

RETHINK THE LATERAL FLOW TEST ROLL-OUT?

Professor Iain Buchan argues that lateral flow tests have been misunderstood and are a useful tool in the fight against COVID-19.



Amid the mountain of scientific work and research generated by the COVID-19 pandemic, the occasional disagreement between experts is inevitable. The concept of lockdown, for example, has been the subject of intense debate. So has the issue of testing for the virus.

The latest dispute over testing flared up in January when the *BMJ* published a blog entry entitled “COVID-19: government must urgently rethink lateral flow test roll out”. The authors claimed lateral flow tests (LFTs) were not fit for mass testing. “Studies have shown that in symptomless people it misses the SARS-CoV-2 virus in a substantial proportion,” they argued. “In the Liverpool pilot study, 60% of infected symptomless people went undetected, including 33% of those with high viral loads who are at highest risk of infecting others.”

The team involved in the Liverpool pilot

study, backed by other public health and infectious disease experts, were swift to rebut. “This document contains factual errors and makes several unsubstantiated allegations and assertions,” they said. Their key concerns were that the blog had demonstrated “persistent and continuing confusion between PCR [polymerase chain reaction] tests... and LFD [LFT].”

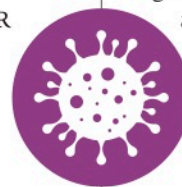
Clinical diagnostic test?

A more formal response entitled “Clarifying the evidence on SARS-CoV-2 antigen rapid tests in public health responses to COVID-19” was published in *The Lancet* in February. One of its authors was Professor Iain Buchan, Chair of Public Health and Clinical Informatics at the University of Liverpool, and lead for the evaluation work for the Liverpool pilot, which offered residents either an LFT or PCR test via local community services. A sample of 6000 residents received both

tests: LFT identified two-fifths of the PCR-positive cases and up to two-thirds of people with high viral loads.

How did Buchan feel when he first saw the Liverpool results being so robustly challenged? “My first reaction was a duty to get the evidence out there as quickly as possible,” he says. “It had to be the usual high-quality science, but also in digestible forms for different audiences, particularly policymakers, to maximise the potential population health gain from appropriate uses of LFT.”

A key error of the critique, he says, was to treat the LFT as though it was a clinical diagnostic test. “A clinical diagnosis is for one patient at a time with an outcome that is unique to them, and not necessarily a condition that they can pass on to other people. PCR was developed as an exclusive, sensitive test for genetic material, the RNA of the virus, to answer the question of whether a person might





have had COVID-19, not whether they have the live virus and could pass it on to someone else. The LFT is different. It's designed to pick up people shedding live virus from the nose or throat. So it's a test of infectiousness, not a test of having been infected at some point."

Test of infectiousness

On average PCR will give a positive result for around 17 days after an infected person stops being infectious. In terms of reducing the risk of transmission, what goes on at the front end is more vital. "There is a short four to eight day window in which people transmit the virus before they get symptoms, if they get symptoms," says Buchan. "But a large proportion don't have the classic symptoms, so they're passing on the virus without realising it. So a test of infectiousness has special relevance for those people, as it enables them to take action and to protect others. That's a public health test

and quite different to a clinical test."

This confusion also fed into the misreading of the results. "If you pick people at random, you're going to get more who are in that 17 days where PCR will be positive but no longer infectious. So the numbers of PCR positives are going to be higher relative to the numbers of LFT positives simply because there are more non-infectious people than infectious. That said, this is a complex set of numbers, but you can't compare them by pretending there is a gold standard."

Since the Liverpool pilot began in November, and in addition to the 6000 asymptomatic people in the city, the LFT has identified more than 16,500 cases in the wider region. "These are people who have had an opportunity to isolate and break the chain of transmission," says Buchan. "This testing has also been popular with communities and the public health services. It has given them a sense of taking control over their own destiny."

Ultimately, an effective public health test for an infectious disease needs to determine as quickly as possible whether somebody is infectious. The goal is rapid

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testing, isolation and contact tracing. "A test that's done in minutes is profoundly more useful than one that requires a laboratory. That's time when someone could be spreading the virus. If you're told in 30 minutes you're positive, you wouldn't go to work that day." The test also needs to be low-cost. "For a rapid test used at scale, you need a lot of kits and you need them to be as cheap as possible."

Another tool

The LFT can also detect new variants – it targets the nucleocapsid, the part of the virus that doesn't change as much as the spike proteins – which, says Buchan, adds to its usefulness as part of the public health arsenal. "You need to take as much risk out of a community as possible, including that of continued lockdown and the long-term consequences. These are important public health considerations. So this is another tool in being able to offer safer reopening at a time when not all the population is covered by the vaccines and when the complete effects of those vaccine are not yet known. The LFT is not a magic bullet, but it is something we have evaluated and found to be very useful at a local level." 