COVID-19 Testing

Doug Melancon, MD |April 2020

Doug Melancon, MD serves as Associate Research Director and as Advent's Healthcare analyst with more than 25 years of experience covering the industry. Prior to joining Advent in 2004, Doug performed Healthcare research and portfolio management for Merlin Biomed Group. He previously worked as a Co-Portfolio Manager and senior healthcare analyst at Merrill Lynch and Morgan Stanley. He is known for his keen ability to distill medical innovation and assess its importance to companies. Doug is a graduate of University of Illinois and received his MBA from University of Illinois's school of business and his MD from University of Pennsylvania's School of Medicine.

Executive Summary

The SARS-COV2 virus which causes the COVID-19 disease has brought much disruption to our lives, our families, and the economy here and abroad. While the headlines seem grim, as infections and fatalities continue to climb and people lose their primary source of income, things will improve in the not too distant future. Before a treatment and/or vaccine arrives, testing will be one of the main tools that can start the easing of social distancing and can help determine which healthcare workers are safe to go to work after exposure to the COVID-19 virus. We are expecting the country to go through regional crises with COVID-19, with the East and West Coast likely starting to resolve first in April, with other parts of the country starting to resolve in May. We do expect the virus to return this fall, but our healthcare infrastructure and surveillance systems will be in place to address the virus much sooner.

Why is testing important?

On March 16th, the WHO Director-General stated the following:

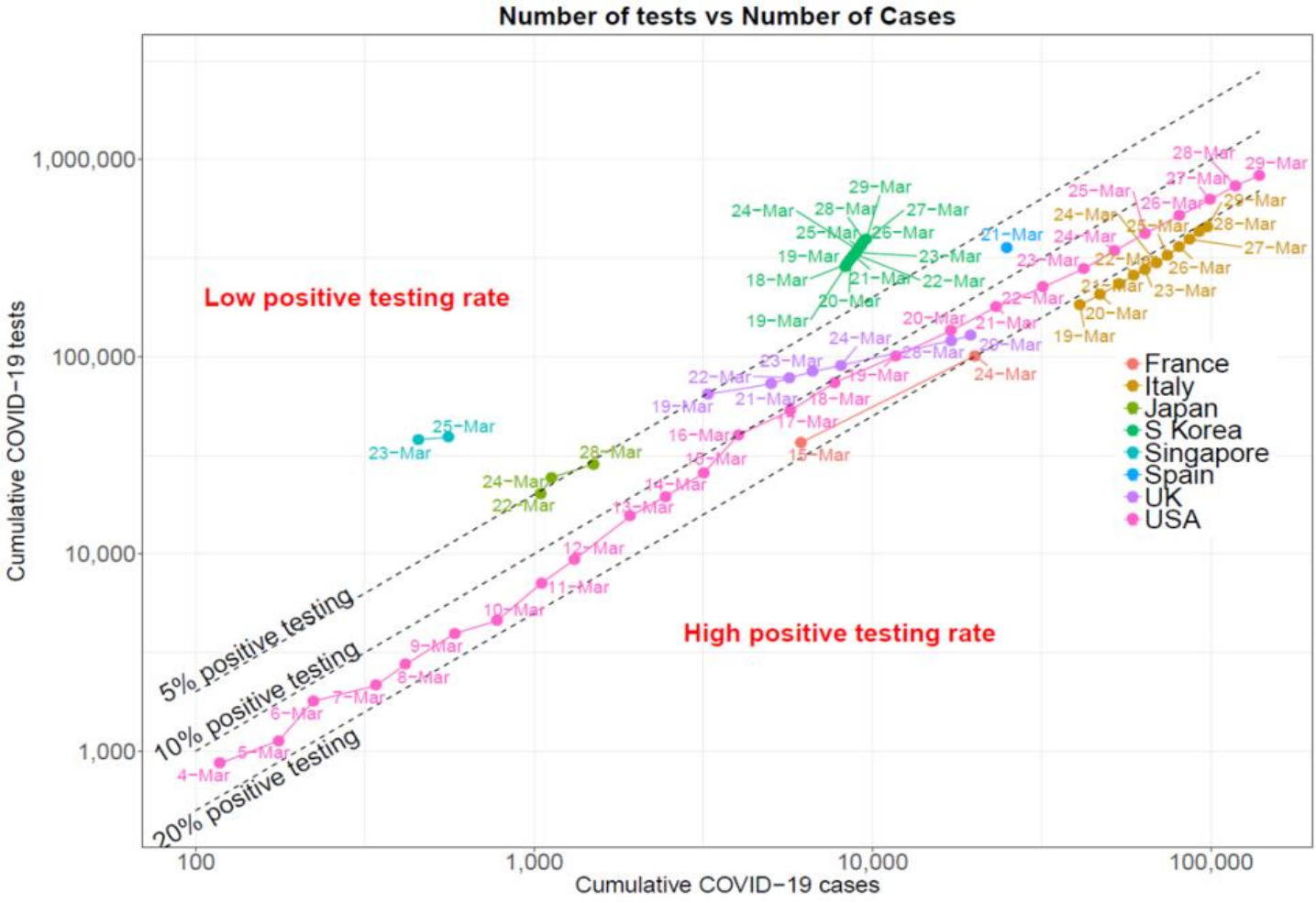
"We have a simple message for all countries: test, test, test. Test every suspected case. If they test positive, isolate them and find out who they have been in close contact with up to 2 days before they developed symptoms, and test those people too."

South Korea has provided one of the best examples of the benefit of widespread testing, isolation of positive patients, and tracing of their contacts. South Korea (population 50mm) set up dozens of drive-thru centers where anyone could get tested, not just people with symptoms, and get an answer within 1-2 days using a PCR test (see below). With its first case identified on January 19th, South Korea started widespread testing in early February and has limited its case rate to 187 per 1mm of the population (test positivity rate less than 5%). Germany also has seen success with testing, helping lead to a low death rate of roughly 0.5% vs over 4% in France and over 1.5% in the US. Germany instituted testing early on, catching younger people coming back from traveling outside the country. With mostly younger people being infected initially, that has helped keep Germany's death rate low.

The United States, with its first case identified on January 20th, is running at a case rate of 429 per 1mm of the population. Italy and Spain, the hardest hits in Europe, have case rates exceeding 1600 per 1mm - those countries did not put in mitigation and testing strategies in place until it was too late.

New York and New Jersey are showing over 35% of conducted tests are positive, as testing is limited to people with symptoms. States with a low number of positive tests also do not have widespread testing. So, the actual number of cases is likely highly underestimated at this point, showing the need for more widespread testing to catch the people with mild or no symptoms yet are still infected and spreading the virus to others.

Until there is widespread testing that shows a decline in the positivity rate in the US, strict mitigation (social distancing) will have to remain in place. Both PCR testing (which detects the presence of the COVID virus) and serological testing (which detects how much of the population has been exposed to the virus and have developed immunity - likely asymptomatic carriers) can be effective.



Source: Morgan Stanley Research, John's Hopkins CSSE, The COVID Tracking Project, Wikipedia, South Korea CDC

Different Test Types

PCR Test

SARS-CoV-2 RNA is detected by a reverse-transcription polymerase chain reaction (RT-PCR). In the United States, testing is performed by the CDC, by local public health departments, by hospitals that have developed and validated their own tests, and by certain commercial reference laboratories.

A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19, although false-positive tests are possible.

Experts say the process, though invasive and uncomfortable, is quite simple and quick, essentially the same as what's done to test for the flu.

Patients have a swab – think of it as a specialized long Q-tip – inserted through their nose to reach what's known as the nasopharyngeal region, from where cells are collected.

"If you were to open your mouth and say 'Ahh' and look straight back, that's the region, right where the respiratory (tract) meets the back of your mouth,'' said Kirsten Hokeness, an immunology expert who teaches at Bryant University in Smithfield, Rhode Island. "The virus likes to latch on there and start replicating.''

If the patient is calm, the swabbing takes a mere 10 seconds or so and is not painful. A jittery patient can make things more difficult.

Once the sample is taken, it is put into a sterile container and sent to a lab, where a chemical is used to pull the cells off the swab and turn the sample into a liquid form. That liquid is then put into a machine that goes through hot and cold cycles to make multiple copies of the virus' ribonucleic acid (RNA), which carries genetic information. The machine looks to match the person's RNA with the coronavirus RNA to determine a positive or negative result (USA Today March 16, 2020)

The person collecting the nasal or oral sample has to be in PPE (Personal Protective Equipment) because the sample is being taken from where the virus typically concentrates, and if the patient sneezes or coughs on the collecting person the virus is transmitted. Ideally, the collecting person puts on fresh PPE for every patient they see, but that is a challenge since PPE is now in such short supply. The swabs are also been reported to be in short supply. LabCorp and Quest, two of the largest commercial testing lab companies, have large machines that can run high volumes of tests. LabCorp now reports it is capable of 30,000 tests per day. More high-volume test machines that can run 1,000 to 5,000 samples per day should be operational in a week or so at the commercial labs. The PCR tests have been taking 5-10 days to return the result because the labs are backed up now. Academic hospitals or other large hospitals are also able to run the tests themselves, but it still can take a few days to get the result at some centers.

In hotspot areas like New York, the PCR tests are being reserved for people being hospitalized with symptoms of COVID-19 and for healthcare professionals.

Starting March 30th, Cepheid began shipments for its Rapid PCR test, which can return a result in an hour.

On March 27th, Abbott Labs announced the approval of a 5-15 minute rapid PCR test that runs on its ID Now point of care platform. Abbott began making shipments of 50,000 tests per day starting April 1st (1 million per month). Along with the approval of its large central lab test, Abbott expects to supply 5 million tests in April.

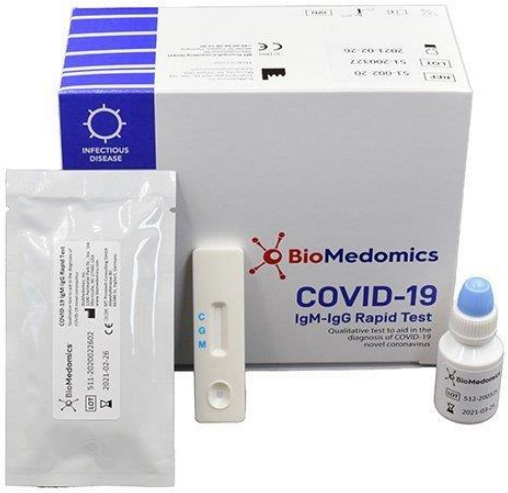
Blood Test (Serology Test)

The serology tests are important, as there is urgent need for rapid testing to quickly identify large numbers of previously infected patients, including asymptomatic carriers. This is important to reduce and prevent virus transmission (isolate asymptomatic carriers and do contact tracing), assure timely treatment of patients, and help return people, especially healthcare workers, to work.

In contrast, serology tests look for specific antibodies (IgG/IgM) that the body has produced to fight the virus. A serological test is advantageous because it can detect antibodies even if a patient has recovered and developed immunity (IgG antibodies), whereas a PCR test can detect the virus only if the person is currently infected. However, both tests might miss cases if samples are taken too early, when the viral load is too low or if the person's body hasn't produced antibodies against the virus yet. For the serologic test, it can take about a week before the body produces ample antibodies. Once a person has developed immunity, it seems they are no longer shedding virus and can be released from isolation.

In addition, the serological test can be collected without the need of PPE or swabs as the virus itself is not in the blood. Taking a simple blood draw or using a fingerpick is very easy and there is no shortage of these supplies. Hence the serological tests are cheaper and easier to scale up than the PCR tests.

These serology tests may help track the progression of the novel coronavirus in individual patients and on a community level. There are many areas in the United States that are not doing much testing now, so we don't know the extent of the virus or if hotspots are developing. They may also help doctors make more informed decisions regarding how to best to care for patients, in addition to other information, such as confirmatory tests, medical history, and symptoms.



The serology test information may be useful in instances where medical resources need to be rationed. Because serology tests measure antibodies, they can help assess the likelihood of past as well as present infection and are meant to be used as an aid to diagnosis in the mid- to later stages of the viral infection. Along with other information, such as the presence/absence of symptoms, the tests may help healthcare professionals assess whether individuals (including healthcare workers) have recovered from the virus.

The serology tests also will help public health officials better understand how much of the U.S. population has been exposed. One important concept in public health is herd immunity – what proportion of the population has developed immunity (either by vaccine or naturally by recovering from infection) to minimize the risk to people who cannot develop immunity or who are at grave risk if they are infected. It is estimated that for COVID-19, roughly 60% of the population needs to have immunity at the herd immunity threshold (other viruses have different levels of herd immunity depending on how infectious they are). Knowing the population immunity level can better drive policy decisions on what areas need to go into strict social distancing (closing schools, businesses, preventing travel) to slow down the spread (flatten the curve) and how much medical resources will be needed in an area.

Singapore has developed an experimental antibody test for COVID-19, China has licensed several, and now there are serological tests becoming available in the US. Henry Schein is distributing a 15-minute test developed by Becton Dickinson and BioMedomics. The 15-minute serological tests require the patient to prick their finger and place a drop of blood on a cassette. The cassette will display if the antibodies are present - something like an at-home pregnancy test. As of now, these serological tests have a small chance of returning a positive result if the person has had a prior infection with other coronaviruses (there are 4 known coronavirus that can cause the common cold). Under the FDA's Emergency Use Authorization that these first-generation serology test kits have been approved, the tests are to be conducted by a healthcare professional or an authorized laboratory.

Conclusion – A Look Ahead

As we look forward to the next few weeks, COVID-19 testing is becoming broader and will inform policy makers on when the economy can begin to restart. Advent has been and will continue to invest in companies with balance sheets and cashflows that are able to withstand this intense economic shock and come out the other side with their prospects intact – within Healthcare, this includes companies such as Biomarin and Sarepta, with their innovative gene therapy programs, Ilumina with its leading genetic sequencing platform important in research, and Becton Dickinson and Danaher with their testing platforms. We have been cautious about investing in companies racing to develop a treatment for COVID-19 as many have been advanced without a clear biological understanding of the virus. Doctors will likely pick the 1 or 2 drugs that end up working the best for the disease and it is just too early to have an idea on which will be those drugs. Thinking longer-term, vaccine approaches to COVID-19 will likely limit the drugs needed for treatment to just the severe patients who get hospitalized.

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No Medical Advice

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