Science & Technical Advisory | Rōpū Tohutohu i te Pūtaiao me te Hangarau

Kōrero Pūtaiao | Science Chat

Ministry of Health | Manatū Hauora

Testing saliva for detection of SARS-CoV-2

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Summary Points

- Testing nasopharyngeal swabs using reverse transcription polymerase chain reaction (RT-PCR) laboratory assays is the recommended reference standard worldwide for the diagnosis of COVID-19.
- Saliva testing is useful as a screening tool, particularly when frequent testing is required.
- Obtaining a saliva sample is less invasive and can be done without a health professional present, reducing possible exposure to SARS-CoV-2 and the need and cost of PPE (personal protective equipment).
- Avoiding contamination of a saliva sample with food or other substances is important as contamination can affect the ability of the laboratory analysis to detect SARS-CoV-2.
- Saliva testing is being used in selected situations overseas and in New Zealand as a complement to screening for SARS-CoV-2 with nasopharyngeal testing.

Explainer: An ideal test is very **sensitive** (high probability of detecting the disease if present) and very **specific** (high probability that those without the disease will screen negative).

Introduction

Different respiratory sample types can be used in testing to identify SARS-CoV-2, the virus that causes COVID-19. Here we discuss the use of saliva samples as a testing option for SARS-CoV-2 detection.

Different samples but same analytic approach

In general, 'saliva testing' refers to the sample that is collected (saliva), as 'nasopharyngeal testing' refers to the use of nasopharyngeal swabs. Both saliva and nasopharyngeal sample types are tested by nucleic acid amplification tests (NAAT). NAAT encompasses several molecular technologies that take genetic material, such as RNA or DNA, and make hundreds of millions of copies until it is able to be detected by a sensor. As SARS-CoV-2 is an RNA-based virus, the NAAT method often used is reverse transcription polymerase chain reaction (RT-PCR). RT-PCR assays are able to detect extremely small amounts of viral RNA in a sample, so they are highly sensitive and often able to detect viral RNA from asymptomatic individuals or after a person has recovered and is no longer infectious. A more detailed and technical description of the RT-PCR process for SARS-CoV-2 can be found in a Nature article here.

Nasopharyngeal testing: current approach and 'gold standard'

Testing nasopharyngeal swabs by RT-PCR is the recommended reference standard used worldwide for the diagnosis of COVID-19 because of the sensitivity and specificity of this testing approach. This is balanced against the less satisfactory features of invasiveness and some discomfort to the person. Nasopharyngeal swabs by RT-PCR are being used for both diagnostic and screening purposes within New Zealand.

The overall performance for nasopharyngeal swab testing by RT-PCR is very high. One systematic review and meta-analysis pooling estimates from 16 studies reported the sensitivity of nasopharyngeal swab testing by RT-PCR for the detection of SARS-CoV-2 was 85% (95% CI, 77-92%) and estimated specificity 99% (95% CI, 97-100%).

Nasopharyngeal testing is undertaken by health professionals and personal protective equipment (PPE) is required for collection of the nasopharyngeal swab from a person. The swab used is a long, flexible shaft made of plastic or metal and tips made of polyester, rayon, or flocked nylon. The person's head is tilted back and the swab inserted into the nose parallel to the palate to swab the posterior nasopharyngeal wall. An instructional video on nasopharyngeal swab collection is provided by the New England Journal of Medicine here.

Minor complications can occur such as nasal bleeds, and there is potential exposure risk to the virus for the health professional collecting the sample. For such reasons, the use of saliva testing as a supplement to nasopharyngeal sample testing has gained interest.

Saliva samples: collection

Saliva samples can be self-collected without supervision, avoiding possible exposure for healthcare professionals and the need and cost of PPE. It can be done in any location. The collection methods are non-invasive and these 'whole saliva' samples can be collected in different ways (drool, spit, cough, using a swab or a saline wash for example). Different collection methods can impact on the quality of the sample. Saliva testing currently being undertaken in New Zealand uses a drool sample (into a vial which is then sealed and transported to the laboratory).

Saliva samples can sometimes be thick and sticky (viscous), making it difficult for laboratories to handle with existing RNA extraction methods and equipment. Contamination of the saliva sample with food or other substances can also affect the ability to detect SARS-CoV-2. Ensuring a non-contaminated sample is a key practical concern. Current New Zealand protocols where saliva testing is in use instruct the individual to abstain from drinking, cleaning teeth, chewing gum, smoking, or vaping for 30 minutes prior to sample collection.

Saliva testing: diagnostic performance

Several systematic reviews have been published comparing various samples for the detection of SARS-CoV-2 to diagnose COVID-19.

Three systematic reviews pooling estimates from multiple studies reported the sensitivity of saliva testing for the detection of SARS-CoV-2 was 83%, 84%, and 85%. Studies to date have not evaluated the clinical utility of one sample type being collected more frequently versus one less frequently, for example a daily saliva sample compared to a weekly nasopharyngeal sample.

There is varying evidence regarding the amount of viral RNA present in saliva compared to nasopharyngeal samples. Two reviews reported a lower amount of viral RNA present in saliva samples compared to nasopharyngeal samples, although there is evidence the amount of viral RNA could be similar in symptomatic patients. There are a number of reasons why the quantity of viral RNA present in the saliva sample could be variable including: disease status (symptomatic, asymptomatic, pre-symptomatic), severity of disease, saliva collection method and age.

Saliva testing: international use

Internationally, New South Wales, Australia began using regular saliva testing among high-risk professionals as a screening programme in January 2021. The Australian Public Health Laboratory Network (PHLN) statement on use of saliva testing as an alternative sample reports that saliva samples are currently used widely internationally where frequent screening is required, for example for quarantine facility workers. Hong Kong uses saliva testing to screen individuals in their compulsory testing programme, for persons arriving at Hong Kong airport, and among those that consider themselves high risk but who are asymptomatic. Singapore and Taiwan also screen incoming travellers with saliva testing.

Nasopharyngeal swabs are the reference standard and used in testing of symptomatic individuals worldwide. However, the Centers for Disease Control (CDC) in the United States, and the European Centre for Disease Prevention and Control (ECDC) both state saliva samples can be used for symptomatic individuals in situations where there are practical difficulties in obtaining a nasophayngeal swab (e.g. being unable to access a healthcare provider to get tested).

Concluding comments

Saliva sampling can be done easily and frequently as it is less invasive than a nasopharyngeal swab. Saliva sampling appears to be nearly as sensitive as the reference standard nasopharyngeal swabbing for detection of SARS-CoV-2. However, further research is anticipated to confirm this as many studies to date have varied in their approach to saliva collection and laboratory analysis.

The limitations of saliva testing for case detection include the quality of the saliva sample (such as food or smoking contamination of the sample), and disease status. A case could be possibly missed if a poor sample is given or the person is very early in their infectious period. However, this may be offset by increased frequency of saliva testing since it is relatively easy to collect samples and is non-invasive. There have been no studies published to date evaluating this testing strategy.

Using saliva samples that are tested by RT-PCR is not a replacement for the use of nasopharyngeal swabs, especially in a diagnostic setting where a person is only tested once. Saliva samples appear to have practical benefit in a screening programme where an individual has to be repeatedly tested, however. The increased frequency could potentially offset some of the limitations of sample integrity and variable amount of viral RNA present. Additionally, self-collection also limits potential SARS-CoV-2 exposure by health professionals.

In New Zealand, use of saliva samples for detection of SARS-CoV-2 has recently been adopted for limited use as a complementary approach to existing screening programmes using nasopharyngeal swabs.