SARS-CoV-2 rapid antigen detection tests

We read with interest the Personal View by Rosanna Peeling and colleagues,[1] who discuss the benefits and limitations of SARS-CoV-2 antigen rapid detection tests (Ag-RDTs) for scaling up diagnostic capacities in different settings. As recent evaluations suggest, Ag-RDTs can reliably detect patients during the initial infective phase of COVID-19 (when patients have high viral loads).[2,3] Fewer data are available for the use of these tests to identify asymptomatic carriers, such as before attending gatherings related to education, work, or travel.[4,5] As the authors emphasise, the screening of asymptomatic individuals in low-prevalence settings is hampered by imperfect specificity.[1] The dilemma that most detected cases represent false positives rather than true infections might require a two-tier approach with molecular confirmation,[1] affecting the practicality and acceptance of such a strategy. Here we suggest alternative strategies to optimise the use of Ag-RDTs in asymptomatic populations with low positivity likelihood.

From September, 2020, to January, 2021, we evaluated an Ag-RTD to screen asymptomatic individuals before surgery or childbirth. 773 people were tested in parallel with STANDARD F COVID-19 Ag fluorescence immunoassay (SD Biosensor, Gyeonggi-do, South Korea) and a commercial RT-PCR (COVID-19 Genesig; Primerdesign, Chandler's Ford, UK)[2] using separate nasopharygeal swabs, following the manufacturers' instructions. The antigen assay was read with an automated device (F2400; SD Biosensor), which provides a quantitative immunofluorenscence index. All individuals tested negative by RT-PCR; however, 67 samples (8·7%) were initially positive by the Ag-RDT (table). We examined alternatives to improve test accuracy in our population. First, we repeated the Ag-RDT of positive samples using the same dilution buffer to calculate the average index, resulting in a reduction of false positives to 42 (5·5%). Second, we raised the cutoff for positivity from 1·0 (recommended by the manufacturer) to 3·0, on the basis of a receiver operating characteristic (ROC) curve which demonstrated optimum diagnostic performance at a cutoff of 3·36 (100% sensitivity; 98·5% specificity). To perform the ROC analysis, 30 RT-PCR-positive samples from patients with early COVID-19 from a previous study were included.[3] This approach reduced false positives to 17 (2·2%), and specificity increased significantly (table). The combination of both strategies showed the highest specificity (99·2%; table).

	Cutoff	Total	True negatives	False positives	Specificity
Manufacturer instructions	≥1·0	773	706	67	91·3 (89·1–93·2)
Testing positive samples twice	≥1·0	767	725	42	94·5 (92·6–96·0)
Using a higher cutoff level	≥3·0	773	756	17	97·8 (96·4–98·7)
Testing positive samples twice and using a higher cutoff level	≥3·0	767	761	6	99·2 (98·2–99·7)

Data are n or % (95% CI), unless otherwise indicated.

Table: **Specificity of an automated fluorescence immunoassay for SARS-CoV-2 antigen in RT-PCR-negative asymptomatic individuals according to testing strategy**

Although further studies are necessary to confirm our results, the presented data suggest that the dilemma of imperfect specificity of Ag-RDTs in asymptomatic populations can be diminished significantly by evaluating testing protocols that maintain the capacity of getting rapid results while increasing the accuracy of the tests.

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