EVIDENCE BRIEF
The Use of Alternate Specimen Collection Methods for COVID-19 PCR Testing

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Summary of Findings

While nasopharyngeal (NP) specimens have been the gold standard collection method for COVID-19 PCR testing, combined swab of throat with anterior nares, or deep nasal specimens, are recommended alternatives to NP specimens. Nasal or throat specimens are acceptable alternative specimen collection sites but have shown to be slightly less sensitive compared to NP specimens for COVID-19 PCR testing.

The collection of combined swab of throat with both anterior nares, nasal or throat specimens can be collected by a broader range of health care professionals, patients or parents of children increasing overall accessibility to COVID-19 testing. These should be collected within a clinical setting to ensure appropriate instructions, labelling and transportation to a laboratory for optimal turnaround time.

The literature on the use of saliva as a specimen for COVID-19 PCR testing is rapidly evolving with the most recent literature reporting slightly less but still acceptable sensitivity for the detection of COVID-19 particularly within the first 7 days of symptom onset. There are several laboratories including Public Health Ontario evaluating performance characteristics on using saliva as a specimen collection method for the detection of COVID-19.

It is also important to note that no single test provides 100% sensitivity in the detection of COVID-19. Therefore, a negative test result should be taken into the context with other information including patient’s signs and symptoms as well as potential exposure history.

Background

The COVID-19 pandemic has highlighted the importance of rapid and accessible testing for identification and isolation of patients with COVID-19. The gold standard method of specimen collection is the nasopharyngeal (NP) specimen. Collection of NP specimens is a controlled act that requires a trained health care provider in full PPE, and a change of full personal protective equipment (PPE) between each individual sample collection. The use of trained health care providers is resource intensive both in terms of personnel as well as in PPE and thus potentially limiting widespread access to testing. Staff, PPE, nor NP swabs are in adequate supply for responding to the global pandemic and thus may limit the number of individuals being tested.

The collection of NP specimens can be uncomfortable for patients and thus not ideal for certain populations such as symptomatic children in the outpatient setting or those requiring repeat sampling.
The use of non-NP specimens could potentially increase the availability and acceptability of testing as well as alleviate pressure on limited resources that are currently used to collect NP swabs.

Several studies have evaluated other respiratory specimens including throat, nasal, and saliva for the detection of respiratory viruses, including COVID-19. These specimen types are faster to collect and are generally more comfortable for the patient. In addition, these specimen types are more amenable to collection by a broader range of health care professionals and observed self-collection, reducing pressures on health care staff.

Performance Characteristics of Respiratory Specimen Types for the Detection of SARS-COV-2 (COVID-19)

Several studies have evaluated the performance characteristics of non-NP respiratory specimens including deep nasal, nasal, throat or saliva for the detection of COVID-19, although, the quality of data for recommending non-NP specimens is rapidly evolving. Overall, the sensitivity of non-NP specimens is lower compared to NP specimens but in the acceptable range.

- Several studies compared the performance characteristics of nasal specimens versus NP specimens and found that the sensitivity of nasal specimens for the detection of COVID-19 varied from 82.6% to 100%.\(^1\)\(^-\)\(^5\) The patient setting among these studies varied from hospitalized patients to out-patient settings. Kojima et al. showed that 82.6% (19/23) of deep nasal specimens were detected when compared to positive NP specimens.\(^1\) Of the 4 negative deep nasal specimens, 2 did not have sufficient quantity for testing, while the other 2 were negative by PCR. There were 4 additional deep nasal specimens that were positive for COVID-19 but negative by NP. Similarly, a study reported by Tu et al reported sensitivity of 94% (95% CI: 84.6 – 100) for nasal, and 96.2% (95% CI: 87.7 – 100) for deep nasal compared to NP.\(^3\)

- A study done by Patel et al reported that 95.2% of paired NP and throat specimens yielded concordant results.\(^6\) Using NP specimens as comparator, throat specimens had a specificity of 97.6% (CI: 93.9% -- 99.5%); sensitivity of 81.8% (CI: 59.7% -- 94.8%); negative predictive value of 96.8% (CI: 92.6% -- 98.7%); and positive predictive value of 85.7% (CI: 65.9% -- 94.9%). The study highlighted that sensitivity of NP specimens was comparatively higher in persons tested later in the illness (>7 days of onset of symptoms).

- Saliva as a possible alternative to NP samples has been reported in few studies for COVID-19 testing. The studies showed that sensitivity in saliva samples varied from 69.2% to 97.1% when compared to NP sample.\(^7\)\(^-\)\(^9\) There was considerable variability in patient settings which could have contributed to the wide range of sensitivity.

A recent meta-analysis study calculated sensitivity of the saliva testing to be 91% (CI: 80%—99%) compared to 98% (CI 89% -- 100%) in NP.\(^10\) The studies included in the meta-analysis were reported to have higher heterogeneity in the saliva test compared to NP tests. The authors also found that viral loads were higher in NP tests compared to saliva tests which would affect the sensitivity of the test. The authors concluded that saliva based testing is promising, though more data is needed. A local study involving hospitalized patients showed a significant difference in the sensitivity between NP swab versus saliva (89% versus 72%).\(^12\)
In addition, standardization and subsequent validation of collection, transportation and storage of saliva samples is required across the Ontario Health Provincial Diagnostics Network to ensure that once introduced, saliva samples can be diverted to the closest laboratory critical to optimizing test turnaround time.

- A recent study from Nova Scotia compared the sensitivity of combined throat swab with nares against NP swab for detection of COVID-19 in an outpatient setting.\(^2\) They collected paired samples from 190 individuals that were being tested for COVID-19. Of 36 patients that tested positive for COVID-19 by at least one method, they reported 91.7% sensitivity for throat/nares swab compared to 94.4% for NP swab.\(^2\)

**Conclusions**

The literature on the use of non-NP specimens for COVID-19 testing is rapidly evolving and expanding. The current quality of evidence is low due to small sample sizes reported in each study with varied patient settings.

- Based on these studies, deep nasal specimens, or a combined swab of throat with both nares, are preferred alternatives to NP specimens for COVID-19 testing by PCR, particularly in the ambulatory setting.

- There is evidence to support the use of nasal (both nares) or throat specimens, as acceptable alternatives to NP specimens. The sensitivity of using non-NP specimen, particularly nasal and throat specimens, in some instances may be lower than NP specimens, but overall appears to be within acceptable limits.

- Combined swab of throat with nares and nasal and throat specimens can be collected by a broader range of health care professionals than NP specimens, or can be performed by self-collection (particularly nares). All specimens collected for COVID-19 PCR testing should occur in a clinical setting to ensure appropriate collection instructions and supervision, labelling and transportation to a laboratory for optimal test turnaround times.

- Based on rapidly evolving literature, saliva testing may also be an acceptable specimen type for detection of COVID-19 testing by PCR though. Several laboratories including Public Health Ontario are currently evaluating performance characteristics of saliva for COVID-19 testing including feasibility of implementing into routine testing in the ambulatory testing.

- Regardless of which sample type or collection method, false negative results do occur, and a single negative COVID-19 test result should be interpreted in the context of signs and symptoms of COVID-19, epidemiological links, and other risk factors.


- For detailed information on acceptable specimen types as well as instructions on sample collection, please refer to the Public Health Ontario [Coronavirus Disease 2019 (COVID-19)-PCR information page](https://www.publichealthontario.ca/en/laboratory-services/test-information-index/covid-19).
The implementation of clear pathways for specimen handling, labelling, storage and transportation, and collection devices is critical to the success of expansion to these modalities.

The use of non-NP specimens and patient-collected specimens for COVID-19 PCR are important tools to increase access to testing, and in the case of self-collected specimens in minimizing healthcare worker exposure & conserving PPE.

References


