Evidence check

8 February 2021

Rapid evidence checks are based on a simplified review method and may not be entirely exhaustive, but aim to provide a balanced assessment of what is already known about a specific problem or issue. This brief has not been peer-reviewed and should not be a substitute for individual clinical judgement, nor is it an endorsed position of NSW Health.

Sample types and collection for COVID-19 diagnostic tests

Evidence check question

Q1. Does COVID-19 diagnostic test performance vary according to whether respiratory swabs or saliva samples are used?

Q2. Does COVID-19 diagnostic test performance vary according to whether respiratory swabs are self-collected, or healthcare worker collected?

In brief

Q1. Test performance of saliva compared with respiratory swabs in reverse transcription polymerase chain reaction (RT-PCR) nucleic acid tests.

- Systematic reviews and meta-analyses have reported that saliva offers sensitivity and specificity for SARS-CoV-2 detection comparable to that of the current standard of nasopharyngeal and throat swabs and is a promising alternative for COVID-19 diagnosis.(1-5) Another meta-analysis reported that diagnostic tests based on salivary specimens are somewhat reliable, but relatively few studies have been carried out and such studies are characterised by low numbers and low sample power.(6)
- Generally, across individual studies there was high agreement between saliva samples and respiratory swabs. There were discrepancies in some studies where only saliva or respiratory swabs were positive.(7-43) The methodological quality of included studies varied.
- The overall mean viral load in saliva samples was lower in some studies.(7, 26) A scoping review concluded no significant difference in viral loads.(44)

Q2. Self-collected versus healthcare worker collected respiratory swabs.

- Self-collected samples for SARS-CoV-2 RT-PCR is a potential strategy to reduce the burden of sample collection, save resources, and reduce the risk of exposure to healthcare workers.(45)
- A review from Alberta Health Services reported a study of 530 participants comparing self-swabbing to healthcare worker collection of nasopharyngeal swabs as a gold standard The sensitivity for detecting SARS-CoV-2 in patient collected tongue, nasal, and mid-turbinate samples was 89.8%, 94.0% and 96.2%, respectively.(45)

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- Since the publication of this review, studies have found that generally, there is substantial agreement between self-collected swabs and swabs collected by healthcare workers. In some studies however there was greater sensitivity in healthcare worker collected samples while in others there was greater sensitivity in self-collected samples.(46-50)
- No sample method or specimen type could detect SARS-CoV-2 infections among all positive participants.(46, 48)

Limitations

Studies published as pre peer review articles have not been included in this review.(51-53) Synthesis of the findings is difficult because of variation in:

- testing protocols
- the definition of a 'saliva sample' is not uniform and the sampling technique would vary from study to study.
- changes in test sensitivity depending on the time since symptom onset
- technical details such as RNA extraction methods (which is not uniform across studies) and the number of PCR cycles
- the lack of longitudinal data of saliva viral content including different viral loads and excretion rates in the disease course.

Behavioural responses to self-collected test results, including potential variation in acting upon and reporting results to public health officials, are not explored in this review. The value of saliva and self-collect sampling may be in the encouragement of ongoing high frequency testing, but studies about the benefit of this have not been extensively studied or reported.

Background

COVID-19 presents important diagnostic challenges. Rapid, point of care testing, saliva samples, and self-collection of swabs have the potential to allow earlier detection of SARS-CoV-2 infection.

There is some evidence that inadequate nasopharyngeal sampling performed by untrained operators in the presence of nasal obstruction can be a relevant case of false-negative findings at RT-PCR.(54, 55)

The presence of SARS-CoV-2 in saliva is evaluated in the peer reviewed literature. In a published letter reporting results of a meta-analysis, the positive rate of saliva for the detection of 2019-nCoV by RT-PCR ranged from 25% to 100%.(56) Collecting saliva in the morning has been identified as a factor to maximise yield.(57) New mouth rinse and gargle sample collection has started to be rolled out in British Columbia, Canada to make testing easier for school age children.(58)

Methods (Appendix 1)

PubMed and google searches were done on the 6 November 2020. Alberta Health services have published a rapid evidence review on self-collected respiratory swabs which included studies published up to 15 July 2020, so studies published after this date were included in question two. Four recent systematic reviews and meta-analysis that were published after the 6 November 2020 search date were added to the results table on the 8 February 2021. Individual studies published past the 6 November 2020 were not included.

Results

Table 1 Test performance of saliva samples

Source	Summary
Peer reviewed sources	
Comparison of Saliva and Nasopharyngeal Swab Nucleic Acid Amplification Testing for Detection of SARS-CoV-2: A Systematic Review and Meta-analysis Butler-Laporte, et al. 2021 (4)	• Systematic review and meta-analysis. • MEDLINE and medRxiv was searched on August 29, 2020. • 16 studies included, 8 peer-reviewed and 8 preprints (5922 unique patients). • In the primary analysis, the saliva NAAT pooled sensitivity was 83.2% and the pooled specificity was 99.2%. • The nasopharyngeal swab NAAT had a sensitivity of 84.8% =and a specificity of 98.9%. • Conclusion: saliva NAAT diagnostic accuracy is similar to that of nasopharyngeal swab NAAT.
The Sensitivity and Costs of Testing for SARS-CoV-2 Infection With Saliva Versus Nasopharyngeal Swabs : A Systematic Review and Meta-analysis Bastos, et al. 2021 (3)	• Systematic review and meta-analysis. • Embase, Medline, medRxiv, and bioRxiv were searched from 1 January to 1 November 2020. • Review included 37 studies with 7332 paired samples. • Against a reference standard of a positive result on either sample, sensitivity of saliva was 3.4 percentage points lower than nasopharyngeal swabs. • Among persons with previously confirmed SARS-CoV-2 infection, saliva's sensitivity was 1.5 percentage points higher than nasopharyngeal swabs. • Among persons without a previous SARS-CoV-2 diagnosis, saliva was 7.9 percentage points less sensitive. • Conclusion: Saliva sampling seems to be a similarly sensitive and less costly alternative to nasopharyngeal swabs.
Performance of Saliva, Oropharyngeal Swabs, and Nasal Swabs for SARS-CoV-2 Molecular Detection: A Systematic Review and Meta-analysis Lee, et al. 2021 (5)	• Systematic review and meta-analysis. • PubMed, Google Scholar, medRxiv, and bioRxiv (last retrieval October 1st, 2020) were searched for comparative studies of alternative specimen types. • 46 studies met the inclusion criteria and included 25 studies on saliva, 11 on nasal swabs (NS), 6 on oropharyngeal (OP) and 4 on oropharyngeal/nasal swabs. • Three specimen types captured lower percent positives compared with nasopharyngeal swabs [NS (82%, 95% CI: 73-90%), OP (84%, 95% CI: 57-100%), saliva (88%, 95% CI: 81 - 93%)], while

Source	Summary
Peer reviewed sources	
	combined OP/NS matched NP performance (97%, 95% CI: 90-100%). • Conclusion: Nasopharyngeal swabs remain the gold standard for diagnosis of SARS-CoV-2, although alternative specimens are promising.
Relative Sensitivity of Saliva and Upper Airway Swabs for Initial Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Ambulatory Patients: Rapid Review O'Leary, 2021 (59)	• Rapid systematic review. • PubMed, medRxiv, and bioRxiv were searched. • 19 studies were included comprising 21 cohorts. • Seven of these cohorts were incorporated into a meta-analysis which suggested that nasopharyngeal swabs are somewhat more sensitive than saliva samples for the diagnosis of early disease in ambulatory patients, such as in drive-through centres or community health centres. • This difference was modest, and the reduced need for personal protective equipment for saliva sampling may justify the difference.
A direct comparison of enhanced saliva to nasopharyngeal swab for the detection of SARS-CoV-2 in symptomatic patients Procop, et al. 2020 (7)	• Study directly compared matched saliva and nasopharyngeal swabs (NPS) specimens from symptomatic patients suspected of having COVID-19. • An enhanced saliva specimen (i.e. strong sniff, elicited cough, and collection of saliva or secretions) was collected and compared with NPS as the gold standard. • Both specimens were tested with the Centers for Disease Prevention and Control 2019 nCoV real-time RT-PCR diagnostic panel. • 216 patients were included. • There was 100% positive agreement (38/38 positive specimens) and 99.4% negative agreement (177/178 negative specimens). • The one discrepant specimen had the presence of SARS-CoV-2 confirmed in the saliva specimen using an alternate United States Food and Drug Administration emergency use authorisation assay. • The overall mean difference in cycle threshold (CT) values for the positive NPS and saliva specimens was −3.61 (95% confidence interval [CI], −5.78 to −1.44; P = 0.002). • The enhanced saliva specimen performed as well as NPS for the qualitative detection of SARS-CoV-2 in symptomatic patients, although the overall mean viral load in saliva was lower.

Source	Summary
Peer reviewed sources	
Saliva as an alternative specimen for molecular COVID-19 testing in community settings and population-based screening Senok, et al. 2020 (8)	• Participants were 401 adults presenting for COVID-19 testing at a community-based screening facility in Dubai. • RT-PCR amplification of SARS-CoV-2 RdRp and N genes was used. • Of the 401 participants, 35 (8.7%) had viral detection in at least one specimen type. • Both swab and saliva were positive in 19 (54.2%) patients, while 7 (20.0%) patients had swab positive/saliva negative results. There were 9 (25.7%) patients with saliva positive/swab negative result. • Using the swab as the reference gold standard, the sensitivity and specificity of saliva were 73.1% (95% CI 52.2-88.4%) and 97.6% (95% CI 95.5-98.9%) while the positive and negative predictive values were 67.9% (95% CI 51.5-80.8%) and 98.1% (95% CI 96.5-99.0%), respectively.
Mass screening of asymptomatic persons for SARS-CoV-2 using saliva Yokota, et al. 2020 (9)	• NPS and saliva samples from two cohorts of asymptomatic persons (contact tracing cohort and airport quarantine cohort) were compared (n=1,924). • The sensitivity of nucleic acid amplification testing with nasopharyngeal and saliva specimens were 86% (90%CI:77-93%) and 92% (90%CI:83-97%), respectively, with specificities greater than 99.9%. • The true concordance probability between the nasopharyngeal and saliva tests was estimated at 0.998 (90%CI:0.996-0.999) on the estimated airport prevalence at 0.3%.
Saliva is a reliable, non-invasive specimen for SARS-CoV-2 detection Vaz, et al. 2020 (10)	• Conventional vs saliva samples testing in 155 participants. • Samples pairs of NPS and oropharyngeal swab (OPS) and saliva were collected. • The sensitivity and specificity of RT-PCR using saliva samples were 94.4% (95% CI 86.4-97.8) and 97.62% (95% CI 91.7-99.3), respectively. • There was an overall high agreement (96.1%) between the two tests.
Saliva as a diagnostic specimen for detection of SARS-CoV-2 in suspected patients: a scoping review Fakheran, et al. 2020 (44)	• Systematic literature review. • Six databases (PubMed, Scopus, The Cochrane Central Register of Controlled Trials [CENTRAL], Science Direct, Web of Science and Google scholar). • Nine studies included.

Source	Summary
Peer reviewed sources	
	• Most of studies included in this review, reported that there is no statistically significant difference between nasopharyngeal or sputum specimens and saliva samples regarding viral load.
Comparing nasopharyngeal swab and early morning saliva for the identification of SARS-CoV-2 Rao, et al. 2020 (11)	• 217 asymptomatic adult male participants in a COVID-19 quarantine centre who had tested positive for SARS-CoV-2 8-10 days prior isolation. • 160 of the 217 (74%) participants tested positive for COVID-19 based on saliva, NPS, or both testing methods. • The detection rate for SARS-CoV-2 was higher in saliva compared to NPS testing (93.1%, 149/160 vs 52.5%, 84/160, p<0.001). • The concordance between the two tests was 45.6% (virus was detected in both saliva and NPS in 73/160), while 47.5% were discordant (87/160 tested positive for one while negative for the other).
Challenges in use of saliva for detection of SARS CoV-2 RNA in symptomatic outpatients Landry, et al. 2020 (12)	• NPS and paired saliva samples were prospectively collected from symptomatic outpatients (n=124). • 35/124 (26.6 %) samples were RT-PCR positive, with 33/35 positive by NPS (sensitivity = 94.3% (95% CI 81.4-99.0%)) and 30/35 by pure saliva (sensitivity = 85.7% (95 % CI 70.6-93.7%)). • There was an overall agreement of 117/124 (94.4%). • The median CT value was significantly lower for NPS than for saliva (p=0.0331).
Prospective study comparing deep throat saliva with other respiratory tract specimens in the diagnosis of novel coronavirus disease 2019 Lai, et al. 2020 (13)	• Study prospectively examined 563 serial samples collected during the virus shedding periods of 50 patients. • Deep throat saliva had the lowest overall RT-PCR-positive rate (68.7% vs 89.4% [sputum] and 80.9% [pooled nasopharyngeal and throat swabs]) and the lowest viral RNA concentration (mean log copy/mL 3.54 vs 5.03 [sputum] and 4.63 [pooled nasopharyngeal and throat swabs]).
Alternative clinical specimens for the detection of SARS-CoV-2: A rapid review Comber, et al. 2020 (60)	• Rapid review including 18 comparative studies (12 of which were for saliva). • For saliva-based studies, the proportion of saliva samples testing positive relative to all positive samples in each study ranged from 82.9% to 100%; detection in nasopharyngeal specimens ranged from 76.7% to 100%; positive agreement between specimens for overall detection ranged from 65.4% to 100%. • The overall quality of the studies included within this review was typically low.

Source	Summary
Peer reviewed sources	
Saliva-based testing for diagnosis of SARS-CoV-2 infection: A meta-analysis Kivela, et al. 2020 (61)	• Letter reporting results of a meta-analysis of diagnostic accuracy studies comparing saliva to NPS or OPS. • 14 studies including 5863 patients were included. • Average sensitivity was 0.85 (95% CI 0.77 to 0.91) and average specificity 0.99 (95% CI 0.98 to 1.00) with saliva-based index test compared to NPS or OPS based reference test. • Positive and negative likelihood ratio was 90 (95% CI 35 to 234) and 0.15 (95% CI 0.10 to 0.23), respectively.
Saliva specimens for detection of severe acute respiratory syndrome coronavirus 2 in Kuwait: A cross-sectional study Altawalah, et al. 2020 (14)	• NPS versus saliva samples in large suspected COVID-19 patients in Kuwait. • NPS and saliva samples pairs were prospectively collected from 891 COVID-19 suspected patients. • Of the 891 patients, 38.61% (344/891) were positive for SARS-CoV-2, 4.83% (43/891) were equivocal, and 56.56% (504/891) were negative with NPS by RT-PCR. • For saliva, 34.23% (305/891) were positive for SARS-CoV-2, 3.14 (28/891) were equivocal, and 62.63% (558/891) were negative. • From 344 confirmed cases with NPS samples, 287 (83.43 %) were positive with saliva specimens. • The diagnostic sensitivity and specificity of RT-PCR for the diagnosis of COVID-19 in saliva were 83.43% (95% CI: 79.07-87.20) and 96.71% (95% CI: 94.85-98.04%), respectively. • An analysis of the agreement between the NPS and saliva specimens demonstrated 91.25% observed agreement.
The effect of sample site, illness duration, and the presence of pneumonia on the detection of SARS-CoV-2 by real-time reverse transcription PCR Sutjipto, et al. 2020 (15)	• 105 patients with suspected or confirmed cases of COVID-19. • Of these 105 participants, 73 had active SARS-CoV-2 infection. • Overall, nasopharyngeal specimens had the highest clinical sensitivity at 85%, followed by throat, 80%, mid-turbinate, 62%, and saliva, 38%-52%. • Clinical sensitivity for nasopharyngeal, throat, mid-turbinate, and saliva was 95%, 88%, 72%, and 44%-56%, respectively, if taken ≤7 days from onset of illness, and 70%, 67%, 47%, 28-44% if >7 days of illness.
SARS-CoV-2 identification and IgA antibodies in saliva: One sample two tests approach for diagnosis Aita, et al. 2020 (16)	• 43 COVID-19 inpatients and 326 screening subjects underwent NPS and saliva collection (Salivette). • NPS and saliva were both SARS-CoV-2 positive in 7 (16%) or both negative in 35 (82%) out of 43 patients with COVID-19. NPS and saliva results did not perfectly match in one patient (saliva positive, NPS negative).

Source	Summary
Peer reviewed sources	
	• Positive molecular results were significantly associated with disease duration (p=0.0049). • 326/326 screening subjects were SARS-CoV-2 negative on both NPS and saliva.
Saliva in the diagnosis of COVID-19: A review and new research directions Fernandes, et al. 2020 (1)	• Systematic review included 28 studies. • Nine studies reported the sensitivity and/or specificity of RT-quantitative PCR (qPCR)analysed saliva specimens as compared with the gold standard diagnosis of throat and nasopharyngeal swabs which varied considerably from 66% to 91.7% and from 97% to 100%, respectively. • When different techniques were used to analyse saliva samples, RT-qPCR, direct RT-qPCR, and RT loop-mediated isothermal amplification had good sensitivity, while the rapid antigen test presented low sensitivity.
Comparison of saliva and oro-nasopharyngeal swab sample in the molecular diagnosis of COVID-19 Guclu, et al. 2020 (17)	• 64 total participants including three groups: group one has confirmed COVID-19, group two has COVID-19 compatible findings by CT and group three were patients presenting to the emergency department with COVID-19 compatible symptoms. • SARS-CoV-2 was detected in 27 (42.2%) patients' saliva samples. • The sensitivity and positive predictive value of saliva samples were 85.2%, specificity and negative predictive value were 89.2%. • The value of kappa agreed (0.744) (statistically significant).
Accuracy and stability of saliva as a sample for reverse transcription PCR detection of SARS-CoV-2 Uwamino, et al. 2020 (18)	• Letter reporting on 32 hospitalised patients with COVID-19 and 115 symptomatic staff. • 32 samples were found positive for both saliva and NPS samples, while 138 were negative for both. • Fifteen samples were positive for NPS samples and negative for saliva samples, and 11 samples were positive for saliva samples and negative for NPS samples. • Saliva and NPS samples displayed 86.7% concordance with kappa coefficient as 0.625.
RT-qPCR assays based on saliva rather than on nasopharyngeal swabs are possible but should be interpreted with caution: results from a systematic review and meta-analysis	• Systematic review and meta-analysis including 14 studies. • Aims: sensitivity and specificity of SARS-CoV-2 viral RNA detection through RT-qPCR based on salivary specimens compared to conventional NPS. • A pooled specificity of 97.7% (95% CI 93.8-99.2) and a pooled sensitivity of 83.4% (95% CI 73.1-90.4).

Source	Summary
Peer reviewed sources	
Ricco, et al. 2020 (6)	• Overall agreement assessed by means of Cohen's kappa equals to 0.750, 95% CI 0.62-0.88 (i.e. moderate agreement). • High heterogeneity and risk of reporting bias across studies.
Saliva as a candidate for COVID-19 diagnostic testing: a meta-analysis Czumbel, et al. 2020 (2)	• Systematic review including eight studies. • 91% (CI 80-99%) sensitivity for saliva tests and 98% (CI 89-100%) sensitivity for NPS tests in previously confirmed COVID-19 patients, with moderate heterogeneity among the studies. • 18 registered, ongoing clinical trials of saliva-based tests for detection of the virus were identified.
Saliva sampling and its direct lysis, an excellent option to increase the number of SARS-CoV-2 diagnostic tests in settings with supply shortages Moreno-Contreras, et al. 2020 (19)	• 253 paired samples from oropharyngeal and nasopharyngeal swabs (183 single swap and 71 with both NPS and OPS) from ambulatory patients (except 3 which were hospitalised patients). • Saliva was self-collected by patients. • All patients had two or more symptoms related to COVID-19. • Of the 182 patients with a single swab collected, 80 (43.9%) were positive for SARS-CoV-2 as determined by either the swab or saliva samples. Of these, 41 (51.2%) were positive as determined by both types of samples, while 28 (35%) were positive only by saliva and not by the swab sample and 11 (13.7%) were positive only by the OPS. In total, out of the 80 individuals found to be positive for the virus, 69 (86.2%) were correctly identified using saliva, while only 52 (65%) were identified with the OPS. • 34 (47.8%) of the 71 patients with two swabs collected were found to be positive for SARS-CoV-2 by either the swabs or the saliva samples. Of these, 19 (55.8%) were positive by both swabs and saliva, while 6 (17.6%) were positive only by saliva and 9 (26.4%) were positive only by the two swab samples. In total, in this group of patients, of the 34 individuals identified as positive for the virus, 25 (73.5%) were identified by testing saliva, while 28 (82.3%) were positive by the swabs.
Deep throat saliva as an alternative diagnostic specimen type for the detection of SARS-CoV-2 Leung, et al. 2020 (20)	• 95 patient-matched paired samples from 62 patients including 29 confirmed patients with COVID-19 and 33 COVID-19 negative patients. • There were no statistical differences between the detection rates of DTS and NPS ($p>0.05$). • The overall agreement between the two sampling methods was 78.9% and the kappa value was 0.58, indicating moderate agreement between these two sample types.

Source	Summary
Peer reviewed sources	
Sensitivity of nasopharyngeal swabs and saliva for the detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Jamal, et al. 2020 (21)	• Of 91 patients with paired samples tested, 72 (79%) had at least one positive specimen. • In 44 (61%) of these 72 patients, both NPS and saliva were positive, in 20 (28%) only the NPS was positive, and in 8 (11%) only saliva was positive (p=0.02) • Using NPS only would have detected 64 of 72 (89%) patients with at least 1 positive specimen and using saliva only would have detected 52 of 72 (72%) patients with at least 1 positive specimen. • Using NPS only would have detected 16 of 17 (94%), 34 of 38 (89%), and 14 of 17 (82%) patients in their first, second, and third or fourth week of illness, respectively. • Using saliva only would have detected 15 of 17 (88%), 25 of 38 (66%), and 12 of 17 (71%) patients in their first, second, and third or fourth week of illness, respectively.
Rapid salivary test suitable for a mass screening program to detect SARS-CoV-2: A diagnostic accuracy study Azzi, et al. 2020 (22)	• Letter reporting a diagnostic accuracy study (n=122). • Primary study reporting on a rapid salivary test. • One hundred fourteen subjects had their salivary sample also analysed by real-time RT-PCR (vs NPS). • In all subjects, sensitivity was 0.91 (95% CI 0.80;0.97). • In all subjects, specificity was 0.60 (95% CI 0.47;0.73).
Posterior oropharyngeal saliva for the detection of SARS-CoV-2 Cheuk, et al. 2020 (23)	• 13772 specimens were identified during the study period, including 2130 posterior OPSand 8438 nasopharyngeal specimens. • 229 same-day posterior OPS- nasopharyngeal specimes paired were identified with posterior OPS and nasopharyngeal specimen positivity of 61.5% (95% CI 55.1-67.6%) and 53.3% (95% CI 46.8-59.6%). • The overall, negative and positive percent agreement were 76.0% (95% CI 70.2-80.9%), 65.4% (95% CI 55.5-74.2%), 85.2% (95% CI 77.4-90.8%). • Better positive percent agreement was observed in posterior OPS-nasopharyngeal specimen obtained within seven days (96.6%, 95% CI 87.3-99.4%) compared with after seven days of symptom onset (75.0%, 95% CI 61.4-85.2%). • Among the 104 positive pairs, the mean difference in Cp value was 0.26 (range: 12.63−14.74), with an overall higher Cp value in NP specimens (Pearson coefficient 0.579).
Comparison of SARS-CoV-2 detection in	• Letter including 76 patients including ten COVID-19 patients.

<table>
<tr><th>Source</th><th>Summary</th></tr>
<tr><td colspan="2">Peer reviewed sources</td></tr>
<tr><td>nasopharyngeal swab and saliva

Iwasaki, et al. 2020 (24)</td><td>
NPS and saliva samples.
<table>
<tr><td>Nasopharyngeal</td><td>Positive</td><td>Negative</td><td>Cohen's kappa analysis</td></tr>
<tr><td>Positive</td><td>8</td><td>1</td><td rowspan="2">κ=0.874 (95%CI, 0.701-1)</td></tr>
<tr><td>Negative</td><td>1</td><td>66</td></tr>
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</td></tr>
<tr><td>Saliva sample as a non-invasive specimen for the diagnosis of coronavirus disease 2019: a cross-sectional study

Pasomsub, et al. 2020 (25)</td><td>

Two-hundred pairs of samples (saliva samples and a standard NPS and throat swab) were collected.
Using nasopharyngeal and throat swab RT-PCR as the reference standard, the prevalence of COVID-19 diagnosed by nasopharyngeal and throat swab RT-PCR was 9.5%.
The sensitivity and specificity of the saliva sample RT-PCR were 84.2% (95% CI 60.4-96.6%), and 98.9% (95% CI 96.1-99.9%), respectively.
Agreement between the two specimens demonstrated 97.5% observed agreement.

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Source	Summary
Peer reviewed sources	
Saliva as a noninvasive specimen for detection of SARS-CoV-2 Williams, et al. 2020 (26)	• Letter including 622 patients that were tested for COVID-19 through a screening clinic in Melbourne. • All patients had NPS, and 522/622 (83.9%) patients also provided saliva. • NPS and saliva specimens underwent nucleic acid extraction on the Qiagen EZ1 platform. • Overall, 39/622 (6.3%; 95% CI, 4.6% to 8.5%) patients had PCR-positive NPS, and 33/39 patients (84.6%; 95% CI, 70.0% to 93.1%) had SARS-CoV-2 detected in saliva. • The median CT value was significantly lower in NPS than saliva, suggestive of higher viral loads in NPS. • To assess specificity, a subset of saliva specimens from 50 patients with PCR-negative swabs was also tested. SARS-CoV-2 was detected in 1/50 (2%; 95% CI, 0.1% to 11.5%) of these saliva samples, which may reflect differing quality of NPS collection.
Evaluating the use of posterior oropharyngeal saliva in a point-of-care assay for the detection of SARS-CoV-2. Chen, et al. 2020 (27)	• NPS and posterior OPS specimens of 58 COVID-19 patients were tested. • SARS-CoV-2 was detected in either NPS or saliva specimens of all patients. • Among them, 84.5% (49/58) tested positive in both NPS and saliva, 10.3% (6/58) tested positive in NPS only, and 5.2% (3/58) tested positive in saliva only. • No significant difference in the detection rate was observed between NPS and saliva (McNemar's test p = 0.5078).
Viral dynamics of SARS-CoV-2 in saliva from infected patients Zhu, et al. 2020 (28)	• Letter including 944 patients from 12 independent cohorts. • When compared to the respiratory tract samples, the sensitivity and specificity of saliva were 86.4% (95% CI 82.8-89.4%) and 97.0% (95% CI 95.0-98.3%), respectively. • Analysis of the concordance revealed a 92.1% observed virus detection accuracy and a firm agreement of diagnosis between the respiratory tract and saliva sample (Kohen's kappa coefficient 0.840, 95% CI 0.805-0.874).
Salivary detection of COVID-19 Caulley, et al. 2020 (29)	• Letter including consecutive, asymptomatic, high-risk persons and those with mild symptoms suggestive of COVID-19 at a centralised testing centre. • Of the 1939 paired swab and saliva samples analysed, SARS-CoV-2 E gene was detected in 70 samples, 80.0% with swabs and 68.6% with saliva.

Source	Summary
Peer reviewed sources	
	• Thirty-four participants (48.6%) tested positive for SARS-CoV-2 on both swab and saliva samples. • Discordant test results were seen in 22 participants (31.4%) who tested positive with swab alone and in 14 (20%) who tested positive with saliva alone. • Swabs were obtained from the nasopharynx in 35.7% of participants who tested positive with saliva alone, compared with 9.1% of participants who tested positive with swab alone.
Comparative evaluation of nasopharyngeal swab and saliva specimens for the molecular detection of SARS-CoV-2 RNA in Japanese patients with COVID-19 Sakanashi, et al. 2020 (30)	• 28 paired clinical specimens of saliva and nasopharyngeal swabs were collected from 12 patients at various time points after symptom onset. • The saliva and nasopharyngeal swab specimens showed 19 and 15 positive results, respectively. • No invalid (PCR inhibition) result was observed for any specimen.
Rapid implementation and validation of a cold-chain free SARS-CoV-2 diagnostic testing workflow to support surge capacity Bosworth, et al. 2020 (31)	• Between the 8 and 30 April 2020, the laboratory tested a total of 1282 healthcare workers for SARS-CoV-2 RNA in throat swabs. • RNA was detected in 54% of those who reported symptoms compatible with COVID-19, but in only 4% who were asymptomatic. • To test against qualitative RT-PCR, a panel of residual RNA preparations from the Queen Elizabeth Hospital which had been extracted and previously tested on the Altona commercial qRT-PCR assay (n=94) or original respiratory samples collected from patients the same day and tested on an Abbott m2000 commercial qualitative qRT-PCR assay (n=26) were used.
Saliva or nasopharyngeal swab specimens for detection of SARS-CoV-2 Wyllie, et al. 2020 (32)	• Letter, 495 asymptomatic health care workers, RT-qPCR was used to test both saliva and nasopharyngeal samples obtained from these persons. • Authors detected SARS-CoV-2 RNA in saliva specimens obtained from 13 persons who did not report any symptoms at or before the time of sample collection. • Of these 13 health care workers, 9 had collected matched NPS specimens by themselves on the same day, and 7 of these specimens tested negative.

Source	Summary
Peer reviewed sources	
Saliva is a reliable tool to detect SARS-CoV-2 Azzi, et al. 2020 (33)	• Salivary samples of 25 COVID-19 patients were analysed by real-time RT-PCR. • All the samples tested positive for the presence of SARS-CoV-2, while there was an inverse association between lactate dehydrogenase and CT values. • Two patients showed positive salivary results on the same days when their pharyngeal or respiratory swabs showed conversion.
Temporal profiles of viral load in posterior oropharyngeal saliva samples and serum antibody responses during infection by SARS-CoV-2: an observational cohort study To, et al. 2020 (34)	• Cohort study at two hospitals in Hong Kong. • 23 patients with laboratory-confirmed COVID-19. • Samples of blood, urine, posterior oropharyngeal saliva, and rectal swabs were obtained. • Serial viral load was ascertained by reverse transcriptase quantitative PCR (RT-qPCR). • The median viral load in posterior oropharyngeal saliva or other respiratory specimens at presentation was 5.2 log10 copies per mL (IQR 4.1-7.0). • Salivary viral load was highest during the first week after symptom onset and subsequently declined with time (slope -0.15, 95% CI -0.19 to -0.11; R2=0.71). • In one patient, viral RNA was detected 25 days after symptom onset.
Consistent detection of 2019 novel coronavirus in saliva To, et al. 2020 (35)	• A total of 12 patients with laboratory-confirmed 2019-nCoV infection in Hong Kong were included. • Saliva specimens were collected at a median of 2 days after hospitalisation (range, 0-7 days). • The 2019-nCoV was detected in the initial saliva specimens of 11 patients (91.7%). • For patient K, the first saliva specimen collected on the day of hospital admission tested negative. • The median viral load of the first available saliva specimens was 3.3 × 106 copies/mL (range, 9.9 × 102 to 1.2 × 108 copies/mL).
Saliva sample pooling for the detection of SARS-CoV-2 Pasomsub, et al. 2020 (36)	• Pooling of saliva specimens for testing by SARS-CoV-2 RT-PCR. • Two hundred RNA specimens. • Of the 40 pools of five samples, there were 27 negative pools. Eleven pools detected of both ORF1ab and N genes, and two pools detected only N gene.

Source	Summary
Peer reviewed sources	
	• RT-PCR of the individual RNA extracted from saliva samples in each positive pool of either one gene or both of the genes was performed. • Saliva pooling does not compromise the sensitivity of viral detection if an increased CT cutoff value and the detection of either gene from the pool are allowed for further individual specimen testing. However, immediate RT-PCR testing should be performed to minimise the effect of storage conditions that can decrease the sensitivity of the testing.
Saliva alternative to upper respiratory swabs for SARS-CoV-2 diagnosis Byrne, et al. 2020 (37)	• 110 patients with COVID-19. • Overall, 12 (10.9%) saliva and 14 (12.7%) nasal and throat swab specimens of 110 paired samples tested positive for SARS-CoV-2 RNA. • Viral loads for all samples ranged from 36 to 3.3 × 106 copies/mL.
Serial semiquantitative detection of SARS-CoV-2 in saliva samples. Mao, et al. 2020 (38)	• Letter. • Inpatients with a diagnosis of COVID-19 provided by real-time RT-PCR on oropharyngeal swabs (n=34). • The CT value of 91 saliva tests was recorded; the median CT value of the ORF1a gene was 36.64 (range 24.10–39.90), and the median CT value of the N gene was 33.99 (range 23.03-39.67). • According to the number of weeks after hospitalisation, the median CT value of the two genes gradually increased, and the amplitude gradually decreased. • The total positive rate of nucleic acid detection from sputum was the highest (67.2%), followed by oropharyngeal swabs (53.1%) and saliva (36%). • The results showed that the total sensitivity, efficiency and specificity of saliva single detection method were 74.10%, 83.90% and 94.40%, respectively. • The overall sensitivity, efficiency and specificity of saliva-sputum combined detection method were 93.40%, 94.00% and 95.20%, respectively.
Detection of SARS-CoV-2 in saliva and characterization of oral symptoms in COVID-19 patients. Chen, et al. 2020 (40)	• To analyse angiotensin-converting enzyme II expression in salivary glands, bulk RNA-seq profiles from four public datasets including 31 COVID-19 patients. • Saliva and oropharyngeal swabs were collected. SARS-CoV-2 nucleic acids in saliva were detected by real-time polymerase chain reaction.

Source	Summary
Peer reviewed sources	
	• Angiotensin-converting enzyme II expression was present at detectable levels in the salivary glands. • 13 cases were tested positive for oropharyngeal swab nucleic acids detection. Among these 13 patients, there were 4 cases with positive nucleic acids detection in saliva, of which 3 cases were critically ill patients on ventilator support.
SARS-CoV-2 presence in the saliva, tears and cerumen of COVID-19 patients. Hanege, et al. 2020 (41)	• 38 COVID-19 patients with a positive real time polymerase chain reaction test. • Saliva, tear and cerumen samples were taken from the patients within 72 hours of the first RT-PCR test. • The highest positivity rate was in saliva (76.3%) followed by tears (55.3%) and cerumen (39.5%). • Viral load in saliva was also significantly higher compared to tears and cerumen ($p<0.001$). • Half of the saliva, tear and cerumen samples obtained from asymptomatic patients contained SARS-CoV-2 genome.
Clinical evaluation of self-collected saliva by quantitative reverse transcription-PCR (RT-qPCR), direct RT-qPCR, reverse transcription-loop-mediated isothermal amplification, and a rapid antigen test to diagnose COVID-19 Nagura-Ikeda, et al. 2020 (42)	• Saliva samples from 103 patients with laboratory-confirmed COVID-19 (15 asymptomatic and 88 symptomatic) were collected on the day of hospital admission. • Of the 103 samples, viral RNA was detected in 50.5 to 81.6% of the specimens by molecular diagnostic tests, and an antigen was detected in 11.7% of the specimens by the rapid antigen test. • Viral RNA was detected at significantly higher percentages (65.6 to 93.4%) in specimens collected within 9 days of symptom onset than in specimens collected after at least 10 days of symptoms (22.2 to 66.7%) and in specimens collected from asymptomatic patients (40.0 to 66.7%).
Hock-a-loogie saliva as a diagnostic specimen for SARS-CoV-2 by a PCR-based assay: A diagnostic validity study Fan, et al. 2020 (43)	• Prospective diagnostic validity study of patients with laboratory-confirmed COVID-19 (n=65). • A total of 195 respiratory tract samples were collected from 65 patients, of which 23 could produce sputum. • In patients who had sputum collected, the detection rate in sputum (95.65%, 22/23) was significantly higher than those in throat swabs (34.78%, 8/23) and nasal swabs (65.22%, 15/23) ($p<0.001$). • Similarly, the detection rate in hock-a-loogie saliva was 88.09% (37/42), significantly higher than those in throat swabs (45.24%, 19/24) and nasal swabs (76.19%, 32/42) ($p<0.001$).

Source	Summary
Peer reviewed sources	
	• SARS-COV-2 detection rates were significantly higher in sputum and hock-a-loogie saliva than those in throat swabs and nasal swabs (p<0.001). • The detection rate of SARS-CoV-2 increased to 76.9% based on either positive throat swab or nasal swab.
The positive rate of saliva for the detection of 2019-nCoV and possible factors related to the sensitivity results Meng, et al. 2020 (56)	• Letter, including a meta-analysis. • 17 studies were included. • The positive rate of saliva for the detection of COVID-19 by RT-PCR ranged from 25% to 100%, and the pooled positive rate of saliva in detecting COVID-19 was 85%. • Morning specimens were more likely to show positive results.

Table 2 Self-collected respiratory swabs

Source	Summary
Peer reviewed sources	
Self-collected anterior nasal and saliva specimens versus health care worker-collected nasopharyngeal swabs for the molecular detection of SARS-CoV-2 Hanson et al. 2020 (46)	• Prospective study, 354 patients included. • Healthcare worker collected NPS to self-collected anterior nasal swabs were compared. • The percent positive agreement between NPS and anterior nasal swabs or saliva was 86.3% (95% CI, 76.7 to 92.9%) and 93.8% (95% CI, 86.0 to 97.9%), respectively. • The percent negative agreement was 99.6% (95% CI, 98.0 to 100.0%) for NPS versus anterior nasal swabs and 97.8% (95% CI, 95.3 to 99.2%) for NPS versus saliva. • More cases were detected by the use of NPS (n=80) and saliva (n=81) than by the use of anterior nasal swabs (n = 70), but no single specimen type detected SARS-CoV-2 infections.
Combined self-collected anterior nasal and oropharyngeal specimens versus provider-collected nasopharyngeal swabs for the detection of SARS-CoV-2 Shakir, et al. 2020 (47)	• Letter to the editor describing a prospective study of self-collected OPS combined with self-collected anterior nasal swabs versus healthcare worker collected NPS from 423 unique patients. • Overall, there was 98.8% qualitative agreement (95CI 97.26-99.61%; kappa =0.97) observed between the dual OPS-anterior nasal swabs and NPS collections.

Source	Summary
Peer reviewed sources	
	• Percent positivity appeared slightly higher for NPS (27.7%) compared to dual collection (27.0%), but this difference did not reach statistical significance. • There were four patients positive for SARS-CoV-2 by NPS only. One patient was positive by OPS-anterior nasal swab spun swab alone.
Self-collected oral fluid and nasal swab specimens demonstrate comparable sensitivity to clinician-collected nasopharyngeal swab specimens for the detection of SARS-CoV-2 Kojima, et al. 2020 (48)	• Patients were non-hospitalised persons tested for SARS-CoV-2 include 45 patients (180 specimens collected, of which 177 yielded results). • Comparison of self-collected oral fluid swab specimens with and without clinician supervision, clinician-supervised self-collected mid-turbinate (nasal) swab specimens, and clinician collected NPS specimens. • Clinician-supervised oral fluid swab specimens detected 26 (90%) of 29 infected individuals, clinician supervised nasal swab specimens detected 23 (85%) of 27, clinician collected posterior NPS specimens detected 23 (79%) of 29, and unsupervised self-collected oral fluid swab specimens detected 19 (66%) of 29. • Supervised oral fluid and nasal swab specimens performed similarly to clinician collected NPS specimens. • No sample type could detect SARS-CoV-2 infections amongst all positive participants.
Comparison of patient-collected and lab technician-collected nasopharyngeal and oropharyngeal swabs for detection of COVID-19 by RT-PCR Abdollahi, et al. 2020 (62)	• 50 study participants. • Two sets of naso- and oropharyngeal swabs were collected, one set by a lab technician and the other by the patients. • The COVID-19 real -time RT-PCR test was performed. • In seven patients all swabs were positive and in 22 patients all swabs were negative. • Discrepancies between results of lab technician collected and patient collected swabs were observed in 12 nasopharyngeal and 13 oropharyngeal specimens. • Positive lab technician collected and negative patient collected samples were observed in 10 and 5 nasopharyngeal and oropharyngeal specimens, respectively. • Negative lab technician collected and positive patient collected samples were observed in two and seven nasopharyngeal and oropharyngeal specimens, respectively. • The overall percentage of agreement was 76%.

Source	Summary
Peer reviewed sources	
Self-collected versus healthcare worker-collected swabs in the diagnosis of severe acute respiratory syndrome coronavirus 2 Therchilsen, et al. 2020 (49)	• 109 participants, of which 19 had SARS-CoV-2-positive results. • Self-collected oropharyngeal and nasal samples versus a healthcare workers collected oropharyngeal sample. • The diagnostic sensitivity of the self-collected and healthcare worker collected swabs was 84.2% and 89.5%, respectively.
Comparison of unsupervised home self-collected midnasal swabs with clinician-collected nasopharyngeal swabs for detection of SARS-CoV-2 infection McCullock, et al. 2020 (50)	• Letter including a cross sectional study of 185 participants. • Among the 185 participants, 41 (22.2%) yielded SARS-CoV-2 positive test results via clinician collected nasopharyngeal swab, home self-collected mid-nasal swab, or both. • 158 participants (85%) were healthcare workers, of whom 14 (9%) tested positive. • Compared with clinician swabs, sensitivity and specificity of home swabs was 80.0% (95% CI, 63-91%) and 97.9% (95% CI, 94-99.5%), respectively. • Cohen kappa statistic was 0.81 (95% CI, 0.70-0.93), suggesting substantial agreement.
Grey literature	
Topic: Self-collection of samples for SARS-CoV-2 RT-PCR testing Alberta Health Services, 2020 (45)	• Self-collecting samples for SARS-CoV-2 RT-PCR has been identified as a potential strategy to reduce the burden of sample collection on the healthcare system, saving resources and reducing potential exposures to healthcare workers. • In the largest study comparing self-swabbing (n=530) the sensitivity for detecting SARS-CoV-2 in patient collected tongue, nasal, and mid-turbinate samples was 89.8% (95% CI: 80.2-100.0), 94.0 (95% CI: 84.6-100.0) and 96.2 (95% CI: 87.7-100.0), respectively, suggesting that nasal and mid-turbinate samples may be the most promising to evaluate. • There is little evidence related to completion rates and costing data. • Further research is required to establish the most appropriate approach to self-collection.

Appendix

PubMed search terms

(2019-nCoV[title/abstract] or nCoV*[title/abstract] or covid-19[title/abstract] or covid19[title/abstract] OR "covid 19"[title/abstract] OR "coronavirus"[MeSH Terms] OR "coronavirus"[title/abstract] OR sars-cov-2[title/abstract] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) AND ("self collect*"[Title/abstract] OR "self test*"[Title/abstract] OR "self swab*"[Title/abstract] OR "self service*"[Title/abstract] OR "self sampl*"[Title/abstract] OR "patient collect*"[Title/abstract] OR "patient administer*"[Title/abstract] OR "at-home test*"[Title/abstract] OR "home collect*"[Title/abstract] OR "home test*"[Title/abstract]) AND (2020/07/15:2020/12/31[pdat])

= 75 hits on 6 November 2020

((2019-nCoV[title/abstract] or nCoV*[title/abstract] or covid-19[title/abstract] or covid19[title/abstract] OR "covid 19"[title/abstract] OR "coronavirus"[MeSH Terms] OR "coronavirus"[title/abstract] OR sars-cov-2[title/abstract] OR "severe acute respiratory syndrome coronavirus 2"[Supplementary Concept]) AND ("saliva"[MeSH Terms] OR "saliva"[Title/Abstract]) AND (2019:2020[pdat])) AND (Diagnostic Tests, Routine[MeSH Terms] OR test*[title/abstract] OR swab*[title/abstract] OR sample*[title/abstract]) AND (2019:2020[dp])

= 167 hits on 6 November 2020

Google and Twitter search terms

Self-collect covid-19 test, health care worker vs self-collect covid-19 test, saliva to detect covid-19, saliva vs NPS to detect covid-19

Inclusion and exclusion criteria

Inclusion	Exclusion

• Comparison study
  ○ self-collected respiratory swabs compared with healthcare worker collected respiratory swabs, or
  ○ saliva samples compared with respiratory swabs
• Systematic reviews including comparative studies
	• Non-comparative studies
	• Studies on efficacy of different assays for the detection of antibodies to SARS-CoV-2 or different extraction methods
	• Narrative reviews
	• ≤10 patients
	• Animal studies
	• Pre peer review studies

Glossary

CI	Confidence interval
CT	Cycle threshold
NPS	Nasopharyngeal swabs
OPS	Oropharyngeal swab
RT-PCR	Reverse transcription polymerase chain reaction
RT-qPCR	Reverse transcription quantitative polymerase chain reaction

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