ANALYSIS

Rapid antigen screening of asymptomatic people as a public health tool to combat COVID-19

Kevin L. Schwartz MD MSc, Allison J. McGeer MD, Isaac I. Bogoch MD MSc


Jurisdictions across Canada have been trying to combat a second wave of the coronavirus disease 2019 (COVID-19) pandemic without using all the available tools. Accumulating evidence has shown that people who are infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) who are either presymptomatic (but subsequently develop symptoms) or paucisymptomatic (have mild symptoms that do not prompt a medical visit) are major contributors to transmission. However, current approaches of testing predominately symptomatic patients and relying on the results of expensive and slow laboratory-based testing for contact tracing have proven inadequate to control the spread of the disease, with associated economic and societal impacts. Frequent rapid antigen testing is a scalable public health tool that can effectively identify asymptomatic and paucisymptomatic people with SARS-CoV-2 infection and improve contact tracing and control of outbreaks.

Why test people who have no symptoms of COVID-19?

A 2020 study of transmission dynamics in Taiwan showed that the infectious period for COVID-19 starts 2–3 days before symptom onset and continues to about 5 days after. Modelling has estimated that more than 50% of SARS-CoV-2 transmissions occur during the presymptomatic period or during asymptomatic infection. A study in which the authors reconstructed transmission in China up to April 2020 found that presymptomatic transmission accounted for a high proportion (40%–90%) of transmissions. Furthermore, higher viral loads have been shown to be significantly associated with higher transmission risk irrespective of symptoms.

Even with ideal public health resources for testing and tracing, the strategy of testing only symptomatic cases will not identify many of the contacts before they transmit infection. A report from the Office of the Auditor General of Ontario indicated that the average time from specimen collection to the start of case and contact management was 4.25 days. In this scenario, for patients who seek testing on their first day of symptoms, on average, contact tracing begins only once virtually all transmissions have occurred and after contacts have started to transmit to others. A testing strategy that would allow detection of presymptomatic and asymptomatic people with SARS-CoV-2 could enhance the overall ability to interrupt viral transmission in Canadian communities. The widespread use of frequent rapid antigen testing could provide this.

What rapid antigen tests are available and how should they be evaluated?

Although many different devices are being produced, the Abbott Panbio lateral flow assay is the only device with Health Canada approval at the time of writing. Lateral flow assays detect a protein...
(antigen) produced by SARS-CoV-2; most devices contain strips precoated with anti-SARS-CoV-2 antibody. After applying a sample from a nasal or nasopharyngeal swab, if antigen is present it will bind to the antibody and generate a coloured line on the device, similar to a home pregnancy kit or rapid test for malaria.7

Laboratory tests fall into 2 main categories: diagnostic and screening tests. A diagnostic test is a clinical approach, typically testing symptomatic people for evidence of disease. Screening is a systematic approach in which asymptomatic people are offered a test that has prognostic value and, for those who screen positive, an intervention can effectively improve outcome. In the context of COVID-19, the goal of screening by rapid antigen testing is to increase the detection of asymptomatic or presymptomatic infection and reduce onward transmission of SARS-CoV-2. Evaluations of rapid screening tests should be designed based on this goal. With this context and goal, test sensitivity of rapid antigen tests compared with testing using reverse transcription-polymerase chain reaction (RT–PCR) is only 1 important characteristic, and a sole focus on sensitivity is misguided.

Whereas RT–PCR is the gold standard diagnostic test for SARS-CoV-2, many instances of positive RT–PCR tests represent noninfectious virus as recovered patients can shed detectable RNA for weeks to months. Cycle threshold (Ct) values are the number of amplification cycles required to detect viral RNA from RT–PCR testing. Although there can be substantial variability of Ct values between different PCR assays and quantification of viral load is difficult and expensive to do, Ct values provide a semiquantitative assessment of viral load, with lower Ct values representing higher viral loads. Mean Ct values between 3 days before and 5 days after symptom onset, when people are most infectious, are less than 25.8 Ct values less than 25 also correlate with the likelihood of viral cultures being positive.9 Rapid antigen tests have higher limits of detection than PCR tests and higher sensitivity in testing when viral concentrations are higher.10 For example, the Panbio rapid antigen test has an overall sensitivity of 73% in symptomatic patients compared with RT–PCR; however, it has a sensitivity of 97% compared with RT–PCR with Ct values less than 25.11 In a study that compared results for a single paired Sofia SARS antigen fluorescent immunoassay and an RT–PCR test among asymptomatic university students at 2 different campuses in Wisconsin, the sensitivity of the rapid test was 41.2% and specificity 98.4%.12 However, the authors of this study also cultured the virus and compared the results from the rapid tests with culture positivity and found that sensitivity was 100% compared with culture-positive samples.

Some have argued that fast result turnaround times and frequency of testing are more important to public health outcomes than test sensitivity in the context of COVID-19.13 Therefore, we should also evaluate the outcomes of screening programs and not solely the performance of screening tests. More meaningful than test accuracy is the extent to which rapid antigen testing identifies cases of COVID-19 during the infectious period and whether ongoing transmission is reduced.

What is the international experience with rapid antigen screening?

Limited pilot testing of rapid antigen screening has been conducted in Canadian provinces, but results are not yet publicly available. Preprint research has reported on the findings of Slovakia’s 2 rounds of countrywide mass testing in October and November 2020; this involved 60 000 (20 000 medical and 40 000 nonmedical) staff and 5 million rapid antigen tests.14 In the first and second rounds, the rate of positivity was 1.01% (range across counties 0.13% to 3.22%) and 0.62% (range 0.28% to 1.65%), respectively, an adjusted decrease in SARS-CoV-2 infections of 61% (95% confidence interval 50%–70%) from the first to second round. A subsequent evaluation in the UK found that the Innova rapid antigen test detected more than 90% of samples with Ct values for RT–PCR less than 25.5 as positive,15 and a program of rapid antigen testing for staff and visitors in long-term care homes was implemented.16

What are the potential harms of rapid antigen screening?

Opponents of the use of rapid antigen tests for screening have argued that the their lower diagnostic sensitivity when compared with RT–PCR makes these tests unsuitable for use because false-negative results may cause potential harms owing to a substantial proportion of infections not being detected.17 This concern arises from the belief that a false-negative test result in a person with a high viral load will be associated with behaviour change that will increase infection risk in the community. Although less than 10% of people in the UK suggested that their behaviour might change to some degree after a negative rapid test, it is not clear that this degree of change would result in a substantial increase in transmission.18 Similar hypotheses have historically been put forward for other public health interventions — for example, arguing that having a negative result for an HIV test would result in higher-risk sexual behaviours, but these have not been confirmed.19 Although behaviour change owing to screening programs requires evaluation, if appropriate and clear communication is conveyed to the public on the meaning of a negative result for a SARS-CoV-2 rapid test, it is unlikely to result in widespread untoward compensatory behaviour change.

As discussed, sensitivity compared with RT–PCR is not the appropriate comparison. Canada’s current approach of symptom- and exposure-based screening detects few infectious asymptomatic cases, and we suggest that improvement in detection would be an improvement on current practice and would likely reduce onward transmissions overall.

The benefits of screening would be proportional to disease prevalence, with greater benefit from higher community risk. At low levels of community circulation, the risk of false-positive test results will exceed the public health benefit. It is difficult to define thresholds in which benefits will be accrued on a population level; however, we would argue that given the destructive social, economic and health care effects of the COVID-19 pandemic, as long as movement restrictions and lockdowns persist, rapid screening is likely to have substantially more benefits to the population than harms.
How can rapid antigen testing be incorporated into Canada’s public health response?

Screening programs that use rapid antigen tests are public health interventions, and settings in which public health benefits can be expected should have programs supported by government that are designed and implemented in collaboration with public health departments. Staffing and logistical challenges are substantial; governments will need to recognize that the cost of these programs will add to rather than replace the costs of current PCR testing and that program costs may substantially exceed test costs.

Settings providing an essential service or manufacturing role, including schools, where direct close contact cannot be avoided, should be considered for such programs. Testing 2–3 times per week is suggested for optimal public health impact.20 In the UK, screening showed lower sensitivity when tests were performed by testers who were not health care workers than when they were performed by health care workers; however, the discrepancy disappeared over a 2-week period, which suggests that workers who are not trained in health care can be taught with experience to adequately perform swabs.16 Preprint research has shown that self-testing may have similar performance to swabs taken by professionals;21 and home-based use needs urgent evaluation to facilitate scalability and minimize biosafety concerns.

Clear communication about the implications and the intent of screening programs are critical. Similarly, additional supportive services, such as paid sick leave for workers and provision of isolation facilities for those who test positive, are needed to remove disincentives for testing.22

Clear messaging from public health leaders on the use and limitations of rapid antigen testing is needed. The public should understand that a negative test result does not preclude the possibility of infection today and certainly not tomorrow. Therefore, other public health measures, such as masking, improved ventilation, hand hygiene, vaccination and physical distancing, will continue to be essential. The goal is not to eliminate individual risk but to reduce population-level risk. Leaders should communicate that a positive test result is not a diagnosis of SARS-CoV-2 infection. The utility of antigen tests is for screening to identify those most likely to be infectious. A positive result for an antigen test still requires confirmation by a PCR test, and a negative result does not exclude infection with a lower viral load or onset of infectiousness hours later. People with symptoms should continue to seek a diagnostic PCR test. Rapid antigen tests are an enhancement of screening forms that many people complete daily before attending work or school. Checking yes to questions on a screening form is not diagnostic of SARS-CoV-2 but should trigger the need to isolate and seek laboratory confirmation.

Evaluation of rapid testing programs will need to include the rate of detection of additional cases, estimates of cases avoided by the intervention, impact on workers, cost of isolation of those with false-positive test results and the possible impact of changed behaviour resulting from negative test results.

Conclusion
Until sufficient vaccine is available to reduce community transmission, the implementation of screening using rapid antigen testing represents an opportunity to reap substantial benefits at the population level in terms of reduced SARS-CoV-2 transmission. Such screening programs will not end the COVID-19 pandemic but, if carefully implemented, could provide an additional layer of safety to current public health strategies by allowing the identification of asymptomatic, presymptomatic and paucisymptomatic infectious individuals, and empowering people to make informed decisions about their own behaviour to reduce the spread of COVID-19. Clear guidance and messaging can mitigate the potential harms of false-negative test results and the impact of false-positive results. To quote Dr. Mike Ryan from the World Health Organization, “Perfection is the enemy of the good.” Although antigen tests are not perfect as diagnostic tests, they are a helpful and currently underutilized public health screening tool in Canada’s COVID-19 response.

References


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Affiliations: Unity Health Toronto (Schwartz); Departments of Medicine (Bogoch), and Laboratory Medicine and Pathobiology (McGeer), and Dalla Lana School of Public Health (Schwartz, McGeer), University of Toronto; Sinai Health System (McGeer); University Health Network (Bogoch), Toronto, Ont.

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Correspondence to: Kevin Schwartz, Kevin.schwartz@unityhealth.to