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RESEARCH ARTICLE

Detection and Stability of SARS-CoV-2 in Three Self-Collected Specimen Types: Flocked Midturbinate Swab (MTS) in Viral Transport Media, Foam MTS, and Saliva

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ABSTRACT Respiratory specimen collection materials shortages hampers severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) testing. We compared specimen alternatives and evaluated SARS-CoV-2 RNA stability under simulated shipping conditions. We compared concordance of RT-PCR detection of SARS-CoV-2 from flocked midturbinate swabs (MTS) in viral transport media (VTM), foam MTS without VTM, and saliva. Specimens were collected between August 2020 and April 2021 from three prospective cohorts. We compared RT-PCR cycle quantification (C_q) for Spike (S), Nucleocapsid (N), and the Open Reading Frame 1ab (ORF) genes for flocked MTS and saliva specimens tested before and after exposure to a range of storage temperatures (4–30°C) and times (2, 3, and 7 days). Of 1,900 illnesses with ≥2 specimen types tested, 335 (18%) had SARS-CoV-2 detected in ≥1 specimen; 304 (91%) were concordant across specimen types. Among illnesses with SARS-CoV-2 detection, 97% (95% confidence interval [CI]: 94–98%) were positive on flocked MTS, 99% (95% CI: 97–100%) on saliva, and 89% (95% CI: 84–93%) on foam MTS. SARS-CoV-2 RNA was detected in flocked MTS and saliva stored up to 30°C for 7 days. All specimen types provided highly concordant SARS-CoV-2 results. These findings support a range of viable options for specimen types, collection, and transport methods that may facilitate SARS-CoV-2 testing during supply and personnel shortages.

IMPORTANCE Findings from this analysis indicate that (1) self-collection of flocked and foam MTS and saliva samples is feasible in both adults and children, (2) foam MTS with VTM and saliva are both viable and reasonable alternatives to traditional flocked MTS in VTM for SARS-CoV-2 detection, and (3) these sample types may be stored and transported at ambient temperatures for up to 7 days without compromising sample quality. These findings support methods of sample collection for SARS-CoV-2 detection

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that may facilitate widespread community testing in the setting of supply and personnel shortages during the current pandemic.

KEYWORDS COVID-19, SARS-CoV-2, sensitivity, respiratory specimens, RT-PCR

Nucleic acid amplification tests (NAATs) such as PCR tests, for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are critical tools for controlling the current coronavirus disease of 2019 (COVID-19) pandemic, but severe shortages of specimen collection materials have hampered testing efforts globally (1, 2). Circulation of SARS-CoV-2 variants of concern highlighted the ongoing need for timely and accurate diagnostic testing (3).

The Centers for Disease Control and Prevention (CDC) recommends upper respiratory tract specimens for initial diagnosis of SARS-CoV-2 infections (4). As of December 2021, CDC-recommended specimen options include nasopharyngeal, nasal midturbinate, anterior nasal, and saliva specimens. Compared to nasopharyngeal specimens, which require collection by trained professionals, nasal midturbinate specimens, anterior nasal specimens, and saliva specimens offer more flexibility because they may be self-collected and may be considered less invasive and more acceptable by patients (5).

Flocked swabs in viral transport medium (VTM) have traditionally been used for both nasopharyngeal and other less invasive nasal midturbinate or anterior nasal specimen collection. However, intermittent shortage of flocked swabs and VTM highlighted the need for valid alternative specimen materials and specimen storage options that do not require VTM. Both dry foam midturbinate swabs (MTS) without VTM (6–8) and saliva specimens (7, 9–23) are promising alternative specimen types for SARS-CoV-2 detection. Although recent publications demonstrated the clinical utility of dry foam MTS and saliva samples for the detection of SARS-CoV-2, data from studies that include both adults and children and utilize consistent methods of specimen collection are limited (14, 15, 24).

Using participant-collected specimens from three ongoing cohort studies of SARS-CoV-2 infection among essential workers and households with adults and children, we compared the performance of flocked MTS in VTM, foam MTS without VTM, and saliva specimens for the identification of SARS-CoV-2 infection. In addition, we evaluated the temporal stability of SARS-CoV-2 RNA from flocked MTS and saliva specimens under a range of storage temperatures and times simulated to mimic a variety of shipping conditions specimens may encounter.

RESULTS

Participant and COVID-like illness event characteristics. During August 2, 2020 to April 10, 2021, 2,903 out of 7,442 (39%) participants reported 3,476 COVID-like illness (CLI) events; 1,616 participants reported 1,900 (55%) CLI events with ≥2 self-collected respiratory specimens (1,896 flocked MTS; 1,035 foam MTS; and 1,866 saliva). Among these 1,616 participants, the median age was 39 years (interquartile range [IQR]: 31–47 years; range: 0–72 years) and 208 (13%) were children aged <18 years. Most participants were from Arizona (47%) or Utah (26%). Fever or feverishness was reported for 713 (38%) of the CLI events with ≥2 self-collected respiratory specimens (Table 1).

Among the 1,900 CLI events with ≥ 2 specimens, all specimen types were collected a median of 2 days after symptom onset (flocked MTS IQR: 0–4 days; foam MTS IQR: 1–4 days; and saliva IQR: 0–4 days). The median time from sample collection to sample receipt at the laboratory was 1 day (IQR: 1–2 days). Over half of flocked MTS and saliva (68% and 66%, respectively) were tested using the TaqPath kit, while most of the foam MTS (100%) were tested using the Lyra Direct Lysis assay (Table 2).

SARS-CoV-2 detection and concordance. Of the 1,900 SARS-CoV-2 CLI events with ≥ 2 specimen types submitted for testing, 335 (18%) had SARS-CoV-2 detected in at least 1 specimen, including 14 (4% of 335) from children <12 years, 8 (2% of 335) from children ages 13–17 years, and 313 (93% of 335) from adults aged ≥18 years. Among these 335 CLI events, 304 (91%) had concordant SARS-CoV-2 positive results across available specimen types, including 12 (86% of 14) from children <12 years and 6 (75% of 8) from children ages

TABLE 1 Characteristics of participants with COVID-19-like illness[a] and with at least 2 specimens submitted for SARS-CoV-2 RT-PCR testing, August 2020 to April 2021

Characteristics	Total[b]
Characteristics of participants	
Total participants	1,616
Age (median, SD)	39 yr, 14.8
Age group	
≤12 yr	170 (11)
13–17 yr	38 (2)
18–49 yr	1,077 (67)
≥50 yr	331 (20)
City/region	
Arizona	769 (47)
Florida	75 (5)
Minnesota	137 (8)
New York	50 (3)
Oregon	111 (7)
Texas	60 (4)
Utah	414 (26)
Occupation[c]	
Health care personnel	709 (44)
Front line worker	554 (34)
Other employment	108 (7)
Age <18 yr[d]	208 (13)
Missing	44 (3)
Characteristics of CLI events	
Total CLI	1,900
CLI with 3 specimens requested[e]: flocked MTS, foam MTS, saliva	1,057 (56)
CLI with 2 specimens requested: flocked MTS and saliva	843 (44)
Fever or feverishness reported	
Yes	713 (38)
No	363 (19)
Missing	824 (43)
Specimens tested	
Flocked MTS	1,886 (99)
Foam MTS[e]	1,010 (96)
Saliva specimen	1,760 (93)

[a]Criteria for CLI included presence of at least one of the following: fever or feverishness, cough, shortness of breath, sore throat, diarrhea, muscle aches, chills, or change in taste or smell.
[b]Values are *n* (%) unless noted otherwise. CLI, COVID-19-like illness; MTS, midturbinate swab; SARS-CoV2, severe acute respiratory syndrome coronavirus 2; C-HEaRT, the Coronavirus Household Evaluation and Respiratory Testing; AZ HEROES, the Arizona Healthcare, Emergency Response, and Other Essential Workers Study; RECOVER, the Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel study.
[c]Occupation criteria are not mutually exclusive.
[d]Participants were not asked about their occupation.
[e]For the C-HEaRT and RECOVER cohorts, participants were asked to collect flocked MTS, foam MTS, and saliva specimens upon symptom onset. For the AZ HEROES cohort, participants were only asked to collect flocked MTS and saliva specimens.

13–17 years. Among 29 CLI events with discordant results between specimen types, SARS-CoV-2 was detected in 24 (83%) saliva specimens and in 17 (59%) flocked MTS specimens in VTM. Among CLI events with SARS-CoV-2 detected on any specimen, 97% (95% confidence interval [CI]: 94-98%) were positive in flocked MTS in VTM, 99% (95% CI: 97–100%) in saliva, and 89% (95% CI: 84–93%) in foam MTS (all $\kappa \geq 0.93$) (Table 3). In a sensitivity analysis considering inconclusive results as positive, the concordance rates between flocked MTS in VTM and saliva ($\kappa = 0.97$) or flocked MTS in VTM and dry foam MTS ($\kappa = 0.94$) remained the same (data not shown).

Four percent of all sample types were collected ≥10 days following symptom onset ($n = 83$ flocked MTS in VTM; $n = 45$ dry foam MTS; $n = 80$ saliva). Among these samples, SARS-CoV-2 was detected in 18 (23%) of saliva and 19 (23%) of flocked MTS in VTM ($P = 0.95$).

Evaluation of SARS-CoV-2 RNA stability. A total of 23 flocked MTS and 19 saliva pools were exposed to 8 combinations of storage temperature and time conditions, representing 336 individual tests. The SARS-CoV-2 C_q values following exposure to experimental conditions

TABLE 2 Specimen collection, transport, and SARS-CoV-2 RT-PCR testing timeline for COVID-19-like illness events where at least two specimens were submitted, August 2020 to April 2021[a]

Characteristics	Flocked MTS, *n* (%)	Foam MTS, *n* (%)	Saliva specimen, *n* (%)
Total specimens collected	1,896	1,035	1,866
Days from symptom onset to specimen collection (median, IQR)	2 days, 0–4 days	2 days, 1–4 days	2 days, 0–4 days
0–2 days	1,180 (62)	649 (63)	1,166 (63)
3–4 days	319 (17)	174 (17)	307 (16)
≥5 days	343 (18)	187 (18)	335 (18)
Missing date	54 (3)	25 (2)	58 (3)
Days from specimen collection to specimen receipt at laboratory (median, IQR)	1 day, 1–2 days	1 day, 1–2 days	1 day, 1–2 days
0–2 days	1,575 (83)	854 (82)	1,562 (84)
3–4 days	201 (11)	144 (14)	199 (11)
≥5 days	66 (3)	28 (3)	65 (3)
Missing date	54 (3)	9 (1)	40 (2)
Days from specimen collection to testing (median, IQR)	2 days, 1–3 days	32 days, 20–50 days	2 days, 1–3 days
0–2 days	1,287 (68)	15 (1)	1,184 (63)
3–4 days	446 (24)	15 (1)	477 (26)
≥5 days	102 (5)	991 (97)	107 (6)
Missing date	61 (3)	14 (1)	98 (5)
Assay platform			
Quidel Lyra SARS-CoV-2 Assay	598 (31)	1,032 (100)	576 (31)
Thermo Fisher TaqPath COVID-19 Combo Kit	1288 (68)	0 (−)	1,228 (66)
Specimen not tested	10 (1)	3 (0)	62 (3)

[a]IQR, interquartile range.

remained consistent with pretest C_q values across both the MTS and saliva specimen collections (Fig. 1 and 2; Table S1 in supplemental material). Across the experimental conditions, the N gene exhibited the greatest stability with mean ΔC_q values of 0.18 and 0.66 for flocked MTS and saliva compared with 0.48 and 1.04 for ORF, and 1.83 and 1.09 for the S gene, respectively ($P < 0.05$; Table S1; Fig. S2). All three viral gene targets had an average ΔC_q of

TABLE 3 Concordance of SARS-CoV-2 RT-PCR detections in flocked MTS in viral transport media, dry foam MTS, and saliva specimens with detection by any specimen type during COVID-19-like illness episodes, August 2020 to April 2021[a]

SARS-CoV-2 detection comparisons[b]	No. (%)	Percent detection[c] no. positive by specimen type/composite positive (%; 95% CI)	Negative predictive value (%; 95% CI)	Percent agreement[d] (Kappa, 95% CI)
Individual specimens				
Flocked MTS (*n* = 1,829)				
Positive	320 (18%)	320/334 (97%; 94–98%)	1,495/1,506 (99%; 99–100%)	
Negative	1,506 (82%)			
Inconclusive	3 (0%)			
Foam MTS (*n* = 1,010)				
Positive	179 (18%)	179/202 (89%; 84–93%)	808/830 (97%; 96–98%)	
Negative	830 (82%)			
Inconclusive	1 (0%)			
Saliva (*n* = 1,757)				
Positive	323 (18%)	323/327 (99%; 97–100%)	1,428/1,432 (100%; 99–100%)	
Negative	1,432 (82%)			
Inconclusive	2 (0%)			
Specimen pairs				
Flocked MTS vs. foam MTS (*n* = 1,002)				0.94 (0.92–0.97)
Flocked MTS vs. saliva (*n* = 1,746)				0.97 (0.96–0.99)
Foam MTS vs. saliva (*n* = 930)				0.93 (0.90–0.96)

[a]Excludes SARS-CoV-2 CLI events where sample viability precluded testing (e.g., unable to amplify internal control or not enough specimen volume for testing) thus resulting in <2 specimen results per CLI event.
[b]Excludes specimens with invalid or missing results: flocked MTS specimen (*n* = 2 missing results), foam MTS specimen (*n* = 18 invalid results and *n* = 2 missing results), and saliva specimen (*n* = 20 invalid results and *n* = 7 missing results).
[c]SARS-CoV-2 percent detection defined as the proportion of specimen type-specific detections among CLI episodes with a detection identified in any specimen collected for that CLI event (composite positive). Excludes specimens with invalid, or missing results. CI, confidence interval.
[d]Discordant results between available and tested specimen types included: 11 negative flocked MTS, 22 negative foam MTS, and 4 negative saliva specimens.

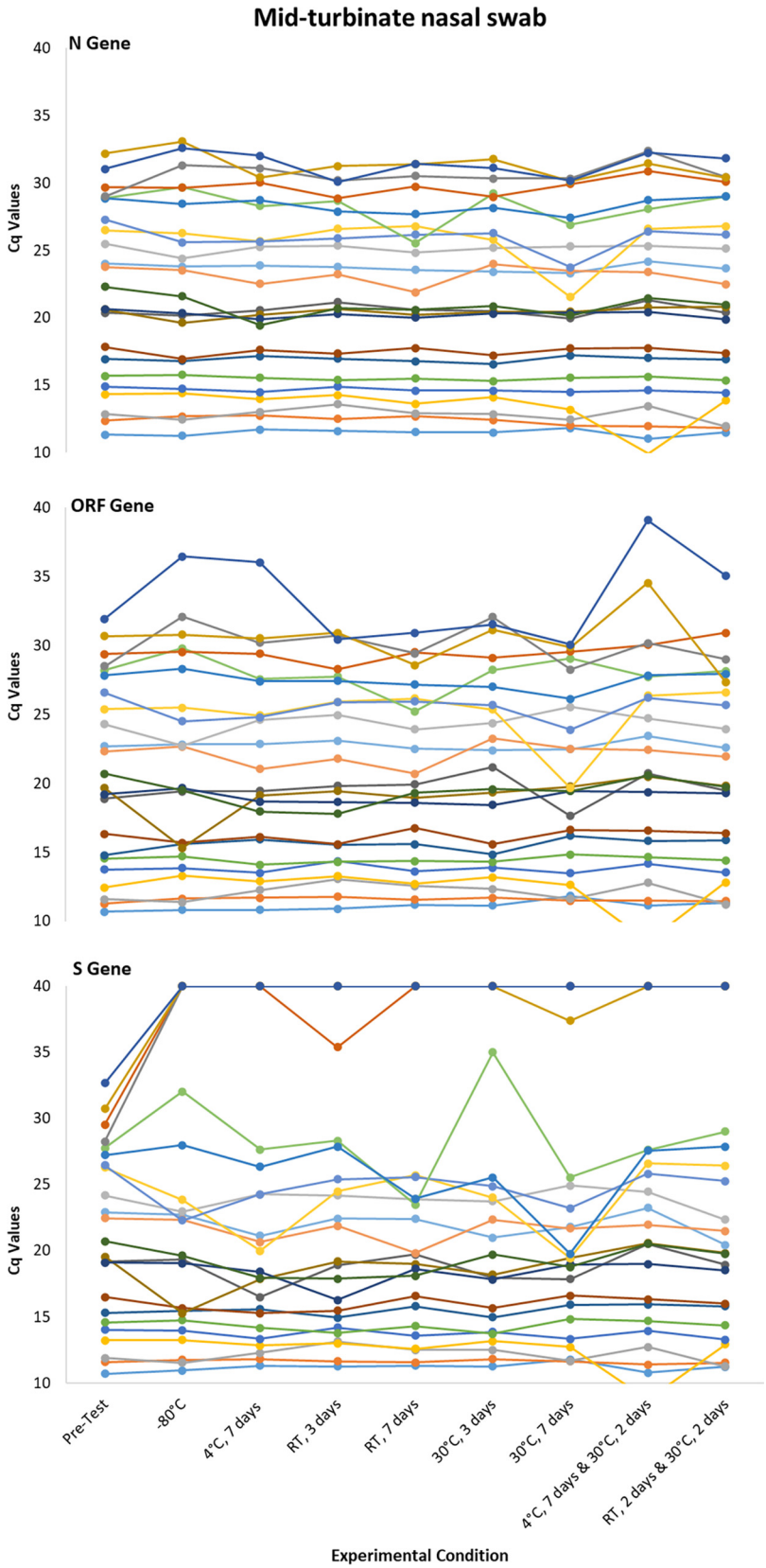

FIG 1 Midturbinate nasal swab cycle quantification (C_q) values before and after exposure to a range of experimental storage temperatures and times using real-time RT-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) Nucleocapsid (N), Open Reading Frame 1ab (ORF1ab) (ORF), and Spike (S) gene targets.

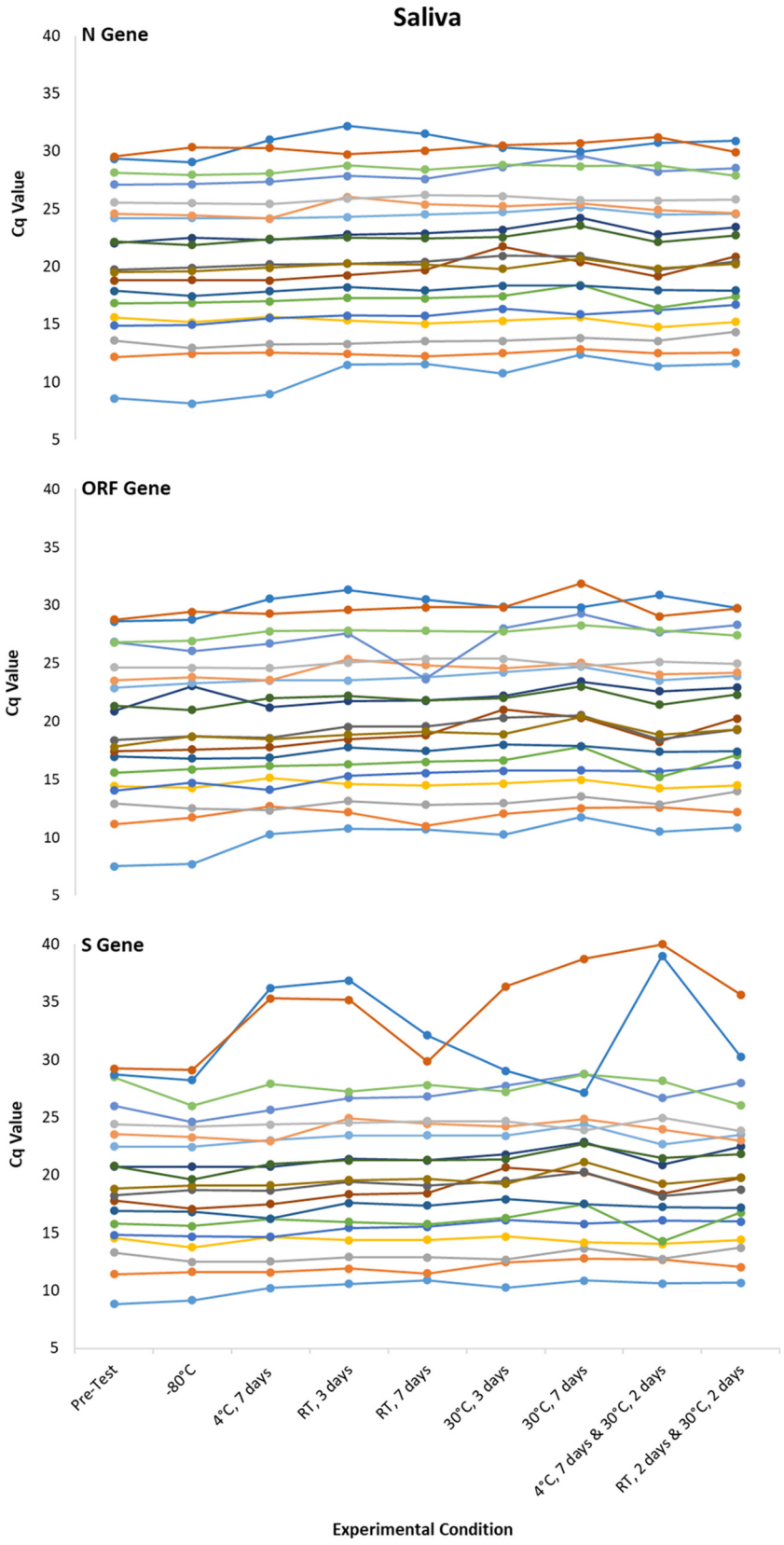

FIG 2 Saliva cycle quantification (C_q) values before and after exposure to a range of experimental storage temperatures and times using real-time RT-PCR for SARS-CoV-2 Nucleocapsid (N), Open Reading Frame 1ab (ORF), and Spike (S) gene targets.

<1 among MTS pools with pretest C_q values <28 (flocked MTS pools 1–17). Among flocked MTS pools with pretest C_q values >28, the S gene fell below the limits of detection (LoD); however, these pools retained positive test interpretations based on N and ORF gene detection (Fig. 1). The N gene result for one pool had a ΔC_q of 1.84 (pool 21) (Table S1). While we observed more variation among saliva specimens, the mean ΔC_q was ≤ 1 for the majority of saliva pools (Table S1).

Only one flocked MTS experimental sample with a high baseline C_q value of 31.89 returned an inconclusive result after the pool was exposed to 4°C for 7 days followed by 30°C for 2 days. Under these conditions, the ΔC_q for all three target genes in the flocked MTS samples were slightly higher, although the difference was not significant (Fig. 1; Fig. S3). In saliva specimens, exposure to elevated temperatures (30°C) for 7 days led to ΔC_q values of >1 (1.77, 1.17, and 1.85) in the S, N, and ORF genes, respectively, compared to their baseline ΔC_q values ($P < 0.05$; Fig. 2; Fig. S3).

DISCUSSION

In this prospective community study that identified 1,900 CLI events among adults and children who self-collected and shipped respiratory specimens at illness onset under real-world conditions, flocked MTS in VTM, dry foam MTS, and saliva specimens yielded comparable SARS-CoV-2 detection rates. Under experimental conditions, SARS-CoV-2 RNA was also highly stable across a wide range of storage times and temperatures with N and ORF gene targets exhibiting more stability than the S-gene target when starting C_q values were higher. Dry foam MTS, which were frozen upon arrival, had an approximate 10% lower sensitivity compared to flocked MTS in VTM and saliva but underwent an additional freeze/thaw cycle and still represents an acceptable alternative if critical. These findings provide additional support for the validity of self-collected dry foam MTS and saliva as alternatives to flocked MTS in VTM. These findings support a range of viable options for specimen types and collection and transport methods that may facilitate large-scale testing for SARS-CoV-2 during supply and personnel shortages.

Our finding that flocked MTS in VTM, foam MTS without VTM, and saliva produced comparable results for detection of SARS-CoV-2 is consistent with published studies. In a pooled analysis of data from studies comparing SARS-CoV-2 detection from MTS in transport media or saliva specimens versus nasopharyngeal swabs, MTS were 95% sensitive (95% CI 83–99%) and saliva specimens collected without coughing were 90% sensitive (95% CI 85–93) (24). Few studies have directly compared SARS-CoV-2 detection from MTS versus saliva (25, 26). An analysis of 31 SARS-CoV-2 positive episodes in which MTS in transport media or saliva were self-collected by adults demonstrated that the two sample types had similar sensitivity for SARS-CoV-2 detection (26). Our analysis expands upon previous studies by assessing flocked MTS in VTM and saliva specimens among both adults and children and documenting that flocked MTS in VTM and saliva had comparable performance in samples collected ≥ 10 days after symptom onset.

Studies evaluating SARS-CoV-2 RNA stability among spiked, mock specimens with predetermined viral dilutions or health care worker collected specimens from hospitalized patients or at-risk health care workers (27–30) demonstrated that SARS-CoV-2 RNA in saliva samples can remain stable for up to 25 days at room temperature. Furthermore, one study concluded that degradation at higher temperature does not impede nuclease activity (28). Our laboratory experiment using self-collected flocked MTS in VTM and saliva from infected individuals demonstrated that SARS-CoV-2 viruses can remain stable during shipping periods of up to 7 days at 20–23°C or up to 30°C for 3 days. Overall pretest and experimental condition C_q were consistent, demonstrating variability for all three viral gene targets in both specimen types with C_q values >28 and only upon exposure to higher environmental temperatures (Fig. 2). Taken together, the laboratory experiment results coupled with the high SARS-CoV-2 detection rate demonstrate that self-collection and shipping of specimens are feasible and viable alternatives for individuals experiencing COVID-19 symptoms.

Several limitations should be considered when interpreting our findings. First, our analysis was limited to specimens collected during symptomatic SARS-CoV-2 infections and

may not be generalizable to specimens collected from asymptomatic persons. Second, we were unable to assess in-home participant adherence to specimen self-collection instructions; however, our findings are more likely to reflect specimen performance under real-world conditions. Third, assessment of SARS-CoV-2 RNA stability under varying storage conditions did not include RNA from dry foam MTS because foam MTS were subjected to one additional freeze-thaw cycle that could have affected pretest C_q values. Furthermore, unlike flocked MTS and saliva samples, dry foam MTS were tested in a reverse transcription-PCR (RT-PCR) platform with limited LoD that could have impacted sample sensitivity. Fourth, our analysis was limited to specimens collected between August 2020 and April 2021, prior to Delta and Omicron variant circulation. A review of recently collected specimens has not identified a difference from the findings reported here (data not shown), but experimental conditions were not replicated. These results many not be generalizable to specimen performance with new variants such as Omicron, which may have different viral loads in different sample types (31).

Self-collected flocked MTS in VTM, foam MTS without VTM, and saliva specimens were comparable for the detection of SARS-CoV-2 among both adults and children in our study. In addition, SARS-CoV-2 RNA from flocked MTS and saliva was stable at up to 20–23°C for up to 7 days under simulated conditions. Giving individuals a choice of sample collection types (i.e., saliva or swab) and transport options may increase the acceptability of SARS-CoV-2 screening programs and reduce the burdens associated with material cost and supply-chain limitations for SARS-CoV-2 detections.

MATERIALS AND METHODS

Participants and Setting. This analysis includes data from participants in three prospective cohorts: the Coronavirus Household Evaluation and Respiratory Testing (C-HEaRT) study (32), the Arizona Healthcare, Emergency Response, and Other Essential Workers Study (AZ HEROES) (33), and the Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) study (34). The C-HEaRT study included 1,361 participants from 357 households with at least 1 child aged $<$18 years in New York City and selected counties in Utah. The AZ HEROES and RECOVER cohorts included 3,226 and 2,855, health care, first responder, and essential/frontline workers, respectively, across six geographic areas in the United States: Arizona, Florida, Minnesota, Oregon, Texas, and Utah.

Design. In all three studies, participants self-collected upper respiratory tract specimens at the onset of symptoms consistent with CLI defined as at least one of the following symptoms: fever or feverishness, cough, shortness of breath, sore throat, diarrhea, muscle aches, chills, or change in taste or smell. In C-HEaRT, adult caregivers collected specimens for children unable to self-collect respiratory samples. In C-HEaRT and RECOVER, participants self-collected two MTS (with a flocked swab placed in VTM and dry foam swab) and saliva. In AZ HEROES, participants collected one flocked MTS placed in VTM and saliva. Participants with CLI events also completed questionnaires about their illness symptoms and the date of onset.

At study enrollment, participants received a verbal orientation to specimen self-collection and preassembled specimen collection kits, including all collection supplies, shipping materials, and printed self-collection instructions. Participants were asked to collect specimens at onset of CLI symptoms. Participants were instructed to blow their nose, wash their hands, and not eat, drink, smoke or chew gum for 30 min prior to specimen collection. Participants self-collected MTS from both nostrils with the same flocked swab and placed the swab in a vial containing 3 mL of VTM. Participants in C-HEaRT and RECOVER cohorts also self-collected a second MTS from both nostrils with a foam swab and placed it in a sterile vial without VTM. Finally, participants were instructed to spit repeatedly without coughing, into a sterile saliva collection container (IBI Scientific, SK-150; and Miraclean Technology Co., Ltd., MSC-001) without VTM until the amount of liquid saliva reached the fill line (~2 mL). Participants either shipped specimens on the same day using padded envelopes with frozen gel packs via overnight courier or stored specimens in biohazard bags at 4°C for up to 72 h and shipped in padded envelopes with frozen gel packs to a centralized laboratory.

At the central laboratory, all samples underwent RNA extraction using the MagMAX Viral/Pathogen Nucleic Acid Isolation Kit on a KingFisher Flex (Thermo Scientific) instrument followed by a real-time RT-PCR detection method using the Quidel Lyra SARS-CoV-2 Assay for (prior to November 2020) or the TaqPath COVID-19 Combo Kit (Applied Biosystems). The TaqPath RT-PCR amplifies and detects regions of three SARS-CoV-2 targets: Spike (S), Nucleocapsid (N), and ORF1ab (ORF) genes. LoD differed between the two RT-PCR assays with TaqPath having a lower LoD than Quidel Lyra SARS-CoV-2 platform for SARS-CoV-2 viral RNA (35, 36). Both RT-PCR platforms were approved under Emergency Use Authorization for the diagnosis of SARS-CoV-2 infection prior to use in this study (37). Flocked MTS in VTM and saliva specimens were processed and tested upon arrival. Foam MTS were stored at −20°C and batch tested on a dry lysis platform, resulting in one potential additional freeze/thaw cycle.

Simulated storage temperatures and times testing. Using specimens that tested positive for all three SARS-CoV-2 gene targets, we combined specimens based on C_q values into separate pools of flocked MTS specimens and saliva that represented a discrete range of C_q values from approximately 10 to 32 (Table S1). Pooling ensured sufficient sample volume for testing all experimental conditions. A total of 24 flocked MTS pools were created from 192 individual specimens, and 20 saliva pools were created from 120 total specimens. Each

pool was retested ("pretest") to confirm the C_q value the pool represented. Eight 250-μL aliquots were created from each specimen pool and exposed to one of the time and temperature conditions and stored at −80°C until RNA extraction. We exposed sample aliquots from flocked MTS in VTM and saliva to eight different storage temperature and time conditions (4°C, 20°C [room temperature], and 30°C for combinations of 2, 3, and 7 days, and −80°C storage) to evaluate the stability of SARS-CoV-2 viral RNA as measured by cycle quantification (C_q) values (Fig. S1). All pretest and experimental specimens were tested using the ThermoFisher TaqPath platform.

Statistical analyses. All CLI events with ≥2 specimen types collected were included in the analysis. Participant demographic and clinical characteristics were described using frequencies for categorical variables and means with standard deviations for continuous variables. Similar to previous studies of influenza virus (38), in the absence of a recognized gold standard for SARS-CoV-2 detection, we defined detection by any of the three specimen types as a true positive. For each specimen type, we calculated the proportion of true positives that were detected as the number of positive samples divided by the number of true positives. We compared the proportion of true positives detected by each specimen type using Chi-square tests. Percent agreement between specimen type pairs was compared using kappa (κ) statistics, excluding inconclusive results (39). Flocked MTS and saliva specimens were retested if they yielded inconclusive results on the first round of testing and those with final inconclusive results to >1 SARS-CoV-2 targets were reported as inconclusive. As a sensitivity analysis, specimens with inconclusive results (3 flocked MTS, 1 foam MTS, and 2 saliva specimens) were analyzed as positive results.

To evaluate stability of flocked MTS in VTM and saliva in simulated shipping conditions, we calculated the change in C_q (ΔC_q) from the pretest to the experimental specimens for viral N, ORF, and S genes. A maximum C_q value of 40 was given to experimental specimens without SARS-CoV-2 detection. All negative ΔC_q values were given a value of 0 (40). We compared the average ΔC_q for each specimen type and gene target across all experimental conditions and for each condition across all specimens using a Student's *t* test. SAS V9.4 software (SAS Institute Inc., Cary, NC) and Microsoft Excel were used for all statistical analyses.

Ethical review. The study protocol was reviewed and approved by the University of Utah Institutional Review Board (IRB) acting as the single IRB for the C-HEaRT study and by the IRBs at all participating sites for AZ HEROES and RECOVER studies. The CDC IRB relied on the review of external IRBs. Informed consent was obtained from all study participants aged ≥18 years. Parents or legal guardians of children aged <18 years provided written informed consent on behalf of their children, and children aged 12–17 years also provided assent to study participation.

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 0.8 MB.

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