verily Covid-19 Testing

Multiple sample collection methods are available for COVID-19 testing. Here are some of the pros and cons of each option.

Introduction

Efforts to enact widespread testing for the COVID-19 pandemic have stressed the supply chain for critical materials needed for the collection, storage and processing of patient specimens. Specifically, severe shortages of swabs for nasopharyngeal (NP) sample collection, personal protective equipment (PPE) for healthcare professionals (HCP) administering collections, and reagents for stabilizing and transporting specimens threaten to hinder increased COVID-19 testing. To mitigate these supply constraints, and to better prepare for future surveillance testing of recurrent outbreaks, alternative testing workflows require continuous re-evaluation Here, we broadly review the most common collection options being used for COVID-19 testing and assess which methods best meet Verily's testing requirements.

Collection Methods

Multiple collection methods exist for obtaining patient samples for diagnostic viral testing. These methods differ in their ability to recover viral particles, which directly impacts the sensitivity of the tests. They also differ in their ease of administration, which often limits where and how the collections can be performed. Because of these variables, Verily has assessed a number of collection approaches in order to choose the most suitable options for any of a number of testing scenarios.

Nasopharyngeal (NP)

NP specimens such as NP swabs and NP aspirates are universally accepted as the diagnostic specimens of choice for any viral respiratory infection due to the high viral loads typically present in the nasopharynx. To collect the specimen, the swab is inserted through the nostril and pushed into the nasopharynx. Despite being the standard for high viral recovery, the collection of NP specimens are relatively invasive and require trained HCPs in full PPE to obtain samples with specialized swabs. This requirement for HCP collection makes them incompatible for home collection and less than ideal for high volume collection processes.

NP aspirates are commonly collected in children <5 years old and are done by instilling 1-1.5 mL of 0.9% sodium chloride into the nostril parallel to the palate, followed by collection of the sample using a catheter. Although this results in high viral recovery, the process is unpleasant and not commonly used, as the sensitivity of swab collected specimens is often more than sufficient [1].

Oropharyngeal (OP)

Similar to NP specimen collection, OP requires trained HCPs in full PPE to obtain samples. OP

sampling is considered easier to perform than NP and is done by placing the swab through the mouth toward the rear wall of the oropharynx. While easier to administer, there is still some question about whether OP collection has the same sensitivity as NP collection when testing for SARS-CoV-2 [2]. Like NP collection, the requirement of an HCP for administration also limits its use.

Mid-turbinate (MT)

MT specimen collection can be self-collected and thus has many logistical benefits over NP and OP specimen collections in terms of large-scale screening, while demonstrating sensitivity comparable to NP specimens for SARS-CoV-2 [3]. To collect the sample, an individual places the swab into the nostril all the way up to the collar on the MT swab, or about 2 cm into the nostril, until resistance is met at turbinates. While MT specimen collection is considered somewhat unpleasant by some individuals, it is significantly more tolerable than either NP or OP collections. It is compatible with self administered collection, typically under the supervision of a healthcare provider. This makes it amenable to high volume testing sites where self administration can reduce the numbers of HCPs required, reduce PPE requirements, and speed up the collection process. It may not be amenable to home collection due to the necessity of a HCP's oversight to facilitate proper collection.

Refer to Verily's white paper "Emerging evidence supports patient-collected mid-turbinate nasal swabs as a practical alternative to nasopharyngeal swabs for COVID-19 testing" for additional details.

Anterior nares (Nasal)

Anterior nares specimen collection does not require trained HCPs and can be easily self-collected with minimal to no discomfort. A swab is used to collect this sample by inserting the tip of the swab into one nostril. The tip is Inserted just until the swab is no longer visible and then the swab is rotated in a circle around the entire inside edge of the nostril. The most extensive comparison to date between NP and nasal sampling for SARS-CoV-2 comes from a recent clinical study of 533 patients using self-collected nasal samples. In this clinical study, the sensitivity of virus detection as compared to the corresponding NP sample was 94.0% (95% CI: 84.6-100.0) and the respective Ct values also demonstrated a high correlation [3]. Because of the ease of administration and high sensitivity to SAR-CoV-2, nasal swabbing is becoming a sample of choice for both unsupervised at home collections and HCP supervised collections sites.

Nasal wash, also referred to as nasal aspirate, should only be collected by trained HCPs. A typical procedure is to flush ~5 mL of 0.9% sodium chloride into the nasal space and then the liquid is collected into a dish. No swabs are needed for this procedure, but the need for HCPs in full PPE makes this method less practical for large-scale deployment.

Saliva

The term saliva specimen is used to describe multiple specimen collection methods. A more descriptive term for the saliva specimen most commonly used to test for SARS-CoV-2 is posterior oropharyngeal saliva (POPS) or "deep throat saliva" and should not be confused with saliva straight from the salivary glands which tend to have lower sensitivity for respiratory viruses [4]. Lower respiratory tract specimen (sputum) is also often grouped in with the term saliva, and only when possible to collect is it recommended by the CDC.

Saliva collection is one of the simplest specimens for individuals to self-collect and in addition it has been used successfully for past respiratory virus detection and therefore is a logical specimen to consider for SARS-CoV-2 detection. While studies are still limited, viral RNA has consistently been

found in the saliva of patients confirmed to have been infected with SARS-CoV-2 [4].

Figure 1. Whatman Indicating FTA Micro Card. Sample area changes from pink to white upon sample collection.

Saliva samples can also be collected using Whatman FTA cards, a filter paper product manufactured by GE Healthcare (**Figure 1**). Samples are collected by having the patient simply spit on the card which act to stabilize and preserve the viral RNA for transport and testing [5]. While there are currently no published studies using FTA cards for SARS-CoV-2 collection and testing, a number of previous studies have demonstrated their efficacy for viral RNA inactivation, preservation, and processing [6].

While viral loads may be lower in saliva samples than in NP swabs, the ability to detect SARS-CoV-2 in patients may be comparable based on early trials, in part due to not needing to dilute samples with viral transport media [4]. The ease of self collection without the requirement of a trained HCP makes saliva collection appropriate for use in situations where an HCP can not be present and is currently being investigated by Verily as a potential collection methodology.

Swab Designs

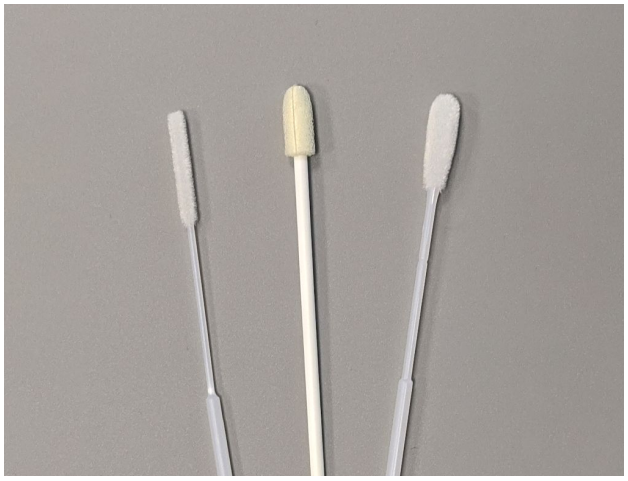

Figure 2. Representative image of swab designs. From left: a flocked, minitip swab suitable for NP sampling; a foam swab for AN sampling; and a flocked swab for AN sampling.

NP, OP, MT, and nasal swabs are tailored for the specific type of specimen collection and, therefore, come in a wide variety of designs.

Generally speaking, NP swabs are the most complex, requiring the most stringent design tolerances due to the specimen location on the rear wall of oropharynx. NP swabs have a narrow, flexible shaft often made of plastic with a carefully designed tip (often made of thin foam, cotton, polyester, flocked nylon, or some other porous/reticulated material) that absorbs and retains fluid while minimizing discomfort to the patient.

OP swabs are designed similarly to NP swabs and are used to reach the posterior pharynx and tonsillar areas.

MT swabs often contain a collar/stopping-point that prevents the tip from entering past the

mid-turbinates of the nasal cavity. In general, swabs are around 2 inches in length and are often flocked and tapered, designed to reach 1 inch inside the nose.

Anterior nares (nasal) swabs are the least restrictive in design and are generally flocked, spun polyester or foam swabs designed to reach 0.5 inches inside the nostril by pressing firmly against the nasal membrane for 10-15 seconds in each nostril. Due to the ease of self collection without the requirement of a HCP, nasal swabs are appropriate for use in situations where a HCP cannot be present. Nasal swabs are currently being investigated by Verily as a potential collection methodology.

The CDC and FDA do not recommend the use of calcium alginate swabs, swabs with wooden shafts, or rayon swabs as they may not be compatible with all molecular testing platforms [8]. Verily thoroughly tests all potential swabs for any potential testing inhibition.

Swab Suppliers and Availability

As of August, 2020, a number of large scale swab manufacturers remain supply constrained due to overall high demand and FEMA contracts. Verily is working with a number of manufacturers with stable supply capabilities in order to ensure availability of swabs applicable to all collection methods that can be used in accordance with FDA authorizations and CDC guidance.

Collection Storage Media

The FDA has published guidance that swabs should immediately be placed into a sterile transport tube containing 2-3mL of either viral transport medium (VTM), Amies transport medium, or sterile saline solution, unless using a test designed to analyze a specimen directly, (e.g., without placement in VTM), such as implemented in some point-of-care test formats. Although no general authorization for other transport media has been established by the FDA, many alternatives such as saline, PBS, and sterile water are being evaluated by Verily.

Regulatory Guidance

Currently the FDA issues authorization for unsupervised collection kits for COVID through the EUA process for manufacturers as well as laboratory developed tests. The FDA has authorized at-home collection kits on a case by case basis including Pixel by LabCorp, the Spectrum Solutions LLC SDNA-1000 Saliva Collection Device and the LAMP Diagnostic assay from Color Genomics[9].

On April 29, 2020, the CDC issued guidance removing NP specimens as the preferred choice for SARS-CoV-2 testing, and instead listed NP, OP, MT, nasal, lower respiratory tract specimen (sputum), NP wash/aspirate or nasal wash/aspirate (NW) as acceptable specimens [8].

As with the CDC, the FDA updated their collection guidelines on July 20, 2020 to permit NP, OP, MT, Nasal specimen collections, but with NP specimens still indicated as the preferred choice [10].

Summary

In the interest of public health which requires an increase in the scale of testing locations across the country, and in light of the current supply limitations, Verily supports the use of multiple collection options as outlined in this paper in accordance with FDA authorizations and CDC guidance.

References

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