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Home Sample Self-Collection for COVID-19 Patients

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Real-time reverse transcription-polymerase chain reaction (qRT-PCR) using specimens collected from nasopharyngeal and/or oropharyngeal swabs is the standard screening approach for coronavirus disease 2019 (COVID-19). While PCR is rapid and highly accurate, it requires costly laboratory equipment and healthcare professionals that limit its use for large-scale screening of mild or asymptomatic patients. Self-collection kits for use in the home could remedy this and have consequently received great attention. In April, 2020, a self-collection kit from LapCorp was the first such kit to be approved by the FDA. In the following month, May 2020, another kit developed by Everlywell received FDA approval, and more kits are evidently on their way to the market in the United Kingdom and elsewhere. Because these home-based, self-collection kits are easy to use and may be more acceptable for patients, they provide a superior screening option for mild or asymptomatic patients under self-quarantine. These kits conserve personal protective equipment and healthcare manpower already in short supply. The primary issues affecting the efficacy of this approach are the potential for inappropriate sampling and insufficient clinical examination. A detailed review of the commercially available kits currently available is provided and their prospective impact is noted during the current pandemic.

1. Introduction

The novel coronavirus, coronavirus disease 2019 (COVID-19), that began in China in December 2019 has spread globally, causing 30.4 million confirmed cases and more than 950 000 deaths worldwide as of September 19th, 2020. COVID-19 screening tests fall into two primary categories: 1) antibody testing; and, 2) PCR-based tests. Antibody tests detect antibodies (IgM, IgA, IgG, or total antibodies) in a blood sample; a positive result indicates a possible previous COVID-19 infection. Samples for this test are usually obtained via finger prick or blood draw by healthcare professionals. However, because seroconversion requires time and is host-dependent, the test may not detect antibodies in patients currently infected with COVID-19 virus.[1,2] Therefore, this test should not be used as a standalone tool to diagnose current infection, but it can be used in combination with other tests. PCR-based tests, a more direct assessment than antibody-based testing, detect the presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral RNA in patients currently afflicted.[3,4] When sampling is properly carried out, PCR testing can be highly accurate.[5] The US Centers for Disease Control and Prevention (CDC) currently recommends the collection of an upper respiratory tract specimen for diagnosing COVID-19, but test specimens from the lower respiratory tract are an option. The common sampling sites and techniques include the nasopharynx, oropharynx, nostril, oral cavity, and respiratory tracts by swabs, wash, and bronchoalveolar lavage.[6]

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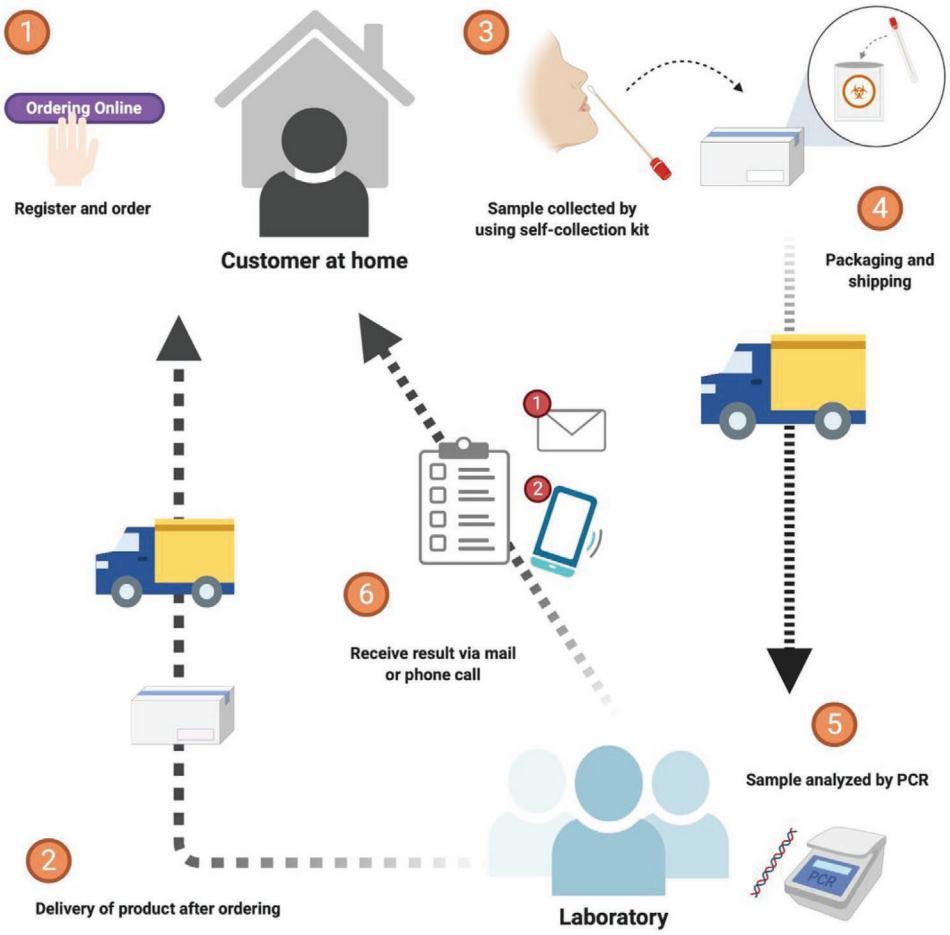

Figure 1. Procedure for self-collection kit approved by the FDA.

Certain sampling methods are technically challenging and should be conducted by healthcare providers, but direct contact with patients places them at high risk of infection despite their use of personal protective equipment (PPE). Moreover, rising COVID-19 cases and high demand for diagnostic tests have led to a shortage of PPE. These factors prompt the development of a platform that is easy to use and distribute for asymptomatic and pre-symptomatic cases. Accordingly, home-based self-collection kits for COVID-19 screening, which have recently been approved for Emergency Use Authorization (EUA) by the FDA, appear to be a reasonable alternative to sampling methods that place demand on healthcare professionals and an already burdened healthcare system. Thus, in this review, we will provide details regarding home-based self-collecting COVID-19 screening tests and provide our perspectives on their possible role(s) during the existing pandemic.

2. Current Progress of Home-Based Self-Collection Test for COVID-19

Thus far, the FDA has issued EUA to two COVID-19 home tests developed by LabCorp,[7] Everlywell,[8] Quest Diagnostics,[9] PrivaPath Diagnostics[10] and Clinical Reference Laboratory.[11] Protocol schematics for both are provided in **Figure 1**. In brief, subjects must first register and complete an online eligibility screening questionnaire before placing a test kit order. The online system not only assesses whether the subjects are suitable, it prevents intentional hoarding. The preferred subject for testing with these self-collecting kits are those who have been exposed to a potential source of infection or have "mild" symptoms, including a fever below 102° Fahrenheit, flu-like symptoms, recent loss of taste or smell, cough or sore throat, and shortness of breath that doesn't limit talking. Both of these home tests request specimen collection from both anterior nares, but not a deep-nostril sample, using a nasal swab. Of note, LabCorp especially advocates the use of Q-tip-like swabs, designed by U.S. Cotton, which are FDA approved and are fully synthetic for COVID-19 testing compatibility. Other companies, such as Private Harley Street[12] and Blue Horizon Medicals[13] in the United Kingdom, also provide COVID-19 home test kits. However, unlike those from LabCorp and Everlywell, these kits ask for samples to be collected by repeatedly brushing the throat, posterior pharynx, and tonsillar areas, and then wiping two nostrils (anterior nostril only) one by one. Interestingly, the same swab is supposed to be used for collecting from each of the sample sites, including the nostrils and the mouth, but not from the tongue. The swabs will are subsequently processed and

shipped overnight to the company laboratory for SARS-CoV-2 viral RNA detection by PCR. The packaging process is supposed to comply with UN 3373, which covers packaging, labelling and shipping regulations for category B infectious substances.[14] Results are provided to test subjects via E-mail, apps, or phone within 3 days. Subjects that test positive are asked to inform their healthcare provider for further clinical examination.

3. What Should We Expect from These Home-Based Self-Collection Tests for COVID-19?

While these home-based self-collection kits offer several advantages (**Table 1**), the seemingly appealing approach of home testing comes with certain features that may undermine its usefulness. Indeed, as mentioned previously, the kits provided by LabCorp and Everlywell specifically request the collection of specimens from anterior nares. It should be noted that, unlike the nasopharynx, oropharynx, or the respiratory tracts, where the secretions from mucous epithelial cells may contribute to the accumulation of viral RNA, the anterior nares can be quite arid.[3] The detection rates of each specimen type differ from patient to patient and may vary with each patient's course of illness.[1] In addition, although RT-PCR analysis can be highly accurate, inappropriate sampling may lead to false negatives. For example, misunderstanding or ignoring the instruction details can lead to sample contamination or insufficient collection. On the other hand, the kits from the Private Harley Street and Blue Horizon Medicals request specimen collection from multiple sites covering oral and nasal cavities using the same swab. Although the instructions do not specify the reasons for such multiple collections, it is speculated that they increase the likelihood of proper sampling. Indeed, relevant studies have reported that a combination of oropharyngeal/nares swab serves as a suitable alternative to nasopharyngeal swabbing, with 91.7% and 94.4% sensitivities, respectively.[15] Meanwhile, these kits prohibit nasal swabbing deep into the nostril, likely because this procedure is very technique-sensitive and potentially dangerous for non-professionals. Moreover, individuals with mild symptoms are the preferred subjects for testing. Because the viral loads of asymptomatic or presymptomatic patients are lower than those with severe symptoms, the accuracy of these home-based self-collection kits may be compromised. Accordingly, an effective collection verification system or guidance, for example, an indicator on the swab to reveal sufficient capture of SARS-CoV-2 nucleic acid, is much needed.

4. What Can We Learn from the Past?

Although laboratory validations of self-collected samples have shown reasonable concordance with healthcare staff collection,[16] it is not clear whether these home-based self-collection kits are of value for COVID-19 screening as specificity and sensitivity for SARS-CoV-2 has not been systemically reported. However, since these kits are mostly based on nasal swabbing, it is worth reviewing the efficacy of nasal swabbing as the primary method for sampling compared to nasopharyngeal swabbing, with an emphasis on the difference in infectivity among distinct viruses. The primary feature that distinguishes nasopharyngeal swabbing from nasal swabbing are the collection sites, the nasopharynx and the nares, respectively. Notably, several previous studies have examined viral infection

Table 1. Differences between self-collection and healthcare professional inspection protocol.

	Self-collection	Healthcare professionals inspection protocol
Age restrictions	1. Private Harley Street Clinic: No 2. Everlywell: 18 years and older	Infants and some older patients not allowed
Material of swab	Cotton swab, Q-tip–like swab	Polyester swab with a plastic shaft swab, sterile Dacron/nylon swab
Testing timing	Test when you think you may have COVID-19 symptoms or between 1 and 5 days after the onset of symptoms	
Sample diagnostic method	Reverse transcriptase-polymerase chain reaction (RT-PCR)	
Sample collection place	1. LapCorp: entire inside edge of the nostril (insert just until the cotton tip of the swab is no longer visible) 2. Everlywell: insert the swab into the nostril, parallel to mouth, about 2–4 cm until resistance is met. 3. Quest Diagnostics: insert the swab into the nostril 4. PrivaPath Diagnositcs: insert the swab into the nostril 5. Clinical Reference Laboratory: individual's saliva be deposited in a collection vial provided. 6. Blue Horizon Medicals: Mouth (Include Tonsile, posterior wall, and Uvula) and nostril (about 2 cm deep) 7. Private Harley Street Clinic: posterior pharynx and tonsillar areas (avoid tongue) and nostril (about 2 cm deep) 8. Right-angled: back of throat How to ensure proper specimen collection: When you collect the specimen from the throat, gagging is necessary. (Everlywell)	Nasopharyngeal: Insert into nasal meatus until reaching the nasal palate, stay for 15 to 30 s and rotate 3–5 times Oropharyngeal: bilateral tonsils and the posterior pharyngeal wall (avoid touching tongue and oral mucosa)

Table 1. (continued).

	Self-collection	Healthcare professionals inspection protocol
Sample preservation way	Collection tube (with 2–3 mL viral preservation medium or sterile saline)	
Sample delivery	About 2–3 days by Express delivery (EX: FedEx, DPD) or Post	No long-term delivery process, but sample should be stored at 4°C and submitted to the laboratory within 2 h. If a delay in testing or shipping is expected, store specimens at –70 °C or below.
Price (Per test)	USA • LapCorp: $ 119 USD • Everlywell: $ 109 USD • Quest Diagnostics: $ 119 USD • PrivaPath Diagnotics: $119 USD • Clinical Reference Laboratory: $175 USD UK • Blue Horizon Medicals: £199 • Private Harley Street Clinic: £250 + £15 delivery • Rightangled: £140	>$500 USD
Result received time	About 1–3 days (after your specimen has been received by the lab)	Within 3 days but it can take longer

detection efficiency using specimens collected from the nasopharynx versus the nares. For example, Irving et al. compared the detection rate of these two sampling sties for diagnosing influenza by PCR and showed a similar sensitivity between nasal swabbing (89%) and nasopharyngeal swabbing (94%).[17] Another study observed good agreement and high detection rates between different swabbing sites for detecting human respiratory syncytial virus in children.[18] A more recent study from Tu et al. found that the detection rates of SARS-CoV-2 using nasal and mid-turbinate samples were 94% and 96.2%, respectively. They also found high correlations with cycle threshold values for nasopharyngeal samples.[19] Kojima et al. also examined the SARS-CoV-2 detection sensitivity using specimens of self-collected oral fluid, nasal swabs, and clinician-collected nasopharyngeal samples.[20] Despite the limited sample size, this study showed that the differences in detection rate between clinician-supervised, self-collected oral fluid, nasal swab specimens, and clinician-collected nasopharyngeal swab specimens were minimal. Taken together, these studies support the use of nasal swabs; however, more studies focusing on COVID-19 detection are needed to establish a definitive conclusion.

5. Current Usage of These Self-Collection Tests

Regarding the current applications of these kits around the world, the detailed numbers of each kit were not easily assessible due to confidentiality. In general, each brand of the home self-collection kit reached 10 000 tests per day and is anticipated to increase. In the USA, a total of 185 participants were enrolled; compared with the clinician swab, the sensitivity and specificity of the home swab were 80.0% (95% CI, 63–91%) and 97.9% (95% CI, 94–99.5%), respectively.[21] The home self-collection kits have presented several advantages, including accessibility outside of the health care system and minimizing personal protective equipment use. This kind of kit is safe and scalable in the pandemic setting, and the home-based strategy should be targeted toward individuals early in illness, when risk of transmission is highest and care seeking less likely.

6. Conclusion

Home-based self-collection of specimens for COVID-19 screening is less invasive, more acceptable, and suitable for

Table 2. Pros and cons of self-collection test.

Advantage	Disadvantages
1. Alleviate the work of medical staff. 2. Collect the specimen by yourself, thus can avoid direct contact between medical staff and symptomatic people, and reduce the risk of cross-infection. 3. Free up more personal protective equipment. 4. Compared to standardized swabbing methods, self-collection is less invasive and more comfortable. 5. Alternative screening method in some places without sufficient medical personnel and resources 6. Receive reports without going to the hospital and avoid potential infection spread.	1. Without professional training, there is no guarantee that enough specimen has been collected, which may lead to false negative results. 2. Inappropriate shipping may influence sample quality. 3. A possible disease transmission pathway.

large scale testing. Thus, although the usefulness for COVID-19 screening has not been comprehensively evaluated, the FDA has approved its EUA use in April. One of the contributions provided by self-collection is a preservation of manpower and resources that can be used for those in greater need. Moreover, self-collection of specimens not only protects medical staff from direct exposure to potentially infected patients but also reduces the risks of transmitting the virus within hospitals. The reduced cost compared to that associated with hospital or health center visits may further increase screening accessibility. However, there are still several limitations to self-collection kits (summarized in the **Table 2**). For example, it is more likely to obtain insufficient or inappropriate specimens without professional training. Further, suboptimal conditions (such as leaks in packaging or improper storage temperatures) during shipping may also affect test results. Moreover, contamination of the package is another concern, as this will produce a new pathway for disease transmission if disinfection and cleaning are not properly carried out before and after the sampling process. Hygeiatouch has developed the RFID-based tracking system to potentially solve these issues. Nonetheless, these kits are still of great value and may have an impactful role during the current pandemic.

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Conflict of Interest

The authors declare no conflict of interest.

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