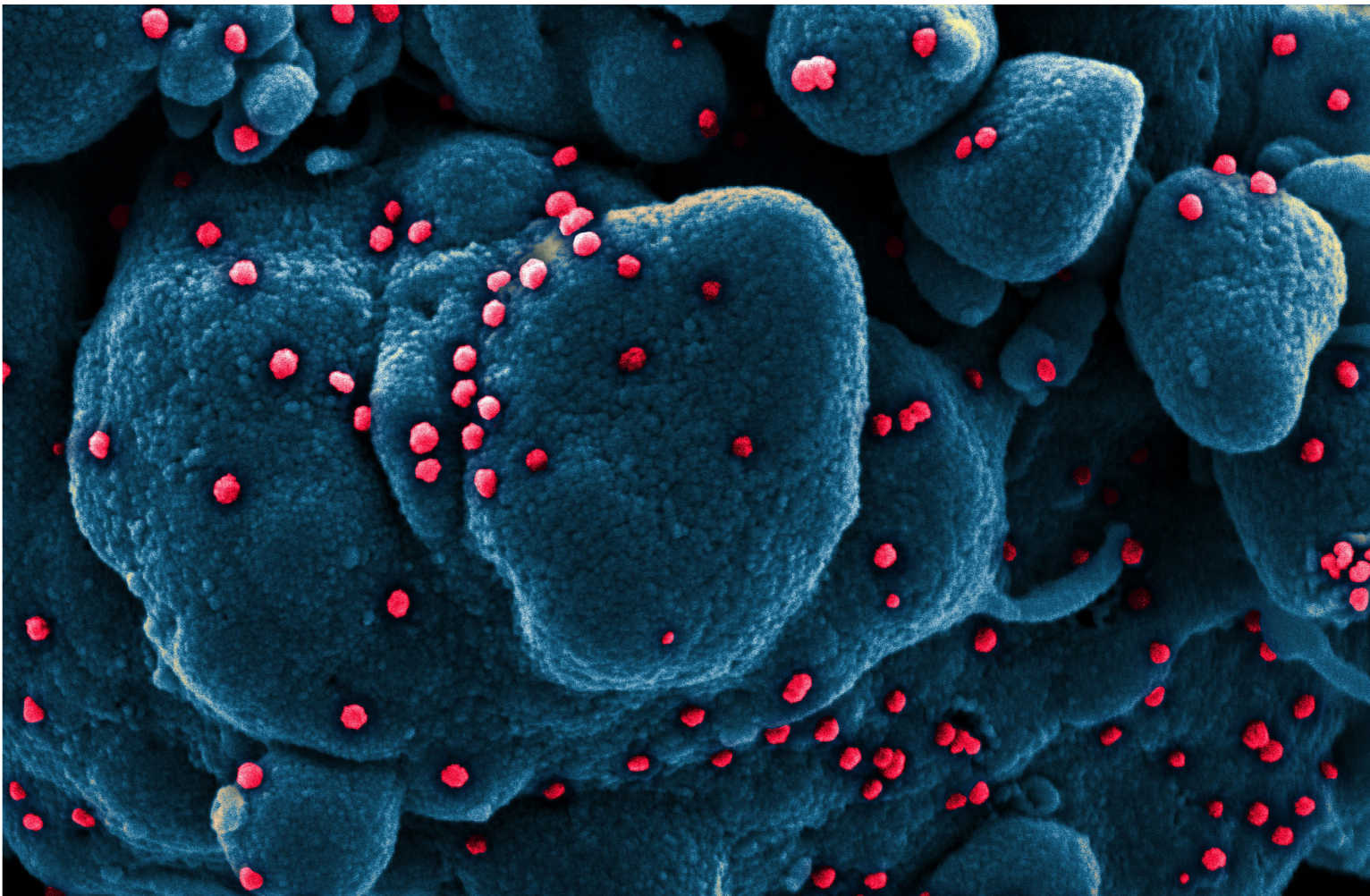# COVID-19:
The CIDRAP Viewpoint

CIDRAP

COVID-19: The CIDRAP Viewpoint

May 20, 2020

Part 3: Smart Testing for COVID-19 Virus and Antibodies

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CIDRAP, founded in 2001, is a global leader in addressing public health preparedness and emerging infectious disease response. Part of the Office of the Vice President for Research (OVPR) at the University of Minnesota, CIDRAP works to prevent illness and death from targeted infectious disease threats through research and the translation of scientific information into real-world, practical applications, policies, and solutions. For more information, visit: www.cidrap.umn.edu.

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Part 3: Smart Testing for COVID-19 Virus and Antibodies

Preface

Welcome to "COVID-19: The CIDRAP Viewpoint," our series of reports that add key information, address issues that haven't garnered the attention they deserve, and reflect the unique expertise among the CIDRAP team and our expert consultants. In our reports we address timely issues with straight talk and clarity. And the steps we recommend are based on our current reality and the best available data. Our goal is to help planners envision some of the situations that might present themselves later this year or next year so that they can take key steps now, while there's still time.

Our first report laid out potential pandemic scenarios, and our second report covered crisis communication.

Our hope is that our efforts can help you plan more effectively and understand the many aspects of this pandemic more clearly—and for you and your family, friends, and colleagues to be safer. Thank you.

– Michael T. Osterholm, PhD, MPH, CIDRAP Director

Introduction

Testing for SARS-CoV-2—the virus that causes COVID-19—is one part of the complex system required to address the pandemic. Testing is essential to confirm infection in cases and contacts, guide patient care, inform our understanding of transmission dynamics, prepare the health system for case surges, and inform the level of economic activity consistent with public health goals for limiting SARS-CoV-2 transmission. Technology to conduct molecular, antigen, and serology tests is now available, and additional technologies will be made available soon.

The requirements for SARS-CoV-2 testing are unprecedented in both their urgency and the need for scalability, which present both technical and policy challenges. Current plans for clinical and public health laboratory testing do not sufficiently address the infrastructure needed to perform such tests. Critical guidance and coordination at the federal level is needed to meet the SARS-CoV-2 testing demand.

SARS-CoV-2 testing depends on a cascade of processes, people, and components that must be in place and accounted for in order for testing to be most effective. Much of the public discussion to date has focused on the availability of testing supplies, such as reagents and swabs, but the ability of laboratories to test for SARS-CoV-2 extends far beyond the availability of test materials. Ambitious proposals that recommend widely testing the population need to consider the merit of widespread testing and how each step in the testing cascade will be maintained. We propose a *"smart testing"* approach to help ensure that the right test is given to the right person at the right time, with test results provided in a timely manner to allow for actions that minimize illness, deaths, and transmission (Figure 1).

Public health agencies, healthcare systems, policy leaders, and the public must be aware of the inherent values, uses, and limitations of SARS-CoV-2 tests and of the cascade of processes required for testing, so that they can plan and respond accordingly.

Testing Fundamentals

The technology to conduct molecular, antigen, and serology tests is now available. Molecular and antigen tests detect the virus and can be used to diagnose acute infection. Diagnostic molecular tests are used to detect the unique genetic sequence of the SARS-CoV-2 virus. Examples of molecular tests are reverse transcription

polymerase chain reaction (RT-PCR) and isothermal amplification. Antigen tests, in contrast, detect proteins on the surface of the virus.

Serology tests don't directly detect the virus but instead measure antibodies to the virus that are present in the blood. Antibody tests can provide evidence of current or previous infection, because they indicate that the body produced an immune response to the virus. It can take over a week for antibodies to form following infection; as such, antibody tests are generally not intended to be

Figure 1. CIDRAP SARS-CoV-2 smart testing framework.

used as a diagnostic tool for confirming acute infection, except in unusual circumstances. Nor is it clear if having antibodies to the virus protects someone from being infected again in the future. The pros and cons of each test should be made clear to policy leaders, public health agencies, healthcare systems, and the public.

Test performance characteristics

Sensitivity and specificity are both measures of how a test performs, and of the ability of the test to detect true-positive and true-negative results. Sensitivity of a test means how well it correctly identifies those who have SARS-CoV-2 infection or antibody (i.e., the true-positive rate). A test that is highly sensitive will detect nearly all true cases; for example, a test that is 90% sensitive will give a positive test result for 90 of 100 people who have the virus infection or antibodies, depending on what you are testing for. A test with low sensitivity will produce more false-negative results compared with a test that has higher sensitivity.

Specificity of a test means how well it correctly identifies those who do not have SARS-CoV-2 infection or antibody. A test that is highly specific will return negative results for nearly all people who do not have the condition. For example, a test that is 95% specific will give a negative test result for 95 of 100 people who do not have the condition. A test with low specificity will produce more false-positive results compared with a test that has higher specificity.

It is important that the end-user of SARS-CoV-2 tests be aware of the likelihood of false-negative test results. This issue was in the national spotlight recently, as the test being used by the White House was found to provide inaccurate results, missing a potentially significant number of infections (FDA 2020b). Within the **smart testing** framework, the use of a point-of-care molecular diagnostic test without confirming a negative result would be identified as a deficiency in the testing protocol. As demonstrated by the White House example, if the purpose of the test is to identify all infected people, negative test results should be confirmed with a high-sensitivity authorized molecular test.

Antigen tests generally have lower sensitivity and, therefore, a greater risk for returning false-negative results. Because of this risk, the US Food and Drug Administration (FDA) recommends that negative results from an antigen test be confirmed with an RT-PCR test prior to making treatment decisions or to prevent the spread of the virus (FDA 2020a).
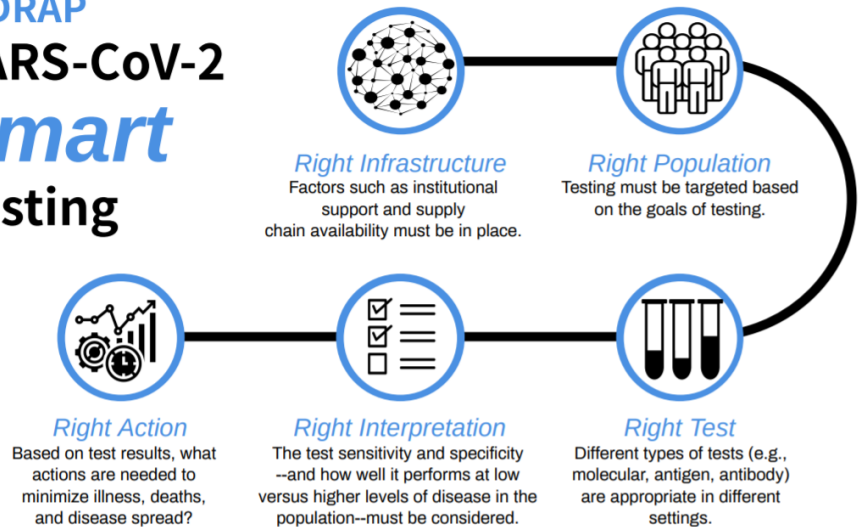
Sensitivity and specificity are characteristics of the diagnostic test itself, but the interpretation of a positive or negative test result varies as prevalence of the condition in the population changes (Figure 2). The likelihood that a positive test result indicates that a person is truly positive increases as more people in the population have the condition; this is called the positive predictive value. When the prevalence of the condition in the population is low, the percentage of false-positive tests may be unacceptably high.

Similarly, the negative predictive value—or the likelihood that a negative test result indicates that a person is truly negative—decreases as more people in the population have the condition. The fundamentals of predictive values are essential to how individuals should be counseled regarding their test results. For example, take a community with 5% antibody prevalence—meaning that 5% have been infected—which is likely the current status for most of the United States. If a patient in that community receives a positive antibody test result with a test that has 95% sensitivity and 95% specificity, the positive predictive value of this test is 50% (Figure 1). This means that 50% of the positive results would not be true-positives. Subsequent decisions based on this result, such as a return to the workforce, may put the individual or their contacts at risk.

The scientific community needs to clearly define how testing should be used most efficiently so that appropriate decisions can be made for clinical care and for public health. A consensus needs to be reached on the level of sensitivity, specificity, and positive and negative predictive values that are acceptable for different uses of the tests. This will vary by population. For example, the willingness to accept false-negative or false-positive tests that detect the virus may be different in hospitalized patients compared to non-hospitalized symptomatic patients compared to asymptomatic (symptom-free) people in the community.

Pressing Issues

1. Testing for SARS-CoV-2 is highly complex, and healthcare providers, public health officials, policymakers, and the public need to understand the nuances, uses, applications, and limitations of testing for the virus that causes COVID-19 and antibodies to it. The success of a testing program should be measured only in part by the number of tests completed.

2. The SARS-CoV-2 testing infrastructure hinges on complex and fragile interdependencies among the availability of materials, supplies, and skilled labor as well as instrument capacity. Shortages in the testing chain supplies (personal protective equipment for those obtaining specimens and for laboratory personnel, tests, pipette tips, tubes, etc.) will leave a gap between the number of tests needed and how many can be performed.

3. SARS-CoV-2 testing plays a critical role in controlling the pandemic, yet tests alone are just one element of a cascade of events that must occur for an effective testing strategy. For the role of testing to be optimized, other elements of the cascade—including infrastructure, processes, people, other essential components, and an action plan—must be in place, operational, and continually monitored.

4. For testing to be maximally effective, coordination across the system and across jurisdictions is necessary. Ideally, this requires federal guidance, leadership, and support, with strong jurisdictional buy-in at the state and local levels.

5. Because of the complexities involved in the SARS-CoV-2 testing cascade, expert oversight involving a blue-ribbon panel is critical.

Authorization of testing

Typically, the FDA regulates the manufacturers of in vitro (laboratory) diagnostic tests, and the US Centers for Medicare and Medicaid Services (CMS) regulates all laboratory testing (except research) performed on humans in the United States through the Clinical Laboratory Improvement Amendments (CLIA).

Its emergency use authorization (EUA) authority allows the FDA to help strengthen the nation's public health protections by facilitating the availability and use of EUA tests in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or conditions when there are no adequate, approved, and available alternatives.

Figure 2. The likelihood that a positive test result indicates that a person is truly positive increases with increasing prevalence.

Traditionally, EUA testing has been performed by the US Centers for Disease Control and Prevention (CDC), state and local health departments, and, at times, regional reference academic and commercial labs. To respond to the COVID-19 pandemic, however, more than 100 EUA tests have been approved, which complicates the situation. SARS-CoV-2 testing requires both hospital and community-wide use on a scale not seen before by hospital, clinical, and public health labs.

In response to challenges encountered by the CDC to rapidly develop RT-PCR tests at the beginning of the pandemic, the FDA invoked emergency provisions to allow the use of COVID-19 test kits without their needing to undergo the agency's standard review for accuracy (Shah & Shuren 2020). The FDA allowed clinical laboratories, in addition to public health laboratories, to conduct testing under an EUA. This greatly expanded both the ability of laboratories to implement testing and the number of laboratories that could test for SARS-CoV-2. Additionally, the FDA implemented an expedited EUA process that enabled laboratories to create their own tests and enabled test manufacturers to provide test kits to laboratories prior to obtaining an EUA, with the stipulation that the lab or manufacturer file an EUA within 15 days of test validation (FDA 2020c). This expedited process applied only to molecular diagnostic tests, such as RT-PCR. This provided regulatory flexibility, while also ensuring some degree of FDA oversight.

The FDA also provided a pathway for serology tests to be marketed in the United States without FDA authorization, requiring only notification to the FDA, through a "pathway D" notification. The rationale for this decision was that serology tests are less complex than molecular tests and are most useful for surveillance, not for COVID-19 diagnosis. This resulted in the introduction of well over 100 serology tests in the United States. After questions about the accuracy of these tests were raised, the FDA has revised its policy to require commercial manufacturers to submit EUA requests within 10 business days from the date they notify the FDA of their validation testing, and provided specific performance threshold recommendations for specificity and sensitivity (FDA 2020c).

In addition, because the pathway D serology tests are not reviewed or categorized by the FDA, these tests are required to be run in a lab certified by CMS as a high-complexity laboratory. However, many of these tests are
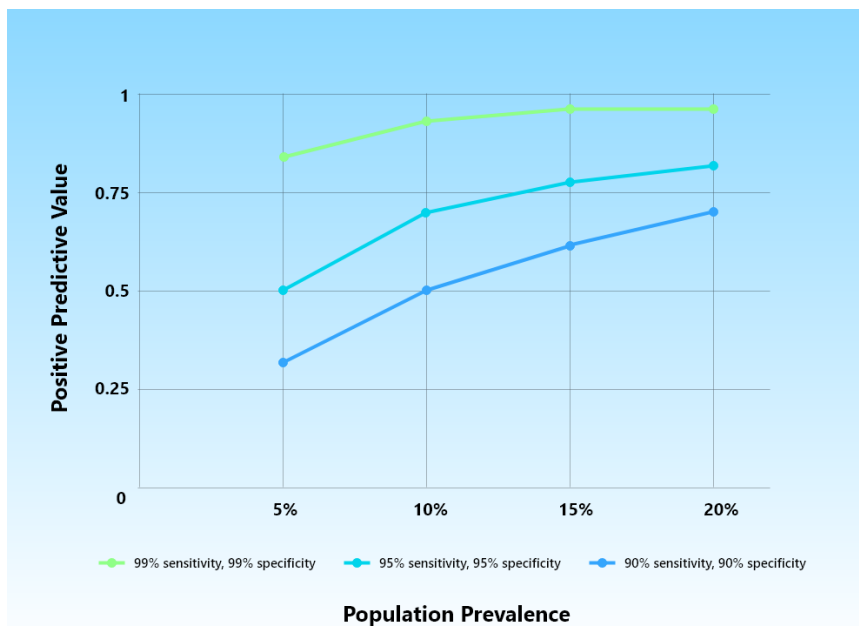
being marketed fraudulently as point-of-care tests, and are not being conducted in a certified lab. This further increases the risk that these tests could provide an inaccurate result, and that the individual receiving the test result will not get the information needed to appropriately interpret the test result.

Use Cases for COVID-19 Testing

Testing for SARS-CoV-2

The question of who should be tested for SARS-CoV-2 should be guided by the local epidemiology of COVID-19 and by test resource availability. The decision of which tests are appropriate for which populations should be driven by the epidemiologic context and by the risk—to both the individual and the public—of false-positive and false-negative results. "Use cases" refers to specific situations for which a test could be used. We present use cases for the detection of SARS-CoV-2 in individuals with symptoms, the detection of SARS-CoV-2 in individuals without symptoms, the detection of SARS-CoV-2 antibody (serology), and serosurveillance—using serology results to assess the prevalence of people who have SARS-CoV-2 antibodies.

This report does not provide an exhaustive list of use cases, but rather examples for how the *smart testing* framework should be applied to SARS-CoV-2 testing. These recommendations are fluid and may change as new data become available. They are based on published documents (CDC 2020, Hanson et al 2020, IDSA 2020, Shah & Shuren 2020).

Detection of SARS-CoV-2 in people with symptoms

- **For clinical care, including case isolation (recommended).** Confirming whether or not a symptomatic person has COVID-19 is essential for appropriate medical management and infection control. If individuals are not ill enough

Recommendations

1. Pandemic messaging needs to move beyond "Test, test, test!" mantras, as the current testing reality is complicated and depends on a cascade of interconnected factors—and our approach must be strategic. We believe that greatly expanding SARS-CoV-2 testing is a critical element in our response to COVID-19. Policymakers, experts, and the public need to understand, however, that the COVID-19 response requires a smart approach to testing that requires the right infrastructure, right population to test, the right test, and the right application of test results before the right actions can be taken.

2. The US secretary of Health and Human Services (HHS) should appoint by July 1, 2020, a blue-ribbon panel of national experts. The panel should include representatives from public health, clinical laboratory, and medicine; the laboratory testing research and development, marketing, and product support industries; ethicists; legal scholars; and elected officials. We have identified eight key objectives for the blue-ribbon panel to address.

3. Every state should immediately develop a comprehensive testing plan using a "smart testing" framework that is consistent with recent guidelines from the Centers for Disease Control and Prevention (CDC) (White House 2020). A smart approach to SARS-CoV-2 testing ensures an infrastructure that provides the right test to the right person at the right time, with timely results allowing for actions that minimize illness, deaths, and transmission (Figure 1).

4. We strongly encourage that HHS review and evaluate the use of testing for SARS-CoV-2 in the public health response to COVID-19 by governments around the world to learn state-of-the-art approaches and best practices that could be incorporated into the US response.

to be hospitalized, they will be instructed to self-isolate and to monitor their symptoms at home. Rapid identification of hospitalized cases can help control the spread of COVID-19 within healthcare systems and enables healthcare workers to conserve personal protective equipment (PPE). If patients are hospitalized, they may be isolated from non-COVID-19 patients and/or managed in the same area as other infected individuals.

- **For disease surveillance and contact tracing (recommended).** Testing of symptomatic persons also serves two important public health purposes: (1) case reporting to public health authorities for surveillance purposes to monitor disease incidence trends in the population and (2) the ability to perform contact tracing by interviewing cases and identifying their contacts to prevent further transmission in the community.

- **For potentially exposed healthcare personnel, including first responders, with mild signs and symptoms (recommended).** The purpose of testing these people is to prevent potential transmission of SARS-CoV-2 to patients or other healthcare workers and first responders. A negative test post-exposure does not necessarily rule out infection.

Detection of SARS-CoV-2 in people without symptoms

Asymptomatic shedding of the virus may be detected with a molecular test or an antigen test. It is not yet clear where, when, and how asymptomatic individuals should be tested. The collection source—such as saliva, throat, nose, or nasopharyngeal sampling—with the highest yield for pre-symptomatic or asymptomatic people is not yet defined. Negative test results among asymptomatic individuals should be interpreted cautiously, as the likelihood of identifying the virus in an infected person increases substantially closer to the time of onset of symptoms. Several potential use cases for testing asymptomatic people are addressed below.

- **For contacts identified through contact tracing (recommended with caveats).** While contacts of confirmed cases are at increased risk of being infected, data are lacking to define the time course

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Key Concepts Defined

- **The CIDRAP SARS-CoV-2 *smart* testing** framework ensures that the right COVID-19 test is available to the right person at the right time, with timely test results guiding actions to minimize illness, deaths, and disease spread.

- **The SARS-CoV-2 testing cascade** is a series of elements essential for optimal testing. These include the availability of materials, supplies, skilled labor, and instrument capacity. The fragile interdependencies among elements in the cascade mean that one lacking element will reduce the number of tests that can be performed.

- The **sensitivity** of a test means how well it can correctly identify those who *have* COVID-19 infection or antibodies.

- The **specificity** of a test means how well it can correctly identify those who *do not have* COVID-19 infection or antibodies.

- The **positive predictive value** of a test is the likelihood that a positive test result indicates that a person is *truly positive* for COVID-19 infection or antibody.

- The **negative predictive value** of a test is the likelihood that a negative test result indicates that a person is *truly negative* for COVID-19 infection or antibody.

- A **use case** is simply a situation in which testing could be used.

between exposure and a positive test result. This complicates the interpretation of testing asymptomatic contacts and the recommendations regarding isolation of an infected person and quarantine of potentially infected people. A negative test post-exposure does not necessarily rule out infection.

- **Epidemiologic or public health research (recommended).** Testing of asymptomatic people can provide important epidemiologic information to improve understanding of COVID-19 transmission dynamics and clinical characteristics, particularly when exposure history is clear. Such studies should be conducted using sound epidemiologic principles and practices with clear objectives defined.
- **Congregate settings (recommended in certain situations).** In some situations, testing of asymptomatic people can be of value. For example, in long-term care facilities or homeless shelters that have case clusters, testing of the presumed exposed population can be used to identify asymptomatic carriers and halt chains of transmission by instituting infection control measures. In such settings, testing asymptomatic people has a clear public health benefit.
- **Universal testing in hospital settings (not recommended).** Universal testing of all patients at the time of admission is of limited value in areas with low prevalence of infection (particularly in the absence of a known exposure) because of the high likelihood of false-positive tests. The lower predictive value of a positive test in this setting makes interpretation of the test result difficult. Hospital admission testing may be warranted in certain situations, however, such as patients with known recent exposure to a COVID-19 case or patients who are immunosuppressed in areas where the virus is circulating.
- **Workplace testing (not recommended except in certain circumstances).** In most situations, workplace testing will not be of value, unless the workplace is a congregate setting as described above or if there is a clear cluster of cases and public health officials have determined that testing would offer a public health benefit. Owing to uncertainties in test performance in asymptomatic individuals because of low prevalence of infection in the population, the meaning of a positive or negative test result in this situation is not clear.
- **Testing in schools or other low-risk settings (not recommended).** In most situations, school-based testing will be of limited value, unless there is a clear cluster of cases and public health officials have determined that testing would offer a public health benefit.
- **Widespread community-based testing (not recommended).** Again, in low-prevalence settings, widespread community testing does not offer a public health benefit because of the varying positive and negative predictive value of the test results.

Detection of SARS-CoV-2 antibody (serology)

Serology tests, or tests that detect antibody in blood, can be used to confirm a recent or past infection. At this time, it is not clear whether antibodies are protective, for how long, and at what level. Given the high likelihood of false-positive tests in a population with low antibody prevalence, antibody test results should be interpreted cautiously.

- **For donor identification (recommended).** Some data suggest that immunoglobulin therapy may be useful as a therapy for COVID-19 cases; therefore, antibody tests may be used to identify convalescent plasma donors.
- **For clinical management to confirm recent infection (recommended in certain situations).** In limited situations, antibody testing may be warranted in a highly suspected case for whom RT-PCR and antigen testing are negative. For example, later in the clinical course, viral RNA or antigens may be below the level of detection. If a clinician has a strong suspicion that the patient has COVID-19 and has been ill for a long

enough period to develop antibodies, then antibody testing may have a role if the test result would influence clinical management.

- **For testing of healthcare workers to determine immune status (recommendation unclear).** In areas of high prevalence of infection, where healthcare workers have routinely cared for COVID-19 patients and past exposure is highly likely, some hospitals have instituted testing of healthcare workers, particularly for those who have had a compatible clinical illness. The implications of a positive test, however, remain unclear. For example, data are not available to determine if the presence of antibodies confers protective immunity or, if so, how long protective immunity lasts. In low-prevalence areas, where the likelihood of exposure is low, antibody testing of healthcare workers likely offers little benefit. Of note: serology should not be used to determine access to PPE.

- **For workplace testing, other than healthcare settings, to determine immune status (not recommended).** At this time, widespread workplace antibody testing is not recommended. Given the increased probability for false-positive antibody tests in a population with low antibody prevalence, and the uncertainty as to whether antibody following infection confers protective levels of immunity, antibody testing in such settings will likely not offer measurable public health benefit.

- **For issuing immunity "passports" (not recommended).** Antibody testing for the purpose of certifying that someone has antibodies against SARS-CoV-2 is not recommended because of concerns with test performance in situations with low prevalence of infection and the lack of understanding regarding whether an antibody test confers immunity (to what degree and for how long) (WHO 2020).

SARS-CoV-2 serosurveillance

- **Public health surveillance and research (recommended with rationale and caveats).** Serosurveillance can be used to estimate the percentage of a population with antibodies and presumed recent infection (taking into consideration issues with test performance identified above). Antibody tests to assess seroconversion should be used for public health surveillance and research, in close collaboration with epidemiologists, biostatisticians, and other public health professionals to ensure that the sampling methodology is sound and allows for extrapolation of results to the population of interest. Reporting of serology surveillance studies should be transparent regarding their sampling and recruitment strategies and clearly articulate potential sampling biases.

Priority testing hierarchy for settings in which test resources are limited

The need for testing will likely far outpace testing capacity, particularly during surges. When test resources are limited, we recommend priority testing with molecular or antigen tests as appropriate, given the limitations discussed above, based on the following hierarchy (CDC 2020):

1. Those with symptoms who are critically ill and hospitalized

2. Symptomatic healthcare workers and first responders, symptomatic individuals in congregate living facilities, and symptomatic essential workers

3. Symptomatic individuals in the community

4. Asymptomatic people living in congregate settings (e.g., long-term care facilities or homeless shelters) for the purpose of infection control

Infrastructure to Support Testing

Laboratory testing is a complex collection of many parts that collectively provide a test result. Testing infrastructure includes the physical and organizational pillars needed to provide and support testing initiatives. Laboratories require adequate facilities with features such as air-handling systems and biosafety cabinets to ensure staff safety and specimen integrity and informatics systems capable of automatically and seamlessly receiving and reporting test results. The infrastructure needed to provide testing requires funding, test supplies, test consumables, and technical laboratory oversight to ensure regulatory and quality oversight but also extends to programs and support services.

To date, much of the initial response to laboratory testing has relied on public health and commercial laboratories. Despite the fact that a critical segment of SARS-CoV-2 potential testing capacity is in hospital laboratories, federal and many state officials have relied on commercial clinical and public health laboratories for this testing. Hospital-based SARS-CoV-2 testing must be further used to meet testing demands and accessibility. Laboratory testing must be paired with state support at local and institution levels. This requires financial support and the timely allocation of necessary materials, supplies, and skilled labor as well as instrument capacity.

> "Effective testing for SARS-CoV-2 will require a concerted effort that combines laboratory testing technologies with other critical components to optimize a US public health response that includes increased SARS-CoV-2 testing.

Expert state and local public health collaboration is needed to support the testing infrastructure and relies on the identification of the critical populations for testing using a *smart* approach. Test results for individual patients must be communicated and acted upon.

The COVID-19 Testing Cascade

Several key components in the testing cascade are often overlooked but must be considered by policy makers, public health agencies, hospital administrators, and the public. Much public discussion has focused on the availability of testing technologies and supplies, but the ability of laboratories to test for SARS-CoV-2 extends far beyond that. Effective testing for SARS-CoV-2 will require a concerted effort that combines laboratory testing technologies with other critical components to optimize a US public health response that includes increased SARS-CoV-2 testing.

Material capacity

The rush for widespread testing has created unprecedented global demand for essential test components. Shortages have been most acute for nucleic acid extraction reagents—which are chemicals needed to conduct the test—and supplies, particularly for the high-throughput tests. Laboratories have shifted to use research use only (RUO) reagents, but these reagents are also in short supply, and reliance on RUO reagents for mass SARS-CoV-2 testing could lead to shortages in research laboratories. Manufacturers have introduced tests with great fanfare, which has created high demand for the product. Manufacturing, though, has not increased quickly enough to meet demand, with test reagents still in short supply.

Even if reagents are available for a particular extraction platform, shortages in other necessary components required for automated testing platforms such as deep-well plates, filter tips, cartridges, and reaction vessels

limit total testing capacity. For example, some statewide plans to roll out mass testing have been postponed because of the unavailability of deep-well plates even when ample reagent was available. Furthermore, the use of replacement materials may compromise the reliability of the tests because swabs, reaction vessels, and reagents are specific to individual tests. Because each element is part of the FDA submission for test approval, substitution of any one of the components can cause serious diagnostic problems.

Reagents have been prioritized to laboratories conducting high-throughput testing, and while this increases the total testing capacity, it means that smaller laboratories, many of which provide testing for underserved and vulnerable populations, are unable to get reagents. Small laboratories have needed to send their specimens to reference laboratories, resulting in delay, and turnaround time at commercial laboratories can be lengthy as a large volume of specimens are funneled to these large labs.

We recommend that attempts to centralize and coordinate reagent and material distribution at the national and state level be transparent. Laboratories should be consulted about their real-time need and the quantity required to meet the demand for testing in their community. For example, swabs should not be delivered without also ensuring access to viral transport media for the swabs once the sample is collected.

Instrument capacity

As new technologies become available, there is likely very limited capacity to increase the manufacturing of additional parts and the assembly of instruments. Under usual laboratory circumstances, instruments require standard maintenance over time. Running these instruments at maximum capacity to meet the rapidly increasing SARS-CoV-2 testing demand will require additional service calls and parts and will result in instrument down-time. Space in the laboratory to store new instruments and run additional tests is an additional consideration. Quality control material and calibrators are also in very short supply.

Skilled labor availability

Laboratories have adapted to increased instrument capacity by adding shifts and running instruments continuously to meet demand. This increases the need for trained technicians for instrument installation, servicing, and trouble-shooting. This work may require highly trained biomedical engineers to be available on site, and waiting for engineers' availability may lead to instrument down-time and delayed result reporting. For the limited number of point-of-care tests that are approved to be used in CLIA-waived settings, challenges might arise because these tests can be run with limited oversight of quality assurance.

Instrument use and availability

Manufacturers that are introducing new tests are overpromising and underdelivering reagents and supplies for their testing platforms. Manufacturing has not ramped up quickly enough to meet the demand, however, and reagents for instruments are still in short supply.

Many SARS-CoV-2 tests share their testing platform with other viral pathogens; these opportunity costs must be accounted for in any planning. An increase in SARS-CoV-2 testing inevitably means that other necessary medical tests will not be run, and if they are still run, the turnaround time for routine labs will be extended. The demand for routine lab testing in many parts of the county has decreased, but it will increase over time as patients need hospital and clinic services. We will need to balance the demand for increasing SARS-CoV-2 tests with providing routine lab testing as hospitals and clinics begin to increase the number of routine (non-COVID-19) visits. One area that is likely to be most affected is testing for sexually transmitted infections (STIs), as these tests often use the same instruments as the SARS-CoV-2 tests. Increasing STI transmission due to a lack of testing and timely treatment could create an additional public health burden.

SARS-CoV-2 test results need to be reported to the individual or group that can take appropriate action with the information. Test results should be returned as quickly as possible, both for the individual's care and for disease control. COVID-19 transmission while waiting for results to be returned is a concern, especially in a hospital or congregate living setting. For the timely return of test results, laboratory reports need to include all essential information to ensure that the result is for the right patient, results are described, and necessary information to interpret the result is included. Such information includes test limitations, potential for cross-reactivity, and the percentage of false-negative or false-positive results. To help meet the need for testing, professionals have established new COVID-19 test sites and are collecting specimens in many non-traditional locations, such as drive-through testing locations and at home. This disrupts the usual patient-provider relationship. This increases the likelihood that reports may not get back to patients, and, if they do, there is no healthcare provider to help them interpret the results.

Furthermore, public health agencies frequently request epidemiologically relevant information that may not be routinely collected by the provider, such as county of residence and travel history. While many hospital and clinical labs are familiar with reporting requirements, many of the newly established COVID-19 testing sites are not. For example, to initiate contact tracing, the individual's address and phone number are necessary, but this information is not always provided to public health officials with the test results. This ultimately leads to inaccurate case counts and a delay in starting contact tracing. Ideally, results should be electronically transmitted from the instrument to the provider and to the local public health agencies in real time.

Finally, testing should be able to be acted on. For example, to limit disease spread, a realistic plan should be developed for isolation for patients who are diagnosed as having COVID-19 and are living in congregate settings, such as long-term care facilities or shelters.

A Blue-Ribbon Panel of National Experts: A Critical Agenda

We recommend that the US secretary of Health and Human Services (HHS) appoint by July 1, 2020, a blue-ribbon panel of national experts. The panel should include representatives from public health, clinical laboratory, and medicine; the laboratory testing research and development, marketing, and product support industries; ethicists; legal scholars; and elected officials. Key objectives for the blue-ribbon panel should include:

- Define the use cases for testing in various settings (e.g., clinical, surveillance, research, public health).
- Identify global supply-chain issues and develop concrete and measurable steps to address them.
- Clearly identify national guidelines for both virus (i.e., diagnostic) and antibody detection (i.e., serology) testing.
- Determine realistic testing strategies for each setting, given realistic limitations and laboratory capacity.
- Develop a strategy for how testing should be used to monitor COVID-19 hot spots and waves of infections.
- Define optimal performance characteristics of tests, depending on how the test will be used (for symptomatic vs asymptomatic cases, etc.).
- Identify steps necessary to create a streamlined national laboratory testing reporting system and defined reporting standards.
- Generate mechanisms, in coordination with the states, to (1) monitor testing requirements across the country, (2) ensure that resources are allocated and available in areas where they are needed most, (3) ensure that testing capabilities are maintained as needed across jurisdictions, and (4) promote transparency at the state and national levels with regard to resource allocation issues.

- Review rapidly evolving new testing technologies and modalities (i.e. saliva testing) and provide timely recommendations for their use based on *smart testing* principles.

Conclusion

The current testing reality is complicated and depends on a cascade of interconnected factors—and our approach must be strategic. We believe that greatly expanding SARS-CoV-2 testing is a critical element in our response to COVID-19. Policymakers, experts, and the public need to understand, however, that the COVID-19 response requires a smart approach to testing that requires the right infrastructure, right population to test, the right test, and the right application of test results before the right actions can be taken.

We recommend that the US secretary of Health and Human Services (HHS) appoint by July 1, 2020, a blue-ribbon panel of national experts from multiple disciplines. We have identified eight priority areas that need to be addressed nationally before we can maximize our SARS-CoV-2 testing strategy.

Although a blue-ribbon panel can address these crucial priorities, every state should immediately develop a comprehensive testing plan using a *smart testing* framework consistent with CDC guidelines. A smart approach to SARS-CoV-2 testing helps ensure that the right test is given to the right person at the right time, with test results allowing for actions to minimize illness, deaths, and transmission. This must be done as soon as possible, as the primary impact of this pandemic will occur in the next 12 to 18 months.

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