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

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Introduction

Since its discovery, the SARS-CoV-2 virus has created a global pandemic of COVID-19.[1] As of August 2, 2021, more than 198 million infections were reported worldwide.[2] Typical symptoms include fatigue, fever, cough, and anosmia or dysgeusia.

Outbreak management has been hindered by high transmission rates and limitations in testing capacity. Effective public health tools are needed for rapid and early detection. The current diagnostic standard is quantitative real-time polymerase chain reaction (qRT-PCR), but its cost and long turnaround times limit its utility for widespread surveillance. Lack of surveillance has caused severe societal disruption.

Rapid antigen tests that permit new cases to isolate immediately can be important surveillance tools.[3] A longitudinal comparison between antigen tests performed at home and qRT-PCR has not previously been performed, to our knowledge. Here, we describe implementation of high-frequency testing using inexpensive, at-home, semiquantitative, direct antigen rapid tests (DARTs) and compare their performance with that of qRT-PCR on self-collected nasal specimens.

Methods

This cohort study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for observational studies and was conducted after review and approval by the Advarra institutional review board. Participants provided written informed consent signed electronically.

The study included 257 affiliates of 3 coworking laboratories in Cambridge and Boston, Massachusetts. The prevalence of COVID-19 in this area during the study was between less than 1% and 8%. Individuals self-collected nasal swab specimens twice weekly at home during a 6-month period. DART was performed at home, and the findings were compared with laboratory qRT-PCR tests.[4,5] Symptom information was collected contemporaneously. Self-reported race and ethnicity were collected in accordance with Department of Health and Human Services and Food and Drug Administration reporting guidelines for non–laboratory-based tests.

Table. Sensitivity Data

Day	Positive specimens, No.		Sensitivity of DART, % (95% CI)[a]	Combined sensitivity, No. of specimens/total No. of specimens (%) [95% CI]
	DART	qRT-PCR		
0	1	1	100.0 (2.5-100.0)	25/26 (96.2) [88.8-100.0]
1	3	4	75.0 (19.4-99.4)	
2	11	11	100.0 (61.5-99.8)	
3	10	10	100.0 (71.5-100.0)	
4	7	9	77.8 (40.0-97.2)	28/33 (84.9) [71.5-98.2]
5	8	8	100.0 (63.1-100.0)	
6	7	9	77.8 (40.0-97.2)	
7	6	7	85.7 (42.1-99.6)	

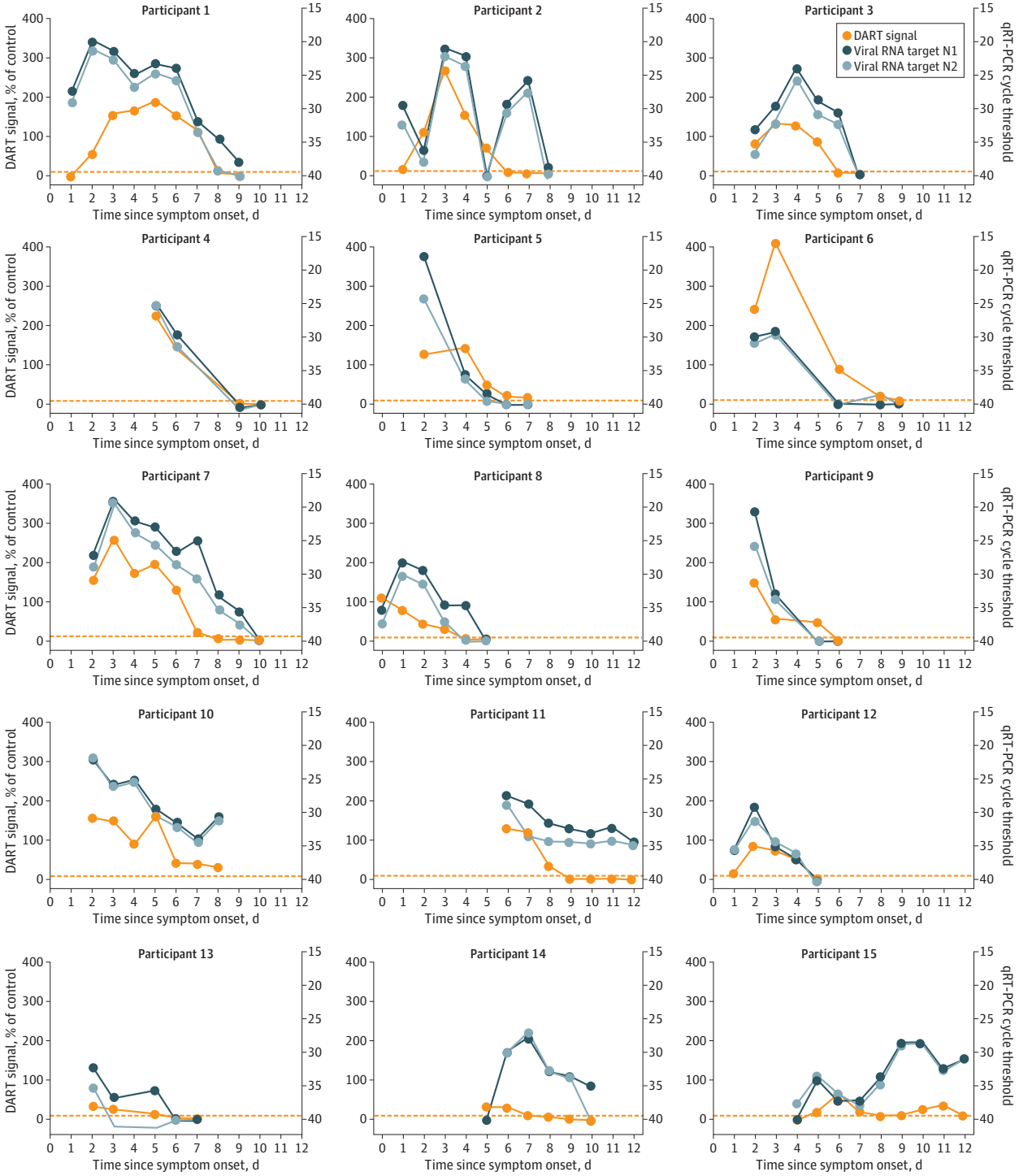
Abbreviations: DART, direct antigen rapid test; qRT-PCR, quantitative real-time polymerase chain reaction.

[a] The sensitivity of DART was calculated for days 0 to 12 of symptoms; 60 of 76 swabs were positive, for sensitivity of 78.9% (95% CI, 69.1%-88.8%). Specificity of DART was calculated using the number of negative DART specimens divided by the total number of corresponding negative qRT-PCR samples (2791 of 2875 specimens) for specificity of 97.1% (95% CI, 96.3%-97.8%). A detailed description of statistical analysis methods can be found in the eAppendix in the Supplement.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Figure. Longitudinal Analysis of SARS-CoV-2 Nucleocapsid and Viral Genome Levels



Graphs show longitudinal analysis of SARS-CoV-2 nucleocapsid and viral genome levels using an at-home, semiquantitative direct antigen rapid test (DART) and quantitative real-time polymerase chain reaction (qRT-PCR) for 15 positive participants. The orange lines represent the DART data for each individual, the dark blue lines represent the viral RNA target N1, and the light blue lines represents the viral target N2. The x-axis corresponds to number of days after first reported symptoms, with 0 indicating 1 day before symptoms onset. The left y-axis corresponds to background subtracted DART signal normalized to the control line for each test. The right y-axis corresponds to the cycle threshold of viral RNA targets N1 and N2 in each sample. DART results less than 10% of control are considered negative results, which is indicated by the orange dashed line.

The 95% CIs for sensitivity and specificity were calculated using generalized estimating equations in Rstudio version 4.1.0 (R Project for Statistical Computing) with a working independence correlation structure accounting for clusters of multiple tests per individual. The 2-sided binomial Clopper-Pearson method was used to calculate 95% CIs for day-by-day sensitivity for days 0 to 7 of symptoms, when there was a maximum of 1 test per individual. See the eAppendix and the eFigure in the Supplement for additional details.

Results

A total of 257 participants were enrolled (median age, 35 years; range, 21-72 years). Among the participants, 120 (46.7%) were women, 161 (62.6%) were White, 49 (19.1%) were Asian, 29 (11.3%) were Hispanic, and 8 (3.1%) were Black. A total of 2951 pairs of nasal swabs were self-collected by participants and tested by qRT-PCR and DART. The sensitivity of DART within days 0 to 12 of symptom onset was 78.9% (60 of 76 swabs; 95% CI, 69.1%-88.8%), and the specificity of DART was 97.1% (2791 of 2875 swabs; 95% CI, 96.3%-97.8%) (**Table**).

The duration of SARS-CoV-2 nucleocapsid and RNA detection for individual infections ranged from 1 to 12 days, with peak levels observed between 2 and 6 days of symptoms (median, 3 days). The sensitivity of DART was calculated for each day. DART sensitivity was 96.2% (25 of 26 swabs; 95% CI, 88.8%-100.0%) within days 0 to 3 of symptoms (Table).

Of the 257 individuals, 15 contracted COVID-19. Twice-weekly DART detected 15 of 15 of infections (100%). The **Figure** shows the performance of DART compared with qRT-PCR. Results were plotted relative to days after symptoms onset. Eleven participants tested positive on day 1 or 2. One was pre-symptomatic the day of their initial DART positive result. One infection was detected by qRT-PCR 1 day before DART. For 1 positive participant, DART detected infection 1 day before qRT-PCR did.

Discussion

We sought to validate the effectiveness of DART and to test whether at-home testing with DART could prevent the spread of SARS-CoV-2 in a coworking environment. In this cohort study of 257 individuals who collected 2951 sample pairs over the course of 6 months, we found that twice-weekly surveillance with DART detected infections in 15 individuals, with 96.2% sensitivity on days 0 through 3 of symptoms. Detection on day 3 is almost as effective as detection on day 1 for reducing the incidence of COVID-19, if 75% of a population is surveilled.[6] The prevalence of disease dictates the frequency of testing and its effectiveness for controlling potential outbreaks. Limitations of this study include low infection rates among the study population. During this study, the prevalence of COVID-19 was between less than 1% and 8%.

Use of twice-weekly DART testing allowed the activities of the coworking sites to continue safely during the pandemic. Most of the positive participants reported that they did not recognize symptoms of COVID-19 until they received a positive result. Policies that rely on self-reported symptoms miss or delay detection and allow viral spread within communities. Frequent at-home testing with DART allows infected individuals to be identified and quarantined immediately. Such surveillance can prevent viral transmission in in-person work environments or other social settings.

ARTICLE INFORMATION

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Acquisition, analysis, or interpretation of data: All authors.

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SUPPLEMENT.

eAppendix. Supplemental Methods
eReferences.
eFigure. Overview of Study Design