There Are Not Enough COVID-19 Tests. There Are Also Too Many COVID-19 Tests.

By Maggie Koerth
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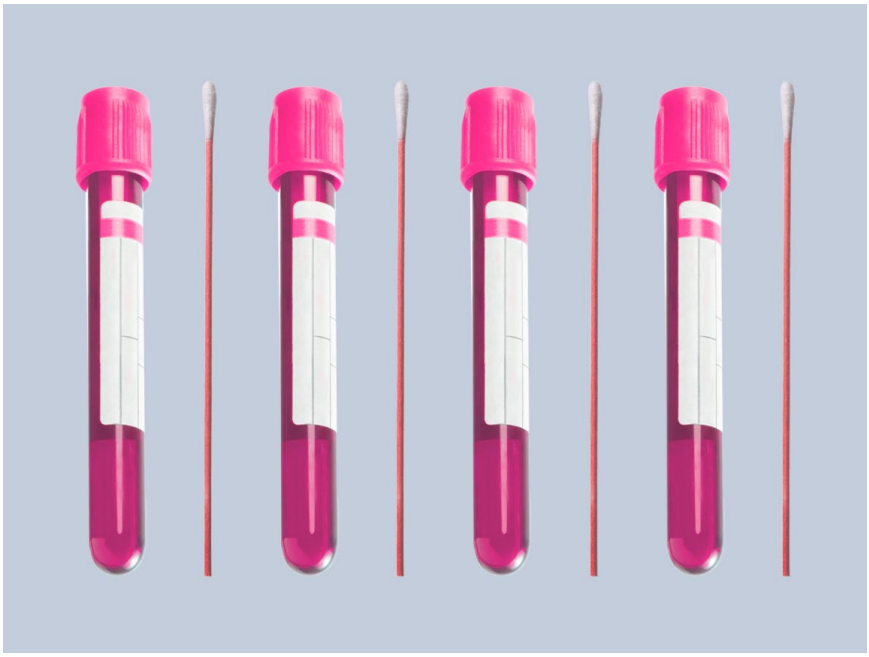

There are still not enough Americans being tested for COVID-19, but there are now many, many ways to be tested. The U.S. started this pandemic with a single diagnostic test, administered solely by the Centers for Disease Control and Prevention. But there are now 57 different tests that have been granted emergency approval by the Food and Drug Administration and more than 190 laboratories are conducting them. The FDA says it is aware of hundreds more tests in various stages of development. Press releases touting the latest and greatest fill the inboxes of journalists like viruses replicating in a cell.

It's an overwhelming jumble, and even some experts have lost count of how many new tests are out there. The proliferation has helped the country drastically increase its testing capacity. "We went from zero tests a day to … something. I don't know, but well

over 100,000 tests a day. In that one month," said Dr. Alex Greninger, assistant director of the University of Washington's Clinical Virology Laboratory.

But experts say we still don't have enough tests to safely do something as complicated as reopen the economy. Yet the test development process has been optimized for speed, rather than quality. Somehow, we're simultaneously not moving fast enough while also moving a little too fast.

The tests for COVID-19 fall into two basic categories: direct tests, which look for the presence of the virus in a patient, and indirect tests, which look for antibodies that show a patient's immune system has encountered the virus at some point. We'll need both to safely emerge from the confines of social isolation, said Scott Becker, chief executive officer of the Association of Public Health Laboratories. The direct tests are critical for finding infected people, tracing who they have been in contact with and isolating them before they can pass the virus to others. The indirect (or "serological") tests, administered across broad swaths of the population, can help public health experts understand how the virus spreads and how people build immunity to it.

So far, Americans have primarily been dealing with direct tests. When you've heard about the tests where people are getting extra-long Q-tips stuck up their noses, those are direct.

Although a number of the new direct tests involve special machines designed by the tests' developers for this purpose, the basic science behind them can be done on common pieces of lab equipment that already exist in lots of places. To ramp up our testing capacity quickly, a lot of that equipment has been called into service — a sort of scientific version of the evacuation of Dunkirk, with research and diagnostic labs across the country setting aside their regular work to take up the cause. "Everybody has their homebrew test," said Dr. Davey Smith, a research virologist at the University of California, San Diego. "Anybody who has a thermocycler has basically turned it into a testing platform."

But we still aren't able to test enough people fast enough. Ideally, Greninger said, we'd have a single testing platform that would allow a medical worker to take a sample from

a patient, put it directly into a machine with little hands-on time and quickly process thousands of tests over the course of a single day.

When those features aren't all in one package, it essentially means that you need more people and more equipment — and both are in short supply. Researchers still don't have enough of the chemicals they need to run direct tests. For years, it was cheaper to manufacture those key ingredients overseas and keep just enough of the product on hand. Nobody had stockpiles. A global pandemic increased demand at the same time it decreased access to the supply, and while companies are now making the chemicals in the U.S., we've still not caught up to the quantities needed, Smith said.

And some of the best tests still have serious drawbacks, Greninger said. Take Cepheid's Xpert Xpress, a direct testing system that processes samples in little cartridges that pop into a specialized machine. "A Cepheid is a fantastic instrument, but you can run one cartridge every 45 minutes," he said. "If you have a wall of Cepheids, you could potentially do 1,000 tests a day. But you have to own 100 of those little instruments." Another test that's gotten a lot of press, from Abbott Laboratories, takes 13 minutes to deliver negative results (it takes less time to process a positive sample — but most samples will be negative). However, it requires a lot of hands-on labor, he told me. And people, Greninger and Smith said, are in nearly as short of supply as chemicals.

If the number of direct tests has exploded, then the number of indirect tests is like a star going supernova. While only four have received an Emergency Use Authorization from the FDA, the agency says it has been notified by 98 test developers that they are offering tests for sale. That's significant because of the approach the FDA is taking to new indirect tests. Usually, companies would have to go through years of research to prove, document and verify the quality and effectiveness of a new test before it could earn FDA approval. Now, though, the agency is allowing the entire approval process to be sidestepped, saying it won't object to any new test being used by the public so long as the developers tell the FDA about their test and don't try to make false claims about what it can do. If they want to get an EUA, the developers can voluntarily document how well their test works and send the data to the FDA — after the test is already in use.

These indirect tests are crucial, experts told me. They can turn up a false negative if you take them too soon, without giving your body enough time to build up antibodies. But they're the tool epidemiologists need in order to get a better handle on how many Americans are actually contracting this virus, and who has and hasn't built up some level of immunity.

That means dozens of tests — not including the four tests with an EUA — are being sold despite never having submitted data to the FDA to show how well they work (or even prove they do). They are being sold and used, but may not be useful. "There's a lot of stuff out there of dubious quality," Becker told me. The city of Laredo, Texas, spent $500,000 on serology tests it later determined to be "unreliable and unusable." The same thing happened in the United Kingdom — only to the tune of $20 million.

"It's the wild, wild west," Smith told me, and that's even before you get into the fact that few of these tests — whether serological or diagnostic — have been checked against each other to make sure there aren't big differences in the results they each turn up. Counties, states and individual hospital systems are all using different tests and testing platforms, Smith said, but we don't really know at this point if one swabbed sample would produce the same result in California as in South Carolina. "I don't want to belabor this and say it was a mistake [to move so quickly]. It's not," Smith said. "Better to get tests out there even if some were marginally good. They were good enough for the moment. But now we need to figure out how we validate this."

That kind of cross-checking is going to be a big part of how we move forward. And so is simply getting more access to needed supplies. For example, one of the world's biggest suppliers of medical swabs was in Italy — which obviously threw a wrench in supply chains when the country was hit hard by the coronavirus. Now the FDA is relaxing rules on the types of swabs that can be used, opening up opportunities for U.S. manufacturers to design and produce new types. But at the same time, it's also relaxed the rules on how swab samples can be taken — steps that make the diagnostic tests less invasive for patients, but could result in a higher rate of false negatives.

Trying to test more while also maintaining quality control is a hard balance to strike. But there are some ways to walk that line that are less fraught than others. Maybe one of the first things we need to do, Greninger said, is get everybody on the same page about testing criteria. Some laboratories are not reaching their testing capacity because the hospitals they serve are only allowing a narrow swath of people to get tested. Making better use of the tools we have would be a step in the right direction.

Ultimately, a lot of these problems are just about the learning curve for figuring out something totally new, Becker told me. "We've never had to stand up lab capacity across our country and around the world at the same time," he said. "We've had outbreaks and SARS and MERS, but that wasn't this. We've never done this before."

Source: https://fivethirtyeight.com/features/there-are-not-enough-covid-19-tests-there-are-also-too-many-covid-19-tests/