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Rolling out COVID-19 antigen rapid diagnostic tests: the time is now

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A year into the COVID-19 pandemic, many questions remain regarding how testing, combined with other measures—eg, personal protection, physical distancing, and vaccines—could help curb SARS-CoV-2 transmission. In *The Lancet Infectious Diseases*, Yap Boum and colleagues[1] give us a glimpse of what is possible when diagnostics are used wisely.

Molecular testing is the method of choice for detecting SARS-Cov-2 infection. But when capacity is restricted, supplies are inconsistent, or delays are experienced in providing results, what alternative technologies and strategies can be adopted for COVID-19 case detection? Boum and colleagues presented the results of PCR, antigen-based, and antibody-based rapid diagnostic tests in individuals with symptomatic COVID-19 during the first, second, and third week after onset of symptoms, and in asymptomatic individuals who volunteered for testing or were contacts of COVID-19 cases.[1]

Antigen-based rapid diagnostic test sensitivity was 80·0% (95% CI 71·0–88·0) in the first 7 days after symptom onset and 76·0% (59·0–88·0) in the second week post-symptom onset, dropping to 19·0% (6·0–38·0) by week three, compared with PCR. Conversely, the sensitivity of antibody-based rapid diagnostic testing increased with duration of illness, from 26·8% sensitivity (18·3–36·8) in week one to 76·4% (70·1–82·0) 14 days after symptom onset. To improve case detection among symptomatic individuals, Boum and colleagues used their data to evaluate a diagnostic algorithm combining use of antigen rapid diagnostic tests with PCR confirmation of samples negative at antigen rapid diagnostic tests.[1] In week one, 60% of symptomatic patients tested positive by PCR and 54% of symptomatic patients tested positive by antigen-based rapid diagnostic test. The advantages to this approach are that it is not only highly sensitive (94% on days 0–7 after onset of symptoms), providing most patients with results in 15 min, but also cost-saving, reducing the cost of PCR testing by almost 50% (if antigen rapid tests can detect 54% of infected people in this population, then PCR testing is only needed for the remaining 46% of people who test antigen negative—compared with using PCR on everyone, this has a cost saving of nearly 50%). However, after the first week post-symptom onset, although use of antigen-based rapid diagnostic testing improves the sensitivity of case detection, it is limited by low specificity, which translates into high numbers of false-positive samples that require PCR confirmation. Therefore, timing is everything: the reduced costs and quicker turnaround time of this diagnostic algorithm should prompt decision makers to encourage people to present for testing earlier. Early diagnosis and isolation of individuals with COVID-19 to interrupt transmission remain a key strategy for pandemic control.

For screening of asymptomatic individuals, the usefulness of antigen-based rapid diagnostic tests depends on both the purpose of testing and the prevalence of COVID-19 in the population to be screened. For triaging of those who can return to school, work, attend mass gatherings, or travel, it is important that antigen-based rapid diagnostic tests has a high negative predictive value, so that those who test negative are truly negative.[2] When used instead for case-finding among, for example, contacts of cases, as in Boum and colleagues' study,[1] it is important that individuals identified as antigen-based rapid diagnostic test-positive are truly infected with SARS-CoV-2, meaning a high positive predictive value. Boum and colleagues[1] evaluated an algorithm combining antigen-based rapid diagnostic test screening with antibody-based rapid diagnostic test screening of those who tested antigen-based test-negative, followed by PCR confirmation of IgM-positive samples. This case finding strategy unfortunately only has a sensitivity of 34% (95% CI 23·0–44·0), which is marginally better than PCR alone, with a specificity of 92·0% (88·0–96·0), yielding a low positive predictive value.

The use of antibody-based tests in an algorithm to increase sensitivity of detection in people presenting late in their illness or who are asymptomatic is useful but requires tests with specificity of 98% or more to be effective. In Boum and colleagues' study,[1] none of the antibody-based rapid diagnostic tests appear to have had sufficiently high specificity compared with a laboratory-based assay for this algorithm to be helpful.

Combining antibody-based rapid diagnostic tests with antigen-based diagnostic tests might also be useful to increase sensitivity of case detection, as has been shown for dengue.[3] This combination might also be useful in determining the phase of an individual's infection, and derive information on potential for transmission and protection.

Diagnostic algorithms that maximise the advantages of each type of test and use them in combination to mitigate risks of underdiagnosing and overdiagnosing COVID-19 are important tools for pandemic control, especially when we are concerned about the rapid spread of variants of concern. As the diagnostic target of most antigen tests is the nucleocapsid protein and most of the mutations of the variants of concern are on the spike protein, countries should not hesitate to roll out antigen testing. Scaling up testing in tandem with appropriate public health measures and vaccine rollout might effectively contribute to our lives returning to some level of normalcy.

We declare no competing interests.

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The interplay between COVID-19 restrictions and vaccination

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An intervention is only as effective as the extent to which people are willing to adopt recommended measures. One obstacle to the success of COVID-19 interventions, especially in the USA, has been the politicisation of control measures, including the adoption of masks and physical distancing. Interplay between acceptance of non-pharmaceutical interventions and vaccination shapes local transmission dynamics. Despite the importance of human behaviour to the epidemiological trajectory, the integration of these interdependent factors into COVID-19 vaccination models has rarely been done. In *The Lancet Infectious Diseases*, Peter Jentsch and colleagues[1] account for these considerations in their assessment of COVID-19 mortality under different vaccination programmes.

Multifaceted approaches are necessary to control the spread of SARS-CoV-2, particularly in the months before widespread vaccination coverage is achieved. However, the staunch opposition to non-pharmaceutical interventions among a substantial proportion of some populations has hampered control of the outbreak. Only 65% of Americans report consistently wearing a mask in public.[2,3] The willingness to wear a mask in public was also found to be heterogeneous among different regions in the USA and across time.[2,3] For example, willingness to wear a mask regularly varied from 57% in the midwest region to 87% in the northeast region.[3] This heterogeneity in behaviour is especially precarious given that vaccine uptake is similarly clustered. As of March 4, 2021, the median proportion of the population who had received at least one dose of COVID-19 vaccine across the nine states in the northeast region was 6% greater than the median for the 12 states in the midwest.[4] Conversely, regions with lower adherence to non-pharmaceutical interventions will require higher levels of herd immunity to interrupt transmission and could prolong the epidemic throughout the country and beyond by continuously seeding cases.

Risk perceptions are fundamental drivers of behavioural shifts.[5] Consequently, the adoption of non-pharmaceutical interventions is likely to wane as vaccination becomes more widespread and prevalence falls. Even before the effects of vaccination campaigns are fully realised, their initiation could boost optimism which might, in turn, lead to the relaxation of non-pharmaceutical interventions. Jentsch and colleagues[1] developed an innovative multilevel epidemiological model accounting for the temporal response of public health authorities in concert with alternative vaccination strategies, integrating population acceptance of non-pharmaceutical interventions using game theory. By considering the effect of vaccination on the implementation and practice of non-pharmaceutical interventions, the projected burden of COVID-19 during a vaccination campaign is more realistic than if these components were neglected.