The ongoing coronavirus disease 2019 (COVID-19) pandemic has spread rapidly across the world and is a leading cause of mortality [1, 2]. Current strategies for prevention and control rely in part on timely identification of infections, followed by isolation of cases and quarantine of their close contacts. While most efforts have focused on identification of symptomatic cases, some patients are asymptomatic early in the infection period (ie, presymptomatic), and other infected persons may remain asymptomatic throughout the course of their infection [3, 4]. Traditional approaches for viral detection involve collection of invasive nasopharyngeal swabs by health care providers at health care facilities and transport in specialized media. There is an increasing interest in widespread testing at the community level, which could provide better opportunities for early detection and preventive action [5–7]. Given physical distancing considerations, self-collected specimens (eg, anterior nasal swabs and saliva) are important alternatives for field and community studies, but their performance has not been extensively evaluated. Identifying reliable, sensitive, alternative approaches to self-collection of respiratory specimens is important for improving case detection, especially among individuals with mild or subclinical infection [8].

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) demonstrates tropism for the upper respiratory tract, especially during the initial days of infection [9, 10]. Accordingly, previous studies have proposed the use of saliva as a specimen for identification of SARS-CoV-2 infection [11–14]. Saliva specimens can be self-collected and could provide a simple, more acceptable noninvasive method for diagnosis [8, 15].

**Background.** Anterior nasal swabs (ANS) are established specimen collection methods for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection detection. While saliva (SA) specimens provide an alternative, few studies have comprehensively characterized the performance of SA specimens in longitudinal studies.

**Methods.** We compared SARS-CoV-2 detections between paired self-collected ANS and SA specimens from a household transmission study. Participants recorded symptoms and paired ANS and SA specimens daily for 14 days. Specimens were tested using RT-PCR. We calculated the proportion of detections identified by each specimen type among the detections from both types combined. We computed percent agreement and Kappa statistics to assess concordance in detections. We also computed estimates stratified by presence of symptoms and examined the influence of traditional and inactivating transport media on the performance of ANS.

**Results.** We examined 2535 self-collected paired specimens from 216 participants. Among 1238 (49%) paired specimens with detections by either specimen type, ANS identified 77.1% (95% CI, 74.6% to 79.3%) and SA 81.9% (1014; 95% CI, 79.7% to 84.0%), with a difference of 4.9% (95% CI, 1.4% to 8.5%). Overall agreement was 80.0%, and Kappa was 0.6 (95% CI, 0.5 to 0.6). Nevertheless, the difference in the proportion of detections identified by ANS and SA using traditional and inactivating transport media was 32.5% (95% CI, 26.8% to 38.0%) and −9.5% (95% CI, −13.7% to −5.2%), respectively. Among participants who remained asymptomatic, the difference in detections between SA and ANS was 51.2% (95% CI, 31.8% to 66.0%) and 26.1% (95% CI, 0% to 48.5%) using traditional and inactivating media, respectively.

**Conclusions.** Self-collected saliva specimens provide a noninvasive alternative to nasal swabs, especially to those collected in traditional transport media, for longitudinal field studies that aim to detect both symptomatic and asymptomatic SARS-CoV-2 infections.

**Keywords.** SARS-CoV-2; diagnostic; saliva; PCR; COVID.
Furthermore, collection of saliva does not require swabs, refrigeration, or specialized transport media [16], which could be advantageous when there is limited availability of specimen collection materials. Self-collected saliva specimens could also allow rapid viral identification during both symptomatic and asymptomatic infections [5–7] and subsequent sequencing. In an ongoing prospective study of transmission of SARS-CoV-2 infections in households, paired self-collected anterior nasal swabs and saliva specimens were examined to determine the performance of these approaches and the concordance in viral detection between these specimen types. These assessments encompassed periods without infections as well as symptomatic and asymptomatic infection periods.

METHODS

Study Population
This study was nested within an ongoing prospective case-ascertained household transmission study and included samples collected from April to November 2020 [17, 18]. We defined an index case as the first household member presenting with COVID-like symptoms who lived with at least 1 other household member and who tested positive for SARS-CoV-2 infection through clinical diagnostic reverse transcription polymerase chain reaction (RT-PCR) testing on a nasopharyngeal sample collected at ambulatory walk-in clinics located in the Nashville metropolitan area. Individuals living in correctional facilities, long-term care facilities, boarding schools, hostels, dormitories, or other similar institutionalized/congregate settings were not eligible for the study. After electronic written informed consent was obtained from index cases and household members, participants were remotely enrolled and instructed in the self-collection of saliva (SA) and anterior nasal swab (ANS) specimens and use of Vanderbilt Research Electronic Data Capture (REDCap) electronic questionnaires. Participants completed daily symptom diaries and self-collected paired specimens daily for 14 days. Symptoms ascertained included fever/feverish/chills, cough, sore throat, runny nose, nasal congestion, fatigue/feeling run down, wheezing, trouble breathing/shortness of breath, chest tightness/chest pain, loss of smell/loss of taste, headache, abdominal pain, diarrhea, vomiting, and muscle or body aches.

Patient Consent
The Vanderbilt University Institutional Review Board reviewed and approved the study [17, 18]. Written informed consent was obtained from all participants at enrollment. This study was also reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted in accordance with applicable federal law and CDC policy [19, 20].

Self-Collection of Specimens
Enrolled participants were remotely instructed on the self-collection of respiratory specimens. Because of the

self-collection nature of the study, collection of nasopharyngeal swabs was not considered; instead, the study focused on self-collection of ANS and SA specimens. Printed instructions and a video demonstrating self-collection procedures were reviewed and discussed with study participants. After swabbing the anterior nares with a flocked swab (Floqswebs, COPAN, Brescia, Italy), the swab was placed into transport media. During the initial period of the study, from April 21 through July 23, 2020, self-collected ANS specimens were collected in traditional viral transport media (Remel MicroTest M4RT, Lenexa, KS, USA), which required the participants to refrigerate the specimens until a study field team retrieved the specimens. Viral transport media for ANS specimens was subsequently replaced (from July 24 through November 20, 2020) by molecular transport media that rapidly inactivates viruses, bacteria, and pathogens within the sample (Primestore, Longhorn Vaccines & Diagnostics LLC, Bethesda, MD, USA). An additional advantage of this inactivating transport media is that it can be stored at room temperature after specimen collection, with an average reported stability of 117 days [21]. For the self-collection of SA specimens, participants were instructed to wait at least 30 minutes after eating, drinking, or brushing teeth, passively accumulate saliva in their mouths for ~10 seconds, and then gently drop the saliva into the provided sterile urine collection cup for ~1 minute (~6 times total) [11]. Parents of young children were asked to help their children with specimen collections, as appropriate. If SA specimens could not be collected by young children, only ANS specimens were collected. All self-collected specimen tubes and cups were tightly closed after daily sample collection, placed in a resealable biohazard bag, and stored in another resealable plastic bag. During the aforementioned initial study period, SA specimens were refrigerated until a study field team came to retrieve them; after that period, specimens were kept at room temperature. All self-collected specimens were retrieved by the study field teams every 3–4 days and transported within a locked hard-shell container to the research laboratory, where specimens were aliquoted and preserved at ~80°C until testing. For the present study, only participants who provided paired ANS and SA specimens were included.

Research RT-PCR Testing
Specimens were tested for SARS-CoV-2 based on methods provided in the CDC Emergency Use Authorization (EUA) protocol, “CDC 2019-Novel Coronavirus (2019-nCoV) Real-Time RT-PCR Diagnostic Panel” [22]. Low-volume and/or overly viscous SA specimens were supplemented with phosphate-buffered saline (PBS) to a maximum total volume of 600 μL (maximum of 500 μL added PBS) before extraction. Total nucleic acid extracts were prepared using the MagNA Pure LC Total Nucleic Acid Isolation Kit and MagNA PURE LC 2.0 automated extraction platform (Roche). Extracts were tested for protocol-specified SARS-CoV-2 nucleocapsid gene N1 and N2
targets using the StepOnePlus, QuantStudio 3, and QuantStudio 6-Flex real-time PCR systems (ABI). Initial co-detection of N1 and N2 was deemed valid and final; results were accepted without additional testing. Specimens for which either N1 or N2 was detected in the absence of the other were retested, usually in duplicate for both targets, and the lowest N1 and N2 cycle threshold (Ct) values obtained upon retesting were accepted as final. Each extract also was evaluated for RNase P (RNP) as an endogenous control for specimen adequacy and successful extraction; an initial RNP Ct ≥40 was followed by re-extraction from the original specimen and retested. Test results were used to classify specimens as positive (both N1 and N2 Ct values <40) or negative (both N1 and N2 Ct values ≥40). Suboptimal specimens (RNP Ct value ≥40) and inconclusive results (either N1 or N2 Ct value ≥40 and the other <40) were excluded from analyses.

**Statistical Analysis**

We summarized participant characteristics using frequencies and medians (and interquartile ranges [IQRs]) for categorical and continuous variables as appropriate. As there was no established reference standard for specimen collection and identification of SARS-CoV-2 infection in the study, sensitivity was not calculated. As an alternative, we computed the proportion of detections identified by ANS and SA relative to the combined detections from either one of the specimen types [11]. As RT-PCR is highly specific [11], examination of proportions of negative detections by specimen types was not conducted. We compared these proportions by calculating the difference in proportions and 95% CI while accounting for the paired nature of the data, and also tested whether this estimate was statistically different from 0 using a Pearson chi-square test. We also estimated the agreement in positive and negative detections between ANS and SA specimens, computed the percent agreement, and compared the discordance in detections between specimen types using McNemar tests. To account for chance agreement, we calculated the Kappa statistic [23].

We estimated the proportion of detections identified by ANS and SA specimens, as well as the agreement in viral detection between specimen types overall and stratified by age (ie, children [<18 years] vs adults), participant type (ie, index case vs household contacts), and presence of symptoms. To examine the influence of symptoms on the proportions detected by each specimen type and agreement in detections, we classified paired self-collected specimens into mutually exclusive groups according to the presence of symptoms on the collection date: asymptomatic periods before symptoms developed (presymptomatic), currently symptomatic periods, asymptomatic periods after symptomatic periods (postillness), and asymptomatic periods in participants who reported no symptoms throughout follow-up (continuously asymptomatic). We also examined specimen type performance among paired specimens collected from participants with incident symptomatic disease during or after the first 7 days following disease onset. To examine the influence of different transport media, we stratified estimates based on use of traditional viral transport media and inactivating transport media. Analyses were conducted in R 4.0.3 (R Foundation, Vienna, Austria) and Stata 16 (StataCorp, College Station, TX, USA).

**RESULTS**

Among 256 participants enrolled during the study period, there were 3325 ANS and 2852 SA specimens collected. After exclusion of subjects with only 1 type of specimen collected, suboptimal specimens, or inconclusive results, we examined a total of 2535 paired ANS and SA specimens from 216 study participants (83 index cases and 133 household contacts) (Table 1). The median number of paired samples per participant (IQR) was 13 (11–14). The median age of participants (IQR) was 29 (21–48) years, 42% were males, and 76% were non-Hispanic White. Overall, 20% had underlying comorbidities, including asthma (9%), cardiovascular diseases (6%), and diabetes (4%). The median interval between disease onset among index cases and enrollment (IQR) was 1 (0–2) days.

**Proportion of Detections Identified by ANS and SA Specimens**

A total of 954 of the 2535 ANS specimens (37.6%) and 1014/2535 (40.0%) SA specimens were positive for SARS-CoV-2. A total of 1238 (49%) paired specimens were positive in either the ANS or SA specimen type. Among all these viral detections, ANS identified 77.1% (95% CI, 74.6% to 79.3%), whereas SA identified 81.9% (95% CI, 79.7% to 84.0%), for an absolute difference of 4.9% (95% CI, 1.4% to 8.5%). Similar differences in detections, with more detections by SA than ANS, were observed in children, adults, and contacts, but there was no difference among index cases (Figure 1A; Supplementary Table 1).

When paired specimens were classified according to the presence of symptoms, there were no significant differences between specimen types collected from subjects with symptoms or during presymptomatic periods. However, the proportion of detections by SA was higher than by ANS specimens collected during postillness periods. Among individuals who remained continuously asymptomatic throughout study follow-up, the proportion of detections by SA was significantly higher (83.9%; 95% CI, 74.8% to 90.2%) than by ANS (46.0%; 95% CI, 35.9% to 56.4%) (Figure 1A; Supplementary Table 1).

Among specimens self-collected by individuals who developed symptomatic disease, the overall proportion of detections by SA and ANS was 79.8% and 76.6%, respectively (difference, 3.2%; 95% CI, −1.3% to 7.7%). Similar patterns were observed among index cases. While the proportion of detections by either SA or ANS was highest during the first week after disease onset, the proportion of detections by SA was generally
lower than detections by ANS during that period (Figure 1B; Supplementary Table 1).

The proportion of detections by ANS was higher when specimens were collected in inactivating transport media compared with traditional viral transport media. This difference was consistent across subgroups, including children, adults, index cases, and household contacts (Figure 2A & B; Supplementary Table 2). Likewise, when we evaluated groups according to the presence of symptoms, the proportion of detections by ANS specimens generally increased with the use of inactivating transport media. However, the proportion of detections by ANS specimens among subjects who remained asymptomatic throughout follow-up was consistently lower than by SA specimens, regardless of the transport media used (Figure 2B; Supplementary Table 2).

Agreement in Detections Between ANS and SA Specimens
Among the total 2535 paired specimens, overall agreement was 80.0% (McNemar test $P = .009$), with agreement on negative results at 51.2% and agreement on positive results at 28.8%; the Kappa statistic was 0.6 (95% CI, 0.5 to 0.6). Among children, agreement was 81.8% ($P = .036$) overall, and the Kappa statistic was 0.6 (95% CI, 0.5 to 0.7). Similarly, among adults, agreement was 79.5% overall ($P = .067$), and the Kappa was 0.6 (95% CI, 0.5 to 0.6). Agreement between paired ANS and SA specimens collected from index cases and household contacts was 67.0% ($P = .693$) and 78.7% ($P < .001$), respectively. The corresponding Kappa statistics were 0.3 (95% CI, 0.2 to 0.4) and 0.7 (95% CI, 0.6 to 0.7) (Table 2).

When we examined agreement based on the presence of symptoms, agreement was consistently high and ranged between 71.1% and 91.1% among groups. Among paired specimens collected from symptomatic participants, the Kappa statistic was 0.5 (95% CI, 0.5 to 0.6). The corresponding Kappa statistic for paired specimens collected from participants who remained consistently asymptomatic throughout their observation period was 0.4 (95% CI, 0.3 to 0.5) (Table 2).

Among 1185 specimens from 103 participants with symptomatic disease, the agreement between SA and ANS was 70.1% ($P = .184$). During the first week of disease, agreement was 86.4% ($P < .001$). In subsequent days, the agreement was 63.1% ($P = .003$). The Kappa statistic overall, during the first week, and thereafter was 0.4 (95% CI, 0.3 to 0.5), 0.6 (95% CI, 0.5 to 0.7), and 0.3 (95% CI, 0.2 to 0.3), respectively. While agreement in detections was lower among specimens from index cases than from household contacts, consistently lower agreement was observed in specimens collected after the first week following disease onset in both index cases and household contacts (Table 2).

A total of 814 paired specimens were collected using traditional transport media. The agreement in detections was 76.7%,

Table 1. Characteristics of Participants Enrolled in a Case-Ascertained Household Transmission Study of SARS-CoV-2—Nashville, TN, April–November 2020

| Characteristic                          | Index Case (n = 83) | Household Contact (n = 133) | Total (n = 216) |
|----------------------------------------|--------------------|-----------------------------|-----------------|
| Sex, % (No.)                           |                    |                             |                 |
| Female                                 | 63.7 (52)          | 55.6 (74)                   | 58.3 (126)      |
| Male                                   | 37.3 (31)          | 44.4 (69)                   | 41.7 (90)       |
| Ethnicity/race, % (No.)                |                    |                             |                 |
| Non-Hispanic White                     | 77.1 (64)          | 74.4 (99)                   | 75.5 (163)      |
| Non-Hispanic Black                     | 7.2 (6)            | 3.8 (5)                     | 5.1 (11)        |
| Hispanic                               | 15.7 (13)          | 18.8 (25)                   | 17.6 (38)       |
| Other/mixed/unknown                    | 0.0 (0)            | 3.0 (4)                     | 1.9 (4)         |
| Age, median (IQR), y                   | 29 (24–48)         | 31 (18–47)                  | 29 (21–48)      |
| Age group, % (No.)                     |                    |                             |                 |
| <18 y                                  | 16.9 (14)          | 24.1 (32)                   | 21.3 (46)       |
| 18–49 y                                | 60.2 (50)          | 54.9 (73)                   | 56.9 (123)      |
| 50–64 y                                | 16.9 (14)          | 14.3 (19)                   | 15.3 (33)       |
| >65 y                                  | 6.5 (5)            | 6.8 (9)                     | 6.5 (14)        |
| Any underlying condition, % (No.)      |                    |                             |                 |
| Asthma                                 | 10.8 (9)           | 8.3 (11)                    | 9.3 (20)        |
| Other chronic lung disease             | 0.0 (0)            | 1.5 (2)                     | 0.9 (2)         |
| Cardiovascular                         | 4.8 (4)            | 6.8 (8)                     | 5.6 (12)        |
| Diabetes                               | 4.8 (4)            | 3.8 (5)                     | 4.2 (9)         |
| Cancer                                 | 2.4 (2)            | 0.8 (1)                     | 1.4 (3)         |
| Immunocompromising condition           | 1.2 (1)            | 1.5 (2)                     | 1.4 (3)         |
| Extreme obesity                        | 2.4 (2)            | 2.3 (3)                     | 2.3 (5)         |
| Kidney disease                         | 0.0 (0)            | 1.5 (2)                     | 0.9 (2)         |
| Smoke cigarettes                       | 1.2 (1)            | 1.5 (2)                     | 1.4 (3)         |

Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
with a Kappa statistic of 0.5 (95% CI, 0.5 to 0.6). When specimens were collected in inactivating transport media (n = 1721), the agreement was 81.5%, and the corresponding Kappa statistic was 0.6 (95% CI, 0.6 to 0.7). Estimated agreement and Kappa were highest among specimens collected using inactivating transport media including estimates for children, adults, index cases, and household contacts, and among most groups based on presence of symptoms (Table 3).

**DISCUSSION**

Among self-collected paired SA and ANS specimens, SA specimens identified a higher proportion of SARS-CoV-2 detections, especially among specimens collected during asymptomatic periods. The overall agreement in viral detection between SA and ANS specimens was moderate. These findings indicate that self-collected SA specimens can be used for identification of SARS-CoV-2 infections in longitudinal field studies and community testing programs.

While several specimen types are currently accepted for identification of SARS-CoV-2 infections, many rely on collection by trained health care providers at health care facilities [24]. Given pandemic physical distancing recommendations and the increasing interest in detecting infections in the community, self-collection of specimens can be a valuable alternative, particularly for field-based studies. Several studies have reported good diagnostic performance of SA specimens for detection of SARS-CoV-2 infections using nasopharyngeal and anterior nasal swabs for comparisons [11–14]. A recent study compared the performance of self-collected ANS and

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**Figure 1.** Proportion of SARS-CoV-2 detections identified by self-collected saliva and anterior nasal swab specimens from participants enrolled in a case-ascertained household transmission study, (A) overall and by age, index, and symptomatic subgroups and (B) by phases of disease (symptomatic participants only). Dots represent the point estimates, and horizontal bars represent the 95% CIs. *Significant difference between specimen types. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
SA specimens with health care worker–collected nasopharyngeal swabs and demonstrated that more SARS-CoV-2 infections were detected by nasopharyngeal swabs and saliva than by ANS [14]. Nevertheless, most prior studies focused on single cross-sectional assessments among hospitalized patients or persons presenting to outpatient clinics or in isolation facilities, but very few have characterized diagnostic performance continuously over the natural course of infection.

Building upon this prior evidence, our ongoing study of SARS-CoV-2 transmission within households presented an ideal opportunity to evaluate the performance of 2 types of self-collected specimens. We found a difference in the proportion of detections between SA and ANS, favoring SA specimens, that was consistent among children, adults, and household contacts. The difference was most remarkable when the person was asymptomatic. Importantly, the difference was greatest among the group of participants who remained asymptomatic throughout their follow-up. While similar differences in test sensitivity between symptomatic and asymptomatic subjects have been documented in evaluations of antigen detection tests [25], the reasons for these differences are not completely clear. Previous studies suggest that viral loads among asymptomatic patients are similar to those of symptomatic patients [26]; however, other studies suggest that asymptomatic infections are associated with lower viral loads [27]. Nevertheless, the relevance of infected individuals who remain asymptomatic in disease transmission is well recognized [28], and practical, accurate approaches for viral detection are crucial to inform isolation of

Figure 2. Proportion of SARS-CoV-2 detections identified by self-collected saliva and anterior nasal swab specimens from participants enrolled in a case-ascertained household transmission study, (A) overall and by subgroups using traditional transport media and (B) overall and by subgroups using inactivating transport media. Dots represent the point estimates, and horizontal bars represent the 95% CIs. *Significant difference between specimen types. Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
### Table 2. Agreement by RT-PCR for SARS-CoV-2 RNA Between Saliva and Anterior Nasal Swab Specimens Self-Collected by Participants Enrolled in A Case-Ascertained Household Transmission Study of SARS-CoV-2—Nashville, TN, April–November 2020

| Subjects | Negative Agreement | Positive Agreement | Observed Agreement, % | McNemar P Value | Kappa (95% CI) |
|----------|--------------------|--------------------|-----------------------|-----------------|----------------|
| Overall (n = 216) | 129/2535 (51.2) | 730/2535 (28.8) | 80.0 | .009 | 0.6 (0.5 to 0.6) |
| Children (n = 46) | 319/548 (58.2) | 129/548 (23.5) | 81.8 | .036 | 0.6 (0.5 to 0.7) |
| Adults (n = 170) | 978/1987 (49.2) | 601/1987 (30.2) | 79.5 | .067 | 0.6 (0.5 to 0.6) |
| Index (n = 83) | 242/951 (25.4) | 395/951 (41.5) | 670 | .693 | 0.3 (0.3 to 0.4) |
| Contacts (n = 133) | 1055/1584 (66.6) | 335/1584 (21.1) | 878 | <.001 | 0.7 (0.6 to 0.7) |

Presence of symptoms

| Presence of symptoms | Overall (n = 216) | Children (n = 46) | Adults (n = 170) | Index (n = 83) | Contacts (n = 133) |
|----------------------|-------------------|------------------|------------------|----------------|------------------|
| Contuously asymptomatic (n = 54) | 545/632 (86.2) | 26/632 (4.1) | 90.3 | <.001 | 0.4 (0.3 to 0.5) |
| Presymptomatic (n = 43) | 99/135 (73.3) | 24/135 (17.8) | 91.1 | .386 | 0.7 (0.6 to 0.9) |
| Postillness (n = 108) | 320/620 (51.6) | 121/620 (19.5) | 71.1 | .052 | 0.4 (0.3 to 0.4) |
| Symptomatic (n = 159) | 333/1148 (29.0) | 559/1148 (48.7) | 77.7 | .851 | 0.5 (0.5 to 0.6) |

During the phases of the disease (symptomatic participants only)

| During the phases of the disease | Overall (n = 216) | Children (n = 46) | Adults (n = 170) | Index (n = 83) | Contacts (n = 133) |
|---------------------------------|-------------------|------------------|------------------|----------------|------------------|
| 1st week (n = 101) | 56/361 (15.5) | 220/278 (79.1) | 84.9 | <.001 | 0.4 (0.3 to 0.5) |
| After 1st week (n = 81) | 316/824 (38.3) | 175/673 (26) | 84.6 | <.001 | 0.5 (0.6 to 0.7) |
| 1st week (n = 20) | 40/83 (48.2) | 36/83 (43.4) | 91.6 | .45 | 0.8 (0.6 to 1.1) |
| After 1st week (n = 20) | 90/151 (59.6) | 28/151 (18.5) | 78.1 | <.001 | 0.5 (0.3 to 0.6) |

Negative agreement refers to the proportion of paired samples that had no detected infections by either specimen type. Positive agreement refers to the proportion of paired samples that had detected infections by both specimen types. Observed agreement refers to the proportion of paired samples that had positive or negative agreement between specimen types.

Interpretation of the Kappa statistic for agreement: ≤0 = poor; 0.01–0.20 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.8 = substantial; and 0.81–1 = almost perfect [23].

Abbreviations: RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

### Table 3. Agreement by RT-PCR for SARS-CoV-2 RNA Between Self-Collected Saliva and Anterior Nasal Swab Specimens in Traditional Transport Media vs Inactivating Transport Media From Participants Enrolled in a Case-Ascertained Household Transmission Study of SARS-CoV-2—Nashville, TN, April–November 2020

| Subjects | Negative Agreement | Positive Agreement | Observed Agreement, % | McNemar P Value | Kappa (95% CI) |
|----------|--------------------|--------------------|-----------------------|-----------------|----------------|
| Traditional transport media Overall (n = 77) | 390/814 (47.9) | 234/814 (28.7) | 76.7 | <.001 | 0.5 (0.5 to 0.6) |
| Children (n = 13) | 71/129 (55.0) | 29/129 (22.5) | 77.5 | <.001 | 0.5 (0.4 to 0.7) |
| Adults (n = 64) | 319/685 (46.6) | 205/685 (29.9) | 76.5 | <.001 | 0.5 (0.5 to 0.6) |
| Index (n = 31) | 72/322 (22.4) | 136/322 (42.2) | 64.6 | <.001 | 0.3 (0.2 to 0.4) |
| Contacts (n = 46) | 318/492 (64.6) | 98/492 (19.9) | 84.6 | <.001 | 0.6 (0.5 to 0.7) |
| Presence of symptoms Contuously asymptomatic (n = 17) | 136/177 (76.8) | 18/177 (10.2) | 870 | <.001 | 0.5 (0.4 to 0.7) |
| Presymptomatic (n = 19) | 61/70 (87.1) | 3/70 (4.3) | 91.4 | >.99 | 0.5 (0.2 to 0.7) |
| Postillness (n = 37) | 98/200 (49.0) | 38/200 (19.0) | 68.0 | <.001 | 0.4 (0.2 to 0.5) |
| Symptomatic (n = 60) | 95/367 (25.9) | 175/367 (47.7) | 73.6 | <.001 | 0.5 (0.4 to 0.6) |
| Inactivating transport media Overall (n = 155) | 907/1721 (52.7) | 496/1721 (28.8) | 81.5 | <.001 | 0.6 (0.6 to 0.7) |
| Children (n = 36) | 248/419 (59.2) | 100/419 (23.9) | 83.1 | .635 | 0.6 (0.5 to 0.7) |
| Adults (n = 119) | 659/1302 (50.6) | 396/1302 (30.4) | 81.0 | <.001 | 0.6 (0.6 to 0.7) |
| Index (n = 58) | 170/629 (27.0) | 259/629 (41.2) | 68.2 | <.001 | 0.4 (0.3 to 0.4) |
| Contacts (n = 97) | 737/1092 (67.5) | 237/1092 (21.7) | 69.2 | .519 | 0.7 (0.7 to 0.8) |
| Presence of symptoms Contuously asymptomatic (n = 40) | 409/455 (89.9) | 8/455 (1.8) | 91.6 | .074 | 0.3 (0.2 to 0.3) |
| Presymptomatic (n = 24) | 38/65 (58.5) | 21/65 (32.3) | 90.8 | .221 | 0.8 (0.6 to 1.0) |
| Postillness (n = 75) | 222/420 (52.9) | 83/420 (19.8) | 72.6 | .005 | 0.4 (0.3 to 0.5) |
| Symptomatic (n = 110) | 238/781 (30.5) | 384/781 (49.2) | 79.6 | <.001 | 0.6 (0.5 to 0.7) |

Negative agreement refers to the proportion of paired samples that had no detected infections by either specimen type. Positive agreement refers to the proportion of paired samples that had detected infections by both specimen types. Observed agreement refers to the proportion of paired samples that had positive or negative agreement between specimen types.

Interpretation of the Kappa statistic for agreement: ≤0 = poor; 0.01–0.20 = slight; 0.21–0.40 = fair; 0.41–0.60 = moderate; 0.61–0.8 = substantial; and 0.81–1 = almost perfect [23].

Abbreviations: RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
these cases and quarantine of their close contacts. Additionally, saliva may be particularly useful in longitudinal field studies that strive for identification of both symptomatic and asymptomatic SARS-CoV-2 infections.

We also observed that there were increased detections when self-collected ANS specimens were placed in inactivating transport media that was stable at room temperature compared with traditional transport media kept under refrigerated conditions. We postulate that the requirement for refrigeration and the time interval for transportation of specimens to the laboratory could have impacted specimen integrity and the performance of self-collected ANS specimens kept in traditional viral transport media. While inactivating transport media reduce risk of contamination during handling and transporting specimens [29] and allow detailed virus characterization through sequencing, their use precludes the ability to isolate the infectious virus for further study. Of note, there are different inactivating transport media alternatives, and consideration of media selection should include compatibility with the requirements of downstream testing platforms.

This study has several important strengths. First, the design and intense daily follow-up of the household contacts allowed collection of a number of sequential specimens quickly after exposure and disease onset. This is in contrast with other studies that rely on single sets of specimens, often collected several days after disease onset. Second, our study allowed characterization of agreement and performance during different periods of the natural course of infection, including days with and without symptoms. Furthermore, by using paired samples for our comparisons, we minimized the influence of other factors that may influence viral detections. Third, we examined a large number of self-collected specimens, providing good precision for our estimates and enabling study of planned subgroups. Fourth, testing followed previously described protocols [22].

Our study has several limitations. First, because of the pandemic, specimens were self-collected by study participants and included ANS and SA specimens, but nasopharyngeal swabs were not collected. Nevertheless, previous studies have shown that self-collection of respiratory specimens for SARS-CoV-2 detection provides a reliable alternative [30]. Second, our estimates of the proportion of infections identified by each specimen type were derived from a composite reference, given the absence of a reference standard for identification of viral infections in our study [11]. Third, we compared viral detections based on molecular identification of viral genetic material, but viability of viruses in the specimens was not directly evaluated. Fourth, our measures of symptoms were based on daily self-report, which may be subject to misclassification [31]. Fifth, while we provided consistent instructions for self-collection of saliva samples, the collected volume was variable, and some samples were supplemented with phosphate-buffered saline to facilitate extraction due to low volume and/or viscosity challenges, which may have diluted some samples and interfered with detections. Lastly, given that paired samples were not tested in parallel, the use of different testing platforms and specimen differences, we only used Ct values to define detections [22] but did not examine Ct value distributions or differences in viral loads between specimen types.

Taken together, these findings demonstrate that self-collection of SA specimens provides an alternative to ANS (especially to those self-collected in traditional transport media) for identification of both symptomatic and asymptomatic SARS-CoV-2 infections that is practical, noninvasive, and less burdensome in field studies and for COVID-19 testing and control strategies.

**Supplementary Data**

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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*Disclaimer.* The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the US Centers for Disease Control and Prevention. Names of specific vendors, manufacturers, or products are included for public health and informational purposes; inclusion does not imply endorsement of the vendors, manufacturers, or products by the Centers for Disease Control and Prevention or the US Department of Health and Human Services.

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