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SYNOPSIS

Review of "Validation of an At-Home Direct Antigen Rapid Test for COVID-19"

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Article citation: Harmon A, Chang C, Salcedo N, Sena B, Herrera BB, Bosch I, et al. Validation of an at-home direct antigen rapid test for COVID-19. JAMA Netw Open. 2021;4(8):e2126931. Available from: https://doi.org/10.1001/jamanetworkopen.2021.26931

One-minute summary

- The authors describe implementation of twice-weekly testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) among 257 participants in Boston and Cambridge, Massachusetts, United States (US), using inexpensive, at-home, semiquantitative, direct antigen rapid tests (DARTs). In addition, the authors compare the performance of DART and quantitative reverse transcription polymerase chain reaction (qRT-PCR; assumed gold standard) on self-collected nasal specimens.
- Participants were tested over a 6-month period, with 2,951 DART-qRT-PCR test pairs collected in total (1–27 pairs per person). Participants included laboratory personnel from three laboratories.
- DART clinical accuracy using nasal swabs was, as compared to qRT-PCR:
    - Sensitivity within 0-12 days of symptom-onset: 78.9% (60/76 swabs; 95% confidence interval [CI]: 69.1–88.8)
    - Sensitivity within 0–3 days of symptom-onset: 96.3% (26/27 swabs; 95% CI: 89.5–100.0)
    - Specificity: 97.1% (2,791/2,875 swabs; 95% CI: 96.3–97.8)
- SARS-CoV-2 nucleocapsid protein and RNA detection occurred from 1–12 days after symptom-onset, peaking at 2–6 days (median = 3).
- Fifteen participants developed Coronavirus Disease 2019 (COVID-19) during the study. Twice-weekly DART detected 15/15 infections and 11/15 participants were positive on day 1 or 2.
- The authors concluded that a DART program allows for quick identification and quarantine of infected individuals, potentially preventing SARS-CoV-2 transmission at in-person work environments or other social settings.

Additional information

- DARTs were based on the E25Bio, Inc. lateral flow immunoassay test platform with semiquantitative measurement of the test line pixel intensity using participant-captured images and image processing software.
- The median age of participants was 35 years (range: 21–72) and 46.7% of participants were female. The majority of participants were white (62.6%), followed by Asian (19.1%), Hispanic (11.3%) and Black (3.1%).
- Of the 15 positive cases, 11 cases tested positive on day 1 or 2 of symptom-onset, one case was presymptomatic when tested positive by DART, one case was detected by qRT-PCR one day before DART, and DART detected one infection one day before qRT-PCR.
- Most of the positive participants did not recognize they were symptomatic until they received a positive result.
- If there was a positive DART, then the participant quarantined at home pending result of the q-RT-PCR sample. If the qRT-PCR was positive, then the participant remained isolated at home and continued to self-collect nasal swabs for DART and qRT-PCR for up to 10 days.
- One limitation of the study mentioned by the authors was that there was a low prevalence of COVID-19 within the population during the study, which was <1–8%.

PHO reviewer's comments

- COVID-19 can be highly transmissible from those with minimal or no symptoms.[1,2] Antigen testing positivity correlates with the most common infectious period of 1–2 days prior to 5 days following symptom-onset.[3]
- When used for screening, a positive antigen test should be confirmed with a molecular-based test due to the small chance of false positive results (2.9% false positive rate according to this study). Although not the primary aim or targeted population of this study, it should be noted that individuals with symptoms of COVID-19 are best to seek a PCR-based test due to the higher analytic sensitivity to detect lower amounts of virus. PCR-based testing is not amenable to screening due to the relatively slow turnaround time and cost.
- This validation study demonstrates the high sensitivity of antigen testing for individuals during a period of likely high infectiousness (sensitivity 96.3% on days 0 through 3 of symptoms). Home-based rapid antigen screen testing can identify infectious pre-symptomatic or pauci-symptomatic individuals with COVID-19.
- Most cases in this study did not recognize they had symptoms of COVID-19 until observing the positive test result. On one hand, this could suggest a benefit for serial screening if individuals under-recognize their symptoms. On the other hand, it would be important to address the impact of serial screening if individuals under-recognize their symptoms due to being enrolled in serial screening and having a recent negative antigen test influencing their symptoms self-assessment.
- It is not clear from the study what symptom information was collected from the participants (i.e., whether the question was having symptoms or not, or actually using a checklist for individual symptoms) and whether this could have resulted in participants not recognizing they

were symptomatic. It would have been interesting to correlate the findings with the actual symptoms experienced and their severity. This analysis can inform the population that can be effectively targeted by a similar program.

- According to the study figure, all 15 positive participants were symptomatic. It is unclear whether infected individuals that remained asymptomatic throughout their infectious period were excluded from the analysis, or whether the study population included no truly asymptomatic infections. If there were no asymptomatic infections in the studied population, generalizability of the study outcomes may be limited to presymptomatic individuals or symptomatic individuals underrecognizing their symptoms.

- It is also not clear from the study the exposure history of the participants who tested positive, which might impact the cost-effectiveness of broad rolling out of such a testing screening program if the alternative is for the high-risk contacts to self-isolate and be followed up by public health units.

- The antigen test used in this study is not available in Ontario. The method of analysing signal intensity from a lateral flow immunoassay band using image capture and an image processing software is also not available in Ontario. It is unclear how the software analysis approach, using a 10% line intensity threshold from the control line to define a positive result, impacted result interpretation as opposed to visual reading of band intensity (the primary method of defining a positive from a negative result with antigen assays currently available in the province).

- The study protocol included recruitment of individuals previously known to be positive for COVID-19, as well as repeat testing of individuals once known to be positive throughout the study period. It is unclear how the inclusion of known positive individuals in the sampled population affected the analysis of test performance.

- Participants consisted of laboratory personnel that may or may not have received specific training on the use of the antigen test in this study. Previous studies have described differences in test accuracy and usability when evaluating use by laboratory-trained professionals compared to use by the general population.

- In Ontario, positive antigen test results are not reportable to public health units. Effectively communicating the next steps for those receiving a positive antigen test result and facilitating confirmatory testing is key for an effective rollout of such program.

- Factoring in the vaccination status for positive participants might also impact the findings and the ability to recognize the symptoms once infected; however, this may be unlikely due to evidence breakthrough cases can be as infectious as non-vaccinated cases.[4]

- Frequent home-based asymptomatic antigen screening can be combined with other public health interventions to detect individuals that are most likely infectious to limit transmission of COVID-19 in work environments or other settings with direct close contact. However, cost-effectiveness analysis may be helpful to inform which population (e.g., fully vaccinated versus non-fully vaccinated, those exposed to COVID-19, those working in areas with high incidence of COVID-19) would benefit most from such a program.

- It is unclear if the conflicts of interest disclosed by the authors (including financial interest in the company manufacturing the antigen test evaluated) have had any impact on the representation of study outcomes.

Literature cited

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