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# Asymptomatic rapid testing for SARS-CoV-2

## Liverpool study confirms low test sensitivity in a mass screening setting

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Community mass testing for SARS-CoV-2 using rapid lateral flow antigen detection tests is being used internationally, under national (eg, United Kingdom<sup>1</sup> or Slovakia<sup>2</sup>) and regional policies (eg, United States<sup>3</sup> and Spain<sup>4</sup> among others). The aim is to detect asymptomatic people, enable rapid self-isolation, and prevent the spread of covid-19, but there has been precious little evidence about whether it is effective. In a Cochrane review of accuracy of rapid antigen tests for SARS-CoV-2, none of the 48 studies screened an asymptomatic cohort in the community.<sup>5</sup> The evaluation of the roll-out of community mass testing in Liverpool, UK, by Garcia-Fiñana and colleagues (doi:10.1136/bmj.n1637) therefore provides an important advance in our understanding of how rapid antigen tests perform in asymptomatic populations when deployed at scale.<sup>6</sup>

In the Liverpool study, the Innova SARS-CoV-2 antigen rapid lateral flow test was offered to all adults attending asymptomatic testing sites, a subset of whom also provided samples for confirmatory polymerase chain reaction (PCR) tests. Of 5869 participants, 74 tested positive for SARS-CoV-2 using the PCR test (prevalence 1.3%). The overall sensitivity of the rapid test was 40.0% (95% confidence interval 28.5% to 52.4%), meaning that it detected only four in 10 people who tested positive by PCR. Although reverse-transcriptase polymerase chain reaction (RT-PCR) can detect even the smallest amount of viral RNA, rapid antigen tests directly capture viral proteins and so accuracy is highly dependent on viral load. Some have argued that those with high viral loads >10<sup>6</sup> RNA copies/mL are most likely to transmit infection,<sup>7,8</sup> but observational evidence also suggests that transmission can occur at much lower viral loads.<sup>9–11</sup> In this study only 11 participants had viral loads of >10<sup>6</sup> RNA copies/mL, so the estimates of sensitivity for the lateral flow test in these 11 participants have wide confidence intervals, from 58.7% to 99.8%. More sensitive tests will be needed to reliably detect people at the start of infection, when viral loads are low and rapidly increasing.<sup>12–14</sup>

Test specificity was exceptionally high at 99.94% and is supported by similar results in other studies.<sup>15</sup> However, the balance between benefit and harms from testing is dependent on prevalence. Testing a population of 50 million twice a week would produce more than 200 000 false positive results each month, with relatively few infected people detected at low prevalence of SARS-CoV-2.

This study, alongside previous Public Health England evaluations of the Innova lateral flow test,<sup>15</sup> provides an excellent example of how early phase test evaluations overestimate test accuracy. The Innova test was one of the first to pass the tests set by PHE

and was bought in large quantities by the UK government.<sup>16</sup> Sensitivity was 96% in the manufacturer validation (in people with symptoms),<sup>17</sup> 74% in known infected people from a community setting,<sup>15</sup> but just 40% in the prospective evaluation by Garcia-Fiñana and colleagues in an asymptomatic community setting.

The observed deterioration in sensitivity is firstly because the test has been applied beyond its intended use in populations.<sup>18</sup> The manufacturer recommends testing people with symptoms soon after symptom onset thus ensuring higher viral load and greater test sensitivity. It is worth noting that the US Food and Drug Administration has recalled the test and withdrawn it from sale, in part because of cited imprecision in the manufacturer's accuracy claims.<sup>19,20</sup> Secondly, the prospective study design used by Garcia-Fiñana and colleagues is less biased than some previous evaluations using retrospective designs with known cases and controls.<sup>21</sup>

The most important question about community mass testing is whether it works to reduce transmission. Unfortunately, we do not yet know the answer. A study that randomised the offer of repeated testing in asymptomatic people versus no offer of testing by geographical area would be best placed to answer that, and any country considering implementation of mass testing would do a great service to knowledge by randomising the roll-out. The impact of testing depends on more than the accuracy of the test.<sup>22</sup> Other factors at play include low adherence to self-isolation in those testing positive,<sup>23</sup> limited uptake of testing skewed towards those at lowest risk of SARS-CoV-2,<sup>24</sup> misuse of lateral flow tests (people with symptoms using the quicker lateral flow tests rather than the more sensitive PCR tests),<sup>25</sup> and false negative rapid test results giving false reassurance.<sup>9,26</sup>

This Liverpool pilot has delivered excellent data on test accuracy and at great speed as part of the roll-out. More studies such as this in the context of the covid-19 pandemic are crucial to delivering evidence based government policy. Further studies are urgently needed to ascertain whether population mass testing using lateral flow tests has any impact on transmission and to measure the harms of this massive scale screening.

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