Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

SARS-CoV-2 rapid antigen detection tests

Authors' reply

We thank Sotirios Fouzas for his interest in our Personal View.[1] Fouzas' conclusion that the excellent negative predictive value of antigen-based rapid diagnostic tests (Ag-RDTs) is misleading has provided us with an opportunity to address common misunderstandings regarding SARS-CoV-2 Ag-RDTs.

The required performance characteristics of a test should be aligned to the purpose of testing. For confirming clinical diagnosis, one needs the most sensitive and specific test possible to ensure the patient is correctly diagnosed and treated. In this case, a molecular test would be the best option. However, when a test is used as a public health tool to ensure a safe environment, then we need an Ag-RDT with a high negative predictive value, while reliably identifying those with high viral loads so that they can be excluded from entry into the safe environment. Infectivity studies showed that the threshold for transmission corresponds to cycle threshold (Ct) values of less than 25, or approximately 10^6 viral copies per mL sample.[2] Ag-RDTs that can reliably detect individuals with these Ct values would be fit for purpose.

It is also important to understand the reasons for the variation in sensitivity of Ag-RDTs in asymptomatic, presymptomatic, and symptomatic populations in the published literature. The reference standard for evaluating Ag-RDTs is usually a molecular test, but studies have shown that while infected individuals shed infectious virus up to 9 days after symptom onset, they can remain RNA positive for weeks, when the test is likely detecting RNA fragments rather than infectious virus.[3] Two major sources of variation in sensitivity arise from different molecular tests being used as reference standards and the proportions of patients with high or low viral loads being recruited for the studies. In the end, the most important question is whether an Ag-RDT is sufficiently sensitive to detect those who might be at risk of transmitting SARS-CoV-2 infection. The sensitivity of most Ag-RDTs exceeds 96% in individuals with Ct values of less than 25.[4]

From a practical viewpoint, Ag-RDTs that are affordable, disposable, single-use cassettes that require minimal training and can return results in 15–20 min are much more feasible as a screening tool than are molecular tests, which are more costly, instrument-dependent, and of limited deployability. We agree with Larremore and colleagues[5] that test sensitivity is secondary to frequency of screening and time to result.

Finally, the excellent negative predictive value of Ag-RDTs is a mathematical computation of probability based on test sensitivity and prevalence of infection in the population. It is not misleading as long as one is clear about the purpose of testing and how the sensitivity of a test is derived.

We declare no competing interests.

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