Acing the tests

Testing is critical in fight against COVID, and in answering question of when it is safe to go back to work

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MULTIPLE COUNTRIES HAVE started conducting at scale randomised antibody seroprevalence studies to understand the prevalence and trends of COVID-19 infection in specific hotspots, including in Munich, Santa Clara in the US and Italy.

Based on current guidelines and available research, rapid antibody tests alone are not reliable as a diagnostic tool or for contact tracing. Further, these tests have lower specificity and sensitivity as compared to molecular assay tests — like RT-PCR — leading to a higher incidence of false negatives and positives. A positive on the antibody test merely means that the person has been exposed to COVID-19 and developed antibodies. The negative test means that the person has not been exposed to COVID-19 and may be susceptible in the future. Hence, as per the recently announced ICMR guidelines on the use of rapid antibody kits, they can be potentially used for epidemiological and surveillance studies at a community level.

These studies can help understand the spread of the infection in hotspots, probable nature of spread in terms of asymptomatic vs symptomatic carriers, facilitate policy-making and help in evaluating the impact of different protocols and policies. However, these studies must be designed carefully along with experienced medical and epidemiology professionals to be able to draw meaningful conclusions. Based on learnings from the research team at the Stanford School of Medicine, the following critical factors must be ensured while designing and conducting the study: Selection, testing methodology and robust statistical analysis.

Well-thought-through study participant selection methodology should be developed to ensure representativeness of actual population demographic and to minimise selection bias.

Appropriate testing methodology and kits should be selected to ensure high specificity and sensitivity, and implementation challenges must be factored in — for example, pooled RT-PCR testing vs rapid antibody kits, or both. The sample size for such tests should be determined by appropriate statistical analysis driven by demographics and the accuracy of the tests being used. The Santa Clara and Munich-based studies have used a sample size of approximately 3,000 participants.

Robust statistical analysis is needed to determine the appropriate sample size, accounting for multiple factors such as the specificity and sensitivity of the tests used, as well as to draw conclusions from the study to understand prevalence.

While Mumbai and other cities have significantly ramped up diagnostic RT-PCR based testing, this is still insufficient to understand the potential spread of the infection especially in the asymptomatic population in hotspots such as the slums in Dharavi. Targeted studies to understand the prevalence of the infection could be carried out for selected hotspots, such as Red Zones, which can help the authorities to plan and prepare better. This will also help in the progress of epidemiological research on the disease.

The study could be led by an academic institute of repute, as in the Santa Clara study in which Stanford University led the research supported by either government or private labs approved to undertake COVID testing. The estimated costs are known for various testing methods. For the Stanford study, the cost of the rapid antibody kits was approximately $7 per kit.

Many countries (including India) and states have reported deficiencies in the output of antibody tests. A variety of antibody tests were validated in a study done by the University of California, San Francisco and the Harvard Medical School. The New York Times reported on the study's results on April 26.

Makers of the antibody tests defend their research and point out how antibody tests have been wrongly used. US-based Sure Biotech has helped develop more than 200 rapid tests for viruses such as HIV, herpes and hepatitis. The company's antibody tests have had a specificity of 100 per cent in one study. On countries reporting a high number of false positives, Sheryl Dunn of Biosure writes "some users don't understand how to use the serology tests. They are less for diagnostic and more for testing for past infections. If you use serology tests between Day 1-14, during a current infection period, they catch only a proportion of the true positive cases. They are a supplement to PCR tests, which test for current infections but so far are not as portable."

The science of testing is evolving. Scientists are cooperating with each other faster than the speed of sound. Our questions to researchers in the Stanford study elicited a quick response (it helped that many of the researchers are of Indian origin). Bill Gates said in a recent interview that we "need to get to the bottom of this" — referring to understanding how much the virus has spread in communities. Researchers are racing to give the answer. It may soon be possible to self-test, just by wiping your nose and providing a swab of saliva via mail to a lab. Academics at IIT Delhi are sequencing bits of the COVID genome and making tests that are affordable. Testing is critical in the fight against COVID and in finding an answer to when it is safe to go back to work.

The writers are part of the Mahacovid, a voluntary informal group including foundations, management consulting firms, companies, public officials and experts in public health and data analytics who are working on the ground in Mumbai, Maharashtra to help in fighting the Covid 19 pandemic. This article is based on conversations with researchers around the world