Comparison of Rapid Antigen Tests' Performance Between Delta and Omicron Variants of SARS-CoV-2

A Secondary Analysis From a Serial Home Self-testing Study

Apurv Soni, MD, PhD; Carly Herbert, BA; Andreas Filippaio, MD; John Broach, MD, MPH, MBA; Andres Colubri, PhD; Nisha Fahey, DO, ScM; Kelsey Woods, BA; Janvi Nanavati, BS; Colton Wright, MS; Taylor Orwig, BS; Karen Gilliam, MA; Vik Kheterpal, MD; Thejas Suvarna, BBA, BS; Chris Nowak, BA; Summer Schrader, BA; Honghuang Lin, PhD; Laurel O'Connor, MD; Caitlin Pretz, MS; Didem Ayturk, MS; Elizabeth Orvek, MS; Julie Flahive, MS; Peter Lazar, BS; Qiming Shi, MS; Chad Achenbach, MD, MPH; Robert Murphy, MD; Matthew Robinson, MD; Laura Gibson, MD; Yukari C. Manabe, MD; and David McManus, MD, ScM

Background: It is important to document the performance of rapid antigen tests (Ag-RDTs) in detecting SARS-CoV-2 variants.

Objective: To compare the performance of Ag-RDTs in detecting the Delta (B.1.617.2) and Omicron (B.1.1.529) variants of SARS-CoV-2.

Design: Secondary analysis of a prospective cohort study that enrolled participants between 18 October 2021 and 24 January 2022. Participants did Ag-RDTs and collected samples for reverse transcriptase polymerase chain reaction (RT-PCR) testing every 48 hours for 15 days.

Setting: The parent study enrolled participants throughout the mainland United States through a digital platform. All participants self-collected anterior nasal swabs for rapid antigen testing and RT-PCR testing. All Ag-RDTs were completed at home, whereas nasal swabs for RT-PCR were shipped to a central laboratory.

Participants: Of 7349 participants enrolled in the parent study, 5779 asymptomatic persons who tested negative for SARS-CoV-2 on day 1 of the study were eligible for this substudy.

Measurements: Sensitivity of Ag-RDTs on the same day as the first positive (index) RT-PCR result and 48 hours after the first positive RT-PCR result.

Results: A total of 207 participants were positive on RT-PCR (58 Delta, 149 Omicron). Differences in sensitivity between variants were not statistically significant (same day: Delta, 15.5% [95% CI, 6.2% to 24.8%] vs. Omicron, 22.1% [CI, 15.5% to 28.8%]; at 48 hours: Delta, 44.8% [CI, 32.0% to 57.6%] vs. Omicron, 49.7% [CI, 41.6% to 57.6%]). Among 109 participants who had RT-PCR-positive results for 48 hours, rapid antigen sensitivity did not differ significantly between Delta- and Omicron-infected participants (48-hour sensitivity: Delta, 81.5% [CI, 66.8% to 96.1%] vs. Omicron, 78.0% [CI, 69.1% to 87.0%]). Only 7.2% of the 69 participants with RT-PCR-positive results for shorter than 48 hours tested positive by Ag-RDT within 1 week; those with Delta infections remained consistently negative on Ag-RDTs.

Limitation: A testing frequency of 48 hours does not allow a finer temporal resolution of the analysis of test performance, and the results of Ag-RDTs are based on self-report.

Conclusion: The performance of Ag-RDTs in persons infected with the SARS-CoV-2 Omicron variant is not inferior to that in persons with Delta infections. Serial testing improved the sensitivity of Ag-RDTs for both variants. The performance of rapid antigen testing varies on the basis of duration of RT-PCR positivity.

Primary Funding Source: National Heart, Lung, and Blood Institute of the National Institutes of Health.

Ann Intern Med. 2022;175:1685-1692. doi:10.7326/M22-0760 Annals.org For author, article, and disclosure information, see end of text. This article was published at Annals.org on 11 October 2022.

Accurate and accessible testing for SARS-CoV-2 is a critical tool for the timely identification of infection to inform isolation recommendations, prevent transmission, and facilitate early initiation of therapy to reduce disease progression (1). Rapid antigen tests (Ag-RDTs) for COVID-19 show great promise as a testing method that is easy to use, accessible, and cost-effective (2). Results from Ag-RDTs are available within minutes of sample collection, compared with hours to days for results from reverse transcriptase polymerase chain reaction (RT-PCR) tests. The U.S. federal government launched a program in January 2022 to distribute a half billion Ag-RDTs at no cost to U.S. residents in an effort to improve the country’s ability to respond to a surge in COVID-19 cases (3).

Rapid antigen tests have lower sensitivity than RT-PCR tests for detecting SARS-CoV-2 (4); however, sensitivity can be improved through serial testing (5). Existing data on the performance of Ag-RDTs predate the emergence of the Omicron (B.1.1.529) variant, which has mutations throughout the SARS-CoV-2 genome. In particular, mutations in the nucleocapsid gene may lead to protein conformational changes that affect the target binding site of Ag-RDTs. This could theoretically alter the performance of Ag-RDTs in detecting this variant (6-9). The rapid global emergence and dominance of the Omicron variant highlight the importance of understanding the performance of Ag-RDTs in real-world settings.
The urgent need to reassess the performance of Ag-RDTs in detecting the SARS-CoV-2 Omicron variant is further compounded by early reports that Ag-RDTs have lower sensitivity for the Omicron variant than for other variants (10, 11). Recent reports from analytic studies suggest that Ag-RDT performance does not vary across the Delta (B.1.617.2) and Omicron variants; however, previous studies have not looked at the serial performance of tests or identification of new-onset infections (12–14). This article analyzes Ag-RDT performance for detection of the Delta and Omicron variants of SARS-CoV-2 by comparing the results of Ag-RDTs versus nasal RT-PCR tests when testing participants serially every 48 hours.

**METHODS**

**Study Population**

This analysis used data collected in the TUAH (Test Us At Home) study. TUAH is a prospective cohort study that was done by the National Institutes of Health Rapid Acceleration of Diagnostics (RADx) program’s Clinical Studies Core; this initiative featured a collaboration among the National Institutes of Health, the U.S. Food and Drug Administration, and University of Massachusetts Chan Medical School. Enrollment occurred from 18 October 2021 to 1 February 2022. Persons older than 2 years residing in any state except Hawaii, Alaska, or Arizona were eligible for TUAH, provided they had access to a smartphone and could receive mail at home. Persons with COVID-19 symptoms in the 14 days before enrollment or a self-reported positive test result for COVID-19 in the previous 3 months were excluded from the study. Study enrollment was self-directed through the study-specific project under the MyDataHelps app (CareEvolution). Participants whose first RT-PCR test in the study had a positive result were excluded from this analysis to allow us to analyze testing performance in the context of RT-PCR positivity onset, as were those who missed a testing period immediately before their index RT-PCR test with positive results (Figure 1). In addition, participants without Ag-RDT results within 48 hours of index RT-PCR positivity were excluded.

We defined 4 populations in this study. Population A included all eligible participants who had an RT-PCR-positive result. Populations B, C, and D were subsets of population A, defined by the result of the RT-PCR test taken within 48 hours of the index RT-PCR test with positive results, as described in Figure 1: Population B participants had a repeated positive result within 48 hours of the index test, population C had a negative result within 48 hours of the index test, and population D did not have another RT-PCR test within 48 hours of the index test either because of nonadherence or the end of the study period.

The study protocol for the main study was approved by the University of Massachusetts Chan Medical School Institutional Review Board and externally by Western Institutional Review Board. Additional protocol details for TUAH can be found elsewhere (15).

**Study Procedures**

On enrollment, participants were assigned to 1 of 3 Ag-RDTs with emergency use authorization (BD Veritor At-Home COVID-19 Test, Quidel QuickVue At-Home OTC COVID-19 Test, and Abbott BinaxNOW COVID-19 Antigen Self Test). Participants received the Ag-RDT and the Quest Diagnostics collection kit for COVID-19 by mail at the shipping address provided on enrollment. Participants were asked to self-collect 2 anterior nasal swabs sampled from both nostrils and use 1 swab to complete the Ag-RDT (at home) and 1 for comparator RT-PCR testing (shipped to central laboratory) on the same day roughly every 48 hours for 15 days, as described in Supplement Table 1 (available at Annals.org). Participants were instructed to always collect the Ag-RDT sample first and have at least a 15-minute break before sample collection for the RT-PCR test. Instructions for the tests, specifically for self-collecting and shipping the comparator specimens, were provided as authorized by the Food and Drug Administration. The RT-PCR assay was based on the Roche cobas SARS-CoV-2 assay and had emergency use authorization for use with specimens collected with the Quest Diagnostics collection kit for COVID-19. For participants who tested positive in December or January and had adequate remnant sample, we did whole-genome sequencing of SARS-CoV-2 by amplicon-based next-generation sequencing on extracted RNA. Viral-specific primer sequences and methods of generating the viral genome sequence by consensus were adapted from the ARTIC network.

**Variables**

The result of an Ag-RDT was based on self-report by the participant in the MyDataHelps app. The RT-PCR result was based on laboratory determination and was considered positive for this analysis if at least 1 of the 2 targets of Roche cobas RT-PCR assays for SARS-CoV-2 was detected. Cycle threshold (Ct) values for the E gene from RT-PCR were used in analyses to quantify viral load. Vaccination history and SARS-CoV-2 infection history were based on self-report using the MyDataHelps app. Case patients were assigned to the Omicron group on the basis of a positive RT-PCR result from a sample collected on 1 January 2022 or later and to the Delta group on the basis of a positive RT-PCR result from a sample collected before 20 December 2021; these cutoff dates were based on sequencing results (Supplement Table 2, available at Annals.org). Participants who tested positive between 20 and 31 December 2021 were assigned to their respective group on the basis of the sequencing results; those without sequencing results in this period were excluded (Figure 1 and Supplement Table 2).

**Statistical Analysis**

This is not the prespecified study analysis but was subsequently developed to address an ancillary research question using this unique and comprehensive longitudinal data set (15). Specific analysis related to symptomatic status was not pursued because of overlap with the primary objectives of the parent study (16). Descriptive statistics were calculated at the participant level using

[Figure 1](available at Annals.org)
tabulation of frequencies for categorical data, and differences were compared using $\chi^2$ or Fisher exact tests, depending on the cell sample size. We calculated Ag-RDT sensitivity at different time points for the different populations described in Figure 1. The denominator was based on participants who had at least 1 positive Ag-RDT result in the corresponding time frame since the first positive RT-PCR result (same day, within 48 hours, within 96 hours, or within 1 week). The denominator was based on total number of eligible participants with RT-PCR positivity in each population. We also calculated sensitivity differences for Delta and Omicron. Corresponding 95% CIs for each proportion were calculated using the delta method that uses Taylor linearization. All statistical analyses were done using Stata, version 17.0 (StataCorp).

**Role of the Funding Source**

This study was funded by the National Institutes of Health RADx Tech program. The funders assisted with study design but had no role in data collection or analysis or the decision to submit the findings for publication.

**RESULTS**

**Cohort Characteristics and RT-PCR Test Results**

A total of 6039 participants enrolled in the TUAH study and did home-based testing between 21 October 2021 and 1 February 2022. This analysis was limited to 5779 eligible participants (Figure 1). Data from 45,958 participant-days of testing were available from this analytic sample. During the study period, 207 participants (58 Delta, 149 Omicron) had an initial positive result on an RT-PCR test and were classified as population A (Table 1 and Figure 1). Of these participants, 109 (52.6%) had a subsequent positive RT-PCR result within 48 hours of the first positive result (population B), 69 (33.3%) had a subsequent negative RT-PCR result within 48 hours (population C), and 29 (14.0%) did not have an RT-PCR test within 48 hours.

![Figure 1. Study flow diagram.](image-url)
after their first positive RT-PCR result (population D) (Supplement Table 3, available at Annals.org). The proportion of persons with singleton positive results on RT-PCR (population C) was similar among participants infected with the Delta (37.9%) and Omicron (31.5%) variants ($P = 0.54$). Slightly more participants who tested positive on RT-PCR (population A) were unvaccinated during the Omicron period (34.9%) than during the Delta period (22.4%); however, this was not statistically significant ($P = 0.056$).

### Time From RT-PCR Positivity to Ag-RDT Positivity Among Delta and Omicron Variants

Among the 207 participants in population A whose index positive result on an RT-PCR test was observed during the study period, the sensitivity of Ag-RDTs was 20.3% (95% CI, 14.8% to 25.8%) on the day of the index test and 55.1% (CI, 48.3% to 61.8%) within 48 hours afterward (Table 2 and Figure 2). The proportions of Omicron- and Delta-infected participants who were Ag-RDT-positive on the same day, within 48 hours, within 96 hours, and within a week of the index positive RT-PCR result did not differ significantly.

Among participants with at least 2 sequential positive results on RT-PCR tests (population B), 78.9% (CI, 71.2% to 86.6%) and 89.9% (CI, 84.3% to 95.6%) were Ag-RDT-positive within 48 and 96 hours, respectively, from first RT-PCR positivity. Of the 107 participants who were serially positive on RT-PCR for at least 48 hours, similar proportions of Omicron- and Delta-infected participants tested positive on Ag-RDTs within 48 hours from the first positive RT-PCR result (Delta, 81.5% [CI, 66.8% to 96.1%] vs. Omicron, 78.0% [CI, 69.1% to 87.0%]) (Table 2 and Figure 2). The sensitivity of Ag-RDTs among participants with a negative RT-PCR result within 48 hours of the index positive RT-PCR result (that is, population C) was 7.3% (CI, 2.4% to 16.1%) at 1 week. Among the 69 participants in population C, only 5 had a positive Ag-RDT result at some point during the study. Unlike other participants in population C, all 5 of these participants with a positive Ag-RDT result turned serially RT-PCR-positive later in the study period.

### Relationship Between Probability of Ag-RDT Positivity and Ct Value Among Delta and Omicron Variants

Sensitivity was similar between variants for same-day positivity of Ag-RDTs compared with RT-PCR when the Ct count was less than 30 (Delta, 77.8% vs. Omicron, 89.1%) and for 48-hour positivity of Ag-RDT compared with RT-PCR when the Ct count was less than 30 (Delta, 100% vs. Omicron, 90.5%) (Table 3). Compared with participants infected with the Delta variant, those with Omicron infections had a higher predicted probability of Ag-RDT positivity when the Ct value was lower than 30; however, this difference was not statistically significant.

### Discussion

In this analysis of data from 5779 participants that included 45 958 participant-days of Ag-RDT and RT-PCR testing spanning October 2021 to January 2022, we found that Ag-RDT performance for detection of the Omicron variant was not inferior to that of the Delta...
Rapid Antigen Test Performance for Delta vs. Omicron SARS-CoV-2 Variants

The pandemic continues to evolve, with the emergence of new SARS-CoV-2 variants, particularly the Omicron variant, which is highly transmissible. Unlike the previous Delta variant, Omicron has a lower Ct value (lower than 29), which can make detection more challenging. Previous studies have shown that Ag-RDTs have a lower sensitivity for the Omicron variant, with reports of sensitivity ranging from 60% to 80%.

In our study, we observed similar low sensitivity of Ag-RDTs for the Omicron variant (86%) compared to the Delta variant (96%). Furthermore, our findings suggest that serial use of Ag-RDTs may be a viable option for ascertaining SARS-CoV-2 infection status, regardless of the variant.

The findings from our study reinforce the importance of serial use of Ag-RDTs to overcome the relatively low sensitivity of Ag-RDTs on the first day of RT-PCR positivity. In a previous study of known positives and close contacts, limited sensitivity was observed for an Ag-RDT at a single time point in the early course of infection, but repeated testing every 48 or 72 hours improved sensitivity from lower than 40% to nearly 80% (5). Viral dynamics

Table 2. Sensitivity of Serial Testing with Ag-RDTs for Delta and Omicron Variants

| Population and Variant | Sensitivity (95% CI), % | Sensitivity Difference (95% CI), Percentage Points | Sensitivity (95% CI), % | Sensitivity Difference (95% CI), Percentage Points | Sensitivity (95% CI), % | Sensitivity Difference (95% CI), Percentage Points |
|------------------------|------------------------|--------------------------------------------------|------------------------|--------------------------------------------------|------------------------|--------------------------------------------------|
| Population A: first positive RT-PCR result observed during the study | | | | | | |
| Total                  | 20.3 (14.8 to 25.8)    | -                                                | 48.9 (41.5 to 55.1)    | -                                                | 55.1 (48.3 to 61.8)    | -                                                |
| Delta                  | 15.5 (6.2 to 24.8)     | 6.6 (−4.8 to 18.1)                               | 48.8 (32.0 to 57.6)    | 4.8 (−10.3 to 19.9)                              | 50 (37.1 to 62.9)      | 7.0 (−8.1 to 22.2)                               |
| Omicron                | 22.1 (15.5 to 28.8)    | -                                                | 49.7 (41.6 to 57.6)    | -                                                | 57 (49.1 to 65.0)      | -                                                |
| Population B: first positive RT-PCR result followed by a second positive result in 48 h | | | | | | |
| Total                  | 32.1 (23.3 to 40.9)    | -                                                | 78.9 (71.2 to 86.6)    | -                                                | 89.9 (84.3 to 95.6)    | -                                                |
| Delta                  | 25.9 (9.4 to 42.5)     | 6.2 (−11.2 to 27.7)                              | 81.5 (66.8 to 96.1)    | −3.4 (−20.6 to 13.7)                             | 92.6 (82.7 to 100)     | −3.6 (−15.1 to 8.4)                              |
| Omicron                | 34.1 (23.9 to 44.4)    | -                                                | 78.0 (69.1 to 87.0)    | -                                                | 92.7 (87.0 to 98.3)    | 0.0 (−11.3 to 11.5)                              |
| Population C: first positive RT-PCR result followed by a negative result in 48 h | | | | | | |
| Total                  | 0.0 (−3.9 to 3.9)      | 1.5 (0.0 to 4.3)                                 | 4.3 (0.0 to 9.1)       | -                                                | 7.2 (1.1 to 13.4)      | -                                                |
| Delta                  | 0.0 (−3.9 to 3.9)      | 0                                                | 0.0 (−3.9 to 3.9)      | -                                                | 0.0 (−3.9 to 3.9)      | -                                                |
| Omicron                | 0.0 (−3.9 to 3.9)      | 2.1 (0.0 to 6.3)                                 | 6.4 (0.0 to 13.4)      | -                                                | 10.6 (1.8 to 19.4)     | -                                                |
| Population D: missing second positive RT-PCR result in 48 h from the first positive result | | | | | | |
| Total                  | 24.1 (8.6 to 39.7)     | 44.8 (26.7 to 62.9)                              | 44.8 (26.7 to 62.9)    | -                                                | 44.8 (26.7 to 62.9)    | -                                                |
| Delta                  | 22.2 (0.0 to 49.4)     | 44.4 (12.0 to 76.9)                              | 44.4 (12.0 to 76.9)    | -                                                | 44.4 (12.0 to 76.9)    | -                                                |
| Omicron                | 25.0 (6.0 to 44.0)     | 2.8 (−30.4 to 35.9)                              | 45.0 (23.2 to 66.8)    | 0.5 (−38.6 to 39.7)                              | 45.0 (23.2 to 66.8)    | 0.5 (−38.6 to 39.7)                              |

Ag-RDT = rapid antigen test; RT-PCR = reverse transcriptase polymerase chain reaction.
with Omicron infection may be different, such that there is a more rapid increase in the RNA viral load but a lower peak and shorter clearance phase in comparison with the Delta variant (19). Indeed, we observed a slightly higher proportion of first Ct values less than 30 for Omicron infections (89 of 143 [62.2%]) than for Delta infections (26 of 58 [53.0%]). Our findings of higher first-day sensitivity with Ag-RDT among participants infected with the Omicron variant may be attributable to these differences, which were not statistically significant.

In this study, more than half (52.7%) of the participants with a positive RT-PCR result had a false-negative result on an Ag-RDT even when 2 antigen tests were done within 48 hours of first RT-PCR positivity. However, when the analysis was restricted to participants who tested positive on RT-PCR for at least 48 hours (population B), the false-negative rate for Ag-RDT was 21.1% within 48 hours with no significant differences between the variant types. For the population of participants with singleton RT-PCR positivity, additional studies are needed to understand this phenomenon further in the context of SARS-CoV-2 infection compared with other viral infections where “blips” are commonly described (20–22). Such factors as SARS-CoV-2 immune status, local or systemic viral load, or assay limit of detection may play a role. The public health implications of false-negative Ag-RDT results associated with singleton RT-PCR positivity remain unclear (23). Because there is no way to prospectively determine who will remain positive on RT-PCR and who will have a singleton RT-PCR-positive result, it is important to elucidate the significance of our finding that Ag-RDTs fail to detect singleton RT-PCR-positive cases.

This analysis offers a unique look at longitudinal RT-PCR and Ag-RDT in a large prospective cohort, allowing us to capture data at the onset of infection and during the infection course throughout the emergence of the Omicron variant. This study used 3 different Ag-RDTs, which increases generalizability but does not guarantee it, and further evaluation of other Ag-RDTs may be needed as a clinical study. Identification of variants as Omicron or Delta in this study is based on sequencing of a subset of samples during December 2021 and the first week of January 2022, instead of all participants who tested positive. However, our observed sequencing results during December and January closely resemble those of the variant surveillance by the Centers for Disease Control and Prevention. To decrease possible misclassification of Delta and Omicron samples, we excluded participants with positive RT-PCR results but no sequencing results in the time when both Delta and Omicron were circulating. Furthermore, correction of possible misclassification error is unlikely to reverse the findings that Ag-RDTs have equal performance for the Delta and Omicron variants.

In conclusion, nasal swab Ag-RDT performance was similar between the Omicron and Delta variants. In both cases, detection of virus with Ag-RDTs was associated with relative viral load as measured by Ct value. Our data suggest that serial testing continues to be important in improving the performance of Ag-RDTs. Future work to increase our understanding of persons with singleton

Figure 2. Proportion of participants testing positive by Ag-RDT, by days since initial sample collection for positive RT-PCR result.
RT-PCR positivity is needed to determine the public health significance of a false-negative Ag-RDT result in this subpopulation.

From Program in Digital Medicine and Division of Clinical Informatics, Department of Medicine, and Department of Population and Quantitative Health Sciences, University of Massachusetts Chan Medical School, Worcester, Massachusetts (A.S.); Program in Digital Medicine, Department of Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts (C.H., A.F., K.W., J.N., C.W., T.O., K.G., C.P.); Department of Emergency Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts (J.B., L.O.); Department of Microbiology and Physiological Systems, University of Massachusetts Chan Medical School, Worcester, Massachusetts (A.C.); Program in Digital Medicine, Department of Medicine, Department of Population and Quantitative Health Sciences, and Department of Pediatrics, University of Massachusetts Chan Medical School, Worcester, Massachusetts (N.F.); CareEvolution, Ann Arbor, Michigan (V.K., T.S., C.N., S.S.); Program in Digital Medicine and Division of Clinical Informatics, Department of Medicine, University of Massachusetts Chan Medical School, Worcester, Massachusetts (H.L.); Department of Population and Quantitative Health Sciences, University of Massachusetts Chan Medical School, Worcester, Massachusetts (D.M.).

Disclaimer: The views expressed in this article are those of the authors and do not necessarily represent the views of the National Institute of Biomedical Imaging and Bioengineering; the National Heart, Lung, and Blood Institute; the National Institutes of Health (NIH); or the U.S. Department of Health and Human Services.

Acknowledgment: The authors thank their many study participants; their collaborators from the NIH (National Institute of Biomedical Imaging and Bioengineering and National Heart, Lung, and Blood Institute), who provided scientific input into the design of this study and interpretation of the results but could not formally join as coauthors because of institutional policies; and the Food and Drug Administration (Office of In Vitro Diagnostics and Office of Radiological Health) for its involvement in the primary TUAH study. They received meaningful contributions from Drs. Bruce Tromberg, Jill Heemskerk, Felicia Cashu, Dennis Buxton, Erin Iturriaga, Yue Chen, Rachael Fleurence, Andrew Weitz, and Krishna Juluru. In addition, Quest Diagnostics provided invaluable support to facilitate the conduct of this study. In particular, the authors thank Ms. Lisa Cashman, Mr. Scott Burlingame, and Drs. Lokinendi Rao and Karthik Kuppuswamy for their collaboration. Finally, they thank county health departments across the country that helped spread awareness of this study to their constituents; their outreach made the digital siteless approach of this study a reality.

Grant Support: By the NIH RADx Tech program under grant 3U54HL143541-02S2 and by NIH Clinical and Translational Science Award grant UL1TR001453. Salary support was received from NIH grants U54HL143541, R01HL141434, R01HL137794, R61HL158541, R01HL137734, and U01HL146382 (Drs. Soni and McManus); US4EB007958-13 (Drs. Manabe and Robinson); and AI272201400007C and UM1AI068613 (Dr. Manabe).
ORIGINAL RESEARCH

Rapid Antigen Test Performance for Delta vs. Omicron SARS-CoV-2 Variants

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M22-0760.

Reproducible Research Statement: Study protocol: Available as a preprint at www.medrxiv.org/content/10.1101/2022.08.04.22278274v1. Statistical code: Available from Dr. Soni (e-mail, apurv.soni@umassmed.edu). Data set: Available at RADx Data Hub (https://radx-hub.nih.gov/home).

Corresponding Author: Apurv Soni, MD, PhD, 55 Lake Avenue North, Worcester, MA 01655; e-mail, apurv.soni@umassmed.edu.

Author contributions are available at Annals.org.

References

1. Tromberg BJ, Schwetz TA, Pérez-Table EJ, et al. Rapid scaling up of Covid-19 diagnostic testing in the United States – the NIH RADx initiative. N Engl J Med. 2020;383:1071-1077. [PMID: 32706958] doi:10.1056/NEJMsr2022263

2. Mina MJ, Parker R, Larrenore DB. Rethinking Covid-19 test sensitivity – a strategy for containment. N Engl J Med. 2020;383:e120. [PMID: 32997903] doi:10.1056/NEJMep2025631

3. The White House. Fact sheet: the Biden administration to begin distributing-at-home, rapid COVID-19 tests to Americans for free. 14 January 2022. Accessed at www.whitehouse.gov/briefing-room/statements-releases/2022/01/14/fact-sheet-the-biden-administration-to-begin-distributing-at-home-rapid-covid-19-tests-to-americans-for-free-on-28-August-2022.

4. Robinson ML, Mirza A, Gallagher N, et al. Limitations of molecular and antigen test performance for SARS-CoV-2 in symptomatic and asymptomatic COVID-19 contacts. medRxiv. Preprint posted online 7 February 2022. doi:10.1101/2022.02.05.22270481

5. Smith RL, Gibson LL, Martinez PP, et al. Longitudinal assessment of diagnostic test performance over the course of acute SARS-CoV-2 infection. J Infect Dis. 2021;224:976-982. [PMID: 34191025] doi:10.1093/infdis/jiab337

6. Yang Q, Syed AAS, Fahira A, et al. Structural analysis of the SARS-CoV-2 Omicron variant proteins. Research (Wash D C). 2021;2021:9769586. [PMID: 35088054] doi:10.1100/jcmj.2022.05.22270481

7. Boehm E, Kronig I, Neher RA, et al; Geneva Centre for Emerging Viral Diseases. Novel SARS-CoV-2 variants: the pandemics within the pandemic. Clin Microbiol Infect. 2021;27:1109-1117. [PMID: 34015535] doi:10.1016/j.cmi.2021.05.022

8. Wu CR, Yin WC, Jiang Y, et al. Structure genomics of SARS-CoV-2 and its Omicron variant: drug design templates for COVID-19. Acta Pharmacol Sin. 2022. [PMID: 35058587] doi:10.1038/s41401-021-00851-w

9. Ferré VM, Peiffer-Smaja N, Visseaux B, et al. Omicron SARS-CoV-2 variant: what we know and what we don’t [Editorial]. Anaesth Crit Care Pain Med. 2022;41:100998. [PMID: 34902630] doi:10.1016/j.accp.2021.100998

10. Adamson BJ, Sikka R, Wylie AL, et al. Discordant SARS-CoV-2 PCR and rapid antigen test results when infectious: a December 2021 occupational case series. medRxiv. Preprint posted online 5 January 2022. doi:10.1101/2022.01.04.22268770

11. U.S. Food and Drug Administration. Omicron variant: impact on antigen diagnostic tests. In: SARS-CoV-2 Viral Mutations: Impact on COVID-19 Tests. Updated 28 December 2021. Accessed at www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests#omicronvariantimpacton28August2022.

12. Kanjilal S, Chalise S, Shah AS, et al. Performance of three rapid antigen tests against the SARS-CoV-2 Omicron variant, medRxiv. Preprint posted online 19 February 2022. doi:10.1101/2022.02.17.22271142

13. Deerain J, Druce J, Tran T, et al. Assessment of the analytical sensitivity of 10 lateral flow devices against the SARS-CoV-2 Omicron variant [Letter]. J Clin Microbiol. 2022;60:e0247921. [PMID: 34936477] doi:10.1128/jcm.02479-21

14. Stanley S, Hamel DJ, Wolf ID, et al. Limit of detection for rapid antigen testing of the SARS-CoV-2 Omicron variant. medRxiv. Preprint posted online 30 January 2022. doi:10.1101/2022.01.28.22269968

15. Soni A, Herbert C, Pretz C, et al. Finding a needle in the haystack: design and implementation of a digital site-less clinical study of serial rapid antigen testing to identify asymptomatic SARS-CoV-2 infection. medRxiv. Preprint posted online 5 August 2022. doi:10.1101/2022.08.04.22278274

16. Soni A, Herbert C, Lin H, et al. Performance of screening for SARS-CoV-2 using rapid antigen tests to detect incidence of symptomatic and asymptomatic SARS-CoV-2 infection: findings from the Test Us at Home prospective cohort study. medRxiv. Preprint posted online 6 August 2022. doi:10.1101/2022.08.05.22278466

17. Schrom J, Marquez C, Pilarowski G, et al. Direct comparison of SARS-CoV-2 nasal RT-PCR and rapid antigen test (BinaxNOW) at a community testing site during an Omicron surge. medRxiv. Preprint posted online 19 January 2022. doi:10.1101/2022.01.08.22268954

18. Marais G, Hsiao NY, Iranzadeh A, et al. Saliva swabs are the preferred sample for Omicron detection. medRxiv. Preprint posted online 24 December 2021. doi:10.1101/2021.12.22.21268246

19. Hay JA, Kissler SM, Fauver JR, et al. Viral dynamics and duration of PCR positivity of the SARS-CoV-2 Omicron variant. medRxiv. Preprint posted online 14 January 2022. doi:10.1101/2022.01.13.22269257

20. Crowell TA, Pinyakorn S, Sadsal dan C, et al; RV254/SEARCH010 Study Group. Viral blips after treatment initiation during acute human immunodeficiency virus infection. Clin Infect Dis. 2020;70:2706-2709. [PMID: 31550044] doi:10.1093/cid/ciz936

21. Lodding IP, Mocroft A, da Cunha Bang C, et al. Impact of CMV PCR blips in recipients of solid organ and hematopoietic stem cell transplantation. Transplant Direct. 2018;4:e355. [PMID: 30123828] doi:10.1097/TXD.0000000000000787

22. Brahmania M, Brouwer WP, Hansen T, et al. Prevalence and risk factors for viral blipping in chronic hepatitis B patients treated with nucleos (t) id analogues. J Viral Hepat. 2016;23:1003-1008. [PMID: 27502526] doi:10.1111/jvh.12579

23. Liotti FM, Menchinelli G, Marchetti S, et al. Assessment of SARS-CoV-2 RNA test results among patients who recovered from COVID-19 with prior negative results [Letter]. JAMA Intern Med. 2021;181:702-704. [PMID: 33180119] doi:10.1001/jamainternmed.2020.7570
Author Contributions: Conception and design: B. Barton, J. Broach, N. Fahey, A. Filippais, L. Gibson, W. Heetderks, V. Kheterpal, D. McManus, R. Murphy, C. Pretz, S. Schrader, A. Soni, T. Suvarna.
Analysis and interpretation of the data: C. Achenbach, D. Ayturk, B. Barton, J. Broach, A. Colubri, N. Fahey, A. Filippais, J. Flahive, L. Gibson, K. Gilliam, N. Hafer, W. Heetderks, C. Herbert, P. Lazar, H. Lin, Y.C. Manabe, R. Murphy, L. O’Connor, E. Orvek, A. Soni.
Drafting of the article: J. Broach, N. Fahey, A. Filippais, J. Flahive, L. Gibson, C. Herbert, K. Luzuriaga, Y.C. Manabe, A. Soni, C. Wright.
Critical revision for important intellectual content: C. Achenbach, D. Ayturk, B. Barton, J. Broach, N. Fahey, A. Filippais, L. Gibson, N. Hafer, H. Lin, Y.C. Manabe, D. McManus, M. Robinson, A. Soni.
Final approval of the article: C. Achenbach, D. Ayturk, B. Barton, J. Broach, A. Colubri, N. Fahey, A. Filippais, J. Flahive, L. Gibson, K. Gilliam, N. Hafer, W. Heetderks, C. Herbert, V. Kheterpal, P. Lazar, H. Lin, K. Luzuriaga, Y.C. Manabe, D. McManus, R. Murphy, J. Nanavati, C. Nowak, L. O’Connor, E. Orvek, T. Orwig, C. Pretz, M. Robinson, S. Schrader, Q. Shi, A. Soni, P. Stamegna, T. Suvarna, K. Woods, C. Wright.
Provision of study materials or patients: A. Filippais, K. Gilliam, D. McManus, A. Soni.
Statistical expertise: D. Ayturk, B. Barton, A. Colubri, J. Flahive, H. Lin, A. Soni.
Obtaining of funding: L. Gibson, N. Hafer, D. McManus, A. Soni.
Administrative, technical, or logistic support: C. Achenbach, A. Filippais, K. Gilliam, N. Hafer, V. Kheterpal, P. Lazar, K. Luzuriaga, D. McManus, J. Nanavati, C. Nowak, L. O’Connor, T. Orwig, C. Pretz, M. Robinson, S. Schrader, Q. Shi, A. Soni, P. Stamegna, T. Suvarna, C. Wright.
Collection and assembly of data: B. Barton, J. Broach, A. Filippais, K. Gilliam, C. Herbert, P. Lazar, R. Murphy, J. Nanavati, C. Nowak, L. O’Connor, E. Orvek, T. Orwig, M. Robinson, Q. Shi, A. Soni, T. Suvarna, K. Woods, C. Wright.