach.

***Transport of Samples and Equipment*:** Commercial testing companies, such as Quest, operate their own transport infrastructure. An equivalent transport mechanism is not currently available to the states. However, alternatives could be explored, such as bulk contracting with UPS or FedEx for rapid transit. The states could also collaborate with federal and state agencies, such as the Department of Defense and National Guard, to address required transport and logistics.

A Model Solution

The Mayo Clinic has created a digital platform that can serve as a model for addressing interoperability challenges such as management of test samples, billing, and results reporting across multiple laboratory systems. The platform allows hospitals around the globe to perform tests that their own lab systems are unable to perform. To function effectively, the platform requires standardized ordering of tests, transporting them via FedEx to laboratories around the country for processing, billing insurance companies, and entering results in electronic medical records. While designed for hospital-to-hospital interoperability, recently the platform was enhanced to be able to send SARS-CoV-2 tests from hospitals around the country to the Broad Institute, demonstrating the feasibility and versatility of this approach. In addition, multiple technological and data management organizations, like the US Digital Service, have volunteered to support the U.S.'s pandemic response. Working with and on behalf of the Alliance, they may be able to develop a platform like the Mayo platform at little or no cost.

OPERATIONALIZING THE ALLIANCE

In order to implement actions to expand testing capacity, ensure cross-state interoperability of capacity, and lessen the need for testing, the Alliance will need to establish an operations center to serve as a communications, information, and logistics hub for its national testing strategy. The operations center would serve as a resource for monitoring lab testing capacity in partner states, coordinating efforts to utilize excess testing capacity to meet critical testing priorities, manage a rotating stock of rapidly deployable point-of-care diagnostic supplies, and assisting with the implementation of interoperability guidelines.

The operations center would be tasked with expanding the testing capacity and resource utilization of Alliance members to eliminate >24-hour delays in testing within the next 4-6 weeks. The center would incorporate specialists in medical logistics, procurement, laboratory management, health care billing, epidemiology, hospital management, infectious diseases, and community and school health in order to guide their actions. It would be empowered to direct shared resources to areas with the greatest need, based on public health advice. For example, it would:

- Monitor testing capacity and demand at high-throughput testing facilities, such as the Broad Institute, and provide guidance for redirecting tests to those facilities for analysis when surplus test capacity is available.
- Coordinate transfer of reagents between labs to fill shortfalls and allow all labs to operate at full testing capacity.

The COVID Collaborative stands ready to support the establishment of the Alliance and operations center by facilitating negotiations, supplying curated technical assistance, and providing a platform for real-time problem solving.

SOLVING THIS CRISIS – AND THE NEXT

By expanding testing capacity, promoting interstate cooperation and coordination, and overcoming barriers to interoperable testing and reporting of SARS-CoV-2 cases, the Governors' COVID Action Alliance can reduce transmission of SARS-CoV-2 within and beyond state borders. The Alliance provides the platform for a nationally coordinated, state managed, and locally/clinically implemented testing strategy. It is designed to ensure that testing with the greatest need is performed expeditiously, while building capacity to ensure that all other testing can be performed as rapidly as possible, with no more than 24-hour turnaround times.

Resolving testing delays now will prepare the country for control of the virus over the medium- and long-term. In particular, new approaches to surveillance testing that are rapidly becoming available will work best in contexts where the virus is being suppressed, rather than rapidly spreading.

The Alliance can also help navigate other thorny logistical problems that arise from the COVID19 epidemic, including effective contact tracing and the provision and distribution of PPE. Moreover, establishing a platform for rapid deployment of diagnostic technologies to community testing centers will inform the deployment of vaccines and refrigeration equipment to community vaccination centers once a vaccine becomes available.

The COVID19 epidemic will, unfortunately, not be the last health security crisis this country faces. However, collaborative state leadership through the Governors' COVID Action Alliance will help resolve the current testing crisis, while helping us face together the unique challenges future crises will bring.

GLOSSARY OF KEY TERMS

- **Antigen:** A molecule or molecular structure that is present in a pathogen. In the context of SARS-CoV-2 testing, an antigen refers to proteins found in the virus that can be detected.

- **Antigen Testing:** Testing platforms designed to detect viral proteins (instead of the viral genome, which is detected via RT-qPCR). Antigen testing is considered to be less sensitive than RT-qPCR, but has sufficient sensitivity in currently approved platforms to be used diagnostically.

- **CLIA:** The Clinical Laboratory Improvement Amendments, a federal regulation overseen by the Centers for Medicare and Medicaid Services, that governs the licensure of clinical laboratories in the United States. This law allows the federal government to set regulations for clinical laboratories and the testing protocols that they can perform; these regulations are then administered by the states.

- **High-throughput testing:** SARS-CoV-2 testing that can be conducted rapidly on a large number of samples in parallel. This refers to testing that is highly automated, either through a single testing platform (such as the Hologic Panther or Roche *cobas*) or through a defined workflow in which individual steps are automated and can be conducted at scale (for example, automated RNA extraction from patient samples and automated RT-qPCR protocols).

- **Point-of-Care/Point-of-Use:** Testing that can be performed directly at the site of sample collection. This often refers to systems that can be used directly in local clinics or hospitals without having to send the patient sample to an outside testing facility.

- **RT-qPCR Testing:** A molecular biology technique that uses nucleic acid specific probes to amplify target RNA. In a testing setting, probes that are specific to the SARS-CoV-2 genome are used to amplify multiple segments of the genome, if present. The amplified product is then detected using a fluorescent dye. If there is no SARS-CoV-2 genome present in the sample, then no amplification occurs and, as a result, nothing is detected.

- **Reagents:** The essential components required for SARS-CoV-2 testing. This includes chemicals and plastic equipment that can be used to isolate the SARS-CoV-2 genome for detection and perform the RT-qPCR reaction that detects the genome. The reagents necessary vary based on equipment used to perform the test and some reagents are compatible with specific testing devices.

- **SARS-CoV-2:** A coronavirus that is the causative agent of coronavirus disease 2019 (COVID-19). Previously known as nCoV-2019 or hCoV-2019, it is believed to have originated in Wuhan, China following a case of zoonotic transmission (transmission from animals).

APPENDIX A: TESTING NEEDS AND TYPES OF TESTING

SARS-CoV-2 testing modalities each have their pros and cons. Scaling up testing is not just a numbers game – rather it requires matching the most appropriate test with the desired goals of testing. We briefly summarize the different types and goals of testing programs that aim to identify active infections below.

Types of Tests Currently in Use

There are only three ways to test for SARS-CoV-2 currently in widespread use. Two of these, the Reverse Transcriptase quantitative Polymerase Chain Reaction (RT-qPCR) and the Isothermic Nucleic Acid Amplification Technology (iNAAT) detect viral genetic material called RNA. The third, the Lateral Flow Assay (LFA), detects viral proteins, or antigens.

Because of its high sensitivity and specificity, RT-qPCR tests are considered the 'gold standard' test to confirm SARS-CoV-2 infections. RT-qPCR tests range from modular, "high complexity" tests, in which viral RNA is extracted from a nasal swab and then that RNA is amplified using a test kit to detect SARS-CoV-2 RNA on a separate device to "moderate complexity" tests in which a single platform, with manufacturer-specific reagents runs the entire assay. High complexity tests can use one of a number of RNA extraction kits (produced by several different manufacturers) to extract the viral RNA and then use any test kit that starts with RNA as the input material – these tests are versatile and potentially less subject to supply bottlenecks at this point in time. Moderate complexity tests perform the same RT-qPCR reaction to detect the SARS-CoV-2 as high-complexity tests, but do so in an automated fashion in a single machine, minimizing human handling of the sample – however, these machines are traditionally only compatible with test kits produced by the manufacturer (the Roche *cobas* system primarily runs assays with Roche reagents), which results in capacity being dictated by the availability of both the device and the specific test kit.

Both of high complexity and moderate complexity RT-qPCR assays must be conducted in a CLIA-certified laboratory. RT-qPCR machines can run between 2-96 tests/hour according to a survey done by the American Public Health Laboratory Network.[19] There is a tradeoff between speed of testing result and quantity of tests that can be run since centralized labs that house multiple high throughput and automated platforms require that test samples be transported, batched, and reported. This process takes at least 24 hours, and currently can be subject to multi day delays. On the other hand, point-of-care RT-qPCR machines (including moderate complexity devices) process fewer tests but can give on-site patients results within 1-2 hours.

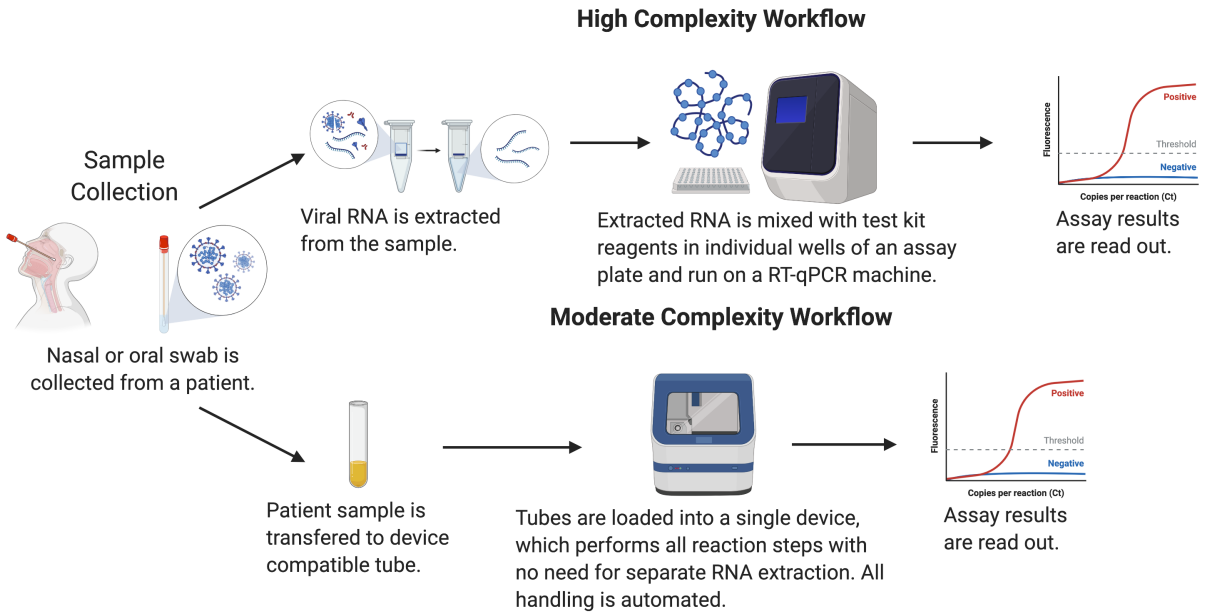
iNAAT PCR-testing gives rapid results and the vast majority are point-of-care machines that can be installed in clinics. Of note, many of these tests have CLIA-waived status, meaning that they can be used in a number of settings outside of a clinical laboratory. The Abbott ID NOW machine is the most well-known iNAAT testing platform. It has been found to be most accurate when samples were run on site, per the manufacturer protocol. However, testing sample transit, storage, and delays in actually testing the samples decrease the sensitivity of this significantly. These tests are limited by the availability of test reagents specific to the device in question. For example, Abbott produces a finite number of reagents that are compatible with the ID NOW platform.

LFA tests are point-of-use tests. Like pregnancy tests, they employ a cartridge on which saliva or nasal secretions are applied. Lower sensitivity than viral molecular tests described above are a consideration, but LFA tests are affordable and convenient. These tests are rapid, typically delivering results in 15-30 minutes. As they detect SARS-CoV-2 antigens, not the genome, they do not require additional processing steps, such as RNA extraction, prior to delivering a result.

Table 1: Types of Testing

Test Type	Systems	Speed	Throughput	Sensitivity	Comments
RT-qPCR	Lab-developed tests, commerical test kits	2-4 hours	Varies with configuration*	High	Can be conducted with high- or low-throughput protocols; highly interchangeable components.
Commerical RT-qPCR assays	Roche *cobas*, Hologic Panther	2-8 hours	Up to ~1,000 tests per day	High	Highly optimized workflow; readily deployable; limited by availability of reagents and no interoperability between systems.
iNAAT	Abbott ID NOW	15-60 minutes	-	Moderately high	Limited by test cartridges that can be produced and distributed by manufacturers; can be nonspecific if protocols not followed.
LFA	Sofia II	15-30 minutes	-	Moderate	Limited by production capacity; lower specificity relative to RT-qPCR.

Chart 1: High-Complexity versus Moderate-Complexity RT-qPCR Testing



Goals of Testing

Over the course of the epidemic, testing has been employed for different purposes.

Testing can limit the spread of COVID-19 in hospitals to other patients and health workers; especially in the case of moderately to severely ill patients who present to acute care facilities which receive tests to confirm their diagnosis. The primary goals of this type of testing is to not only to diagnose patients but also to prevent them from spreading the infection to other patients and healthcare workers. Point-of-care RT-qPCR tests are the best suited for this context because they are sensitive and specific, and results can be rapidly obtained on site. If hospitals have their own internal labs, they can process the tests on site and third-party insurance is billed for the test as part of the overall care the patient receives in the hospital. Hospitals that don't have their own labs may contract with a commercial testing company.

Testing prevents community transmission over the period when cases are rising: Mildly ill patients or people who have been exposed to an infected person receive a test to see if they have contracted the disease, ideally before they are able to spread it to others. Again, RT-qPCR has been the test of choice, although iNAAT is also appropriate if sensitivity and specificity can be maintained. LFA tests are a second-best choice if molecular testing cannot be accessed in a timely way. It is better to have an imperfect but timely test than a delayed one or none at all. Testing venues have included primary care centers as well as pop up testing sites run by state's Departments of Public Health. The difference between these two testing venues is often who pays for the test: if testing is conducted in primary health care centers, third party insurance may cover the costs, while the state may finance pop-up testing center tests. Commercial testing companies are often the entities that run tests from both primary care clinics and pop-up testing centers.

Testing is the best way to monitor community progression of the disease. Surveillance testing involves testing people routinely, regardless of symptoms, in order catch people with early infections before they can transmit to others. This strategy has been deployed to detect early outbreaks in vulnerable populations including long term care facility residents and people who are incarcerated. LFA tests are preferred in this situation because they are point-of-use, don't require special equipment and are inexpensive. They don't require people to travel to testing facilities or to send large numbers of tests to central labs. The major drawback to LFA testing is its relative low sensitivity compared to molecular tests. This is partially compensated for by routine, repeated testing. Payment for LFA testing has largely been done through public health programs or privately by employers who are testing their workers. Billing via third party insurance companies faces several challenges Because LFA tests are done outside of health facilities that have the administrative processes in place to bill for the test. Also, insurance companies have not been directed to pay for surveillance testing in people who are asymptomatic. The more broadly and regularly used LFA testing becomes, the greater the expense of LFA testing programs. iNAAT testing could also be readily utilized for surveillance testing, provided testing is conducted rapidly at point-of-use and the demand for more sensitive nucleic acid testing has not surpassed capacity.

On the Horizon

Multiple new approaches to testing have been mentioned in the news. These new approaches are in various stages of development, with many promising to be a game changer in terms of our nation's testing capabilities. While we find these exciting, we should not wait for these before we act to address the testing crisis in the very short term.

The cavalry on the horizon includes:

Next Generation Sequencing: Next generation sequencing (NGS) platforms are capable of running thousands of samples in parallel as a result of indexing capabilities. The first FDA-approved SARS-CoV-2 NGS diagnostic is the Illumina COVID-seq protocol, which allows up to 3,072 tests to be run in parallel. One benefit of NGS is that mutations in the virus can be identified during each sequencing run. These tests require significant installed capacity, such as next generation sequencers, workflows that facilitate indexing of samples, and significant capacity to process over 3,000 nasal swabs per run. If these barriers are overcome or systems are established in settings with high-throughput processing capabilities, NGS could be used to expand testing capacity significantly over the next three months.

Point-of-use testing modalities including CRISPR: CRISPR-based technologies offer the potential for point-of-use testing that can be conducted at home or in a clinical office. While these technologies have potential, current protocols require sample incubation at constant temperature, which may be difficult to achieve at home. Additionally, these tests are lower sensitivity (though sufficient for detecting infection) and have not received FDA approval. These tests, if approved, could be produced at scale within three to six months.

Pooled testing: Pooled testing allows multiple patient samples to be combined and analyzed at once; if one pool is positive, then each sample is run individually to identify the infected patient. A benefit of pooled testing is that numerous negative samples can be identified at once. However, pooled testing is constrained by percent positive rates in an area; in areas with high rates of transmission, pools cannot be efficiently run. Multiple SARS-CoV-2 diagnostics were approved for pooled testing; however, expansion of pooled testing depends on as additional test modalities being approved (currently each approved test must be separately approved for pooled testing) and testing facilities developing workflows and sample management protocols for pooled testing.

Table 2: Uses of Testing & Testing Modalities Based on Context

	Preferred Test	Alternate Tests	Capacity Necessary
Preventing the spread in health systems	RT-qPCR	iNAAT (when RT-qPCR is not available)	Sufficient capacity to test patients and exposed staff. Necessary capacity will vary by health care system.
Stopping community transmission	iNAAT	RT-qPCR, LFA	Sufficient capacity to test known contacts and meet symptomatic testing needs in local clinics.*
Surveillance testing in communities	LFA	iNAAT, RT-qPCR (pooled)	Sufficient capacity to achieve percent positive rates below 3% of all tests and target potential outbreak zones (schools, businesses, etc.).*
			*capacity should reach at least ~1.8 million tests per day combined to achieve 3% positive test rate.

[1] Office of Governor Larry Hogan. "Governors of Maryland, Louisiana, Massachusetts, Michigan, Ohio, and Virginia Announce Major Bipartisan Interstate Compact For Three Million Rapid Antigen Tests". August 4, 2020. https://governor.maryland.gov/2020/08/04/governors-of-maryland-louisiana-massachusetts-michigan-ohio-and-virginia-announce-major-bipartisan-interstate-compact-for-three-million-rapid-antigen-tests/

[2] Cassady, Daniel. "Testing Demand Declines Across 22 States—And Experts Aren't Quite Sure Why". *Forbes*. August 5, 2020. https://www.forbes.com/sites/danielcassady/2020/08/05/testing-demand-declines-across-22-states-and-experts-arent-quite-sure-why/#7dd893ce550f

[3] Cuomo, Andrew. "Let's End the Wait for Coronavirus Test Results. Here's How." *The New York Times.* July 31, 2020. https://www.nytimes.com/2020/07/31/opinion/coronavirus-testing-cuomo.html?smid=em-share

[4] Sheridan, Kate. "This tiny Texas company is running most of the drive-thru Covid-19 testing in the U.S." *STAT News.* August 3, 2020. https://www.statnews.com/2020/08/03/etruenorth-tiny-company-running-covid-19-company/?utm_source=STAT+Newsletters&utm_campaign=f38fda374e-MR_COPY_01&utm_medium=email&utm_term=0_8cab1d7961-f38fda374e-152835942

[5] Tromberg et al. "Rapid Scaling Up of Covid-19 Diagnostic Testing in the United States — The NIH RADx Initiative". *The New England Journal of Medicine*. July 22, 2020. https://www.nejm.org/doi/full/10.1056/NEJMsr2022263

[6] *Ibid.*

[7] COVID Local is a joint project of the Georgetown University Center for Global Health Science and Security, Talus Analytics, Nuclear Threat Initiative, and the Center for Global Development designed to provide local governments with information on how to protect their communities from pandemics (https://covid-local.org/). The Harvard Global Health Institute partnered with numerous organizations to provide guidance on key metrics to guide the coronavirus response (https://globalhealth.harvard.edu/key-metrics-for-covid-suppression-researchers-and-public-health-experts-unite-to-bring-clarity-to-key-metrics-guiding-coronavirus-response/). Resolve to Save Lives is an initiative of Vital Strategies, supported by the Bill and Melinda Gates Foundation and Bloomberg Philanthropies, the established a series of metrics and performance indicators for COVID-19 analytics (https://preventepidemics.org/wp-content/uploads/2020/07/Tracking-COVID-19-in-the-United-States-Report.pdf).

[8] Office of the Governor of Minnesota. "Governor Walz, Mayo, U of M Announce COVID-19 Testing Breakthrough". April 22, 2020. https://mn.gov/governor/news/#/detail/appId/1/id/429435

[9] Office of the Governor of Maine. "Mills Administration Secures Major COVID-19 Testing Expansion for Maine". May 7, 2020. https://www.maine.gov/governor/mills/news/mills-administration-secures-major-covid-19-testing-expansion-maine-2020-05-07

[10] See endnote 4.

[11] Eisenstadt, Leah. "How Broad Institute converted a clinical processing lab into a large-scale COVID-19 testing facility in a matter of days". The Broad Institute. March 27, 2020. https://www.broadinstitute.org/news/how-broad-institute-converted-clinical-processing-lab-large-scale-covid-19-testing-facility

[12] Bleicher, Ariel. "How to Build a COVID Testing Lab in Eight Days". *UCSF Magazine.* Summer 2020. https://www.ucsf.edu/magazine/covid-testing-lab

[13] IGI Testing Consortium. "Blueprint for a pop-up SARS-CoV-2 testing lab". *Nature Biotechnology*. June 18, 2020. https://www.nature.com/articles/s41587-020-0583-3

[14] Cima, Greg. "Animal health laboratories aid testing for COVID-19 in people". American Veterinary Medical Association. June 1, 20202. https://www.avma.org/javma-news/2020-06-01/animal-health-laboratories-aid-testing-covid-19-people

[15] Chan Zuckerberg Initiative. "UCSF, CZI, CZ Biohub, & the State of California Partner to Expand & Utilize Clinical Testing Capacity for COVID-19". March 19, 2020. https://chanzuckerberg.com/newsroom/ucsf-chan-zuckerberg-initiative-biohub-california-partner-expand-testing-capacity-covid-19/

[16] Harvard Global Health Institute. "The Path to Zero: Suppressing COVID-19 through TTSI". https://globalepidemics.org/wp-content/uploads/2020/06/TTSI_general_briefing_v3-1.pdf

[17] Udugama et al. "Diagnosing COVID-19: The Disease and Tools for Detection". *ACS Nano*. March 30, 2020. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7144809/

[18] Radiological Society of North America. "CT provides best diagnosis for COVID-19." Refers to study published in *Radiology*. February 26, 2020. https://www.rsna.org/en/news/2020/February/COVID-19-CT-Diagnosis-Study

[19] Association of Public Health Laboratories. "Laboratory and Testing Resources: COVID-19 Test Characteristics." http://www.aphl.org/programs/preparedness/Crisis-Management/_layouts/15/WopiFrame.aspx?sourcedoc=/programs/preparedness/Crisis-Management/Documents/COVID-test-summaries.xlsx&action=default