

Rapid Antigen Test Sensitivity for Asymptomatic COVID-19 Screening

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Abstract

Introduction: Operating in-person instruction, residential living, and other activities at institutions of higher education (IHEs) in the context of the pandemic of severe acute respiratory syndrome–coronavirus 2 (SARS-Cov2) have posed a multitude of challenges. Identification of asymptomatic cases at IHEs is crucial, as a large reservoir of virus can potentially develop among students. Unfortunately, despite the advantages, rapid antigen tests (RATs) have variously been shown to perform poorly when used with asymptomatic individuals.

Methods: In order to address the appropriateness of RAT use in screening asymptomatic populations like those at IHEs, we conducted a rapid review of published evaluations of RATs available in the United States, where sensitivity and specificity were reported specifically from asymptomatic populations. We extracted sensitivity and specificity for asymptomatic populations reported in each article, along with location and important notes. The data are presented narratively.

Results: A total of 11 articles were included for evaluation and presentation, representing tests from four manufacturers. Sensitivity ranged from 35.8% to a high of about 71%, with caveats to the higher number about exposure. Both the low and high sensitivity rates were observed in Abbott BinaxNOW RATs. Due to heterogeneity and publishing differences, a meta-analysis was not feasible, but RAT tests in asymptomatic populations tended to identify roughly half of those identified as infected via reverse transcription-polymerase chain reaction. Specificity ranged from 97.8% to 100%.

Conclusion: The results of this rapid review indicate serious issues in misidentifying asymptomatic individuals as COVID-19 negative, when in fact they are infected and carrying the SARS-Cov2 virus.

Introduction

Operating in-person instruction, residential living, and other activities at institutions of higher education (IHEs) in the context of the pandemic of severe acute respiratory syndrome–coronavirus 2 (SARS-Cov2) has posed a multitude of challenges. The SARS-Cov2 virus causes Coronavirus Disease 2019 (COVID-19), a serious and potentially deadly illness. IHEs present a particularly difficult problem, because they mix younger, and potentially asymptomatic, carriers of the virus, with high-density residential circumstances, and frequent interactions with older individuals (instructors, administrators, facility staff, etc) who may be at elevated risk for

severe outcomes. The rapid identification of SARS-Cov2 at the start of instructional periods (eg, academic years or semesters), as well as throughout the period in areas of medium-to-high community transmission, has been crucial to controlling outbreaks.

A key component of infection control at IHEs has been the use of systematic screening and surveillance, achieved by testing regimens. At the time of this writing, the US Centers for Disease Control and Prevention (CDC) recommends testing upon entry, and at least once per week thereafter, of students in moderate-to-high transmission areas, with considerations given to vaccination status and other issues.¹ However, implementation of asymptomatic testing can present a massive, previously unbudgeted expense for IHEs, and additionally draws resources from clinical ascertainment of symptomatic patients. Additionally, the de facto gold standard for SARS-Cov2 infection determination involves reverse-transcriptase polymerase chain reaction (RT-PCR) testing of samples obtained via nasopharyngeal (NPG) swab, which is expensive, resource-intensive, and not often feasible to do rapidly.² A variety of other methods have arisen in the face of the challenges of RT-PCR testing, including the use of easily-collected salivary PCR-based tests,³ the pooling of samples,⁴ and the use of rapid antigen tests (RATs) that are inexpensive, potentially self-administered, and generally produce results in 10-15 minutes.⁵ This combination of low cost, ease of administration, and rapid results have led many institutions to consider using RATs for large-scale, asymptomatic screening.

Identification of asymptomatic cases at IHEs is crucial, as a large reservoir of virus can potentially develop among students. Unfortunately, despite the advantages, RATs have variously been shown to perform poorly when used with asymptomatic individuals. In order to address the appropriateness of RAT use in screening asymptomatic populations like those at IHEs, we conducted a rapid review of published evaluations of RATs, where sensitivity and specificity were reported specifically from asymptomatic populations.

Methods

Data Sources/Search Strategy

Our review aimed to collect and assess evaluations of SARS-Cov2 RATs (a) that are approved for use in the United States, and (b) for which sensitivity and specificity in asymptomatic people have been explicitly reported. We conducted an initial literature search using the PubMed interface of MEDLINE in May 2021-August 2021, using iterations of the term "Covid-19 Rapid Antigen Tests," and then initiated a rapid, functional review of abstracts and titles for appropriateness. We then repeated our search using Ovid MEDLINE (R) and In-Process, In-Data-Review and Other Non-Indexed Citations 1946 to October 26, 2021 using the search string "[((assessment OR evaluation) AND (COVID OR COVID-19) and (asymptomatic OR presymptomatic) AND ("rapid antigen test" OR "rapid antigen tests" OR rapid antigen OR RAT))]."

The literature search was updated again in January 2022, using the same terms in PubMed and OVID.

Inclusion/Exclusion Criteria

At the time of this writing, there are 45 rapid antigen tests that have been granted emergency use authorization (EUA) by the US Food and Drug Administration (FDA). Studies were selected if they (a) evaluated rapid antigen tests that have been granted EUA by the FDA, and (b) were conducted among asymptomatic populations. Any studies conducted outside of the United States were excluded. We also eliminated reports that were duplicative, such as documents first disseminated on preprint servers, that were later published in peer-reviewed journals.

Data Extraction

We extracted sensitivity and specificity for asymptomatic populations reported in each article, along with location and important notes. The data are presented narratively.

Results

The initial search of identified 61 articles in PubMed with search terms of “COVID-19 rapid antigen tests,” and another 18 articles in Ovid MEDLINE. The update in January 2022 using PubMed produced 54 articles with search terms of “COVID-19 ‘rapid antigen test’ asymptomatic,” and 35 articles with search terms of “COVID-19 ‘rapid antigen tests’ asymptomatic.” Identical terms from the previous MEDLINE via OVID search were used again, which resulted in 31 articles. Out of these 199 articles, 77 articles were eligible for screening, after eliminating duplicate and preprint articles; 11 of these articles, representing tests from four manufacturers, met criteria has having assessed the performance of rapid antigen tests among asymptomatic individuals with COVID-19 within the United States only.^{2,5-14} The overall processing of search results is detailed in a PRISMA diagram (Figure 1).

Sensitivity ranged from 35.8% to a high of about 71%, with caveats to the higher number about exposure. Both the low and high sensitivity rates were observed in Abbott BinaxNOW RATs. Due to heterogeneity and publishing differences, a meta-analysis was not feasible, but RAT tests in asymptomatic populations tended to identify roughly half of those identified as infected via RT-PCR. Specificity ranged from 97.8% to 100%. The results are fully displayed in Table 1.

Conclusions

A challenge of rapid antigen tests usage among asymptomatic individuals includes the low sensitivity of the tests and the need for confirmation tests with RT-PCR tests as recommended by the FDA’s EUA. The results of this rapid review indicate serious issues in misidentifying asymptomatic individuals as COVID-19 negative, when in fact they are infected and carrying the SARS-Cov2 virus. The implication in a college population is twofold: infections among individuals living in congregate settings are potentially missed; and a false negative test may lead to an assumption that one is infection-free, and lead such individuals to behave as though they are infection-free in a college setting, where group living, social gatherings, in-class attendance, and events are frequent parts of daily life.

Although RATs appear to have sensitivity issues in asymptomatic individuals, there is still a benefit to using them for detecting and monitoring COVID-19 infections. A major advantage of RATs is the speed of their results compared to RT-PCR tests. This is especially useful for screening in the case RT-PCR tests are unavailable.¹² As such, RATs may be useful in identifying those who are actually infectious, and may help screen individuals at the start of an acute event or gathering. Additionally, RATs have proven successful in detecting the emergent Omicron variant.¹⁵ There is also utility in frequent use of RATs to identify those who have a high enough viral load for detection via this modality.¹⁶ However, few if any institutions are using RATs with the daily or constant frequency required for this approach. Finally, new approaches to antigen testing may yield better results in asymptomatic populations in the future.¹⁷

This rapid review should be viewed with several limitations in mind. First, in order to share results quickly, we relied upon one review pass, and did not search grey literature or other databases beyond the two main interfaces that access MEDLINE. However, the results we observed are consistent, and we believe it is unlikely that a report exists outside of MEDLINE that would contradict the fundamental concerns about RAT sensitivity revealed in the 11 articles included in this rapid review. It is also notable that sensitivity results have reported in the peer-reviewed literature for only four RATs, to our knowledge, representing a small minority of the 45 RATs available in the United States within the timeframe of this review. Additionally, we do not believe that a meta-analysis would be feasible, given variations in reporting style and populations across the 11 articles. In this case, we believe that the narratively-presented results speak for themselves. Additionally, there are reports that fell outside of our inclusion/exclusion criteria that nonetheless replicate the findings we report here.^{18,19}

In summary, we have deep concerns about the use of RATs for broad, weekly screening in asymptomatic populations, such as within IHEs, as they have a high probability of missing infected individuals due to low sensitivity. Pooled sampling techniques that allow for quicker and more efficient use of RT-PCR based testing are a much better alternative if one is needed.²⁰

Tables and Figures

Figure 1: PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Diagram

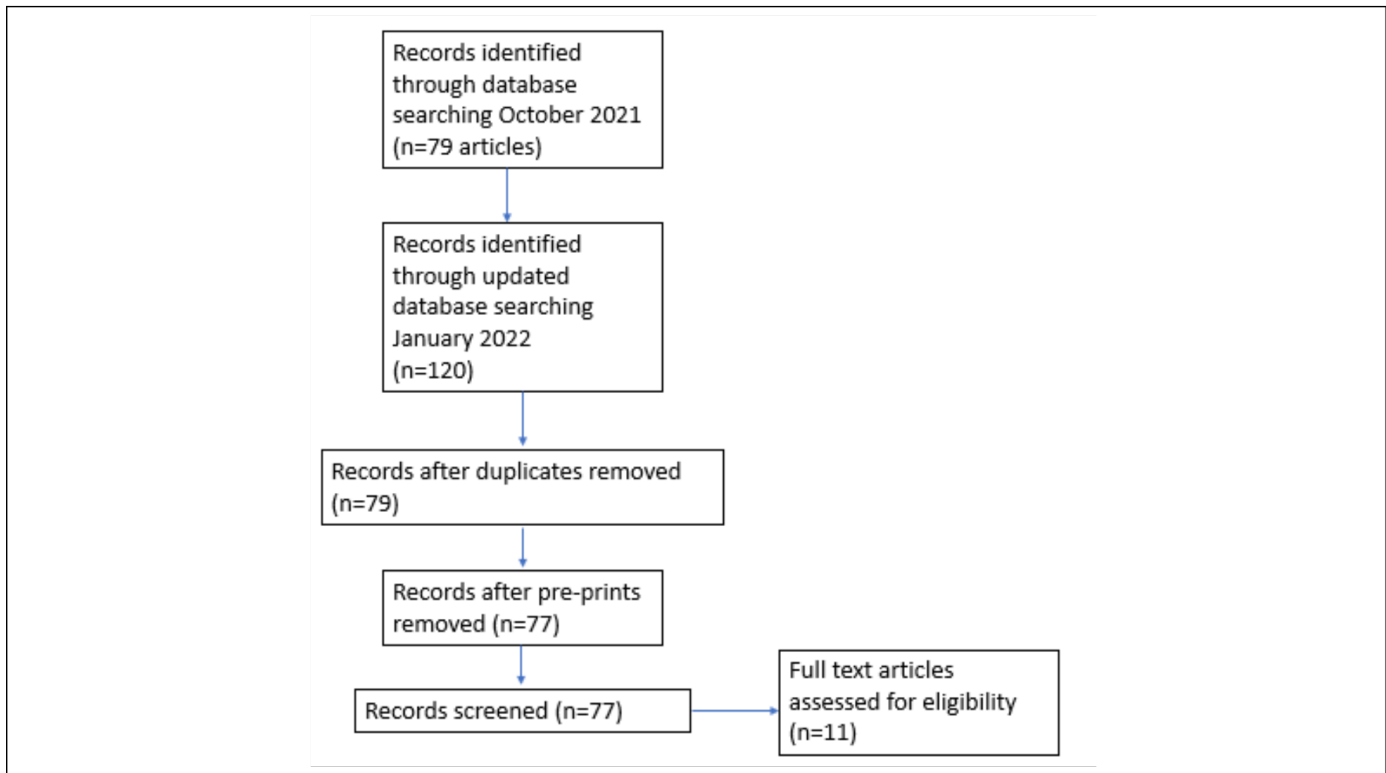


Table 1: Rapid Antigen Tests Performance Among Asymptomatic COVID-19 Infections (United States Only)

Name of Test	Sensitivity % (95% CI)	Specificity % (95% CI)	Notes	Site	Source
Abbott BinaxNOW rapid antigen test	57.7% (95% CI, 36.9%–76.6%) (15 of 26)	100% (99.6%–100%) (845 of 845)	Not asymptomatic but based upon absence of PCR threshold	San Francisco	Pilarowski G (2021)
Abbott BinaxNOW rapid antigen test	70.2% (95% CI, 56.6 to 81.6)	99.6% (95% CI, 98.9 to 99.9)	Asymptomatic adults	Massachusetts	Pollock NR (2021)
	65.4% (95% CI, 55.6 to 74.4)	99.0% (95% CI, 98.0 to 99.6)	Asymptomatic children	Massachusetts	
Abbott BinaxNOW COVID-19 Ag card (BinaxNOW)	35.8 (27.3–44.9) % (95% CI)	99.8 (99.6–100.0) % (95% CI)	Asymptomatic persons aged ≥10 years	Pima County, Arizona	Prince-Guerra, JL (2021)
Abbot BinaxNOW™ rapid SARS-CoV-2 antigen assay	51.1% (95% CI: 42.5% to 59.7%) (Positive concordance)		Positive concordance was 64.4% (95% CI: 53.4% to 74.4%) among symptomatic children and 51.1% (95% CI: 42.5% to 59.7%) among asymptomatic children.	Los Angeles County	Sood N (2021)
Abbot BinaxNOW COVID-19 antigen card	53.3%	100%		University of Utah	Okoye NC (2021)
Abbot BinaxNOW coronavirus disease 2019 (COVID-19) Ag card test (BinaxNOW)	51.6%		The sensitivity of the BinaxNOW coronavirus disease 2019 (COVID-19) Ag Card test (BinaxNOW) was 51.6% among asymptomatic healthcare employees relative to real-time reverse transcriptase polymerase chain reaction (rRT-PCR). (n=159)	Little Rock, Arkansas	James AE (2021)
Abbot BinaxNOW rapid antigen COVID-19 test	71% (95% CI 61%, 80%)	Greater than 99%	Asymptomatic individuals with potential exposure 82% (95% CI 66%, 91%) Asymptomatic no exposure 64% (95% CI 51%, 76%) for those with no exposure	Baltimore Convention Center Field Hospital	Siddiqui ZK (2021)
Abbot BinaxNOW COVID-19 rapid antigen test	Low number of patients testing positive by the molecular and/or antigen tests, which limits any conclusions that can be made about the sensitivity of antigen testing	99.8%	Asymptomatic patients undergoing COVID-19 preprocedural/ surgical screening	United States	Stokes NL (2021)
Access Bio CareStart COVID-19 antigen test	50.0% (95% CI, 41.0–59.0)	99.1% (95% CI, 98.3–99.6)	Asymptomatic adults	Massachusetts	Pollock NR (2021)
	51.4% (95% CI, 34.4–68.1)	97.8% (95% CI, 94.5–99.4)	Asymptomatic children	Massachusetts	
Quidel rapid antigen test	Unclear	100%	In asymptomatic individuals the Ag test detected less than half of those who had been infected with SARS-CoV-2 <i>but identified 86% of those who were contagious and likely to spread the virus.</i>	University of Arizona	Harris DT (2021)
Sofia SARS Antigen Fluorescent Immunoassay (FIA) (Quidel Corporation)	41.2% (seven of 17)	98.4% (840 of 854)	Among 871 paired specimens from asymptomatic participants, 21 (2.4%) were antigen-positive and 17 (2.0%) were real-time RT-PCR-positive. Antigen testing sensitivity was 41.2% (7 of 17), specificity was 98.4% (840 of 854), PPV was 33.3% (7 of 21), and NPV was 98.8% (840 of 850).	Wisconsin	Pray IW (2021)

Abbreviations: PCR, Polymerase chain reaction; PPV, positive predictive value; NPV, negative predictive value.

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