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Perspective

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# Testing in a Pandemic — Improving Access, Coordination, and Prioritization

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The moment a new lethal virus begins spreading in human populations, public health authorities and the communities they serve enter a race against time to prevent a major outbreak.

Success depends on tracking viral spread rapidly from its early stages to identify people who are infected and protect those who aren't.

With SARS-CoV-2, the United States lost that race. Nearly a year into the U.S. outbreak, the national case count exceeds 20 million. Most of the country is still not doing enough testing. When tests are performed, the organizations processing them often fail to achieve fast enough turnaround times (ideally, 1 to 2 days) to permit effective contact-tracing efforts. On average, Americans wait 4 days to receive a test result; 10% of Americans have waited 10 days or more. And testing is beset by racial disparities.[1] Many people are now asking why these failures persist. The answer is twofold.

First, we failed to build and scale up sufficient capacity for diagnostic tests in clinical laboratories. During the first month of the U.S. response, our highly centralized regulatory system prevented many laboratories from joining production efforts. Once a pathway was opened, leaders of most clinical laboratories either didn't know how to navigate regulations or lacked the capacity and resources to produce their own tests. Today, only 45 of 260,000 U.S. laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) standards have received emergency use authorizations (EUAs) to produce their own laboratory-developed tests (LDTs), and 197 are using tests of their own that have been validated but have not yet been approved by the Food and Drug Administration (FDA).[2] Even the FDA's August 2020 decision to allow laboratories to establish Covid-19 LDTs without premarket approval failed to encourage further production by the vast majority of clinical microbiology laboratories, and potentially added more hurdles, given that liability protections under the Public Readiness and Emergency Preparedness Act disappeared in the absence of EUA coverage.

A simple technological solution was available: polymerase chain reaction (PCR). A highly sensitive and specific nucleic acid testing technology, PCR is well suited for clinical testing and easily adaptable for new pathogens. Yet most clinical laboratories have not used it to develop their own tests. Instead, we became dependent on commercial manufacturers, creating a system that leads to price gouging: in some instances, prices of Covid tests have reached $2,315.[3]

Simultaneously, the federal government did not adequately use its power to support expansion of production capacity in clinical laboratories. The Defense Production Act (DPA) could have been used to fund broad, distributed production of tests and to forcefully check otherwise-unfettered capitalism. Instead, according to the Congressional Research Service, the Trump administration's invocation of the DPA was "sporadic" and "narrow": of the $1 billion allotted by the Coronavirus Aid, Relief, and Economic Security (CARES) Act for production of personal protective equipment and testing materials, $688 million was redirected to Department of Defense expenses.[4]

Second, our leadership never created a coherent national prioritization strategy for the distribution of limited testing capacity. Meanwhile, the current administration, professional sports teams, businesses, colleges, and others began testing many thousands of asymptomatic people — sometimes daily — often while surrounding communities struggled to meet basic clinical testing needs. Asymptomatic surveillance testing is a useful addition to a robust testing strategy, but when testing and resources are scarce, it is wasteful and can even be ineffective in protecting the groups surveyed, as the White House outbreak demonstrates. The more we delay prioritizing and creating the infrastructure needed for hypothesis-driven testing (e.g., symptomatic persons, contacts, high-risk groups) on a massive scale, the more we risk containment failure.

Other countries have shown responsible leadership, prioritization, and coordination. From the pandemic's outset, a distributed network of German laboratories had the expertise and capacity needed to rapidly develop and implement PCR tests, facilitated by their centralized national health care system. They overcame supply shortages through standardized criteria prioritizing symptomatic cases, and with clinical cases largely under control by May, they responsibly shifted to asymptomatic surveillance testing of at-risk communities. Similarly, molecular biologists throughout Africa started developing PCR-based tests for SARS-CoV-2 in early February.

By building distributed capacity and prioritizing resources in response to public health demands, the United States, too, can transform our trajectory in fighting this pandemic — and preempting future ones. The essential steps are clear.

First, we need to support clinical laboratories to build LDTs and navigate regulations with ease and speed. Continued test shortages prove that funneling resources into a few commercial companies alone is not enough. To quickly respond to emergent viruses or new variants of existing viruses, and to provide stopgaps to prevent spread, we must empower the FDA, the Centers for Disease Control and Prevention (CDC), and the public health community to support — by means of clear regulatory processes and training — broader, distributed capacity to build and administer tests in clinical labs.

The FDA can simplify regulatory processes for LDTs and provide resources for navigating a rigorous but nononerous authorization process. Rather than remove oversight altogether, the agency should set and maintain common standards and straightforward expectations for regulatory processing of tests, with quality and efficiency being paramount. Particularly during an outbreak, they should provide greater resources to support applicants and give regular updates on the timeline for approval.

The CDC, public health departments, and others can provide training courses and materials for creating clinical grade LDTs that meet FDA standards, for troubleshooting, and for completing clinical validation. We have seen firsthand that such LDT creation is possible, through our hospital network in West and Central Africa (https://acegid.org) and at Massachusetts General Hospital, where we established a real-time reverse-transcriptase–PCR LDT for SARS-CoV-2 within a week after the FDA began allowing it.[5]

Second, research and development resources must be provided. Grants, loans, and incentives should be broadly administered under Title III of the DPA to enable clinical laboratories to acquire the equipment, consumables, and reagents needed for building, validating, and conducting tests. The allocation authority of the DPA should be used to encourage fair and need-based allocation of scarce testing supplies to laboratories in regions of high transmission risk.[4] We believe that the United States also requires either a new national institute or far greater support for existing ones to provide a range of resources to all test developers, including engineered and patient clinical samples and reagents, within short time frames. As a federal entity, such an institute could enable a centralized alloca-

tion strategy for diagnostic development resources at reasonable cost, under the DPA.

Third, we need to prioritize test distribution. Successful containment of Covid-19 requires a prioritization strategy for facilitating equitable access to tests according to need. In communities where the demand remains unmet, decision makers will have to redirect existing clinical grade testing to symptomatic people, contacts, and high-prevalence areas before spending resources on surveillance testing of low-risk persons. To enable a full economic reopening of the United States, non–clinical grade tools could be dedicated to surveillance and to identifying potential asymptomatic cases for clinical investigation. Simple PCR tests administered outside CLIA settings, and other easy-to-use surveillance tools such as loop-mediated isothermal amplification — a highly specific, cost-effective, rapid, and scalable technology — are currently being explored as potential alternatives.

*An audio interview with Dr. Sabeti is available at NEJM.org*

As we fight Covid-19 and prepare for new threats, including a potentially pandemic-level strain of influenza, we need to pave a better path. We believe that our leaders need to motivate and support a laboratory-based testing model that enables broad and distributed production capacity. We must build a national system that operates according to rapid regulatory processes with clear, rigorous standards, facilitates innovation and training, provides resources for ongoing test development, and prioritizes supplies on the basis of need. Before Covid-19, virologists predicted the emergence of a novel "Disease X." It's here now, and we still have not contained it. When "Disease Y" arrives, will we have learned?

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# *Roman Catholic Diocese of Brooklyn v. Cuomo* — The Supreme Court and Pandemic Controls

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On November 25, 2020, as Americans prepared to celebrate Thanksgiving during a pandemic, the U.S. Supreme Court, by a 5-to-4 vote, undermined states' ability to control that pandemic. In *Roman Catholic Diocese of Brooklyn v. Cuomo*,[1] the Court temporarily enjoined limits on in-person religious worship imposed by New York Governor Andrew Cuomo. Although the injunction will have little effect because the restrictions were no longer in place by the time of the ruling, the decision has the potential to upend public health law during the current pandemic and afterward.

Since March 2020, U.S. governors have placed numerous restrictions on public gatherings in an effort to reduce transmission of SARS-CoV-2. Many of these restrictions have been challenged in court as violating a broad array of constitutional rights, including free exercise of religion, freedom of speech, and the right to travel. Initially, most courts rejected these claims, citing the Supreme Court's 1905 decision in *Jacobson v. Massachusetts*, which upheld a Cambridge, Massachusetts, regulation