Performance Characteristics of the Abbott BinaxNOW SARS-CoV-2 Antigen Test in Comparison to Real-Time Reverse Transcriptase PCR and Viral Culture in Community Testing Sites during November 2020

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ABSTRACT Point-of-care antigen tests are an important tool for SARS-CoV-2 detection. Antigen tests are less sensitive than real-time reverse transcriptase PCR (rRT-PCR). Data on the performance of the BinaxNOW antigen test compared to rRT-PCR and viral culture by symptom and known exposure status, timing during disease, or exposure period and demographic variables are limited. During 3 to 17 November 2020, we collected paired upper respiratory swab specimens to test for SARS-CoV-2 by rRT-PCR and Abbott BinaxNOW antigen test at two community testing sites in Pima County, Arizona. We administered a questionnaire to capture symptoms, known exposure status, and previous SARS-CoV-2 test results. Specimens positive by either test were analyzed by viral culture. Previously we showed overall BinaxNOW sensitivity was 52.5%. Here, we showed BinaxNOW sensitivity increased to 65.7% among currently symptomatic individuals reporting a known exposure. BinaxNOW sensitivity was lower among participants with a known exposure and previously symptomatic (32.4%) or never symptomatic (47.1%) within 14 days of testing. Sensitivity was 71.1% in participants within a week of symptom onset. In participants with a known exposure, sensitivity was highest 8 to 10 days postexposure (75%). The positive predictive value for recovery of virus in cell culture was 56.7% for BinaxNOW-positive and 35.4% for rRT-PCR-positive specimens. Result reporting time was 2.5 h for BinaxNOW and 26 h for rRT-PCR. Point-of-care antigen tests have a shorter turnaround time than laboratory-based nucleic acid amplification tests, which allows for more rapid identification of infected individuals. Antigen test sensitivity limitations are important to consider when developing a testing program.

KEYWORDS COVID-19, SARS-CoV-2, Abbott BinaxNOW SARS-CoV-2 Ag Card, antigen test, viral culture

A s of 16 June 2021, the FDA has given Emergency Use Authorization for 28 SARS-CoV-2 antigen (Ag) diagnostic tests, including the Abbott BinaxNOW COVID-19 Ag Card point-of-care test (BinaxNOW) (1). The BinaxNOW test is a point-of-care lateral-flow

antigen test, and results are read visually within 15 to 30 min, which is quicker than laboratory-based testing, such as real-time reverse transcriptase PCR (rRT-PCR). BinaxNOW is currently authorized for emergency use in individuals within the first week of symptom onset (2). However, the Centers for Medicare and Medicaid Services (CMS) exercises enforcement discretion under Clinical Laboratory Improvement Amendments (CLIA) for the duration of the pandemic for the use of SARS-CoV-2 point-of-care tests on asymptomatic individuals outside the test's EUA (3), when these tests are conducted considering FDA's frequently asked questions (FAQs) (4). The FDA FAQs note that screening asymptomatic individuals for COVID-19 using a highly sensitive test if rapid turnaround time is available should be the first option. However, consideration to use less sensitive point-of-care tests is given for situations, such as when highly sensitive tests are not available, turnaround times are long, or considering the type of setting (e.g., serial testing in congregate care settings), and is at the discretion of the health care provider. Asymptomatic screening is an important detection strategy (5) and the use of point-of-care antigen tests can increase access to testing, but performance characteristics should be carefully considered.

Prior studies (6–14) have examined BinaxNOW antigen test performance; however, detailed data on the association of antigen test performance compared to rRT-PCR and viral culture by key epidemiologic characteristics, such as symptom and known exposure status, timing during infection, and demographic variables, are limited. An earlier brief report (15) analyzing these data showed high specificity for BinaxNOW but low sensitivity in specimens from either symptomatic (64.2%) or asymptomatic persons (35.8%) and showed improved sensitivity compared to rRT-PCR when limiting the analysis to culture-positive specimens. However, given the increasing reliance on rapid tests for screening programs, a more granular analysis on the performance of antigen tests is warranted. Here, we build on the previous report to assess BinaxNOW antigen test performance by additional participant characteristics, including symptom and known exposure status, days postsymptom onset and/or known exposure, and demographic variables, including age, gender, and race/ethnicity in two community testing sites during a time of high prevalence (16). We also assessed the BinaxNOW antigen test performance in relation to rRT-PCR cycle threshold (C_T) values and viral isolation in cell culture. Some of the previously published values are repeated here to give context and clarity.

MATERIALS AND METHODS

Setting. During 3 to 17 November 2020, participants were recruited from two community testing sites in Pima County, Arizona. A convenience sample of individuals ≥10 years of age who presented for testing were offered a concurrent BinaxNOW antigen and rRT-PCR test. This evaluation occurred prior to SARS-CoV-2 vaccine FDA EUA approval and availability (17); thus, all participants included were unvaccinated, with the exception of a small number of volunteers who may have participated in early phases of the vaccine clinical trials. We did not collect data on whether individuals previously participated in SARS-CoV-2 vaccine clinical trials. We obtained verbal agreement to participate from adults and assent from minors. Staff administered an electronic questionnaire to participants via REDCap, assessing current or 14 days of symptom history, number of days since symptom onset, known exposure to a diagnosed COVID-19 case (during prior 14 days), number of days since last known exposure, and whether individuals tested positive in the past 90 days. The list of symptoms was selected based on the Council of State and Territorial Epidemiologists COVID-19 2020 Interim Case Definition (18). We obtained demographic data from the Pima County Health Department (PCHD). The protocol for this evaluation was reviewed by the Centers for Disease Control and Prevention (CDC) and determined to be nonresearch and was conducted consistent with applicable federal law and CDC policy as defined in 45 CRF 46.102(l)(2) (19).

Swab collection procedure and BinaxNOW testing and results reporting. We collected paired upper respiratory swab specimens for rRT-PCR and BinaxNOW antigen testing from all persons agreeing to participate. A health care professional collected a bilateral anterior nasal (AN) swab first for BinaxNOW testing according to the manufacturer's instructions for use (2), immediately followed by a bilateral nasopharyngeal (NP) swab for rRT-PCR testing per the standard of care at the testing sites. Additional details on swab collection and BinaxNOW quality control, testing, and results reporting are included in the supplemental material.

Real-time RT-PCR testing. NP swabs were stored in phosphate-buffered saline (PBS) at 4°C and analyzed within 24 to 48 h by rRT-PCR for detection of SARS-CoV-2 using either the CDC 2019-nCoV rRT-PCR diagnostic panel (CDC rRT-PCR assay) for detection of SARS-CoV-2 (n = 2,582) (20) or the Fosun COVID-19 rRT-PCR detection kit (Fosun rRT-PCR assay) (n = 837) (21). Both rRT-PCR assays were performed and

reported according to the FDA Emergency Use Authorization Instructions for Use, with modifications that are described here. All modifications were validated by the commercial laboratory using a bridging study to the EUA-authorized test according to the FDA's Policy for Coronavirus Disease-2019 Tests During the Public Health Emergency (22). For both rRT-PCR assays, RNA was extracted using the Omega BioMek (Norcross, GA)-Thermo Fisher Scientific KingFisher RNA extraction platform, and the rRT-PCR instrument platform used was the Light Cycler 480 Instrument II (Roche Sequencing Solutions). Additional details on swab collection and BinaxNOW quality control, testing, and results reporting are included in the supplemental material.

SARS-CoV-2 viral isolation. Residual rRT-PCR swabs ($n = 274$) from individuals who tested positive by either rRT-PCR or BinaxNOW were analyzed by viral culture as described previously (23) and in the supplemental material. To preserve viral infectivity, the residual rRT-PCR swabs in PBS were stored at $-80°C$ after rRT-PCR testing and within 72 h of collection and shipped to the CDC overnight on dry ice for viral culture.

Statistical analysis. Using the rRT-PCR result as the reference, we calculated analytic performance characteristics, including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and 95% confidence intervals (CIs) using the exact binomial method. We analyzed test performance by patient characteristics, including symptom timing and known exposure history, and calculated turnaround time for results reporting for antigen and rRT-PCR results. Statistical analysis was limited to data collected from specimens tested by the CDC rRT-PCR assay when using the nucleocapsid 1 (N1) cycle threshold value as a variable, because the two rRT-PCR assays detect different SARS-CoV-2 gene targets and C_T values are not comparable across different assays. The CDC rRT-PCR assay detects targets N1 and N2 while the Fosun rRT-PCR assay detects N, E, and ORF1a. We calculated the PPV for isolation in viral culture for BinaxNOW and rRT-PCR using viral culture as the reference. We used chi-square or Spearman's rho for test of significance. All statistical analyses were performed using SAS (V9.4, Cary, NC). Figures were created using GraphPad PRISM v9.0.

Data availability. Data are available upon request. Data will be shared in a manner that is compliant with all local and U.S. government laws and regulations and that protects human subjects' patient confidentiality.

RESULTS

Participant characteristics. We collected 3,419 paired specimens from 3,302 participants aged 10 and older that also had complete testing and survey data (see Fig. S1 in the supplemental material). Of these, 161 (4.7%) were BinaxNOW positive and 299 (8.7%) were rRT-PCR positive (Table 1). Of the 299 rRT-PCR-positive specimens, 228 (76.3%) were tested by the CDC rRT-PCR assay and 71 (23.7%) by the Fosun rRT-PCR assay. Of the 3,302 participants, 97 participated twice and 10 participated three times; no significant differences in BinaxNOW test performance were observed when including only the first paired test results. The average time from test site registration to reporting of test results was 2.5 h for BinaxNOW and 26 h for rRT-PCR.

One-third of participants (31.4%) identified as Hispanic/Latino, 51.1% identified as White, non-Hispanic/Latino, and 4.6% as other race, non-Hispanic/Latino (Table 1). As reported on the day of testing, 827 (24.2%) specimens were from participants experiencing symptoms (currently symptomatic), 624 (18.3%) from individuals asymptomatic but reported symptoms in the past 14 days (previously symptomatic), and 1,968 (57.6%) from individuals who reported no symptoms in the past 14 days (never symptomatic). One-third (33.3%) of participants reported a known exposure within the past 14 days to a diagnosed COVID-19 case (Table 1). Participants with a known exposure were more likely to test positive than those with no known exposure by rRT-PCR (14.2% versus 6.0%, $P \leq 0.0001$) or BinaxNOW (8.2% versus 3.0%, $P \leq 0.0001$). rRT-PCR test positivity was at least twice as high among Hispanic/Latino participants (14%) than non-Hispanic participants (White, 6.0%; other race, 7.0%). rRT-PCR positivity among children 10 to 17 years was 9.3%, similar to adults 18 to 49 (9.4%) and 50 to 64 years (9.3%) (Table 1).

BinaxNOW test performance by symptom and known exposure status. BinaxNOW sensitivity was 65.7% among currently symptomatic individuals reporting a known exposure and 61.8% for those without a known exposure (Table 2). Specificity was 100% for both groups. BinaxNOW sensitivity was lower among participants with a known exposure and previously symptomatic (32.4%) or never symptomatic (47.1%); specificity was 100.0% and 99.8% in each group, respectively. Among participants who were never symptomatic in the 14 days prior to testing, BinaxNOW sensitivity was higher among individuals who reported a known exposure (47.1%) than among those without a known exposure (36.1%). Among participants who were either currently or previously symptomatic, NPV for the BinaxNOW antigen test was lower in participants reporting a

TABLE 1 Characteristics of persons providing paired upper respiratory swabs ($N = 3,419$)[a] for BinaxNOW and rRT-PCR[b] for SARS-CoV-2 at two community-based testing sites[c]

Characteristic	Total	rRT-PCR positive	BinaxNOW antigen positive
Total no. (%)	3,419 (100.0)	299 (8.7)	161 (4.7)
Sex, no. (%)			
Male	1,290 (37.7)	138 (10.7)	74 (5.7)
Female	1,681 (49.2)	127 (7.6)	76 (4.5)
Undisclosed	448 (13.1)	34 (7.6)	11 (2.5)
Race/ethnicity, no. (%)			
White, non-Hispanic/Latino	1,747 (51.1)	105 (6.0)	56 (3.2)
Other race,[d] non-Hispanic/Latino	158 (4.6)	11 (7.0)	6 (3.8)
Hispanic/Latino	1,075 (31.4)	150 (14.0)	86 (8)
Unknown race or ethnicity	439 (12.8)	33 (7.5)	13 (3.0)
Age (yr), no. (%)			
10–17	236 (6.9)	22 (9.3)	10 (4.2)
18–49	1,885 (55.1)	178 (9.4)	91 (4.8)
50–64	743 (21.7)	69 (9.3)	41 (5.5)
≥ 65	555 (16.2)	30 (5.4)	19 (3.4)
Median age (yr, range)	41 (10–95)	38 (11–84)	40 (13–84)
Symptom[e] and exposure[f] status, no. (%)			
Currently symptomatic	827 (24.2)	176 (21.3)	113 (13.7)
Exposure	366 (10.7)	108 (36.1)	71 (44.1)
No exposure	461 (13.5)	68 (22.7)	42 (26.1)
Previously symptomatic	624 (18.3)	70 (11.2)	24 (3.8)
Exposure	216 (6.3)	37 (12.4)	12 (7.5)
No exposure	407 (11.9)	33 (11.0)	12 (7.5)
Never symptomatic	1,968 (57.6)	53 (2.7)	24 (1.2)
Exposure	556 (16.3)	17 (5.7)	10 (6.2)
No exposure	1,412 (41.3)	36 (12.0)	14 (8.7)
Exposure[f]	1138 (33.3)	162 (54.2)	93 (57.8)
No exposure	2281 (66.7)	137 (45.8)	68 (42.2)
Median days since last known exposure (range)	5 (0–14)	3 (0–14)	4 (0–14)
Median days since symptom onset (range)	4 (0–210)	4 (0–45)	3 (0–14)
Tested positive in past 90 days,[g] no. (%)			
Yes	179 (5.2)	83 (46.4)	22 (12.3)
No	3,239 (94.7)	216 (6.7)	139 (4.3)

[a]Includes 107 individuals who presented multiple times for testing during the evaluation and were included more than once in the analysis.

[b]rRT-PCR performed using the CDC 2019-nCoV diagnostic panel for detection of SARS-CoV-2 ($n = 2,582$) or the Fosun assay ($n = 837$).

[c]Table includes data from a previous brief report (15).

[d]Other race includes Black/African American, American Indian/Alaska Native, Asian, Native Hawaiian/Pacific Islander.

[e]Participants were asked if they had symptoms in 14 days prior to testing and/or at the time of testing, here we classified currently symptomatic as ≥1 symptom at time of test. Previously symptomatic was defined as having symptoms in the 14 days prior to but not on the day of test, and those never symptomatic were defined as reporting no symptoms in the 14 days prior to or on day of test.

[f]Self-reported being a known close contact (within 6 ft for ≥15 min) in the 14 days prior to day of testing with a person diagnosed with COVID-19.

[g]Individuals self-identified as previously having a positive test and noted test type was rRT-PCR ($n = 160$), antigen ($n = 7$), or test type was unknown ($n = 12$). Additionally, 5 individuals responded not knowing or declined to answer whether they tested positive in the previous 90 days (grouped with "no" responses); 1 individual for which the response was not recorded was excluded from the total.

known exposure compared to those who did not (currently symptomatic, known exposure, 87.5%, no known exposure, 93.8%; previously symptomatic, known exposure, 87.8%, no known exposure, 94.4%). For participants who were never symptomatic, NPV for the BinaxNOW test was the same (98.4%) regardless of known exposure status. Excluding participants who tested positive in the previous 90 days, overall BinaxNOW sensitivity increased from 52.5% to 63.0%, a trend seen across all symptom and known exposure groups and most pronounced in the previously symptomatic group (32.9% compared to 51.9%) (Table 2).

TABLE 2 Statistics for Abbott BinaxNOW COVID-19 antigen test compared to rRT-PCR by symptom and exposure status

Symptom[a] and exposure[b] status	N (%)	No. Ag⁻/no. RT-PCR⁺	No. Ag⁺/no. RT-PCR⁻	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All participants[c]	3,419 (100)	142/299	4/3,120	52.5 (46.7–58.3)	99.9 (99.7–100)	97.5 (93.6–99.0)	95.6 (95.1–96.1)
Currently symptomatic[c]	827 (24.2)	63/176	0/651	64.2 (56.6–71.3)	100.0 (99.4–100)	100.0 (96.8–100)	91.2 (88.8–93.1)
Exposure	366 (44.2)	37/108	0/258	65.7 (56.0–74.6)	100.0 (98.6–100)	100.0 (95.0–100)	87.5 (83.1–91.0)
No Exposure	461 (55.7)	26/68	0/393	61.8 (49.2–73.3)	100.0 (99.1–100)	100.0 (91.6–100)	93.8 (91.0–95.9)
Previously symptomatic	624 (18.2)	47/70	1/554	32.9 (22.1–45.1)	99.8 (99.0–100)	95.8 (78.9–99.9)	92.2 (89.7–94.2)
Exposure	216 (34.6)	25/37	0/179	32.4 (18.0–49.8)	100.0 (98.0–100)	100.0 (73.5–100)	87.7 (82.4–91.9)
No Exposure	408 (65.4)	22/33	1/375	33.3 (18.0–51.8)	99.7 (98.5–100)	91.7 (60.0–98.8)	94.4 (93.0–95.6)
Never symptomatic	1,968 (57.6)	32/53	3/1,915	39.6 (26.4–54.0)	99.8 (99.5–100)	87.5 (67.6–97.3)	98.4 (97.7–98.9)
Exposure	556 (28.2)	9/17	2/539	47.1 (23.0–72.2)	99.6 (98.7–100)	80.0 (44.4–97.5)	98.4 (96.9–99.2)
No Exposure	1,412 (71.7)	23/36	1/1,376	36.1 (20.8–53.8)	99.9 (99.6–100)	92.9 (66.1–99.8)	98.4 (97.5–98.9)
Participants who did not report a positive[d] test in the previous 90 days (N = 3,239)							
All Participants	3,239 (100)	80/216	3/3,024	63.0 (56.2–69.4)	99.9 (99.7–100)	97.8 (93.6–99.3)	97.4 (97.0–97.8)
Currently symptomatic	771 (23.8)	42/144	0/627	70.8 (62.7–78.1)	100.0 (99.4–100)	100.0 (96.4–100)	93.7 (91.6–95.4)
Exposure	332 (43.0)	22/84	0/248	73.8 (63.1–82.8)	100.0 (98.5–100)	100.0 (94.2–100)	91.9 (87.9–94.8)
No exposure	439 (56.9)	20/60	0/379	66.7 (53.3–78.3)	100.0 (99.0–100)	100.0 (91.2–100)	95.0 (92.4–96.9)
Previously symptomatic	554 (17.1)	13/27	0/527	51.9 (31.9–71.3)	100.0 (99.3–100)	100.0 (76.8–100)	97.6 (95.9–98.7)
Exposure	182 (32.8)	6/12	0/170	50.0 (21.1–78.9)	100.0 (97.8–100)	100.0 (54.1–100)	96.6 (92.7–98.7)
No exposure	371 (67.0)	7/15	0/356	53.3 (26.6–78.7)	100.0 (99.0–100)	100.0 (63.1–100)	98.1 (96.1–99.2)
Never symptomatic	1,915 (59.1)	25/45	3/1,870	44.4 (29.6–60.0)	99.8 (99.5–100)	87.0 (66.4–97.2)	98.7 (98.1–99.1)
Exposure	542 (28.3)	6/14	2/528	57.1 (28.9–82.3)	99.6 (98.6–100)	80.0 (44.4–97.5)	98.9 (97.6–99.6)
No exposure	1,373 (71.7)	19/31	1/1,342	38.7 (21.8–57.8)	99.9 (99.6–100)	92.3 (64.0–99.8)	98.6 (97.8–99.2)

[a]Participants were asked if they had symptoms in the 14 days prior to testing and/or at the time of testing. Here, we classified currently symptomatic as ≥1 symptom at the time of testing. Those classified as previously symptomatic reported symptoms in the 14 days prior to but not on day of test and those classified as never symptomatic reported no symptoms in the 14 days prior to or on day of test.
[b]Self-reported being a known close contact (within 6 ft for ≥15 min) in the 14 days prior to day of testing with a person diagnosed with COVID-19.
[c]Previously reported data from a brief report (15).
[d]Individuals self-identified as previously having a positive test for SARS-CoV-2 in the 90 days prior and noted that test type was by rRT-PCR (n = 160), antigen (n = 7), or, in some cases, test type was unknown (n = 12).

Symptomatic, known exposure status, and BinaxNOW performance by participant demographics. Hispanic/Latino persons were more likely to report current symptoms (30.3%, $P \leq 0.0001$) or known exposure to a diagnosed COVID-19 case (45.4%, $P \leq 0.0001$) (see Table S1 in the supplemental material). BinaxNOW sensitivity was 56.7% in Hispanic/Latino compared to 50.9% in non-Hispanic/Latino persons. Among never symptomatic participants, BinaxNOW sensitivity was 52.4% in Hispanic/Latino individuals compared to 32.1% in non-Hispanic/Latino individuals (Table S1).

In children 10 to 17 years, BinaxNOW sensitivity was 40.9% compared to 53.4% in adults $\geq$18 years (Table S1). Among participants who were never symptomatic, BinaxNOW sensitivity was 16.7% in children 10 to 17 years and increased with age (18 to 49 years, 30.4%; 50 to 64 years, 46.6%; and $\geq$65 years, 66.7%) (Table S1). The proportion of symptomatic children 10 to 17 years (20.8%) and adults $\geq$65 years (17.8%) was lower than that for adults 18 to 49 years (26.5%) or 50 to 64 years (24%) (Table S1). The proportion of participants with a known exposure was highest in children 10 to 17 years old and decreased with age. Across all age groups, BinaxNOW sensitivity was higher in individuals with a known exposure compared to those without a known exposure, but the difference was greatest in children ages 10 to 17 years (53.8% versus 22.2%) (Table S1).

BinaxNOW test performance by days since symptom onset and days postexposure. BinaxNOW sensitivity was highest within the first 7 days of symptom onset (71.1%) and decreased as days postsymptom onset increased (50.0% on days 8 to 10 and 37.5% on days 11 to 14) (Table 3). In individuals who were more than 14 days postsymptom onset, 100% (6/6) of the rRT-PCR-positive specimens were BinaxNOW negative, and none of these specimens was culture positive. Moreover, 5 of these 6 individuals self-identified as having a positive test in the 90 days prior to testing during the evaluation period, suggesting a longer period of rRT-PCR positive/BinaxNOW negative in the later stages of infection. Postexposure, BinaxNOW sensitivity was highest during days 5 to 7 (65.8%) and days 8 to 10 (75.0%) and lowest during 0 to 3 days (48.0%) and 11 to 14 days (46.7%) (Table 4). Culture positivity was highest during days 3 to 10 postexposure.

C_T values. In specimens analyzed with the CDC rRT-PCR assay and with N1 C_T values <29 (n = 125), which represents the 50th percentile of N1 C_T values in the data set, BinaxNOW sensitivity was 81.6%. Furthermore, median N1 C_T values were lowest in specimens from currently symptomatic individuals (exposed, 24.6; not exposed, 25.8), but higher in specimens from previously symptomatic (exposed, 31.2; not exposed, 30.0) and never symptomatic individuals (not exposed, 32.1) (Fig. 1).

In specimens from symptomatic participants, there was a positive correlation between N1 C_T values and the days postsymptom onset (Spearman rho, 0.24; $P < 0.0001$), suggesting the amount of viral RNA is high during early infection and decreases over time (Fig. 2A). Specimens positive by antigen and culture had a low median N1 C_T value (22.0), and all were collected within 7 days of symptom onset (Fig. 2A). During the postexposure period, median N1 C_T values were highest during 0 to 2 days (29.2) and 11 to 14 days (33.0) (Fig. 2B).

Viral culture results. Thirty-five percent (90/271) of rRT-PCR positive specimens had culturable virus. Among specimens with concordant BinaxNOW- and rRT-PCR-positive results, 57.8% (85/147) were positive by viral culture, and among antigen false-negative specimens, 8.9% (11/124) had culturable virus (Table S2). No virus was cultured among BinaxNOW-positive/rRT-PCR-negative specimens (n = 3) (15). A total of 41.7% (68/163) of currently symptomatic individuals positive by rRT-PCR were culture positive compared to 25.0% (16/64) of previously symptomatic individuals and 27.3% (12/44) of individuals never symptomatic (Table S2). All specimens BinaxNOW negative yet rRT-PCR and culture positive had N1 C_T values of <28 (median C_T, 23.2; interquartile range [IQR], 19.4 to 26.9).

Among specimens from currently symptomatic participants, culture positivity was highest within 7 days of symptom onset (50.4%) (Table 3). Less than 10% of specimens from individuals between 8 and 14 days of symptom onset had culturable virus, and virus was not isolated after 14 days of symptom onset (Table 3). Among specimens from participants with a known exposure, culture positivity was 23.9% during days 0 to 2 and 55.5% between days 3 and 10 postexposure. No culturable virus was detected in rRT-PCR-positive specimens collected from individuals beyond 10 days postexposure (Table 4).

TABLE 3 Statistics for Abbott BinaxNOW COVID-19 antigen test[a] and culture positivity by days postsymptom onset among individuals experiencing COVID-19 symptoms at time of test

Days postsymptom onset	No. symptomatic	No. culture positive/total[c] (%)	No. Ag−/no. RT-PCR+ (false negative)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All participants (N = 823)[b]							
≤3	382	39/78 (50.0)	25/84	70.2 (59.3–79.7)	100.0 (98.8–100)	100.0 (93.9–100)	92.3 (88.8–94.9)
4–7	280	27/53 (50.9)	16/58	72.4 (59.1–83.3)	100.0 (98.3–100)	100.0 (91.6–100)	93.3 (89.3–96.1)
8–10	43	1/12 (8.3)	6/12	50.0 (21.1–78.9)	100.0 (88.8–100)	100.0 (54.1–100)	83.8 (68.0–93.8)
11–14	63	1/14 (7.1)	10/16	37.5 (15.2–65.6)	100.0 (54.1–100)	100.0 (54.1–100)	82.5 (70.1–91.2)
>14	55	0/6 (0.0)	6/6	0.0 (−)	98.0 (92.7–100)	0.0 (−)	89.1 (77.7–95.9)
Participants who did not report a positive[d] test in the previous 90 days (N = 767)[b]							
≤3	376	39/76 (51.3)	24/82	70.7 (59.6–80.3)	100.0 (98.7–100)	100.0 (93.8–100)	92.5 (88.9–95.1)
4–7	266	26/45 (57.8)	12/50	76.0 (61.8–86.9)	100.0 (98.3–100)	100.0 (90.7–100)	94.7 (91.0–97.2)
8–10	35	1/5 (20.0)	2/5	60.0 (14.7–94.7)	100.0 (88.4–100)	100.0 (29.2–100)	93.8 (79.2–99.2)
11–14	48	1/4 (25.0)	3/6	50.0 (11.8–88.2)	100.0 (91.6–100)	100.0 (29.2–100)	93.3 (81.7–98.6)
>14	42	0/1 (0.0)	1/1	0.0 (−)	100.0 (91.6–100)	0.0 (−)	97.6 (87.4–99.9)

[a]Abbott BinaxNOW COVID-19 antigen test performance based on comparison to rRT-PCR.

[b]Excluded 4 participants who reported being symptomatic at the time of test but did not recall the number of days or date since symptom onset.

[c]Denominator includes the total number of residual rRT-PCR-positive specimens analyzed by viral culture.

[d]Individuals self-identified as previously having a positive test for SARS-CoV-2 in the 90 days prior and noted that test type was by rRT-PCR (n = 49) or antigen (n = 2), or, in some cases, test type was unknown (n = 5).

**TABLE 4** Statistics for Abbott BinaxNOW COVID-19 antigen test[a] and culture positivity by days postexposure

Days postexposure	Total no. with exposure	Culture positive/total[b] (%)	No. Ag−/no. RT-PCR+ (false negative)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
All participants (n = 1,138)							
<3	365	17/71 (23.9)	39/75	48.0 (36.3–59.9)	100 (98.7–100)	100 (90.3–100)	88.2 (84.2–91.4)
3–4	177	10/20 (50.0)	8/22	63.6 (40.7–82.8)	99.4 (96.5–100)	93.3 (68.1–99.8)	95.1 (90.5–97.8)
5–7	377	20/33 (60.6)	13/25	65.8 (48.7–80.4)	100 (98.9–100)	100 (86.3–100)	96.3 (93.8–98.0)
8–10	124	5/10 (50.0)	3/12	75.0 (42.8–94.5)	100 (96.8–100)	100 (66.4–100)	97.4 (92.6–99.5)
11–14	95	0/13 (0.0)	8/15	46.7 (21.3–73.4)	98.8 (93.2–100)	87.5 (47.4–99.7)	90.8 (82.7–96.0)
Participants who did not report positive[c] test in previous 90 days (N = 1,056)							
<3	321	15/41 (36.6)	16/44	63.6 (47.8–77.6)	100.0 (98.7–100)	100.0 (87.7–100)	94.5 (91.3–96.8)
3–4	172	10/18 (55.6)	7/20	65.0 (40.8–84.6)	99.3 (96.4–100)	92.9 (66.1–99.8)	95.6 (91.1–98.2)
5–7	366	19/28 (67.9)	9/33	72.7 (54.5–86.7)	100.0 (98.9–100)	100.0 (85.7–100)	97.4 (95.1–98.8)
8–10	120	5/9 (55.6)	9/11	81.8 (48.2–97.7)	100.0 (96.7–100)	100.0 (66.4–100)	98.2 (93.6–99.8)
11–14	77	0/1 (0.0)	0/2	100.0 (15.8–100)	98.7 (92.8–100)	66.7 (9.4–99.2)	100.0 (95.1–100)

[a]Abbott BinaxNOW COVID-19 antigen test performance based on comparison to rRT-PCR.
[b]Denominator includes the total number of residual rRT-PCR-positive specimens analyzed by viral culture.
[c]Individuals self-identified as previously having a positive test for SARS-CoV-2 in the 90 days prior and noted that test type was by rRT-PCR (n = 74) or antigen (n = 3) or, in some cases, test type was unknown (n = 5).
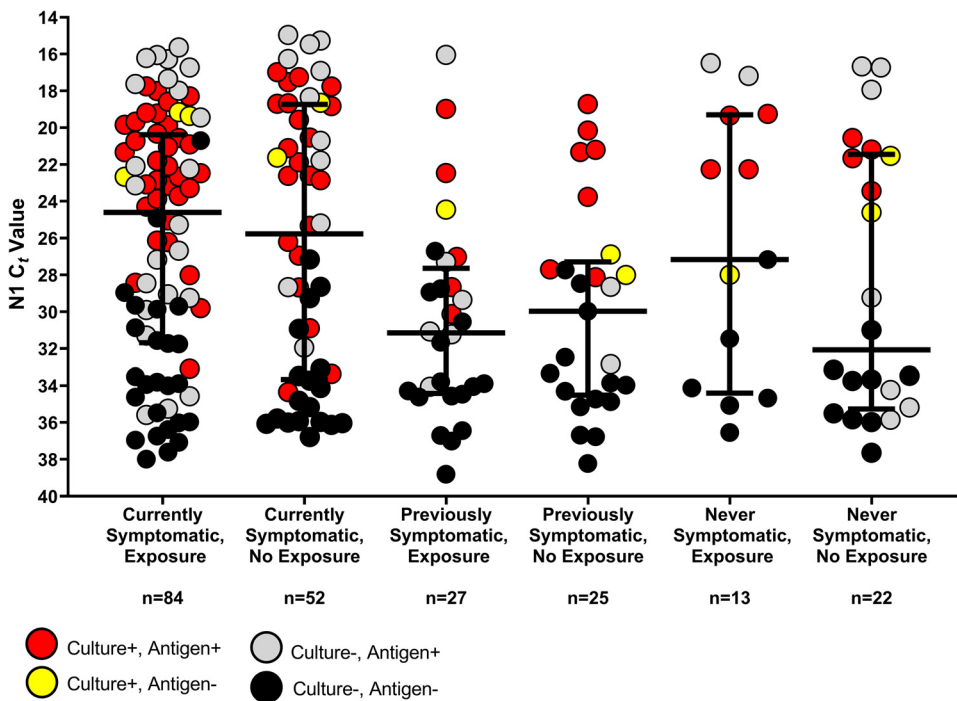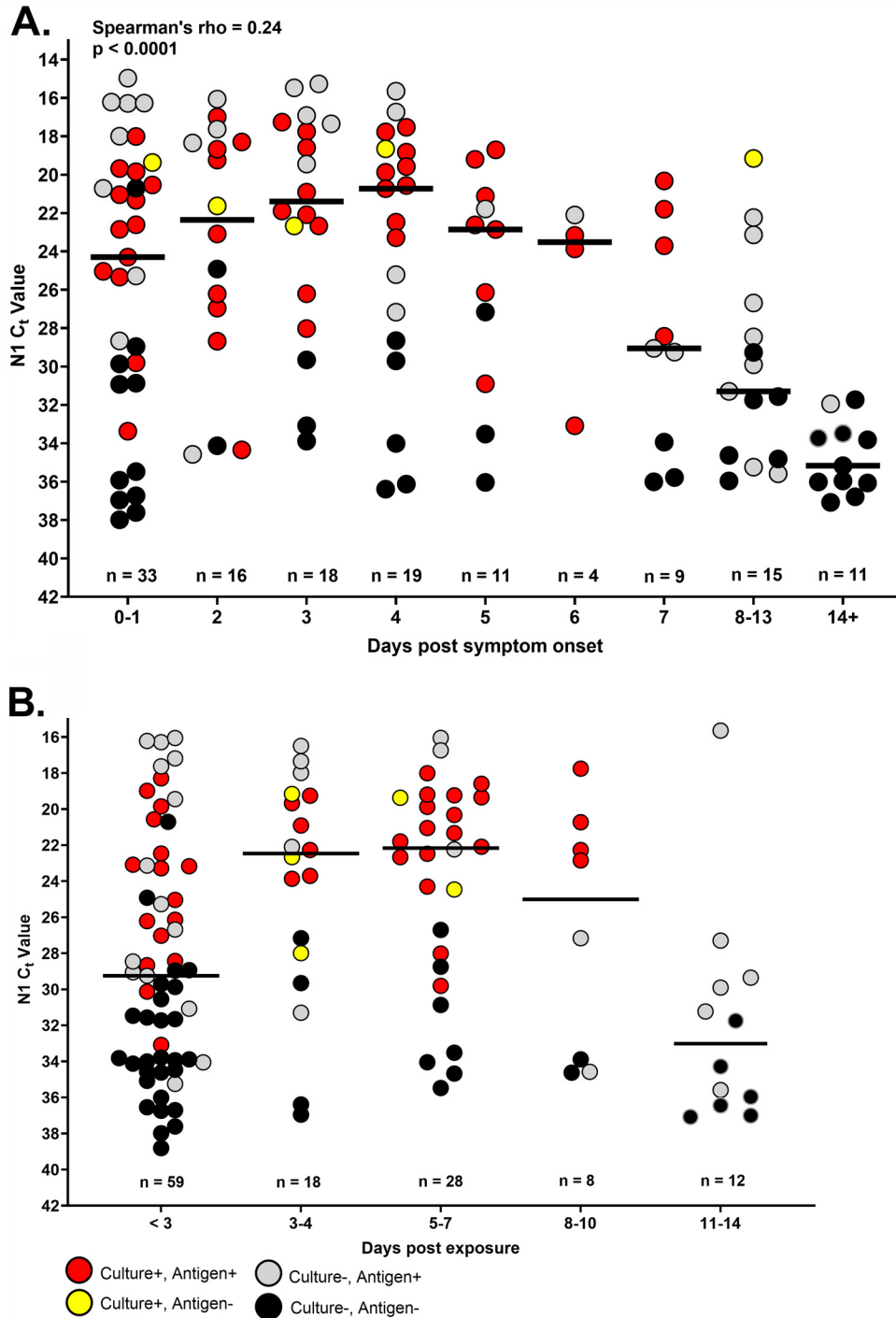
FIG 1 Distribution of N1 cycle threshold values for samples positive by CDC 2019-nCoV rRT-PCR diagnostic panel, viral culture, and Abbott BinaxNOW COVID-19 antigen test by symptom and exposure groups. The distributions of N1 C_T values from rRT-PCR-positive specimens were compared for specimens analyzed with the CDC 2019-nCoV rRT-PCR diagnostic panel for detection of SARS-CoV-2 and were also analyzed by viral culture ($n = 224$). C_T values are represented on the y axis in descending order to indicate that lower C_T values represent larger amounts of RNA in the specimen. The median C_T values and interquartile range (IQR) for the groups are currently symptomatic and exposed, 24.6 (IQR, 20.4 to 31.6), and not exposed, 25.8 (IQR, 18.8 to 33.6); in previously symptomatic and exposed, 31.1 (IQR, 28.0 to 34.4), and not exposed, 30.0 (IQR, 27.7 to 34.3), and in never symptomatic and exposed, 27.2 (IQR, 19.3 to 34.1), and not exposed, 32.1 (IQR, 21.5 to 35.2). Colors indicate the antigen and culture test result of the specimen (red, culture positive/antigen positive; yellow, culture positive/antigen negative; gray, culture negative/antigen positive; black, culture negative/antigen negative).

Among all participants, BinaxNOW PPV for virus isolation was 56.7% compared to rRT-PCR PPV for virus isolation, which was 35.4% (Table 5). In specimens with N1 C_T values of <29, the BinaxNOW PPV for viral isolation was 66.7% compared to rRT-PCR PPV for virus isolation, which was 63.7%. The PPV for virus isolation was lowest among specimens from never symptomatic individuals with no known exposure (antigen PPV, 30.8%; RT-PCR PPV, 20.0%) (Table 5). A sensitivity analysis that included specimens as culture positive if rRT-PCR positive and that, when added to cell culture, showed cytopathic effects yet did not met the culture-positive criteria of being two C_T values lower than the clinical specimen C_T showed that overall BinaxNOW PPV for virus isolation was 70.6% compared to 43.2% for rRT-PCR PPV for virus isolation.

DISCUSSION

As previously reported, BinaxNOW sensitivity was 35.8% among specimens from asymptomatic and 64.2% among participants who reported ≥1 symptom on the day of testing (15). We expanded these analyses and demonstrate that BinaxNOW antigen sensitivity and culture positivity were highest within 7 days of symptom onset. BinaxNOW test performance also differed by symptom and known exposure status and by population demographics, which may be due to differences in test-seeking behavior. Individuals with a known exposure had higher test positive rates, which resulted in lower NPV for BinaxNOW among currently or previously symptomatic persons. Virus isolation was more frequently achieved with samples that were BinaxNOW positive than rRT-PCR positive. Positive BinaxNOW test results were returned on average 23.5 h faster than rRT-PCR results, allowing for more rapid identification and isolation of

FIG 2 Distribution of N1 C_T values for samples positive by CDC 2019-nCoV rRT-PCR diagnostic panel by viral culture and Abbott BinaxNOW COVID-19 antigen test by days since symptom onset or days postexposure. (A) Distribution of N1 C_T values for rRT-PCR-positive specimens tested by CDC 2019-nCoV rRT-PCR diagnostic panel by days postsymptom onset. Median N1 C_T values for 0 to 1 days postsymptom onset is 24.3; for day 2, 22.3; for day 3, 21.4; for day 4, 20.7; for day 5, 22.8; for day 6, 23.5; for day 7, 20.0; for days 8 to 13, 31.3; and days 14+, 35.2. (B) Distribution of N1 C_T values for rRT-PCR-positive specimens tested by CDC 2019-nCoV rRT-PCR diagnostic panel by days postexposure. Median N1 C_T values for 0 to 2 days postexposure is 29.2; for days 3 to 4, 22.5; for days 5 to 7, 22.1; for days 8 to 10, 25.0; and for days 11 to 14, 33.0. C_T values are represented on the y axis in descending order to indicate that lower C_T values represent larger amounts of RNA in the specimen.

TABLE 5 PPV for Abbott BinaxNOW COVID-19 antigen test and rRT-PCR test for virus isolation by symptom and exposure status

Parameter	PPV for virus isolation (95% CI)	
	BinaxNOW Ag test	rRT-PCR
Overall	56.7 (48.3–64.3)	35.4 (29.7–41.4)
N1 C_T value <29	66.7 (56.6–75.7)	63.7 (54.6–72.1)
Currently symptomatic	59.4 (49.5–69.9)	41.7 (34.1–49.7)
Exposed	56.1 (43.3–68.3)	40.0 (30.3–50.3)
Not exposed	65.0 (48.3–79.4)	44.4 (31.9–57.5)
Previously symptomatic	56.5 (34.5–76.8)	25.0 (15.0–37.4)
Exposed	45.5 (16.8–76.7)	18.2 (7.0–35.5)
Not exposed	66.7 (34.9–90.1)	32.3 (16.7–51.4)
Never symptomatic	42.9 (21.8–66.0)	27.3 (15.0–42.8)
Exposed	62.5 (24.5–91.5)	42.9 (17.7–71.1)
Not exposed	30.8 (10.0–61.4)	20.0 (7.7–38.6)
Days postsymptom onset		
≤3	65.6 (51.4–77.8)	50.0 (38.5–61.5)
4–7	65.0 (48.3–79.4)	50.9 (36.8–65.0)
8–10	0 (–)	8.3 (0.2–38.5)
11–14	20.0 (0.5–71.6)	7.1 (0.2–33.9)
>14	—[a]	—[a]
Days postexposure		
<3	47.2 (30.4–64.5)	23.9 (14.6–35.5)
3–4	53.9 (25.1–80.8)	50.0 (27.2–72.8)
5–7	81.8 (59.7–94.8)	60.6 (42.1–77.1)
8–10	71.4 (29.0–96.3)	50.0 (18.7–81.3)
11–14	—[a]	—[a]

[a]—, no culture-positive specimens for this group.

potentially infectious individuals. However, if BinaxNOW had been the only test administered, almost half of those with a positive rRT-PCR result, including almost 9% with culturable virus, would not have been identified for isolation and contact tracing.

Across other studies, BinaxNOW sensitivity varied between 64.4% and 96.5% among symptomatic persons (6, 8, 10–13) and between 20.0% and 70.2% among asymptomatic participants (9, 14). Several factors may contribute to variability in test performance, including differences in population characteristics, the timing during disease course, test operator training (7), and methodological differences, such as the comparator rRT-PCR assay, specimen type, and collection method.

Persons who tested positive and reported no symptoms on the day of testing likely included postsymptomatic or presymptomatic individuals, those who did not recognize mild symptoms, and those who never develop symptoms. Previously symptomatic individuals were more likely to be in the later stages of disease course when viral loads were lower, viral isolation was less likely, and there was a higher probability for presence of noninfectious, defective viral particles or residual RNA molecules, which could explain why BinaxNOW sensitivity was lowest in these individuals. BinaxNOW sensitivity increased when excluding results from individuals who tested positive in the 90 days prior, yet sensitivity was still lower than that in many other published studies (6, 8, 11, 12). Individuals in this evaluation may have sought repeat testing after their initial positive to obtain a negative result per work or school requirements. It is important to interpret antigen testing within the context of the individual's clinical status and whether they had a previous positive result.

Nearly a third of individuals sought testing for known exposure to a diagnosed COVID-19 case and were more than twice as likely to test positive compared to those without known exposure. NPV was lower for individuals exposed and either currently or previously symptomatic. For individuals with a known exposure, BinaxNOW sensitivity was low within the first 2 days postexposure, highest during days 8 to 10 postexposure, and decreased

thereafter. Using an antigen test during the early postexposure period may increase the risk of a false-negative result. The CDC's guidance on options to shorten the quarantine length period note that asymptomatic individuals may discontinue quarantine after day 7 with a negative test result, which must occur $\geq$5 days postexposure and can discontinue quarantine after day 10 without a test (24). Our data suggest that using a single antigen test instead of a more sensitive nucleic acid amplification test (NAAT) for reducing quarantine length would result in higher residual postquarantine transmission risk, which should be weighed against the benefits of reducing quarantine length.

Children 10 to 17 years old had a similar prevalence of SARS-CoV-2 infection as adults 18 to 64 years and were more likely to have a known exposure but less likely to be symptomatic, which highlights the importance of vaccination against SARS-CoV-2 for all children as they become eligible. For children not yet eligible for vaccination, prevention measures including surveillance testing will continue to be important (25, 26).

A third of participants in this evaluation identified as Hispanic/Latino, and test positivity in this group was more than double that of non-Hispanic/Latino groups. A higher proportion of symptomatic individuals and those reporting known exposure to a diagnosed COVID-19 case identified as Hispanic/Latino. Our data suggest Hispanic/Latino persons seek testing only when more symptomatic or with a known exposure, similar to other findings (27). Structural barriers to care access disproportionally affect the Hispanic/Latino community and highlight the importance of improving health equity (28). Point-of-care tests can increase access to testing, which may be particularly important for Hispanic/Latino communities who have been shown to be disproportionately affected by COVID-19 (28–31).

PPV for viral isolation was higher for BinaxNOW than rRT-PCR, indicating a positive antigen test is more predictive of the ability to culture virus than a positive rRT-PCR. The ability to isolate virus from a clinical specimen in cell culture indicates that the person who provided the clinical specimen was shedding infectious virus at the time of specimen collection (23, 32). Moreover, BinaxNOW sensitivity was higher in specimens with N1 C_T values of <29 (81.6%). The PPV for viral isolation improved in specimens with N1 C_T values of <29 for both BinaxNOW and rRT-PCR, but the difference was most pronounced in rRT-PCR specimens. Although C_T values cannot be used as a quantitative measure of viral load or for clinical decision-making, they are informative on relative amounts of RNA or nucleocapsid 1 gene within a specimen. These data show that BinaxNOW demonstrated acceptable performance to detect SARS-CoV-2 infection from individuals who likely have high viral loads and may be more likely to transmit live virus to others. However, the antigen test missed 11.5% of culture-positive specimens. Not implementing confirmatory NAAT or serial antigen testing may result in undetected cases and potentially lead to secondary transmission. Many biological and environmental variables can affect the outcome of virus culture (32), and the inability to isolate virus from a clinical specimen should not be interpreted to mean a person is not infectious or not capable of transmission. Thus, it is hard to ascertain how many infectious persons a single BinaxNOW test may fail to detect in the absence of confirmatory NAAT testing, especially among asymptomatic persons or those without known exposure.

There were several limitations to this investigation. The data here are cross-sectional, and presymptomatic individuals could not be identified. NP swabs have been shown to have increased sensitivity compared with nasal swabs (33). Here, the nasal swab for BinaxNOW testing was collected first and may have reduced sensitivity of the NP swab. This evaluation was conducted during a time when SARS-CoV-2 vaccines were not yet available, and test sensitivity may be different in vaccinated individuals due to lower viral loads (34, 35). The proportion of participants with unknown race or ethnicity limits the conclusions that can be drawn here. This investigation evaluated the Abbott BinaxNOW COVID-19 Ag card and cannot be generalized to other antigen tests, including the two available self-administered versions of the BinaxNOW test. Specimens were collected into PBS, which may have affected the ability to isolate infectious virus, although a recent study (36) demonstrated that SARS-CoV-2 infectious virus stability was not impacted when specimens were stored in PBS at 4°C for up to 35 days. Finally, there were 21 specimens with positive antigen and rRT-PCR results and low C_T values but were culture negative. The cell culture for these specimens showed

evidence of cytopathic effects and had presence of SARS-CoV-2 RNA as detected by rRT-PCR in the first passage culture, but viral recovery was not two C_T values lower than the corresponding clinical specimen C_T. A sensitivity analysis was conducted to include specimens not meeting this conservative two C_T value difference between output virus compared to the clinical specimen C_T value as culture positive. The sensitivity analysis showed improved PPV overall, but results still support the conclusion that PPV for viral culture is higher for BinaxNOW than rRT-PCR. Nevertheless, the interpretation of whether these specimens had culturable virus present was challenging and represents a limitation.

This investigation included a diverse population and was conducted at two community testing sites in an area of high SARS-CoV-2 prevalence during the evaluation. Collection of exposure and symptom status data in conjunction with viral culture allowed for a more detailed description of test performance. As shown here, BinaxNOW antigen testing within the first week of symptoms and/or around days 5 to 7 after known exposure can lead to early detection and isolation. Given the limitations of the BinaxNOW test, confirmatory testing with highly sensitive NAATs can be considered under certain circumstances (37). Symptomatic individuals with a high likelihood of SARS-CoV-2 infection may need confirmatory testing with an NAAT after a negative antigen test (37). Although BinaxNOW specificity was high, as prevalence decreases, confirmation of positive antigen test may be needed if there is low likelihood of SARS-CoV-2 infection (37). Antigen tests can be an important tool for increasing testing frequency and improving equitable access to testing. These tests provide rapid results and can be easily implemented in hard-to-reach populations via mobile testing units or community clinics, where more complex laboratory testing is not feasible.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.
SUPPLEMENTAL FILE 1, PDF file, 0.2 MB.

REFERENCES

1. U.S. Food and Drug Administration. 2021. In vitro diagnostics EUAs–antigen diagnostic tests for SARS-CoV-2. FDA, Silver Spring, MD. https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/in-vitro-diagnostics-euas-antigen-diagnostic-tests-sars-cov-2.
2. Abbott Diagnostics. 2020. BinaxNOW COVID-19 Ag card (PN 195–000)—instructions for use. https://www.fda.gov/media/141570/download.
3. CMS. 2020. Updated CLIA SARS-CoV-2 molecular and antigen point of care test enforcement discretion. https://www.cms.gov/files/document/clia-sars-cov-2-point-care-test-enforcement-discretion.pdf.
4. U.S. Food and Drug Administration. 2020. COVID-19 test uses: FAQs on testing for SARS-CoV-2. FDA, Silver Spring, MD. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/covid-19-test-uses-faqs-testing-sars-cov-2.
5. U.S. Department of Health and Human Services. 2020. Coronavirus (COVID-19) testing: expanding access to coronavirus (COVID-19) testing. https://www.hhs.gov/coronavirus/testing/index.html.
6. Pollock NR, Jacobs JR, Tran K, Cranston AE, Smith S, O'Kane CY, Roady TJ, Moran A, Scarry A, Carroll M, Volinsky L, Perez G, Patel P, Gabriel S, Lennon NJ, Madoff LC, Brown C, Smole SC. 2021. Performance and implementation evaluation of the Abbott BinaxNOW rapid antigen test in a high-through-put drive-through community testing site in Massachusetts. J Clin Microbiol 59:e00083-21. https://doi.org/10.1128/JCM.00083-21.
7. Pilarowski G, Lebel P, Sunshine S, Liu J, Crawford E, Marquez C, Rubio L, Chamie G, Martinez J, Peng J, Black D, Wu W, Pak J, Laurie MT, Jones D, Miller S, Jacobo J, Rojas S, Rojas S, Nakamura R, Tulier-Laiwa V, Petersen M, Havlir DV, DeRisi J. 2021. Performance characteristics of a rapid severe acute respiratory syndrome coronavirus 2 antigen detection assay at a

public plaza testing site in San Francisco. J Infect Dis 223:1139–1144. https://doi.org/10.1093/infdis/jiaa802.

8. Shah MM, Salvatore PP, Ford L, et al. 2021. Performance of repeat BinaxNOW SARS-CoV-2 antigen testing in a community setting, Wisconsin, November-December 2020. Clin Infect Dis https://doi.org/10.1093/cid/ciab309.

9. Okoye NC, Barker AP, Curtis K, Orlandi RR, Snavely EA, Wright C, Hanson KE, Pearson LN. 2021. Performance characteristics of BinaxNOW COVID-19 antigen card for screening asymptomatic individuals in a university setting. J Clin Microbiol 59:e03282-20. https://doi.org/10.1128/JCM.03282-20.

10. Sood N, Shetgiri R, Rodriguez A, Jimenez D, Treminino S, Daflos A, Simon P. 2021. Evaluation of the Abbott BinaxNOW rapid antigen test for SARS-CoV-2 infection in children: implications for screening in a school setting. PLoS One 16:e0249710. https://doi.org/10.1371/journal.pone.0249710.

11. Pilarowski G, Marquez C, Rubio L, et al. 2020. Field performance and public health response using the BinaxNOW TM Rapid SARS-CoV-2 antigen detection assay during community-based testing. Clin Infect Dis https://doi.org/10.1093/cid/ciaa1890.

12. McKay SL, Tobolowsky FA, Moritz ED, Hatfield KM, Bhatnagar A, LaVoie SP, Jackson DA, Lecy KD, Bryant-Genevier J, Campbell D, Freeman B, Gilbert SE, Folster JM, Medrzycki M, Shewmaker PL, Bankamp B, Radford KW, Anderson R, Bowen MD, Negley J, Reddy SC, Jernigan JA, Brown AC, McDonald LC, Kutty PK, CDC Infection Prevention and Control Team and the CDC COVID-19 Surge Laboratory Group. 2021. Performance evaluation of serial SARS-CoV-2 rapid antigen testing during a nursing home outbreak. Ann Intern Med 174:945–951. https://doi.org/10.7326/M21-0422.

13. James AE, Gulley T, Kothari A, Holder K, Garner K, Patil N. 2021. Performance of the BinaxNOW coronavirus disease 2019 (COVID-19) antigen card test relative to the severe acute respiratory coronavirus virus 2 (SARS-CoV-2) real-time reverse transcriptase polymerase chain reaction (rRT-PCR) assay among symptomatic and asymptomatic healthcare employees. Infect Control Hosp Epidemiol https://doi.org/10.1017/ice.2021.20.

14. Tinker SC, Szablewski CM, Litvintseva AP, Drenzek C, Voccio GE, Hunter MA, Briggs S, Heida DE, Folster J, Shewmaker PL, Medrzycki M, Bowen MD, Bohannon C, Bagarozzi D, Petway M, Rota PA, Kuhnert-Tallman W, Thornburg N, Prince-Guerra JL, Barrios LC, Tamin A, Harcourt JL, Honein MA, CDC Surge Laboratory Group. 2021. Point-of-care antigen test for SARS-CoV-2 in asymptomatic college students. Emerg Infect Dis 27:2662–2665. https://doi.org/10.3201/eid2710.210080.

15. Prince-Guerra JL, Almendares O, Nolen LD, Gunn JKL, Dale AP, Buono SA, Deutsch-Feldman M, Suppiah S, Hao L, Zeng Y, Stevens VA, Knipe K, Pompey J, Atherstone C, Bui DP, Powell T, Tamin A, Harcourt JL, Shewmaker PL, Medrzycki M, Wong P, Jain S, Tejada-Strop A, Rogers S, Emery B, Wang H, Petway M, Bohannon C, Folster JM, MacNeil A, Salerno R, Kuhnert-Tallman W, Tate JE, Thornburg NJ, Kirking HL, Sheiban K, Kudrna J, Cullen T, Komatsu KK, Villanueva JM, Rose DA, Neatherlin JC, Anderson M, Rota PA, Honein MA, Bower WA. 2021. Evaluation of Abbott BinaxNOW rapid antigen test for SARS-CoV-2 infection at two community-based testing sites–Pima County, Arizona, November 3–17, 2020. MMWR Morb Mortal Wkly Rep 70:100–105. https://doi.org/10.15585/mmwr.mm7003e3.

16. CDC. 2021. COVID data tracker: COVID-19 integrated county view, Arizona, Pima County. https://covid.cdc.gov/covid-data-tracker/#county-view.

17. FDA. 2021. FDA approves first COVID-19 vaccine. https://www.fda.gov/news-events/press-announcements/fda-approves-first-covid-19-vaccine.

18. CDC. 2020. Coronavirus disease 2019 (COVID-19) 2020 interim case definition, approved August 5, 2020. CSTE position statement. https://wwwn.cdc.gov/nndss/conditions/coronavirus-disease-2019-covid-19/case-definition/2020/08/05/.

19. Code of Federal Regulations. 2009. Title 45. Public welfare. CFR part 46.102(l)(2), 21 CFR part 56, 42 USC Sect 241(d), 5 USC Sect. 552a, 44 U.S.C. Sect. 3501 et seq. https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/ohrpregulations.pdf.

20. U.S. Food and Drug Administration. 2020. CDC 2019-novel coronavirus (2019-nCoV) real-time RT-PCR diagnostic panel—instructions for use. https://www.fda.gov/media/134922/download.

21. Fosun Pharma USA. 2020. Instruction for use: Fosun COVID-19 RT-PCR detection kit. https://www.fda.gov/media/137120/download.

22. FDA. 2020. Policy for coronavirus disease-2019 tests during the public health emergency (revised). https://www.fda.gov/regulatory-information/search-fda-guidance-documents/policy-coronavirus-disease-2019-tests-during-public-health-emergency-revised.

23. Harcourt J, Tamin A, Lu X, Kamili S, Sakthivel SK, Murray J, Queen K, Tao Y, Paden CR, Zhang J, Li Y, Uehara A, Wang H, Goldsmith C, Bullock HA, Wang L, Whitaker B, Lynch B, Gautam R, Schindewolf C, Lokugamage KG, Scharton D, Plante JA, Mirchandani D, Widen SG, Narayanan K, Makino S, Ksiazek TG, Plante KS, Weaver SC, Lindstrom S, Tong S, Menachery VD, Thornburg NJ. 2020. Severe acute respiratory syndrome coronavirus 2 from patient with coronavirus disease, United States. Emerg Infect Dis 26:1266–1273. https://doi.org/10.3201/eid2606.200516.

24. CDC. 2020. Science brief: options to reduce quarantine for contacts of persons with SARS-CoV-2 infection using symptom monitoring and diagnostic testing. https://www.cdc.gov/coronavirus/2019-ncov/science/science-briefs/scientific-brief-options-to-reduce-quarantine.html.

25. CDC. 2021. Guidance for COVID-19 prevention in K-12 schools. https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/k-12-guidance.html.

26. Lanier WA, Babitz KD, Collingwood A, Graul MF, Dickson S, Cunningham L, Dunn AC, MacKellar D, Hersh AL. 2021. COVID-19 testing to sustain in-person instruction and extracurricular activities in high schools–Utah, November 2020-March 2021. MMWR Morb Mortal Wkly Rep 70:785–791. https://doi.org/10.15585/mmwr.mm7021e2.

27. Chamie G, Marquez C, Crawford E, et al. 2020. SARS-CoV-2 community transmission disproportionately affects Latinx population during shelter-in-place in San Francisco. Clin Infect Dis https://doi.org/10.1093/cid/ciaa1234.

28. Cantos VD, Rebolledo PA. 2020. Structural vulnerability to COVID-19 among Latinx communities in the United States. Clin Infect Dis 73:S136–S137. https://doi.org/10.1093/cid/ciaa1378.

29. Zelner J, Trangucci R, Naraharisetti R, Cao A, Malosh R, Broen K, Masters N, Delamater P. 2021. Racial disparities in coronavirus disease 2019 (COVID-19) mortality are driven by unequal infection risks. Clin Infect Dis 72:e88–e95. https://doi.org/10.1093/cid/ciaa1723.

30. Moore JT, Ricaldi JN, Rose CE, Fuld J, Parise M, Kang GJ, Driscoll AK, Norris T, Wilson N, Rainisch G, Valverde E, Beresovsky V, Agnew Brune C, Oussayef NL, Rose DA, Adams LE, Awel S, Villanueva J, Meaney-Delman D, Honein MA, COVID-19 State, Tribal, Local, and Territorial Response Team. 2020. Disparities in incidence of COVID-19 among underrepresented racial/ethnic groups in counties identified as hotspots during June 5–18, 2020–22 States, February-June 2020. MMWR Morb Mortal Wkly Rep 69:1122–1126. https://doi.org/10.15585/mmwr.mm6933e1.

31. Hollis ND, Li W, Van Dyke ME, Njie GJ, Scobie HM, Parker EM, Penman-Aguilar A, Clarke KEN. 2021. Racial and ethnic disparities in incidence of SARS-CoV-2 infection, 22 US states and DC, January 1-October 1, 2020. Emerg Infect Dis 27:1477–1481. https://doi.org/10.3201/eid2705.204523.

32. Killerby ME, Ata Ur Rasheed M, Tamin A, et al. 2021. Shedding of culturable virus, seroconversion, and 6-month follow-up antibody responses in the first 14 confirmed cases of COVID-19 in the United States. J Infect Dis 224:771–776. https://doi.org/10.1093/infdis/jiab125.

33. Pinninti S, Trieu C, Pati SK, Latting M, Cooper J, Seleme MC, Boppana S, Arora N, Britt WJ, Boppana SB. 2021. Comparing nasopharyngeal and midturbinate nasal swab testing for the identification of severe acute respiratory syndrome coronavirus 2. Clin Infect Dis 72:1253–1255. https://doi.org/10.1093/cid/ciaa882.

34. McEllistrem MC, Clancy CJ, Buehrle DJ, Lucas A, Decker BK. 2021. Single dose of a mRNA SARS-CoV-2 vaccine is associated with lower nasopharyngeal viral load among nursing home residents with asymptomatic COVID-19. Clin Infect Dis https://doi.org/10.1093/cid/ciab263.

35. Levine-Tiefenbrun M, Yelin I, Katz R, Herzel E, Golan Z, Schreiber L, Wolf T, Nadler V, Ben-Tov A, Kuint J, Gazit S, Patalon T, Chodick G, Kishony R. 2021. Initial report of decreased SARS-CoV-2 viral load after inoculation with the BNT162b2 vaccine. Nat Med 27:790–792. https://doi.org/10.1038/s41591-021-01316-7.

36. Fukuta M, Mao ZQ, Morita K, Moi ML. 2021. Stability and infectivity of SARS-CoV-2 and viral RNA in water, commercial beverages, and bodily fluids. Front Microbiol 12:667956. https://doi.org/10.3389/fmicb.2021.667956.

37. CDC. 2021. Coronavirus disease 2019 (COVID-19): interim guidance for antigen testing for SARS-CoV-2. CDC, Atlanta, GA. https://www.cdc.gov/coronavirus/2019-ncov/lab/resources/antigen-tests-guidelines.html.