COVID-19 Testing and a Path out of the Pandemic

Gigi Gronvall

Address correspondence to this author at: Johns Hopkins Center for Health Security, Department of Environmental Health and Engineering, Baltimore, Maryland, United States. Email ggronvall@jhu.edu.

For the US, COVID-19 testing is here to stay. The White House's "Path out of the Pandemic" announcement on September 10, 2021 calls for increased access to COVID-19 testing and testing programs, including for schools and for employees of businesses larger than 100 people who are not vaccinated.(1) To increase the availability of tests, the Defense Production Act has been invoked by the Administration to increase manufacturing, free pharmacy testing has been expanded, and home rapid antigen tests will be sold at reduced prices by major retailers. This plan is a welcomed ramp-up of testing capacity which will help address current shortages of tests and long delays in getting test results. It will be important, however, for the US government to not only address the current demands for testing but to anticipate what testing needs are likely for the future, and plan for them. Testing needs are increasing and will change—though not disappear—when cases of COVID-19 eventually decline.

Testing must be accessible, timely, and verifiable

Many people have a recurrent need to produce a verifiable, timely, negative test result to gain access to their employment, flights, school, camp, cruises, or other events. A COVID-19 negative test result has become a de facto "passport" for access, even for vaccinated people. However, negative test results are time-limited and so tests must be repeated often to prove that someone does not have an active SARS-CoV-2 infection. A verifiable test result (for example, from a diagnostics laboratory or a pharmacy) is often required 72 hours before an event/activity that requires it for access, which places a premium on accessible testing appointments within that 72-hour window and a quick turnaround time for testing results. For schools with pooled COVID-19 testing programs, one positive pool test may send an entire class for testing to identify the positive case(s), and to determine who may continue in-person learning and who must quarantine. While many schools perform individual tests after a positive result as a matter of policy, a positive pool test result can lead to a scramble for parents and guardians to get results as soon as possible, before the school testing can be performed, so they can identify if their child has COVID-19.

Rapid antigen tests can be more useful if home-use is verifiable or if batching could be more user-friendly

Rapid antigen tests are in many ways superior to molecular laboratory tests to identify actively infectious people.(2) The tests provide results quickly, within 20 minutes, so immediate action can be taken, unlike the delays of 24-72 hours (or more) for a laboratory test. Unlike PCR tests, there is no amplification step in the rapid antigen test, so a positive result may be more indicative of an infectious case. In contrast, a person who is recovering from COVID-19 and is no longer infectious may continue to test positive in PCR tests for weeks or longer; the positive test result therefore does not indicate infectiousness. One significant drawback of the rapid antigen test, however, is its verifiability—a person may test at home, but the result will not usually be verified by a third party, and thus this test will not be useful for flights, returning to school or work, or access to other activities. There are video-call services that can verify results, where medical technicians directly observe a person giving themselves a test and see the result, but these testing services are higher priced than a rapid antigen test purchased from a pharmacy.

Verification of a test result using an antigen test can be achieved if the test is given at the point of desired access and is therefore verifiable by the test-giver (for example, a testing service that performs a

rapid antigen test just before boarding a flight, or before entering school). However, to accomplish testing at the point of entry there are logistical hurdles of processing tests. For example, some school systems have put into place “test to stay” protocols, in which close contacts of an infected student are not quarantined but allowed to attend school if they are tested every day. While this maximizes learning in person for the 98% of students who are affected by a quarantine and are not likely to become positive for COVID-19, this testing strategy requires school nurses to process a lot of tests, depending upon the pool size.(3) As rapid antigen tests need to be read within a certain time—the Abbott BinaxNow test requires it to be read within 20 minutes—this organizational hurdle for performing and reading rapid tests may be difficult for all school systems to achieve, particularly as school nurses have to attend to other issues in addition to COVID-19 testing. Validating the test result accuracy beyond that time limit would help school nurses use the tests on more people.

A strategy is needed for false results, particularly as COVID-19 cases decline

Organizations that require negative COVID-19 tests for access to on-site employment, in-school learning, or access to events and activities need a strategy for dealing with false results from COVID-19 tests. *False negative* results from a COVID-19 test are a problem for public health, because if someone tests negative but is actually infectious, they may end up sparking a cluster of disease. However, it is the *false positive* cases which cause an immediate problem for the organization that is using testing as a passport for access to activities. Major social and economic disruptions from quarantines, missed flights, and denied access to employment, paid-for cruises and concerts are immediate challenges for an organization doing the testing and risks personal confrontations. If a confirmatory COVID-19 test is given after a positive test, a potentially contradictory result will likely come too late for the person who hoped to use the test to gain access to a flight, cruise, or other activity.

False results are rare with tests that are highly specific and sensitive, but they do occur, and can be statistically predicted. Furthermore, the accuracy of the test depends not only on the test itself, but on the prevalence of disease within the population. As COVID-19 cases decline, the probability that a person who receives a positive test result actually has the disease, i.e. the positive predictive value, also declines. As COVID-19 tests are used for access to desired and paid for activities, as cases wane, a growing percentage of people will be declined access based on false results. For diseases in which accuracy is medically important even in low-prevalence settings, such as HIV/AIDS, the standard is to administer up to three sequential tests for increased accuracy. A similar standard should be considered for COVID-19 tests once case counts decline or in low prevalence settings.

Learning from past mistakes in testing and becoming better prepared for future health security threats

From the beginning of the pandemic, access to reliable COVID-19 testing in the US has been marked by failures, delays, and missteps. At first, diagnostic tests were slow to be rolled out. Due to the delays in reliable diagnostic testing, many people thought that they may have already been infected by SARS-CoV-2 and were potentially immune. There was talk of “immune passports” which could exempt the previously infected from public health measures including quarantine, if people could demonstrate that they had recovered from COVID-19. This began a “wild west” for serological (antibody) testing. Manufacturers rushed to fill the market with tests that received FDA emergency use authorization but were often not accurate.(4) There was an all-too-brief period where there appeared to be enough access and availability of testing in many parts of the country. As vaccine became available and

vaccination clinics prioritized, however, mass testing sites started to curtail their hours and shut down completely. In the spring of 2021, when it was announced that vaccinated people did not have to continue to test, rapid antigen testing sales decreased, and manufacturing curtailed. Then came the delta variant: cases went up, and COVID-19 testing again became a scarce resource. At-home rapid antigen tests were hoarded and are largely not available in drugstores, and there are significant delays in laboratory tests.(5)

The mixed record of COVID-19 testing in the US, with alternating cycles of accessibility and shortages, should be an indication that improvements are necessary to anticipate testing needs and that manufacturers need to be incentivized to be prepared for future health security threats. It also indicates the strong demand for testing and verification of health information, which is important for COVID-19 and for future epidemics. For now, as a path out of the pandemic, we must ensure that testing for COVID-19 is accessible, verifiable, fast, and accurate.

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