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Lateral flow tests cannot rule out SARS- CoV-2 infection

People testing negative must stick to infection control recommendations

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Lateral flow devices for asymptomatic mass testing are proving controversial.[1] At the heart of the matter is a flawed process, with the decision to implement society-wide "Moonshot" testing made before robust field evaluations of the tests were completed.[2] Subsequent selective emphasis of unrealistic performance estimates[3] has caused confusion. Little surprise we are now in a mess.

Tests have to be fit for the purpose to which they are put. Innova lateral flow assays for repeat asymptomatic testing are being distributed to care homes, universities, NHS staff, public health teams, and now schools. Ministers and other proponents have stated that negative results will show who is free from infection.[4-6] The tests appeal because they are cheap, do not need a laboratory, give results in 30 minutes, and are easy to distribute. But their performance as a "test to enable" is lacking.

The government commissioned the University of Oxford and Public Health England's Porton Down laboratory to evaluate rapid tests for covid-19, including Innova's.[7] The two relevant field studies recruited people from NHS test and trace centres, mainly those with symptoms. Detection rates (sensitivity) were 73% (95% confidence interval 64% to 85%) when tested by skilled NIHR research nurses and 79% (73% to 85%) when tested by Porton Down laboratory scientists.[8 9] But testing by test centre employees (following written instructions) achieved sensitivity of just 58% (52% to 63%). This is important, because it is closest to the circumstances for staff, student, visitor, and community testing.

Government announcements have described sensitivity as "high," quoting detection rates of "76.8%"[3] or "nearly 80%,"[10] obtained by pooling results from two groups of highly experienced staff and excluding test centre staff. When questioned, the secretary of state for health said he "was not familiar" with the 58% figure.[11] The government press release announcing the results of the evaluation says that over 95% of cases with high viral loads were detected, although it confusingly also includes a statement that all were detected.[3]

Preliminary data from mass screening of largely asymptomatic people shows even lower sensitivity. Tucked into annex B of a government guide to community testing[12] is the statement: "In the field evaluation in Liverpool, compared to PCR tests, these tests picked up 5 out of 10 of the cases PCR detected and more than 7 out of 10 cases with higher viral loads, who are likely to be the most infectious."

If a test misses 50% of infections, people with a negative result are not in the clear—their chances of active infection are simply half what they were before the test. Nobody can be considered free of risk of transmitting infection. Failing to identify 30% of people with high viral loads is six times worse than the almost 5% missed in the Porton Down/Oxford evaluation, and of particular concern.

Allowing half of infected people, and one third of those with high viral loads, to unwittingly take the virus into hospitals, family homes, and care homes will not reduce the spread of the infection and could put lives at risk. Diligent maintenance of social distancing, personal protection, and other infection prevention control measures remains vital for people with a negative result.

Uncertainties remain about who is actually infectious. "High viral load" has wrongly become synonymous with "infectious," with tests being described equally wrongly as tests of infectiousness. Both scientists and politicians have used this wording, with the prime minister stating that lateral flow tests would "identify people who are infectious ... allowing those who are not infectious to continue as normal."[5]

The assumption that people with a negative lateral flow test cannot be infectious, is also embedded in a key simulation model used to promote mass testing.[13] It's still unclear how viral load and ease of viral culture from people with PCR positive results relate to level of infectivity. Although evidence suggests that virus can be more easily cultured from people with higher viral loads,[14] it can also be cultured from people with lower viral loads.[15] Also, detected viral load varies according to how much biological material is caught on a swab,[16] and it is not yet clear whether SARS-CoV-2 can be spread when virus cannot be cultured at all.

Innova's poor sensitivity in asymptomatic people in field settings should have been expected. The largest and most realistic study within the Porton Down/Oxford evaluation (of tests done by test centre employees) reported only a 58% detection rate, even in mainly symptomatic people. Innova recommends use of the test only in people with symptoms and states: "Negative results do not rule out SARS-CoV-2 infection and should not be used as the sole basis for treatment or patient management decisions, including infection control decisions."[17] The World Health Organization says negative antigen rapid diagnostic test results "should not remove a contact from quarantine requirements." [18]

Whatever decision making process the UK government used, it ignored key evidence and dismissed expert international advice. The result is a considerable burden on care home staff, universities, NHS staff, public health teams, and schools, with minimal additional safety compared

with existing risk mitigation measures. Asymptomatic lateral flow testing is an unhelpful diversion from the important task of vaccination rollout.[19]

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