Field performance and public health response using the BinaxNOW™ Rapid SARS-CoV-2 antigen detection assay during community-based testing

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Abstract

Among 3,302 persons tested for SARS-CoV-2 by BinaxNOW™ and RT-PCR in a community setting, rapid assay sensitivity was 100%/98.5%/89% using RT-PCR Ct thresholds of 30, 35 and none. The specificity was 99.9%. Performance was high across ages and those with and without symptoms. Rapid resulting permitted immediate public health action.

Key Words: Community-based SARS-CoV-2 testing; asymptomatic SARS-CoV-2 infection

Introduction

Breaking SARS-CoV-2 community transmission chains requires rapid identification and isolation of infectious persons. Up to forty percent of infected persons may not have symptoms, despite harboring high levels of virus [1]. Further, standard testing models pose multiple barriers to the effective use of testing for epidemic control, including testing access restricted to symptomatic persons, difficult appointment scheduling, long turnaround times, and structural barriers including health insurance, monolingual services, and location of testing sites far from communities most impacted. Deploying rapid antigen tests with high field performance through the use of community-based test-and-respond models [2] could address these barriers and increase the identification of the most infectious persons. Importantly, compared to a standard RT-PCR assay, use of these tests could rapidly permit identification and isolation of persons with high levels of virus, disrupting forward transmission chains [3].

We evaluated the Abbott BinaxNOW™ Covid-19 antigen card rapid assay performance for detection of persons with high levels of virus and measured the time to isolation in a community walk-up "test and respond" program.

Methods

Study Setting and Procedures

We conducted this study through an academic, community (Latino Task Force) and public health department partnership (Unidos en Salud). We offered testing at a plaza under tents in an urban commercial transport hub in the Mission neighborhood in San Francisco, a setting of ongoing community transmission, predominantly among Latinx persons. Community workers conducted door-to-door mobilization in 3 census tracts surrounding the testing site four days prior to testing. Persons of all ages, with or without symptoms, registered on site. After consent, trained community

volunteers conducted a brief survey that included demographic information and COVID-19 symptoms. Certified lab assistants collected bilateral anterior nasal swab for BinaxNOW™ (cards provided by State of California Department of Public Health) according to manufacturer instructions, immediately followed by a separate bilateral swab for RT-PCR. BinaxNOW™ results were read on site by certified technician readers [4,5]. We returned rapid antigen test results via secure messaging within an hour of testing. Persons with a positive rapid antigen test received a follow-up phone call within 2 hours. Staff provided counseling and offered a city-sponsored hotel stay for isolation. Persons choosing to isolate at home had immediate same-day access to home services, including health education and food delivery, administered through a community-led outreach program [6]. Health department contact tracing was initiated immediately on return of a positive BinaxNOW™ result.

RT-PCR was completed by RenegadeBio using RenegadeXP™ technology. Anterior nares swabs were collected into proprietary viral transport media, then lysed. Lysate was transferred directly to a multiplex RT-PCR reaction with primers/probes for the nucleoprotein gene of SARS-CoV-2. Positive results were confirmed by the standard CDC methodology using Qiagen viral RNA purification kits and singleplex RT-PCR detection of the nucleoprotein gene.

Assay sensitivity and specificity with 95% confidence intervals were calculated using RT-PCR cycle thresholds (Ct) below 30 and 35 (corresponding to high viral levels associated *in vitro* with virus viability) [7–9]. Time to reporting was calculated from time of registration to time of test results notification. Time to isolation was calculated from symptom onset for those persons who were symptomatic prior to or at the time of testing.

Ethics statement

The UCSF Committee on Human Research determined that the study met criteria for public health surveillance. All participants provided informed consent for dual testing.

Results

We tested 3,302 persons over 6 days between November 22 and December 1; 99 were aged <13 years, 110 aged 13-18 years, and 3,093 aged >18 years. Participants were 45.4% female, and 53.0% male. Reported ethnicity was 65.6% LatinX, 9.2% Asian, 16.9% White, 1.6% American Indian and 2.5% Black. Of all persons tested, 30.9% self-reported possible COVID-19 symptoms. At this site, equipped with 3 testing tents each with 4 technicians and 1 data entry volunteer, we were able to test approximately 100 persons/hour.

There were 237 persons overall who were RT-PCR positive (7.2% prevalence), and 211 (6.4%) persons who were also rapid test positive. RT-PCR prevalence was 19/99 (19.4%) among children < 13 years of age, and 16/110 (14.5%) among teens 13-18 years of age. 95 RT-PCR(+) persons (40.1%) were asymptomatic and 7 (3.0%) had a symptoms that started >7 days prior to testing.

The BinaxNOW™ test exhibited high sensitivity and specificity for persons with high levels of virus (Ct <30 or <35), both overall and stratified by age and presence of symptoms (Table 1). Sensitivity using a Ct cutoff of 30 was 100% (95%CI: 97.9-100%) for the full study population, 100% (95%CI: 73.5-100%) among persons <13 years, and 100% (95%CI: 73.5-100%) among persons 13-18 years. Among 102 persons who were asymptomatic or whose symptom onset was >7 days before testing, sensitivity for a Ct cutoff of 30 was 100% (95%CI: 94-100%). Persons with and without symptoms exhibited a similar range of Ct levels by RT-PCR (Figure 1). Three individuals were rapid test positive and RT-PCR test negative; one had symptoms (cough). Overall test specificity was 99.9% (95%CI: 99.7-100%).

For persons with a positive rapid antigen test, the median time from on-site registration to electronic results notification (N=211) was 62 minutes (IQR: 47-82 minutes). Phone calls followed within one hour. Among symptomatic persons with a positive rapid antigen test (N=134), the median time from symptom onset to isolation using BinaxNOW™ antigen test results was 3 days (IQR: 2-5 days).

Discussion

SARS-CoV-2 pandemic control calls for fast, low-barrier, high-performing field assays accessible to people who will not otherwise be tested or who will receive results too late for results to make a difference. The US government has purchased 150 million BinaxNOW™ cards, yet their use to date has been limited due to gaps in information about performance and assessment of public health activation. Our data show that these tests are readily deployed in a field setting at scale for children and adults, can rapidly identify persons with high levels of virus including those who are asymptomatic, and can lead to immediate public health action.

A major benefit of using this high performing rapid test was the speed with which results were returned (approximately one hour from walk-up registration to return). This permitted immediate public health action for persons infected with high levels of virus, who are most likely to be infectious [3,10,11]. Upon receipt of a positive rapid test result, we activated an isolation protocol offering city sponsored hotels or home isolation with supportive services. In addition, contact tracing was initiated 24-48 hours earlier than would have been possible through routine city sponsored RT-PCR testing. The use of this technology further allowed rapid mass screening in an outside setting

easily accessed by communities at high risk of ongoing transmission. This test is much less costly than RT-PCR and does not require a machine to read.

Integration of rapid antigen testing within community-based test and respond initiatives could contribute to reduced transmission via several mechanisms, including more complete and earlier detection of infectious persons made possible by increased access to low-barrier testing. Even without these benefits, however, the reduction in turn-around-time alone afforded by BinaxNOW™ (approximately one hour) as compared to an RT-PCR turnaround of 4 days could potentially eliminate four highly infectious days that would otherwise be spent out of isolation (of a typical 10 day maximum potential isolation period for non-hospitalized patients) [3,10].

We found high sensitivity and specificity for the BinaxNOW™ assay, including in asymptomatic persons and children. These results expand on, and are concordant with, our previous report which found a BinaxNOW™ detection level of ~$2x10^4$ viral RNA copies based on titration experiments [12]. Heterogeneity in the relationship between Ct and viral load across RT-PCR platforms complicates direct comparisons of raw Ct values; however, we find BinaxNOW™ reliably detects persons with low Ct, correlating to high viral load. Rapid tests may miss individuals at the earliest rise in virus levels, a limitation which can be addressed through repeat rapid testing [3,10]. Rapid tests may also miss the latter end of the viral dynamic curve (which can last for weeks), a period during which virus levels are low and a person is not thought to be infectious; some have suggested the lower sensitivity of the assay during this period could reduce hardship resulting from unnecessary isolation.

SARS-CoV-2 RT-PCR testing remains the gold standard for diagnosis. Even with a rapid test specificity of 99.9%, the percent of false positives needs to be considered. Our data suggest false positives will be 2% or less when SARS CoV-2 prevalence is above 5%. For populations with a 2% prevalence the false positivity rate would be 5.1%. We used these tests in a high prevalence community setting, where RT-PCR confirmation may not be required outside the research context. In

other settings with lower prevalence, confirmatory RT-PCR would be required, particularly among persons without symptoms or exposures.

Our low-barrier testing model incorporating the rapid BinaxNOW™ assay and linked with supportive follow-up services could identify more infectious persons faster, decrease the time to isolation, and interrupt transmission chains. As national vaccine roll-out is implemented, strategic testing strategies remain a key part of the public health response.

NOTES

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Potential conflicts:

Dr. Havlir reports non-financial support from Abbott, outside the submitted work; **None of the other authors has any potential conflicts.**

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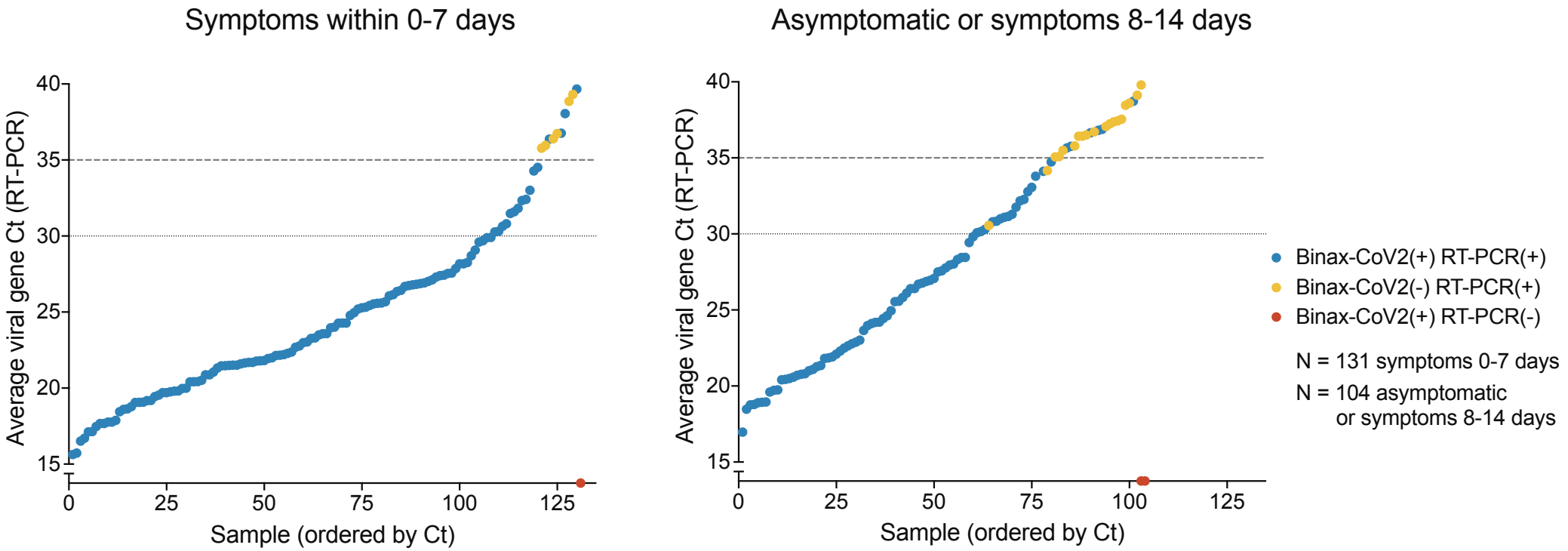
Table 1. Sensitivity and Specificity of BinaxNOW™ Stratified by Age and Symptoms

Populations	BinaxNOW Performance	All	Symptom onset within 7 days*	Asymptomatic or symptom onset > 7 days ago
All ages (N = 3,302) Value (95% CI)	**CT = 30 cutoff**			
	Sensitivity	100% (171/171, 95%CI: 97.9-100%)	100% (108/108, 95%CI: 96.6-100%)	100% (60/60, 95%CI: 94-100%)
	Specificity	98.6% (3088/3131, 95%CI: 98.2-99%)	97% (546/563, 95%CI: 95.2-98.2%)	98.9% (2317/2342, 95%CI: 98.4-99.3%)
	CT = 35 cutoff			
	Sensitivity	98.5% (201/204, 95%CI: 95.8-99.7%)	100% (120/120, 95%CI: 97-100%)	97.5% (77/79, 95%CI: 91.2-99.7%)
	Specificity	99.6% (3085/3098, 95%CI: 99.3-99.8%)	99.1% (546/551, 95%CI: 97.9-99.7%)	99.7% (2315/2323, 95%CI: 99.3-99.9%)
	No CT cutoff			
	Sensitivity	89% (211/237, 95%CI: 84.3-92.7%)	95.4% (124/130, 95%CI: 90.2-98.3%)	81.4% (83/102, 95%CI: 72.4-88.4%)
	Specificity	99.9% (3062/3065, 95%CI: 99.7-100%)	99.8% (540/541, 95%CI: 99-100%)	99.9% (2298/2300, 95%CI: 99.7-100%)
Ages < 13 Years (N = 99) Value (95% CI)	**CT = 30 cutoff**			
	Sensitivity	100% (12/12, 95%CI: 73.5-100%)	100% (3/3, 95%CI: 29.2-100%)	100% (9/9, 95%CI: 66.4-100%)
	Specificity	96.6% (84/87, 95%CI: 90.3-99.3%)	91.7% (11/12, 95%CI: 61.5-99.8%)	97.1% (68/70, 95%CI: 90.1-99.7%)
	CT = 35 cutoff			
	Sensitivity	93.3% (14/15, 95%CI: 68.1-99.8%)	100% (3/3, 95%CI: 29.2-100%)	91.7% (11/12, 95%CI: 61.5-99.8%)
	Specificity	98.8% (83/84, 95%CI: 93.5-100%)	91.7% (11/12, 95%CI: 61.5-99.8%)	100% (67/67, 95%CI: 94.6-100%)
	No CT cutoff			
	Sensitivity	78.9% (15/19, 95%CI: 54.4-93.9%)	80% (4/5, 95%CI: 28.4-99.5%)	78.6% (11/14, 95%CI: 49.2-95.3%)
	Specificity	100% (80/80, 95%CI: 95.5-100%)	100% (10/10, 95%CI: 69.2-100%)	100% (65/65, 95%CI: 94.5-100%)
Ages 13-18 Years	**CT = 30 cutoff**			
	Sensitivity	100% (12/12,	100% (8/8,	100% (4/4,

(N = 110) Value (95% CI)		95%CI: 73.5-100%)	95%CI: 63.1-100%)	95%CI: 39.8-100%)
	Specificity	96.9% (95/98, 95%CI: 91.3-99.4%)	100% (13/13, 95%CI: 75.3-100%)	96.1% (73/76, 95%CI: 88.9-99.2%)
	CT = 35 cutoff			
	Sensitivity	100% (14/14, 95%CI: 76.8-100%)	100% (8/8, 95%CI: 63.1-100%)	100% (6/6, 95%CI: 54.1-100%)
	Specificity	99% (95/96, 95%CI: 94.3-100%)	100% (13/13, 95%CI: 75.3-100%)	98.6% (73/74, 95%CI: 92.7-100%)
	No CT cutoff			
	Sensitivity	93.8% (15/16, 95%CI: 69.8-99.8%)	100% (8/8, 95%CI: 63.1-100%)	87.5% (7/8, 95%CI: 47.3-99.7%)
	Specificity	100% (94/94, 95%CI: 96.2-100%)	100% (13/13, 95%CI: 75.3-100%)	100% (72/72, 95%CI: 95-100%)

* Symptom onset date missing for 229 persons.

Figure 1. RT-PCR Ct values and BinaxNOW™ rapid antigen test results of participants, stratified according to COVID-19 symptoms. Average viral Ct values of all individuals with positive RT-PCR and/or rapid antigen test results (N=245 total) plotted in ascending order of Ct. Each point represents one individual. Blue points are individuals whose samples were positive for both rapid antigen test (BinaxNOW™) and RT-PCR test. Yellow circles represent individuals who were RT-PCR(+), but rapid test negative. Red circles represent individuals with a positive rapid antigen test and negative RT-PCR test result.


Symptoms within 0-7 days
Asymptomatic or symptoms 8-14 days
Average viral gene Ct (RT-PCR)
40
35
30
25
20
15
0
25
50
75
100
125
Sample (ordered by Ct)
Binax-CoV2(+) RT-PCR(+)
Binax-CoV2(-) RT-PCR(+)
Binax-CoV2(+) RT-PCR(-)
N = 131 symptoms 0-7 days
N = 104 asymptomatic
or symptoms 8-14 days