Smart Testing for Optimizing Pandemic Response

SUMMARY

Diagnostic testing has been, and remains, important for our national response to COVID-19. Testing is utilized to diagnose disease in symptomatic patients, screen for asymptomatic carriers, and conduct epidemiologic surveillance to assess the pandemic in order to develop and monitor the effectiveness of public health interventions. Unfortunately, testing during the COVID-19 pandemic has not been as effective as it could be due to the lack of a coherent, coordinated national testing strategy. This has resulted in the inability to target scarce testing resources, including reagents, supplies and testing personnel to where they are needed the most and will have the greatest impact. The following actions should be taken to improve the COVID-19 testing situation in the United States:

- Develop and implement a national testing strategy for the SARS-CoV-2 virus
- Address supply chain issues that have led to shortages of testing reagents and supplies
- Monitor the ongoing development and field evaluation of new diagnostic tests,
- Perform national surveillance for emerging mutations in the viral, and use this information, when necessary, to modify the national pandemic mitigation strategy.

INTRODUCTION

The public health response to an emerging infectious disease pandemic relies on timely and accurate data to assess disease prevalence, transmission routes, and effectiveness of interventions designed to reduce morbidity and mortality. Laboratory testing conducted by the US Centers for Disease Control and Prevention (CDC), state and local public health laboratories, and clinical and commercial laboratories provides much of the data used by epidemiologists to assess and respond to the situation. This data is supplemented by the recent addition of testing sites conducting rapid point-of-care testing.

Traditionally, CDC and public health laboratories perform testing for the initial detection of the novel threat until clinical and commercial laboratories can implement testing, if high volume testing becomes necessary. Once testing in clinical settings is widespread, public health laboratories typically focus much of their testing on protecting at-risk populations and surveillance-based testing, such as outbreak investigation and monitoring the effectiveness of public health interventions. Prior to COVID-19, this progression of testing from CDC to public health laboratories to clinical and commercial labs was predictable, if not always entirely smooth. However, the rollout of COVID-19 testing in the United States has been anything but predictable and smooth and could perhaps best be characterized as chaotic.

Early delays in the dissemination of a diagnostic test for COVID-19 were supplanted by a veritable explosion of laboratory-developed tests, commercial test kits and testing services. This created a myriad of problems that has led to a chronic shortage of testing materials and an inconsistent and uncoordinated approach to testing, which has contributed to an ineffective pandemic response from a laboratory testing standpoint. It is imperative that, in order to make the best use of scarce testing resources including supplies, equipment, and testing personnel, that we develop and implement a coordinated testing strategy for where we are in the current pandemic, plan for post-vaccine testing, and develop a plan to ensure optimal and appropriate use of laboratory testing for future infectious disease threats.

WHAT WAS THE IMPACT OF LACK OF A COORDINATED TESTING STRATEGY FOR COVID-19?

Laboratory testing for SARS-CoV-2, the virus that causes COVID-19, was critical to detecting the introduction of COVID-19 into the United States. And while there was an initial delay due to problems with CDC's test for the SARS-

CoV-2 virus, a major issue that has limited testing is a shortage of testing reagents and consumable supplies, such as laboratory plastics, as well as supplies for collection of specimens at the point-of-care. This shortage, in addition to the ill-timed federal declaration that "anybody who wants a test can get a test," increased the demand for testing at a time when tests were not widely available and when testing should have been targeted to where it was most needed. The shortage of supplies and reagents has never been resolved, and the recent surge in COVID-19 disease has put further stress on the supply chain, which is accompanied by a lack of qualified personnel to fill laboratory vacancies. In addition, there has been a proliferation of rapid antigen tests, including those for home use, that have been deployed to screen asymptomatic individuals. While these no doubt have value if used properly based on CDC guidance, these tests have the potential to be deployed in high-risk settings and collection performed by inexperienced persons, further adding to the concern. The authorization of home testing has introduced yet another variable that can impact the quality of test results.

While is clear that testing is an important component to understanding the course of the pandemic and to helping control the spread of the virus, the current approach of attempting to test all individuals when COVID-19 disease is widespread is not effective as evidenced by the recent surge of disease which has occurred despite a dramatic increase in testing. While screening of asymptomatic or pre-symptomatic individuals in congregate living and other social settings is critical to controlling the spread of disease, it is important to note that expanded testing in the absence of a well-defined action plan may in fact be counterproductive if people fail to observe physical distancing and mask wearing following a negative test result or while awaiting a test result. Expanded screening should be conducted following the guidance provided by the CDC for asymptomatic and pre-symptomatic infection with SARS-CoV-2.[1] This guidance notes that expansion may not be feasible if testing resources are limited, but does not provide guidance on how to ensure that testing resources are utilized most efficiently in order to conserve resources for higher-priority testing. Rapid antigen tests may be beneficial when more accurate PCR-based testing is limited as long as CDC guidance for the use of these tests is followed.[2] Guidance for the use of newly-approved tests that are available without a prescription has not been provided, and the impact and utility of these tests remains to be determined.

WHAT CAN BE DONE TO IMPROVE TESTING DURING THE CURRENT PANDEMIC?

Develop a national plan to support a smart-testing strategy

A Center for Infectious Disease Research and Policy (CIDRAP)[3] report titled "CIDRAP Viewpoint Part 3: Smart Testing for COVID-19 Virus and Antibodies" defines smart testing as:

- Having the right infrastructure to ensure quality testing
- Testing the right population using a test suitable for the setting and end-use of the data
- Providing the right interpretation of the test
- Implementing the right action based on the test results.

The report detailed a number of use cases as examples of how smart testing should be applied to achieve the best possible outcome while maximizing stewardship of scarce testing resources. Because many of the supply shortages and inappropriate test utilization is due to lack of a national testing plan, the report also recommended that the federal government establish a panel of experts to address the myriad issues surrounding testing for COVID-19; however this was never adopted.

Since a national testing plan has not been implemented to address COVID-19 testing, CIDRAP's recommendation to convene an expert panel at the federal level to develop recommendations for a national testing strategy should be implemented. This is a necessary step to optimize the use of testing with goals to improve management of the pandemic as well as to address supply and staffing shortages. The expert panel should base their recommendations on available scientific data and should seek input from professional public health organizations whose members will be impacted by the panel's recommendations. The testing strategy should be a living document that provides for changes to address new testing technologies, as well as changes in the phase of the pandemic. Absent federal government engagement, it would be beneficial for professional organizations to self-organize to develop a mutually agreed-upon testing strategy.

1 CDC. Guidanced for Expanded Screening Testing to Reduce Silent Spread of SARS-CoV-2. Updated December 3, 2020. Available from https://www.cdc.gov/coronavirus/2019-ncov/php/open-america/expanded-screening-testing.html.
2 CDC. Interim Guidance for Antigen TEsting for SARS-CoV-2. Updated December 16, 2020. Available from https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html.
3 CIDRAP. COVID-19: The CIDRAP Viewpoint Part 3: Smart Testing for COVID-19 Virus Antibodies. May 20, 2020. Available from https://www.cidrap.umn.edu/sites/default/files/public/downloads/cidrap-covid19-viewpoint-part3.pdf.

The panel should develop a smart testing framework that:

- Defines testing roles and responsibilities, including public health laboratories, clinical and commercial laboratories, and point-of-care testing.
- Identifies priority populations to be tested in order to:
  - o Diagnose disease in symptomatic individuals
  - o Protect vulnerable populations by screening of asymptomatic and pre-symptomatic individuals
  - o Monitor disease prevalence and the effectiveness of public health interventions.
- Describes the accuracy of diagnostic and screening tests and develop best practices for test utilization and interpretation, including frequency and timing of testing, and prioritization of populations to be tested when reagents and/or testing personnel are in short supply.
- Provides action plans to address screening test results from asymptomatic and pre-symptomatic individuals and populations. These plans should take into account the likelihood of false-positive and false-negative results for the diagnostic or screening test to be utilized, the critical impact of a false-negative or false-positive result, and address the need and process for confirmatory testing.
- Collects and evaluates scientific data on the effectiveness of expanded testing for pandemic interventions such as contact tracing and screening of asymptomatic and pre-symptomatic individuals to enable the expert panel to develop data-driven best practices and recommendations.
- Ensures that actionable data collected is accurate and transmitted to public health departments in a timely manner to ensure that control measures can be implemented as appropriate.
- Provides the flexibility to adapt to new testing technologies and to changes in the pandemic that may warrant a change in testing strategy. The plan should be assessed and updated at regular intervals or as needed to account for changes that impact the types of tests that available and changes in at-risk populations or outbreak settings.
- Establishes and maintains a dynamic virologic surveillance system with sequencing capacity to monitor genetic changes in the virus that may impact the effectiveness of public health interventions including vaccines and therapeutics or increases the transmissibility or disease severity of the virus. The system should be geographically and demographically representative and include a pathway to conduct additional studies to further characterize genetic mutations.

Prepare for the post-vaccine phase of the pandemic

With much of the diagnostic and screening testing now conducted by clinical and commercial laboratories and distribution of vaccines has begun, a program to evaluate the impact of immunization should be developed. Public health laboratories may wish to begin testing to assess vaccine efficacy, vaccine failure and conducting molecular subtype surveillance to monitor changes in the virus that could impact the ability to detect and control the virus. Similar to influenza surveillance, such testing should be prioritized with baseline targets established using a statistical approach. Federal funding should be provided to public health laboratories and to epidemiologists specifically for this purpose, as well as to collect and transmit data to a central location for storage and analysis.

HOW CAN PANDEMIC TESTING BE IMPROVED IN THE FUTURE?

COVID-19 will not be the only pandemic that laboratorians face, and the problems that led to the failure of our response must be addressed to be better prepared for the next pandemic. A robust national testing framework needs to be created that includes guidance from public health laboratories to ensure a more orderly and predictable rollout of testing in the future and to provide for an adequate supply chain and workforce. Messaging of the test plan needs to be consistent and expectations should be set in such a way that they are appropriate and realistic, without a political overtone. To improve the current situation with the COVID-19 pandemic, the following issues must be addressed:

Implement actions to address supply shortages. Supply shortages of everything from nucleic acid extraction reagents to ancillary supplies such as consumable plastics to specimen collection materials such as swabs and viral transport media have plagued the effective implementation of testing that continues at this writing. Laboratories have spent an inordinately large amount of time “chasing reagents,” switching from test platform to test platform, validating methods and training staff and maintaining documentation of all of these activities to meet regulatory requirements. While it is nearly impossible to predict what the next novel pandemic agent will be, it is likely that molecular testing will be important in the initial phase of

testing. To facilitate stockpiling of reagents and supplies and to reduce time required to validate test methods and train staff on multiple platforms, the following should be considered:

- A federal stockpile of consumable plastics, many of which have long expiration dates, and reagents that are used with the standardized instrumentation should be established, along with a system to define when supplies expire. A system to distribute unused reagents that have expired or are nearing their expiration date to research or other non-diagnostic laboratories should also be developed to reduce waste. The federal government should prioritize the need to obtain and stockpile reagents from US manufacturers rather than international manufacturers to limit the dependence on non-US sources.
- Standardization of equipment and supplies should be maximized in order facilitate development of a national stockpile of supplies and reagents. The US Food and Drug Administration (FDA) has noted that it would be "more effective to authorize a small number of well-designed, well-developed and validated tests run on common high-throughput platforms, followed by a few point-of-care tests, all of which are manufactured in large quantities, than to simultaneously develop and authorize scores of diagnostics."[4] Implementation of this recommendation must be done with input from public health and clinical laboratories and with input, but without undue pressure, from manufacturers. While standardization is crucial, it is important to recognize that diversification is also important to ensure that testing supplies are available in the event of supply chain shortages. Instrumentation should include options for low-, medium-, and high-throughput testing. Funding must be made available to ensure laboratories are able to purchase and maintain equipment. While standardization is desirable to ensure a robust pandemic response, it is recognized that different jurisdictions may have different needs and constraints, and there is a need to balance innovation with preparedness. Therefore, there must be some flexibility built into the system to enable the implementation of novel technologies as they are developed.

Create a national testing system. A robust national laboratory testing program needs to be designed that includes all of the major laboratory systems (i.e., public health, clinical, commercial and federal laboratories) so they can work together on best practices during a pandemic instead of competing with each other for resources. It has been suggested that the Department of Health and Human Services (HHS) establish an office on national laboratory policy that could serve in a coordinating role.[5]

- The role of each laboratory should be defined. The plans should include a description of what resources are required to be able to implement testing rapidly while ensuring quality and accuracy of results. Plans should define how testing can support a response during and after a pandemic. An effective plan should not only address testing, but should include public health strategies to optimize the impact of testing.
- A coalition/council of laboratories of all types should be convened to provide ongoing feedback regarding testing roles and functionality of the national plan during a pandemic situation. This council should work closely with epidemiologists and physicians to ensure that the need for test data to monitor and control the pandemic is being met. It will be important to define the role of testing at various phases of the pandemic, especially addressing the recognition that we have never been able to identify cases early enough to contain a pandemic with contact tracing.

Improve data collection and sharing. Data collection and sharing is critical to understanding and controlling the pandemic. A nationwide interoperative data collection system must be established that includes governmental laboratories such as CDC and state and local public health laboratories as well as clinical and commercial laboratories. The system should include a mechanism for collecting data from non-traditional sites, which has been particularly problematic with COVID-19. Manufacturers must ensure that data generated on point-of-care systems can be reported electronically and in real-time to public health departments. There should be consensus as to what demographic data needs to be collected to monitor the pandemic. Public health surveillance frequently requires data that are not normally collected by clinical and commercial laboratories, and there needs to be seamless coordination and integration of clinical and public health data. APHL can play an important role in developing the partnerships necessary to develop a set of universal data fields.

Update regulatory requirements. Problems with the rollout of the CDC emergency use authorization (EUA) test for COVID-19, coupled with the inability of laboratories to implement their own laboratory diagnostic tests, led to a widely-publicized lengthy delay in testing. FDA ultimately relaxed their requirements for laboratories and test kit manufacturers, which increased the availability of testing, but allowed a flood of tests of sometimes questionable quality to enter the market. In addition, there was little or no guidance as to how these tests should be utilized and how the results should be interpreted and confirmed. This is particularly concerning now that a test that is available without a prescription has been approved for home use.

4 Shren J. and Stenzel T. (2020). COVID-19 Molecular Diagnostic Testing—Lessons Learned. New England Journal of Medicine 2020; 383:e97. Available from https://www.nejm.org/doi/full/10.1056/NEJMp2023830.

5 Toney, D., Pentella, M., Blank, E., & Becker, S. (2021). Creating a Blueprint for the Future: Lessons Learned From Public Health Laboratories in the COVID-19 Response. Journal of Public Health Management and Practice : 27 Suppl 1, S101–S105. Available from. https://doi.org/10.1097/PHH.0000000000001285

- At the federal level, HHS should convene a panel to revisit the EUA process and how FDA regulates tests during an emergency to make the system more efficient, while ensuring quality of testing. The federal panel should work with FDA to develop a system that works within and builds on the existing laboratory regulatory infrastructure, rather than replacing it solely with the more stringent EUA process.
- Reagent shortages necessitated laboratories to frequently implement and validate new protocols. Staffing shortages necessitated training personnel to conduct testing and ensuring that they were competent. The process of validating tests, training staff and generating the accompanying documentation is a time-consuming and resource-intensive activity. FDA has noted that there needs to be a common approach to validating test design and performance regardless of whether there is an emergency.[6] However the requirements for test validation during a non-emergency, were too burdensome to fulfill during the COVID-19 pandemic and were modified "on the fly." To ensure consistency, FDA, CDC, and the Center for Medicare and Medicaid Services (CMS) should develop and publish standardized and streamlined procedures for rapid validation of new tests so that they are in place prior to a pandemic to ensure test quality while allowing staff and reagents to be dedicated to diagnostic testing. Likewise, a streamlined process for emergency training of staff should be developed prior to the next infectious disease pandemic. This process should include competencies and basic skills required for staff to perform testing, data entry and other laboratory functions.

Ensure quality of testing. Quality assurance must be maintained for all testing, whether it is laboratory-based or point-of-care, but this activity has been difficult to sustain due to the rapid proliferation of test kits and testing laboratories. FDA should implement post-market surveillance of all diagnostic and screening tests that receive an EUA during a pandemic or other health emergency and make the information available to enable optimization of testing recommendations. CMS must be provided with the resources to ensure that newly established laboratories are capable of providing data of acceptable quality. This information should be made public for users considering contracts with these laboratories to ensure that they are reputable and their performance has been vetted. CMS should develop procedures that provide flexibility in enabling labs to meet quality standards in the least burdensome way during a pandemic situation.

Improve communication. Communication during the COVID-19 pandemic has been particularly ineffective, especially as concerns the availability and role of testing and the meaning and interpretation of test results by both clinicians and patients. Messaging to the public must be realistic, truthful, coordinated and consistent at both state and federal levels. The popular media was quick to pick up on overly optimistic promises of test availability from federal officials as well as from test manufacturers. Federal agencies distributed testing instruments to public health laboratories with great fanfare, without ensuring that test kits were available and sustainable. This resulted in unrealistic expectations by the public and placed undue burden on testing laboratories and individuals collecting specimens. Pandemic plans should define how mainstream and social media can partner with public health to support programs to adequately respond to an outbreak by helping to disseminate scientifically valid and consistent information to the public.

Provide adequate funding. Finally, the federal government must provide for adequate funding to support a national laboratory infrastructure that is prepared to recognize and address an outbreak situation as it occurs. Public health laboratories, and the public health system in general, have been underfunded for many years and reimbursements to clinical laboratories have also declined. Funding has been provided to states for testing, however money alone cannot resolve a shortage of reagents and supplies, or a lack of qualified laboratory testing staff. Additionally, it should be noted that the funding that has been provided is not sufficient to sustain testing at the level that laboratories are currently performing. Adequate funding and reimbursements are critical to ensuring that a strong laboratory network can be created and sustained.

6 Shren J. and Stenzel T. (2020). COVID-19 Molecular Diagnostic Testing—Lessons Learned. New England Journal of Medicine 2020; 383:e97. Available from https://www.nejm.org/doi/full/10.1056/NEJMp2023830.

Association of Public Health Laboratories

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