



**Health
Information
and Quality
Authority**

An tÚdarás Um Fhaisnéis
agus Cáilíocht Sláinte

Evidence summary for accuracy of molecular and antigen detection tests for the diagnosis of COVID-19 using alternative clinical specimens or sites

21 August 2020

Evidence summary for accuracy of molecular and antigen detection tests for the diagnosis of COVID-19 using alternative clinical specimens or sites

Key points

- The current standard of care in Ireland for the detection of SARS-CoV-2 comprises provider-collected combined nasopharyngeal-oro-pharyngeal specimens tested through RT-PCR. The use of alternative clinical specimens, such as saliva or nasal, may offer less-invasive options with potential benefits in terms of improved patient comfort, reduced transmission risk for healthcare providers, and the possibility of a self-collected method.
- This evidence summary focused on the accuracy of molecular (for example RT-PCR) and antigen detection tests using saliva or nasal specimens in SARS-CoV-2 detection compared with RT-PCR tested nasopharyngeal specimens. Twenty-four studies were identified with 16 including data relevant to saliva specimens and nine to nasal specimens.
- The collection methods for saliva and nasal specimens were inconsistent between studies with various procedures described, and often little detail provided.
- Twelve studies directly compared saliva and nasopharyngeal specimens using the same RT-PCR technique. Two studies noted equal detection between specimen types, while five displayed higher rates of detection with saliva relative to nasopharyngeal specimens, and five showed higher rates with nasopharyngeal relative to saliva specimens. Positive detection by saliva ranged from 82.9% to 100%; detection by nasopharyngeal ranged from 76.7% to 100%. Positive agreement between samples for overall detection ranged from 65.4% to 100%.
- Four studies compared saliva specimens tested with other molecular or antigen tests (loop-mediated isothermal amplification [n=2], point-of-care isothermal amplification [n=1], and a rapid antigen detection test [n=1]) with RT-PCR tested nasopharyngeal specimens. Each of these alternative methods were noted to produce a degree of false positive and or false negative tests when compared with the reference standard RT-PCR.
- For direct RT-PCR comparisons between nasal and nasopharyngeal specimens, from seven available datasets, one study noted equal detection between

specimen types, four noted higher rates of detection with nasopharyngeal relative to nasal specimens, and two showed higher rates with nasal relative to nasopharyngeal specimens. Positive detection by nasal swabs ranged from 81.9% to 100%; detection by nasopharyngeal specimens ranged from 70% to 100%. Positive agreement between samples for overall detection ranged from 62.3% to 100%.

- Three studies compared nasal specimens tested with a point-of-care isothermal amplification technology with RT-PCR tested nasopharyngeal specimens. Across studies, this test presented 62 (7.7%) false negatives tests from 807 paired comparisons with the reference standard RT-PCR.
- The methodological quality of included studies was generally low. Important variables such as patient recruitment and flow, symptom presence and duration, and index test parameters and conduct were often poorly reported. Additionally, nine of the 24 included studies are preprints, which have not yet been peer-reviewed.
- For direct RT-PCR comparisons, the results of this review indicated an inconsistency in the detection of SARS-CoV-2 by the specimens included; often with neither the nasopharyngeal or index specimens (saliva and nasal) detecting all positive cases and sometimes these specimens tested positive for SARS-CoV-2 while the nasopharyngeal specimen was negative.
- Evidence for the use of these specimens with other molecular or antigen tests, which are not RT-PCR based, is very limited. However, the limited data suggests that such tests may be associated with a higher degree of false positive and or false negative results, reducing confidence in their use overall.
- Depending on the test environment and purpose, saliva and nasal specimens may offer a viable alternative to traditional test specimens for RT-PCR testing (for example the collection of these specimens may be more acceptable in paediatric populations). Use should be contingent on validation studies confirming performance in the intended setting. No study within this review reported on differences in resource use, or assessed provider and patient satisfaction with the different specimen types. As additional studies are published in this rapidly emerging area, more robust conclusions may be drawn about the overall value of these clinical specimens for the diagnosis of COVID-19.

Evidence summary for accuracy of molecular and antigen detection tests for the diagnosis of COVID-19 using alternative clinical specimens or sites

The Health Information and Quality Authority (HIQA) has developed a series of 'Evidence Summaries' to assist the Clinical Expert Advisory Group (EAG) in supporting the National Public Health Emergency Team (NPHE) in their response to COVID-19. These summaries are based on specific research questions. This evidence summary was developed to address the following research question:

What is the accuracy of molecular and antigen detection tests for the diagnosis of COVID-19 using alternative clinical specimens or sites compared with RT-PCR tested nasopharyngeal (with or without oropharyngeal) or lower respiratory tract clinical samples?

Background

The accurate and timely detection of SARS-CoV-2 facilitates public health surveillance, response and control measures during the COVID-19 pandemic. The current standard of care in Ireland for the detection of SARS-CoV-2 (the virus that causes COVID-19) involves testing of clinician-collected combined nasopharyngeal-oropharyngeal specimens with reverse transcription polymerase chain reaction (RT-PCR). RT-PCR is considered the 'gold standard' in diagnostics for the detection of SARS-CoV-2 ribonucleic acid (RNA) in the acute phase of infection.⁽¹⁾ A growing body of research is emerging for additional tests of viral material, including rapid diagnostic tests and near patient testing (point-of-care) that may provide advantages in terms of the speed or convenience of testing. In the United States, a number of these tests have obtained Food and Drug Administration (FDA) approval under Emergency Use Authorizations in the context of the COVID-19 pandemic.⁽²⁾ This is reflected in guidance from the Centers for Disease Prevention and Control (CDC) which, in addition to traditional RT-PCR-based tests, includes antigen tests for the detection of viral material as well as other molecular tests, such as loop-mediated isothermal amplification (LAMP) based tests and isothermal amplification point-of-care tests.⁽³⁾

The selection of sites for the retrieval of clinical specimens to test for the presence of viral material has potential implications for the overall accuracy of the diagnostic test utilised.⁽²⁾ An evidence summary from HIQA, published 15 April 2020, highlighted positive detection rates of SARS-CoV-2 through RT-PCR tests across a range of clinical samples and tests sites including nasopharyngeal, oropharyngeal,

sputum, faecal matter, urine, blood, ocular, and blood.⁽⁴⁾ The clinical sample sites were noted to be inconsistent in their detection of viral material for SARS-CoV-2, with discordance highlighted between clinical samples. Current guidance from the Health Protection Surveillance Centre (HSPC),⁽⁵⁾ the World Health Organization (WHO),⁽¹⁾ and the UK National Health Service (NHS)⁽⁶⁾ endorse the collection of upper respiratory specimens through nasopharyngeal combined with oropharyngeal swabs for the routine testing of SARS-CoV-2, with the collection of lower respiratory samples (bronchoalveolar lavage, endotracheal aspirate or sputum) in more severe illness. Updated guidance from the CDC in the US has extended to permit the collection of one of the following: nasopharyngeal swab, oropharyngeal swab, nasopharyngeal aspirate, mid-turbinate anterior nasal swab, with the latter two having the option of a self-collection method by the patient.⁽³⁾

The collection of nasopharyngeal swabs by healthcare workers involves an invasive technique that is uncomfortable for the patient, with one study noting significant discomfort relative to other nasal specimen collection in both adult and paediatric populations.⁽⁷⁾ A relative degree of skill is required by the provider, and due to risk of transmission, the procedure necessitates substantial personal protective equipment. Other issues include the potential for a shortage of swabs during large scale testing initiatives.⁽²⁾ Alternative specimens from the upper respiratory tract, such as saliva or nasal, may offer a means to mitigate these limitations, with the additional benefit of potentially offering a 'self-collection' method by the patient.

Methods for the collection of such alternative clinical specimens can vary. Saliva may be collected by a patient pooling saliva in their mouth before spitting into a sterile container, repeatedly spitting into a container without pooling, coughing and pooling in their mouth before expelling into a container (termed 'deep throat') or by a passive drooling technique.⁽²⁾ Collection of specimens from the nasal cavity typically involves the use of a swab, but is distinct from nasopharyngeal specimens in terms of the depth of swab insertion.⁽⁸⁾ While nasopharyngeal specimen collection typically involves the insertion of a swab to a distance in line with a patient's ear, nasal cavity specimens involve less invasive collection with swab insertion to 1cm (anterior) or 2.5cm (mid-turbinate) depending on the sample needed, typically with the same swab used in both nostrils.^(8, 9)

Methods

The processes as outlined in HIQA's *'Protocol for evidence synthesis support - COVID-19'*, available on www.hiqa.ie, were followed throughout the conduct of this review.⁽¹⁰⁾ Below is a summary of all relevant evidence comparing alternative clinical specimens or sites (specifically saliva or nasal) with RT-PCR tested nasopharyngeal

(with or without oropharyngeal) or lower respiratory tract specimens identified from 30 December 2019 until 20 July 2020.

For consistency, data presented for RT-PCR comparisons of specimen types were used to calculate positive agreement between specimens. Given that the same form of test was being conducted for each specimen type, a positive result with one or both specimens was considered an overall positive result. The detection of each specimen type was then calculated relative to all positive cases. The positive agreement between specimens was calculated as the proportion of results where both specimens were positive (numerator) relative to overall positives (denominator). Data comparing other molecular or antigen tests with RT-PCR tests are presented in a standard fashion of diagnostic accuracy (with the RT-PCR test considered the reference-standard) with results extracted directly from each study.

Results

Twenty-four relevant studies were identified within this review, with all being classified as cross-sectional in nature.⁽¹¹⁻³⁴⁾ Fourteen studies were from the United States,^(12, 13, 16-18, 20, 23-25, 28-30, 32, 34) with three from Hong Kong,^(14, 15, 21) two each from Australia,^(31, 33) and France,^(22, 27) and one each from Italy,⁽¹¹⁾ Japan,⁽¹⁹⁾ and Thailand.⁽²⁶⁾ The median number of participants included in the studies was 94 and ranged from 18 to 524. Twelve studies were conducted in adults, or likely to be adults from the summary statistics provided;^(11, 12, 14, 19-24, 26, 27, 34) four studies included adult and paediatric populations,^(15, 17, 30, 31) and eight studies did not provide demographic details of participants.^(13, 16, 18, 25, 28, 29, 32, 33) Three studies were conducted exclusively in healthcare workers.^(22, 24, 34) Fifteen studies were conducted in ambulatory settings,^(12, 13, 17, 18, 20, 22, 24-26, 28, 30-34) two in hospitalised inpatients,^(14, 15) three in mixed settings,^(11, 23, 35) and four were unclear in their settings.^(19, 21, 27, 29) The majority of studies included symptomatic, or clinically suspected cases, with the exception of Wyllie et al.⁽³⁴⁾ who exclusively examined asymptomatic healthcare workers as part of surveillance testing.

Fifteen of the included studies examined saliva specimens,^(11, 13-15, 19, 21-23, 25, 26, 28, 29, 32-34) seven examined nasal specimens,^(12, 16, 18, 24, 27, 30, 31) and two included both specimen types.^(17, 20) All specimen types were compared with nasopharyngeal specimens. The results are outlined by specimen type with summaries of the included studies for saliva and nasal specimens provided in Table 1 and Table 2, respectively.

Saliva specimens

Seventeen of the included studies examined saliva specimens compared with RT-PCR tested nasopharyngeal specimens.^(11, 13-15, 17, 19-23, 25, 26, 28, 29, 32-34) For the index test, 12 directly compared specimens using the same RT-PCR test,^(11, 13-15, 17, 19-21, 23, 25, 26, 28, 33, 34) two compared specimens using different RT-PCR tests (with one including another comparison to a novel rapid salivary antigen test),^(11, 13) two used loop-mediated isothermal amplification (LAMP) based tests,^(22, 32) and one used an isothermal amplification point-of-care test (Abbot ID NOW).⁽²⁹⁾

Collection method

The included studies varied in the methods used to collect saliva specimens. Seven studies collected samples by participants spitting saliva into a sterile container,^(19, 23, 25, 26, 32-34) four studies used posterior oropharyngeal or deep throat saliva,^(14, 15, 20, 21) one study used a drooling technique,⁽¹¹⁾ and five studies did not provide information on collection methods.^(13, 17, 22, 28, 29) Six studies included a statement regarding cessation of oral intake or hygiene for a period of time prior to sample collection.^(11, 14, 15, 17, 23, 34)

Ten studies reported self-collection of saliva, although the level of supervision was often unclear,^(14, 15, 19, 21, 23, 25, 26, 28, 32, 34) one study included both self-collected and clinician-collected specimens,⁽²⁰⁾ while five studies did not provide any detail on who the sample was collected by.^(11, 13, 17, 22, 29)

Detection of SARS-CoV-2: Direct RT-PCR comparisons using same technique

Twelve studies compared RT-PCR tested saliva and nasopharyngeal specimens using the same RT-PCR technique, with 11 being in suspected SARS-CoV-2 cases; one study was in confirmed COVID-19 patients.^(11, 13-15, 17, 19-21, 23, 25, 26, 28, 33, 34) Two studies noted equal detection between specimen types, while five displayed higher detection rates with saliva relative to nasopharyngeal specimens, and five showed higher detection rates with nasopharyngeal relative to saliva specimens. As shown in Table 3, detection by nasopharyngeal specimens ranged from 76.7% to 100% relative to all positive cases. Detection by saliva relative to all positive cases ranged from 82.9% to 100%. Positive agreement of detection by saliva specimens relative to nasopharyngeal ranged from 82.5% to 100%. Positive agreement between specimens for overall detection ranged from 65.4% to 100%. A graphical representation of the detection of all positive cases by each specimen type is provided in Figure 1.

One study that examined routine surveillance of 98 asymptomatic healthcare workers based on occupational exposure did not detect any cases using nasopharyngeal specimens, though it detected two cases using saliva.⁽³⁴⁾ Given the

nature of this study, it has been excluded from the summary statistics provided above.

In 229 paired samples from 95 suspected SARS-CoV-2 cases, Cheuk et al.⁽¹⁵⁾ highlighted a higher overall detection by saliva specimens compared with nasopharyngeal (88.7% vs 76.7%), with a positive agreement of saliva relative to nasopharyngeal of 85.2% (104/122) and an overall positive agreement between specimen types of 65.4% (104/159). Of the 58 confirmed COVID-19 cases, 51 were symptomatic at the time of testing. Specifically for 21 paired samples from seven paediatric participants, 13/21 were positive by saliva while 11/21 were positive by nasopharyngeal, and five were negative by both specimen types.

Kojima et al.⁽²⁰⁾ highlighted a higher overall detection of SARS-CoV-2 by supervised self-collected saliva specimens compared with clinician-collected nasopharyngeal swabs (89.7% vs 79.3%) in 45 adults tested in the community. The agreement between saliva and nasopharyngeal samples was 86.9% (20/23), with 69% (20/29) overall positive agreement between specimen types. Of note, the authors reported higher detection rates by saliva specimens collected while supervised by clinicians (26/29) versus unsupervised collection (19/29). Twenty-one of the tested participants reported active symptoms.

In 95 paired samples from 62 suspected SARS-CoV-2 cases, Leung et al.⁽²¹⁾ reported greater overall detection with saliva specimens compared with nasopharyngeal (87.9% vs 77.6%). Positive agreement of saliva relative to nasopharyngeal was 84.0% (38/45), with overall positive agreement between specimen types of 65.5% (38/58). No clinical information was provided.

In 91 suspected SARS-CoV-2 cases, who were symptomatic and tested in ambulatory settings, Miller et al.⁽²⁵⁾ noted slightly higher detection by saliva compared with nasopharyngeal (97.2% vs 94.0%), and overall positive agreement between samples of 91.6% (33/36). These results were reflected by two RNA extraction kits used, with a slightly lower agreement seen with a third kit (one fewer saliva specimens tested positive).

Iwasaki et al.⁽¹⁹⁾ reported comparable rates of detection between both specimen types relative to all positive cases (90% vs 90%) in a sample of 76 suspected SARS-CoV-2 cases, with positive agreement of saliva relative to nasopharyngeal of 87.5% (8/9) and overall positive agreement between specimen types of 80% (8/10). Confirmed cases were reported to have mild-moderate disease.

McCormik-Baw et al.⁽²³⁾ noted comparable rates of detection between nasopharyngeal and saliva specimens (98% vs 96%) in 155 suspected cases tested

within a hospital setting. The positive agreement of saliva relative to nasopharyngeal was 96% (47/49) with overall positive agreement between samples of 94% (47/50). No demographic or clinical detail was provided.

In an Emergency Use Authorization study for a SARS-CoV-2 assay, the Rutgers Clinical Laboratory⁽²⁸⁾ reported complete agreement between nasopharyngeal and saliva specimens with 30 positive and 30 negative tests from symptomatic SARS-CoV-2 suspected cases in three ambulatory care settings. No demographic or clinical detail was provided.

In 58 COVID-19 confirmed patients, with specimens tested within 24 hours of the diagnostic test, Chen et al.⁽¹⁴⁾ presented higher overall detection by nasopharyngeal specimens relative to saliva (94.8% vs 89.7%). Positive agreement of saliva specimens relative to nasopharyngeal was 89.0% (49/55) with positive agreement between specimens being 84.5% (49/58). The authors further noted full concordance between an in-house assay and a point-of-care PCR-based test (Xpert Xpress, Cepheid). No detail regarding clinical characteristics was provided.

Griesemer et al.⁽¹⁷⁾ reported higher overall detection by nasopharyngeal specimens compared with saliva in 463 individuals tested for SARS-CoV-2 in an ambulatory testing environment (98% vs 82.9%). Positive agreement of saliva relative to nasopharyngeal was 82.5% (85/103) and an overall positive agreement between specimen types was 81.0% (85/105). No clinical characteristics were provided.

An Australian study conducted by Williams et al.⁽³³⁾ of testing within an ambulatory test setting presented matched results for 89 suspected SARS-CoV-2 cases. Overall, a higher number of infections were detected with nasopharyngeal swabs compared with saliva specimens (97.5% vs 85%). Positive detection of saliva relative to the reference was 84.6% (33/39), with an overall positive agreement of 82.5% (33/40). No demographic or clinical detail was provided.

Pasomsub et al.⁽²⁶⁾ reported higher rates of detection with combined nasopharyngeal and oropharyngeal swabs compared with saliva specimens in 200 adults tested at an acute respiratory clinic in Thailand (90.4% vs 85.7%). Saliva detection relative to the reference was 84.2% (16/19) and overall positive agreement between samples 76.2% (16/21).

Wyllie et al.⁽³⁴⁾ enrolled 98 asymptomatic healthcare workers for continuous self-collected specimen testing over a two week period. The authors noted that saliva specimens detected SARS-CoV-2 in two cases which were not identified by nasopharyngeal specimens. Results should be interpreted within the context of the low overall positivity rate within this study as testing was based on occupational

exposure; however, they equate to 0% (0/2) detection by nasopharyngeal specimens and 100% (2/2) detection by saliva.

Detection of SARS-CoV-2: RT-PCR comparisons using different techniques

Two studies compared nasopharyngeal and saliva specimens, but differed in the RT-PCR test used for each specimen type (Table 1). Given the possible confounding nature of this difference, these studies are presented separately below.^(11, 13)

Azzi et al.⁽¹¹⁾ noted higher detection of SARS-CoV-2 with saliva specimens in 113 paired samples (93.2% vs 44.0%) from a mixed setting of inpatient and ambulatory testing, with 42 (34.4%) participants symptomatic at the time of testing. Positive agreement of saliva relative to nasopharyngeal specimens was 84.6% (22/26), with 37.3% (22/59) overall positive agreement between samples.

Becker et al.⁽¹³⁾ noted higher detection of SARS-CoV-2 with nasopharyngeal swabs compared with saliva specimens from 85 participants within a community testing environment (88.2% vs 64.7%). Positive agreement of saliva relative to nasopharyngeal swabs was 60% (9/15), with 52.9% (9/17) overall positive agreement between samples. No details on clinical characteristics were provided.

Detection of SARS-CoV-2: Other molecular and antigen-based tests

Four studies compared additional molecular- or antigen-based saliva tests with RT-PCR confirmed nasopharyngeal specimens. As noted in the methods section, the results of these studies are presented in a standard fashion of diagnostic accuracy whereby RT-PCR nasopharyngeal is treated as the reference standard. Two examined loop-mediated isothermal amplification (LAMP) based tests,^(22, 32) one examined an isothermal amplification point-of-care test (Abbott ID NOW),⁽²⁹⁾ and one examined a novel rapid salivary antigen test.⁽¹¹⁾ The results of these studies are summarised in Table 4.

For LAMP- based testing, in 93 healthcare workers from a single hospital L'Helgouach et al.⁽²²⁾ noted one positive test (that was subsequently confirmed) that was not originally detected by RT-PCR nasopharyngeal specimens and four false positive tests. In a study of 18 suspected SARS-CoV-2 cases tested in ambulatory settings, Wei et al.⁽³²⁾ highlighted complete positive agreement with nasopharyngeal-based RT-PCR testing and further noted a case determined as positive by saliva LAMP-based testing that was deemed indeterminate by nasopharyngeal. Neither LAMP-based study reported false negatives relative to the reference comparator.

Using the Abbott ID NOW test, SoRelle et al.⁽²⁹⁾ noted no false positives, but five false negatives relative to the reference RT-PCR nasopharyngeal test in 67 suspected

SARS-CoV-2 cases. Collectively, the results indicated a positive agreement of 78.2% (18/23) and negative agreement of 100% (44/44). Of note, the authors highlighted potentially low viral loads as contributing to the discrepancy seen.

A novel rapid salivary antigen test, evaluated by Azzi et al.⁽¹¹⁾ categorised two cases as false negatives and 51 as false positives relative to RT-PCR nasopharyngeal testing, with a positive agreement of 92.9% (26/28) and negative agreement of 41.6% (38/91). However, follow-up RT-PCR testing on 49 of the saliva specimens (two samples excluded due to RT-PCR technical failure) categorised as false positives indicated that 28 were positive, giving some additional weight to the index test. Of note, as described above, RT-PCR testing varied between the two specimen types within this study. The remaining false positives (23/51) were determined to be technical errors with the novel test stemming from difficulties in accurately differentiating colour indicators of results.

Sample sufficiency and spoilage

Details regarding sample sufficiency were reported by one of the 16 studies concerning saliva specimens within this review,⁽²⁰⁾ with one insufficient sample (out of 45) noted for unsupervised oral fluid collection, and no insufficient samples for clinician supervised oral fluid collection or nasopharyngeal swab samples.

Azzi et al.⁽¹¹⁾ noted the exclusion of six saliva specimens due to technical failure with RT-PCR testing but did not provide any further detail.

Nasal specimens

Nine of the included studies compared nasal specimens with nasopharyngeal specimens.^(12, 16-18, 20, 24, 27, 30, 31) Six studies compared different specimen types (one containing two separate nasal specimen types) analysed using the same RT-PCR test,^(17, 20, 24, 27, 30, 31) and three studies compared nasal specimens analysed using the Abbott ID NOW test with nasopharyngeal specimens analysed with an RT-PCR test.^(12, 16, 18)

Collection method

Precise details of collection of nasal specimens were not well reported by the included studies. However, the majority reported use of a swab with four studies highlighting specimen collection through one nostril only,^(20, 24, 27, 31) three reporting collection from both nostrils,^(12, 16, 30) and one study collecting separate anterior and mid-turbinate nasal specimens for comparison.⁽³⁰⁾

Four studies reported self-collection of nasal specimens,^(20, 23, 30, 31) one reported collection by a clinician,⁽²⁷⁾ and four did not provide details on who samples were collected by.^(12, 16-18)

Detection of SARS-CoV-2: Direct RT-PCR comparisons

Six studies compared RT-PCR-tested nasal and nasopharyngeal specimens, with one study examining anterior and mid-turbinate nasal swabs separately. All studies were conducted in suspected SARS-CoV-2 cases.^(17, 20, 24, 27, 30, 31) One study noted equal detection between specimen types, four noted higher detection rates with nasopharyngeal relative to nasal specimens, and two showed higher rates with nasal relative to nasopharyngeal specimens. As shown in Table 3, detection by nasopharyngeal specimens ranged from 70% to 100% relative to all positive cases. Detection by nasal specimens ranged from 81.9% to 100% relative to all positive cases. Positive agreement between specimens for overall detection ranged from 62.3% to 100%. Positive agreement of detection by nasal specimens relative to the nasopharyngeal specimens ranged from 81.0% to 100%. A graphical representation of the detection of all positive cases by each specimen type is provided in Figure 1.

In 463 suspected SARS-CoV-2 cases tested in ambulatory settings, Griesemer et al.⁽¹⁷⁾ presented higher detection rates by nasopharyngeal specimens compared with nasal (98.1% vs 81.9%). Positive agreement of nasal relative to nasopharyngeal specimens was 83.5% (86/103), and there was 81.9% overall positive agreement between the two specimen types. No clinical information was provided.

Péré et al.⁽²⁷⁾ noted higher detection with clinician-collected nasopharyngeal swabs compared with clinician-collected nasal swabs in 44 symptomatic SARS-CoV-2 suspected cases (100% vs 89.1%). Positive agreement of nasal relative to nasopharyngeal and overall positive cases was 89.1% (33/37). The authors highlighted that the discordant results were likely related to low viral loads.

Tu et al.⁽³⁰⁾ compared self-collected nasal swabs and mid-turbinate swabs with clinician-collected nasopharyngeal swabs in 498 and 504 symptomatic individuals, respectively, in ambulatory testing settings. Nasopharyngeal specimens detected a higher number of cases compared with nasal (98.0% vs 94.1%) or mid-turbinate swabs (100% vs 96.2%). Positive agreement relative to the nasopharyngeal swab was 94.0% (47/50) for nasal specimens and 96.2% (50/52) for mid-turbinate, with overall positive agreements of 92.2% (47/51) and 96.2% (50/52), respectively.

Kojima et al.⁽²⁰⁾ noted higher detection by self-collected nasal specimens compared with clinician-collected nasopharyngeal specimens in paired samples from 43 suspected SARS-CoV-2 cases in an ambulatory setting (85.1% vs 70%). Positive

agreement of nasal relative to nasopharyngeal was 90.5% (19/21), with 70.3% (19/27) overall positive agreement between specimen types. Twenty-one individuals reported active symptoms.

In 158 symptomatic healthcare workers tested for SARS-CoV-2 in ambulatory settings, McCulloch et al.⁽²⁴⁾ reported greater detection with self-collected nasal swabs compared with clinician-collected nasopharyngeal swabs (85.7% vs 78.6%). Positive agreement of nasal specimens relative to nasopharyngeal was 81.0% (9/11), with overall positive agreement being 62.3% (9/14).

Wehrhahn et al.⁽³¹⁾ compared self-collected nasal swabs with clinician-collected combined nasopharyngeal and oropharyngeal swabs in 166 symptomatic suspected SARS-CoV-2 cases in an ambulatory testing environment. Complete agreement was noted for both specimen types for positive (13/13) and negative (153/153) results.

Detection of SARS-CoV-2: Other molecular and antigen-based tests

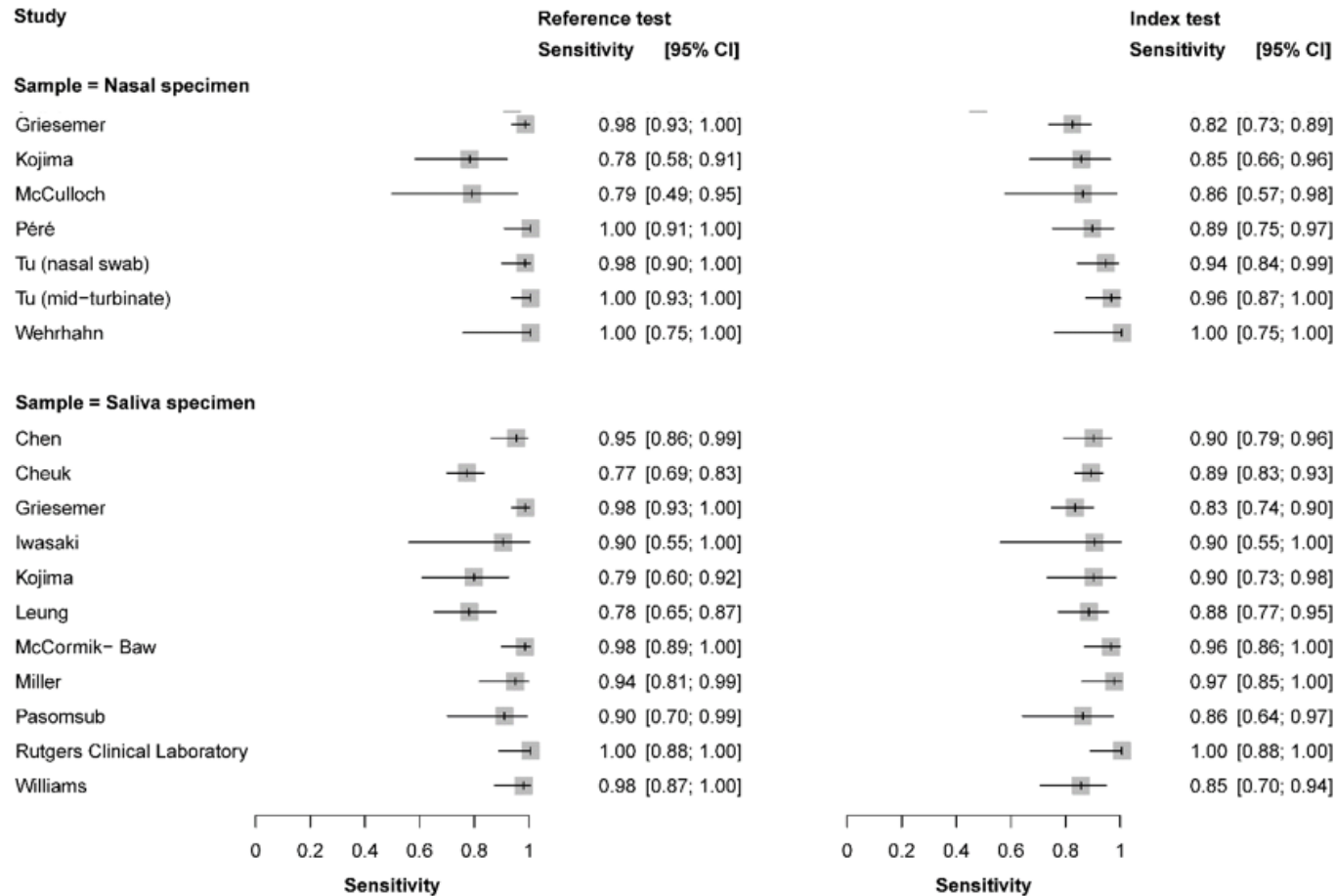
Three studies compared additional molecular or antigen-based nasal tests with RT-PCR confirmed nasopharyngeal specimens, all of which used an isothermal amplification point of care test (Abbott ID NOW test).^(12, 16, 18) As noted in the methods section, the results of these studies are presented in a standard fashion of diagnostic accuracy whereby RT-PCR nasopharyngeal is treated as the reference standard.

In the largest sample of 524 symptomatic participants tested in a mixed setting by Harrington et al.⁽¹⁸⁾, the authors noted two false positive and 47 false negatives with the nasal Abbott ID NOW test compared with RT-PCR-tested nasopharyngeal specimens. Positive agreement was noted in 139/186 (74.7%) of results and negative agreement in 336/338 (99.4%). The authors noted differences in detection were likely due to higher limits of detection in the test or lower viral loads in the nasal specimens. Subsequent repeat testing of the nasal specimens with RT-PCR, deemed one false positive to be a true positive. Providing similar reasoning for false negative tests, Basu et al.⁽¹²⁾ highlighted one false positive and 14 false negatives in 101 suspected SARS-CoV-2 patients tested in an emergency department with 54.8% (17/31) positive agreement and 98.6% (69/70) negative agreement between tests. Cradic et al.⁽¹⁶⁾ noted just one false negative in 182 suspected SARS-CoV-2 cases tested in a mixed testing environment, resulting in a positive agreement of 92.3% (12/13) and negative agreement of 100% (169/169), albeit with a generally lower overall positivity rate than the other studies included in this review.

Sample sufficiency and spoilage

With regards to sample sufficiency, one study reported this outcome for nasal specimens with Kojima et al.⁽²⁰⁾ highlighting that two of 45 self-collected nasal swabs were insufficient for testing.

Figure 1. Sensitivity of direct RT-PCR-tested specimens relative to all positive cases



Note: As all tests were RT-PCR based, any positive case was considered positive regardless of what specimen type it was detected by. These studies are limited to those where the same RT-PCR test was used for both specimen types.

Methodological quality of included studies

Overall, the methodological quality of included studies was generally low. Participant selection was rated as introducing a high risk of bias in seven of the 24 studies.^(13, 14, 20, 23, 25, 31, 33) In four studies, this was due to the non-consecutive recruitment of patients.^(13, 20, 23, 31) In three studies, this was because of inappropriate exclusions which may have resulted in a biased population.^(14, 25, 33) Due to limited reporting of how patients were recruited, 12 studies had an unclear risk of bias in this domain.^(11, 15, 16, 19, 21, 22, 27-30, 32, 34)

The index test was rated as introducing a high risk of bias in three studies.^(14, 32, 33) This was because the index test results were interpreted with the results of the reference test already known, and hence there was no blinding in these three studies.^(14, 32, 33) There were limited details on how and when the index test was conducted and or interpreted in 19 studies, and hence these studies had an unclear risk of bias in this domain.

Given that studies needed to analyse nasopharyngeal (with or without oropharyngeal) specimens or lower respiratory tract specimens using an RT-PCR test as per WHO recommendations in order to be included, there were few concerns regarding the reference standard across all studies. With the exception of one study where there was some uncertainty regarding the validity of an in-house developed assay used for RT-PCR,⁽³¹⁾ the reference standard was rated as introducing a low risk of bias in the remaining 23 studies.

Patient flow and timing was rated as introducing a high risk of bias in six studies.^(14, 15, 29, 31-33) In three studies, this was because not all patients were included in the analysis.^(14, 32, 33) In the other three studies, this was because not all patients received the same reference standard.^(15, 29, 31) There was also some uncertainty as to the timing of the tests, and hence three studies had an unclear risk of bias in this domain.^(18, 21, 24)

There were high concerns for the applicability of the included patients for the review question given differences in the included populations in four studies, including concerns around specific inclusion criteria or the potential for a portion representing surveillance of confirmed cases.^(15, 21, 25, 33) There were high concerns for the applicability of the index test for the review question, given observed divergence from manufacturers' instructions in four studies,^(12, 14, 15, 27) and varying skill levels for the conduct of the index test among users in one study.⁽¹⁸⁾ However, there were low concerns for the applicability of the reference standard for the review question across all included studies.

Additionally, nine included studies are as yet only published as pre-prints so have not been formally peer-reviewed; this raises additional concerns about overall quality and the potential for results to change prior to final publication.^(13, 17, 20, 22, 25, 28, 29, 32, 34)

Discussion and conclusion

The results of this review highlight that detection rates of SARS-CoV-2 vary between testing of saliva, nasal, and nasopharyngeal specimens. A reasonable evidence base was presented for direct RT-PCR comparisons between the index specimens of interest to this review and nasopharyngeal specimens. The rates of positive detection and discordance between specimens highlight inconsistencies in detection of the virus between specimen types, frequently with neither the index nor the reference test detecting all positive cases. For studies using the same RT-PCR assay for both index and reference test, those using saliva specimens detected the same number or more cases than those using nasopharyngeal specimens in seven out of 12 studies, while those using nasal specimens detected the same number or more cases than those using nasopharyngeal specimens in three out of seven included datasets. The evidence base for the use of these specimen types with additional molecular or antigen tests was limited; however, concerns were raised with regards to the rates of false results presented. That is to say, there was a higher rate of incorrect results with specimens analysed using these tests. The included studies used a variety of methods to collect the index specimens of interest, which were not always well described. The overall quality of the studies included within this review was typically low. Important variables such as patient recruitment and flow, symptom presence and duration, and index test parameters and conduct were often poorly reported. Nine of the 24 included studies are as yet only published as preprints, and have not yet been formally peer-reviewed. Additionally, the majority of studies were conducted in adult, or likely to be adult, populations with only one providing a sub-set of data for children which may limit the overall generalisability of the findings of this review.

The collection methods for nasopharyngeal specimens were typically reported as being a standardised procedure with clinician collection. However, the procedure for collecting saliva and nasal specimens varied. Saliva collection included spitting in sterile containers, collection of deep throat or posterior oropharyngeal saliva, and the use of a drooling technique. Nasal specimen collection was consistently swab orientated; however, it varied in terms of one or both nostrils being sampled and the precise site investigated. Furthermore, the description of these procedures often lacked detail, as did specifications on whether they were self-collected by the participants, collected under direction or supervision by the clinician, or collected by

the clinician. The variety of collection methods has implications for the specificity of the specimen collected, ease of collection, equipment required, and required experience level of the clinician.⁽²⁾ Furthermore, little detail was provided by the included studies with regards to sample sufficiency or test spoilage, which is surprising given the known pre-analytical and analytical challenges associated with these types of tests.⁽³⁶⁾ This may reflect a retrospective approach whereby only samples which were analysed in full were eligible for inclusion. Furthermore, no study within this review assessed implications for resource use or participant and provider satisfaction with each type of specimen collection. These considerations would provide meaningful information for decision-making overall.

For studies directly comparing nasopharyngeal with saliva specimens using the same RT-PCR test, two studies highlighted equal detection between specimen types, while five displayed higher rates of detection with nasopharyngeal relative to saliva specimens, and five showed higher rates with saliva relative to nasopharyngeal. It is worth noting that frequently neither specimen type detected all positive cases, and all studies noted detection of SARS-CoV-2 in at least 80% of positive cases using saliva specimens. Similarly with regards to nasal specimens, although typically a higher rate of detection was seen with nasopharyngeal specimens, nasal specimens identified SARS-CoV-2 in at least 80% of positive cases in all included datasets.

For the direct comparisons within this review, as the same form of test (RT-PCR) was being used with variation in a component (specimen type), an assumption was made that a positive test indicates a positive case regardless of the sample used. This reflects the view that false positive results using RT-PCR for the detection of SARS-CoV-2 are rare and typically represent technical errors or contamination rather than accuracy.⁽³⁷⁻³⁹⁾ However, false negatives with RT-PCR testing for SARS-CoV-2 are well-documented with a number of influencing factors including timing of specimen collection relative to symptom onset, sufficiency of collected specimens, and test parameters.⁽³⁷⁻³⁹⁾ For example, in a retrospective analysis by Fang et al.,⁽⁴⁰⁾ sensitivity of nasopharyngeal specimens tested with RT-PCR compared with chest CT was estimated to be 71%. A negative RT-PCR test therefore does not rule out SARS-CoV-2, particularly in those with high clinical suspicion.⁽⁴¹⁾ For this reason, the WHO and ECDC recommend caution in terms of a negative test if a person meets the clinical case definition with a re-test advised a number of days later,^(1, 42) given notable increases in viral load particularly in the early stages of infection.⁽³⁸⁾ Viral load has been noted to peak and reduce at different rates depending on the clinical specimen used.^(43, 44) As such, false negative test results may occur if specimens are tested during the early incubation period or late convalescent phase of infection, when virus levels may be undetectable depending on the specimen used. Of note, although not the premise of this review, viral loads reported by studies were

typically higher in nasopharyngeal than saliva specimens,^(33, 45) with generally longer viral shedding times.^(33, 45, 46) Similarly, lower viral loads were noted with a number of studies for nasal specimens.^(12, 18) Such considerations may be important in terms of decision-making for the timing of use of saliva and nasal specimens in testing for the presence of SARS-CoV-2.⁽²⁾

A substantial number of false negatives were reported with the Abbott ID NOW isothermal amplification point-of-care test in the one saliva and three nasal studies employing this test.^(12, 16, 18, 29) Again, such false negatives may be reflective of the viral load of the selected specimens of interest, the limits of detection of the test itself or a combination of both.^(2, 18) Of note, this test has received FDA approval for use for the diagnosis of COVID-19 under an Emergency Use Authorization.⁽⁴⁷⁾ Conversely, the LAMP-based methodologies employed by two saliva-based studies did not detect false negatives, but highlighted the potential for false positives. Such findings are not inconsistent with previous investigations of LAMP technology and appear to reflect an increased risk of contamination within the test procedures.⁽⁴⁸⁾ Lastly, this review noted only one antigen detection test which investigated the use of saliva specimens. The test appeared to be novel, with a large number of false positives identified which the authors noted as technical in nature.⁽¹¹⁾ Collectively, evidence for saliva and nasal specimens tested by these alternate methods compared with RT-PCR-tested nasopharyngeal specimens is limited and does not appear to support their use.

As highlighted, the use of alternative clinical specimens to nasopharyngeal swabs may offer potential benefits, including: reduced invasiveness of the technique, patient comfort, reduced risk transmission for healthcare workers and provide alternative methods if faced with swab shortages during large scale testing initiatives.⁽²⁾ Additionally, such specimens offer the potential for a patient-collected procedure which has implications for personal protective equipment use, the settings in which testing can be conducted, the acceptability of testing, and the scale of testing performed.^(2, 3) With such benefits, a potentially reduced sensitivity may be tolerable in certain circumstances, such as large scale testing or testing of children.

In conclusion, the studies included within this review showed that detection rates of SARS-CoV-2 vary with saliva, nasal, and nasopharyngeal specimens. While the evidence for use of these specimens with alternate molecular and antigen tests was very limited, a reasonable evidence-base was presented for direct RT-PCR-based comparisons. These comparisons highlighted variability in the detection rates relative to all positive cases and discordance in agreement; often with neither the index specimen of interest (saliva or nasal) nor the nasopharyngeal specimens detecting all cases. Depending on the testing environment, population, and available

resources, the benefits of these alternative clinical specimens may offer a viable alternative to the standard approach. Use should be contingent on validation studies confirming performance in the intended setting. There was a lack of consistency in methods used to collect the saliva and nasal specimens, and the quality of included studies was generally low. It may be possible to draw more robust conclusions about the overall value of these clinical specimens for the detection of SARS-CoV-2 in suspected cases as additional studies are published in this rapidly emerging area.

Table 1. Summary of identified saliva specimen studies

Author Country Sample size Study design Status: DOI	Patient demographics Setting Clinical characteristics Time between samples	Index specimen Test Gene target Threshold Collection method Self- or provider- collected	Reference specimen Test Gene target Threshold Collection method	Primary outcome results
<p>Azzi 2020 Italy N= 122 Cross-sectional study Published https://doi.org/10.1016/j.jinf.2020.06.042</p>	<p>Population: Suspected SARS-CoV-2 cases Population demographics: Mean age 53.5 (SD=19.8), 40 males (32.8%) Setting: Three independent medical areas in a single hospital:</p> <ul style="list-style-type: none"> ▪ COVID-19 wards (inpatients) ▪ Emergency Room (patients at high risk of COVID-19) ▪ Area for Healthcare workers (subjects at low risk of COVID-19) <p>Clinical characteristics: 42 (34.4%) symptomatic at the time of sample collection Time between samples: Simultaneous collection</p>	<p>Index sample: Salivary sample Test: Test 1:</p> <ul style="list-style-type: none"> ▪ Rapid Salivary Test (point of need antigen detection test using Lateral Flow Assay (LFA) (Abcam, cat ab270537)) <p>Test 2:</p> <ul style="list-style-type: none"> ▪ rRT-PCR (Luna® Universal qPCR Master Mix (New England BioLab)) <p>Threshold: NR Target: Test 1:</p> <ul style="list-style-type: none"> ▪ Viral Spike protein <p>Test 2:</p> <ul style="list-style-type: none"> ▪ NR <p>Collection method: 1ml sample through drooling technique in the morning Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swabs Test: rRT-PCR (GeneFinder™ COVID19 Plus RealAmp PCR kit (ELITechGroup)) Threshold: NR Gene target: RdRp, E, and N Collection method: NR</p>	<p>Detection rate: Test 1- Rapid salivary antigen test vs nasopharyngeal RT-PCR (n=119):</p> <ul style="list-style-type: none"> ▪ 28/119 positive by nasopharyngeal and 91 negative ▪ 79/119 positive by rapid saliva and 40 negative ▪ 2 positive by nasopharyngeal and negative by rapid saliva ▪ 53 positive by rapid saliva and negative by nasopharyngeal ▪ Study reported sensitivity- 0.93 (95% CI: 0.77 to 0.99) ▪ Study reported specificity- 0.42 (95% CI: 0.32 to 0.53) <p>Note: 28 positive saliva antigen samples (initially categorised as false positives) also tested positive by saliva RT-PCR</p> <p>Test 2- Saliva RT-PCR vs nasopharyngeal RT-PCR (n=113):</p> <ul style="list-style-type: none"> ▪ 26/113 positive by nasopharyngeal and 87/113 negative ▪ 55/113 positive by saliva and 58/113 negative ▪ 4 positive by nasopharyngeal and negative by saliva ▪ 33 positive by saliva and negative

				by nasopharyngeal Spoilage and sufficiency: 3 subjects were excluded from the analysis because their rapid salivary test failed and 6 subjects with technically failed RT-PCR for saliva.
<p>Becker 2020 United States N=88 Cross-sectional study Preprint: https://doi.org/10.1101/2020.05.11.20092338</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: No information provided</p> <p>Setting: Community testing environment</p> <p>Clinical characteristics: NR</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Salivary sample</p> <p>Test: RT-PCR in 2 separate labs with different primers used (PrimerDesign COVID-19 assay and TaqPath Multiplex RT-PCR COVID-19 assay).</p> <p>Threshold: NR</p> <p>Gene target: ORF1ab, RdRp,</p> <p>Collection method: 33 and 55 saliva specimens were collected using Orasure OM-505 Microbiome and OGD-610 DNA collection kits, respectively. No further detail provided</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swabs</p> <p>Test: RT-PCR (CDC RT-qPCR assay)</p> <p>Threshold: NR</p> <p>Gene target: ORF1ab, RdRp</p> <p>Collection method: NR</p>	<p>Detection rate: PrimerDesign assay:</p> <ul style="list-style-type: none"> ▪ 9/88 positive in both samples ▪ 6/88 positive nasopharyngeal and negative saliva sample ▪ 6/88 indeterminate with nasopharyngeal, 2/88 indeterminate with saliva sample ▪ 62/88 negative in both samples ▪ Study reported nasopharyngeal sensitivity: 98.9% (95% CI: 67.6%-99.7%) ▪ Study reported saliva sensitivity: 69.2% (95% CI: 38.6%-97.6%)
<p>Chen 2020 Hong Kong N=58 Cross-sectional study Published: https://doi.org/10.1080/22221751.2020.1775133</p>	<p>Population: COVID-19 inpatients</p> <p>Population demographics: Median age 38 years (IQR 31–52), 28 males (48.2%)</p> <p>Setting:</p>	<p>Index sample: Salivary sample (posterior oropharyngeal)</p> <p>Test:</p> <ul style="list-style-type: none"> ▪ Test 1: RT-PCR (In house dependent SARS-CoV-2 RNA polymerase/Helicase (RdRp/Hel) real-time RT– 	<p>Reference sample: Nasopharyngeal swab</p> <p>Test:</p> <ul style="list-style-type: none"> ▪ Test one: RT-PCR (In house dependent SARS-CoV-2 RNA polymerase/Helicase (RdRp/Hel) real-time RT–PCR assay 	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 49/58 (84.5%) tested positive with both nasopharyngeal and saliva ▪ 6/58 (10.3%) tested positive in nasopharyngeal and negative in saliva ▪ 3/58 (5.2%) tested positive in saliva and negative in nasopharyngeal <p>Note: 100% concordance between in-</p>

	<p>Inpatient setting of a single hospital</p> <p>Clinical characteristics:</p> <p>NR</p> <p>Time between samples:</p> <p>On the same day</p>	<p>PCR assay</p> <ul style="list-style-type: none"> Test 2: RT-PCR (Xpert Xpress, Cepheid, Sunnyvale, CA) <p>Threshold:</p> <p>NR</p> <p>Gene Target:</p> <p>E and N2</p> <p>Collection method:</p> <p>Patients were asked to cough up saliva by clearing the throat and spit about 1 mL of posterior oropharyngeal saliva directly into a sterile bottle in the early morning before mouth rinsing or breakfast</p> <p>Self- or provider- collection:</p> <p>Self-collection. NR if supervised or unsupervised</p>	<ul style="list-style-type: none"> Test two: RT-PCR (Xpert Xpress, Cepheid, Sunnyvale, CA) <p>Threshold:</p> <p>NR</p> <p>Gene target:</p> <p>E and N2</p> <p>Collection method:</p> <p>The swab was gently inserted up the nostril towards the pharynx until resistance was felt and was then rotated 3 times to obtain epithelial cells</p>	<p>house laboratory based and point of care tests</p>
<p>Cheuk 2020</p> <p>Hong Kong</p> <p>N= 95 (229 paired samples)</p> <p>Cross-sectional study</p> <p>Published:</p> <p>https://doi.org/10.1093/cid/ciaa797</p>	<p>Population:</p> <p>Suspected SARS-CoV-2 cases (n=95)</p> <p>Population demographics:</p> <p>Median age 36 years (range 4–92), 57 males (60%).</p> <p>Setting:</p> <p>Inpatient setting of a single hospital</p> <p>Clinical characteristics:</p> <p>51 confirmed COVID-19 patients with 7 being</p>	<p>Index sample:</p> <p>Salivary sample (posterior oropharyngeal)</p> <p>Test:</p> <ul style="list-style-type: none"> rRT-PCR (Cobas z480 real-time PCR analyser; Roche Diagnostics, Mannheim, Germany) <p>Threshold:</p> <p>Ct value ≤ 40 considered positive</p> <p>Gene Target:</p>	<p>Reference sample:</p> <p>Nasopharyngeal swab and nasopharyngeal aspirate (majority were nasopharyngeal swab- 70.3%)</p> <p>Test:</p> <p>rRT-PCR (Cobas z480 real-time PCR analyser; Roche Diagnostics, Mannheim, Germany)</p> <p>Threshold:</p> <p>Ct value ≤ 40 considered positive</p> <p>Gene target:</p> <p>E</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> 104/229 positive by both samples 70/229 negative by both samples 18 positive by nasopharyngeal and negative by saliva 37 positive by saliva and negative nasopharyngeal Study reported positive agreement 85.2% (95% CI 77.4 to 90.8) Study reported negative agreement 65.4% (95% CI 55.5 to 74.2) Study reported overall agreement 76.0% (95% CI 70.2 to 80.9) <p>Note: Positive agreement within 7 days</p>

	<p>asymptomatic. Samples taken across duration of illness</p> <p>Time between samples:</p> <p>On the same day</p>	<p>E</p> <p>Collection method:</p> <p>Patients were asked to clear saliva from back of throat into a sterile container as soon as possible after waking up, before any eating, drinking or teeth brushing.</p> <p>Self- or provider- collection:</p> <p>Self- collection. NR if supervised or unsupervised</p>	<p>Collection method:</p> <p>Insertion of a flock swab into the nostril parallel to the palate with a rotatory motion to a depth equal to the distance from the nostril to the tragus. Aspirate was collected using a catheter connected one end to a mucus trap and the other end to a vacuum source, which is then inserted into the nasopharynx similar to NPS to the nasopharynx for aspirate nasopharyngeal secretion into the mucus trap</p>	<p>of symptom onset 96.6% (95% CI 87.3 to 99.4)</p> <p>Paediatric population:</p> <p>Of 21 paired samples from 7 paediatric patients:</p> <p>8/21 positive by both specimen 5/21 negative by both specimen 5 positive by saliva and negative by nasopharyngeal 3 positive by nasopharyngeal and negative by saliva</p>
<p>Griesemer et al</p> <p>United States</p> <p>N=463</p> <p>Cross-sectional study</p> <p>Preprint: https://doi.org/10.1101/2020.06.16.20133041</p>	<p>Population:</p> <p>Suspected SARS-CoV-2 cases</p> <p>Population demographics:</p> <p>Age range 3-105 years.</p> <p>Setting:</p> <p>Two outpatient ambulatory clinics</p> <p>Clinical characteristics:</p> <p>NR</p> <p>Time between samples:</p> <p>Simultaneous collection</p>	<p>Index sample:</p> <p>Salivary sample</p> <p>Test:</p> <p>rRT-PCR (CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold:</p> <p>Ct value < 45 considered positive</p> <p>Gene target:</p> <p>N</p> <p>Collection method:</p> <p>Saliva samples were collected in sterile 50mL conical tubes, and patients were instructed to refrain from eating, drinking, chewing gum or tobacco, or smoking, 30 minutes prior to collection.</p> <p>Self- or provider- collection:</p> <p>NR</p>	<p>Reference sample:</p> <p>Nasopharyngeal swabs</p> <p>Test:</p> <p>rRT-PCR (CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold:</p> <p>Ct value < 45 considered positive</p> <p>Gene target:</p> <p>N</p> <p>Collection method:</p> <p>NR</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 103/463 positive by nasopharyngeal and 360 negative ▪ 87/463 positive by saliva and 376 negative ▪ 18 positive by nasopharyngeal and negative by saliva ▪ 2 positive by saliva and negative by nasopharyngeal

<p>Iwasaki 2020 Japan N=76 Cross-sectional study Published: 10.1016/j.jinf.2020.05.071</p>	<p>Populations: 1. SARS-CoV-2 infected patients (n=10) 2. Suspected SARS-CoV-2 cases (n=66)</p> <p>Population demographics: Median age: COVID-19 patients 69 (range 30 to 97). No demographic detail for suspected cases</p> <p>Setting: Single hospital</p> <p>Clinical characteristics: Most COVID-19 patients had mild-moderate disease. Median day of sampling was 9 days (range 3-19 days) after symptom onset</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Salivary sample</p> <p>Test: RT-qPCR ((One-Step Real-Time RTPCR Master Mixes (Thermo Fisher Scientific, Waltham, USA) and tepOnePlus Real Time PCR System (Thermo Fisher Scientific))</p> <p>Gene target: NR</p> <p>Threshold: NR</p> <p>Collection method: Spit into sterile container</p> <p>Self- or provider- collection: Self-collected with the exception of one patient. Level of supervision NR</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-qPCR ((One-Step Real-Time RTPCR Master Mixes (Thermo Fisher Scientific, Waltham, USA) and tepOnePlus Real Time PCR System (Thermo Fisher Scientific))</p> <p>Gene target: NR</p> <p>Threshold: NR</p> <p>Collection method: The swab was passed through the nostril until reaching the posterior nasopharynx and slowly removed while rotating</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 9/76 positive by nasopharyngeal, 67 negative ▪ 9/76 positive by saliva, 67 negative ▪ 1 positive by nasopharyngeal and negative by saliva ▪ 1 positive by saliva and negative by nasopharyngeal
<p>Kojima 2020 United States N= 45 Cross-sectional study Preprint: https://doi.org/10.1101/2020.04.11.20062372</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Median age 42 years (Interquartile range 31 to 52 years)</p> <p>Setting: Samples collected in participant homes</p> <p>Clinical characteristics: 29 positive for SARS-CoV-2 from at least one specimen type collected (Oral fluid,</p>	<p>Index sample: Oral fluid sample</p> <p>Test: RT-qPCR (CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: NR</p> <p>Gene target: N</p> <p>Collection method: Participants were instructed to cough deeply 3-5 times collecting</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-qPCR (CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: NR</p> <p>Gene target: N</p> <p>Collection method: Posterior using the recommended</p>	<p>Detection rate: 16/45 (35.6%) negative with both samples. 29/45 (64.4%) participants identified as positive by at least one specimen. No single specimen type detected all those with infection:</p> <ul style="list-style-type: none"> ▪ Clinician-supervised oral fluid swab specimens detected 26/29 (90%) ▪ Unsupervised self-collected oral fluid swab specimens detected 19/29 (66%) ▪ Clinician-collected posterior nasopharyngeal swab specimens detected 23/29 (79%).

	<p>nasal swab, nasopharyngeal swab). 21 reported active symptoms. Range 2-21 days from symptom onset to sample collection.</p> <p>Time between samples:</p> <p>All samples collected within a 30 minute window.</p>	<p>any phlegm or secretions in their mouth, rub the swab on both cheeks, above and below the tongue, both gums, and on the hard palate for a total of 20 seconds to ensure the swab was saturated with oral fluid</p> <p>Self- or provider- collection:</p> <ol style="list-style-type: none"> 1. Unsupervised self-collected oral fluid sample 2. Clinician supervised oral fluid sample. 	<p>medical technique</p>	<p>Spoilage and sufficiency:</p> <p>One insufficient unsupervised oral fluid</p>
<p>Leung et al</p> <p>Hong Kong</p> <p>N=62 (95 matched pairs)</p> <p>Cross-sectional study</p> <p>Published: https://doi.org/10.1002/jmv.26258</p>	<p>Population:</p> <p>Suspected SARS-CoV-2 cases</p> <p>Population demographics:</p> <p>mean age 42 years (SD=17.1), 26 males (41.9%)</p> <p>Setting:</p> <p>Single hospital</p> <p>Clinical characteristics:</p> <p>29 confirmed patients with COVID-19</p> <p>Time between samples:</p> <p>On the same day</p>	<p>Index sample:</p> <p>Salivary sample (posterior oropharyngeal)</p> <p>Test:</p> <p>RT-PCR (lightMix Modular SARS-CoV (COVID19) E-gene detection kit (TIB Molbiol, Berlin, Germany)</p> <p>Threshold:</p> <p>NR</p> <p>Gene target:</p> <p>E, RdRp</p> <p>Collection method:</p> <p>Patients were provided clear instructions to collect saliva from the deep throat (posterior oropharyngeal) in a sterile sputum container</p> <p>Self- or provider- collection:</p> <p>Self-collection. NR level of supervision.</p>	<p>Reference sample:</p> <p>Nasopharyngeal swab</p> <p>Test:</p> <p>RT-PCR (lightMix Modular SARS-CoV (COVID19) E-gene detection kit (TIB Molbiol, Berlin, Germany)</p> <p>Threshold:</p> <p>NR</p> <p>Gene target:</p> <p>E, RdRp</p> <p>Collection method:</p> <p>Collected by nursing staff using flocked swabs</p>	<p>Detection rate:</p> <p>Total 58 positives:</p> <ul style="list-style-type: none"> ▪ 45/95 positive by nasopharyngeal, 50 negative ▪ 51/95 positive by saliva, 44 negative ▪ 13 positive by saliva and negative by nasopharyngeal ▪ 7 positive by nasopharyngeal and negative by saliva ▪ Study reported overall agreement: 78.9% (69.1%-86.4%)

<p>L'Helgouach 2020 France N=93 Cross-sectional study Preprint: https://doi.org/10.1101/2020.05.30.20117291</p>	<p>Population: Health care workers</p> <p>Population demographics: Mean age 37.1 (SEM=1.1), 22 males (34.1%)</p> <p>Setting: Single hospital</p> <p>Clinical characteristics: Testing based on symptomatic case-finding or close exposure with an index case. 15 (16.1%) symptomatic</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Salivary sample</p> <p>Test: RT-LAMP (EasyCoV)</p> <p>Collection method: NR</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-PCR (Allplex 2019-nCov assay kit, Seegene, Korea)</p> <p>Threshold: Ct value < 35 considered positive</p> <p>Gene target: RdRp, E and N</p> <p>Collection method: NR</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 88/93 negative with both tests ▪ 5/93 negative with nasopharyngeal and positive with EasyCoV saliva <ul style="list-style-type: none"> ○ 4/5 deemed to be false positives and one true positive (confirmed by RT-PCR saliva)
<p>McCormik-Baw 2020 United States N= 156 Cross-sectional study Published: 10.1128/JCM.01109-20</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Mean age 47.8 years, 90 males (58%)</p> <p>Setting: Emergency department and inpatients from COVID positive hospital unit</p> <p>Clinical characteristics: Unventilated participants.</p> <p>Time between samples: NR</p>	<p>Index sample: Salivary sample</p> <p>Test: rRT-PCR (Cepheid Xpert Xpress SARS-CoV-2 PCR test, Sunnyvale, CA)</p> <p>Gene target: E and N2</p> <p>Threshold: Detection of both targets or N2 alone is considered positive and detection of E alone is considered presumptive positive</p> <p>Collection method: Recommended that patients not</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: rRT-PCR (Cepheid Xpert Xpress SARS-CoV-2 PCR test, Sunnyvale, CA)</p> <p>Gene target: E and N2</p> <p>Threshold: Detection of both targets or N2 alone is considered positive and detection of E alone is considered presumptive positive</p> <p>Collection method: Collected in a standard fashion</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 49/156 positive with nasopharyngeal, 106 negative ▪ 47/156 positive with saliva, 107 negative ▪ 47 positive with both samples, 105 negative with both samples ▪ 1 sample was positive by saliva, and negative by nasopharyngeal

		<p>have any food, drink, tobacco or gum for 30 minutes prior to collection. Saliva was collected in sterile urine cups or sterile 50 ml conical tubes. 5 ml of saliva was requested; however, specimens were considered acceptable if approximately 1 ml saliva was submitted.</p> <p>Self- or provider- collection: Clinician present but uncertain if clinician collected or supervised. Encouraged to collect saliva not sputum collection.</p>		
<p>Miller 2020 United States Cross-sectional study N= 91 Preprint: https://doi.org/10.1101/2020.06.05.20122721</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: NR</p> <p>Setting: Two ambulatory primary care clinics</p> <p>Clinical characteristics: Symptomatic</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Saliva sample</p> <p>Test: RT-qPCR (CFX384 Touch Real-Time PCR Detection System with CFX Manager software version 3.1 (Bio-Rad Laboratories)).</p> <p>Gene target: RdRp, N</p> <p>Threshold: 5 copies/μL</p> <p>Collection method: Spit into sterile container. Collected using the Orasure Oragene®·Dx (OGD-510).</p> <p>Self- or provider- collection: Supervised self-collection</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-qPCR (CFX384 Touch Real-Time PCR Detection System with CFX Manager software version 3.1 (Bio-Rad Laboratories)).</p> <p>Gene target: RdRp, N</p> <p>Threshold: 5 copies/μL</p> <p>Collection method: Clinician collected. No further information provided.</p>	<p>Detection rate: 3 RNA extraction utilised: Identical results for MagMAX™ Viral/Pathogen Nucleic Acid Isolation Kit and Maxwell RSC TNA Viral Kit (Promega Corporation)</p> <ul style="list-style-type: none"> ▪ 34 positive by nasopharyngeal, 57 negative ▪ 35 positive by saliva, 56 negative ▪ 2 positive by saliva and negative by nasopharyngeal ▪ 1 positive by nasopharyngeal and negative by saliva ▪ Study reported positive agreement 97.1% (95% CI 85.1 to 99.5) ▪ Study reported negative agreement 96.5% (95%CI 88.1 to 99.0) <p>Maxwell® HT Viral TNA Kit (Promega Corporation)</p> <ul style="list-style-type: none"> ▪ 34 positive by nasopharyngeal, 57 negative

				<ul style="list-style-type: none"> ▪ 34 positive by saliva, 57 negative ▪ 1 positive by saliva and negative by nasopharyngeal ▪ 1 positive by nasopharyngeal and negative by saliva ▪ Positive agreement 97.1% (95% CI 85.1 to 99.5) ▪ Negative agreement 98.2% (95% CI 90.7 to 99.7)
<p>Pasomsub 2020 Thailand N=200 Cross-sectional study Published: https://doi.org/10.1016/j.cmi.2020.05.001</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Patients >18 years. Median age 36 (Interquartile range 28-48), 69 males (34.5%),</p> <p>Setting: Acute respiratory infection clinic at a single hospital</p> <p>Clinical characteristics: Median onset of symptoms before testing 3 days (interquartile range 2 to 7).</p> <p>Time between samples: Consecutive collection</p>	<p>Index sample: Salivary sample</p> <p>Test: RT-PCR (SARS-CoV-2 Nucleic Acid Diagnostic Kit (San-sure, Changsha, China) using the CFX96 Real-Time Detection System (Bio-Rad, Hercules, CA, USA)</p> <p>Gene Target: ORF1AB and N</p> <p>Threshold: Both target genes Ct value < 38</p> <p>Limit of detection: 200 copies/sample</p> <p>Collection method: Patients were asked to provide a saliva sample, void of coughing, in a sputum collection container</p> <p>Self- or provider- collection: Self-collected. Level of supervision unclear</p>	<p>Reference sample: Combined Nasopharyngeal and throat swabs</p> <p>Test: RT-PCR (SARS-CoV-2 Nucleic Acid Diagnostic Kit (San-sure, Changsha, China) using the CFX96 Real-Time Detection System (Bio-Rad, Hercules, CA, USA)</p> <p>Gene Target: ORF1AB and N</p> <p>Threshold: Both target genes Ct value < 38</p> <p>Limit of detection: 200 copies/sample</p> <p>Collection method: Collected as per standard protocol</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 16/200 positive by both samples, 179/200 negative by both samples ▪ 19/200 positive by nasopharyngeal/throat, 181 negative ▪ 18/200 positive by saliva, 182 negative. ▪ 2 positive by saliva and negative by nasopharyngeal/throat ▪ 3 positive by nasopharyngeal/throat and negative by saliva

<p>Rutgers Clinical Genomics Laboratory United States N=60 Cross-sectional study (Accelerated Emergency Use Authorization published by Food and Drug Administration) https://www.fda.gov/media/136875/download</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: No demographic information provided</p> <p>Setting: Three ambulatory care centres</p> <p>Clinical characteristics: Symptomatic patients</p> <p>Time between samples: Both sample sites collected within 10 minutes of each other.</p>	<p>Index sample: Salivary sample</p> <p>Test: rRT-PCR (Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay based on a modification of the previously authorised ThermoFisher Applied Biosystems TaqPath COVID-19 Combo Kit)</p> <p>Gene target: N, S and, ORF1ab</p> <p>Threshold: Two of three Ct value <37 Limit of detection: 200 copies/ml</p> <p>Collection method: Each patient was provided with instructions for self-collection of saliva using a commercial saliva collection device.</p> <p>Self- or provider- collection: Self-collected under supervision of clinician</p>	<p>Reference sample: Nasopharyngeal or oropharyngeal swab</p> <p>Test: rRT-PCR (Rutgers Clinical Genomics Laboratory TaqPath SARS-CoV-2 Assay based on a modification of the previously authorised ThermoFisher Applied Biosystems TaqPath COVID-19 Combo Kit)</p> <p>Gene target: N, S and, ORF1ab</p> <p>Threshold: Two of three Ct value <37 Limit of detection: 200 copies/ml</p> <p>Collection method: Collected in a standard fashion</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 30/60 positive by both samples, 30/60 negative by both samples ▪ Study reported positive agreement: 100% (30/30) (95% CI 88.7 to 100%). ▪ Study reported negative agreement: 100% (30/30) (95% CI 88.7 to 100%).
<p>SoRelle 2020 United States N=67 Cross-sectional study Preprint: https://doi.org/10.1101/2020.06.01.20119198</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: NR</p> <p>Setting: NR</p> <p>Clinical characteristics:</p>	<p>Index sample: Salivary sample</p> <p>Test: Abbott ID NOW (point-of-care isothermal amplification-based platform)</p> <p>Limit of detection: 2000 copies/mL</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-PCR (Xpert® Xpress SARS-CoV-2 (Cepheid, Sunnyvale, CA) or Real-Time SARS-CoV-2 (Abbott Molecular, Des Plaines, IL) RT-PCR assays)</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 23/67 positive by nasopharyngeal, 44 negative ▪ 18/67 positive by Abbott ID NOW saliva, 49 negative <ul style="list-style-type: none"> ○ 5 false negatives

	Symptomatic Time between samples: Paired samples	Gene target: E, N Collection method: NR Self- or provider- collection: NR	Threshold: NR Gene target: E, N Collection method: NR	
Wei 2020 United States Cross-sectional study N=18 Preprint: https://doi.org/10.1101/2020.06.13.20129841	Population: Suspected SARS-CoV-2 cases Population demographics: NR Setting: Ambulatory testing clinics Clinical characteristics: NR Time between samples: Simultaneous collection	Index sample: Salivary sample Test: Modified RT-LAMP for point of care with saliva specifically (HP-LAMP) Threshold: 2 viral copies per µL Gene target: Orf1ab Collection method: Spitting ~1mL saliva in a clean sterile tube Self- or provider- collection: Self-collected. Level of supervision NR	Reference sample: Nasopharyngeal swab Test: RT-PCR (Roche Cobas 6800 system) Threshold: 0.10-0.15 copies/microliter Gene target: E, N Collection method: Followed CDC recommended protocol	Detection rate: HP-LAMP performed on four positive samples, two indeterminate and 12 randomly selected negative samples: <ul style="list-style-type: none"> ▪ 4/18 positive by nasopharyngeal, 12 negative, 2 indeterminate ▪ 5/18 positive by LAMP saliva, 13 negative ▪ One positive and one negative by LAMP saliva were indeterminate by nasopharyngeal
Williams 2020 Australia N= 89 Cross-sectional study Published: 10.1128/JCM.00776-20	Population: Suspected SARS-CoV-2 cases Population demographics: No demographic information provided Setting: Ambulatory screening clinic at a single hospital	Index sample: Salivary sample Test: RT-PCR (multiplex RT-PCR test for SARS-CoV-2 and other seasonal coronaviruses (coronavirus typing [8-well] assay; AusDiagnostics, Mascot, Australia)	Reference sample: Nasopharyngeal swab Test: RT-PCR (multiplex RT-PCR test for SARS-CoV-2 and other seasonal coronaviruses (coronavirus typing [8-well] assay; AusDiagnostics, Mascot, Australia)	Detection rate: <ul style="list-style-type: none"> ▪ 39/89 positive by nasopharyngeal, 50 negative ▪ 34 positive by saliva, 55 negative ▪ 6 positive by nasopharyngeal and negative by saliva ▪ 1 positive by saliva and negative by nasopharyngeal

	<p>Clinical characteristics: NR</p> <p>Time between samples: Consecutive</p>	<p>Threshold: NR</p> <p>Collection method: Patients were asked to pool saliva in their mouth for 1-2 minutes prior to collection, and gently spit 1-2 ml of saliva into a 25ml collection pot.</p> <p>Self- or provider- collection: Self-collected. Level of supervision unclear</p>	<p>Threshold: NR</p> <p>Collection method: NR</p>	
<p>Wyllie 2020 United States N= 98 Cross-sectional study Preprint: https://doi.org/10.1101/2020.04.16.20067835</p>	<p>Population: Asymptomatic healthcare workers at moderate- high risk of exposure (n=98)</p> <p>Population demographics: Mean age 36 years (Range 22-67), 16 males (16%).</p> <p>Setting: Single hospital</p> <p>Clinical characteristics: Asymptomatic</p> <p>Time between samples: NR</p>	<p>Index sample: Salivary sample</p> <p>Test: RT-PCR (CDC SARS-CoV-2 RT-PCR assay)</p> <p>Gene target: N</p> <p>Threshold: Ct value < 38</p> <p>Collection method: Asked to avoid food, water and brushing of teeth until the sample was collected. Asked to repeatedly spit into a sterile urine cup until roughly a third full of liquid. Every 3 days for 2 weeks</p> <p>Self- or provider- collection: Self-collected. Level of supervision unclear</p>	<p>Reference sample: Nasopharyngeal and/ or oropharyngeal swab</p> <p>Test: RT-PCR (CDC SARS-CoV-2 RT-PCR assay)</p> <p>Gene target: N</p> <p>Threshold: Ct value < 38</p> <p>Collection method: Self-collected nasopharyngeal swab every 3 days for a period of 2 weeks.</p>	<p>Detection Rate:</p> <ul style="list-style-type: none"> ▪ 2/98 positive by saliva, 96 negative ▪ 98 negative by nasopharyngeal ▪ 2 positive by saliva and negative by nasopharyngeal

Table 2. Summary of identified nasal site studies

Author	Patient demographics	Index specimen	Reference specimen	Primary outcome results
Country	Setting	Test	Test	
Sample size	Clinical characteristics	Gene target	Gene target	
Study design	Time between samples	Threshold	Threshold	
Status: DOI		Collection method	Collection method	
		Self- or provider- collected		
<p>Basu 2020</p> <p>United States</p> <p>N= 101</p> <p>Cross-sectional study</p> <p>Published: 10.1128/JCM.01136-20</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Age range 28 to 90 years</p> <p>Setting: Emergency departments of hospital group</p> <p>Clinical characteristics: Time since symptoms range 1 day to 1 month</p> <p>Time between samples: Collected in parallel</p>	<p>Index sample: Dry nasal (both nares)</p> <p>Test: Abbott ID Now COVID-19 (Abbott Diagnostics Scarborough, Inc., Scarborough, ME)</p> <p>Threshold: 125 genome equivalents/mL</p> <p>Target: RdRp</p> <p>Collection method: Obtained from both nares with swabs supplied with the Abbott assay. No further information provided</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-PCR (Xpert Xpress SARS-CoV-2 test (Cepheid, Sunnyvale) CA)</p> <p>Threshold: 250 copies/mL</p> <p>Gene target: N2, E</p> <p>Collection method: Obtained using flocked swabs from one nostril only</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 17 positive with both samples, 69 negative with both samples ▪ 31/101 positive by RT-PCR nasopharyngeal, 70 negative ▪ 18/101 positive by Abbott nasal, 83 negative ▪ 14 positive by RT-PCR nasopharyngeal and negative by Abbott nasal ▪ 1 positive by Abbott nasal and negative by nasopharyngeal RT-PCR ▪ Study reported: positive agreement 54.8% (95% CI 37.8 to 70.8). ▪ Study reported negative agreement: 98.6% (95% CI 92.3 to 99.7). ▪ Study reported positive predictive value: 94.4% (95% CI 74.3 to 99.0) ▪ Study reported negative predictive value (NPV): 83.1% (95% CI 73.7 to 89.7) <p>Note: Authors highlight low viral loads may have contributed to discordance for false negatives</p>

<p>Cradic 2020 United States N= 182 Cross-sectional study Published: 10.1093/AJCP/AQAA097</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: NR</p> <p>Setting: Emergency department and inpatients of a single hospital</p> <p>Clinical characteristics: Symptomatic</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Dry nasal swab</p> <p>Test: Abbott ID NOW (Abbott Diagnostics, Inc., Scarborough, ME)</p> <p>Threshold: NR</p> <p>Target: RdRp</p> <p>Collection method: Collected using a single swab to sample both nares</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-PCR (DiaSorin Molecular Simplexa COVID-19 Direct EUA assay (DiaSorin Molecular))</p> <p>Threshold: NR</p> <p>Gene target: S, ORF1ab</p> <p>Collection method: Collected using a flocked swab</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 12 positive by both samples, 169 negative by both ▪ 13/182 positive with RT-PCR nasopharyngeal, 169 negative ▪ 12/182 positive with Abbott nasal, 170 negative ▪ 1 positive RT-PCR nasopharyngeal and negative by Abbott nasal ▪ Study reported positive agreement 92% (95% CI 0.67 to 0.99) ▪ Study reported negative agreement 100% (95% CI 0.98 to 1.00)
<p>Griesemer et al United States N=463 Cross-sectional study Preprint: https://doi.org/10.1101/2020.06.16.20133041</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Age range 3-105 years.</p> <p>Setting: Two outpatient ambulatory clinics</p> <p>Clinical characteristics: NR</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Nasal swab</p> <p>Test: rRT-PCR (CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: Ct value < 45 considered positive</p> <p>Gene target: N</p> <p>Collection method: NR</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swabs</p> <p>Test: rRT-PCR (CDC 2019 nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: Ct value < 45 considered positive</p> <p>Gene target: N</p> <p>Collection method: NR</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 86 positive with both samples, 360 negative with both ▪ 103/463 positive by nasopharyngeal, 360 negative ▪ 86/463 positive by nasal swab, 377 negative ▪ 17 positive in in nasopharyngeal and negative in nasal <p>Note: two additional samples positive by saliva and negative by nasal and nasopharyngeal</p>

<p>Harrington 2020 United States N=524 Cross-sectional study Published: 10.1128/JCM.00798-20</p>	<p>Population: SARS-CoV-2 suspected cases</p> <p>Population demographics: NR</p> <p>Setting: Three emergency departments and 2 immediate care centres</p> <p>Clinical characteristics: Symptomatic</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Nasal swab</p> <p>Test: Abbott ID NOW (Abbott Diagnostics, Inc., Scarborough, ME)</p> <p>Threshold: NR</p> <p>Target: NR</p> <p>Collection method: NR</p> <p>Self- or provider- collection: NR</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-PCR (Abbott RealTime SARS-CoV-2 (ACOV) assay performed on the Abbott m2000 system (Abbott Molecular Inc., Des Plaines, IL)</p> <p>Threshold: NR</p> <p>Gene target: NR</p> <p>Collection method: NR</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 139 positive with both samples, 336 negative with both samples ▪ 186/524 positive on with RT-PCR nasopharyngeal, 338 negative ▪ 141/524 positive with Abbott nasal, 383 negative ▪ 47 positive with RT-PCR nasopharyngeal and negative with Abbott nasal ▪ 2 positive with Abbott nasal and negative with RT-PCR nasopharyngeal (follow up testing deemed one to be true positive) ▪ Study reported positive agreement 74.73% (95% CI 67.74 to 80.67) ▪ Study reported negative agreement 99.41% (95% CI 97.64 to 99.89) <p>Note: Authors noted difference in detection likely due to higher limits of detection and lower viral loads</p>
<p>Kojima 2020 United States N= 45 Cross-sectional study Preprint: https://doi.org/10.1101/2020.04.11.20062372</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Median age 42 (IQR range 31 to 52)</p> <p>Setting: Samples collected in participant homes</p> <p>Clinical characteristics: 29 positive for SARS-CoV-2 from at least 1 specimen type</p>	<p>Index sample: Nasal swab</p> <p>Test: RT-qPCR (CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: NR</p> <p>Gene target: N</p> <p>Collection method:</p>	<p>Reference sample: Nasopharyngeal swab</p> <p>Test: RT-qPCR (CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel)</p> <p>Threshold: NR</p> <p>Gene target: N</p> <p>Collection method:</p>	<p>Detection rate: 27 known positives (including other specimen types)</p> <ul style="list-style-type: none"> ▪ 18/43 participants negative with both samples. ▪ 19/43 positive by both samples. ▪ 23/43 positive by nasal, 20 negative ▪ 21/43 positive by nasopharyngeal, 22 negative ▪ 2 positive by nasopharyngeal and negative by nasal ▪ 4 positive by nasal and negative

	collected (Oral fluid, nasal swab, nasopharyngeal swab). 21 reported active symptoms. Range 2-21 days from symptom onset to sample collection. Time between samples: All samples collected within a 30 minute window.	Insert the swab into one nostril to the depth of 3-4 cm, rotate the swab for 5 to 10 seconds Self- or provider- collection: Supervised self-collection	Posterior using the recommended medical technique	by nasopharyngeal Spoilage and sufficiency: Two insufficient supervised, self-collected nasal swabs
McCulloch 2020 United States N=158 Cross-sectional study Published: 10.1001/jamanetworkopen.2020.16382	Population: Suspected SARS-CoV-2 cases: <ul style="list-style-type: none">Symptomatic healthcare workers presenting to drive-through SARS-CoV-2 testing clinics Population demographics: NR Setting: Drive through testing clinics (nasopharyngeal) and participants own homes (nasal) Clinical characteristics: Symptomatic cases Time between samples: Appears to be close time points of collection	Index sample: Mid-nasal swab Test: RT-PCR (AgPath-ID system master mix on the real-time ABI 7500 instrument) Threshold: NR Gene target: N Collection method: Home swab collection kit containing a flocced mid-nasal swab. Participants instructed to insert swab 1 inch in nostril, press against and rotate swab 5 times. Self- or provider- collection: Unsupervised self-collection	Reference sample: Nasopharyngeal swab Test: RT-PCR (AgPath-ID system master mix on the real-time ABI 7500 instrument) Threshold: NR Gene target: N Collection method: Collected by medical assistants and nurses	Detection rate: <ul style="list-style-type: none">9 samples positive with both, 150 negative with both11/154 samples positive by nasopharyngeal, 143 negative12/154 samples positive by nasal, 142 negative2 samples positive by nasopharyngeal and negative by nasal3 samples positive by nasal and negative by nasopharyngeal Spoilage and sufficiency: Three inconclusive results for nasal swabs and one inconclusive for nasopharyngeal. No further information provided
Péré 2020 France N= 44	Population: Suspected SARS-CoV-2 cases Population demographics:	Index sample: Nasal swab Test:	Reference sample: Nasopharyngeal swab Test:	Detection rate: <ul style="list-style-type: none">33 positive with both samples and 7 negative by both samples

<p>Cross-sectional study Published: https://doi.org/10.1128/JCM.00721-20</p>	<p>Median age 63 years (Range 18 to 94 years), 23 males (52.3%) Setting: Single hospital Clinical characteristics: Symptomatic Time between samples: Simultaneous collection</p>	<p>RT-PCR (Allplex 2019-nCoV assay (Seegene, Seoul, Korea)) Threshold: NR Target: E, N, RdRp Collection method: Nasal swabs were inserted in the nostril until they hit the inferior concha rotated 5 times, and removed. The test was conducted in only 1 nostril. Self- or provider- collection: Clinician collected</p>	<p>RT-PCR (Allplex 2019-nCoV assay (Seegene, Seoul, Korea)) Threshold: NR Gene target: E, N, RdRp Collection method: Nasopharyngeal swabs were inserted in the nostril until they hit the back of the nasopharyngeal cavity rotated five times, and removed. The test was conducted in only one nostril.</p>	<ul style="list-style-type: none"> ▪ 37/44 positive by nasopharyngeal, 7 negative ▪ 33/44 positive by nasal, 11 negative ▪ Sensitivity 89.2% (95% CI 75.3 to 95.7) <p>Note: Authors highlight that a number of discordant results related to low viral loads</p>
<p>Tu 2020 United States N= 504 Cross-sectional study Published: 10.1056/NEJMc2016321</p>	<p>Population: Suspected SARS-CoV-2 cases Population demographics: Age range 15 months to 94 years, 403 males Setting: Five ambulatory clinics Clinical characteristics: Symptomatic. Mean time since first symptoms >6 days for all sample types Time between samples: Simultaneous collection</p>	<p>Index sample: Nasal and mid turbinate samples Test: rRT-PCR (Quest Diagnostics, San Juan Capistrano, CA) Threshold: NR Gene target: NR Collection method: Nasal samples: Foam swab inserted in the vertical position into 1 nasal passage until gentle resistance, swab left in place for 10-15 seconds, rotating the swab, and repeating the procedure on the other side with</p>	<p>Reference sample: Nasopharyngeal swab Test: rRT-PCR (Quest Diagnostics, San Juan Capistrano, CA) Threshold: NR Gene target: NR Collection method: Collected by a health care worker using a polyester tipped swab passed along the floor of the nose until meeting gentle resistance as it touched the posterior pharynx, rotated several times</p>	<p>Detection rate: Nasopharyngeal versus nasal swab (n= 498)</p> <ul style="list-style-type: none"> ▪ 47 positive with both samples, 447 negative with both samples ▪ 50/498 positive with nasopharyngeal, 448 negative ▪ 48/498 positive with nasal, 450 negative ▪ 1 positive with nasal and negative with nasopharyngeal ▪ 3 positive with nasopharyngeal and negative with nasal ▪ Study reported sensitivity 94.0% (97.5% CI 83.8 to 100.0) <p>Nasopharyngeal versus Mid-turbinate (n=504)</p> <ul style="list-style-type: none"> ▪ 50 positive with both samples, 452 negative with both samples

		<p>the same swab.</p> <p>Mid- turbinate: nylon flocked swab inserted in the horizontal position until gentle resistance swab left in for 10-15 seconds on each side, rotating the swab, repeating in the other nostril with the same swab</p> <p>Self- or provider- collection: Self-collected with instruction</p>		<ul style="list-style-type: none"> ▪ 52/504 positive with nasopharyngeal, 452 negative, ▪ 50/504 positive with mid-turbinate, 454 negative ▪ 2 positive with nasopharyngeal and negative with mid-turbinate ▪ Study reported sensitivity 96.2% (97.5% CI 87.0 to 100)
<p>Wehrhahn 2020 Australia N= 166 Cross-sectional study Published: https://doi.org/10.1016/j.jcv.2020.104417</p>	<p>Population: Suspected SARS-CoV-2 cases</p> <p>Population demographics: Median age 40 (range 9–81) years, 40% male</p> <p>Setting: Ambulatory testing clinic</p> <p>Clinical characteristics: Symptomatic. Mean time between symptom onset and collection 4.8 days (range 2 to 9 days)</p> <p>Time between samples: Simultaneous collection</p>	<p>Index sample: Nasal swab</p> <p>Test: RT-PCR (an in-house developed Taqman assay)</p> <p>Threshold: NR</p> <p>Target: E and N</p> <p>Collection method: Swabs were inserted as far as comfortably possible and at least 2–3 cm inside one nostril, rotating the swab 5 times and leaving in place for 5–10 seconds.</p> <p>Self- or provider- collection: Self-collected</p>	<p>Reference sample: Nasopharyngeal and oropharyngeal combined swab</p> <p>Test: RT-PCR (an in-house developed Taqman assay)</p> <p>Threshold: NR</p> <p>Gene target: E and N</p> <p>Collection method: Flocked NP swab and a foam throat swab</p>	<p>Detection rate:</p> <ul style="list-style-type: none"> ▪ 13 positive on both samples, 153 negative on both samples ▪ No discordant results

Table 3. Detection rates of SARS-CoV-2 for RT-PCR comparisons

Study	Positive (any specimen)	Positive (reference)	Positive (index)	Detection by index relative to reference (%)	Positive agreement between specimens	Negative (reference)	Negative (index)	Negative (both specimens)
Saliva specimen- Same RT-PCR technique used for both specimen types								
Chen (n=58) [^]	58	55 (94.8%)	52 (89.7%)	49/55 (89.0%)	49/58 (84.5%)			
Cheuk (n=95, 229 paired samples)	159	122 (76.7%)	141 (88.7%)	104/122 (85.2%)	104/159 (65.4%)	107	88	70
Griesemer (n=463)	105	103 (98%)	87 (82.9%)	85/103 (82.5%)	85/105 (81.0%)	360	376	358
Iwasaki (n=76) [^]	10	9 (90%)	9 (90%)	8/9 (87.5%)	8/10 (80%)	67	67	66
Kojima (n=45) [`]	29	23 (79.3%)	26 (89.7%)	20/23 (86.9%)	20/29 (69%)	22	19	16
Leung (n=62, 95 paired samples)	58	45 (77.6%)	51 (87.9%)	38/45 (84.0%)	38/58 (65.5%)	50	44	37
McCormik- Baw (n=156)	50	49 (98%)	48 (96%)	47/49 (96%)	47/50 (94%)	106	107	105
Miller (n=91) ⁺	36	34 (94.0%)	35 (97.2%)	33/34 (97.1%)	33/36 (91.6%)	57	56	55
Pasomsub (n=200)	21	19 (90.4%)	18 (85.7%)	16/19 (84.2%)	16/21 (76.2%)	181	182	179
Rutgers Clinical Laboratory (n=60)	30	30 (100%)	30 (100%)	30/30 (100%)	30/30 (100%)	30	30	30
Williams (n= 89)	40	39 (97.5%)	34 (85%)	33/39 (84.6%)	33/40 (82.5%)	50	55	49
Wyllie (n=98)	2	0 (0.0%)	2 (100%)	Non-estimable	Non-estimable	98	96	96
Saliva specimen- Different RT-PCR techniques used for each specimen type								
Azzi (n=113)	59	26 (44.0%)	55 (93.2%)	22/26 (84.6%)	22/59 (37.3%)	87	58	54
Becker (n=85)	17	15 (88.2%)	11 (64.7%)	9/15 (60%)	9/17 (52.9%)	64	72	62
Nasal specimen- Same RT-PCR technique used for both specimen types								
Griesemer (n=463)	105 ["]	103 (98.1%)	86 (81.9%)	86/103 (83.5%)	86/105 (81.9%)	360	377	360
Kojima (n=43)	27 ["]	21 (70.0%)	23 (85.1%)	19/21 (90.5%)	19/27 (70.3%)	22	20	18
McCulloch (n=154)	14	11 (78.6%)	12 (85.7%)	9/11 (81.0%)	9/14 (62.3%)	143	142	140
Péré (n=44)	37	37 (100%)	33 (89.1%)	33/37 (89.1%)	33/37 (89.1%)	7	11	7
Tu (n=498) <i>Nasal swab</i>	51	50 (98.0%)	48 (94.1%)	47/50 (94.0%)	47/51 (92.2%)	448	450	447
Tu (n=504) <i>Mid-turbinate</i>	52	52 (100%)	50 (96.2%)	50/52 (96.2%)	50/52 (96.2%)	452	454	452
Wehrhahn (n=166)	13	13 (100%)	13 (100%)	13/13 (100%)	13/13 (100%)	153	153	153

[^] Includes COVID-19 confirmed patients

[`] Results for clinician supervised oral fluid collection

⁺ Results reference to MagMAX™ Viral/Pathogen Nucleic Acid Isolation and Maxwell RSC TNA Viral kits

["] Two positives confirmed by saliva

Table 4. Detection rates of SARS-CoV-2 for other molecular and antigen tests compared with RT-PCR

Study Reference sample(s)	Positive (reference)	Positive (index)	False positives	Positive agreement between samples	Negative (reference)	Negative (index)	False negatives	Negative agreement between samples
Saliva specimen- RT-LAMP								
L'Helgouach (n=93)	0	5*	4*	Non-estimable	93	88	0	88/93 (94.6%)
Wei (n=18)"	4	5 ⁺	0	4/4 (100%)	12	13	0	12/12 (100.0%)
Saliva specimen- Abbott ID NOW								
SoRelle (n= 67)	23	18	0	18/23 (78.2%)	44	49	5	44/44 (100%)
Saliva specimen- Rapid Salivary Antigen test								
Azzi (n=119)^	28^	79^	51^	26/28 (92.9%)	91	40	2	38/91 (41.6%)
Nasal specimen- Abbott ID NOW								
Basu (n=101)	31	18	1	17/31 (54.8%)	70	83	14	69/70 (98.6%)
Cradic (n= 182)	13	12	0	12/13 (92.3%)	169	170	1	169/169 (100%)
Harrington (n=524)	186	141	2~	139/186 (74.7%)	338	383	47	336/338 (99.4%)

*4/5 identified as false positives, one case confirmed with follow up RT-PCR saliva

"Modified RT-LAMP (HP-LAMP)

+ One test positive and one test negative by RT-LAMP which were indeterminate by RT-PCR

^51 initially determined as false positives; however follow up with RT-PCR on saliva indicated that 28/49 (two not analysed) samples positive

~Subsequent testing deemed one false positive to be a true positive

References

1. World Health Organization. Laboratory testing strategy recommendations for COVID-19: interim guidance. 2020.
2. National University of Singapore School of Public Health. COVID-19 Science Report: Diagnostics. 2020.
3. Centers for Disease Control and Prevention. Interim Guidelines for Collecting, Handling, and Testing Clinical Specimens for COVID-19. 2020.
4. Health Information and Quality Authority. Evidence Summary for COVID-19 Clinical Samples. 2020.
5. Health Protection Surveillance Centre. Laboratory Guidance for COVID-19 2020 [Available from: <https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/laboratoryguidance/>].
6. National Health Service (NHS) United Kingdom. Guidance and standard operating procedure COVID-19 virus testing in NHS laboratories. 2020.
7. Frazee BW, de la Guardia AR-H, Alter H, Chen CG, Fuentes EL, Holzer AK, et al. Accuracy and discomfort of different types of intranasal specimen collection methods for molecular influenza testing in emergency department patients. *Annals of Emergency Medicine*. 2018;71(4):509-17. e1.
8. Infectious Diseases Society of America. Infectious Diseases Society of America Guidelines on the Diagnosis of COVID-19 2020 [Available from: <https://www.idsociety.org/practice-guideline/covid-19-guideline-diagnostics/>].
9. Centers for Disease Prevention and Control. Nasal (Anterior Nasal) Specimen Collection for SARS-CoV-2 Diagnostic Testing 2020 [Available from: <https://www.cdc.gov/coronavirus/2019-ncov/downloads/OASH-nasal-specimen-collection-fact-sheet.pdf>].
10. Health Information and Quality Authority. Protocol for evidence synthesis support - COVID-19. 2020.
11. Azzi L, Baj A, Alberio T, Lualdi M, Veronesi G, Carcano G, et al. Rapid salivary test suitable for a mass screening program to detect SARS-CoV-2: A DIAGNOSTIC ACCURACY STUDY. *Journal of Infection*. 2020.
12. Basu A, Zinger T, Inghima K, Woo K-m, Atie O, Yurasits L, et al. Performance of Abbott ID NOW COVID-19 rapid nucleic acid amplification test in nasopharyngeal swabs transported in viral media and dry nasal swabs, in a New York City academic institution. *Journal of Clinical Microbiology*. 2020.
13. Becker D, Sandoval E, Amin A, De Hoff P, Leonetti N, Lim YW, et al. Saliva is less sensitive than nasopharyngeal swabs for COVID-19 detection in the community setting. *medRxiv*. 2020.
14. Li Y, Qian H, Hang J, Chen X, Hong L, Liang P, et al. Evidence for probable aerosol transmission of SARS-CoV-2 in a poorly ventilated restaurant. *medRxiv*. 2020.
15. Cheuk S, Wong Y, Tse H, Siu HK, Kwong TS, Chu MY, et al. Posterior oropharyngeal saliva for the detection of SARS-CoV-2. *Clinical Infectious Diseases*. 2020.
16. Cradic K, Lockhart M, Ozbolt P, Fatica L, Landon L, Lieber M, et al. Clinical Evaluation and Utilization of Multiple Molecular In Vitro Diagnostic Assays for the Detection of SARS-CoV-2. *American Journal of Clinical Pathology*. 2020.
17. Griesemer SB, Van Slyke G, Ehrbar D, Strle K, Yildirim T, Centurioni DA, et al. Evaluation of specimen types and saliva stabilization solutions for SARS-CoV-2 testing. *medRxiv*. 2020.
18. Harrington A, Cox B, Snowdon J, Bakst J, Ley E, Grajales P, et al. Comparison of Abbott ID Now and Abbott m2000 methods for the detection of SARS-CoV-2 from

- nasopharyngeal and nasal swabs from symptomatic patients. *Journal of Clinical Microbiology*. 2020.
19. Iwasaki S, Fujisawa S, Nakakubo S, Kamada K, Yamashita Y, Fukumoto T, et al. Comparison of SARS-CoV-2 detection in nasopharyngeal swab and saliva. *The Journal of infection*. 2020.
 20. Kojima N, Turner F, Slepnev V, Bacelar A, Deming L, Kodeboyina S, et al. Self-Collected Oral Fluid and Nasal Swabs Demonstrate Comparable Sensitivity to Clinician Collected Nasopharyngeal Swabs for Covid-19 Detection. *medRxiv*. 2020.
 21. Leung ECm, Chow VCy, Lee MKp, Lai RWm. Deep throat saliva as an alternative diagnostic specimen type for the detection of SARS-CoV-2. *Journal of Medical Virology*.
 22. L'Helgouach N, Champigneux P, Santos-Schneider F, Molina L, Espeut J, Alali M, et al. EasyCOV: LAMP based rapid detection of SARS-CoV-2 in saliva. *medRxiv*. 2020.
 23. McCormick-Baw C, Morgan K, Gaffney D, Cazares Y, Jaworski K, Byrd A, et al. Saliva as an Alternate Specimen Source for Detection of SARS-CoV-2 in Symptomatic Patients Using Cepheid Xpert Xpress SARS-CoV-2. *Journal of Clinical Microbiology*. 2020.
 24. McCulloch DJ, Kim AE, Wilcox NC, Logue JK, Greninger AL, Englund JA, et al. Comparison of Unsupervised Home Self-collected Midnasal Swabs With Clinician-Collected Nasopharyngeal Swabs for Detection of SARS-CoV-2 Infection. *JAMA Network Open*. 2020;3(7).
 25. Miller M, Jansen M, Bisignano A, Mahoney S, Wechsberg C, Albanese N, et al. Validation of a Self-administrable, Saliva-based RT-qPCR Test Detecting SARS-CoV-2. *medRxiv*. 2020.
 26. Pasomsub E, Watcharananan SP, Boonyawat K, Janchompoo P, Wongtabtim G, Sukswan W, et al. Saliva sample as a non-invasive specimen for the diagnosis of coronavirus disease-2019 (COVID-19): a cross-sectional study. *Clinical Microbiology and Infection*. 2020.
 27. Péré H, Podglajen I, Wack M, Flamarion E, Mirault T, Goudot G, et al. Nasal swab sampling for SARS-CoV-2: a convenient alternative in times of nasopharyngeal swab shortage. *Journal of clinical microbiology*. 2020;58(6).
 28. Rutgers Clinical Genomics Laboratory. ACCELERATED EMERGENCY USE AUTHORIZATION (EUA) SUMMARY SARS-CoV-2 ASSAY. FDA approval, . 2020.
 29. SoRelle J, Mahimainathan L, McCormick-Baw C, Cavuoti D, Lee F, Bararia A, et al. Evaluation of symptomatic patient saliva as a sample type for the Abbott ID NOW COVID-19 assay. *medRxiv*. 2020.
 30. Tu Y-P, Jennings R, Hart B, Cangelosi G, Wood R, Wehber K, et al. Patient-collected tongue, nasal, and mid-turbinate swabs for SARS-CoV-2 yield equivalent sensitivity to health care worker collected nasopharyngeal swabs. *medRxiv*. 2020.
 31. Wehrhahn MC, Robson J, Brown S, Bursle E, Byrne S, New D, et al. Self-collection: an appropriate alternative during the SARS-CoV-2 pandemic. *Journal of Clinical Virology*. 2020:104417.
 32. Wei S, Kohl E, Djandji A, Morgan S, Whittier S, Mansukhani M, et al. Field-deployable, rapid diagnostic testing of saliva samples for SARS-CoV-2. *medRxiv*. 2020.
 33. Williams E, Bond K, Zhang B, Putland M, Williamson DA. Saliva as a non-invasive specimen for detection of SARS-CoV-2. *Journal of Clinical Microbiology*. 2020.
 34. Wyllie AL, Fournier J, Casanovas-Massana A, Campbell M, Tokuyama M, Vijayakumar P, et al. Saliva is more sensitive for SARS-CoV-2 detection in COVID-19 patients than nasopharyngeal swabs. *Medrxiv*. 2020.

35. Callahan C, Lee R, Lee G, Zulauf KE, Kirby JE, Arnaout R. Nasal-Swab Testing Misses Patients with Low SARS-CoV-2 Viral Loads. medRxiv. 2020.
36. Lippi G, Simundic A-M, Plebani M. Potential preanalytical and analytical vulnerabilities in the laboratory diagnosis of coronavirus disease 2019 (COVID-19). Clinical Chemistry and Laboratory Medicine (CCLM). 2020;1(ahead-of-print).
37. Patel R, Babady E, Theel ES, Storch GA, Pinsky BA, George KS, et al. Report from the American Society for Microbiology COVID-19 international summit, 23 march 2020: value of diagnostic testing for SARS-CoV-2/COVID-19. Am Soc Microbiol; 2020.
38. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. Jama. 2020.
39. Wikramaratna P, Paton RS, Ghafari M, Lourenco J. Estimating false-negative detection rate of SARS-CoV-2 by RT-PCR. medRxiv. 2020.
40. Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of chest CT for COVID-19: comparison to RT-PCR. Radiology. 2020:200432.
41. Lippi G, Sanchis-Gomar F, Henry BM, Mattiuzzi C. Updates on laboratory investigations in coronavirus disease 2019 (COVID-19). Acta bio-medica : Atenei Parmensis. 2020;91(3).
42. European Centre for Disease Prevention and Control. Questions and answers regarding laboratory topics on SARS-CoV-2. 2020.
43. Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, et al. Detection of SARS-CoV-2 in different types of clinical specimens. Jama. 2020;323(18):1843-4.
44. Health Information and Quality Authority. Evidence summary for COVID-19 viral load over course of infection. 2020.
45. Iwasaki S, Fujisawa S, Nakakubo S, Kamada K, Yamashita Y, Fukumoto T, et al. Comparison of SARS-CoV-2 detection in nasopharyngeal swab and saliva. medRxiv; 2020.
46. Becker D, Sandoval E, Amin A, De Hoff P, Diets A, Leonetti N, et al. Saliva is less sensitive than nasopharyngeal swabs for COVID-19 detection in the community setting. medRxiv; 2020.
47. FDA. Emergency Use Authorisation: Abbott ID NOW COVID-19 2020 [Available from: <https://www.fda.gov/media/136522/download>].
48. Tomita N, Mori Y, Kanda H, Notomi T. Loop-mediated isothermal amplification (LAMP) of gene sequences and simple visual detection of products. Nature protocols. 2008;3(5):877-82.

Published by the Health Information and Quality Authority (HIQA).

For further information please contact:

Health Information and Quality Authority

George's Court

George's Lane

Smithfield

Dublin 7

D07 E98Y